NTP TECHNICAL REPORT

ON THE

# TOXICOLOGY AND CARCINOGENESIS STUDIES OF PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER

(CAS NO. 57018-52-7)

# IN F344/N RATS AND B6C3F$_1$ MICE

# AND A TOXICOLOGY STUDY OF PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER IN MALE NBR RATS

(INHALATION STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

March 2004

NTP TR 515

NIH Publication No. 04-4449

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

## FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Technical Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals. The prechronic and chronic studies were conducted in compliance with Food and Drug Administration (FDA) Good Laboratory Practice Regulations, and all aspects of the chronic studies were subjected to retrospective quality assurance audits before being presented for public review.

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology and carcinogenesis studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. The interpretive conclusions presented in this Technical Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of a chemical's carcinogenic potential.

Details about ongoing and completed NTP studies are available at the NTP's World Wide Web site: http://ntp-server.niehs.nih.gov. Abstracts of all NTP Technical Reports and full versions of the most recent reports and other publications are available from the NIEHS' Environmental Health Perspectives (EHP) http://ehp.niehs.nih.gov (866-541-3841 or 919-653-2590). In addition, printed copies of these reports are available from EHP as supplies last. A listing of all the NTP Technical Reports printed since 1982 appears at the end of this Technical Report.

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# CONTENTS


**ABSTRACT** . . . . . 7

**EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY** . . . . . 12

**TECHNICAL REPORTS REVIEW SUBCOMMITTEE** . . . . . 13

**SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS** . . . . . 14

**INTRODUCTION** . . . . . 15

**MATERIALS AND METHODS** . . . . . 21

**RESULTS** . . . . . 35

**DISCUSSION AND CONCLUSIONS** . . . . . 65

**REFERENCES** . . . . . 73

**APPENDIX A** **Summary of Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether** . . . . . 81

**APPENDIX B** **Summary of Lesions in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether** . . . . . 123

**APPENDIX C** **Summary of Lesions in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether** . . . . . 159

**APPENDIX D** **Summary of Lesions in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether** . . . . . 201

**APPENDIX E** **Genetic Toxicology** . . . . . 239

**APPENDIX F** **Clinical Pathology Results** . . . . . 249

**APPENDIX G** **Biomarkers of Exposure** . . . . . 259

**APPENDIX H** **Renal Toxicity Results** . . . . . 263

**APPENDIX I** **Organ Weights and Organ-Weight-to-Body-Weight Ratios** . . . . . 267

**APPENDIX J** **Reproductive Tissue Evaluations and Estrous Cycle Characterization** . . . . . 273

**APPENDIX K** **Chemical Characterization and Generation of Chamber Concentrations** . . . . . 277

**APPENDIX L** **Ingredients, Nutrient Composition, and Contaminant Levels in NTP-2000 Rat and Mouse Ration** . . . . . 289

APPENDIX M Sentinel Animal Program . . . . . 293

APPENDIX N Single-Exposure Toxicokinetic Studies in F344/N Rats and B6C3F$_1$ Mice . . . . . 297

## SUMMARY


### Background

Propylene glycol mono-*t*-butyl ether is used as a solvent in all-purpose cleaners, inks, and nail polish lacquers. We studied the effects of propylene glycol mono-*t*-butyl ether on male and female rats and mice to identify potential toxic or cancer-related hazards to humans.

### Methods

We exposed groups of male and female rats and mice to air containing vapors of propylene glycol mono-*t*-butyl ether at concentrations of 75, 300, or 1,200 parts per million (ppm) for 6 hours per day, 5 days a week for 2 years. Untreated control animals were housed in similar exposure chambers but without chemical exposure for comparison. Tissues from more than 40 sites were examined for every animal.

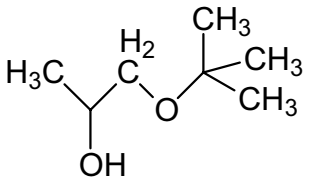
### Results

Rats receiving 1,200 ppm propylene glycol mono-*t*-butyl ether weighed less on average than the control animals. Tumors were seen in the liver and kidney of a few male rats exposed to propylene glycol mono-*t*-butyl ether. No increases in the numbers of tumors were seen in female rats. In male and female mice there were large increases in the numbers of liver tumors compared with the control animals.

### Conclusions

We conclude that propylene glycol mono-*t*-butyl ether caused cancer in the liver of male and female mice. Propylene glycol mono-*t*-butyl ether did not cause cancer in female rats, and its effect on the liver and kidney of male rats was considered uncertain.

# ABSTRACT




**PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER**

CAS No. 57018-52-7

Chemical Formula: $C_7H_{16}O_2$ Molecular Weight: 132.2

**Synonyms:** 1-(1,1-Dimethylethoxy)-2-propanol; 1-methyl-2-*tert*-butoxyethanol; propylene glycol mono-*tert*-butyl ether; *tert*-butoxypropanol; 1-*tert*-butoxy-2-propanol; 1-*tertiary*-butoxypropan-2-ol
**Trade names:** Arcosolv PTB

Propylene glycol mono-*t*-butyl ether is used as a solvent for all-purpose cleaners, electronic chemicals, inks, adhesives, nail polish lacquers, and other water-reducible coatings. Propylene glycol mono-*t*-butyl ether was nominated for study by the United States Consumer Product Safety Commission because of its widespread use, potential for human exposure, and the lack of adequate toxicological, chronic toxicity, and carcinogenicity information. Male and female F344/N rats and B6C3F$_1$ mice were exposed to propylene glycol mono-*t*-butyl ether (at least 99% pure) by inhalation for 2 weeks, 3 months, or 2 years. The chemical structure of propylene glycol mono-*t*-butyl ether indicated a potential to induce $\alpha$2u-globulin nephropathy, a male-specific renal syndrome characterized by the accumulation of hyaline droplets in the proximal tubule epithelium of F344/N rats. Thus, male NBR rats, which do not develop this condition, were exposed to propylene glycol mono-*t*-butyl ether concurrently with F344/N rats for 2 weeks for comparison of renal lesion development. Genetic toxicology studies were conducted in *Salmonella typhimurium,* cultured Chinese hamster ovary cells, and mouse peripheral blood erythrocytes.

## 2-Week Study in Rats

Groups of five male and five female F344/N rats and five male NBR rats were exposed to 0, 75, 150, 300, 600, or 1,200 ppm propylene glycol mono-*t*-butyl ether vapor 6 hours per day, 5 days per week for 16 days. All rats survived to the end of the study, and mean body weights of exposed groups were similar to those of the chamber controls. Renal toxicity studies were performed in male F344/N and NBR rats. The number of cells labeled with proliferating cell nuclear antigen and the labeling index (number of labeled nuclei/total nuclei) in the left kidney of 1,200 ppm male F344/N rats were significantly greater than those in the chamber controls. No significant differences in labeling indices were noted in NBR rats. Kidney weights of 600 ppm male F344/N rats were significantly increased. Liver weights of male and female F344/N rats exposed to 600 and 1,200 ppm and

male NBR rats exposed to 1,200 ppm were significantly increased.

## 2-Week Study in Mice

Groups of five male and five female B6C3F$_1$ mice were exposed to 0, 75, 150, 300, 600, or 1,200 ppm propylene glycol mono-*t*-butyl ether 6 hours per day, 5 days per week for 17 days. All mice survived to the end of the study. Mean body weights of 1,200 ppm female mice were significantly greater than those of the chamber control group. Liver weights of 600 and 1,200 ppm males and of 300 ppm or greater females were significantly increased.

## 3-Month Study in Rats

Groups of 25 male and 20 female F344/N rats were exposed to 0, 75, 150, 300, 600, or 1,200 ppm propylene glycol mono-*t*-butyl ether vapor 6 hours per day, 5 days per week for 2 (five male renal toxicity rats), 4 or 6 (10 male and 10 female clinical pathology rats), or 14 (10 core study rats) weeks. All core study rats survived to the end of the study. Mean body weight gains of 1,200 ppm males and 600 and 1,200 ppm females were significantly increased.

At week 12, urinalysis results indicated that exposure of rats to propylene glycol mono-*t*-butyl ether caused increases in urine volume, glucose and protein concentrations, and the activities of aspartate aminotransferase in males and increases in the activities of lactate dehydrogenase and *N*-acetyl-ß-D-glucosaminidase in males and females. Renal toxicity studies were performed on male rats sacrificed at 2 and 6 weeks and at the end of the study. In kidney tissue examined for cell proliferation, the numbers of PCNA-labeled cells and labeling indices in exposed groups of rats were generally significantly greater than those of the chamber controls at all three time points. Exposure-related increases in $\alpha$2u-globulin concentrations in males occurred throughout the study.

Kidney weights of all exposed groups of males and of 300 ppm or greater females and liver weights of all exposed groups of males and 600 ppm or greater females were increased. Incidences of renal tubule regeneration and granular casts in the medulla of the kidney in exposed rats were increased, and the severities of hyaline droplets generally increased with increasing exposure concentration.

## 3-Month Study in Mice

Groups of 10 male and 10 female B6C3F$_1$ mice were exposed to 0, 75, 150, 300, 600, or 1,200 ppm propylene glycol mono-*t*-butyl ether 6 hours per day, 5 days per week for 14 weeks. All mice survived to the end of the study. Final mean body weights of 300 and 1,200 ppm males and mean body weight gains for 150, 300, and 1,200 ppm males were significantly less than those of the chamber control group. Liver weights of 600 and 1,200 ppm males and females were significantly increased. The estrous cycle length of 1,200 ppm females was significantly increased. The incidences of minimal to mild centrilobular hypertrophy of the liver were significantly increased in 600 ppm males and 1,200 ppm males and females. The incidence of minimal squamous metaplasia of the respiratory epithelium of the nose was significantly increased in 1,200 ppm males.

## 2-Year Study in Rats

Groups of 50 male and 50 female F344/N rats were exposed to 0, 75, 300, or 1,200 ppm propylene glycol mono-*t*-butyl ether vapor 6 hours per day, 5 days per week for 104 weeks. Survival of 300 ppm males was less than that of the chamber controls. Mean body weights of 1,200 ppm males and females were less than those of the chamber controls during the second year of the study. In 1,200 ppm males and females the excretion of propylene glycol mono-*t*-butyl ether glucuronide in urine, expressed as the metabolite to creatinine ratios, were generally significantly less than those in the groups exposed to 75 or 300 ppm.

Incidences of renal tubule hyperplasia, renal tubule hyaline droplet accumulation, papilla mineralization, and transitional epithelial hyperplasia were increased in most exposed groups of males. Marginally increased incidences of renal tubule adenoma and adenoma or carcinoma (combined) occurred in 300 and 1,200 ppm males. The severities of chronic nephropathy increased with increasing exposure concentration in males and females and were significantly increased in all exposed groups of males and in 1,200 ppm females. The incidences of hepatocellular adenoma occurred with a positive trend in

male rats. The incidences of basophilic foci of the liver were significantly increased in all exposed groups of males; the incidence of clear foci of the liver was significantly increased in 1,200 ppm females. The incidences of hyaline degeneration of the olfactory epithelium in all exposed groups of males and females and the incidence of corneal mineralization in 1,200 ppm females were significantly increased.

## 2-Year Study in Mice

Groups of 50 male and 50 female B6C3F$_1$ mice were exposed to 0, 75, 300, or 1,200 ppm propylene glycol mono-*t*-butyl ether vapor 6 hours per day, 5 days per week for 104 weeks. Survival of exposed groups of mice was similar to that of the chamber control groups throughout the study. Mean body weights of 1,200 ppm females were slightly less than those of the chamber control group at the end of the study. Clinical findings included ataxia, shallow breathing, and lethargy in 1,200 ppm mice during the first 6 months of the study and pale foci of the eyes in 1,200 ppm females in the last month of the study.

The incidences of hepatocellular adenoma, hepatocellular adenoma or carcinoma (combined), and hepatoblastoma occurred with positive trends in males and females, and the incidences in the 1,200 ppm groups were increased. The incidences of eosinophilic foci and multinucleated hepatocytes in 1,200 ppm males and eosinophilic foci in 1,200 ppm females were significantly increased. The incidence of mild corneal mineralization was significantly increased in 1,200 ppm females.

## Genetic Toxicology

Propylene glycol mono-*t*-butyl ether was mutagenic in *S. typhimurium* strain TA97 in the absence of liver S9 activation enzymes; negative results were obtained with strain TA97 in the presence of rat or hamster liver S9 enzymes, in strains TA98, TA100, and TA1535 with and without S9, and in strain TA1537 without S9. Propylene glycol mono-*t*-butyl ether did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells, with or without S9. Propylene glycol mono-*t*-butyl ether induced a small but significant increase in the frequency of micronucleated normochromatic erythrocytes in peripheral blood of female mice in the 3-month study; no significant increase in micronucleated normochromatic erythrocytes was seen in male mice, and percentages of polychromatic erythrocytes were similar in the exposed and chamber control groups.

## Conclusions

Under the conditions of this 2-year inhalation study, there was *equivocal evidence of carcinogenic activity** of propylene glycol mono-*t*-butyl ether in male F344/N rats based on marginally increased incidences of renal tubule and liver neoplasms. There was *no evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in female F344/N rats exposed to 75, 300, or 1,200 ppm. There was *clear evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in male and female B6C3F$_1$ mice based on increased incidences of liver neoplasms.

Exposure of male rats to propylene glycol mono-*t*-butyl ether resulted in nonneoplastic lesions of the kidney characteristic of $\alpha$2u-globulin accumulation. Exposure to propylene glycol mono-*t*-butyl ether resulted in nonneoplastic lesions of the liver and nose in male and female rats, the liver in male and female mice, and the eyes in female rats and mice. Kinetic and biomarker studies indicated that clearance was saturated at the 1,200 ppm exposure for both rats and mice.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 12. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 14.

**Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Propylene Glycol Mono-*t*-butyl Ether**

| | Male F344/N Rats | Female F344/N Rats | Male $B6C3F_1$ Mice | Female $B6C3F_1$ Mice |
|---|---|---|---|---|
| **Concentrations in air** | Chamber control, 75, 300, or 1,200 ppm | Chamber control, 75, 300, or 1,200 ppm | Chamber control, 75, 300, or 1,200 ppm | Chamber control, 75, 300, or 1,200 ppm |
| **Body weights** | 1,200 ppm group less than the chamber control group | 1,200 ppm group less than the chamber control group | Exposed groups similar to the chamber control group | 1,200 ppm groups slightly less than the chamber control group |
| **Survival rates** | 27/50, 29/50, 16/50, 22/50 | 33/50, 34/50, 28/50, 36/50 | 35/50, 40/50, 40/50, 37/50 | 39/50, 36/50, 42/50, 39/50 |
| **Nonneoplastic effects** | Kidney: renal tubule hyperplasia (standard evaluation - 0/50, 3/50, 7/49, 19/50; standard and extended evaluations - 10/50, 20/50, 23/49, 30/50); hyaline droplet accumulation (1/50, 2/50, 9/49, 17/50); renal papilla mineralization 0/50, 8/50, 28/49, 41/50); transitional epithelium hyperplasia (2/50, 1/50, 6/49, 15/50); severity of chronic nephropathy (1.9, 2.3, 2.9, 3.5)<br><br>Liver: basophilic foci (6/50, 18/50, 15/49, 17/50)<br><br>Nose: olfactory epithelium hyaline degeneration (0/50, 25/49, 45/49, 50/50) | Kidney: severity of chronic nephropathy (1.5, 1.6, 1.7, 2.1)<br><br>Liver: clear cell foci (12/49, 13/50, 11/50, 27/50)<br><br>Nose: olfactory epithelium hyaline degeneration (10/49, 22/49, 48/50, 50/50)<br><br>Eye: corneal mineralization (0/49, 0/50, 0/50, 10/50) | Liver: eosinophilic foci (9/50, 14/49, 11/50, 29/50); multinucleated hepatocytes (27/50, 23/49, 24/50, 46/50) | Liver: eosinophilic foci (11/49, 10/50, 9/50, 27/49)<br><br>Eye: corneal mineralization (1/50, 2/50, 0/50, 20/48) |
| **Neoplastic effects** | None | None | Liver: hepatocellular adenoma (18/50, 23/49, 26/50, 36/50); hepatocellular carcinoma (9/50, 8/49, 13/50, 11/50); hepatocellular adenoma or carcinoma (25/50, 26/49, 33/50, 41/50); hepatoblastoma (0/50, 0/49, 1/50, 5/50) | Liver: hepatocellular adenoma (14/49, 8/50, 10/50, 37/49); hepatocellular carcinoma (4/49, 8/50, 7/50, 10/49); hepatocellular adenoma or carcinoma (18/49, 14/50, 16/50, 41/49); hepatoblastoma (0/49, 0/50, 0/50, 2/49) |

## Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Propylene Glycol Mono-*t*-butyl Ether

| | Male F344/N Rats | Female F344/N Rats | Male $B6C3F_1$ Mice | Female $B6C3F_1$ Mice |
|---|---|---|---|---|
| **Equivocal findings** | Kidney: renal tubule adenoma (standard evaluation - 1/50, 1/50, 3/49, 2/50; standard and extended evaluations combined - 1/50, 2/50, 5/49, 4/50); renal tubule adenoma or carcinoma (standard evaluation - 1/50, 1/50, 3/49, 3/50; standard and extended evaluations combined - 1/50, 2/50, 5/49, 5/50)<br><br>Liver: hepatocellular adenoma (3/50, 0/50, 2/49, 6/50) | None | None | None |
| **Level of evidence of carcinogenic activity** | Equivocal evidence | No evidence | Clear evidence | Clear evidence |
| **Genetic toxicology** | | | | |
| *Salmonella typhimurium* gene mutations: | Positive in strain TA97 without S9; negative in strains TA98, TA100, and TA1535 with and without S9; negative in strain TA1537 without S9 | | | |
| Sister chromatid exchanges<br>Cultured Chinese hamster ovary cells *in vitro:* | Negative with and without S9 | | | |
| Chromosomal aberrations<br>Cultured Chinese hamster ovary cells *in vitro:* | Negative with and without S9 | | | |
| Micronucleated erythrocytes<br>Mouse peripheral blood *in vivo:* | Negative in males; weak positive in females | | | |

## EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

The National Toxicology Program describes the results of individual experiments on a chemical agent and notes the strength of the evidence for conclusions regarding each study. Negative results, in which the study animals do not have a greater incidence of neoplasia than control animals, do not necessarily mean that a chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a chemical is carcinogenic for laboratory animals under the conditions of the study and indicate that exposure to the chemical has the potential for hazard to humans. Other organizations, such as the International Agency for Research on Cancer, assign a strength of evidence for conclusions based on an examination of all available evidence, including animal studies such as those conducted by the NTP, epidemiologic studies, and estimates of exposure. Thus, the actual determination of risk to humans from chemicals found to be carcinogenic in laboratory animals requires a wider analysis that extends beyond the purview of these studies.

Five categories of evidence of carcinogenic activity are used in the Technical Report series to summarize the strength of the evidence observed in each experiment: two categories for positive results **(clear evidence and some evidence);** one category for uncertain findings **(equivocal evidence);** one category for no observable effects **(no evidence);** and one category for experiments that cannot be evaluated because of major flaws **(inadequate study).** These categories of interpretative conclusions were first adopted in June 1983 and then revised in March 1986 for use in the Technical Report series to incorporate more specifically the concept of actual weight of evidence of carcinogenic activity. For each separate experiment (male rats, female rats, male mice, female mice), one of the following five categories is selected to describe the findings. These categories refer to the strength of the experimental evidence and not to potency or mechanism.

- **Clear evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.
- **Some evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.
- **Equivocal evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemical related.
- **No evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing no chemical-related increases in malignant or benign neoplasms.
- **Inadequate study** of carcinogenic activity is demonstrated by studies that, because of major qualitative or quantitative limitations, cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

For studies showing multiple chemical-related neoplastic effects that if considered individually would be assigned to different levels of evidence categories, the following convention has been adopted to convey completely the study results. In a study with clear evidence of carcinogenic activity at some tissue sites, other responses that alone might be deemed some evidence are indicated as "were also related" to chemical exposure. In studies with clear or some evidence of carcinogenic activity, other responses that alone might be termed equivocal evidence are indicated as "may have been" related to chemical exposure.

When a conclusion statement for a particular experiment is selected, consideration must be given to key factors that would extend the actual boundary of an individual category of evidence. Such consideration should allow for incorporation of scientific experience and current understanding of long-term carcinogenesis studies in laboratory animals, especially for those evaluations that may be on the borderline between two adjacent levels. These considerations should include:

- adequacy of the experimental design and conduct;
- occurrence of common versus uncommon neoplasia;
- progression (or lack thereof) from benign to malignant neoplasia as well as from preneoplastic to neoplastic lesions;
- some benign neoplasms have the capacity to regress but others (of the same morphologic type) progress. At present, it is impossible to identify the difference. Therefore, where progression is known to be a possibility, the most prudent course is to assume that benign neoplasms of those types have the potential to become malignant;
- combining benign and malignant tumor incidence known or thought to represent stages of progression in the same organ or tissue;
- latency in tumor induction;
- multiplicity in site-specific neoplasia;
- metastases;
- supporting information from proliferative lesions (hyperplasia) in the same site of neoplasia or in other experiments (same lesion in another sex or species);
- presence or absence of dose relationships;
- statistical significance of the observed tumor increase;
- concurrent control tumor incidence as well as the historical control rate and variability for a specific neoplasm;
- survival-adjusted analyses and false positive or false negative concerns;
- structure-activity correlations; and
- in some cases, genetic toxicology.

## NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS
### TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the draft NTP Technical Report on propylene glycol mono-*t*-butyl ether on May 22, 2003, are listed below. Subcommittee members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, subcommittee members have five major responsibilities in reviewing the NTP studies:

- to ascertain that all relevant literature data have been adequately cited and interpreted,
- to determine if the design and conditions of the NTP studies were appropriate,
- to ensure that the Technical Report presents the experimental results and conclusions fully and clearly,
- to judge the significance of the experimental results by scientific criteria, and
- to assess the evaluation of the evidence of carcinogenic activity and other observed toxic responses.

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## SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On May 22, 2003, the draft Technical Report on the toxicology and carcinogenesis studies of propylene glycol mono-*t*-butyl ether received public review by the National Toxicology Program's Board of Scientific Counselor's Technical Reports Review Subcommittee. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. A.M. Doi, NIEHS, introduced the toxicology and carcinogenesis studies of propylene glycol mono-*t*-butyl ether by discussing the uses of the chemical and the rationale for study, describing the experimental design, reporting on survival, body weight, and kidney toxicity effects, and commenting on compound-related neoplastic and nonneoplastic lesions. The proposed conclusions for the 2-year inhalation studies in rats were *equivocal evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in male F344/N rats based on marginally increased incidences of renal tubule and liver neoplasms. Renal tubule neoplasms occurred at concentrations where there was evidence of $\alpha$2u-globulin nephropathy. There was *no evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in female F344/N rats. There was *clear evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in male and female B6C3F$_1$ mice based on increased incidences of liver neoplasms.

Dr. Roberts, the first principal reviewer, questioned whether *equivocal evidence* was the most appropriate conclusion for the male rat study but agreed with the other conclusions. He stated that the inclusion of NBR rats and the special attention paid to the question of $\alpha$2u-globulin were useful.

Dr. Boekelheide, the second principal reviewer, stated that the studies had been carefully analyzed and agreed with the proposed conclusions.

Dr. Walker, the third principal reviewer, questioned the significance of the renal tumors and liver adenomas in male rats and the liver neoplasms in mice.

Dr. Doi explained that renal tumors are rare in rats and the potential trend in liver adenomas, though not dose related, was consistent with *equivocal evidence of carcinogenic activity*. Dr. J.K. Haseman, NIEHS, noted that the significance of the trend test derived from the spacing of the doses, with the lowest dose being close to the control value. He also observed that the control rate was at the upper end of the historical range.

Dr. Doi explained the reasons for the choice of *clear evidence of carcinogenic activity* for the mouse studies. The incidences of liver adenoma and of multiple adenoma were markedly increased in the 1,200 ppm group. The incidences of carcinoma were also elevated, and uncommon malignant hepatoblastomas were also seen in exposed mice.

Dr. W. Faber, representing the Lyondell Chemical Co., argued that propylene glycol mono-*t*-butyl ether should not be considered genotoxic because of a positive response in one *Salmonella* strain and a small increase in the micronucleus test. He also suggested that the 1,200 ppm concentration exceeded the maximally tolerated dose.

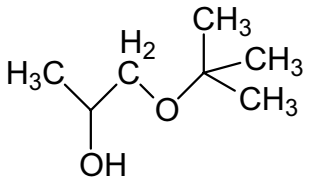
Dr. Roberts noted that the Technical Report made no overall conclusions of genotoxicity beyond listing individual test results.

Dr. J.R. Bucher, NIEHS, defended the dose selection, noting that any clinical signs of toxicity observed were brief and transient and that the 1,200 ppm groups did not exceed the criteria of survival, body weight changes, or other toxicity.

Dr. Bucher also described two additions proposed to the concluding statement: a comment that the nonneoplastic lesions in male rats were characteristic of $\alpha$2u-globulin accumulation and a statement that kinetic and biomarker studies indicated that clearance was saturated at the 1,200 ppm exposure concentration both for rats and mice.

Dr. Roberts moved, and Dr. Vore seconded, that the proposed conclusions to the report be accepted. Dr. Walker proposed an amendment that the conclusion for female mice be changed to *some evidence of carcinogenic activity.* That amendment failed for lack of a second. The original motion was approved unanimously with eight votes.

# INTRODUCTION



**PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER**

CAS No. 57018-52-7

Chemical Formula: $C_7H_{16}O_2$ Molecular Weight: 132.2

**Synonyms:** 1-(1,1-Dimethylethoxy)-2-propanol; 1-methyl-2-*tert*-butoxyethanol; propylene glycol mono-*tert*-butyl ether; *tert*-butoxypropanol; 1-*tert*-butoxy-2-propanol; 1-*tertiary*-butoxypropan-2-ol
**Trade name:** Arcosolv PTB

## Chemical and Physical Properties

Propylene glycol mono-*t*-butyl ether is one of several monoalkyl ethers of propylene glycol. It is a colorless liquid with a boiling point of 151° C, a specific gravity of 0.87, and a vapor pressure of 3.7 mm Hg at 25° C. It is combustible and has a flash point of 45° C (open cup). It is partly soluble in water, and is miscible with most organic solvents (Greany and Gillman, 1989; Boatman, 2001). The solubility in water is ≥100 mg/mL at 19° C (NTP, 2001).

## Production, Use, and Human Exposure

Propylene glycol mono-*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. It is then distilled to produce around 99% of the alpha isomer, 1-*tert*-butoxy-propan-2-ol (Gupta, 1987). Because glycol ethers display properties of both alcohols and ethers, they exhibit dual solubility in water and solvents and can be employed in a variety of applications (Brucker and Warren, 2001). The commercial uses of propylene glycol mono-*t*-butyl ether include all-purpose cleaners, electronic chemicals, inks, adhesives, nail polish lacquers, and other water-reducible coatings (Anonymous, 1985; Heckman, 1986; Gupta, 1987; Kessler, 1989; Nudy and Johnston, 1990). Propylene glycol mono-*t*-butyl ether is listed in the 1994 High Production Volume Chemical List posted by the Environmental Protection Agency, and its 1993 production volume was estimated to be between 6 and 10 million pounds (Boatman, 2001). Propylene glycol mono-*t*-butyl ether was formulated to replace ethylene glycol monobutyl ether, the largest volume alkyl glycol produced, after concern emerged regarding its potential toxic effects (Begley, 1986).

Due to the high production volume and widespread use, there is a high potential for occupational and consumer exposure as a result of contact with propylene glycol mono-*t*-butyl ether-containing products mainly via inhalation and dermal absorption. Occupational exposures during the manufacturing process are thought to be low since the manufacturing process is largely enclosed (Boatman, 2001). In the United States, occupational exposure limits have not been established by the American Conference of Governmental Industrial Hygienists, the National Institute for Occupational Safety and Health, or the Occupational Safety and Health Administration for propylene glycol mono-*t*-butyl ether.

## ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

### *Experimental Animals*

Radiolabeled propylene glycol mono-*t*-butyl ether was rapidly absorbed from the gastrointestinal tract of male Fischer F344/N rats after administration by gavage (NTP, 1994). By 72 hours, 87% to 100% of the radiolabeled dose was eliminated, and less than 6% of the dose remained in the carcasses of rats following single oral doses ranging from 3.8 to 377 mg/kg. The distribution of radioactivity in various tissues was similar regardless of the administered oral dose. The predominant route of elimination was via the urine (48% to 67% of the dose), and the main urinary metabolite (23% to 52% of metabolites) observed in all dosed groups was propylene glycol mono-*t*-butyl ether glucuronide. Propylene glycol mono-*t*-butyl ether sulfate was identified at lower levels (7% to 13%) in the urine.

Dermal absorption of radiolabeled propylene glycol mono-*t*-butyl ether was reported to be greater in male B6C3F$_1$ mice (close to 8%) than in male Fischer 344/N rats, with approximately 3% absorption (NTP, 1994). This apparent species difference in absorption may be related to the temporal effects (absorption versus evaporation) in penetrating the thinner skin barrier of the mouse. In both species, the vast majority of the radiolabeled propylene glycol mono-*t*-butyl ether volatilized from the skin surface before absorption could occur. Excretion of the absorbed compound occurred mainly via the urine, with approximately 2% to 5% of the dose in mice and 2% of the dose in rats being recovered within 72 hours. In a metabolic pattern similar to that seen following oral administration, the major urinary metabolites seen in rats were propylene glycol mono-*t*-butyl ether glucuronide and sulfate. Radioactivity in the urine of the B6C3F$_1$ mouse was insufficient for conducting metabolite analysis.

In addition to being conjugated, propylene glycol mono-*t*-butyl ether is also hypothesized to be partly metabolized by *O*-dealkylation to propylene glycol in a similar fashion to propylene glycol mono-*n*-butyl ether. Although direct metabolism studies have not been conducted with propylene glycol mono-*n*-butyl ether, a scheme has been suggested where it is partly conjugated to sulfates and glucuronides followed by excretion in the urine, and partly metabolized to propylene glycol via microsomal *O*-dealkylation (Verschuuren, 1996). Propylene glycol is in turn further metabolized to lactic acid and pyruvic acid, which enter the tricarboxylic acid cycle, resulting in ultimate elimination as carbon dioxide (Miller, 1987). The excretion of 22% to 26% of the administered oral dose of propylene glycol mono-*t*-butyl ether as expired carbon dioxide in rats was reported by NTP (1994). This finding is consistent with the metabolism of propylene glycol mono-*t*-butyl ether to carbon dioxide via *O*-dealkylation, but this pathway remains to be demonstrated.

Intravenous bolus administration of radiolabeled propylene glycol mono-*t*-butyl ether to male Fischer 344/N rats revealed a mean elimination half-life of 16 minutes and a mean clearance of 25.1 mL/minute/kg (NTP, 1994). Biliary excretion studies demonstrated that 40% of a radiolabeled intravenous dose was recovered in the bile as propylene glycol mono-*t*-butyl ether glucuronide. However, only 11% or less of the radioactive dose was recovered in the feces, suggesting that the metabolite underwent hydrolysis in the intestine and the parent chemical was reabsorbed.

### *Humans*

Systemic exposures to propylene glycol mono-*t*-butyl ether may occur in humans from inhalation and dermal contact with products containing this solvent. Glycol ethers have been shown to be capable of penetrating the human skin, and the absorption rate of monoethylene and diethylene glycol ethers was shown to decrease with increasing molecular weight or increasing boiling point of glycol ethers within a specific series (Dugard *et al*., 1984). However, subsequent studies by Larese Filon *et al.* (1999) implied that the water and lipid solubility of a compound would prevail over molecular weight in predicting the skin permeation of glycol ethers, because permeation rates are only indirectly linked to molecular weight. Accordingly, propylene glycol mono-*t*-butyl ether is likely to be dermally absorbed at a rate comparable with propylene glycol mono-*n*-butyl ether, which was shown to exhibit a permeation rate of $0.017 \pm 0.005$ g/cm$^2$ per hour in human skin *in vitro* (Larese Filon *et al*., 1999).

## TOXICITY

### *Experimental Animals*

No deaths or abnormal clinical signs were observed in male or female Sprague-Dawley rats exposed to 2,680 mg/m$^3$ (~550 ppm) propylene glycol mono-*t*-butyl ether for 4 hours in a whole-body inhalation study by the ARCO Chemical Company (Boatman, 2001). In this study, the animals were observed for 14 days and then

necropsied. Mild hepatic extra-medullary hematopoiesis (small foci of hematopoietic cells in some portal triads) was seen in two of the five rats of each sex exposed to propylene glycol mono-*t*-butyl ether. In a separate study, male and female Fischer 344/N rats were exposed to propylene glycol mono-*t*-butyl ether at concentrations of 28 to 709 ppm, 6 hours per day, 5 days per week for 13 weeks (Boatman, 2001). Animals were sacrificed after 4 weeks, at the end of the 13-week exposure period, or following a 3-week recovery period. No differences in mortality or body weight were noted. Hematology and clinical chemistry parameters were unaltered, and urinalysis data revealed no signs of renal injury. Increases in liver, kidney, and spleen weights were not considered to be treatment related, due to the absence of accompanying histopathology or clinical chemistry alterations. Testicular degeneration, described as damage to the seminiferous tubules, occurred in one of ten animals at the end of the 4-week and 13-week exposures. However, this finding was not reported to be treatment related in view of its low severity, its unilateral occurrence, and because it is a common lesion in rats of the particular age used in the study (not specified). Absence of alterations in the bone marrow, blood and thymus were particularly noted. The no-observed-adverse-effect level for this study was 709 ppm, the highest concentration tested.

Studies by the ARCO Chemical Company using rabbits (strain and gender not specified) showed that 24-hour dermal application of 2 g/kg of propylene glycol mono-*t*-butyl ether resulted in no deaths, adverse clinical signs, or body weight effects over a 14-day observation period (Boatman, 2001). The compound was applied to the abraded, clipped skin of rabbits using an occlusive wrap. Transient erythema and persistent desquamation, atonia, erythema, fissures, discoloration, and thickened skin were noted at the site of application in some treated animals. In separate studies, it was reported that the application of propylene glycol mono-*t*-butyl ether to the clipped skin of albino rabbits at both abraded and nonabraded areas using an occlusive wrap for 24 hours resulted in slight erythema and desquamation over a 7-day period, leading to the conclusion that propylene glycol mono-*t*-butyl ether had a slight skin irritation potential (Boatman, 2001).

The oral $LD_{50}$ of propylene glycol mono-*t*-butyl ether in male and female Sprague-Dawley rats was determined to be 3,771 mg/kg body weight in a study by the ARCO Chemical Company (Boatman, 2001). Rats treated with 2,239 to 4,467 mg/kg displayed lethargy, ataxia, prostration, irregular breathing, lacrimation, crusty eyes, and yellow and brown-stained fur. In addition to these clinical signs, animals that died during the study showed crusty muzzle, salivation, red-stained fur, and emaciation and had decreased body weights. Necropsies conducted in animals that did not survive to the end of the study revealed red and dark-stained areas of the lungs, in addition to damage to the stomach and the liver (no details provided). Survivors displayed similar lung damage and mild dilation of kidney pelvises.

The ARCO Chemical Company tested the eye irritation potential of propylene glycol mono-*t*-butyl ether in rabbits (strain and gender not specified) by instilling 0.1 mL of neat chemical into their eyes (Boatman, 2001). Reversible corneal opacity was seen in most treated animals; washing the eyes immediately following treatment lessened the duration of this alteration. Additional transient signs of irritation, such as redness, chemosis, and discharge, were also observed. The compound was considered a severe eye irritant in its neat form. Subsequent studies reported that propylene glycol mono-*t*-butyl ether had a slight irritation potential when applied to the eye of albino rabbits (strain and gender not specified) as a 20% aqueous solution (Boatman, 2001).

Structurally related propylene glycol mono-*n*-butyl ether was shown to cause mild or no toxic effects following inhalation exposures. No signs of toxicity were reported in Fischer 344/N rats (gender not specified) exposed to saturated vapors of propylene glycol mono-*n*-butyl ether for 4 hours, or 600 ppm (7 hours per day, for 9 days, over a 2-week period) in studies by the DOW Chemical Company (Boatman, 2001). In two separate studies by the Union Carbide Corporation, the main treatment-related effects in female Fischer 344/N rats exposed to 600 ppm (7 hours per day, for 31 days), and male and female rats exposed to 600 ppm (6 hours per day, for 9 days over an 11-day interval) propylene glycol mono-*n*-butyl ether were increased liver weights (Boatman, 2001). Additional mild eye lesions following 300 and 600 ppm exposures were also seen in the latter experiment. Studies with the shorter chained propylene glycol monomethyl ether by the DOW Chemical Company showed no deaths in Fischer 344/N rats (gender not specified) following single 6-hour exposures at concentrations of 6,038 or 7,559 ppm, although signs of narcosis were noted (Boatman, 2001). In short-term inhalation studies, Fischer 344/N rats and $B6C3F_1$ mice were exposed to concentrations of 300 to 3,000 ppm

propylene glycol monomethyl ether, 6 hours per day for 9 days over an 11-day interval (Miller *et al*., 1981). Exposure to 3,000 ppm resulted in increased liver weights in male rats in addition to central nervous system depression and decreases in specific gravity of the urine in both sexes of rats. No other gross or histopathological changes were seen in either rats or mice.

Ethylene glycol ethers have been shown to be much more toxic than propylene glycol ethers. Ethylene glycol monomethyl ether, for instance, has been shown to cause a variety of adverse effects in male and female Fischer 344 rats following inhalation exposures to 1,000 ppm, 6 hours per day for 9 days over an 11-day interval (Miller *et al*., 1981). Effects included decreases in red and white blood cell counts, reduction in bone marrow cellularity, and lymphoid cell depletion in the thymus. Hematologic effects were also seen in male and female Fischer 344 rats following exposures to 86 or 245 ppm ethylene glycol monobutyl ether, 6 hours per day for 9 days (Dodd *et al*., 1983). Statistically significant depressions of red blood cell (RBC) count, hemoglobin and mean corpuscular hemoglobin (MCH) concentration, in addition to increases in nucleated erythrocytes, reticulocytes, and lymphocytes were seen in the 245 ppm group. A subsequent 90-day study in rats exposed to 77 ppm ethylene glycol monobutyl ether, 6 hours per day, 5 days per week, resulted in significant decreases in RBC count and hemoglobin concomitant with an increase in MCH in females (Dodd *et al*., 1983). In both studies with ethylene glycol monobutyl ether, there was a substantial reversal of the affected blood parameters during a postexposure recovery period in the short-term study and at the conclusion of the 90-day exposure period.

Differences in toxicity among ethylene and propylene glycol ethers are largely attributed to the differences in their metabolism. While propylene glycol ethers undergo *O*-dealkylation to form propylene glycol, ethylene glycol ethers are metabolized to the corresponding toxic alkoxyacetic acids by alcohol dehydrogenase and are ultimately metabolized to carbon dioxide (Miller *et al*., 1983, 1984).

### *Humans*

No toxicity studies of propylene glycol mono-*t*-butyl ether in humans were found in the literature.

## Reproductive and Developmental Toxicity

### *Experimental Animals*

Studies by the ARCO Chemical Company using pregnant New Zealand rabbits examined the effect of whole-body inhalation exposures to 229 to 984 ppm propylene glycol mono-*t*-butyl ether, 6 hours per day on days 7 through 9 of gestation (Boatman, 2001). In these studies, there were no signs of toxicity or behavioral, body weight, or hematological effects in the dams. Fetal morphology was similarly unaltered. The no-observed-adverse-effect level in this study was the highest concentration examined (984 ppm). In a similar but separate study, pregnant Charles River CDF rats were exposed to propylene glycol mono-*t*-butyl ether at concentrations of 0, 230, 726, or 990 ppm, 6 hours per day on days 6 through 15 of gestation (Boatman, 2001). No fetotoxicity or developmental abnormalities were reported in the fetuses, although dams from the mid and high exposure groups showed statistical increases in absolute and relative liver weights, and one half of the dams from the high-exposure group were described as pale over the duration of the exposure period.

Structurally related propylene glycol mono-*n*-butyl ether has been shown to have no developmental or teratogenic effects in Wistar rats or New Zealand White rabbits following dermal administration (Gibson *et al*., 1989; Verschuuren, 1996). Similarly, propylene glycol monomethyl ether, which has a shorter alkyl chain, has shown no reproductive or developmental effects in the Wistar-derived Alderly Park strain when pregnant females were exposed on days 6 to 17 of gestation or when male rats were exposed for 10 days at 200 or 600 ppm (Doe *et al*., 1983). No teratogenic effects were seen in Fischer 344/N rats or New Zealand White rabbits exposed to concentrations of 500 to 3,000 ppm of propylene glycol monomethyl ether, with the exception of delayed fetal skeletal ossification in the high dose group (Hanley *et al*., 1984). An inhalation reproductive study was conducted in Sprague-Dawley rats with propylene glycol monomethyl ether at concentrations of 300 to 3,000 ppm, administered prior to and after mating and during gestation and lactation for two generations (Carney *et al*., 1999). Marked parental toxicity accompanied by decreases in the survival, litter size, and body weights of the offspring was observed in the high dose

groups and delays in puberty onset and hepatic and renal histological alterations also occurred. All of these findings appeared to be secondary to parental toxicity (Carney *et al*., 1999). No treatment-related effects were seen at lower concentrations. Propylene glycol monomethyl ether administered in drinking water to CD-1 mice following the NTP Reproductive Assessment by Continuous Breeding protocol (Chapin and Sloane, 1997) had no effect on fertility or reproductive parameters (NTP, 1986). However, there was some evidence of probable developmental toxicity, expressed as reduced pup weights at birth.

Ethylene glycol ethers, in contrast, have been demonstrated to cause severe adverse effects, mainly on the reproductive system. Ethylene glycol monoethyl and monomethyl ethers have been shown to cause testicular atrophy, teratogenicity, and fetotoxicity in addition to myelotoxicity (ECETOC, 1995). Interestingly, the target of longer alkyl chain length ethylene glycols, such as ethylene glycol monobutyl ether, is not the reproductive system because their main toxic effects are related to their hemolytic action (Bartnik *et al*., 1987; Ghanayem, 1996).

### *Humans*

No reproductive or developmental toxicity studies of propylene glycol mono-*t*-butyl ether in humans were found in the literature.

## Carcinogenicity

### *Experimental Animals*

No information regarding the carcinogenic effects of propylene glycol mono-*t*-butyl ether in experimental animals was found in the literature. However, some evidence of carcinogenic activity was shown for ethylene glycol monobutyl ether (or 2-butoxyethanol) following whole body exposures to air concentrations of 62.5 to 250 ppm carried out for 6 hours per day, 5 days per week for up to 2 years in B6C3$F_1$ mice (NTP, 2000). These conclusions were based on increased incidences of forestomach squamous cell papillomas or carcinomas in female mice and to a lesser extent in males, as well as increased incidences of hemangiosarcomas of the liver in male mice in the highest exposure groups.

### *Humans*

No epidemiology studies of propylene glycol mono-*t*-butyl ether were found in the literature.

## Genetic Toxicity

No published genetic toxicity data for propylene glycol mono-*t*-butyl ether were found in a review of the literature.

## Study Rationale

Propylene glycol mono-*t*-butyl ether was nominated by the U.S. Consumer Product Safety Commission based on its widespread use, potential for human exposure, and the lack of adequate toxicological, chronic toxicity, and carcinogenicity information. Inhalation studies were conducted because inhalation is a major route of exposure to humans. Initially, the highest exposure concentration of propylene glycol mono-*t*-butyl ether (1,200 ppm) used in the current studies was based on the maximum attainable vapor concentration that could be generated without aerosolization in the exposure chambers.

Propylene glycol mono-*t*-butyl ether is structurally related to propylene glycol monomethyl ether, a compound that has been shown to induce male rat-specific nephropathy related to $\alpha$2u-globulin accumulation in the renal tubules (Bus *et al.*, 1992). Male NBR rats, in particular, do not produce hepatic $\alpha$2u-globulin, and as a consequence, do not develop $\alpha$2u-globulin-related nephropathy (Chatterjee *et al.*, 1989; Dietrich and Swenberg, 1991). Thus, male NBR rats were exposed to propylene glycol mono-*t*-butyl ether, concurrently with F344/N rats, for comparison of renal lesion development in the 2-week study.

# MATERIALS AND METHODS

## Procurement and Characterization of Propylene Glycol Mono-*t*-butyl Ether

Propylene glycol mono-*t*-butyl ether was obtained from Aldrich Chemical Company, Inc. (Milwaukee, WI), in three lots (00406CN, 00603PG, and 14301ER). Lots 00406CN and 00603PG were combined, assigned a new lot number (8359-126-01), and used in the 2-week and 3-month studies; lot 14301ER was used during the 2-year studies. Identity and purity analyses were conducted by the analytical chemistry laboratory, Research Triangle Institute (Research Triangle Park, NC) and the study laboratory (Appendix K). Reports on analyses performed in support of the propylene glycol mono-*t*-butyl ether studies are on file at the National Institute of Environmental Health Sciences.

The chemical, a clear liquid, was identified as propylene glycol mono-*t*-butyl ether by infrared and nuclear magnetic resonance spectroscopy and by gas chromatography/mass spectrometry (GC/MS). The moisture content of lot 14301ER was determined by Karl Fischer titration. The purity of each lot was determined by elemental analyses and gas chromatography. Elemental analyses for carbon, hydrogen, oxygen, nitrogen, and sulfur were in agreement with the theoretical values for propylene glycol mono-*t*-butyl ether. Karl Fischer titration indicated 0.05% ± 0.01% water. Gas chromatography indicated one major peak and one impurity with an area greater than 0.1% relative to the major peak for both lots. The overall purity was determined to be 99% or greater.

To ensure stability, the bulk chemical was stored at room temperature, in metal drums under a nitrogen headspace. Stability was monitored using gas chromatography. No degradation of the bulk chemical was detected.

## Vapor Generation and Exposure System

Propylene glycol mono-*t*-butyl ether was pumped through a preheater and into the top of a heated glass column filled with glass beads to increase the surface area for evaporation. Heated nitrogen entering the column from below vaporized the chemical as it conveyed it out of the generator to a condenser column. The vapor was transported to the exposure room at an elevated temperature to prevent condensation.

In the exposure room, the vapor was mixed with heated air before it entered a short vapor distribution manifold. The pressure in the distribution manifold was kept fixed to ensure constant flows through the manifold and into the chambers. Electronically actuated metering valves controlled flow to each chamber. Metering valves in the chambers automatically opened to the established setting and allowed vapor to flow through individual temperature-controlled delivery lines to each exposure chamber. The vapor was then injected into the chamber inlet duct where it was diluted with conditioned chamber air to achieve the desired exposure concentration.

The study laboratory designed the inhalation exposure chamber (Harford Systems Division of Lab Products, Inc., Aberdeen, MD) so that uniform vapor concentrations could be maintained throughout the chamber with the catch pans in place. The total active mixing volume of each chamber was 1.7 $m^3$. A small particle detector (Type CN, Gardner Associates, Schenectady, NY) was used with and without animals in the exposure chambers to ensure that propylene glycol mono-*t*-butyl ether vapor, and not aerosol, was produced. The maximum attainable vapor concentration that could be generated without aerolization was 1,200 ppm, which was thus selected as the highest exposure concentration for the initial studies. No particle counts above the minimum resolvable level (approximately 200 particles/$cm^3$) were detected.

## Vapor Concentration Monitoring

The propylene glycol mono-*t*-butyl ether concentrations in the exposure chambers were monitored by an on-line gas chromatograph. Samples were drawn from each exposure chamber approximately every 24 minutes using a 12-port stream select valve. The on-line

chromatograph was checked throughout the day for instrument drift against an on-line standard of propylene glycol mono-*t*-butyl ether in nitrogen supplied by a diffusion tube standard generator. The on-line gas chromatograph was calibrated monthly by a comparison of chamber concentration data to data from grab samples that were collected with charcoal sampling tubes, extracted with ethyl acetate containing di(ethylene glycol) butyl ether as an internal standard, and analyzed by an off-line gas chromatograph. The volumes of gas were sampled at a constant flow rate ensured by a calibrated critical orifice. The off-line gas chromatograph was calibrated with gravimetrically prepared standards of propylene glycol mono-*t*-butyl ether containing di(ethylene glycol) butyl ether as an internal standard.

## Chamber Atmosphere Characterization

Buildup and decay rates for chamber vapor concentrations were determined with animals present in the chambers. At a chamber airflow rate of 15 air changes per hour, the theoretical value for the time to achieve 90% of the target concentration after the beginning of vapor generation ($T_{90}$) and the time for the chamber concentration to decay to 10% of the target concentration after termination of vapor generation ($T_{10}$) was approximately 12.5 minutes. Based on experimental data, a $T_{90}$ value of 12 minutes was selected for the studies.

Evaluations of chamber uniformity and persistence and monitoring for propylene glycol mono-t-butyl ether degradation impurities were conducted periodically throughout the studies by gas chromatography. With the exception of the 75 ppm exposure chamber uniformity, which showed slightly higher within-port variability due to a faulty valve during the 2-week studies, chamber uniformity was maintained; no degradation was detected.

## 2-Week Studies

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Taconic Laboratory Animals and Services (Germantown, NY); male NCI Black Reiter (NBR) rats were obtained from Charles River Laboratories (Frederick, MD). On receipt, the F344/N rats and mice were approximately 4 weeks old; the NBR rats were approximately 6 to 7 weeks old. Rats were quarantined for 34 days and were approximately 9 (F344/N) or 10 to 11 (NBR) weeks old on the first day of the studies. Mice were quarantined for 12 days and were approximately 6 weeks old on the first day of the study. Groups of five male and five female F344/N rats and mice and five NBR rats were exposed to propylene glycol mono-*t*-butyl ether at concentrations of 0, 75, 150, 300, 600, or 1,200 ppm, 6 hours plus $T_{90}$ (12 minutes) per day, 5 days per week for 16 (rats) or 17 (mice) days. Feed was available *ad libitum* except during exposure periods; water was available *ad libitum*. Rats and mice were housed individually. Clinical findings were recorded on days 6 and 13 and at the end of the studies**.** The animals were weighed initially, on days 6 and 13, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 1.

Concentrations of α2u-globulin and soluble protein were measured in male F344/N rats from each exposure group. The right kidney was removed, frozen in liquid nitrogen, and stored at –70° C until analysis. Each right kidney was thawed, a volume of 67 mM sodium/potassium phosphate buffer (pH 7.2) equivalent to twice the recorded fresh weight of the sample was added, and the sample was homogenized for 30 to 60 seconds using a tissue homogenizer (Tekmar Co., Cincinnati, OH). Approximately 500 µL of the well-mixed kidney homogenate was removed and stored at –70° C in 1.5 mL plastic screw-cap vials. The remainder of the homogenate was centrifuged at 3,000 g for 15 minutes, and the supernatant was drawn off and stored at –70° C in 1.5 mL plastic screw-cap vials. The protein content of each supernatant was measured in a 1:50 dilution (in phosphate-buffered saline-Tween) using the Pyrogallol Red Assay.

Homogenates diluted to 1:50,000 were analyzed for α2u-globulin using a competitive indirect ELISA technique. The amount of α2u-globulin was measured by comparing the relative fluorescent signal intensity in the study samples to that observed with known amounts of α2u-globulin present in calibration standards. Calibration standards and ELISA control standards (negative and positive) were plated in predetermined wells on 96-well microtiter plates. Calibration standards were assayed in triplicate. Each study sample was assayed in quadruplicate and randomized with respect to its relative position on the ELISA plate.

For cell proliferation analyses, the left kidney (bisected longitudinally) and a piece of duodenum were removed from all male and female rats and fixed in 10% neutral buffered formalin for 24 hours. The tissues were then processed, embedded in paraffin, and sectioned to a thickness of 5 µm. Tissues from all groups of male F344/N rats and the chamber control and 1,200 ppm NBR rats were stained with Mallory-Heidenhain for

protein and proliferating cell nuclear antigen (PCNA; PC-10 clone, Dako, Carpinteria, CA). Tissues from the remaining exposure groups of male NBR rats were stained with hematoxylin and eosin (H&E) and PCNA. Tissues from female F344/N rats were stained with H&E only. The duodenum and kidney were assessed qualitatively for adequate labeling. Approximately 2,000 proximal tubule nuclei were counted from each kidney stained with PCNA, and counts of labeled and total nuclei were recorded.

Necropsies were performed on all rats and mice. The right kidney, liver, and lung were weighed. Histopathologic examinations were performed on all chamber control and 1,200 ppm rats and mice. Table 1 lists the tissues and organs examined.

## 3-Month Studies

The 3-month studies were conducted to evaluate the cumulative toxic effects of repeated exposure to propylene glycol mono-*t*-butyl ether and to determine the appropriate exposure concentrations to be used in the 2-year studies.

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Taconic Laboratory Animals and Services. On receipt, the rats and mice were approximately 4 weeks old. Animals were quarantined for 13 (males) or 14 (females) days and were approximately 6 weeks old on the first day of the studies. Before the studies began, five male and five female rats and mice were randomly selected for parasite evaluation and gross observation for evidence of disease. Serologic analyses were performed on five male and five female sentinel rats and mice at week one and on five male and five female control rats and mice at the end of the studies using the protocols of the NTP Sentinel Animal Program (Appendix M).

Groups of 10 male and 10 female rats and 10 male and 10 female mice were exposed to propylene glycol mono-*t*-butyl ether at concentrations of 0, 75, 150, 300, 600, or 1,200 ppm, 6 hours plus $T_{90}$ (12 minutes) per day, 5 days per week for 14 weeks. Additional groups of 10 male and 10 female rats were exposed to the same concentrations for 6 weeks for clinical pathology and renal toxicity analyses; additional groups of five male rats were exposed to the same concentrations for 2 weeks for renal toxicity analyses. Feed was available *ad libitum* except during exposure periods and during urine collection; water was available *ad libitum*. Rats and mice were housed individually. Clinical findings were recorded weekly for rats and mice. The animals were weighed initially, weekly, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 1.

Animals were anesthetized with carbon dioxide, and blood was collected from the retroorbital sinus of clinical pathology rats on days 3 and 23 and from core study rats at the end of the study for hematology and clinical chemistry analyses; blood was collected from the supraorbital sinus of mice at the end of the study for hematology. Blood samples for hematology analyses were placed in tubes containing potassium EDTA. Packed cell volume; hemoglobin concentration; erythrocyte, platelet, and leukocyte counts; mean cell volume; mean cell hemoglobin; and mean cell hemoglobin concentration were determined using a Roche Cobas Helios (Roche Diagnostics, Branchburg, NJ). Manual hematocrit value was determined using a Damon/IEC MB microcentrifuge (International Equipment Company, Needham Heights, MA) and a Damon/IEC capillary reader for comparison to Cobas values for packed cell volume. Blood smears for mice and rats were stained with Wright/Giemsa stain in a Wescor 7100 Aerospray Slide Stainer (Wescor, Inc., Logan, UT). Leukocyte differential counts for mice and rats were based on classifying a minimum of 100 white cells. Reticulocytes were stained with New Methylene Blue and enumerated as a reticulocyte:erythrocyte ratio using the Miller disc method (Brecher and Schneiderman, 1950). Blood samples for clinical chemistry analyses were placed in tubes without anticoagulant, allowed to clot, and centrifuged. During week 12, core study male and female rats were placed in metabolism cages, and urine was collected over ice, protected from light for 16 hours. Table 1 lists the parameters measured.

At the end of the 3-month studies, samples were collected for sperm count and motility and vaginal cytology evaluations in core study rats and mice exposed to 0, 300, 600, or 1,200 ppm. The parameters evaluated are listed in Table 1. For 12 consecutive days prior to scheduled terminal sacrifice, the vaginal vaults of the females were moistened with saline, if necessary, and samples of vaginal fluid and cells were stained. Relative numbers of leukocytes, nucleated epithelial cells, and large squamous epithelial cells were determined and used to ascertain estrous cycle stage (i.e., diestrus, proestrus, estrus, and metestrus). Male animals were evaluated for sperm count and motility. The left testis

and left epididymis were isolated and weighed. The tail of the epididymis (cauda epididymis) was then removed from the epididymal body (corpus epididymis) and weighed. Test yolk (rats) or modified Tyrode's buffer (mice) was applied to slides and a small incision was made at the distal border of the cauda epididymis. The sperm effluxing from the incision were dispersed in the buffer on the slides, and the numbers of motile and nonmotile spermatozoa were counted for five fields per slide by two observers. Following completion of sperm motility estimates, each left cauda epididymis was placed in buffered saline solution. Caudae were finely minced, and the tissue was incubated in the saline solution and then heat fixed at 65° C. Sperm density was then determined microscopically with the aid of a hemacytometer. To quantify spermatogenesis, the testicular spermatid head count was determined by removing the tunica albuginea and homogenizing the left testis in phosphate-buffered saline containing 10% dimethyl sulfoxide. Homogenization-resistant spermatid nuclei were counted with a hemacytometer.

Renal toxicity studies were performed on male rats. To determine levels of α2u-globulin in each exposure group, the right kidney was collected from five renal toxicity study males at 2 weeks, five clinical pathology males at 6 weeks, and five core study males at terminal sacrifice. The right kidney was removed, cut in half, and stored at –70° C until analysis.

The kidney homogenate for determination of α2u-globulin was prepared as described for the 2-week study. Homogenates diluted to 1:10,000 with PBS-Tween were analyzed for α2u-globulin using a competitive indirect ELISA technique. The amount of α2u-globulin was measured by comparing the relative fluorescent signal intensity in the study samples to that observed with known amounts of α2u-globulin present in calibration standards. Calibration standards and ELISA control standards (negative and positive) were plated in predetermined wells on 96-well microtiter plates. Calibration standards were assayed in triplicate. Each study sample was assayed in quadruplicate and randomized with respect to its relative position on the ELISA plate.

For each exposure group, the left kidney and a piece of duodenum were collected from five male renal toxicity rats at 2 weeks, five male clinical pathology rats at 6 weeks, and five male core study rats at terminal sacrifice and prepared as described for the 2-week study. Sections from each kidney were stained with Mallory-Heidenhain for protein and PCNA (PC-10 clone, Dako) for determination of cell proliferation indices. The duodenum and kidney were qualitatively assessed as described for the 2-week study.

Necropsies were performed on all core study animals. The heart, right kidney, liver, lung, right testis, and thymus were weighed. Tissues for microscopic examination were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 4 to 6 µm, and stained with hematoxylin and eosin. Testes were fixed in plastic and sectioned to a thickness of 1 µm. Complete histopathologic examinations were performed on all chamber control and 1,200 ppm animals, and tissues were examined to a no-effect level. Table 1 lists the tissues and organs routinely examined.

## 2-Year Studies

### Study Design

Groups of 50 male and 50 female rats and mice were exposed to propylene glycol mono-*t*-butyl ether at concentrations of 0, 75, 300, or 1,200 ppm, 6 hours plus $T_{90}$ (12 minutes) per day, 5 days per week for 104 weeks.

### Source and Specification of Animals

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Taconic Laboratory Animals and Services for use in the 2-year studies. Rats were quarantined for 13 days and mice were quarantined for 12 days before the beginning of the studies. Five male and five female rats and mice were randomly selected for parasite evaluation and gross observation of disease. Rats and mice were approximately 6 weeks old at the beginning of the studies. The health of the animals was monitored during the studies according to the protocols of the NTP Sentinel Animal Program (Appendix M).

### Animal Maintenance

Rats and mice were housed individually. Feed was available *ad libitum* except during exposure and urine collection periods. Water was available *ad libitum*. Cages and racks were changed weekly. Further details of animal maintenance are given in Table 1. Information on feed composition and contaminants is provided in Appendix L.

### Clinical Examinations and Pathology

All animals were observed twice daily. Body weights were recorded initially, and clinical findings and body weights were recorded approximately every 4 weeks

through week 89, every 2 weeks beginning at week 92, and at the end of the studies.

Complete necropsies and microscopic examinations were performed on all core study rats and mice. At necropsy, all organs and tissues were examined for grossly visible lesions, and all major tissues were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 4 to 6 µm, and stained with hematoxylin and eosin for microscopic examination. For all paired organs (e.g., adrenal gland, kidney, ovary), samples from each organ were examined. For extended evaluation of renal proliferative lesions, kidneys of male and female rats were step sectioned at 1 mm intervals to obtain three to four additional sections from each kidney with a maximum of eight additional sections per animal. Tissues examined microscopically are listed in Table 1.

Microscopic evaluations were completed by the study laboratory pathologist, and the pathology data were entered into the Toxicology Data Management System. The slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit. The slides, individual animal data records, and pathology tables were evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, the slide and tissue counts were verified, and the histotechnique was evaluated. For the 2-year studies, a quality assessment pathologist evaluated slides from all tumors and all potential target organs, which included the kidney, liver, and nose of male and female rats, the urinary bladder and testes in male rats, and the eye in female rats. The liver, teeth, and eyes of male and female mice, the forestomach and lung of male mice, and the uterus of female mice were reviewed.

The quality assessment report and the reviewed slides were submitted to the NTP Pathology Working Group (PWG) chairperson, who reviewed the selected tissues and addressed any inconsistencies in the diagnoses made by the laboratory and quality assessment pathologists. Representative histopathology slides containing examples of lesions related to chemical administration, examples of disagreements in diagnoses between the laboratory and quality assessment pathologists, or lesions of general interest were presented by the chairperson to the PWG for review. The PWG consisted of the quality assessment pathologist and other pathologists experienced in rodent toxicologic pathology. This group examined the tissues without any knowledge of dose groups or previously rendered diagnoses. When the PWG consensus differed from the opinion of the laboratory pathologist, the diagnosis was changed. Final diagnoses for reviewed lesions represent a consensus between the laboratory pathologist, reviewing pathologist(s), and the PWG. Details of these review procedures have been described, in part, by Maronpot and Boorman (1982) and Boorman *et al.* (1985). For subsequent analyses of the pathology data, the decision of whether to evaluate the diagnosed lesions for each tissue type separately or combined was generally based on the guidelines of McConnell *et al.* (1986).

## Biomarkers of Exposure

Five male and five female chamber control core study rats and mice (data not provided) and 10 male and 10 female core study rats and mice from each exposed group were randomly selected for urinary metabolite analyses at 2 weeks. Urine was also collected from the same animals at 6 and 14 (rats) or 16 (mice) weeks. Animals were placed in metabolism cages for 16 hours after three consecutive days of exposure, and urine was collected over ice. Urine volume and creatinine concentration were measured on a Cobas Fara II chemistry system, then the samples were frozen at –70° C pending metabolite analysis.

Concentrations of propylene glycol mono-*t*-butyl ether sulfate and propylene glycol mono-*t*-butyl ether glucuronide were determined by liquid chromatography/tandem mass spectrometry as described by Battelle (1997). A buffer was prepared by dissolving 120 mg ammonium formate and 2.0 mL formic acid in 500 mL deionized water and then diluting with an equal volume of methanol. An internal standard solution of target concentrations of 3.2 µg propylene glycol mono-*t*-butyl ether sulfate-$d_5$ and 6.4 µg propylene glycol mono-*t*-butyl ether glucuronide-$d_5$ in buffer was added to 20 µL aliquots of urine and mixed thoroughly. Samples were injected into a Microsorb C18 column (250 mm × 4.6 mm ID, 5 µm; Rainin Instrument Co., Woburn, MA), and metabolites were eluted isocratically using a 19 mM ammonium formate/50% methanol mobile phase at 0.5 mL/minute in a triple quadrupole mass spectrometer (TSQ 7000, Finnigan MAT, San Jose, CA) with an electron spray ionization source. Metabolite ratios were determined by dividing metabolite concentration by creatinine concentration; further division by exposure concentration yielded normalized ratios.

**TABLE 1**
**Experimental Design and Materials and Methods in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| 2-Week Studies | 3-Month Studies | 2-Year Studies |
|---|---|---|
| **Study Laboratory** | | |
| Battelle Toxicology Northwest (Richland, WA) | Battelle Toxicology Northwest (Richland, WA) | Battelle Toxicology Northwest (Richland, WA) |
| **Strain and Species** | | |
| F344/N rats<br>NBR rats<br>$B6C3F_1$ mice | F344/N rats<br>$B6C3F_1$ mice | F344/N rats<br>$B6C3F_1$ mice |
| **Animal Source** | | |
| F344/N rats and $B6C3F_1$ mice: Taconic Laboratory Animals and Services (Germantown, NY)<br>NBR rats: Charles River Laboratories (Frederick, MD) | Taconic Laboratory Animals and Services (Germantown, NY) | Taconic Laboratory Animals and Services (Germantown, NY) |
| **Time Held Before Studies** | | |
| Rats: 34 days<br>Mice: 12 days | 13 days (males) or 14 days (females) | Rats: 13 days<br>Mice: 12 days |
| **Average Age When Studies Began** | | |
| F344/N Rats: 9 weeks<br>NBR Rats: 10-11 weeks<br>Mice: 6 weeks | 6 weeks | 6 weeks |
| **Date of First Exposure** | | |
| July 22, 1996 | December 9 (males) or 10 (females), 1996 | Rats: October 6, 1997<br>Mice: September 29, 1997 |
| **Duration of Exposure** | | |
| 6 hours plus $T_{90}$ (12 minutes) per day, 5 days per week for 16 (rats) or 17 (mice) days | 6 hours plus $T_{90}$ (12 minutes) per day, 5 days per week for 14 weeks | 6 hours plus $T_{90}$ (12 minutes) per day, 5 days per week for 104 weeks |
| **Date of Last Exposure** | | |
| Rats: August 6, 1996<br>Mice: August 7, 1996 | Rats: March 10 (females) or 12 (males), 1997<br>Mice: March 11 (females) or 13 (males), 1997 | Rats: October 1, 1999<br>Mice: September 24, 1999 |
| **Necropsy Dates** | | |
| Rats: August 7, 1996<br>Mice: August 8, 1996 | Rats: March 11 (females) or 13 (males), 1997<br>Mice: March 12 (females) or 14 (males), 1997 | Rats: October 4-7, 1999<br>Mice: September 27-October 1, 1999 |
| **Average Age at Necropsy** | | |
| F344/N rats: 11 weeks<br>NBR rats: 13-14 weeks<br>Mice: 8 weeks | 19 weeks | 110 weeks |
| **Size of Study Groups** | | |
| F344/N rats: 5 males and 5 females<br>NBR rats: 5 males<br>Mice: 5 males and 5 females | Rats: 25 males and 20 females<br>Mice: 10 males and 10 females | Core studies: 50 males and 50 females |

**TABLE 1**
**Experimental Design and Materials and Methods in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| 2-Week Studies | 3-Month Studies | 2-Year Studies |
|---|---|---|
| **Method of Distribution**<br>Animals were distributed randomly into groups of approximately equal initial mean body weights. | Same as 2-week studies | Same as 2-week studies |
| **Animals per Cage**<br>1 | 1 | 1 |
| **Method of Animal Identification**<br>Tail tattoo | Tail tattoo | Tail tattoo |
| **Diet**<br>NTP-2000 pelleted diet, (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum* except during exposure periods, changed weekly | Same as 2-week studies, except irradiated. Available *ad libitum* except during exposure and urine collection periods. | Same as 3-month studies |
| **Water**<br>Tap water (City of Richland municipal supply) via automatic watering system (Edstrom Industries, Waterford, WI), available *ad libitum* | Same as 2-week studies, except softened by study laboratory | Same as 2-week studies |
| **Cages**<br>Stainless-steel wire bottom (Hazleton Systems, Inc., Aberdeen, MD), changed weekly | Same as 2-week studies | Stainless-steel wire bottom (Lab Products, Inc., Seaford, DE), changed weekly |
| **Chamber Air Supply Filters**<br>Single HEPA (Northland Filter System International, Mechanicville, NY); charcoal (RSE, New Baltimore, MI); Purafil (Environmental Systems, Lynnwood, WA) | Same as 2-week studies | Single HEPA (Environmental Filter, Santa Rosa, CA); charcoal (RSE, New Baltimore, MI); Purafil (Environmental Systems, Lynnwood, WA) |
| **Chambers**<br>Stainless steel with excreta pan suspended below each cage unit (Lab Products, Inc., Aberdeen, MD), changed weekly | Same as 2-week studies | Same as 2-week studies (Lab Products, Inc., Seaford, DE) |
| **Chamber Environment**<br>Temperature: 75° ± 3° F<br>Relative humidity: 55% ± 15%<br>Room fluorescent light: 12 hours/day<br>Chamber air changes: 15/hour | Same as 2-week studies | Same as 2-week studies |
| **Exposure Concentrations**<br>0, 75, 150, 300, 600, or 1,200 ppm | 0, 75, 150, 300, 600, or 1,200 ppm | 0, 75, 300, or 1,200 ppm |
| **Type and Frequency of Observation**<br>Observed twice daily; animals were weighed initially, on days 6 and 13, and at the end of the studies; clinical findings were recorded on days 6 and 13 and at the end of the studies. | Observed twice daily; animals were weighed initially, weekly, and at the end of the studies; clinical findings were recorded weekly. | Observed twice daily; animals were weighed and clinical findings were recorded initially (body weights), every 4 weeks for weeks 5 through 89, every 2 weeks beginning week 92, and at the end of the studies. |

**TABLE 1**
**Experimental Design and Materials and Methods in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| 2-Week Studies | 3-Month Studies | 2-Year Studies |
|---|---|---|
| **Method of Sacrifice** | | |
| Carbon dioxide asphyxiation. | Same as 2-week studies | Same as 2-week studies |
| **Necropsy** | | |
| Necropsies were performed on all animals. Organs weighed were right kidney, liver, and lung. | Necropsies were performed on all animals. Organs weighed were heart, right kidney, liver, lung, right testis, and thymus. | Necropsies were performed on all core study animals. |
| **Clinical Pathology** | | |
| None | Blood was collected from the retroorbital sinus of clinical pathology rats on days 3 and 23 and from core study rats at the end of the study for hematology and clinical chemistry. Blood was collected from the supraorbital sinus of mice at the end of the study for hematology. Core study rats were placed in metabolism cages for 16-hour urine collection during week 12.<br>***Hematology:*** hematocrit; packed red cell volume; hemoglobin; erythrocyte, reticulocyte, nucleated erythrocyte, and platelet counts; mean cell volume; mean cell hemoglobin; mean cell hemoglobin concentration; and leukocyte counts and differentials.<br>***Clinical chemistry:*** urea nitrogen, creatinine, total protein, albumin, alanine aminotransferase, alkaline phosphatase, sorbitol dehydrogenase, and total bile acids.<br>***Urinalysis:*** volume, specific gravity, creatinine, glucose, protein, *N*-acetyl-β-D-glucosaminidase, alkaline phosphatase, aspartate aminotransferase, lactate dehydrogenase, and γ-glutamyltransferase. | None |

**TABLE 1**
**Experimental Design and Materials and Methods in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| 2-Week Studies | 3-Month Studies | 2-Year Studies |
|---|---|---|
| **Histopathology** | | |
| Histopathology was performed on chamber control and 1,200 ppm rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined to the no-effect level: kidney (female F344/N rats, male NBR rats, and male and female mice), liver, lung, and nose. The kidney was also examined in all groups of male F344/N rats. | Complete histopathology was performed on chamber control and 1,200 ppm core study rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined to the no-effect level: adrenal gland, bone with marrow, brain, clitoral gland, esophagus, gallbladder (mice), heart with aorta, large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, ileum), kidney, larynx, liver, lung and mainstream bronchi, lymph nodes (mandibular, mesenteric, bronchial, and mediastinal), mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, skin, spleen, stomach (forestomach and glandular), testis with epididymis and seminal vesicle, thymus, thyroid gland, trachea, urinary bladder, and uterus. | Complete histopathology was performed on core study rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined: adrenal gland, bone with marrow, brain (three sections in mice), clitoral gland, esophagus, eyes, gallbladder (mice), harderian gland (rats), heart with aorta, large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, ileum), kidney, larynx, liver, lung with bronchi, lymph nodes (mandibular, mesenteric, bronchial, & mediastinal), mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, skin, spleen, stomach (forestomach and glandular), testis with epididymis and seminal vesicle, thymus, thyroid gland, trachea, urinary bladder, uterus, and Zymbal's gland. |
| **Sperm Motility and Vaginal Cytology** | | |
| None | At the end of the studies, sperm samples were collected from core study male animals in the chamber control, 300, 600, and 1,200 ppm groups for sperm motility evaluations. The following parameters were evaluated: spermatid heads per testis and per gram testis, spermatid counts, and epididymal spermatozoal motility and concentration. The left cauda, left epididymis, and left testis were weighed. Vaginal samples were collected for 12 days during the last two weeks of the studies from females exposed to 0, 300, 600, or 1,200 ppm for vaginal cytology evaluations. The percentage of time spent in the various estrous cycle stages and estrous cycle length were evaluated. | None |
| **Renal Toxicity Studies in Rats** | | |
| Concentrations of $\alpha$2u-globulin and soluble protein in the right kidney were measured in male F344/N rats at terminal sacrifice. For assessment of cell proliferation, left kidney sections from male F344/N rats and NBR rats were stained with PCNA and examined for labeled cells. | For each exposure group, concentrations of $\alpha$2u-globulin in the right kidney were measured in 5 male renal toxicity rats at 2 weeks, 5 males randomly selected from clinical pathology rats at 6 weeks, and 5 males randomly selected from core study animals at terminal sacrifice. Left kidney sections from the same male rats were stained with Mallory-Heidenhain for protein and PCNA for assessment of cell proliferation indices. | None |

**TABLE 1**
**Experimental Design and Materials and Methods in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| 2-Week Studies | 3-Month Studies | 2-Year Studies |
|---|---|---|
| **Biomarkers of Exposure** | | |
| None | None | Urine was collected during a 16-hour period from five male and five female chamber control rats and mice and 10 male and 10 female core study rats and mice from each exposed group at 2, 6, and 14 (rats) or 16 (mice) weeks. Parameters measured included urine volume and creatinine, propylene glycol mono-*t*-butyl ether sulfate , and propylene glycol mono-*t*-butyl ether glucuronide concentrations. |

# Statistical Methods

## Survival Analyses

The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals found dead of other than natural causes were censored from the survival analyses; animals dying from natural causes were not censored. Statistical analyses for possible dose-related effects on survival used Cox's (1972) method for testing two groups for equality and Tarone's (1975) life table test to identify dose-related trends. All reported P values for the survival analyses are two sided.

## Calculation of Incidence

The incidences of neoplasms or nonneoplastic lesions are presented in Tables A1, A5, B1, B5, C1, C5, D1, and D5 as the numbers of animals bearing such lesions at a specific anatomic site and the numbers of animals with that site examined microscopically. For calculation of statistical significance, the incidences of most neoplasms (Tables A3, B3, C3, and D3) and all nonneoplastic lesions are given as the numbers of animals affected at each site examined microscopically. However, when macroscopic examination was required to detect neoplasms in certain tissues (e.g., harderian gland, intestine, mammary gland, and skin) before microscopic evaluation, or when neoplasms had multiple potential sites of occurrence (e.g., leukemia or lymphoma), the denominators consist of the number of animals on which a necropsy was performed. Tables A3, B3, C3, and D3 also give the survival-adjusted neoplasm rate for each group and each site-specific neoplasm. This survival-adjusted rate (based on the Poly-3 method described below) accounts for differential mortality by assigning a reduced risk of neoplasm, proportional to the third power of the fraction of time on study, to animals that do not reach terminal sacrifice.

## Analysis of Neoplasm and Nonneoplastic Lesion Incidences

The Poly-k test (Bailer and Portier, 1988; Portier and Bailer, 1989; Piegorsch and Bailer, 1997) was used to assess neoplasm and nonneoplastic lesion prevalence. This test is a survival-adjusted quantal-response procedure that modifies the Cochran-Armitage linear trend test to take survival differences into account. More specifically, this method modifies the denominator in the quantal estimate of lesion incidence to approximate more closely the total number of animal years at risk. For analysis of a given site, each animal is assigned a risk weight. This value is one if the animal had a lesion at that site or if it survived until terminal sacrifice; if the animal died prior to terminal sacrifice and did not have a lesion at that site, its risk weight is the fraction of the entire study time that it survived, raised to the kth power.

This method yields a lesion prevalence rate that depends only upon the choice of a shape parameter for a Weibull hazard function describing cumulative lesion incidence over time (Bailer and Portier, 1988). Unless otherwise specified, a value of k=3 was used in the analysis of site-specific lesions. This value was recommended by Bailer and Portier (1988) following an evaluation of neoplasm onset time distributions for a variety of site-specific neoplasms in control F344 rats and $B6C3F_1$ mice (Portier *et al.,* 1986). Bailer and Portier (1988) showed that the Poly-3 test gave valid results if the true value of k was anywhere in the range from 1 to 5. A further advantage of the Poly-3 method is that it does not require lesion lethality assumptions. Variation introduced by the use of risk weights, which reflect differential mortality, was accommodated by adjusting the variance of the Poly-3 statistic as recommended by Bieler and Williams (1993).

Tests of significance included pairwise comparisons of each exposed group with controls and a test for an overall exposure-related trend. Continuity-corrected Poly-3 tests were used in the analysis of lesion incidence, and reported P values are one sided. The significance of lower incidences or decreasing trends in lesions is represented as 1– P with the letter N added (e.g., P=0.99 is presented as P=0.01N).

## Analysis of Continuous Variables

Two approaches were employed to assess the significance of pairwise comparisons between exposed and control groups in the analysis of continuous variables. Organ and body weight data, which historically have approximately normal distributions, were analyzed with the parametric multiple comparison procedures of Dunnett (1955) and Williams (1971, 1972). Hematology, clinical chemistry, urinalysis, spermatid, and epididymal spermatozoal data, which have typically skewed distributions, were analyzed using the nonparametric multiple comparison methods of Shirley (1977) (as modified by Williams, 1986) and Dunn (1964). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of the dose-related trends and to determine whether a trend-sensitive test (Williams' or Shirley's test) was more appropriate for pairwise

comparisons than a test that does not assume a monotonic dose-related trend (Dunnett's or Dunn's test). Prior to statistical analysis, extreme values identified by the outlier test of Dixon and Massey (1951) were examined by NTP personnel, and implausible values were eliminated from the analysis. Average severity values were analyzed for significance with the Mann-Whitney U test (Hollander and Wolfe, 1973). Because vaginal cytology data are proportions (the proportion of the observation period that an animal was in a given estrous stage), an arcsine transformation was used to bring the data into closer conformance with a normality assumption. Treatment effects were investigated by applying a multivariate analysis of variance (Morrison, 1976) to the transformed data to test for simultaneous equality of measurements across exposure concentrations. The Tukey-Kramer test (Westfall, 1999) was used to assess the significance of the comparisons between groups for the urinary biomarker data.

### Historical Control Data

The concurrent control group represents the most valid comparison to the treated groups and is the only control group analyzed statistically in NTP bioassays. However, historical control data are often helpful in interpreting potential treatment-related effects, particularly for uncommon or rare neoplasm types. For meaningful comparisons, the conditions for studies in the historical database must be generally similar. One significant factor affecting the background incidence of neoplasms at a variety of sites is diet. In 1995, the NTP incorporated a new diet (NTP-2000) that contains less protein and more fiber than the NIH-07 diet used previously in toxicity and carcinogenicity studies (Rao, 1996, 1997). The current NTP historical database contains all 21 studies that use the NTP-2000 diet with histopathology findings completed up to the present. A second potential source of variability is route of administration. In general the historical database for a given study will include studies using the same route of administration, and the overall incidences of neoplasms for all routes of administration are included for comparison.

## Quality Assurance Methods

The 3-month and 2-year studies were conducted in compliance with Food and Drug Administration Good Laboratory Practice Regulations (21 CFR, Part 58). In addition, as records from the 2-year studies were submitted to the NTP Archives, these studies were audited retrospectively by an independent quality assurance contractor. Separate audits covered completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and a draft of this NTP Technical Report. Audit procedures and findings are presented in the reports and are on file at NIEHS. The audit findings were reviewed and assessed by NTP staff, and all comments were resolved or otherwise addressed during the preparation of this Technical Report.

## Genetic Toxicology

The genetic toxicity of propylene glycol mono-*t*-butyl ether was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium,* sister chromatid exchanges and chromosomal aberrations in cultured Chinese hamster ovary cells, and increases in the frequency of micronucleated erythrocytes in mouse peripheral blood. The protocols for these studies and the results are given in Appendix E.

The genetic toxicity studies have evolved from an earlier effort by the NTP to develop a comprehensive database permitting a critical anticipation of a chemical's carcinogenicity in experimental animals based on numerous considerations, including the molecular structure of the chemical and its observed effects in short-term *in vitro* and *in vivo* genetic toxicity tests (structure-activity relationships). The short-term tests were originally developed to clarify proposed mechanisms of chemical-induced DNA damage based on the relationship between electrophilicity and mutagenicity (Miller and Miller, 1977) and the somatic mutation theory of cancer (Straus, 1981; Crawford, 1985). However, it should be noted that not all cancers arise through genotoxic mechanisms.

DNA reactivity combined with *Salmonella* mutagenicity is highly correlated with induction of carcinogenicity in multiple species/sexes of rodents and at multiple tissue sites (Ashby and Tennant, 1991). A positive response in the *Salmonella* test was shown to be the most predictive *in vitro* indicator for rodent carcinogenicity (89% of the *Salmonella* mutagens are rodent carcinogens) (Tennant *et al.,* 1987; Zeiger *et al.,* 1990). Additionally, no battery of tests that included the *Salmonella* test improved the predictivity of the *Salmonella* test alone. However, these other tests can provide useful information on the

types of DNA and chromosomal damage induced by the chemical under investigation.

The predictivity for carcinogenicity of a positive response in acute *in vivo* bone marrow chromosome aberration or micronucleus tests appears to be less than that in the *Salmonella* test (Shelby *et al.,* 1993; Shelby and Witt, 1995). However, clearly positive results in long-term peripheral blood micronucleus tests have high predictivity for rodent carcinogenicity (Witt *et al.,* 2000); negative results in this assay do not correlate well with either negative or positive results in rodent carcinogenicity studies. Because of the theoretical and observed associations between induced genetic damage and adverse effects in somatic and germ cells, the determination of *in vivo* genetic effects is important to the overall understanding of the risks associated with exposure to a particular chemical. Most organic chemicals that are identified by the International Agency for Research on Cancer as human carcinogens, other than hormones, are genotoxic. The vast majority of these are detected by both the *Salmonella* assay and rodent bone marrow cytogenetics tests (Shelby, 1988; Shelby and Zeiger, 1990).

# RESULTS

## RATS

### 2-WEEK STUDY

All male and female F344/N and male NBR rats survived to the end of the study (Tables 2 and 3). Final mean body weights and body weight gains of all exposed groups of rats were similar to those of the chamber controls. There were no clinical findings related to propylene glycol mono-*t*-butyl ether exposure.

**TABLE 2**
**Survival and Body Weights of F344/N Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Concentration (ppm) | Survival[a] | Mean Body Weight[b] (g) | | | Final Weight Relative to Controls (%) |
|---|---|---|---|---|---|
| | | Initial | Final | Change | |
| **Male** | | | | | |
| 0 | 5/5 | 167 ± 3 | 219 ± 7 | 52 ± 4 | |
| 75 | 5/5 | 172 ± 3 | 225 ± 4 | 54 ± 1 | 103 |
| 150 | 5/5 | 168 ± 2 | 217 ± 6 | 49 ± 5 | 99 |
| 300 | 5/5 | 167 ± 2 | 221 ± 4 | 54 ± 4 | 101 |
| 600 | 5/5 | 172 ± 3 | 222 ± 5 | 50 ± 3 | 101 |
| 1,200 | 5/5 | 170 ± 3 | 214 ± 5 | 44 ± 3 | 97 |
| **Female** | | | | | |
| 0 | 5/5 | 121 ± 2 | 147 ± 2 | 26 ± 1 | |
| 75 | 5/5 | 123 ± 1 | 148 ± 3 | 26 ± 3 | 101 |
| 150 | 5/5 | 122 ± 1 | 145 ± 3 | 22 ± 2 | 98 |
| 300 | 5/5 | 122 ± 2 | 147 ± 3 | 25 ± 2 | 100 |
| 600 | 5/5 | 123 ± 2 | 144 ± 4 | 21 ± 2 | 98 |
| 1,200 | 5/5 | 122 ± 3 | 144 ± 4 | 22 ± 2 | 97 |

[a] Number of animals surviving at 2 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Differences from the chamber control group are not significant by Dunnett's test.

**TABLE 3**
**Survival and Body Weights of Male NBR Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Concentration (ppm) | Survival[a] | Mean Body Weight[b] (g) | | | Final Weight Relative to Controls (%) |
|---|---|---|---|---|---|
| | | Initial | Final | Change | |
| 0 | 5/5 | 249 ± 5 | 288 ± 4 | 38 ± 2 | |
| 75 | 5/5 | 248 ± 5 | 284 ± 4 | 36 ± 4 | 99 |
| 150 | 5/5 | 239 ± 9 | 285 ± 9 | 46 ± 10 | 99 |
| 300 | 5/5 | 245 ± 4 | 283 ± 2 | 38 ± 3 | 98 |
| 600 | 5/5 | 247 ± 5 | 281 ± 5 | 34 ± 3 | 98 |
| 1,200 | 5/5 | 248 ± 7 | 281 ± 7 | 33 ± 2 | 98 |

[a] Number of animals surviving at 2 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Differences from the chamber control group are not significant by Dunnett's test.

Cell proliferation analyses were performed on male F344/N and NBR rats (Tables H1 and H2). The number of labeled cells and the labeling index in the left kidney of 1,200 ppm F344/N males were significantly greater than those of the chamber controls. No significant differences in labeling indices were noted in NBR males. Concentrations of α2u-globulin were measured for male F344/N rats (Table H1); the α2u-globulin/soluble protein ratios in exposed rats were not significantly different from that in the chamber controls.

Kidney weights of 600 ppm male F344/N rats were significantly greater than those of the chamber controls (Table I1). Liver weights of male and female F344/N and male NBR rats in the 1,200 ppm groups were significantly increased (Tables I1 and I2); liver weights of 600 ppm male F344/N rats were also increased. There were no exposure-related histopathological changes in the liver.

Mild hyaline droplet accumulation occurred in the kidneys of all male F344/N rats (data not shown). Chamber control rats had fine, bright pink, intracytoplasmic protein granules/droplets in the proximal renal cortical tubules, whereas the granules/droplets in the tubules of exposed rats were irregularly shaped, larger, or conglomerates of several droplets. There were no exposure-related kidney changes in male NBR rats or female F344/N rats.

*Exposure Concentration Selection Rationale*: Because there were no effects of propylene glycol mono-*t*-butyl ether on survival or body weights of male or female F344/N rats or male NBR rats in the 2-week study, and because the incidences of kidney lesions in exposed male F344/N rats were mild and not significantly increased, exposure concentrations selected for the 3-month inhalation study in F344/N rats were 0, 75, 150, 300, 600, and 1,200 ppm. The highest exposure concentration was maintained for the 3-month study because it was the maximum attainable vapor concentration that could be generated without aerosolization in the exposure chambers.

## 3-Month Study

All rats survived to the end of the study (Table 4). Final mean body weights of all exposed groups were similar to those of the chamber controls; final mean body weight gains of 1,200 ppm males and 600 and 1,200 ppm females were greater than those of the chamber controls.

**Table 4**
**Survival and Body Weights of Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Concentration (ppm) | Survival[a] | Mean Body Weight[b] (g) | | | Final Weight Relative to Controls (%) |
|---|---|---|---|---|---|
| | | Initial | Final | Change | |
| **Male** | | | | | |
| 0 | 10/10 | 102 ± 3 | 309 ± 4 | 207 ± 4 | |
| 75 | 10/10 | 100 ± 3 | 320 ± 5 | 220 ± 4 | 104 |
| 150 | 10/10 | 98 ± 3 | 309 ± 4 | 211 ± 5 | 100 |
| 300 | 10/10 | 95 ± 3 | 314 ± 5 | 219 ± 6 | 102 |
| 600 | 10/10 | 93 ± 3 | 310 ± 7 | 216 ± 5 | 100 |
| 1,200 | 10/10 | 99 ± 3 | 327 ± 7 | 227 ± 6* | 106 |
| **Female** | | | | | |
| 0 | 10/10 | 93 ± 2 | 179 ± 4 | 87 ± 4 | |
| 75 | 10/10 | 89 ± 2 | 180 ± 3 | 91 ± 2 | 101 |
| 150 | 10/10 | 90 ± 3 | 185 ± 4 | 95 ± 3 | 103 |
| 300 | 10/10 | 95 ± 3 | 187 ± 4 | 91 ± 3 | 104 |
| 600 | 10/10 | 90 ± 3 | 187 ± 4 | 97 ± 3* | 104 |
| 1,200 | 10/10 | 92 ± 2 | 189 ± 4 | 96 ± 2* | 105 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Williams' or Dunnett's test.
[a] Number of animals surviving at 3 months/number initially in group
[b] Weights and weight changes are given as mean ± standard error.

The hematology, clinical chemistry, and urinalysis data are shown in Table F1. In male rats, a minimal decrease in the erythron, evidenced by small decreases in hematocrit values, hemoglobin concentrations, and erythrocyte counts occurred at 14 weeks. This change was observed in groups exposed to 300 ppm or greater, but there was no apparent exposure-concentration relationship for the response. On day 23, hemoglobin concentrations were minimally decreased in 600 and 1,200 ppm males; hematocrit values and erythrocyte counts were unaffected. On days 3 and 23, several exposed male groups (primarily the 600 and 1,200 ppm groups) demonstrated small increases in reticulocyte counts. The increases in reticulocyte counts were transient and despite the presence of minimal erythron decrease, did not persist until 14 weeks. In female rats, minimal transient decreases in the erythron and reticulocyte counts occurred on day 23 in the 1,200 ppm group; these effects were not apparent at 14 weeks. Though observed statistically as exposure concentration-related, none of the erythron changes in male or female rats were considered to be clinically significant.

In 1,200 ppm rats, leukocyte counts were decreased by approximately 40% on days 3 and 23, reflecting decreases in lymphocyte and monocyte counts. Low leukocyte counts persisted in the female rats at 14 weeks, but to a reduced extent. In contrast, leukocyte counts were increased in all exposed groups of males at 14 weeks. The cause of the leukocyte changes, specifically the decreases or increases in lymphocytes and monocytes, was unknown but may suggest some alteration in peripheral distribution rather than a change in production.

On day 3, a transient increase in serum bile acid concentration occurred in nearly all of the exposed groups; by day 23, this effect persisted in 300 ppm or greater males and 1,200 ppm females. At 14 weeks, bile acid concentrations were similar in exposed and chamber control groups. On day 23, an exposure concentration-related decrease in alanine aminotransferase activity occurred in males and females. The effect was transient in females with no decrease at 14 weeks, but persisted in all exposed groups of males at 14 weeks.

On days 3 (males) and 23 (males and females), serum creatinine concentrations were increased in the 1,200 ppm groups compared to the chamber controls. The effect was more prominent in males and, on day 23, the creatinine concentration was approximately twofold higher than in the chamber controls. This effect was transient however, and was not apparent at 14 weeks.

At week 12, urinalysis results for exposed groups of male rats demonstrated increases in urine volumes, glucose and protein concentrations, and activities of aspartate aminotransferase, lactate dehydrogenase, and *N*-acetyl-ß-D-glucosaminidase (Tables 5 and F1). A polyuria, evidenced by an approximately twofold increase in urine volume, occurred in 600 and 1,200 ppm male rats. The urine of the affected groups was characterized by a mean specific gravity (1.013) that was at or above that of glomerular filtrate (1.008-1.012) and similar to values obtained for chamber control animals, suggesting that the increased urine volumes were probably not related to contamination of the specimens with drinking water. The mechanism for the increased urine output was unknown.

Increases in urine glucose and protein concentrations occurred in essentially all exposed groups of males, urine glucose/mg creatinine was increased approximately 25% to 50%, compared to the chamber controls. Urine protein/mg creatinine increased approximately 20% to 70% in exposed groups of males. Increased activities of aspartate aminotransferase and lactate dehydrogenase per mg creatinine occurred in all exposed groups of males. Exposed groups of female rats were much less affected, as minimal increases in lactate dehydrogenase and *N*-acetyl-ß-D-glucosaminidase per mg creatinine occurred in groups exposed to 150 ppm or greater and 600 and 1,200 ppm, respectively.

**TABLE 5**
**Selected Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-Butyl Ether[a]**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| **Male** | | | | | | |
| Volume (mL/16 hours) | 12.2 ± 1.8 | 19.0 ± 2.6 | 19.8 ± 3.1 | 13.9 ± 2.3 | 25.3 ± 3.7** | 26.8 ± 2.7** |
| Specific gravity | 1.017 ± 0.002 | 1.012 ± 0.002 | 1.014 ± 0.002 | 1.020 ± 0.003 | 1.013 ± 0.002 | 1.013 ± 0.001 |
| Creatinine (mg/dL) | 68.40 ± 8.90 | 50.10 ± 7.04 | 51.00 ± 9.19 | 71.40 ± 10.05 | 40.50 ± 6.12* | 34.00 ± 3.19** |
| Glucose (µg/mg creatinine) | 118 ± 5 | 153 ± 6* | 163 ± 12** | 156 ± 6* | 159 ± 8** | 149 ± 15 |
| Protein (µg/mg creatinine) | 964 ± 43 | 1,256 ± 81** | 1,266 ± 49** | 1,161 ± 44** | 1,293 ± 48** | 1,585 ± 61** |
| Alkaline phosphatase (mU/mg creatinine) | 259 ± 14 | 322 ± 17 | 293 ± 18 | 266 ± 15 | 288 ± 17 | 299 ± 19 |
| Aspartate aminotransferase (mU/mg creatinine) | 9 ± 0 | 52 ± 4** | 61 ± 3** | 59 ± 4** | 52 ± 3** | 78 ± 5** |
| Lactate dehydrogenase (mU/mg creatinine) | 39 ± 1 | 118 ± 15** | 121 ± 6** | 127 ± 6** | 124 ± 7** | 156 ± 9** |
| γ-Glutamyltransferase (U/mg creatinine) | 2.1 ± 0.1 | 2.2 ± 0.1 | 2.2 ± 0.1 | 2.0 ± 0.1 | 2.0 ± 0.1 | 1.8 ± 0.1 |
| *N*-acetyl-β-D-glucosaminidase (mU/mg creatinine) | 14 ± 1 | 23 ± 1** | 23 ± 1** | 22 ± 1** | 24 ± 1** | 27 ± 2** |
| **Female** | | | | | | |
| Volume (mL/16 hours) | 12.0 ± 1.7 | 13.2 ± 1.6 | 10.4 ± 1.5 | 8.0 ± 1.1 | 13.8 ± 2.0 | 10.5 ± 1.9 |
| Specific gravity | 1.013 ± 0.002 | 1.012 ± 0.002 | 1.015 ± 0.002 | 1.020 ± 0.003* | 1.013 ± 0.002 | 1.023 ± 0.004* |
| Creatinine (mg/dL) | 45.00 ± 7.41 | 37.50 ± 4.61 | 44.80 ± 4.94 | 60.00 ± 9.69 | 35.00 ± 4.57 | 52.10 ± 9.44 |
| Glucose (µg/mg creatinine) | 106 ± 3 | 102 ± 4 | 106 ± 6 | 101 ± 3 | 93 ± 6 | 114 ± 4 |
| Protein (µg/mg creatinine) | 91 ± 4 | 158 ± 59 | 89 ± 3 | 94 ± 4 | 93 ± 8 | 105 ± 6 |
| Alkaline phosphatase (mU/mg creatinine) | 184 ± 10 | 172 ± 11 | 159 ± 11 | 177 ± 24 | 188 ± 11 | 186 ± 10 |
| Aspartate aminotransferase (mU/mg creatinine) | 2 ± 1 | 4 ± 1 | 2 ± 0 | 3 ± 0 | 3 ± 1 | 2 ± 0 |
| Lactate dehydrogenase (mU/mg creatinine) | 27 ± 3 | 31 ± 1 | 36 ± 2** | 42 ± 2** | 45 ± 2** | 60 ± 3** |
| γ-Glutamyltransferase (U/mg creatinine) | 0.9 ± 0.1 | 0.9 ± 0.1 | 0.8 ± 0.1 | 1.1 ± 0.2 | 1.2 ± 0.1 | 1.1 ± 0.1 |
| *N*-acetyl-β-D-glucosaminidase (U/mg creatinine) | 13 ± 0 | 13 ± 0 | 13 ± 0 | 13 ± 0 | 14 ± 0* | 15 ± 0** |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error. Statistical tests were performed on unrounded data.

At 2 and 6 weeks and at study termination, five male rats per group were sacrificed for renal toxicity studies. Kidney tissue of male rats was examined for indices of cell proliferation. The numbers of PCNA-labeled cells and labeling indices in exposed males were generally significantly greater than those of the chamber controls at 2 and 6 weeks and at study termination (Tables 6 and H3). In general, exposure-related increases in α2u-globulin concentrations in males occurred throughout the study; the concentrations at 2 weeks (8 weeks of age) were less than those at 6 and 14 weeks (12 and 20 weeks of age, respectively), which was in part due to the age-dependent production of α2u-globulin. The production of α2u-globulin is in general relatively low at 8 weeks of age.

**TABLE 6**
**Selected Renal Toxicity Data for Male Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 5 | 5 | 5 | 5 | 5 | 5 |
| Cells labeled | | | | | | |
| Week 2 | 79.0 ± 2.8 | 80.0 ± 4.2 | 84.4 ± 4.5 | 74.2 ± 3.0 | 96.2 ± 4.3 | 122.4 ± 9.7 |
| Week 6 | 75.0 ± 2.4 | 66.2 ± 2.6 | 72.4 ± 5.4 | 84.6 ± 2.8 | 96.8 ± 1.4 | 109.6 ± 7.4 |
| Week 13 | 69.2 ± 4.3 | 83.2 ± 5.0 | 93.6 ± 3.2 | 87.4 ± 3.0 | 108.4 ± 9.2 | 148.0 ± 9.0 |
| Cells counted | | | | | | |
| Week 2 | 2,210 ± 91 | 2,200 ± 30 | 2,188 ± 48 | 2,158 ± 61 | 2,202 ± 60 | 2,217 ± 74 |
| Week 6 | 2,093 ± 22 | 2,091 ± 50 | 2,149 ± 38 | 2,187 ± 52 | 2,226 ± 28 | 2,214 ± 19 |
| Week 13 | 2,202 ± 52 | 2,200 ± 26 | 2,167 ± 49 | 2,147 ± 41 | 2,151 ± 28 | 2,238 ± 29 |
| Labeling index (%) | | | | | | |
| Week 2 | 3.6 ± 0.1 | 3.6 ± 0.2 | 3.9 ± 0.2 | 3.4 ± 0.1 | 4.4 ± 0.2* | 5.5 ± 0.4** |
| Week 6 | 3.6 ± 0.1 | 3.2 ± 0.1 | 3.4 ± 0.2 | 3.9 ± 0.1 | 4.3 ± 0.0* | 4.9 ± 0.3* |
| Week 14 | 3.2 ± 0.2 | 3.8 ± 0.2 | 4.3 ± 0.2* | 4.1 ± 0.2* | 5.0 ± 0.4** | 6.6 ± 0.4** |
| α2u-Globulin (nmol/g kidney) | | | | | | |
| Week 2 | 21.5 ± 2.4 | 69.2 ± 25.2 | 126.3 ± 34.8 | 171.6 ± 46.0* | 332.6 ± 54.9** | 52.8 ± 15.2 |
| Week 6 | 160.1 ± 63.6 | 437.0 ± 78.9* | 505.6 ± 74.6* | 757.8 ± 120.1** | 670.2 ± 212.0** | 732.4 ± 77.4** |
| Week 14 | 319.0 ± 93.7 | 476.8 ± 73.9 | 525.8 ± 125.0 | 733.6 ± 71.2** | 553.4 ± 85.2* | 708.4 ± 159.1* |
| α2u-Globulin (ng/μg soluble protein) | | | | | | |
| Week 2 | 7.7 ± 0.9 | 28.0 ± 8.8* | 47.9 ± 12.7* | 71.4 ± 18.7** | 138.8 ± 21.4** | 25.6 ± 7.3** |
| Week 6 | 64.7 ± 25.4 | 167.8 ± 27.1* | 184.0 ± 25.5* | 249.2 ± 48.7** | 237.0 ± 73.5* | 250.0 ± 24.7** |
| Week 14 | 113.2 ± 37.0 | 153.0 ± 21.9 | 197.7 ± 44.0 | 218.2 ± 24.5* | 179.0 ± 25.0 | 254.0 ± 44.6* |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunn's or Shirley's test.
** $P \leq 0.01$
[a] Data are presented as mean ± standard error.

Kidney weights of all exposed groups of males and 300 ppm or greater females and liver weights of all exposed males and 600 and 1,200 ppm females were significantly increased (Table I3).

Hyaline droplet accumulation occurred in all chamber control and exposed males at 2 and 6 weeks (data not shown) and at 3 months (Table 7); the severities of this lesion in the exposed groups were generally greater than those in the chamber controls and were more pronounced at week 6 and at 3 months than at week 2. Hyaline droplet accumulation is a change commonly observed in the proximal renal tubule of male rats in 3-month studies (Montgomery and Seely, 1990). The less severe hyaline droplet accumulation at 2 weeks (8 weeks of age) likely reflects the relatively low production of α2u-globulin in male rats at this age. Hyaline droplet accumulation did not occur in females. At 6 weeks, the incidences of minimal renal cortical tubule regeneration were increased in all exposed groups, and granular casts occurred in 300 and 600 ppm males (data not shown). At 3 months, the incidences of renal cortical tubule regeneration and granular casts in 150 ppm or greater male rats were significantly greater than those in the chamber controls, and there was a slight increase in the severity of regeneration with increasing exposure concentration.

Hyaline droplet accumulation consisted of numerous variably-sized, round, brightly eosinophilic droplets within the cytoplasm of the proximal renal tubule epithelial cells. At 3 months, some epithelial cells were greatly expanded by large droplets. Hyaline droplet accumulation was observed and graded using the hematoxylin and eosin-stained sections; however, sections stained with the Mallory-Heidenhain protein to enhance visualization of the droplets were evaluated to verify the initial grading. Tubule regeneration consisted of scattered small clusters of smaller than normal proximal tubules lined by small cuboidal basophilic epithelial cells that were

**TABLE 7**
**Incidences of Nonneoplastic Lesions of the Kidney in Male Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| Number Examined Microscopically | 10 | 10 | 10 | 10 | 10 | 10 |
| Renal Tubule, Regeneration[a] | 6 (1.0)[b] | 9 (1.0) | 10* (1.0) | 10* (1.3) | 10* (1.5) | 10* (1.6) |
| Medulla, Casts Granular | 0 | 0 | 8** (1.0) | 7** (1.1) | 6** (1.0) | 4* (1.0) |
| Renal Tubule, Accumulation, Hyaline Droplet | 10 (1.2) | 10 (1.0) | 10 (2.0) | 10 (2.0) | 10 (2.0) | 10 (2.4) |

* Significantly different ($P \leq 0.05$) from the chamber control group by the Fischer exact test
** $P \leq 0.01$
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

sometimes crowded and had occasional mitotic figures. Regeneration of the renal tubule epithelium is an early component of chronic progressive nephropathy, a common spontaneous syndrome in F344/N rats, particularly males. Granular casts were a minimal change that occurred within the outer stripe of the outer medulla; scattered tubules were filled and dilated two to three times normal size by granular eosinophilic material assumed to be $\alpha$2u-globulin protein and cellular debris (degenerate, sloughed proximal tubule epithelial cells). Granular casts are indicative of cell death and degeneration of renal proximal tubule epithelium.

The incidences of minimal hyaline degeneration of the olfactory epithelium were significantly increased in 600 and 1,200 ppm males and females (males: chamber control, 0/10; 75 ppm, 0/10; 150 ppm, 0/10; 300 ppm, 0/10; 600 ppm, 4/10; 1,200 ppm, 8/10; females: 0/10, 0/10, 0/10, 1/10, 7/10, 10/10). This lesion was most evident in the dorsal meatus of Level II and in the more distal Level III section of the nose and consisted of single, large, round to oval, lightly eosinophilic droplets that expanded the apical cytoplasm of the sustentacular cells.

*Exposure Concentration Selection Rationale*: There were no treatment-related mortality, reductions in body weight gain, or clinical findings in male or female F344/N rats exposed to 0, 75, 150, 300, 600, or 1,200 ppm propylene glycol mono-*t*-butyl ether. The kidney and liver were considered target organs in the 3-month study. Kidney weights were significantly increased in all exposed groups of males and in 300 ppm or greater females. Increases in the incidences of renal tubule hyaline droplet accumulation, cortical regeneration, and medullary granular casts, as well as general concentration-related increases in cell proliferation and $\alpha$2u-globulin, were observed in exposed males. Urinalysis data were consistent with the development of nephropathy in male rats. Liver weights were significantly increased in male and female rats at 600 and 1,200 ppm. These renal and liver effects; however, were not considered sufficiently severe to cause excessive toxicity or to affect survival in a 2-year study. Therefore, 1,200 ppm was considered acceptable as the highest exposure concentration for the 2-year study. Lower concentrations were based on blood clearance data from the single administration toxicokinetic study conducted with 75, 300, and 1,200 ppm (Appendix N). In male and female rats, blood clearance rates of propylene glycol mono-*t*-butyl ether at 1,200 ppm and probably at 300 ppm were not in the linear range (Appendix N). It was not clear whether 75 ppm was within the linear range since a lower concentration was not tested. Therefore, it was decided that one concentration (1,200 ppm) well above the linear range, one concentration (300 ppm) at or near the linear portion, and one concentration (75 ppm) most likely in the linear range would be used.

## 2-YEAR STUDY

### *Survival*

Estimates of 2-year survival probabilities for male and female rats are shown in Table 8 and in the Kaplan-Meier survival curves (Figure 1). Survival of males in the 300 ppm group was less than that of the chamber control group; survival of all exposed groups of females was similar to that of the chamber control group.

### *Body Weights and Clinical Findings*

Mean body weights of 1,200 ppm males and females were less than those of the chamber controls during the second year of the study (Figure 2; Tables 9 and 10). Pale corneal foci were noted in the eyes of females exposed to 1,200 ppm.

**TABLE 8**
**Survival of Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Male** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Moribund | 20 | 15 | 26 | 22 |
| Natural deaths | 3 | 6 | 8 | 6 |
| Animals surviving to study termination | 27 | 29 | 16 | 22 |
| Percent probability of survival at end of study[a] | 54 | 58 | 32 | 44 |
| Mean survival (days)[b] | 676 | 689 | 639 | 671 |
| Survival analysis[c] | P=0.358 | P=0.727N | P=0.031 | P=0.435 |
| **Female** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Moribund | 14 | 12 | 20 | 11 |
| Natural deaths | 3 | 4 | 2 | 3 |
| Animals surviving to study termination | 33 | 34 | 28 | 36 |
| Percent probability of survival at end of study | 66 | 68 | 56 | 72 |
| Mean survival (days) | 675 | 709 | 681 | 698 |
| Survival analysis | P=0.515N | P=0.801N | P=0.419 | P=0.602N |

[a] Kaplan-Meier determinations
[b] Mean of all deaths (uncensored, censored, and terminal sacrifice).
[c] The result of the life table trend test (Tarone, 1975) is in the chamber control column, and the results of the life table pairwise comparisons (Cox, 1972) with the chamber controls are in the exposed group columns. A negative trend or lower mortality in an exposure group is indicated by **N**.

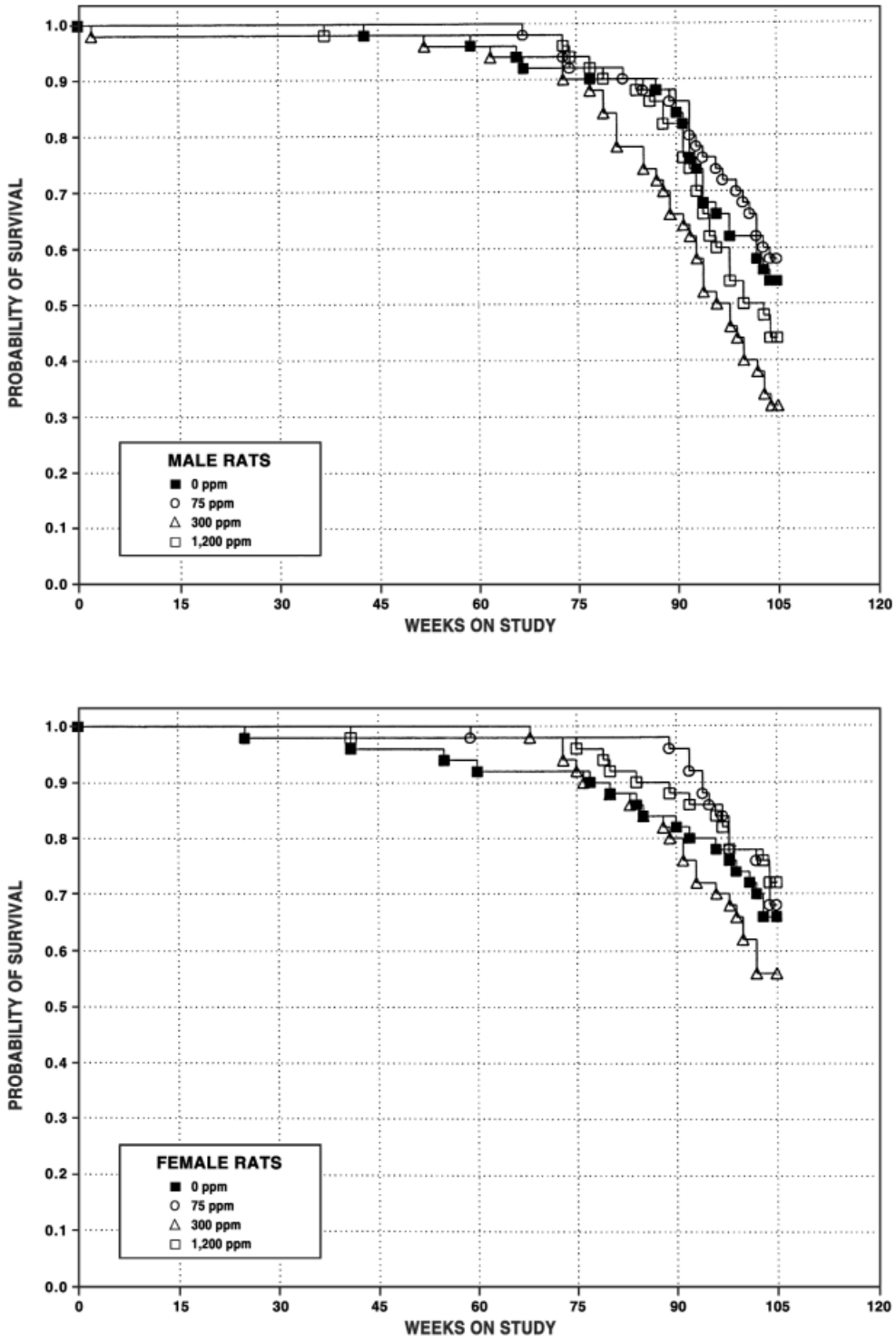



**FIGURE 1**
**Kaplan-Meier Survival Curves for Male and Female Rats**
**Exposed to Propylene Glycol Mono-*t*-butyl Ether by Inhalation for 2 Years**

**TABLE 9**
**Mean Body Weights and Survival of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Weeks on Study | Chamber Control | | 75 ppm | | | 300 ppm | | | 1,200 ppm | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Av. Wt. (g) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors |
| 1 | 98 | 50 | 99 | 101 | 50 | 96 | 98 | 50 | 97 | 99 | 50 |
| 5 | 229 | 50 | 235 | 103 | 50 | 232 | 101 | 49 | 225 | 98 | 50 |
| 9 | 299 | 50 | 305 | 102 | 50 | 301 | 101 | 49 | 294 | 98 | 50 |
| 13 | 342 | 50 | 344 | 101 | 50 | 344 | 101 | 49 | 341 | 100 | 50 |
| 17 | 378 | 50 | 381 | 101 | 50 | 377 | 100 | 49 | 373 | 99 | 50 |
| 21 | 400 | 50 | 402 | 101 | 50 | 399 | 100 | 49 | 392 | 98 | 50 |
| 25 | 424 | 50 | 425 | 100 | 50 | 420 | 99 | 49 | 413 | 98 | 50 |
| 29 | 445 | 50 | 447 | 100 | 50 | 439 | 99 | 49 | 432 | 97 | 50 |
| 33 | 461 | 50 | 464 | 101 | 50 | 453 | 98 | 49 | 445 | 97 | 50 |
| 37 | 472 | 50 | 475 | 101 | 50 | 464 | 98 | 49 | 454 | 96 | 49 |
| 41 | 478 | 50 | 483 | 101 | 50 | 470 | 98 | 49 | 463 | 97 | 49 |
| 45 | 489 | 49 | 495 | 101 | 50 | 481 | 98 | 49 | 475 | 97 | 49 |
| 49 | 500 | 49 | 502 | 100 | 50 | 490 | 98 | 49 | 482 | 96 | 49 |
| 53 | 505 | 49 | 505 | 100 | 50 | 497 | 99 | 48 | 487 | 97 | 49 |
| 57 | 504 | 49 | 505 | 100 | 50 | 499 | 99 | 48 | 491 | 97 | 49 |
| 61 | 514 | 48 | 513 | 100 | 50 | 504 | 98 | 48 | 494 | 96 | 49 |
| 65 | 518 | 48 | 519 | 100 | 50 | 511 | 99 | 47 | 499 | 96 | 49 |
| 69 | 528 | 46 | 528 | 100 | 49 | 517 | 98 | 47 | 505 | 96 | 49 |
| 73 | 535 | 46 | 530 | 99 | 49 | 516 | 97 | 47 | 505 | 94 | 49 |
| 77 | 540 | 46 | 536 | 99 | 46 | 525 | 97 | 45 | 507 | 94 | 47 |
| 81 | 540 | 45 | 538 | 100 | 46 | 523 | 97 | 41 | 510 | 95 | 45 |
| 85 | 537 | 45 | 540 | 100 | 44 | 521 | 97 | 38 | 500 | 93 | 44 |
| 89 | 529 | 44 | 534 | 101 | 44 | 525 | 99 | 34 | 500 | 94 | 41 |
| 92 | 532 | 40 | 530 | 100 | 43 | 522 | 98 | 32 | 496 | 93 | 37 |
| 94 | 536 | 35 | 537 | 100 | 39 | 525 | 98 | 28 | 494 | 92 | 34 |
| 96 | 538 | 33 | 537 | 100 | 37 | 521 | 97 | 26 | 497 | 93 | 30 |
| 98 | 537 | 32 | 537 | 100 | 36 | 519 | 97 | 24 | 494 | 92 | 28 |
| 100 | 536 | 31 | 537 | 100 | 34 | 522 | 97 | 20 | 494 | 92 | 25 |
| 102 | 521 | 31 | 529 | 102 | 32 | 513 | 99 | 19 | 483 | 93 | 25 |
| 104 | 513 | 27 | 519 | 101 | 29 | 514 | 100 | 16 | 481 | 94 | 22 |
| **Mean for weeks** | | | | | | | | | | | |
| 1-13 | 242 | | 246 | 102 | | 243 | 100 | | 239 | 99 | |
| 14-52 | 450 | | 453 | 101 | | 444 | 99 | | 437 | 97 | |
| 53-104 | 527 | | 528 | 100 | | 516 | 98 | | 496 | 94 | |

**TABLE 10**
**Mean Body Weights and Survival of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Weeks on Study | Chamber Control | | 75 ppm | | | 300 ppm | | | 1,200 ppm | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Av. Wt. (g) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors |
| 1 | 88 | 50 | 88 | 100 | 50 | 89 | 100 | 50 | 88 | 99 | 50 |
| 5 | 152 | 50 | 153 | 101 | 50 | 153 | 101 | 50 | 153 | 101 | 50 |
| 9 | 178 | 50 | 176 | 99 | 50 | 176 | 99 | 50 | 177 | 100 | 50 |
| 13 | 194 | 50 | 193 | 99 | 50 | 193 | 99 | 50 | 196 | 101 | 50 |
| 17 | 208 | 50 | 206 | 99 | 50 | 204 | 99 | 50 | 205 | 99 | 50 |
| 21 | 215 | 50 | 216 | 101 | 50 | 215 | 100 | 50 | 212 | 99 | 50 |
| 25 | 224 | 49 | 226 | 101 | 50 | 221 | 99 | 50 | 218 | 98 | 50 |
| 29 | 233 | 49 | 235 | 101 | 50 | 229 | 98 | 50 | 227 | 98 | 50 |
| 33 | 242 | 49 | 244 | 101 | 50 | 236 | 97 | 50 | 233 | 96 | 50 |
| 37 | 250 | 49 | 252 | 101 | 50 | 244 | 98 | 50 | 240 | 96 | 50 |
| 41 | 256 | 48 | 261 | 102 | 50 | 253 | 99 | 50 | 249 | 97 | 49 |
| 45 | 267 | 48 | 273 | 102 | 50 | 262 | 98 | 50 | 258 | 97 | 49 |
| 49 | 279 | 48 | 286 | 103 | 50 | 277 | 99 | 50 | 269 | 97 | 49 |
| 53 | 289 | 48 | 296 | 103 | 50 | 287 | 99 | 50 | 278 | 96 | 49 |
| 57 | 295 | 47 | 303 | 103 | 50 | 295 | 100 | 50 | 284 | 96 | 49 |
| 61 | 305 | 46 | 313 | 103 | 49 | 305 | 100 | 50 | 292 | 96 | 49 |
| 65 | 314 | 46 | 322 | 103 | 49 | 312 | 100 | 50 | 298 | 95 | 49 |
| 69 | 322 | 46 | 330 | 103 | 49 | 319 | 99 | 49 | 304 | 94 | 49 |
| 73 | 331 | 46 | 340 | 103 | 49 | 324 | 98 | 48 | 312 | 94 | 49 |
| 77 | 335 | 46 | 345 | 103 | 49 | 336 | 100 | 45 | 318 | 95 | 48 |
| 81 | 340 | 44 | 348 | 102 | 49 | 338 | 100 | 44 | 321 | 94 | 46 |
| 85 | 343 | 43 | 354 | 103 | 49 | 343 | 100 | 43 | 326 | 95 | 45 |
| 89 | 351 | 42 | 357 | 102 | 49 | 344 | 98 | 40 | 330 | 94 | 44 |
| 92 | 358 | 41 | 362 | 101 | 48 | 344 | 96 | 38 | 333 | 93 | 44 |
| 94 | 362 | 40 | 359 | 99 | 46 | 350 | 97 | 36 | 331 | 91 | 43 |
| 96 | 366 | 40 | 365 | 100 | 43 | 352 | 96 | 36 | 333 | 91 | 42 |
| 98 | 363 | 39 | 362 | 100 | 40 | 350 | 96 | 34 | 335 | 92 | 41 |
| 100 | 366 | 37 | 362 | 99 | 39 | 350 | 96 | 33 | 337 | 92 | 39 |
| 102 | 363 | 35 | 362 | 100 | 38 | 349 | 96 | 30 | 335 | 93 | 39 |
| 104 | 367 | 33 | 356 | 97 | 35 | 349 | 95 | 28 | 330 | 90 | 37 |
| **Mean for weeks** | | | | | | | | | | | |
| 1-13 | 153 | | 153 | 100 | | 153 | 100 | | 154 | 101 | |
| 14-52 | 242 | | 244 | 101 | | 238 | 98 | | 235 | 97 | |
| 53-104 | 339 | | 343 | 101 | | 332 | 98 | | 317 | 94 | |

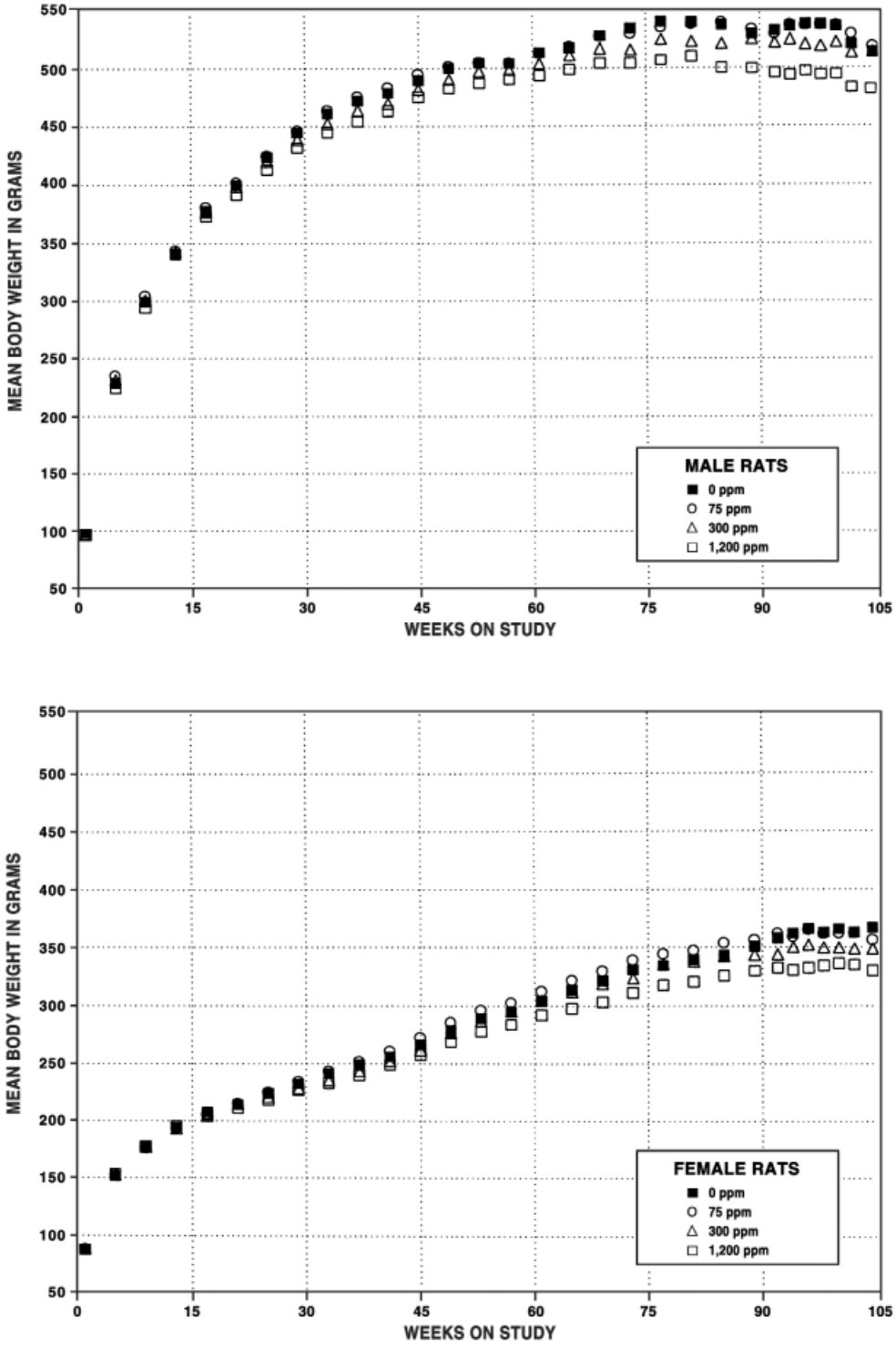



**FIGURE 2**
**Growth Curves for Male and Female Rats**
**Exposed to Propylene Glycol Mono-*t*-butyl Ether by Inhalation for 2 Years**

## *Pathology and Statistical Analyses*

This section describes the statistically significant or biologically noteworthy changes in the incidences of neoplasms and/or nonneoplastic lesions of the kidney, urinary bladder, liver, nose, and eye. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group, and historical incidences for the neoplasms mentioned in this section are presented in Appendix A for male rats and Appendix B for female rats.

*Kidney*: In the standard evaluation of the kidney, the incidences of renal tubule adenoma and adenoma or carcinoma (combined) in 300 and 1,200 ppm males were increased; however the increases were marginal and not statistically significant. Historically, no more than a single kidney neoplasm has been observed in chamber controls compared to two to three in each of the exposed groups (Tables 11, A3, and A4a). The incidences of renal tubule hyperplasia in males increased with increasing exposure concentration, and the incidences in the 300 and 1,200 ppm groups were significantly increased (Tables 11 and A5). A single 1,200 ppm male had a stromal nephroma and a single 1,200 ppm female had a renal tubule adenoma.

Renal tubule hyperplasia consisted of single or multiple expanded cortical tubules composed of increased numbers of tubular epithelial cells arranged in multiple layers that partially or completely filled the tubule. Renal tubule adenomas were discrete proliferative lesions that were larger than focal hyperplasias (generally greater than the combined diameter of 5 normal sized renal tubules). Adenomas tended to have a more complex structure than hyperplasias composed of closely packed tubules and nests of pale basophilic cells and lesser numbers of cells with clear cytoplasm. The carcinoma was an expansive and invasive mass composed of large basophilic to amphiphilic cells that formed large multilayered tubular structures, solid nests, and sheets.

In the kidney, renal tubule hyperplasia, adenoma, and carcinoma are thought to constitute a morphologic and biologic continuum in the progression of proliferative lesions in the renal tubule epithelium. A single section of each kidney was examined microscopically during the initial evaluation. Because the incidences of renal tubule neoplasms in the 300 and 1,200 ppm male rats suggested the possibility of a treatment-related carcinogenic effect, an extended evaluation of the kidney was performed to explore this possibility. The residual formalin-fixed wet kidney tissues (male only) were step-sectioned to obtain an additional 3 to 4 sections per kidney and examined microscopically. In the extended evaluation, additional renal tubule adenomas were identified in each exposed group (Table 11). Additional renal tubule hyperplasias were also identified in the chamber control and all exposed groups. No additional renal tubule carcinomas were identified. In the combined analyses, the incidences of renal tubule adenoma and adenoma or carcinoma (combined) in the exposed groups were marginally increased, however the increases were not statistically significant (Table 11).

Renal tubule oncocytic hyperplasia was identified in two 300 ppm males and a single 1,200 ppm male; however, a low incidence of this lesion is not uncommon in aged males and is not considered to be chemical related. Age-related chronic nephropathy occurred in all exposed males and in most exposed females and chamber control males and females. The severities of nephropathy increased with increasing exposure concentration in males and females, and were significantly increased in all exposed groups of males and in 1,200 ppm females (Tables 11, A5, and B5). Nephrotoxic chemicals frequently exacerbate the severity of nephropathy in both sexes of F344/N rats. Nephropathy consisted of a spectrum of lesions of varying severity that included dilated renal tubules that were empty or contained hyaline (proteinaceous) casts, multifocal tubular epithelial regeneration, glomerular atrophy, thickening of the tubular and glomerular basement membrane, interstitial fibrosis, and mononuclear inflammatory cell infiltrates within the interstitium.

Incidences of mild to moderate renal tubule hyaline droplet accumulation in male rats increased with increasing exposure concentration, and the increases were significant in the 300 and 1,200 ppm groups (Tables 11, A5, and B5). The hyaline droplets were similar to those typically induced in the early stages of $\alpha$2u-globulin nephropathy. In male F344/N rats, synthesis of $\alpha$2u-globulin declines progressively after 12 to 15 months of age, and exposure-related increases should not occur at the end of a 2-year study. In this study, hyaline droplet accumulation was most frequent in male rats that died or were sacrificed relatively early during the course of the study.

There were significant exposure-related increases in the incidences of mineralization in the renal papilla of exposed males (Tables 11 and A5). Mineralization was

**TABLE 11**
**Incidences of Neoplasms and Nonneoplastic Lesions of the Kidney in Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Male** | | | | |
| Number Examined Microscopically | 50 | 50 | 49 | 50 |
| **Single Sections (Standard Evaluation)** | | | | |
| Renal Tubule, Hyperplasia[a] | 0 | 3 (2.3)[b] | 7** (2.7) | 19** (2.4) |
| Nephropathy, Chronic | 46 (1.9) | 50 (2.3)▲ | 49 (2.9)▲ | 50 (3.5)▲ |
| Renal Tubule, Accumulation, Hyaline Droplet | 1 (3.0) | 2 (3.0) | 9** (3.1) | 17** (2.6) |
| Papilla, Mineralization | 0 | 8** (1.0) | 28** (1.6) | 41** (1.0) |
| Pelvis, Transitional Epithelium, Hyperplasia | 2 (1.0) | 1 (1.0) | 6 (1.3) | 15** (1.4) |
| Renal Tubule, Adenoma (includes multiple)[c] | | | | |
| Overall rate[d] | 1/50 (2%) | 1/50 (2%) | 3/49 (6%) | 2/50 (4%) |
| Adjusted rate[e] | 2.4% | 2.3% | 8.1% | 4.9% |
| Terminal rate[f] | 0/27 (0%) | 1/29 (3%) | 1/16 (6%) | 1/22 (5%) |
| First incidence (days) | 655 | 729 (T) | 681 | 683 |
| Poly-3 test[g] | P=0.423 | P=0.754N | P=0.260 | P=0.490 |
| Renal Tubule, Carcinoma | 0 | 0 | 0 | 1 |
| Renal Tubule, Adenoma or Carcinoma[h] | | | | |
| Overall rate | 1/50 (2%) | 1/50 (2%) | 3/49 (6%) | 3/50 (6%) |
| Adjusted rate | 2.4% | 2.3% | 8.1% | 7.3% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 1/16 (6%) | 2/22 (9%) |
| First incidence (days) | 655 | 729 (T) | 681 | 683 |
| Poly-3 test | P=0.214 | P=0.754N | P=0.260 | P=0.295 |
| Stromal Nephroma | 0 | 0 | 0 | 1 |
| **Step Sections (Extended Evaluation)** | | | | |
| Renal Tubule, Hyperplasia | 10 | 20* | 20** | 25** |
| Renal Tubule, Adenoma (includes multiple) | | | | |
| Overall rate | 0/50 (0%) | 1/50 (2%) | 3/49 (6%) | 2/50 (4%) |
| Adjusted rate | 0.0% | 2.3% | 8.0% | 4.9% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 0/16 (0%) | 1/22 (5%) |
| First incidence (days) | —[i] | 729 (T) | 509 | 725 |
| Poly-3 test | P=0.293 | P=0.508 | P=0.100 | P=0.231 |
| **Single Sections and Step Sections (Combined)** | | | | |
| Renal Tubule, Hyperplasia | 10 | 20* | 23** | 30** |
| Renal Tubule, Adenoma (includes multiple) | | | | |
| Overall rate | 1/50 (2%) | 2/50 (4%) | 5/49 (10%) | 4/50 (8%) |
| Adjusted rate | 2.4% | 4.6% | 13.2% | 9.8% |
| Terminal rate | 0/27 (0%) | 2/29(7%) | 1/16 (6%) | 2/22 (9%) |
| First incidence (days) | 655 | 729 (T) | 509 | 683 |
| Poly-3 test | P=0.192 | P=0.511 | P=0.077 | P=0.169 |
| Renal Tubule, Carcinoma | 0 | 0 | 0 | 1 |

**TABLE 11**
**Incidences of Neoplasms and Nonneoplastic Lesions of the Kidney in Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Male** (continued) | | | | |
| Renal Tubule, Adenoma or Carcinoma | | | | |
| Overall rate | 1/50 (2%) | 2/50 (4%) | 5/49 (10%) | 5/50 (10%) |
| Adjusted rate | 2.4% | 4.6% | 13.2% | 12.2% |
| Terminal rate | 0/27 (0%) | 2/29 (7%) | 1/16 (6%) | 3/22 (14%) |
| First incidence (days) | 655 | 729 (T) | 509 | 683 |
| Poly-3 test | P=0.091 | P=0.511 | P=0.077 | P=0.094 |
| **Female** | | | | |
| Number Examined Microscopically | 49 | 50 | 50 | 50 |
| Nephropathy, Chronic | 45 (1.5) | 45 (1.6) | 45 (1.7) | 49 (2.1)▲ |
| Renal Tubule, Adenoma | 0 | 0 | 0 | 1 |

* Significantly different (P≤0.05) from the chamber control group by the Poly-3 test
** P≤0.01
▲ Significantly different (P≤0.01) from the chamber control group by the Mann-Whitney U test
(T) Terminal sacrifice
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked
[c] Historical incidence for 2-year inhalation studies with chamber controls given NTP-2000 diet (mean ± standard deviation): 3/299 (1.0% ± 1.1%), range 0%-2%
[d] Number of animals with neoplasm per number of animals with kidney examined microscopically
[e] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[f] Observed incidence at terminal kill
[g] Beneath the chamber control incidence is the P value associated with the trend test. Beneath the exposed group incidence are the P values corresponding to pairwise comparisons between the chamber controls and that exposed group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice. A lower incidence in an exposed group is indicated by **N**.
[h] Historical incidence 4/299 (1.3% ± 1.0%), range 0%-2%
[i] Not applicable; no neoplasms in animal group

a generally minimal lesion that appeared as small multifocally scattered deposits of mineral within the tubules of the papilla. In some males, the mineral deposits occurred as linear profiles, suggestive of α2u-globulin nephropathy. The incidence of minimal transitional epithelial hyperplasia was significantly increased in 1,200 ppm males and was characterized by increased thickness of the transitional epithelium lining the renal pelvis. Transitional epithelial hyperplasia was considered a component of the exacerbated nephropathy.

*Urinary bladder*: A transitional epithelial carcinoma occurred in the urinary bladder of a 1,200 ppm male, and a transitional epithelial papilloma occurred in the urinary bladder of a 1,200 ppm female (Tables A1 and B1). Although no transitional epithelial carcinomas have been previously observed in 297 male rat chamber controls and only two transitional epithelial papillomas have been observed in 295 female rat chamber controls (Tables A4b and B4), the two urinary bladder neoplasms were not considered related to exposure to propylene glycol mono-*t*-butyl ether. The incidence of transitional epithelial hyperplasia was increased in the 1,200 ppm males (chamber control, 3/50; 75 ppm, 1/49; 300 ppm, 3/49; 1,200 ppm, 6/50; Table A5), however, the increase was not statistically significant.

*Liver*: The incidence of hepatocellular adenoma occurred with a positive trend in male rats, and the incidence in the 1,200 ppm group exceeded the historical range in chamber controls (Tables 12, A3, and A4c). A single incidence of hepatic cholangiocarcinoma occurred in a 1,200 ppm male. Hepatic cholangiocarcinoma has not occurred in 299 male or 297 female historical chamber controls. Hepatocellular adenoma occurred in one chamber control female and two 1,200 ppm females; the marginal increase in females was not significant and not considered related to exposure. The incidences of basophilic foci in all exposed groups of males and the incidence of clear cell foci in 1,200 ppm females were significantly increased (Tables 12, A5, and B5).

*Nose*: The incidences and severities of hyaline degeneration of the olfactory epithelium in males and females increased with increasing exposure concentration and the incidences in all exposed groups were significantly increased (Tables 13, A5, and B5). The incidences of dilatation of the submucosal glands were significantly increased in males exposed to 300 or 1,200 ppm. The incidences of goblet cell hyperplasia in 1,200 ppm males and females were greater than those in the chamber

**TABLE 12**
**Incidences of Neoplasms and Nonneoplastic Lesions of the Liver in Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Male** | | | | |
| Number Examined Microscopically | 50 | 50 | 49 | 50 |
| Basophilic Focus[a] | 6 | 18** | 15** | 17** |
| Clear Cell Focus | 8 | 11 | 11 | 9 |
| Eosinophilic Focus | 0 | 1 | 1 | 2 |
| Hepatocellular Adenoma[b] | | | | |
| Overall rate[c] | 3/50 (6%) | 0/50 (0%) | 2/49 (4%) | 6/50 (12%) |
| Adjusted rate[d] | 7.2% | 0.0% | 5.4% | 14.3% |
| Terminal rate[e] | 2/27 (7%) | 0/29 (0%) | 1/16 (6%) | 2/22 (9%) |
| First incidence (days) | 712 | —[g] | 684 | 537 |
| Poly-3 test[f] | P=0.022 | P=0.112N | P=0.556N | P=0.241 |
| Cholangiocarcinoma | 0 | 0 | 0 | 1 |
| **Female** | | | | |
| Number Examined Microscopically | 49 | 50 | 50 | 50 |
| Basophilic Focus | 39 | 45 | 43 | 40 |
| Clear Cell Focus | 12 | 13 | 11 | 27** |
| Eosinophilic Focus | 1 | 0 | 0 | 1 |
| Hepatocellular Adenoma | 1 | 0 | 0 | 2 |

** Significantly different (P≤0.01) from the chamber control group by the Poly-3 test
[a] Number of animals with lesion
[b] Historical incidence for 2-year inhalation studies with chamber controls given NTP-2000 diet (mean ± standard deviation): 4/299 (1.3% ± 2.4%), range 0%-6%
[c] Number of animals with neoplasm per number of animals with liver examined microscopically
[d] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[e] Observed incidence at terminal kill
[f] Beneath the chamber control incidence is the P value associated with the trend test. Beneath the exposed group incidence are the P values corresponding to pairwise comparisons between the chamber controls and that exposed group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice. A lower incidence in an exposed group is indicated by **N**.
[g] Not applicable; no neoplasms in animal group

**TABLE 13**
**Incidences of Nonneoplastic Lesions of the Nose in Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Male** | | | | |
| Number Examined Microscopically | 50 | 49 | 49 | 50 |
| Olfactory Epithelium, Degeneration, Hyaline[a] | 0 | 25** (1.8)[b] | 45** (3.0) | 50** (3.6) |
| Goblet Cell, Hyperplasia | 1 (1.0) | 1 (1.0) | 2 (2.5) | 15** (1.9) |
| Glands, Dilatation | 1 (2.0) | 2 (1.0) | 7* (1.9) | 15** (1.8) |
| **Female** | | | | |
| Number Examined Microscopically | 49 | 49 | 50 | 50 |
| Olfactory Epithelium, Degeneration, Hyaline | 10 (1.9) | 22** (2.0) | 48** (2.3) | 50** (3.6) |
| Goblet Cell, Hyperplasia | 0 | 0 | 0 | 3 (1.7) |

* Significantly different ($P \leq 0.05$) from the chamber control group by the Poly-3 test
** $P \leq 0.01$
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

controls, and the incidence in 1,200 ppm males was significantly increased. Hyaline degeneration primarily affected the olfactory epithelium lining the dorsal meatus extending ventrally along the dorsal portion of the nasal septum (in the standard Level II histological section of the nose) and the dorsal aspects of the ethmoid turbinates. In affected sites, large eosinophilic globules filled the cytoplasm of the olfactory epithelial cells and that of the adjacent submucosal glands. Submucosal gland dilatation occurred adjacent to the epithelium affected by hyaline degeneration. Goblet cell hyperplasia occurred along the nasal septum (in the standard Level II histological section of the nose); the apical cytoplasm of the affected respiratory epithelium was expanded by large clear vacuoles. Hyaline degeneration and goblet cell hyperplasia are commonly observed in aging rats. In chronic inhalation studies, the incidence and severity may be exacerbated often in an exposure dependent manner. These changes are considered nonspecific adaptive or protective responses to prolonged inhalation of irritants.

*Eye*: Gross observations noted at necropsy included opacity or pale foci in the eyes of females exposed to 1,200 ppm. The incidence of corneal mineralization in 1,200 ppm females was significantly increased (chamber control, 0/49; 75 ppm, 0/50; 300 ppm, 0/50; 1,200 ppm, 10/50; Table B5); however, there was poor correlation between corneal mineralization and the corneal opacity observed at necropsy.

## *Biomarkers of Exposure*

Propylene glycol mono-*t*-butyl ether sulfate and propylene glycol mono-*t*-butyl ether glucuronide excretion data are listed in Table G1. Excretion of the metabolites in urine was not proportional to exposure concentration when expressed as the metabolite to creatinine ratios. Dose proportionality was determined by normalizing the metabolite to creatinine ratios to exposure concentrations and testing for significant differences between exposed groups. Propylene glycol mono-*t*-butyl ether glucuronide is the more useful biomarker since it represents 90% or more of the total of the two metabolites. In 1,200 ppm males and females at all time points, the normalized propylene glycol mono-*t*-butyl ether glucuronide/creatinine ratios were generally significantly less than those in the groups exposed to 75 or 300 ppm.

## MICE

### 2-WEEK STUDY

All mice survived to the end of the study (Table 14). Final mean body weights and body weight gains of 1,200 ppm female mice were greater than those of the chamber controls. There were no clinical findings related to propylene glycol mono-*t*-butyl ether exposure.

Liver weights of 600 and 1,200 ppm males and 300 ppm or greater females were significantly greater than those of the chamber controls (Table I4). No exposure-related lesions occurred in male or female mice.

*Exposure Concentration Selection Rationale*: Because there were generally no effects of propylene glycol mono-*t*-butyl ether on survival or body weights of male or female B6C3F$_1$ mice in the 2-week study and because there were no other exposure-related lesions in addition to increases in liver weights, exposure concentrations selected for the 3-month inhalation study were 0, 75, 150, 300, 600, and 1,200 ppm. The highest exposure concentration was maintained for the 3-month study because it was the maximum attainable vapor concentration that could be generated without aerosolization in the exposure chambers.

**TABLE 14**
**Survival and Body Weights of Mice in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Concentration (ppm) | Survival[a] | Mean Body Weight[b] (g) | | | Final Weight Relative to Controls (%) |
|---|---|---|---|---|---|
| | | Initial | Final | Change | |
| **Male** | | | | | |
| 0 | 5/5 | 20.7 ± 0.3 | 26.1 ± 0.5 | 5.4 ± 0.4 | |
| 75 | 5/5 | 20.2 ± 0.6 | 25.6 ± 0.5 | 5.5 ± 0.6 | 98 |
| 150 | 5/5 | 20.6 ± 0.5 | 25.6 ± 0.7 | 5.0 ± 0.6 | 98 |
| 300 | 5/5 | 20.4 ± 0.2 | 26.6 ± 0.6 | 6.2 ± 0.6 | 102 |
| 600 | 5/5 | 20.7 ± 0.1 | 26.1 ± 0.3 | 5.4 ± 0.3 | 100 |
| 1,200 | 5/5 | 20.4 ± 0.5 | 26.6 ± 0.4 | 6.2 ± 0.8 | 102 |
| **Female** | | | | | |
| 0 | 5/5 | 17.6 ± 0.4 | 21.9 ± 0.3 | 4.4 ± 0.2 | |
| 75 | 5/5 | 17.9 ± 0.3 | 22.0 ± 0.4 | 4.1 ± 0.3 | 100 |
| 150 | 5/5 | 18.5 ± 0.3 | 22.4 ± 0.2 | 3.9 ± 0.4 | 102 |
| 300 | 5/5 | 17.4 ± 0.4 | 21.9 ± 0.4 | 4.5 ± 0.3 | 100 |
| 600 | 5/5 | 18.0 ± 0.3 | 22.0 ± 0.2 | 3.9 ± 0.4 | 100 |
| 1,200 | 5/5 | 17.8 ± 0.5 | 23.4 ± 0.4* | 5.6 ± 0.3* | 107 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunnett's test.
[a] Number of animals surviving at 2 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error.

## 3-Month Study

All mice survived to the end of the study (Table 15). Final mean body weights of 300 and 1,200 ppm males were significantly less than that of the chamber controls, as were mean body weight gains of 150, 300, and 1,200 ppm males. Exposed groups of females weighed slightly more than the chamber controls, but the differences were not significant.

The hematology data for mice are shown in Table F2. In all exposed groups of males, a minimal increase in the erythron occurred at 3 months, evidenced by small increases in hematocrit values, hemoglobin concentrations and erythrocyte counts. Females were unaffected by exposure. The erythron changes in the males were generally statistically significant but not considered to be clinically significant.

**Table 15**
**Survival and Body Weights of Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Concentration (ppm) | Survival[a] | Mean Body Weight[b] (g) | | | Final Weight Relative to Controls (%) |
|---|---|---|---|---|---|
| | | Initial | Final | Change | |
| **Male** | | | | | |
| 0 | 10/10 | 22.0 ± 0.3 | 36.2 ± 0.5 | 14.2 ± 0.5 | |
| 75 | 10/10 | 21.7 ± 0.5 | 35.0 ± 1.0 | 13.2 ± 0.8 | 97 |
| 150 | 10/10 | 21.9 ± 0.3 | 33.6 ± 0.9 | 11.7 ± 0.9* | 93 |
| 300 | 10/10 | 21.6 ± 0.4 | 32.5 ± 0.9* | 10.9 ± 0.6** | 90 |
| 600 | 10/10 | 21.9 ± 0.3 | 34.8 ± 0.7 | 12.9 ± 0.6 | 96 |
| 1,200 | 10/10 | 21.4 ± 0.5 | 33.0 ± 0.7* | 11.6 ± 0.4* | 91 |
| **Female** | | | | | |
| 0 | 10/10 | 18.6 ± 0.6 | 27.6 ± 0.6 | 9.0 ± 0.6 | |
| 75 | 10/10 | 19.4 ± 0.3 | 29.5 ± 0.8 | 10.1 ± 0.6 | 107 |
| 150 | 10/10 | 19.5 ± 0.3 | 28.4 ± 0.4 | 8.9 ± 0.5 | 103 |
| 300 | 10/10 | 19.3 ± 0.4 | 29.9 ± 0.8 | 10.6 ± 0.6 | 108 |
| 600 | 10/10 | 19.6 ± 0.2 | 30.0 ± 0.7 | 10.5 ± 0.7 | 109 |
| 1,200 | 10/10 | 19.3 ± 0.3 | 28.5 ± 0.7 | 9.2 ± 0.6 | 103 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunnett's test
** $P \leq 0.01$
[a] Number of animals surviving at 3 months/number initially in group
[b] Weights and weight changes are given as mean ± standard error.

Liver weights of 600 and 1,200 ppm males and females were significantly greater than those of the chamber controls (Table I5). The estrous cycle length of 1,200 ppm females was longer than that of the chamber controls (Table J4).

The incidences of minimal to mild centrilobular hypertrophy of the liver were significantly increased in 600 and 1,200 ppm males and in 1,200 ppm females (Table 16). Centrilobular hepatocytes were slightly enlarged and had increased amounts of finely granular lightly eosinophilic cytoplasm; the affected hepatocytes also appeared to contain less glycogen, as evidenced by being less vacuolated than surrounding unaffected hepatocytes and hepatocytes in the chamber controls.

The incidence of minimal squamous metaplasia of the respiratory epithelium of the nose in 1,200 ppm males was significantly increased; this lesion also occurred in one 75 ppm and one 1,200 ppm female (Table 16). Metaplasia involved the dorsal aspects and tips of the maxilloturbinates, the tips and lateral aspects of the nasoturbinates and the lateral wall of the nasal passages of the Level I histological section of the nose. In affected sites, three or more layers of squamous to low cuboidal, nonciliated epithelial cells replaced the single layer of normally cuboidal to columnar ciliated respiratory epithelium. These lesions are considered to be protective in response to nasal epithelial irritation.

*Exposure Concentration Selection Rationale*: There were no treatment-related mortality, reductions in body weight gain, or clinical findings in $B6C3F_1$ mice exposed to 0, 75, 150, 300, 600, or 1,200 ppm propylene glycol mono-*t*-butyl ether. In male and female mice, liver weights were increased at 600 and 1,200 ppm. Minimal hepatic centrilobular hypertrophy was observed in very few animals exposed to these concentrations. There were no significant treatment-related hematologic

**TABLE 16**
**Incidences of Nonneoplastic Lesions of the Liver and Nose in Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| Number Examined Microscopically | 10 | 10 | 10 | 10 | 10 | 10 |
| **Male** | | | | | | |
| Liver | | | | | | |
| Centrilobular, Hypertrophy[a] | 0 | 0 | 0 | 0 | 4* (1.0)[b] | 10** (1.8) |
| Nose | | | | | | |
| Respiratory Epithelium, Metaplasia, Squamous | 0 | 0 | 0 | 0 | 0 | 6** (1.0) |
| **Female** | | | | | | |
| Liver | | | | | | |
| Centrilobular, Hypertrophy | 0 | 0 | 0 | 0 | 0 | 5* (1.2) |
| Nose | | | | | | |
| Respiratory Epithelium, Metaplasia, Squamous | 0 | 1 (1.0) | 0 | 0 | 0 | 1 (1.0) |

* Significantly different ($P \leq 0.05$) from the chamber control group by the Fischer exact test
** $P \leq 0.01$
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

effects. The liver effects were not considered sufficiently severe to preclude use of the 1,200 ppm exposure concentration in the 2-year study. Lower concentrations were based on blood clearance data from the single administration toxicokinetic studies conducted with 75, 300, and 1,200 ppm propylene glycol mono-*t*-butyl ether (Appendix N). In male and female mice, blood clearance rates of propylene glycol mono-*t*-butyl ether at 1,200 ppm and probably at 300 ppm were not in the linear range. It was not clear whether 75 ppm was within the linear range since a lower concentration was not tested (Appendix N). Therefore, it was decided that one concentration (1,200 ppm) well above the linear range, one concentration (300 ppm) at or near the linear portion, and one concentration (75 ppm) most likely in the linear range would be used.

## 2-YEAR STUDY

### *Survival*

Estimates of 2-year survival probabilities for male and female mice are shown in Table 17 and in the Kaplan-Meier survival curves (Figure 3). Survival of exposed groups of mice was similar to that of the chamber control groups.

### *Body Weights and Clinical Findings*

Mean body weights of male mice were generally similar to those of the chamber controls throughout the study; those of 1,200 ppm females were slightly less at the end of the study (Tables 18 and 19; Figure 4). Clinical findings included pale foci in the eyes in 23 of 50 1,200 ppm females in the last month of the study.

**TABLE 17**
**Survival of Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Male** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Moribund | 4 | 6 | 6 | 8 |
| Natural deaths | 11 | 4 | 4 | 5 |
| Animals surviving to study termination | 35 | 40 | 40 | 37 |
| Percent probability of survival at end of study[a] | 70 | 80 | 80 | 74 |
| Mean survival (days)[b] | 643 | 526 | 576 | 598 |
| Survival analysis[c] | P=0.927 | P=0.430N | P=0.462N | P=0.931N |
| **Female** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Accidental deaths[d] | 0 | 1 | 0 | 1 |
| Moribund | 8 | 10 | 6 | 4 |
| Natural deaths | 3 | 3 | 2 | 6 |
| Animals surviving to study termination | 39 | 36 | 42[e] | 39[e] |
| Percent probability of survival at end of study | 78 | 74 | 84 | 80 |
| Mean survival (days) | 670 | 660 | 663 | 616 |
| Survival analysis | P=0.878N | P=0.749 | P=0.612N | P=1.000N |

[a] Kaplan-Meier determinations
[b] Mean of all deaths (uncensored, censored, and terminal sacrifice)
[c] The result of the life table trend test (Tarone, 1975) is in the chamber control column, and the results of the life table pairwise comparisons (Cox, 1972) with the chamber controls are in the exposed group columns. A negative trend or lower mortality in an exposure group is indicated by **N**.
[d] Censored from survival analyses
[e] Includes one animal that died during the last week of the study

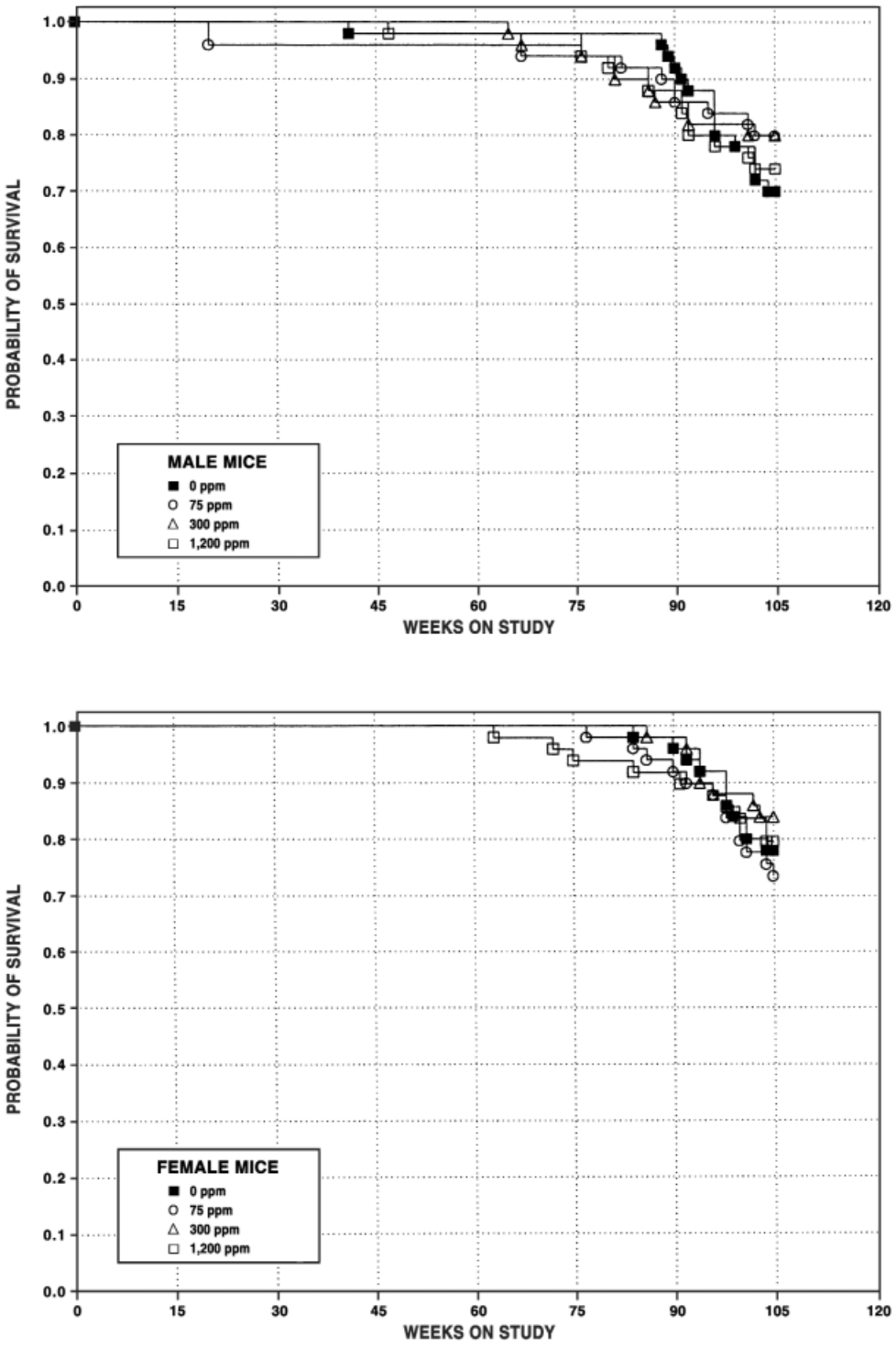



**FIGURE 3**
**Kaplan-Meier Survival Curves for Male and Female Mice**
**Exposed to Propylene Glycol Mono-*t*-butyl Ether by Inhalation for 2 Years**

**TABLE 18**
**Mean Body Weights and Survival of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Weeks on Study | Chamber Control | | 75 ppm | | | 300 ppm | | | 1,200 ppm | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Av. Wt. (g) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors |
| 1 | 21.3 | 50 | 21.5 | 101 | 50 | 21.0 | 99 | 50 | 20.8 | 98 | 50 |
| 5 | 29.2 | 50 | 29.2 | 100 | 50 | 29.0 | 99 | 50 | 29.4 | 101 | 50 |
| 9 | 32.6 | 50 | 32.7 | 100 | 50 | 32.3 | 99 | 50 | 32.3 | 99 | 50 |
| 13 | 35.7 | 50 | 35.5 | 99 | 50 | 35.1 | 98 | 50 | 34.7 | 97 | 50 |
| 17 | 39.4 | 50 | 38.4 | 98 | 50 | 36.8 | 93 | 50 | 37.4 | 95 | 50 |
| 21 | 41.6 | 50 | 41.5 | 100 | 48 | 40.5 | 97 | 50 | 39.5 | 95 | 50 |
| 25 | 43.6 | 50 | 42.8 | 98 | 48 | 42.3 | 97 | 50 | 41.3 | 95 | 50 |
| 29 | 45.5 | 50 | 44.5 | 98 | 48 | 44.6 | 98 | 50 | 43.2 | 95 | 50 |
| 33 | 46.1 | 50 | 46.2 | 100 | 48 | 46.3 | 100 | 50 | 44.8 | 97 | 50 |
| 37 | 49.0 | 50 | 48.0 | 98 | 48 | 48.9 | 100 | 50 | 47.5 | 97 | 50 |
| 41 | 50.1 | 49 | 49.6 | 99 | 48 | 49.9 | 100 | 50 | 49.0 | 98 | 50 |
| 45 | 51.2 | 49 | 50.5 | 99 | 48 | 51.0 | 100 | 50 | 50.6 | 99 | 50 |
| 49 | 51.8 | 49 | 51.5 | 99 | 48 | 51.1 | 99 | 50 | 51.4 | 99 | 49 |
| 53 | 52.9 | 49 | 52.3 | 99 | 48 | 52.1 | 99 | 50 | 52.0 | 98 | 49 |
| 57 | 53.0 | 49 | 53.0 | 100 | 48 | 52.3 | 99 | 50 | 53.5 | 101 | 49 |
| 61 | 53.2 | 49 | 52.6 | 99 | 48 | 52.2 | 98 | 50 | 53.5 | 101 | 49 |
| 65 | 52.5 | 49 | 52.9 | 101 | 48 | 51.5 | 98 | 49 | 53.7 | 102 | 49 |
| 69 | 53.9 | 49 | 53.5 | 99 | 47 | 52.3 | 97 | 48 | 54.4 | 101 | 49 |
| 73 | 54.3 | 49 | 53.7 | 99 | 47 | 52.3 | 96 | 48 | 54.1 | 100 | 49 |
| 77 | 54.3 | 49 | 54.1 | 100 | 47 | 52.6 | 97 | 47 | 54.2 | 100 | 47 |
| 81 | 54.2 | 49 | 53.4 | 99 | 47 | 52.0 | 96 | 46 | 53.6 | 99 | 46 |
| 85 | 53.9 | 49 | 53.0 | 98 | 46 | 51.7 | 96 | 45 | 52.4 | 97 | 46 |
| 89 | 53.0 | 48 | 53.0 | 100 | 45 | 51.5 | 97 | 43 | 51.9 | 98 | 44 |
| 92 | 52.7 | 44 | 52.1 | 99 | 43 | 50.9 | 97 | 43 | 52.0 | 99 | 42 |
| 94 | 51.8 | 44 | 51.9 | 100 | 43 | 51.2 | 99 | 41 | 52.4 | 101 | 40 |
| 96 | 51.5 | 43 | 51.7 | 100 | 42 | 50.2 | 98 | 41 | 51.6 | 100 | 40 |
| 98 | 52.3 | 40 | 51.1 | 98 | 42 | 49.5 | 95 | 41 | 50.9 | 97 | 39 |
| 100 | 51.5 | 39 | 51.1 | 99 | 42 | 49.4 | 96 | 41 | 50.7 | 98 | 39 |
| 102 | 50.7 | 38 | 50.9 | 100 | 41 | 48.8 | 96 | 40 | 50.0 | 99 | 38 |
| 104 | 50.7 | 35 | 50.2 | 99 | 40 | 47.4 | 94 | 40 | 49.2 | 97 | 37 |
| **Mean for weeks** | | | | | | | | | | | |
| 1-13 | 29.7 | | 29.7 | 100 | | 29.4 | 99 | | 29.3 | 99 | |
| 14-53 | 47.1 | | 46.5 | 99 | | 46.4 | 99 | | 45.7 | 97 | |
| 54-104 | 52.7 | | 52.4 | 99 | | 51.0 | 97 | | 52.4 | 99 | |

**TABLE 19**
**Mean Body Weights and Survival of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| Weeks on Study | Chamber Control | | 75 ppm | | | 300 ppm | | | 1,200 ppm | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Av. Wt. (g) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors | Av. Wt. (g) | Wt. (% of controls) | No. of Survivors |
| 1 | 18.1 | 50 | 18.1 | 100 | 50 | 18.2 | 101 | 50 | 18.2 | 101 | 50 |
| 5 | 24.1 | 50 | 24.2 | 100 | 50 | 24.0 | 100 | 50 | 25.3 | 105 | 49 |
| 9 | 27.5 | 50 | 27.2 | 99 | 50 | 27.1 | 99 | 50 | 28.2 | 103 | 49 |
| 13 | 29.5 | 50 | 29.7 | 101 | 50 | 29.1 | 99 | 50 | 30.3 | 103 | 49 |
| 17 | 29.3 | 50 | 33.4 | 114 | 50 | 32.1 | 110 | 50 | 33.9 | 116 | 49 |
| 21 | 35.3 | 50 | 36.5 | 103 | 50 | 34.5 | 98 | 50 | 35.4 | 100 | 49 |
| 25 | 37.4 | 50 | 37.9 | 101 | 50 | 35.7 | 96 | 50 | 37.4 | 100 | 49 |
| 29 | 40.9 | 50 | 41.3 | 101 | 50 | 38.7 | 95 | 50 | 39.5 | 97 | 49 |
| 33 | 42.6 | 50 | 43.9 | 103 | 50 | 41.4 | 97 | 50 | 41.6 | 98 | 49 |
| 37 | 45.5 | 50 | 47.9 | 105 | 50 | 46.0 | 101 | 50 | 45.2 | 99 | 49 |
| 41 | 47.1 | 50 | 50.5 | 107 | 50 | 48.0 | 102 | 50 | 47.3 | 100 | 49 |
| 45 | 49.4 | 50 | 52.4 | 106 | 50 | 51.6 | 105 | 50 | 49.6 | 100 | 49 |
| 49 | 51.2 | 50 | 54.4 | 106 | 50 | 53.3 | 104 | 50 | 50.9 | 99 | 49 |
| 53 | 53.5 | 50 | 57.3 | 107 | 50 | 55.9 | 105 | 50 | 51.9 | 97 | 49 |
| 57 | 55.6 | 50 | 59.7 | 107 | 50 | 57.8 | 104 | 50 | 54.4 | 98 | 49 |
| 61 | 55.8 | 50 | 59.9 | 107 | 50 | 57.7 | 103 | 50 | 54.4 | 98 | 49 |
| 65 | 55.1 | 50 | 59.9 | 109 | 50 | 57.0 | 103 | 50 | 55.2 | 100 | 48 |
| 69 | 57.8 | 50 | 61.1 | 106 | 50 | 59.5 | 103 | 50 | 56.1 | 97 | 48 |
| 73 | 58.5 | 50 | 61.7 | 106 | 50 | 60.5 | 103 | 50 | 56.7 | 97 | 47 |
| 77 | 59.8 | 50 | 62.0 | 104 | 49 | 63.1 | 106 | 50 | 57.5 | 96 | 46 |
| 81 | 59.0 | 50 | 60.7 | 103 | 49 | 62.9 | 107 | 50 | 57.3 | 97 | 46 |
| 85 | 58.6 | 49 | 59.6 | 102 | 48 | 61.8 | 106 | 50 | 55.4 | 95 | 45 |
| 89 | 57.5 | 49 | 57.3 | 100 | 46 | 60.8 | 106 | 49 | 53.9 | 94 | 45 |
| 92 | 56.5 | 47 | 56.3 | 100 | 45 | 59.6 | 106 | 49 | 53.6 | 95 | 44 |
| 94 | 55.8 | 46 | 55.8 | 100 | 44 | 58.7 | 105 | 48 | 53.7 | 96 | 44 |
| 96 | 55.2 | 46 | 54.2 | 98 | 44 | 58.0 | 105 | 45 | 53.3 | 97 | 43 |
| 98 | 54.9 | 44 | 53.6 | 98 | 42 | 57.7 | 105 | 44 | 52.5 | 96 | 42 |
| 100 | 55.8 | 42 | 53.3 | 96 | 39 | 57.5 | 103 | 44 | 52.5 | 94 | 41 |
| 102 | 55.7 | 40 | 52.3 | 94 | 38 | 56.6 | 102 | 44 | 50.8 | 91 | 41 |
| 104 | 53.8 | 40 | 49.6 | 92 | 38 | 55.8 | 104 | 42 | 49.7 | 92 | 39 |
| **Mean for weeks** | | | | | | | | | | | |
| 1-13 | 24.8 | | 24.8 | 100 | | 24.6 | 99 | | 25.5 | 103 | |
| 14-53 | 43.2 | | 45.6 | 106 | | 43.7 | 101 | | 43.3 | 100 | |
| 54-104 | 56.6 | | 57.3 | 101 | | 59.1 | 104 | | 54.2 | 96 | |

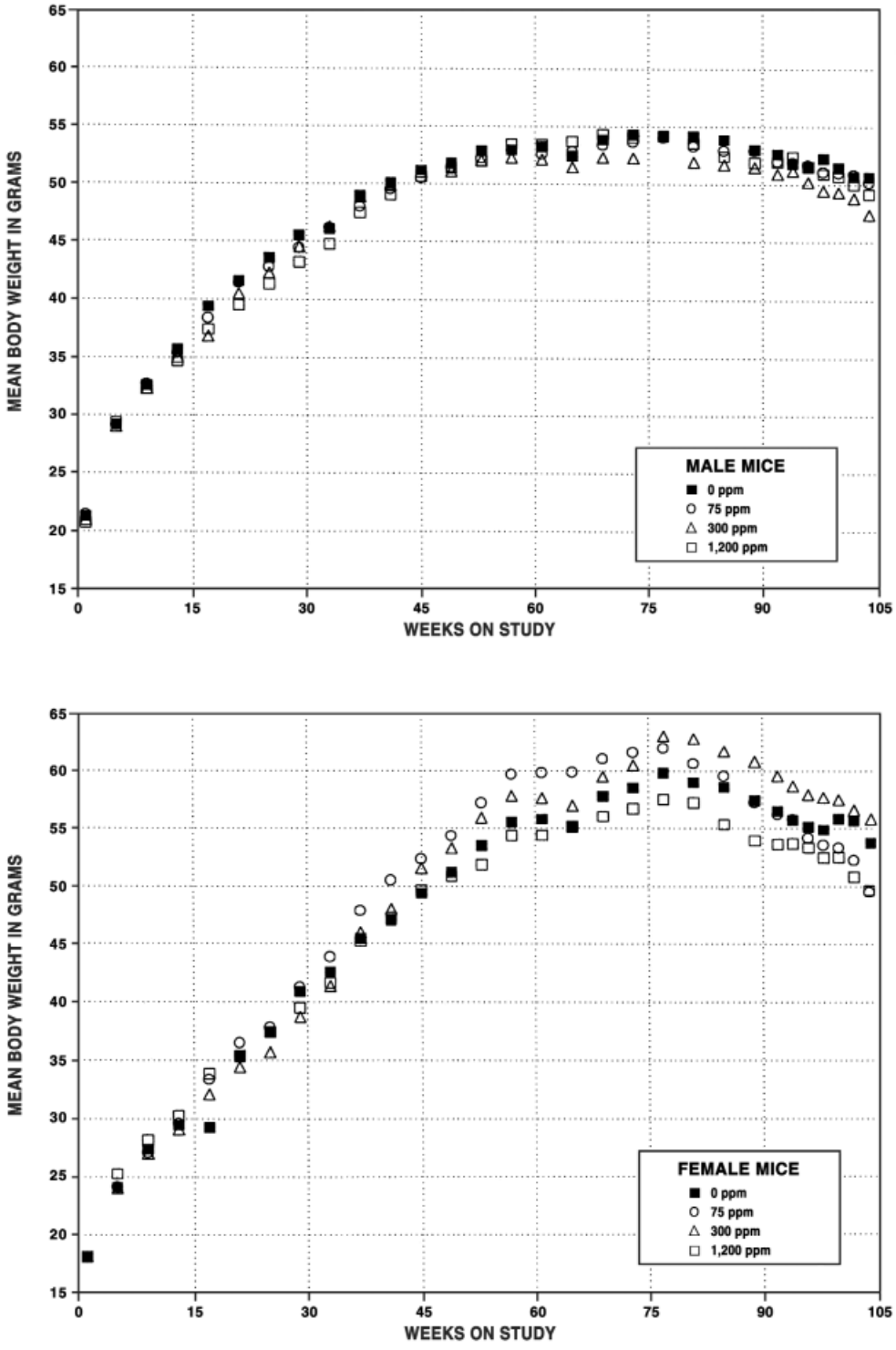



**FIGURE 4**
**Growth Curves for Male and Female Mice**
**Exposed to Propylene Glycol Mono-*t*-butyl Ether by Inhalation for 2 Years**

## *Pathology and Statistical Analyses*

This section describes the statistically significant or biologically noteworthy changes in the incidences of neoplasms and/or nonneoplastic lesions of the liver, eye, and forestomach. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group, and historical incidences for the neoplasms mentioned in this section are presented in Appendix C for male mice and Appendix D for female mice.

*Liver*: The incidences of hepatocellular adenoma, hepatocellular adenoma or carcinoma (combined), and hepatoblastoma occurred with positive trends in males and females, and the incidences in the 1,200 ppm groups were significantly increased (Tables 20, C3, and D3). In males, the incidences of hepatocellular adenoma in all exposed groups and hepatocellular adenoma or carcinoma (combined) in the 1,200 ppm group exceeded the historical ranges in chamber controls; no hepatoblastomas have been observed in historical chamber control male rats (Tables 20 and C4). In females, the incidences of these neoplasms in the 1,200 ppm group exceeded the historical chamber control ranges (Tables 20 and D4) as did the incidence of hepatocellular carcinoma in all exposed groups of females. Adenomas also increased in multiplicity in 300 and 1,200 ppm males and 1,200 ppm females. Hepatocellular adenomas were typically large masses that compressed the surrounding normal parenchyma and frequently bulged from the surface of the liver. There was clear demarcation between adenomas and the adjacent parenchyma with loss of the normal lobular architecture. Component hepatocytes varied tinctorally from eosinophilic to basophilic to vacuolated and were often larger than normal. Many adenomas had cellular atypia, pale eosinophilic cytoplasmic inclusions and proliferating oval cells dispersed among the neoplastic cells. The carcinomas were morphologically consistent with those that occur spontaneously in control mice. They were well vascularized masses with the component neoplastic hepatocyte cells typically arranged as broad trabeculae three or more cells thick. Some carcinomas contained focal areas of necrosis. Hepatoblastomas were also morphologically similar to those that occur spontaneously. They were discrete masses that occurred within or adjacent to hepatocellular adenomas or carcinomas and were composed of dense collections of small basophilic spindle-shaped cells with dark hyperchromatic nuclei and scant cytoplasm. Component cells were arranged around vascular spaces or in irregularly shaped, variably sized cords and nests that frequently had focal areas of necrosis. Mitotic figures were abundant.

The incidences of eosinophilic foci in 1,200 ppm males and females and basophilic foci in 300 ppm males were significantly increased (Tables 20, C5, and D5); the incidence of mixed cell foci in 1,200 ppm males was also increased. Hepatocellular foci were morphologically consistent with those that occur spontaneously in control mice.

The incidence of mild multinucleated hepatocytes was significantly increased in males exposed to 1,200 ppm (Tables 20 and C5). Multinucleated hepatocytes were randomly distributed enlarged hepatocytes that contained three or more nuclei. The severity of this change was mild in general and based on the number of multinucleated hepatocytes observed in liver sections.

*Eye*: Gross lesions noted at necropsy included pale corneal foci in 1,200 ppm females. The incidence of mild corneal mineralization was significantly increased in 1,200 ppm females (chamber controls, 1/50; 75 ppm, 2/50; 300 ppm, 0/50; 1,200 ppm, 20/48; Table D5); corneal mineralization also occurred in 3 of 50 1,200 ppm males (Table C5). In females, chronic inflammation, corneal erosions, and squamous hyperplasia that were generally minimal to mild infrequently accompanied mineralization. The microscopic lesions corresponded to the pale foci (corneal opacities) described clinically or at necropsy. In the females receiving 1,200 ppm, 20 of the 23 identified with corneal foci also had corneal mineralization. Foci described at necropsy were focal and quite small and may have been missed during sectioning. Mineralization occurred as centrally located deposits of mineral along the basement membrane at the stromal-epithelium interface disrupting basal cells and extending into the corneal stroma.

*Forestomach:* The incidences of forestomach inflammation were significantly increased in male mice exposed to 300 ppm and 1,200 ppm (2/48, 3/49, 9/50, 9/50); forestomach squamous epithelial hyperplasia was significantly increased in males exposed to 300 ppm (2/48, 5/49, 9/50, 7/50; Table C5). The severity of these lesions was generally similar to that of the chamber controls (data not shown), and the lesions were not considered to be related to exposure.

**TABLE 20**
**Incidences of Neoplasms and Nonneoplastic Lesions of the Liver in Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Male** | | | | |
| Number Examined Microscopically | 50 | 49 | 50 | 50 |
| Basophilic Focus[a] | 6 | 11 | 16* | 4 |
| Clear Cell Focus | 20 | 18 | 16 | 17 |
| Eosinophilic Focus | 9 | 14 | 11 | 29** |
| Mixed Cell Focus | 0 | 0 | 0 | 4 |
| Hepatocyte, Multinucleated | 27 (1.0)[b] | 23 (1.0) | 24 (1.0) | 46** (1.8) |
| Hepatocellular Adenoma, Multiple | 3 | 7 | 12* | 23** |
| Hepatocellular Adenoma (includes multiple)[c] | | | | |
| Overall rate[d] | 18/50 (36%) | 23/49 (47%) | 26/50 (52%) | 36/50 (72%) |
| Adjusted rate[e] | 38.4% | 51.0% | 57.0% | 76.7% |
| Terminal rate[f] | 13/35 (37%) | 21/40 (53%) | 24/40 (60%) | 29/37 (78%) |
| First incidence (days) | 622 | 705 | 642 | 527 |
| Poly-3 test[g] | P<0.001 | P=0.154 | P=0.052 | P<0.001 |
| Hepatocellular Carcinoma, Multiple | 1 | 1 | 2 | 2 |
| Hepatocellular Carcinoma (includes multiple)[h] | | | | |
| Overall rate | 9/50 (18%) | 8/49 (16%) | 13/50 (26%) | 11/50 (22%) |
| Adjusted rate | 19.2% | 17.7% | 27.1% | 23.7% |
| Terminal rate | 5/35 (14%) | 6/40 (15%) | 7/40 (18%) | 5/37 (14%) |
| First incidence (days) | 630 | 705 | 463 | 560 |
| Poly-3 test | P=0.348 | P=0.535N | P=0.253 | P=0.393 |
| Hepatocellular Adenoma or Carcinoma[i] | | | | |
| Overall rate | 25/50 (50%) | 26/49 (53%) | 33/50 (66%) | 41/50 (82%) |
| Adjusted rate | 52.2% | 57.6% | 68.7% | 85.0% |
| Terminal rate | 16/35 (46%) | 24/40 (60%) | 27/40 (68%) | 31/37 (84%) |
| First incidence (days) | 622 | 705 | 463 | 527 |
| Poly-3 test | P<0.001 | P=0.375 | P=0.071 | P<0.001 |
| Hepatoblastoma[j] | | | | |
| Overall rate | 0/50 (0%) | 0/49 (0%) | 1/50 (2%) | 5/50 (10%) |
| Adjusted rate | 0.0% | 0.0% | 2.2% | 11.2% |
| Terminal rate | 0/35 (0%) | 0/40 (0%) | 1/40 (3%) | 5/37 (14%) |
| First incidence (days) | —[k] | —[l] | 729 (T) | 729 (T) |
| Poly-3 test | P<0.001 | | P=0.497 | P=0.028 |

**TABLE 20**
**Incidences of Neoplasms and Nonneoplastic Lesions of the Liver in Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Female** | | | | |
| Number Examined Microscopically | 49 | 50 | 50 | 49 |
| Basophilic Focus | 3 | 4 | 4 | 2 |
| Clear Cell Focus | 4 | 4 | 6 | 5 |
| Eosinophilic Focus | 11 | 10 | 9 | 27** |
| Hepatocellular Adenoma, Multiple | 6 | 0 | 3 | 32** |
| Hepatocellular Adenoma (includes multiple)[m] | | | | |
| Overall rate | 14/49 (29%) | 8/50 (16%) | 10/50 (20%) | 37/49 (76%) |
| Adjusted rate | 29.8% | 17.1% | 20.8% | 79.3% |
| Terminal rate | 12/39 (31%) | 7/36 (19%) | 10/42 (24%) | 32/39 (82%) |
| First incidence (days) | 680 | 602 | 731 (T) | 519 |
| Poly-3 test | P<0.001 | P=0.112N | P=0.220N | P<0.001 |
| Hepatocellular Carcinoma, Multiple | 0 | 0 | 1 | 2 |
| Hepatocellular Carcinoma (includes multiple)[n] | | | | |
| Overall rate | 4/49 (8%) | 8/50 (16%) | 7/50 (14%) | 10/49 (20%) |
| Adjusted rate | 8.4% | 16.7% | 14.4% | 21.2% |
| Terminal rate | 1/39 (3%) | 3/36 (8%) | 6/42 (14%) | 6/39 (15%) |
| First incidence (days) | 624 | 586 | 600 | 440 |
| Poly-3 test | P=0.109 | P=0.183 | P=0.275 | P=0.071 |
| Hepatocellular Adenoma or Carcinoma[o] | | | | |
| Overall rate | 18/49 (37%) | 14/50 (28%) | 16/50 (32%) | 41/49 (84%) |
| Adjusted rate | 37.8% | 29.2% | 33.0% | 86.2% |
| Terminal rate | 13/39 (33%) | 9/36 (25%) | 15/42 (36%) | 34/39 (87%) |
| First incidence (days) | 624 | 586 | 600 | 440 |
| Poly-3 test | P<0.001 | P=0.249N | P=0.391N | P<0.001 |
| Hepatoblastoma[p] | 0 | 0 | 0 | 2 |

* Significantly different (P≤0.05) from the chamber control group by the Poly-3 test
** P≤0.01
(T) Terminal sacrifice
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked
[c] Historical incidence for 2-year inhalation studies with chamber controls given NTP-2000 diet (mean ± standard deviation): 95/250 (38.0% ± 6.8%), range 30%-46%
[d] Number of animals with neoplasm per number of animals with liver examined microscopically
[e] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[f] Observed incidence at terminal kill
[g] Beneath the chamber control incidence is the P value associated with the trend test. Beneath the exposed group incidence are the P values corresponding to pairwise comparisons between the chamber controls and that exposed group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice. A lower incidence in an exposed group is indicated by **N**.
[h] Historical incidence: 60/250 (24.0% ± 5.8%), range 18%-32%
[i] Historical incidence: 139/250 (55.6% ± 7.3%), range 50%-68%
[j] Historical incidence: 0/250
[k] Not applicable; no neoplasms in animal group
[l] Value of statistic cannot be computed
[m] Historical incidence: 48/248 (19.4% ± 6.9%), range 12%-29%
[n] Historical incidence: 26/248 (10.5% ± 2.1%), range 8%-12%
[o] Historical incidence: 72/248 (29.0% ± 6.8%), range 22%-37%
[p] Historical incidence: 0/248

### *Biomarkers of Exposure*

Propylene glycol mono-*t*-butyl ether sulfate and propylene glycol mono-*t*-butyl ether glucuronide excretion data are listed in Table G2. Excretion of the metabolites in urine was not proportional to exposure concentration when expressed as the metabolite to creatinine ratios. Dose proportionality was determined by normalizing the metabolite to creatinine ratios to exposure concentrations and testing for significant differences between exposed groups. Propylene glycol mono-*t*-butyl ether glucuronide is the more useful biomarker since it represents 95% or more of the total of the two metabolites. No consistent pattern was noted in the data.

## Genetic Toxicology

Propylene glycol mono-*t*-butyl ether, tested over a concentration range of 100 to 10,000 µg/plate, was mutagenic in *Salmonella typhimurium* strain TA97 in the absence of liver S9 activation enzymes; negative results were obtained with strain TA97 in the presence of rat or hamster liver S9 enzymes, and in strains TA98, TA100, and TA1535 with and without S9 (Table E1). Propylene glycol mono-*t*-butyl ether was also nonmutagenic in TA1537 in the absence of S9; it was not tested with S9. Propylene glycol mono-*t*-butyl ether did not induce sister chromatid exchanges (Table E2) or chromosomal aberrations (Table E3) in Chinese hamster ovary cells, with or without S9. In these cytogenetic assays, propylene glycol mono-*t*-butyl ether was tested up to 5,000 µg/mL, the maximum concentration set by the assay protocol. Propylene glycol mono-*t*-butyl ether, administered for 3 months by inhalation over an exposure concentration range of 75 to 1,200 ppm, induced a small but significant increase in the frequency of micronucleated normochromatic erythrocytes in peripheral blood of female mice; no increase in micronucleated normochromatic erythrocytes was seen in male mice (Table E4). The percentages of polychromatic erythrocytes in the exposed groups were similar to those of the chamber control groups.

# DISCUSSION AND CONCLUSIONS

The U. S. Consumer Product Safety Commission nominated propylene glycol mono-*t*-butyl ether for study based on its widespread use, potential for human exposure, and the lack of adequate toxicity and carcinogenicity data. The effects of propylene glycol mono-*t*-butyl ether, administered by whole body inhalation, were studied in male and female F344/N rats, male NBR rats, and male and female B6C3F$_1$ mice.

Several organic chemicals have been shown to produce a renal syndrome exclusive to male rats known as α2u-globulin nephropathy. In this syndrome, renal toxicity is associated with the accumulation of hyaline protein droplets in the cytoplasm of the proximal tubular epithelium (Swenberg *et al.*, 1989; Hard *et al.*, 1993; Swenberg and Lehman-McKeeman, 1999). These droplets contain a filtered protein, α2u-globulin, which is synthesized predominantly in the liver under multihormonal, but mainly androgen control prior to being secreted into the blood (Roy and Neuhaus, 1967; Roy and Raber, 1972; Chan and Neuhaus, 1978; Roy and Chatterjee, 1983). Female rats, mice of either sex, and male NBR rats produce scant if any hepatic α2u-globulin and thus do not develop α2u-globulin nephropathy (MacInnes, *et al.,* 1986; Chatterjee *et al.*, 1989; Lehman-McKeeman and Caudill, 1992). In the kidney of male rats, α2u-globulin is freely filtered across the glomerulus with 40% being excreted in the urine and 60% being reabsorbed in the proximal tubules by endocytosis and slowly hydrolyzed by phagolysosomes (Neuhaus *et al.*, 1981; Lehman-McKeeman *et al.*, 1990). Some chemicals have the ability to bind to α2u-globulin, which is thought to decrease the rate of degradation of α2u-globulin protein and to increase its accumulation. Abnormal accumulation of α2u-globulin, in turn, may result in lysosomal dysfunction, initiating a cycle of cytotoxicity, cell death, and a compensatory increase in cell proliferation that, if chronic, may lead to the promotion of neoplastic lesions (Swenberg *et al.*, 1989; Borghoff *et al.*, 1990). Alternatively, it has been proposed that α2u-globulin may serve as a vector to increase the delivery of a toxicant or protoxicant to proximal tubular cells, so that nephrotoxicity occurs not from the abnormal accumulation and degradation of α2u-globulin, but because chemical levels are elevated in the renal tubules (Melnick, 1992). The class of compounds that produce α2u-globulin nephropathy is structurally diverse. A few general structure-activity relationships for chemicals that induce α2u-globulin accumulation have been compiled in a review by the U.S. Environmental Protection Agency (1991). Propylene glycol mono-*t*-butyl ether contains some structural features, such as an oxygen function or at least one tertiary carbon atom, that have been found in other α2u-globulin binding chemicals. In addition, propylene glycol mono-*t*-butyl ether is structurally related to propylene glycol monomethyl ether, which has been shown to induce α2u-globulin nephropathy in F344/N rats (Bus *et al.*, 1992).

In the current 2-week studies, exposure to propylene glycol mono-*t*-butyl ether had no effect on survival and was characterized by an absence of clinical signs in rats and mice. Some evidence of acute toxicity of propylene glycol mono-*t*-butyl ether was seen in male F344/N rats, which had an exposure-related accumulation of hyaline droplets in the renal proximal tubules. These findings were accompanied by an overall, although not significant, increase in cell proliferation indices and α2u-globulin concentrations, which were suggestive of α2u-globulin-related nephropathy. Some increases in kidney and liver weights occurred in male and female F344/N rats and male NBR rats, but there were no corresponding histopathological changes and the increases appeared to be unrelated to chemical exposure. Increases in liver weights were also seen in exposed male and female B6C3F$_1$ mice. Although liver weight increases in mice were not accompanied by histopathological lesions, there were trends of increasing liver weight with increasing exposure concentration, suggesting that the mouse liver might have been a target for propylene glycol mono-*t*-butyl ether acute toxicity. Likewise, low acute toxicity of propylene glycol mono-*t*-butyl ether has been reported in a whole-body exposure inhalation study in Sprague-Dawley rats (Boatman, 2001). Following a single, 4-hour exposure of approximately 550 ppm propylene glycol mono-*t*-butyl ether, no

deaths or clinical signs were observed and the only treatment-related finding at 14 days after exposure, was mild hepatic extramedullary hematopoiesis consisting of small foci of hematopoietic cells in some portal triads. No further details are provided in this study, but hepatic extramedullary hematopoiesis is known to occur only under pathologic conditions in the adult rat, with frequent involvement of other organs/sites, such as the spleen and the perirenal adipose tissue (Eustis *et al.*, 1990).

In the current 3-month F344/N rat studies, the main target of propylene glycol mono-*t*-butyl ether toxicity was the kidney. Exposure-related increases in renal cell proliferation indices and α2u-globulin concentrations were seen in male rats. In general, the levels of α2u-globulin increased with increasing exposure concentration at all time points, except in the 1,200 ppm group at 2 weeks; levels of α2u-globulin for 1,200 ppm males were higher than those of the chamber controls, but lower than all other exposed groups at 2 weeks. It is possible that the production of α2u-globulin was impaired in this particular group, but the reason for this finding is unknown at this time. The relative increases of α2u-globulin/soluble protein levels with increasing exposure concentration were greater at 2 weeks and 6 weeks (8 and 12 weeks of age, respectively) in comparison to 14 weeks on study (approximately 5 months of age). Overall, the concentrations of α2u-globulin were the lowest at 2 weeks, probably due to age-dependent differences in α2u-globulin production. Low levels of α2u-globulin in male rats are first detectable by 5 to 6 weeks of age; reach maximum levels by approximately 2 to 4 months of age, and gradually decline thereafter (Motwani *et al.*, 1984; MacInnes *et al.*, 1986; Richardson *et al.*, 1987). Increased kidney weights and altered parameters in urine chemistry analyses in male rats provide further indication of renal injury. Increased activities of aspartate aminotransferase, lactate dehydrogenase, and *N*-acetyl-ß-D-glucosaminidase would be consistent with treatment-related renal tubular injury. In addition, increases in urine glucose/mg creatinine could reflect extra-renal hypoglycemia or a renal effect related to proximal convoluted tubule injury and loss of normal glucose reabsorption by the kidney; increases in urine protein/mg creatinine could be either a result of renal tubule injury or a reflection of the increased concentrations of α2u-globulin observed in treated male rats. Polyuria, however, can be related to physiological (e.g., compensatory to increased fluid intake), pharmacological (e.g., diuretic agents) or pathological mechanisms. Based on the specific gravity/osmolality of the urine, pathological mechanisms can be classified as water diuresis (specific gravity below that of glomerular filtrate) or solute diuresis (specific gravity above that of glomerular filtrate). Since the specific gravities of the affected animals were at or above that of glomerular filtrate, a water diuresis mechanism (as with a renal diabetes insipidus) was probably not involved. The severity of renal tubule hyaline droplet accumulation and the incidences of cortical regeneration and medullary granular casts also generally increased with increasing exposure concentration. The male-specific renal lesions observed in propylene glycol mono-*t*-butyl ether exposed rats are characteristic of α2u-globulin nephropathy. Interestingly, increases in kidney weights were also seen in female rats exposed to 300 ppm or greater along with a slight increase in the severity of nephropathy in female rats exposed to 1,200 ppm, and alterations in urine chemistry parameters in female rats exposed to 150 ppm or greater. Although these changes were unaccompanied by histopathologic lesions and were less pronounced than in male rats, they suggest that mechanisms of renal injury independent of α2u-globulin accumulation may have been operative.

Serum urea nitrogen and creatinine concentrations are used as markers of renal function. In general, approximately 75% of the nephrons must be nonfunctional for increased serum urea nitrogen and creatinine concentrations to occur from renal causes. In the male rats, but not females, there was microscopic evidence of kidney lesions that may have influenced the serum creatinine values, but serum urea nitrogen concentrations were unaffected. Furthermore, it has been demonstrated that numerous compounds interfere with the creatinine analytical method resulting in erroneously high values. Thus, it is possible that the parent compound or a metabolite (for example, pyruvate) interfered with the serum creatinine analysis. Besides conjugation, it has been hypothesized that propylene glycol mono-*t*-butyl ether may be partly metabolized to propylene glycol (Verschuuren, 1996). Propylene glycol is further metabolized to lactic and pyruvic acids (Miller, 1987). Thus, an increased pyruvate concentration may have affected the creatinine assay. In a previous 90-day study, dipropylene glycol administered to F344/N rats in drinking water at concentrations up to 80,000 ppm also resulted in increased serum creatinine concentrations (up to fivefold increases) in the absence of increased serum urea nitrogen concentration or severe renal pathology (NTP, 2004a). In that study, it was suggested that metabolism of the dipropylene glycol to pyruvate may have resulted in erroneously high creatinine concentrations.

Liver weights of all exposed F344/N male rats and 600 and 1,200 ppm female rats were increased in an exposure concentration-dependent manner, suggesting that the liver was also a target of propylene glycol mono-*t*-butyl ether toxicity in 3-month studies. It is possible that the increases in liver weight occurred as an adaptive response to altered hepatic function, as evidenced by transient increases in total bile acid concentrations that returned to control levels at study termination. The mechanism for the transient serum bile acid increase was unknown, but serum concentrations may be affected by hepatic injury, altered bile acid metabolism or cholestasis (Hofmann, 1988). In this study, alkaline phosphatase activity, another marker of cholestasis, was either unchanged or decreased (1,200 ppm males and females) suggesting that the transient increases in bile acid concentrations were probably not related to a cholestatic event. Decreases in serum alanine aminotransferase enzyme activity could suggest some alteration in enzyme metabolism/catabolism or release by the liver or enzyme inhibition (Pappas, 1989). In addition, the incidences of hyaline degeneration of the olfactory epithelium were significantly increased in rats exposed to 600 or 1,200 ppm. This nasal lesion is thought to occur as an adaptive or protective response following chemical exposures (Buckley *et al.*, 1985). In a previous 3-month inhalation study with propylene glycol mono-*t*-butyl ether in F344/N rats, no renal, hepatic, or nasal lesions were reported with the exception of increases in kidney weights, which the authors did not consider to be related to chemical exposure; the no-observed-adverse-effect level for propylene glycol mono-*t*-butyl ether was the highest concentration tested, 709 ppm (Boatman, 2001).

In contrast to rats, no kidney lesions were observed in B6C3F$_1$ mice exposed to propylene glycol mono-*t*-butyl ether in the current 3-month studies. Increases in liver weights accompanied by centrilobular hypertrophy were present in male mice exposed to 600 and 1,200 ppm and female mice exposed to 1,200 ppm. Hepatocyte hypertrophy is a lesion often associated with increases in liver weight and is a common finding in xenobiotic-exposed mice (Harada *et al.*, 1999). Lesions in the olfactory epithelium consisted of significant increases in minimal squamous metaplasia in 1,200 ppm male mice. In this type of lesion, layers of stratified squamous epithelium replace the normal epithelium, following inhalation exposure to irritants and toxicants (Herbert and Leininger, 1999). Nasal lesions were also observed in the current 3-month rat study, but these lesions consisted of hyaline degeneration of the olfactory epithelium and were located in more posterior nasal sections. These nasal changes are considered to be protective or adaptive in nature.

No histopathologic changes were noted in the reproductive organs of rats or mice. The only significant reproductive effect of propylene glycol mono-*t*-butyl ether was an increase in the estrous cycle length in 1,200 ppm female mice. Estrous cycle characterization through vaginal cytology showed that the cycle length increase was mainly due to a lengthened diestrus. Oral administration of a related compound, ethylene glycol monomethyl ether, resulted in an increase in estrous cycle length in Swiss CD-1 mice (Chapin and Sloane, 1997). Davis *et al.* (1997) reported suppression of vaginal cyclicity with prolonged diestrus as ethylene glycol monomethyl ether inhibited luteal cell death and maintained progesterone secretion in the cycling female Sprague-Dawley rat. It is possible that the current reproductive toxicity findings associated with propylene glycol mono-*t*-butyl ether may occur via a similar mechanism and hence affect ovarian function. However, these assumptions are only speculative and further studies are needed to establish the toxicological significance of the estrous cycle alteration reported herein.

In the current 2-year rat studies, the kidney was the target organ of propylene glycol mono-*t*-butyl ether toxicity. Age-related chronic nephropathy occurred in most chamber control and exposed rats. This notable spontaneous finding appears in older F344/N rats, being particularly more common and severe in males (Montgomery and Seely, 1990). In the current study, male rats also displayed a significant increase in nephropathy severity relative to controls, as well as exposure-related renal tubule hyperplasia and hyaline droplet accumulation, papilla mineralization, and transitional epithelium hyperplasia. Interestingly, there was a significant increase in the severity of nephropathy in 1,200 ppm female rats, which suggests that exposure-related nephropathy also occurred independent of the $\alpha$2u-globulin mechanism. In the standard single-section evaluation of the kidney, marginal increases in the incidences of renal tubule adenoma and adenoma or carcinoma (combined) occurred in 300 and 1,200 ppm male rats. In a subsequent extended evaluation of kidney step sections, additional renal tubule adenomas, but no additional renal tubule carcinomas, were identified in the exposed groups. Although these are uncommon neoplasms, and their final combined incidences in the 300 and 1,200 ppm males exceeded the ranges in historical chamber controls, they were not significantly different from the concurrent chamber controls. Additionally, in

chamber control animals from an NTP study with Stoddard solvent (NTP, 2004b), the combined incidence of renal tubule adenoma or carcinoma from single and step sections was 4/50; these chamber control incidences were comparable to those seen in the 300 and 1,200 ppm groups in the current study. These results are suggestive of a marginal tumorigenic effect of propylene glycol mono-*t*-butyl ether in the kidney of male rats.

Propylene glycol mono-*t*-butyl ether meets the three required criteria listed by the USEPA (1991) to link the α2u-globulin process and the observed renal neoplasm outcome: 1) increased numbers and size of hyaline droplets in renal proximal tubule cells of treated male rats; 2) the accumulating protein in the hyaline droplets is α2u-globulin; and 3) additional aspects of the pathologic sequence of lesions associated with α2u-globulin nephropathy are present (including formation of granular casts, linear mineralization of the papillary tubules and tubule hyperplasia). In contrast, it only satisfies some of the International Agency for Research on Cancer (IARC) criteria for kidney carcinogenicity through a α2u-globulin-associated response (IARC, 1999). IARC criteria include: 1) lack of genotoxic activity (agent and/or metabolite) based on an overall evaluation of *in vitro* and *in vivo* data, 2) male rat specificity for nephropathy and renal tumorigenicity, 3) induction of the characteristic sequence of histopathological changes in shorter-term studies, of which protein droplet accumulation is obligatory, 4) identification of the protein accumulating in tubule cells as α2u-globulin, 5) reversible binding of the chemical or metabolite to α2u-globulin, 6) induction of sustained increased cell proliferation in the renal cortex, and 7) similarities in dose-response relationship of the tumor outcome with the histopathological end points (protein droplets, α2u-globulin accumulation, cell proliferation). The IARC criteria not satisfied by propylene glycol mono-*t*-butyl ether include: a) lack of genotoxic activity, as the compound was mutagenic in the *Salmonella* test, b) male rat specificity for nephropathy, since increases in kidney weights and alterations in urine chemistry analysis parameters in the 3-month studies and increased severity of chronic nephropathy in the 2-year studies were also seen in exposed females and c) similarities in the dose-response relationship of the tumor outcome with the histopathological endpoints, because the evidence of carcinogenic activity of propylene glycol mono-*t*-butyl ether in male rats was equivocal, and thus, not clearly related to chemical exposure. In addition, the binding of propylene glycol mono-*t*-butyl ether to α2u-globulin was not investigated.

Chemicals that induce renal tumors through α2u-globulin are thought to be essentially nongenotoxic and produce tumors independent of direct genetic damage. Propylene glycol mono-*t*-butyl ether mutagenicity in *Salmonella typhimurium* strain TA97 in the absence of liver S9 activation enzymes (Table E1) would suggest that this chemical has the potential to produce genetic injury. However, not all chemicals that demonstrate mutagenicity in *Salmonella* have been identified as rodent carcinogens. Thus, although a DNA-damage mechanism for propylene glycol mono-*t*-butyl ether carcinogenesis should not be ruled out, it needs to be further investigated. As previously mentioned, female rat nephropathy severity also increased with increasing exposure concentrations, which would be consistent with the male rat nephropathy occurring to some extent through mechanisms other than α2u-globulin accumulation. Additional research is needed to characterize the binding of propylene glycol mono-*t*-butyl ether to α2u-globulin and to clarify the role of the α2u-globulin mechanism in the observed tumor outcome in male rats in the current study.

Additional findings in the current 2-year rat studies included significantly increased incidences of basophilic foci in the liver of all exposed groups of male rats and clear cell foci in 1,200 ppm females. The significance of the increased incidences of these common background lesions is not certain. The increases of both types of foci were not exposure-related, and the incidences of basophilic foci in control and exposed males were unusually low. Hepatocellular foci have been putatively linked to the development of neoplasia in the rodent liver, however their biological significance in the carcinogenic process is still uncertain (Bannasch *et al.*, 1986). In relation to neoplasms, incidences of hepatocellular adenoma occurred with a positive trend in male rats, and the incidence in the 1,200 ppm group exceeded the historical range in chamber controls. It should be noted, however, that the concurrent control rates (6%) reported in this study correspond to the upper end of the range of the chamber control historical incidence (0%-6%). This would suggest that liver neoplasm incidences were overall higher in male rats in the current study. A single incidence of a cholangiocarcinoma appeared in a 1,200 ppm male and was noteworthy because this neoplasm has not been seen in 299 male chamber controls in the NTP database.

In regard to nasal effects, the incidences and severity of hyaline degeneration of the olfactory epithelium were increased with increasing exposure concentrations of propylene glycol mono-*t*-butyl ether in rats. As previously mentioned, this type of nasal change is adaptive or protective following chemical exposure (Buckley *et al.*, 1985), but it is also a very common occurrence in aging rats (St. Clair and Morgan, 1992), appearing both in control and exposed animals (Morgan and Harkema, 1996). In a previous 2-year NTP (2000) study with the related compound ethylene glycol monobutyl ether (2-butoxyethanol), hyaline degeneration of the olfactory epithelium was seen in all exposed groups of male rats (31.2, 62.5, and 125 ppm) and in 62.5 and 125 ppm female rats, but the incidences were not exposure-concentration related, and the lesion was of minimal severity. Dilatation of the submucosal glands and goblet cell hyperplasia, in 300 and 1,200 ppm rats in the current study are most likely also protective or adaptive responses.

In the eyes, corneal opacity or pale foci were noted at gross observation in 1,200 ppm female rats. Microscopically, corneal mineralization was significantly increased in this group, although there was poor individual correlation between these two findings. Previous studies with propylene glycol mono-*t*-butyl ether have shown this chemical to be a severe eye irritant in its neat form (Boatman, 2001). Instillation of 0.1 mL of neat chemical into the eyes of rabbits resulted in transient signs of irritation, as well as reversible corneal opacity. Corneal mineralization, however, has been shown to occur without evidence of other ocular injury and can be found in up to 15% of F344/N rats between 7 and 26 weeks of age (Yoshitomi and Boorman, 1990).

In the current 2-year B6C3$F_1$ mouse study, significant increases in the incidences of hepatocellular foci of the eosinophilic type were seen in males and females exposed to 1,200 ppm; incidences of basophilic foci in 75 and 300 ppm males and mixed cell foci in 1,200 ppm males were also increased. Hepatic foci are more frequently observed in mice treated with hepatocarcinogens than untreated controls and, although there is evidence that putatively links these lesions to the development of hepatocellular neoplasms in the rodent liver, their exact role in hepatocarcinogenesis is still uncertain (reviewed in Harada *et al.*, 1999). They generally precede the development of hepatic neoplasms and may increase in incidence, multiplicity, and/or size with time and administration of hepatocarcinogens. However, while some foci progress to neoplasia, others regress when the inciting carcinogenic stimulus is removed. The biological significance of the increased incidence of multinucleated hepatocytesis unknown. It has been suggested that multinucleated hepatocytes arise by cell fusion rather than cell division and have occurred in hepatic injury of rats following administration of some chemicals, and incidences increase in aged animals (Jones and Butler, 1974).

Incidences of hepatocellular adenoma, hepatocellular adenoma or carcinoma (combined), and hepatoblastoma occurred with positive trends in male mice; with the exception of hepatoblastoma, these incidences also occurred with positive trends in female mice. In 1,200 ppm mice the incidences of hepatocellular adenoma and hepatocellular adenoma or carcinoma (combined) were significantly greater than those in the chamber controls, as was the incidence of hepatoblastoma in 1,200 ppm males. The incidences of hepatocellular adenoma in all exposed groups of males and 1,200 ppm females, hepatocellular carcinoma in all exposed groups of females, hepatocellular adenoma or carcinoma (combined) in 1,200 ppm males and females, and hepatoblastoma in 300 ppm males and 1,200 ppm males and females exceeded the historical control ranges in chamber controls. Hepatocellular adenoma is the most frequent spontaneous liver neoplasm in B6C3$F_1$ mice; hepatocellular carcinoma is also a frequent spontaneous hepatic neoplasm in B6C3$F_1$ mice (Harada *et al.*, 1999). Hepatoblastomas, on the other hand, are very rare neoplasms with an extremely low spontaneous incidence in mice (Harada *et al.*, 1999; Haseman *et al.*, 1998). Hepatoblastomas are considered part of the continuum of hepatocellular neoplasms. With chemicals that are hepatocarcinogens, there appears to be a positive association between increased incidences of hepatoblastoma and increased incidences of hepatocellular carcinoma in mice. Additionally, the malignant potential of hepatoblastoma appears to be similar to that of hepatocellular carcinoma. In general, zero to two hepatoblastomas have occurred in individual control groups in NTP studies; however, as many as five have been observed in one control group in a noninhalation study. In inhalation studies, hepatoblastoma has not been observed in 250 chamber controls. The incidence of hepatoblastoma (5/50) in 1,200 ppm males in the current study is the highest that has been observed in treated mice given the NTP-2000 diet.

In the eyes, pale foci of the cornea were noted in 1,200 ppm female mice at gross observation. These lesions partially corresponded to microscopically

diagnosed corneal mineralization, which occurred almost exclusively in females exposed to 1,200 ppm and was infrequently accompanied by chronic inflammation, corneal erosions, and squamous hyperplasia. Corneal mineralization has been reported to occur as a spontaneous lesion following inflammation or trauma in up to 10% of $B6C3F_1$ mice (Geiss and Yoshitomi, 1999). Interestingly, this abnormality was also significantly increased in female rats exposed to 1,200 ppm in the current F344/N rat study.

Although the incidences of forestomach inflammation and squamous epithelial hyperplasia were increased in select groups of mice, their severity was generally similar to those of the chamber control groups and thus these lesions were not considered to be related to exposure. Lesions of the forestomach are frequently seen in toxicity studies utilizing various routes of exposure. Some NTP inhalation studies have resulted in the development of neoplastic lesions in the forestomach, although the respiratory tract was not affected (NTP, 1996, 2000). This unusual target of toxicity for an inhalation exposure is thought to be a consequence of indirect ingestion of the test chemical through grooming (Leininger *et al.*, 1999).

In both rats and mice, propylene glycol mono-*t*-butyl ether was excreted in the urine as sulfate and glucuronide conjugates, but primarily as the glucuronide. The latter can be used as a biomarker of exposure, as it represents 90% or more of the total of the two metabolites. In general, there was an increase in propylene glycol mono-*t*-butyl ether metabolites, when expressed as the metabolite to creatinine ratios with exposure; the increase, however, was linear with exposure to 75 or 300 ppm, but was supralinear for 1,200 ppm. The excretion of propylene glycol mono-*t*-butyl ether glucuronide/creatinine in urine by 1,200 ppm rats of both sexes was generally significantly less than by the groups exposed to 75 or 300 ppm at all time points, suggesting that elimination by this route was saturated at the highest exposure concentration. No consistent metabolic pattern was noted in mice, although as in rats, glucuronide urinary excretion (normalized to creatinine) was nonlinear with respect to exposure concentration.

There are insufficient data to clearly define the mutagenic potential of propylene glycol mono-*t*-butyl ether or the role that mutagenicity may play in the etiology of the observed tumors in rats and mice. The mutagenic activity observed exclusively in *Salmonella typhimurium* strain TA97 without S9 indicates that propylene glycol mono-*t*-butyl ether operates through a frameshift mechanism in this test system, rather than through base pair substitution, which would have been detected in other *Salmonella* strains sensitive to that mode of action. Strain TA97 carries a mutation in the histidine operon which is a +1 cytosine frameshift mutation resulting in a run of 6 cytosines (Mortelmans and Zeiger, 2000). TA97 is believed to be more sensitive to the action of frameshift mutagens than TA1537, a *Salmonella* strain that also mutates via frameshift, and indeed, no mutagenic activity was observed with propylene glycol mono-*t*-butyl ether in TA1537. A related compound, ethylene glycol monobutyl ether (2-butoxyethanol), was also reported to induce mutations exclusively in the closely-related *S. typhimurium* strain TA97a (Hoflack *et al.*, 1995). However, attempts to replicate the response with ethylene glycol monobutyl ether in TA97a were unsuccessful in another laboratory (Gollapudi *et al.*, 1996). Furthermore, the NTP has tested a number of ethylene glycol ethers, including ethylene glycol monobutyl ether, for mutagenicity in a number of different strains of *S. typhimurium*, including frameshift strains, and uniformly negative results were obtained (Zeiger *et al.*, 1985, 1992; NTP, 2000). A review of the genotoxicity data for ethylene glycol monobutyl ether by Elliott and Ashby (1997) indicated that the chemical was not mutagenic and demonstrated no structural alerts to genotoxicity (Tennant and Ashby, 1991). Thus, the activity seen with propylene glycol mono-*t*-butyl ether in *Salmonella* appears to be an exception to the pattern of negative responses in mutagenicity assays that characterize the majority of glycol ethers.

The weak response seen only in female mice in the *in vivo* micronucleus assay, which detects induced chromosomal damage, may indicate gender-limited sensitivity to the action of propylene glycol mono-*t*-butyl ether. However, if clastogenic activity were postulated to be involved in the induction of liver tumors in mice, the absence of a micronucleus response in male mice would be difficult to interpret. The micronucleus test results in female mice should be interpreted with caution because the response was weak, a similar response was not seen in male mice, and due to the nature of the test, the study was not repeated. However, there is one report in the literature of a micronucleus test conducted with male and female rats exposed short-term by gavage to ethylene glycol monobutyl ether (2-butoxyethanol) that also showed increased frequencies of micronucleated erythrocytes in females only (Ghanayem *et al.*, 2001). Two additional acute rodent bone marrow micronucleus tests were conducted by the NTP with ethylene glycol

monobutyl ether, one in male rats and the other in male mice (unpublished data). In both studies, ethylene glycol monobutyl ether was administered by intraperitoneal injection three times at 24-hour intervals with phosphate-buffered saline as the vehicle. No increase in micronucleated erythrocytes was seen in either study.

## CONCLUSIONS

Under the conditions of this 2-year inhalation study, there was *equivocal evidence of carcinogenic activity** of propylene glycol mono-*t*-butyl ether in male F344/N rats based on marginally increased incidences of renal tubule and liver neoplasms. There was *no evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in female F344/N rats exposed to 75, 300, or 1,200 ppm. There was *clear evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in male and female $B6C3F_1$ mice based on increased incidences of liver neoplasms.

Exposure of male rats to propylene glycol mono-*t*-butyl ether resulted in nonneoplastic lesions of the kidney characteristic of $\alpha$2u-globulin accumulation. Exposure to propylene glycol mono-*t*-butyl ether resulted in nonneoplastic lesions of the liver and nose in male and female rats, the liver in male and female mice, and the eyes in female rats and mice. Kinetic and biomarker studies indicated that clearance was saturated at the 1,200 ppm exposure for both rats and mice.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 12. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 14.

# REFERENCES


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# APPENDIX A
# SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR INHALATION STUDY OF PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER


| | | |
|---|---|---|
| TABLE A1 | Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 82 |
| TABLE A2 | Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 86 |
| TABLE A3 | Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 110 |
| TABLE A4a | Historical Incidence of Renal Tubule Neoplasms in Control Male F344/N Rats | 114 |
| TABLE A4b | Historical Incidence of Urinary Bladder Neoplasms in Control Male F344/N Rats | 115 |
| TABLE A4c | Historical Incidence of Hepatocellular Neoplasms in Control Male F344/N Rats | 116 |
| TABLE A5 | Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 117 |

**TABLE A1**
**Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Moribund | 20 | 15 | 26 | 22 |
| Natural deaths | 3 | 6 | 8 | 6 |
| Survivors | | | | |
| Terminal sacrifice | 27 | 29 | 16 | 22 |
| Animals examined microscopically | 50 | 50 | 50 | 50 |
| **Alimentary System** | | | | |
| Esophagus | (50) | (50) | (49) | (50) |
| Carcinoma, metastatic, thyroid gland | | | | 1 (2%) |
| Intestine large, colon | (49) | (48) | (46) | (48) |
| Polyp adenomatous | 1 (2%) | | | |
| Intestine large, cecum | (47) | (47) | (47) | (45) |
| Intestine small, ileum | (47) | (47) | (43) | (45) |
| Liver | (50) | (50) | (49) | (50) |
| Cholangiocarcinoma | | | | 1 (2%) |
| Hepatocellular adenoma | 3 (6%) | | 2 (4%) | 6 (12%) |
| Histiocytic sarcoma, metastatic, skin | | 1 (2%) | | |
| Mesentery | (13) | (9) | (10) | (7) |
| Stomach, forestomach | (50) | (50) | (49) | (50) |
| Stomach, glandular | (50) | (50) | (49) | (50) |
| Carcinoma | | | | 1 (2%) |
| Muscularis, lipoma | 1 (2%) | | | |
| **Cardiovascular System** | | | | |
| Blood vessel | (50) | (50) | (49) | (50) |
| Aorta, pulmonary artery, sarcoma, metastatic, heart | | | | 1 (2%) |
| Heart | (50) | (50) | (49) | (50) |
| Carcinoma, metastatic, lung | | | | 1 (2%) |
| Pericardium, sarcoma | | | | 1 (2%) |
| **Endocrine System** | | | | |
| Adrenal medulla | (50) | (50) | (49) | (50) |
| Pheochromocytoma malignant | 2 (4%) | | | 2 (4%) |
| Pheochromocytoma complex | | 1 (2%) | | |
| Pheochromocytoma benign | 10 (20%) | 8 (16%) | 8 (16%) | 6 (12%) |
| Bilateral, pheochromocytoma benign | 2 (4%) | | 3 (6%) | 1 (2%) |
| Islets, pancreatic | (50) | (50) | (49) | (50) |
| Adenoma | 4 (8%) | 4 (8%) | 5 (10%) | |
| Carcinoma | | | 1 (2%) | 1 (2%) |
| Parathyroid gland | (49) | (49) | (48) | (49) |
| Carcinoma, metastatic, thyroid gland | | | | 2 (4%) |
| Pituitary gland | (50) | (50) | (49) | (50) |
| Adenoma | 35 (70%) | 27 (54%) | 26 (53%) | 32 (64%) |
| Thyroid gland | (50) | (50) | (49) | (50) |
| C-cell, adenoma | 3 (6%) | 3 (6%) | 3 (6%) | 5 (10%) |
| C-cell, adenoma, multiple | | 1 (2%) | | |
| C-cell, carcinoma | 1 (2%) | 1 (2%) | 3 (6%) | 3 (6%) |
| Follicular cell, adenoma | | 1 (2%) | | 1 (2%) |
| Follicular cell, carcinoma | 1 (2%) | | | 1 (2%) |

**TABLE A1**
**Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **General Body System** | | | | |
| Peritoneum | | (1) | (2) | (2) |
| **Genital System** | | | | |
| Epididymis | (50) | (50) | (49) | (50) |
| Preputial gland | (50) | (50) | (49) | (50) |
| Adenoma | 1 (2%) | | | |
| Carcinoma | 1 (2%) | 2 (4%) | 1 (2%) | 2 (4%) |
| Prostate | (50) | (50) | (49) | (50) |
| Seminal vesicle | (50) | (50) | (49) | (50) |
| Testes | (50) | (50) | (49) | (50) |
| Bilateral, interstitial cell, adenoma | 29 (58%) | 31 (62%) | 30 (61%) | 32 (64%) |
| Interstitial cell, adenoma | 12 (24%) | 14 (28%) | 10 (20%) | 10 (20%) |
| **Hematopoietic System** | | | | |
| Bone marrow | (50) | (50) | (49) | (50) |
| Lymph node | (12) | (7) | (15) | (6) |
| Deep cervical, carcinoma, metastatic, thyroid gland | | 1 (14%) | | |
| Lymph node, bronchial | (24) | (7) | (9) | (21) |
| Carcinoma, metastatic, lung | | | | 1 (5%) |
| Histiocytic sarcoma, metastatic, skin | | 1 (14%) | | |
| Lymph node, mandibular | (1) | (3) | (3) | (1) |
| Carcinoma, metastatic, Zymbal's gland | | 1 (33%) | | |
| Lymph node, mesenteric | (50) | (50) | (49) | (50) |
| Lymph node, mediastinal | (38) | (41) | (46) | (45) |
| Carcinoma, metastatic, lung | | | | 1 (2%) |
| Carcinoma, metastatic, Zymbal's gland | | 1 (2%) | | |
| Histiocytic sarcoma, metastatic, skin | | 1 (2%) | | |
| Sarcoma, metastatic, heart | | | | 1 (2%) |
| Spleen | (50) | (50) | (49) | (50) |
| Thymus | (47) | (46) | (46) | (47) |
| Sarcoma, metastatic, heart | | | | 1 (2%) |
| **Integumentary System** | | | | |
| Mammary gland | (50) | (50) | (49) | (50) |
| Carcinoma | | 2 (4%) | 2 (4%) | 1 (2%) |
| Fibroadenoma | 2 (4%) | 2 (4%) | 3 (6%) | 3 (6%) |
| Skin | (50) | (50) | (49) | (50) |
| Basal cell adenoma | | 1 (2%) | | 3 (6%) |
| Basal cell carcinoma | | | | 1 (2%) |
| Keratoacanthoma | 1 (2%) | | | |
| Squamous cell papilloma | 1 (2%) | | 1 (2%) | 1 (2%) |
| Pinna, neural crest tumor | | 1 (2%) | | |
| Sebaceous gland, adenoma | 1 (2%) | | | |
| Subcutaneous tissue, fibroma | 2 (4%) | 4 (8%) | 2 (4%) | 4 (8%) |
| Subcutaneous tissue, fibrosarcoma | 1 (2%) | | | |
| Subcutaneous tissue, histiocytic sarcoma | | 1 (2%) | | |
| Subcutaneous tissue, lipoma | 1 (2%) | 2 (4%) | 1 (2%) | |
| Subcutaneous tissue, sarcoma | | | | 1 (2%) |
| Subcutaneous tissue, schwannoma benign | | | | 1 (2%) |

**TABLE A1**
**Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Musculoskeletal System** | | | | |
| Bone | (50) | (50) | (49) | (50) |
| Mandible, carcinoma, metastatic, Zymbal's gland | | 1 (2%) | | |
| Mandible, osteosarcoma | 1 (2%) | | | |
| Vertebra, chordoma | | | 1 (2%) | |
| Skeletal muscle | | | (2) | (3) |
| Carcinoma, metastatic, thyroid gland | | | 1 (50%) | |
| Sarcoma, metastatic, skin | | | | 1 (33%) |
| **Nervous System** | | | | |
| Brain | (50) | (50) | (49) | (50) |
| Astrocytoma benign | | | | 1 (2%) |
| **Respiratory System** | | | | |
| Lung | (50) | (50) | (49) | (50) |
| Alveolar/bronchiolar adenoma | | | 1 (2%) | 1 (2%) |
| Alveolar/bronchiolar carcinoma | 1 (2%) | | 1 (2%) | 2 (4%) |
| Carcinoma, metastatic, thyroid gland | | 1 (2%) | 1 (2%) | 1 (2%) |
| Carcinoma, metastatic, Zymbal's gland | | 1 (2%) | | |
| Cholangiocarcinoma, metastatic, liver | | | | 1 (2%) |
| Histiocytic sarcoma, metastatic, skin | | 1 (2%) | | |
| Osteosarcoma, metastatic, bone | 1 (2%) | | | |
| Sarcoma, metastatic, heart | | | | 1 (2%) |
| Pleura | (49) | (50) | (49) | (50) |
| Sarcoma, metastatic, heart | | | | 1 (2%) |
| Trachea | (50) | (49) | (49) | (50) |
| Carcinoma, metastatic, thyroid gland | | | | 1 (2%) |
| **Special Senses System** | | | | |
| Eye | (50) | (49) | (49) | (50) |
| Carcinoma, metastatic, Zymbal's gland | | | | 1 (2%) |
| Zymbal's gland | (44) | (41) | (39) | (46) |
| Carcinoma | 1 (2%) | 2 (5%) | | 2 (4%) |
| **Urinary System** | | | | |
| Kidney | (50) | (50) | (49) | (50) |
| Lipoma | | 1 (2%) | | |
| Sarcoma, metastatic, heart | | | | 1 (2%) |
| Stromal nephroma | | | | 1 (2%) |
| Cortex, renal tubule, adenoma | 1 (2%) | 1 (2%) | 2 (4%) | 2 (4%) |
| Cortex, renal tubule, adenoma, multiple | | | 1 (2%) | |
| Renal tubule, carcinoma | | | | 1 (2%) |
| Urinary bladder | (50) | (49) | (49) | (50) |
| Transitional epithelium, carcinoma | | | | 1 (2%) |

**TABLE A1**
**Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Systemic Lesions** | | | | |
| Multiple organs[b] | (50) | (50) | (50) | (50) |
| Histiocytic sarcoma | | 1 (2%) | | |
| Leukemia mononuclear | 33 (66%) | 31 (62%) | 35 (70%) | 27 (54%) |
| Mesothelioma malignant | 2 (4%) | 2 (4%) | 3 (6%) | 4 (8%) |
| **Neoplasm Summary** | | | | |
| Total animals with primary neoplasms[c] | 50 | 50 | 49 | 50 |
| Total primary neoplasms | 154 | 143 | 145 | 162 |
| Total animals with benign neoplasms | 50 | 50 | 48 | 49 |
| Total benign neoplasms | 110 | 100 | 98 | 109 |
| Total animals with malignant neoplasms | 35 | 34 | 40 | 40 |
| Total malignant neoplasms | 44 | 42 | 47 | 53 |
| Total animals with metastatic neoplasms | 1 | 3 | 2 | 9 |
| Total metastatic neoplasms | 1 | 10 | 2 | 18 |
| Total animals with uncertain neoplasms–benign or malignant | | 1 | | |
| Total uncertain neoplasms | | 1 | | |

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 2 9 6 | 4 0 9 | 4 5 8 | 4 6 5 | 5 3 9 | 6 0 4 | 6 2 5 | 6 3 0 | 6 3 1 | 6 3 9 | 6 4 2 | 6 4 2 | 6 4 6 | 6 5 5 | 6 5 5 | 6 5 6 | 6 6 8 | 6 8 1 | 6 8 4 | 7 1 2 | 7 1 2 | 7 1 8 | 7 2 3 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 2 0 | 0 0 9 | 0 1 9 | 0 3 9 | 0 5 0 | 0 1 4 | 0 2 6 | 0 2 8 | 0 2 5 | 0 2 4 | 0 1 5 | 0 4 7 | 0 1 6 | 0 1 3 | 0 4 6 | 0 4 2 | 0 4 0 | 0 3 1 | 0 2 2 | 0 3 3 | 0 4 4 | 0 1 0 | 0 4 3 | 0 0 2 | 0 0 3 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | | |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | + | + | A | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | A | + | + |
| Intestine small, duodenum | + | + | + | + | A | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | + | + | A | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | A | + | + |
| Intestine small, ileum | + | + | + | + | A | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | A | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular adenoma | | | | | | | | | | | | | | | | | | | | | X | | | | |
| Mesentery | | | | | | | | | | | | | | + | | | | | + | | | + | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Muscularis, lipoma | | | | | | | | | | | | | | | | | | X | | | | | | | |
| Tongue | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tooth | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma malignant | | | | | | | | | | | | | | | | X | | | | | | | | | |
| Pheochromocytoma benign | | X | | | | | | | | | | | | | | | | | | | X | | | | |
| Bilateral, pheochromocytoma benign | | | | | | | | | | | | | | | | | | | | | | | X | | X |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | X | | | | |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | X | | | X | X | | X | X | X | X | | | X | X | X | | X | | X | | | X | X | | X |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | | | | | | | | | | | | | | | | X | X | | | | |
| C-cell, carcinoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Follicular cell, carcinoma | | | | | | | | | | | | | | | | X | | | | | | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | |

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 0 4 | 0 0 5 | 0 0 7 | 0 0 8 | 0 1 1 | 0 1 2 | 0 1 7 | 0 1 8 | 0 2 7 | 0 3 2 | 0 3 4 | 0 3 6 | 0 3 7 | 0 3 8 | 0 4 1 | 0 4 8 | 0 4 9 | 0 1 | 0 0 6 | 0 0 2 | 0 2 3 | 0 2 9 | 0 3 0 | 0 3 5 | 0 4 5 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | X | | | | 1 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hepatocellular adenoma | | X | | | | | | | | | | | | X | | | | | | | | | | | | 3 |
| Mesentery | | + | | | | + | | | + | | + | | + | + | + | | + | | + | | | | | | + | 13 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Muscularis, lipoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Tongue | | | | | | | | | | | + | + | | | | | | | | | | | | | | 2 |
| Tooth | | | | | | | | | | | | | | + | | | | | | | | | | | | 1 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pheochromocytoma malignant | | X | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Pheochromocytoma benign | X | | X | | | X | | | | | | | | X | | X | X | | | | | | X | | X | 10 |
| Bilateral, pheochromocytoma benign | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | X | | | | | X | | | | X | | | | | | | | | | | | | 4 |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | X | | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | | | X | | 35 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| C-cell, adenoma | | | | | | | | | | | | | | | | X | | | | | | | | | | 3 |
| C-cell, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Follicular cell, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 2 9 6 | 4 0 9 | 4 5 8 | 4 6 5 | 5 3 9 | 6 0 4 | 6 2 5 | 6 3 0 | 6 3 1 | 6 3 9 | 6 4 2 | 6 4 2 | 6 4 6 | 6 5 5 | 6 5 5 | 6 5 6 | 6 6 8 | 6 8 1 | 6 8 4 | 7 1 2 | 7 1 2 | 7 1 8 | 7 2 3 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 2 0 | 0 0 9 | 0 1 9 | 0 3 9 | 0 5 0 | 0 1 4 | 0 2 6 | 0 2 8 | 0 2 5 | 0 2 4 | 0 1 5 | 0 4 7 | 0 1 6 | 0 1 3 | 0 4 6 | 0 4 2 | 0 4 0 | 0 3 1 | 0 2 2 | 0 3 3 | 0 4 4 | 0 1 0 | 0 4 3 | 0 0 2 | 0 0 3 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | | + | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Bilateral, interstitial cell, adenoma | | | | | | X | | | | | X | X | X | | | | X | X | | X | X | X | | X | X |
| Interstitial cell, adenoma | | | X | | | | X | | | X | | | | X | | X | | | X | | | | X | | |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | M | | | | | | + | | + | | | | | + | + | | + | | | | | |
| Lymph node, bronchial | M | M | M | M | M | + | M | + | M | M | + | M | M | M | + | + | M | + | M | + | M | M | + | + | + |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | M | + |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Fibroadenoma | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Keratoacanthoma | | | | | | | | | X | | | | | | | | | | | | | | | | |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sebaceous gland, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Subcutaneous tissue, fibroma | | | | | | | | | | | | | | | | | | | | | X | | | | |
| Subcutaneous tissue, fibrosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mandible, osteosarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Osteosarcoma, metastatic, bone | | | | | | | | | | X | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 0 0 4 | 0 0 0 5 | 0 0 0 7 | 0 0 0 8 | 0 0 1 1 | 0 0 1 2 | 0 0 1 7 | 0 0 1 8 | 0 0 2 7 | 0 0 3 2 | 0 0 3 4 | 0 0 3 6 | 0 0 3 7 | 0 0 3 8 | 0 0 4 1 | 0 0 4 8 | 0 0 4 9 | 0 0 1 | 0 0 0 6 | 0 0 2 1 | 0 0 2 3 | 0 0 2 9 | 0 0 3 0 | 0 0 3 5 | 0 0 4 5 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | + | | | | | | | | | | | + | | | | | | | | | | | 3 |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Carcinoma | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Bilateral, interstitial cell, adenoma | X | X | X | X | X | X | X | | | X | X | X | | | X | X | | X | | X | X | X | X | | X | 29 |
| Interstitial cell, adenoma | | | | | | | | X | | | | | X | | | | X | | X | | | | | X | | 12 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | + | | + | + | | | | | | + | | | | + | + | | | | | + | | | | | | 12 |
| Lymph node, bronchial | + | + | M | + | + | + | M | M | + | M | + | M | M | + | + | + | M | M | + | M | M | M | + | + | + | 24 |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | M | M | 1 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node, mediastinal | + | M | M | M | M | M | + | M | + | + | M | + | M | + | + | + | + | + | M | + | + | + | + | + | + | 38 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thymus | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Fibroadenoma | | | | | X | | | | | | | | | | | | | | | | | | | | | 2 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Keratoacanthoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Squamous cell papilloma | | | | | | | | | | | | X | | | | | | | | | | | | | | 1 |
| Sebaceous gland, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, fibroma | | | | | | | X | | | | | | | | | | | | | | | | | | | 2 |
| Subcutaneous tissue, fibrosarcoma | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mandible, osteosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | X | | | | | | | | | | | | | | 1 |
| Osteosarcoma, metastatic, bone | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 2 9 6 | 4 0 9 | 4 5 8 | 4 6 5 | 5 3 9 | 6 0 4 | 6 2 5 | 6 3 0 | 6 3 1 | 6 3 9 | 6 4 2 | 6 4 2 | 6 4 6 | 6 5 5 | 6 5 5 | 6 5 6 | 6 6 8 | 6 8 1 | 6 8 4 | 7 1 2 | 7 1 2 | 7 1 8 | 7 2 3 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 2 0 | 0 0 9 | 0 1 9 | 0 3 9 | 0 5 0 | 0 1 4 | 0 2 6 | 0 2 8 | 0 2 5 | 0 2 4 | 0 1 5 | 0 4 7 | 0 1 6 | 0 1 3 | 0 4 6 | 0 4 2 | 0 4 0 | 0 3 1 | 0 2 2 | 0 3 3 | 0 4 4 | 0 1 0 | 0 4 3 | 0 0 2 | 0 0 3 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lacrimal gland | | | + | | | | | | | | | | | | | | | | | | | | | | |
| Zymbal's gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | M |
| Carcinoma | | | X | | | | | | | | | | | | | | | | | | | | | | |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | X | | | | | | | | | | |
| Urethra | | | | | | | | | | | | | | | | | | | | | | | | | + |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leukemia mononuclear | X | X | | | | X | X | X | X | X | X | X | X | | | X | X | X | | X | X | X | X | X | X |
| Mesothelioma malignant | | | | | | | | | | X | | | | | | | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 00004 | 00005 | 00007 | 00008 | 00011 | 00012 | 00017 | 00018 | 00027 | 00032 | 00034 | 00036 | 00037 | 00038 | 00041 | 00048 | 00049 | 00101 | 00016 | 00021 | 00023 | 00029 | 00030 | 00035 | 00045 | Total Tissues/ Tumors |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lacrimal gland | | | | + | | | | | | | | | | | | | | | | | | | | | | 2 |
| Zymbal's gland | + | M | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | M | + | + | M | + | + | + | 44 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Urethra | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Leukemia mononuclear | X | X | X | X | X | X | | | X | X | | | X | X | X | X | | X | | | | X | | | | 33 |
| Mesothelioma malignant | | | | | | | | | | | | X | | | | | | | | | | | | | | 2 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 4 6 4 | 5 0 9 | 5 0 9 | 5 1 3 | 5 6 9 | 5 9 1 | 6 2 1 | 6 4 2 | 6 4 2 | 6 4 2 | 6 4 8 | 6 5 6 | 6 6 6 | 6 7 5 | 6 8 9 | 6 9 7 | 7 0 5 | 7 0 9 | 7 1 3 | 7 1 9 | 7 2 6 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 0 8 | 2 1 6 | 2 4 6 | 2 1 1 | 2 3 1 | 2 1 9 | 2 4 4 | 2 2 0 | 2 4 0 | 2 4 5 | 2 4 2 | 2 3 6 | 2 2 6 | 2 3 0 | 2 4 1 | 2 0 3 | 2 2 4 | 2 2 3 | 2 1 7 | 2 2 8 | 2 0 2 | 2 0 4 | 2 0 6 | 2 0 7 | 2 1 3 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | A | + | + | + | + | + | + |
| Intestine small, duodenum | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | A | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | A | + | + | + | + | + | + |
| Intestine small, ileum | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | A | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | + | | | | | | | | | + | | + | + | | | | | | + | | |
| Oral mucosa | | | | | | | | | + | | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tooth | | | | | | | | | + | | | | | | | | | | | | | | | |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma complex | | | | | | | | | | | | | | | | | | | | | | | | |
| Pheochromocytoma benign | | | | | | | X | | | X | X | | | X | | | | | | | X | | | |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | X | X | | |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | X | X | | | X | | X | | | X | X | | | X | | X | | X | X | X | X | X | X |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| C-cell, adenoma, multiple | | | | | | | | | | | | | | | | X | | | | | | | | |
| C-cell, carcinoma | | | | | | | X | | | | | | | | | | | | | | | | | |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | X | | | | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 1 8 | 2 1 2 | 2 2 2 | 2 2 5 | 2 2 7 | 2 3 2 | 2 3 3 | 2 3 4 | 2 3 5 | 2 3 7 | 2 3 8 | 2 4 3 | 2 4 8 | 2 4 9 | 2 5 0 | 2 0 1 | 2 0 5 | 2 0 9 | 2 1 0 | 2 1 2 | 2 1 4 | 2 1 5 | 2 2 9 | 2 3 9 | 2 4 7 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Mesentery | | | | | | | | | + | | | | | | | | | + | | + | | | | | + | 9 |
| Oral mucosa | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Tooth | | | + | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pheochromocytoma complex | | | | | | | | | | | | | X | | | | | | | | | | | | | 1 |
| Pheochromocytoma benign | | | | | X | | | | | | | | | | | | | | | | | | | X | X | 8 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | X | | | | | | | | | | | | X | | | | | | 4 |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | 49 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | X | X | X | | X | X | X | X | | | | X | | | X | X | X | X | | | 27 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| C-cell, adenoma | | | | | | | | | X | | | | | | | X | | | | | | | | X | | 3 |
| C-cell, adenoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| C-cell, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | + | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 4 6 4 | 5 0 9 | 5 0 9 | 5 1 3 | 5 6 9 | 5 9 1 | 6 2 1 | 6 4 2 | 6 4 2 | 6 4 2 | 6 4 8 | 6 5 6 | 6 6 6 | 6 7 5 | 6 8 9 | 6 9 7 | 7 0 5 | 7 0 9 | 7 1 3 | 7 1 9 | 7 2 6 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 0 8 | 2 1 6 | 2 4 6 | 2 1 1 | 2 3 1 | 2 1 9 | 2 4 4 | 2 2 0 | 2 4 0 | 2 4 5 | 2 4 2 | 2 3 6 | 2 2 6 | 2 3 0 | 2 4 1 | 2 0 3 | 2 2 4 | 2 2 3 | 2 1 7 | 2 2 8 | 2 0 2 | 2 0 4 | 2 0 6 | 2 0 7 | 2 1 3 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | + | | | | | | | + | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | X | | | | | | | | | | | | | | |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Bilateral, interstitial cell, adenoma | | | | | X | X | X | | | X | | | | X | X | X | X | | | X | | | X | | |
| Interstitial cell, adenoma | X | | | X | | | | X | X | | | X | X | | | | | X | X | | | X | | | X |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | | | | + | | + | | | | + | | | + | | | | | | | | | |
| Deep cervical, carcinoma, metastatic, thyroid gland | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Lymph node, bronchial | M | M | M | M | M | M | M | M | M | M | + | M | M | + | M | M | M | M | M | + | M | M | M | M | M |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mandibular | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M |
| Carcinoma, metastatic, Zymbal's gland | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | M | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, Zymbal's gland | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | X | | | | | | | | | | | | | | | | | X |
| Fibroadenoma | | | | | | | | X | | | | | | | | | | | | | | | | X | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Basal cell adenoma | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Pinna, neural crest tumor | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, fibroma | | | | X | | | | | | | | | X | | | | | | | | | | | | |
| Subcutaneous tissue, histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mandible, carcinoma, metastatic, Zymbal's gland | X | | | | | | | | | | | | | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 1 1 8 | 2 1 2 1 | 2 2 1 2 | 2 2 2 5 | 2 2 3 7 | 2 3 2 2 | 2 3 3 3 | 2 3 3 4 | 2 3 3 5 | 2 3 3 7 | 2 3 3 8 | 2 4 4 3 | 2 4 4 8 | 2 4 4 9 | 2 5 0 0 | 2 0 0 1 | 2 0 0 5 | 2 0 0 9 | 2 1 1 0 | 2 1 1 2 | 2 1 1 4 | 2 1 1 5 | 2 2 2 9 | 2 3 3 9 | 2 4 4 7 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | | X | | | | | | | | | | | | | | 2 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Bilateral, interstitial cell, adenoma | X | X | X | | X | X | X | | X | X | | X | X | X | X | X | X | | X | X | X | X | X | X | X | 31 |
| Interstitial cell, adenoma | | | | X | | | | X | | | X | | | | | | | X | | | | | | | | 14 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | | | | | | | | | + | | | | + | | | | + | | | | | | | | | 7 |
| Deep cervical, carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, bronchial | M | M | M | M | + | M | M | M | M | M | + | + | M | M | M | M | M | M | M | M | M | M | M | + | M | 7 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Lymph node, mandibular | M | M | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 3 |
| Carcinoma, metastatic, Zymbal's gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node, mediastinal | + | M | + | + | + | M | + | + | + | + | + | + | M | M | M | + | + | + | + | + | + | + | + | + | M | 41 |
| Carcinoma, metastatic, Zymbal's gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thymus | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | M | 46 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Fibroadenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Basal cell adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pinna, neural crest tumor | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, fibroma | | | | | | | | | | | | | | X | | | | | | | | | | X | | 4 |
| Subcutaneous tissue, histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Subcutaneous tissue, lipoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 2 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mandible, carcinoma, metastatic, Zymbal's gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 4 6 4 | 5 0 9 | 5 0 9 | 5 1 3 | 5 6 9 | 5 9 1 | 6 2 1 | 6 4 2 | 6 4 2 | 6 4 2 | 6 4 8 | 6 5 6 | 6 6 6 | 6 7 5 | 6 8 9 | 6 9 7 | 7 0 5 | 7 0 9 | 7 1 3 | 7 1 9 | 7 2 6 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 0 8 | 2 1 6 | 2 4 6 | 2 1 1 | 2 3 1 | 2 1 9 | 2 4 4 | 2 2 0 | 2 4 0 | 2 4 5 | 2 4 2 | 2 3 6 | 2 2 6 | 2 3 0 | 2 4 1 | 2 0 3 | 2 2 4 | 2 2 3 | 2 1 7 | 2 2 8 | 2 0 2 | 2 0 4 | 2 0 6 | 2 0 7 | 2 1 3 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, thyroid gland | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Carcinoma, metastatic, Zymbal's gland | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | + | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lacrimal gland | | | | | | | | | | | | | | | | | | | | | | | | | |
| Zymbal's gland | + | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | M | + | + | + | + | + | M | + | + |
| Carcinoma | X | | | | | | | | | | | | | | | | | | | | | | | | X |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lipoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Urinary bladder | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leukemia mononuclear | | | | | X | X | | X | | X | X | X | X | X | | X | | X | | X | X | | X | | X |
| Mesothelioma malignant | | X | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 1 8 | 2 2 1 | 2 2 2 | 2 2 5 | 2 2 7 | 2 3 2 | 2 3 3 | 2 3 4 | 2 3 5 | 2 3 7 | 2 3 8 | 2 4 3 | 2 4 8 | 2 4 9 | 2 5 0 | 2 0 1 | 2 0 5 | 2 0 9 | 2 1 0 | 2 1 2 | 2 1 4 | 2 1 5 | 2 2 9 | 2 3 9 | 2 4 7 | Total Tissues/ Tumors |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Carcinoma, metastatic, Zymbal's gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lacrimal gland | | | | | | | | | | | | | | | | | + | | | | | | | | | 1 |
| Zymbal's gland | + | + | + | M | + | M | + | + | + | + | + | + | + | + | M | + | + | + | M | + | + | + | M | + | + | 41 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lipoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | | | | X | | | | | | | | 1 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Leukemia mononuclear | X | | X | X | | X | | | X | X | X | X | X | X | X | | | X | X | | X | | X | X | X | 31 |
| Mesothelioma malignant | | | | X | | | | | | | | | | | | | | | | | | | | | | 2 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 0 0 9 | 3 6 1 | 4 3 1 | 5 0 9 | 5 0 9 | 5 3 7 | 5 5 0 | 5 5 0 | 5 6 1 | 5 6 5 | 5 6 5 | 5 9 0 | 5 9 3 | 6 0 5 | 6 1 1 | 6 1 9 | 6 2 1 | 6 3 4 | 6 4 2 | 6 4 6 | 6 4 6 | 6 5 2 | 6 5 6 | 6 5 6 | 6 7 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 1 8 | 4 3 4 | 4 4 4 | 4 0 7 | 4 0 2 4 | 4 4 7 | 4 2 2 | 4 3 8 | 4 1 3 | 4 0 9 | 4 1 5 | 4 1 6 | 4 2 0 | 4 1 7 | 4 1 9 | 4 2 8 | 4 4 5 | 4 1 4 | 4 4 1 | 4 3 5 | 4 4 2 | 4 2 6 | 4 0 2 | 4 1 2 | 4 2 9 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | A | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + |
| Intestine large, rectum | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + |
| Intestine large, cecum | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + |
| Intestine small, duodenum | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + |
| Intestine small, jejunum | A | + | A | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | A | + | + | + |
| Intestine small, ileum | A | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + |
| Liver | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | | | | | | | + | | | | | | | | + | + | | | + | + | | + |
| Pancreas | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tongue | | | | | | + | | | | | | | | | | | | | | + | | | | | |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adrenal medulla | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma benign | | | | | | | | | | X | | | | | | | | | | | | | | | |
| Bilateral, pheochromocytoma benign | | | | | | | | | | | | | | | | | | | | | | | | | |
| Islets, pancreatic | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | X | | X | | | | |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid gland | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary gland | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | X | | | | | X | | | | | X | X | | X | X | X | X | X | | X | X | X | X |
| Thyroid gland | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | | | | | | | | | | | | | | X | | | | | | | |
| C-cell, carcinoma | | | | | X | | | | X | | | | | | | | | | | | | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | + | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | + | | | | | | | | | | |
| Epididymis | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Penis | | | | | | | | | | | | | | | | | | | | | | | | | |
| Preputial gland | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Prostate | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Seminal vesicle | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Testes | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Bilateral, interstitial cell, adenoma | | | | | | X | X | | X | X | X | X | | | X | | | X | | | X | X | X | X | |
| Interstitial cell, adenoma | | | X | X | X | | | | | | | | X | | | X | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 6 8 1 | 6 8 4 | 6 9 0 | 6 9 6 | 6 9 7 | 7 0 9 | 7 1 6 | 7 1 8 | 7 2 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 3 1 | 4 0 1 8 | 4 1 0 | 4 3 6 | 4 3 2 | 4 2 3 | 4 4 6 | 4 4 9 | 4 5 0 | 4 0 3 | 4 0 4 | 4 0 6 | 4 1 1 | 4 3 0 | 4 3 3 | 4 3 7 | 4 4 0 | 4 4 3 | 4 0 1 | 4 0 0 5 | 4 2 1 | 4 2 5 | 4 2 7 | 4 3 9 | 4 4 8 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine large, colon | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Intestine large, rectum | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine large, cecum | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, duodenum | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, jejunum | + | + | A | A | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 42 |
| Intestine small, ileum | + | + | A | A | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 43 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Hepatocellular adenoma | | X | | | | | | | | | | | | X | | | | | | | | | | | | 2 |
| Mesentery | + | | + | | | | | | | | + | | | | | | + | | | | | | | | | 10 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Tongue | | | | | | | | | | | | | | | + | | | | | | | | | | | 3 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pheochromocytoma benign | X | X | X | X | | | | X | | | | | | | | | | | | X | X | | | | | 8 |
| Bilateral, pheochromocytoma benign | | | | | | X | | | X | | | | | X | | | | | | | | | | | | 3 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | X | | X | | | | | | | | | | | | | | X | | | | | | | | 5 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | X | | | | | 1 |
| Parathyroid gland | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | | | | X | X | | X | X | X | X | | X | | | X | X | | | X | X | | X | | X | 26 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| C-cell, adenoma | | | | X | | | | | | | | | | | | | | | | X | | | | | | 3 |
| C-cell, carcinoma | | | | | | | | X | | | | | | | | | | | | | | | | | | 3 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | | | | | | | | | | | + | | | | 2 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | | | | | | | | | + | | | 2 |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Penis | | | | | | + | | | | | | | | | | | | | | | | | | | | 1 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Bilateral, interstitial cell, adenoma | | X | X | | X | | X | | X | X | X | X | | X | X | | X | X | X | X | X | X | X | X | X | 30 |
| Interstitial cell, adenoma | X | | | | | X | | | X | | | | X | | | X | | | | | | | | | | 10 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 0 0 9 | 3 6 1 | 4 3 1 | 5 0 9 | 5 0 9 | 5 3 7 | 5 5 0 | 5 5 0 | 5 6 1 | 5 6 5 | 5 6 5 | 5 9 0 | 5 9 3 | 6 0 5 | 6 1 1 | 6 1 9 | 6 2 1 | 6 3 4 | 6 4 2 | 6 4 6 | 6 4 6 | 6 5 2 | 6 5 6 | 6 5 6 | 6 7 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 1 8 | 4 3 4 | 4 4 4 | 4 0 7 | 4 2 4 | 4 4 7 | 4 2 2 | 4 3 8 | 4 1 3 | 4 1 0 | 4 1 5 | 4 1 6 | 4 2 0 | 4 1 7 | 4 1 9 | 4 2 8 | 4 4 5 | 4 1 4 | 4 4 1 | 4 3 5 | 4 4 2 | 4 2 6 | 4 0 2 | 4 1 2 | 4 2 9 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | + | + | | + | | | | + | | + | | + | + | + | | | | + | | + | | |
| Lymph node, bronchial | M | M | M | M | M | M | M | M | M | M | + | M | + | M | + | + | M | M | M | M | M | M | M | M | + |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | + | M | M | M | + | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mesenteric | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | A | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | M |
| Spleen | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | A | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | M |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Fibroadenoma | | | | | | | | | | | | | | | | | X | | X | | | | | | |
| Skin | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, fibroma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Vertebra, chordoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Skeletal muscle | | | | | | | | | + | | | | | | + | | | | | | | | | | |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | X | | | | | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Carcinoma, metastatic, thyroid gland | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Nose | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Zymbal's gland | A | M | + | M | + | + | M | + | + | + | + | + | M | M | + | + | + | + | + | + | + | M | M | + | M |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 6 8 1 | 6 8 4 | 6 9 0 | 6 9 6 | 6 9 7 | 7 0 9 | 7 1 6 | 7 1 8 | 7 2 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 3 1 | 4 0 1 8 | 4 1 0 | 4 3 6 | 4 3 2 | 4 2 3 | 4 4 6 | 4 4 9 | 4 5 0 | 4 0 3 | 4 0 4 | 4 0 6 | 4 1 1 | 4 3 0 | 4 3 3 | 4 3 7 | 4 4 0 | 4 4 3 | 4 0 1 | 4 0 5 | 4 2 1 | 4 2 5 | 4 2 7 | 4 3 9 | 4 4 8 | Total Tissues/ Tumors |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node | + | | | | | + | + | | | | | | | | + | + | | | | | | | | | | 15 |
| Lymph node, bronchial | + | + | M | + | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | 9 |
| Lymph node, mandibular | M | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 3 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node, mediastinal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma | | X | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Fibroadenoma | | | | | | | | | | | | | | | | | | | | | | | | | X | 3 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Squamous cell papilloma | | | | | | | X | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, fibroma | | | | | X | | | | | | | X | | | | | | | | | | | | | | 2 |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Vertebra, chordoma | | | | | | | | | X | | | | | | | | | | | | | | | | | 1 |
| Skeletal muscle | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Alveolar/bronchiolar adenoma | | | | | X | | | | | | | | | | | | | | | | | | | | | 1 |
| Alveolar/bronchiolar carcinoma | | | | | X | | | | | | | | | | | | | | | | | | | | | 1 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Zymbal's gland | + | + | + | + | M | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 39 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 0 0 9 | 3 6 1 | 4 3 1 | 5 0 9 | 5 0 9 | 5 3 7 | 5 5 0 | 5 5 0 | 5 6 1 | 5 6 5 | 5 6 5 | 5 9 0 | 5 9 3 | 6 0 5 | 6 1 1 | 6 1 9 | 6 2 1 | 6 3 4 | 6 4 2 | 6 4 6 | 6 4 6 | 6 5 2 | 6 5 6 | 6 5 6 | 6 7 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 1 8 | 4 3 4 | 4 4 4 | 4 0 7 | 4 2 4 | 4 4 7 | 4 2 2 | 4 3 8 | 4 1 3 | 4 0 9 | 4 1 5 | 4 1 6 | 4 2 0 | 4 1 7 | 4 1 9 | 4 2 8 | 4 4 5 | 4 1 4 | 4 4 1 | 4 3 5 | 4 4 2 | 4 2 6 | 4 0 2 | 4 1 2 | 4 2 9 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cortex, renal tubule, adenoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| Urethra | | | | | | | | | | | | | | | | | | | | | | | | | |
| Urinary bladder | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leukemia mononuclear | | X | | X | X | X | X | X | | X | X | | X | | X | X | X | | X | | X | X | X | X | |
| Mesothelioma malignant | | | | | | | | | X | | | X | | | | | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 681 | 684 | 690 | 696 | 697 | 709 | 716 | 718 | 722 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 43 1 | 40 8 | 41 0 | 43 6 | 43 2 | 42 3 | 44 6 | 44 9 | 45 0 | 50 3 | 00 4 | 00 6 | 01 1 | 43 0 | 43 3 | 43 7 | 44 0 | 44 3 | 40 1 | 00 5 | 02 1 | 42 5 | 42 7 | 43 9 | 44 8 | Total Tissues/ Tumors |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Cortex, renal tubule, adenoma | X | | | | | | | | | | | | | X | | | | | | | | | | | | 2 |
| Cortex, renal tubule, adenoma, multiple | | | | | | | | | X | | | | | | | | | | | | | | | | | 1 |
| Urethra | | | | | | | | | + | | | | | | | | | | | | | | | | | 1 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Leukemia mononuclear | X | X | X | | | X | X | X | | | X | X | | X | X | X | X | X | X | X | | X | | X | X | 35 |
| Mesothelioma malignant | | | | | | | | | | | | | | | | | | | | | | X | | | | 3 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 2 5 4 | 5 0 9 | 5 1 8 | 5 3 7 | 5 5 0 | 5 8 2 | 5 9 8 | 6 1 2 | 6 1 6 | 6 3 1 | 6 3 5 | 6 3 5 | 6 3 9 | 6 4 8 | 6 4 8 | 6 5 5 | 6 5 6 | 6 6 2 | 6 6 3 | 6 6 6 | 6 8 1 | 6 8 3 | 6 8 4 | 6 9 6 | 6 9 8 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 1 4 | 6 2 5 | 6 3 8 | 6 3 3 | 6 4 0 | 6 0 9 | 6 0 5 | 6 3 9 | 6 4 3 | 6 1 0 | 6 0 6 | 6 2 8 | 6 0 8 | 6 0 1 | 6 1 9 | 6 0 3 | 6 0 7 | 6 3 5 | 6 4 4 | 6 0 2 | 6 1 8 | 6 4 6 | 6 3 6 | 6 5 0 | 6 2 3 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Intestine large, colon | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | A | + | + | A |
| Intestine small, duodenum | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + |
| Intestine small, jejunum | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | A |
| Intestine small, ileum | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | A | + | + | A |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cholangiocarcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular adenoma | | | | X | | | | | | | | | | | | X | | | | | X | | | | X |
| Mesentery | | | | | | | + | + | | | | | | | | | | | + | | | | | + | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tongue | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tooth | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Aorta, pulmonary artery, sarcoma, metastatic, heart | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | X | |
| Pericardium, sarcoma | | | X | | | | | | | | | | | | | | | | | | | | | | |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma malignant | | | | | | | | | | | | | | | | | | | X | | | | | | |
| Pheochromocytoma benign | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bilateral, pheochromocytoma benign | | | | | | | | | | | | | | | | | | | | | | | | | |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | X | | X | | | | X | X | X | X | X | | X | X | | X | | X | | X | X | X | X |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| C-cell, carcinoma | | | | | | | | | | | | | | | | | | | | | X | | | | |
| Follicular cell, adenoma | | | | | | X | | | | | | | | | | | | | | | | | | | |
| Follicular cell, carcinoma | | | | | | | | | | | | | | | | | | | | | | | X | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 716 | 724 | 725 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 649 | 617 | 612 | 611 | 620 | 622 | 626 | 629 | 630 | 631 | 632 | 641 | 642 | 648 | 604 | 613 | 615 | 616 | 621 | 624 | 627 | 634 | 637 | 645 | 647 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 45 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 45 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Cholangiocarcinoma | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular adenoma | | | | X | | | X | | | | | | | | | | | | | | | | | | | 6 |
| Mesentery | | + | | | | | | | | | | + | | | | | | | | + | | | | | | 7 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | X | | | | | | | | | | | | | | | 1 |
| Tongue | | | | | | | | | | | | | | | | | | | | | | | + | | | 1 |
| Tooth | | | | | | | | | | | | | | | | | | + | | | | | | | | 1 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Aorta, pulmonary artery, sarcoma, metastatic, heart | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pericardium, sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pheochromocytoma malignant | | | | | | | | | | | | | | X | | | | | | | | | | | | 2 |
| Pheochromocytoma benign | | | X | X | | | | | | | | X | | | X | | | | | X | | | | | X | 6 |
| Bilateral, pheochromocytoma benign | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | X | | | 2 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | X | X | | X | X | X | | | X | X | | X | X | X | X | X | | X | X | X | X | X | | | 32 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| C-cell, adenoma | | X | | | | | X | | | | | X | | | | | | X | | | | | X | | | 5 |
| C-cell, carcinoma | | | | X | | | | | | | | | | | | | | | | | | | X | | | 3 |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Follicular cell, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | + | | | | | + | | | | | | | | | | | | | | 2 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 2 5 4 | 5 0 9 | 5 1 8 | 5 3 7 | 5 5 0 | 5 8 2 | 5 9 8 | 6 1 2 | 6 1 6 | 6 3 1 | 6 3 5 | 6 3 5 | 6 3 9 | 6 4 8 | 6 4 8 | 6 5 5 | 6 5 6 | 6 6 2 | 6 6 3 | 6 6 6 | 6 8 1 | 6 8 3 | 6 8 4 | 6 9 6 | 6 9 8 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 1 4 | 6 2 5 | 6 3 8 | 6 3 3 | 6 4 0 | 6 0 9 | 6 0 5 | 6 3 9 | 6 4 3 | 6 1 0 | 6 0 6 | 6 2 8 | 6 0 8 | 6 0 1 | 6 1 9 | 6 0 3 | 6 0 7 | 6 3 5 | 6 4 4 | 6 0 2 | 6 1 8 | 6 4 6 | 6 3 6 | 6 5 0 | 6 2 3 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Bilateral, interstitial cell, adenoma | | X | | X | | X | | X | X | | | | X | X | | X | | | X | | | | | X | X |
| Interstitial cell, adenoma | | | X | | | | X | | | | | | | | X | | X | | | | X | | X | | |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | | | | | | | | | | | + | | | + | | | + | | | + | | |
| Lymph node, bronchial | + | + | M | M | + | M | + | + | M | + | M | + | M | + | M | M | M | M | + | + | M | M | M | + | + |
| Carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | X | |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | M | + | + | + | + | + | + | + | M |
| Carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | X | |
| Sarcoma, metastatic, heart | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, heart | | | X | | | | | | | | | | | | | | | | | | | | | | |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Fibroadenoma | | | | | | | | | | | | | | | | | X | X | | | | | | | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Basal cell adenoma | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Basal cell carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | X | | | | | |
| Subcutaneous tissue, fibroma | | | | | | | | | | | | | | | | X | | | | | | | | | |
| Subcutaneous tissue, sarcoma | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Subcutaneous tissue, schwannoma benign | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skeletal muscle | + | | | | | | | | | | | | + | | | | | | | | | | | | |
| Sarcoma, metastatic, skin | | | | | | | | | | | | | X | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Astrocytoma benign | | | | | | | | | | | | X | | | | | | | | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 1 6 | 7 2 4 | 7 2 5 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 4 9 | 6 1 7 | 6 1 2 | 6 1 1 | 6 2 0 | 6 2 2 | 6 2 6 | 6 2 9 | 6 3 0 | 6 3 1 | 6 3 2 | 6 4 1 | 6 4 2 | 6 4 8 | 6 0 4 | 6 1 3 | 6 1 5 | 6 1 6 | 6 2 1 | 6 2 4 | 6 2 7 | 6 3 4 | 6 3 7 | 6 4 5 | 6 4 7 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | | | | | | | | + | | | | 1 |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | X | | | | 2 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Bilateral, interstitial cell, adenoma | X | X | X | | X | X | X | X | X | X | X | X | X | | | X | X | X | X | | X | X | X | X | X | 32 |
| Interstitial cell, adenoma | | | | X | | | | | | | | | | X | X | | | | | X | | | | | | 10 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | | | | | | | | | | | + | | | | | | | | | + | | | | | | 6 |
| Lymph node, bronchial | + | M | + | + | M | + | M | M | + | M | + | M | M | + | + | M | M | M | M | M | + | M | M | M | M | 21 |
| Carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | M | M | 1 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node, mediastinal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | 45 |
| Carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, heart | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | 47 |
| Sarcoma, metastatic, heart | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Fibroadenoma | | | | | | | | | | | | | | | | | | | | | | | | | X | 3 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Basal cell adenoma | | | | X | | | | | | | | | | | | | | | X | | | | | | | 3 |
| Basal cell carcinoma | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, fibroma | | | | | X | | | | | X | | | | | | | | | | X | | | | | | 4 |
| Subcutaneous tissue, sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, schwannoma benign | | | | | | X | | | | | | | | | | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Skeletal muscle | | | | | | | | | | | | | | | | | | | | | | | | | + | 3 |
| Sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Astrocytoma benign | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 2 5 4 | 5 0 9 | 5 1 8 | 5 3 7 | 5 5 0 | 5 8 2 | 5 9 8 | 6 1 2 | 6 1 6 | 6 3 1 | 6 3 5 | 6 3 5 | 6 3 9 | 6 4 8 | 6 4 8 | 6 5 5 | 6 5 6 | 6 6 2 | 6 6 3 | 6 6 6 | 6 8 1 | 6 8 3 | 6 8 4 | 6 9 6 | 6 9 8 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 1 4 | 6 2 5 | 6 3 8 | 6 3 3 | 6 4 0 | 6 0 9 | 6 0 5 | 6 3 9 | 6 4 3 | 6 1 0 | 6 0 6 | 6 2 8 | 6 0 8 | 6 0 1 | 6 1 9 | 6 0 3 | 6 0 7 | 6 3 5 | 6 4 4 | 6 0 2 | 6 1 8 | 6 4 6 | 6 3 6 | 6 5 0 | 6 2 3 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | X | | | | | X | | |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | X | | | | |
| Cholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sarcoma, metastatic, heart | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mesothelioma malignant, metastatic, peritoneum | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sarcoma, metastatic, heart | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | X | | |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, Zymbal's gland | | | | | | | | | | | | | | | | | | | | | | | | | |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lacrimal gland | | | | | | | | | | | | | | | | | | + | | | | | | | |
| Zymbal's gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, heart | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Stromal nephroma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | | | X | | | |
| Renal tubule, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Urethra | | | | | | | | | | | | | | | | | | | | | | | | | |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Transitional epithelium, carcinoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leukemia mononuclear | X | X | | X | | X | X | X | | | | | | X | | X | X | | | X | | | | X | X |
| Mesothelioma malignant | | | | | | | | | | | | | | | | | | X | X | | | | | | |

**TABLE A2**
**Individual Animal Tumor Pathology of Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 716 | 724 | 725 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 64 49 | 61 17 | 61 12 | 61 21 | 62 20 | 62 02 | 62 26 | 62 69 | 63 30 | 63 31 | 63 32 | 64 41 | 64 42 | 64 48 | 60 44 | 61 43 | 61 15 | 61 16 | 62 21 | 62 24 | 62 27 | 63 34 | 63 37 | 64 45 | 64 47 | Total Tissues/ Tumors |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | | | | | | | | | | | X | | | 1 |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Cholangiocarcinoma, metastatic, liver | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, heart | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mesothelioma malignant, metastatic, peritoneum | | | | | | | | | | | | X | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, heart | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | + | 1 |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, Zymbal's gland | | | | | | X | | | | | | | | | | | | | | | | | | | | 1 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lacrimal gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Zymbal's gland | M | + | + | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | M | + | + | + | + | + | 46 |
| Carcinoma | | | | | | X | | | | | | | | | | | | X | | | | | | | | 2 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Sarcoma, metastatic, heart | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Stromal nephroma | | | | | | | | | | | | | | | | | | X | | | | | | | | 1 |
| Cortex, renal tubule, adenoma | | | | X | | | | | | | | | | | | | | | | | | | | | | 2 |
| Renal tubule, carcinoma | | | | | | | | | | | | | | | | | X | | | | | | | | | 1 |
| Urethra | | + | | | | | | + | | | | | | | | | | | | | | | | | | 2 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Transitional epithelium, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Leukemia mononuclear | X | X | | | X | | | X | X | X | X | | X | | | X | X | | X | X | | X | | X | X | 27 |
| Mesothelioma malignant | | | | | | | X | | | | | X | | | | | | | | | | | | | | 4 |

**TABLE A3**
**Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Adrenal Medulla: Benign Pheochromocytoma** | | | | |
| Overall rate[a] | 12/50 (24%) | 8/50 (16%) | 11/49 (22%) | 7/50 (14%) |
| Adjusted rate[b] | 28.1% | 17.9% | 28.8% | 17.2% |
| Terminal rate[c] | 9/27 (33%) | 3/29 (10%) | 3/16 (19%) | 5/22 (23%) |
| First incidence (days) | 409 | 621 | 565 | 724 |
| Poly-3 test[d] | P=0.247N | P=0.189N | P=0.570 | P=0.173N |
| **Adrenal Medulla: Benign, Complex, or Malignant Pheochromocytoma** | | | | |
| Overall rate | 14/50 (28%) | 9/50 (18%) | 11/49 (22%) | 9/50 (18%) |
| Adjusted rate | 32.6% | 20.2% | 28.8% | 22.0% |
| Terminal rate | 10/27 (37%) | 4/29 (14%) | 3/16 (19%) | 6/22 (27%) |
| First incidence (days) | 409 | 621 | 565 | 663 |
| Poly-3 test | P=0.321N | P=0.138N | P=0.450N | P=0.195N |
| **Kidney (Renal Tubule): Adenoma (Single Sections)** | | | | |
| Overall rate | 1/50 (2%) | 1/50 (2%) | 3/49 (6%) | 2/50 (4%) |
| Adjusted rate | 2.4% | 2.3% | 8.1% | 4.9% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 1/16 (6%) | 1/22 (5%) |
| First incidence (days) | 655 | 729 (T) | 681 | 683 |
| Poly-3 test | P=0.423 | P=0.754N | P=0.260 | P=0.490 |
| **Kidney (Renal Tubule): Adenoma (Step Sections)** | | | | |
| Overall rate | 0/50 (0%) | 1/50 (2%) | 3/49 (6%) | 2/50 (4%) |
| Adjusted rate | 0.0% | 2.3% | 8.0% | 4.9% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 0/16 (0%) | 1/22 (5%) |
| First incidence (days) | —[e] | 729 (T) | 509 | 725 |
| Poly-3 test | P=0.293 | P=0.508 | P=0.100 | P=0.231 |
| **Kidney (Renal Tubule): Adenoma (Single and Step Sections)** | | | | |
| Overall rate | 1/50 (2%) | 2/50 (4%) | 5/49 (10%) | 4/50 (8%) |
| Adjusted rate | 2.4% | 4.6% | 13.2% | 9.8% |
| Terminal rate | 0/27 (0%) | 2/29 (7%) | 1/16 (6%) | 2/22 (9%) |
| First incidence (days) | 655 | 729 (T) | 509 | 683 |
| Poly-3 test | P=0.192 | P=0.511 | P=0.077 | P=0.169 |
| **Kidney (Renal Tubule): Adenoma or Carcinoma (Single Sections)** | | | | |
| Overall rate | 1/50 (2%) | 1/50 (2%) | 3/49 (6%) | 3/50 (6%) |
| Adjusted rate | 2.4% | 2.3% | 8.1% | 7.3% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 1/16 (6%) | 2/22 (9%) |
| First incidence (days) | 655 | 729 (T) | 681 | 683 |
| Poly-3 test | P=0.214 | P=0.754N | P=0.260 | P=0.295 |
| **Kidney (Renal Tubule): Adenoma or Carcinoma (Step Sections)** | | | | |
| Overall rate | 0/50 (0%) | 1/50 (2%) | 3/49 (6%) | 2/50 (4%) |
| Adjusted rate | 0.0% | 2.3% | 8.0% | 4.9% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 0/16 (0%) | 1/22 (5%) |
| First incidence (days) | — | 729 (T) | 509 | 725 |
| Poly-3 test | P=0.293 | P=0.508 | P=0.100 | P=0.231 |
| **Kidney (Renal Tubule): Adenoma or Carcinoma (Single and Step Sections)** | | | | |
| Overall rate | 1/50 (2%) | 2/50 (4%) | 5/49 (10%) | 5/50 (10%) |
| Adjusted rate | 2.4% | 4.6% | 13.2% | 12.2% |
| Terminal rate | 0/27 (0%) | 2/29 (7%) | 1/16 (6%) | 3/22 (14%) |
| First incidence (days) | 655 | 729 (T) | 509 | 683 |
| Poly-3 test | P=0.091 | P=0.511 | P=0.077 | P=0.094 |

**TABLE A3**
**Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Liver: Hepatocellular Adenoma** | | | | |
| Overall rate | 3/50 (6%) | 0/50 (0%) | 2/49 (4%) | 6/50 (12%) |
| Adjusted rate | 7.2% | 0.0% | 5.4% | 14.3% |
| Terminal rate | 2/27 (7%) | 0/29 (0%) | 1/16 (6%) | 2/22 (9%) |
| First incidence (days) | 712 | — | 684 | 537 |
| Poly-3 test | P=0.022 | P=0.112N | P=0.556N | P=0.241 |
| **Lung: Alveolar/bronchiolar Adenoma or Carcinoma** | | | | |
| Overall rate | 1/50 (2%) | 0/50 (0%) | 1/49 (2%) | 3/50 (6%) |
| Adjusted rate | 2.4% | 0.0% | 2.7% | 7.3% |
| Terminal rate | 1/27 (4%) | 0/29 (0%) | 0/16 (0%) | 1/22 (5%) |
| First incidence (days) | 729 (T) | — | 697 | 662 |
| Poly-3 test | P=0.075 | P=0.492N | P=0.733 | P=0.299 |
| **Mammary Gland: Fibroadenoma** | | | | |
| Overall rate | 2/50 (4%) | 2/50 (4%) | 3/50 (6%) | 3/50 (6%) |
| Adjusted rate | 4.8% | 4.6% | 8.0% | 7.3% |
| Terminal rate | 2/27 (7%) | 1/29 (3%) | 1/16 (6%) | 1/22 (5%) |
| First incidence (days) | 729 (T) | 642 | 621 | 656 |
| Poly-3 test | P=0.413 | P=0.678N | P=0.451 | P=0.494 |
| **Mammary Gland: Fibroadenoma or Carcinoma** | | | | |
| Overall rate | 2/50 (4%) | 3/50 (6%) | 5/50 (10%) | 4/50 (8%) |
| Adjusted rate | 4.8% | 6.9% | 13.1% | 9.7% |
| Terminal rate | 2/27 (7%) | 2/29 (7%) | 1/16 (6%) | 1/22 (5%) |
| First incidence (days) | 729 (T) | 642 | 593 | 656 |
| Poly-3 test | P=0.354 | P=0.521 | P=0.179 | P=0.332 |
| **Pancreatic Islets: Adenoma** | | | | |
| Overall rate | 4/50 (8%) | 4/50 (8%) | 5/49 (10%) | 0/50 (0%) |
| Adjusted rate | 9.6% | 9.2% | 13.3% | 0.0% |
| Terminal rate | 3/27 (11%) | 3/29 (10%) | 1/16 (6%) | 0/22 (0%) |
| First incidence (days) | 712 | 726 | 642 | — |
| Poly-3 test | P=0.046N | P=0.624N | P=0.435 | P=0.063N |
| **Pancreatic Islets: Adenoma or Carcinoma** | | | | |
| Overall rate | 4/50 (8%) | 4/50 (8%) | 6/49 (12%) | 1/50 (2%) |
| Adjusted rate | 9.6% | 9.2% | 15.9% | 2.5% |
| Terminal rate | 3/27 (11%) | 3/29 (10%) | 2/16 (13%) | 1/22 (5%) |
| First incidence (days) | 712 | 726 | 642 | 729 (T) |
| Poly-3 test | P=0.124N | P=0.624N | P=0.304 | P=0.186N |
| **Pituitary Gland (Unspecified Site): Adenoma** | | | | |
| Overall rate | 35/50 (70%) | 27/50 (54%) | 26/49 (53%) | 32/50 (64%) |
| Adjusted rate | 74.8% | 58.2% | 61.7% | 70.5% |
| Terminal rate | 21/27 (78%) | 16/29 (55%) | 9/16 (56%) | 15/22 (68%) |
| First incidence (days) | 296 | 509 | 431 | 518 |
| Poly-3 test | P=0.382 | P=0.060N | P=0.121N | P=0.404N |
| **Skin: Basal Cell Adenoma** | | | | |
| Overall rate | 0/50 (0%) | 1/50 (2%) | 0/50 (0%) | 3/50 (6%) |
| Adjusted rate | 0.0% | 2.3% | 0.0% | 7.4% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 0/16 (0%) | 2/22 (9%) |
| First incidence (days) | — | 729 (T) | —[f] | 698 |
| Poly-3 test | P=0.038 | P=0.508 | — | P=0.114 |

**TABLE A3**
**Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Skin: Basal Cell Adenoma or Carcinoma** | | | | |
| Overall rate | 0/50 (0%) | 1/50 (2%) | 0/50 (0%) | 4/50 (8%) |
| Adjusted rate | 0.0% | 2.3% | 0.0% | 9.8% |
| Terminal rate | 0/27 (0%) | 1/29 (3%) | 0/16 (0%) | 2/22 (9%) |
| First incidence (days) | — | 729 (T) | — | 698 |
| Poly-3 test | P=0.009 | P=0.508 | — | P=0.057 |
| **Skin: Squamous Cell Papilloma, Keratoacanthoma, Basal Cell Adenoma, or Basal Cell Carcinoma** | | | | |
| Overall rate | 2/50 (4%) | 1/50 (2%) | 1/50 (2%) | 5/50 (10%) |
| Adjusted rate | 4.8% | 2.3% | 2.7% | 12.2% |
| Terminal rate | 1/27 (4%) | 1/29 (3%) | 0/16 (0%) | 2/22 (9%) |
| First incidence (days) | 631 | 729 (T) | 716 | 666 |
| Poly-3 test | P=0.040 | P=0.490N | P=0.546N | P=0.205 |
| **Skin (Subcutaneous Tissue): Fibroma** | | | | |
| Overall rate | 2/50 (4%) | 4/50 (8%) | 2/50 (4%) | 4/50 (8%) |
| Adjusted rate | 4.8% | 9.0% | 5.4% | 9.8% |
| Terminal rate | 1/27 (4%) | 2/29 (7%) | 1/16 (6%) | 3/22 (14%) |
| First incidence (days) | 712 | 513 | 697 | 655 |
| Poly-3 test | P=0.359 | P=0.363 | P=0.649 | P=0.327 |
| **Skin (Subcutaneous Tissue): Fibroma, Fibrosarcoma, or Sarcoma** | | | | |
| Overall rate | 3/50 (6%) | 4/50 (8%) | 2/50 (4%) | 5/50 (10%) |
| Adjusted rate | 7.2% | 9.0% | 5.4% | 12.1% |
| Terminal rate | 2/27 (7%) | 2/29 (7%) | 1/16 (6%) | 3/22 (14%) |
| First incidence (days) | 712 | 513 | 697 | 639 |
| Poly-3 test | P=0.283 | P=0.531 | P=0.557N | P=0.348 |
| **Testes: Adenoma** | | | | |
| Overall rate | 41/50 (82%) | 45/50 (90%) | 40/49 (82%) | 42/50 (84%) |
| Adjusted rate | 89.3% | 93.0% | 87.5% | 89.8% |
| Terminal rate | 25/27 (93%) | 28/29 (97%) | 16/16 (100%) | 22/22 (100%) |
| First incidence (days) | 458 | 464 | 431 | 509 |
| Poly-3 test | P=0.529N | P=0.377 | P=0.527N | P=0.616 |
| **Thyroid Gland (C-Cell): Adenoma** | | | | |
| Overall rate | 3/50 (6%) | 4/50 (8%) | 3/49 (6%) | 5/50 (10%) |
| Adjusted rate | 7.2% | 9.2% | 8.0% | 12.3% |
| Terminal rate | 1/27 (4%) | 3/29 (10%) | 1/16 (6%) | 4/22 (18%) |
| First incidence (days) | 712 | 697 | 634 | 724 |
| Poly-3 test | P=0.299 | P=0.520 | P=0.608 | P=0.340 |
| **Thyroid Gland (C-Cell): Carcinoma** | | | | |
| Overall rate | 1/50 (2%) | 1/50 (2%) | 3/49 (6%) | 3/50 (6%) |
| Adjusted rate | 2.4% | 2.3% | 7.9% | 7.3% |
| Terminal rate | 0/27 (0%) | 0/29 (0%) | 0/16 (0%) | 2/22 (9%) |
| First incidence (days) | 668 | 621 | 509 | 681 |
| Poly-3 test | P=0.213 | P=0.752N | P=0.270 | P=0.295 |
| **Thyroid Gland (C-Cell): Adenoma or Carcinoma** | | | | |
| Overall rate | 4/50 (8%) | 5/50 (10%) | 6/49 (12%) | 7/50 (14%) |
| Adjusted rate | 9.5% | 11.4% | 15.6% | 17.1% |
| Terminal rate | 1/27 (4%) | 3/29 (10%) | 1/16 (6%) | 5/22 (23%) |
| First incidence (days) | 668 | 621 | 509 | 681 |
| Poly-3 test | P=0.216 | P=0.526 | P=0.313 | P=0.241 |

**TABLE A3**
**Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **All Organs: Mononuclear Cell Leukemia** | | | | |
| Overall rate | 33/50 (66%) | 31/50 (62%) | 35/50 (70%) | 27/50 (54%) |
| Adjusted rate | 69.9% | 67.0% | 76.7% | 59.1% |
| Terminal rate | 16/27 (59%) | 19/29 (66%) | 12/16 (75%) | 13/22 (59%) |
| First incidence (days) | 296 | 569 | 361 | 254 |
| Poly-3 test | P=0.121N | P=0.466N | P=0.300 | P=0.183N |
| **All Organs: Malignant Mesothelioma** | | | | |
| Overall rate | 2/50 (4%) | 2/50 (4%) | 3/50 (6%) | 4/50 (8%) |
| Adjusted rate | 4.8% | 4.5% | 7.9% | 9.7% |
| Terminal rate | 1/27 (4%) | 1/29 (3%) | 1/16 (6%) | 2/22 (9%) |
| First incidence (days) | 639 | 509 | 561 | 662 |
| Poly-3 test | P=0.227 | P=0.678N | P=0.451 | P=0.327 |
| **All Organs: Benign Neoplasms** | | | | |
| Overall rate | 50/50 (100%) | 50/50 (100%) | 48/50 (96%) | 49/50 (98%) |
| Adjusted rate | 100.0% | 100.0% | 99.8% | 99.9% |
| Terminal rate | 27/27 (100%) | 29/29 (100%) | 16/16 (100%) | 22/22 (100%) |
| First incidence (days) | 296 | 464 | 431 | 509 |
| Poly-3 test | P=1.000N | — | P=1.000N | P=1.000N |
| **All Organs: Malignant Neoplasms** | | | | |
| Overall rate | 35/50 (70%) | 34/50 (68%) | 40/50 (80%) | 40/50 (80%) |
| Adjusted rate | 73.0% | 70.8% | 85.5% | 84.2% |
| Terminal rate | 17/27 (63%) | 19/29 (66%) | 13/16 (81%) | 20/22 (91%) |
| First incidence (days) | 296 | 464 | 361 | 254 |
| Poly-3 test | P=0.079 | P=0.492N | P=0.096 | P=0.128 |
| **All Organs: Benign or Malignant Neoplasms** | | | | |
| Overall rate | 50/50 (100%) | 50/50 (100%) | 49/50 (98%) | 50/50 (100%) |
| Adjusted rate | 100.0% | 100.0% | 100.0% | 100.0% |
| Terminal rate | 27/27 (100%) | 29/29 (100%) | 16/16 (100%) | 22/22 (100%) |
| First incidence (days) | 296 | 464 | 361 | 254 |
| Poly-3 test | P=1.000 | — | P=1.000N | — |

(T) Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, kidney, liver, lung, pancreatic islets, pituitary gland, testes, and thyroid gland; for other tissues, denominator is number of animals necropsied.
[b] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the chamber control incidence is the P value associated with the trend test. Beneath the exposed group incidence are the P values corresponding to pairwise comparisons between the chamber controls and that exposed group. The Poly-3 test accounts for the differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in an exposed group is indicated by **N**.
[e] Not applicable; no neoplasms in animal group
[f] Value of statistic cannot be computed.

**TABLE A4a**
**Historical Incidence of Renal Tubule Neoplasms in Control Male F344/N Rats**[a]

| Study | Incidence in Controls | | |
|---|---|---|---|
| | Adenoma | Carcinoma | Adenoma or Carcinoma |
| **Historical Incidence: Inhalation Studies** | | | |
| Decalin | 1/50 | 0/50 | 1/50 |
| Indium phosphide | 0/50 | 0/50 | 0/50 |
| Naphthalene | 0/49 | 0/49 | 0/49 |
| Propylene glycol mono-*t*-butyl ether | 1/50 | 0/50 | 1/50 |
| Stoddard solvent IIC | 0/50 | 1/50 | 1/50 |
| Vanadium pentoxide | 1/50 | 0/50 | 1/50 |
| **Overall Historical Incidence: Inhalation Studies** | | | |
| Total (%) | 3/299 (1.0%) | 1/299 (0.3%) | 4/299 (1.3%) |
| Mean ± standard deviation | 1.0% ± 1.1% | 0.3% ± 0.8% | 1.3% ± 1.0% |
| Range | 0%-2% | 0%-2% | 0%-2% |
| **Overall Historical Incidence** | | | |
| Total (%) | 4/1,055 (0.4%) | 1/1,055 (0.1%) | 5/1,055 (0.5%) |
| Mean ± standard deviation | 0.5% ± 0.9% | 0.1% ± 0.5% | 0.6% ± 0.9% |
| Range | 0%-2% | 0%-2% | 0%-2% |

[a] Data as of March 3, 2003

**TABLE A4b**
**Historical Incidence of Urinary Bladder Neoplasms in Control Male F344/N Rats**[a]

| Study | Incidence in Controls | |
|---|---|---|
| | Carcinoma | Papilloma |
| **Historical Incidence: Inhalation Studies** | | |
| Decalin | 0/50 | 0/50 |
| Indium phosphide | 0/50 | 0/50 |
| Naphthalene | 0/48 | 1/48 |
| Propylene glycol mono-*t*-butyl ether | 0/50 | 0/50 |
| Stoddard solvent IIC | 0/50 | 0/50 |
| Vanadium pentoxide | 0/49 | 0/49 |
| **Overall Historical Incidence: Inhalation Studies** | | |
| Total (%) | 0/297 (0%) | 1/297 (0.3%) |
| Mean ± standard deviation | | 0.4% ± 0.8% |
| Range | | 0%-2% |
| **Overall Historical Incidence** | | |
| Total (%) | 0/1,051 (0%) | 4/1,051 (0.4%) |
| Mean ± standard deviation | | 0.4% ± 0.8% |
| Range | | 0%-2% |

[a] Data as of March 3, 2003

**TABLE A4c**
**Historical Incidence of Hepatocellular Neoplasms in Control Male F344/N Rats**[a]

| Study | Incidence in Controls | |
|---|---|---|
| | Adenoma | Carcinoma |
| **Historical Incidence: Inhalation Studies** | | |
| Decalin | 0/50 | 0/50 |
| Indium phosphide | 0/50 | 0/50 |
| Naphthalene | 1/49 | 1/49 |
| Propylene glycol mono-*t*-butyl ether | 3/50 | 0/50 |
| Stoddard solvent IIC | 0/50 | 0/50 |
| Vanadium pentoxide | 0/50 | 0/50 |
| **Overall Historical Incidence: Inhalation Studies** | | |
| Total (%) | 4/299 (1.3%) | 1/299 (0.3%) |
| Mean ± standard deviation | 1.3% ± 2.4% | 0.3% ± 0.8% |
| Range | 0%-6% | 0%-2% |
| **Overall Historical Incidence** | | |
| Total (%) | 10/1,059 (0.9%) | 5/1,059 (0.5%) |
| Mean ± standard deviation | 0.9% ± 1.6% | 0.5% ± 1.1% |
| Range | 0%-6% | 0%-4% |

[a] Data as of March 3, 2003

**TABLE A5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Moribund | 20 | 15 | 26 | 22 |
| Natural deaths | 3 | 6 | 8 | 6 |
| Survivors | | | | |
| Terminal sacrifice | 27 | 29 | 16 | 22 |
| Animals examined microscopically | 50 | 50 | 50 | 50 |
| **Alimentary System** | | | | |
| Intestine large, rectum | (50) | (48) | (47) | (48) |
| Diverticulum | 1 (2%) | | | |
| Intestine large, cecum | (47) | (47) | (47) | (45) |
| Hemorrhage | | | 1 (2%) | |
| Necrosis | | 1 (2%) | | |
| Intestine small, duodenum | (48) | (47) | (47) | (47) |
| Epithelium, hyperplasia | | | | 1 (2%) |
| Intestine small, jejunum | (47) | (47) | (42) | (46) |
| Epithelium, hyperplasia | | | | 1 (2%) |
| Intestine small, ileum | (47) | (47) | (43) | (45) |
| Epithelium, hyperplasia | | | | 1 (2%) |
| Liver | (50) | (50) | (49) | (50) |
| Basophilic focus | 6 (12%) | 18 (36%) | 15 (31%) | 17 (34%) |
| Clear cell focus | 8 (16%) | 11 (22%) | 11 (22%) | 9 (18%) |
| Degeneration, cystic | 1 (2%) | | 1 (2%) | 3 (6%) |
| Eosinophilic focus | | 1 (2%) | 1 (2%) | 2 (4%) |
| Fatty change | 3 (6%) | | | 1 (2%) |
| Hepatodiaphragmatic nodule | 1 (2%) | 6 (12%) | 11 (22%) | 5 (10%) |
| Necrosis | | | 3 (6%) | 1 (2%) |
| Thrombosis | 1 (2%) | | | |
| Vacuolization cytoplasmic | 3 (6%) | 1 (2%) | 2 (4%) | 1 (2%) |
| Bile duct, cyst | 1 (2%) | | | |
| Bile duct, dilatation | | | 1 (2%) | |
| Bile duct, hyperplasia | | | 1 (2%) | 1 (2%) |
| Hepatocyte, regeneration | | | 1 (2%) | |
| Mesentery | (13) | (9) | (10) | (7) |
| Necrosis | 13 (100%) | 9 (100%) | 10 (100%) | 5 (71%) |
| Thrombosis | | | | 1 (14%) |
| Fat, hemorrhage | | 1 (11%) | | |
| Oral mucosa | | (1) | | |
| Ulcer | | 1 (100%) | | |
| Pancreas | (50) | (50) | (49) | (50) |
| Acinus, atrophy | | 1 (2%) | 1 (2%) | |
| Artery, inflammation | | | | 1 (2%) |
| Stomach, forestomach | (50) | (50) | (49) | (50) |
| Hyperplasia, squamous | 2 (4%) | 1 (2%) | 2 (4%) | 4 (8%) |
| Inflammation, suppurative | 1 (2%) | | | |
| Necrosis | | | 1 (2%) | |
| Ulcer | 3 (6%) | | 3 (6%) | 4 (8%) |

[a] Number of animals examined microscopically at the site and the number of animals with lesion

**TABLE A5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Alimentary System** (continued) | | | | |
| Stomach, glandular | (50) | (50) | (49) | (50) |
| Erosion | | | 3 (6%) | |
| Mineralization | | | 1 (2%) | |
| Necrosis | 1 (2%) | | | 1 (2%) |
| Ulcer | | | 1 (2%) | |
| Epithelium, hyperplasia | | | | 1 (2%) |
| Tongue | (2) | | (3) | (1) |
| Epithelium, hyperplasia | 2 (100%) | | 3 (100%) | 1 (100%) |
| Tooth | (1) | (2) | | (1) |
| Malformation | | 1 (50%) | | |
| Peridontal tissue, inflammation | 1 (100%) | 1 (50%) | | 1 (100%) |
| **Cardiovascular System** | | | | |
| Blood vessel | (50) | (50) | (49) | (50) |
| Pulmonary artery, degeneration, mucoid | | | 1 (2%) | |
| Heart | (50) | (50) | (49) | (50) |
| Cardiomyopathy | 7 (14%) | 6 (12%) | 4 (8%) | 7 (14%) |
| Inflammation, focal, suppurative | | | 1 (2%) | |
| Atrium, thrombosis | 1 (2%) | | 1 (2%) | |
| Myocardium, fibrosis | | 1 (2%) | | |
| Myocardium, necrosis | 1 (2%) | | | |
| **Endocrine System** | | | | |
| Adrenal cortex | (50) | (50) | (49) | (50) |
| Hyperplasia | | 1 (2%) | | 3 (6%) |
| Mineralization | | | 1 (2%) | |
| Necrosis | 1 (2%) | | | |
| Vacuolization cytoplasmic | 6 (12%) | 14 (28%) | 6 (12%) | 9 (18%) |
| Adrenal medulla | (50) | (50) | (49) | (50) |
| Hyperplasia | 6 (12%) | 4 (8%) | 11 (22%) | 9 (18%) |
| Thrombosis | | | 1 (2%) | |
| Islets, pancreatic | (50) | (50) | (49) | (50) |
| Hyperplasia | | | 1 (2%) | 1 (2%) |
| Parathyroid gland | (49) | (49) | (48) | (49) |
| Hyperplasia | 1 (2%) | | | |
| Pituitary gland | (50) | (50) | (49) | (50) |
| Angiectasis | 1 (2%) | 3 (6%) | 1 (2%) | |
| Atrophy | | | | 1 (2%) |
| Cyst | | 1 (2%) | | |
| Hemorrhage | 1 (2%) | 1 (2%) | 2 (4%) | |
| Hyperplasia | 5 (10%) | 2 (4%) | 4 (8%) | 2 (4%) |
| Thyroid gland | (50) | (50) | (49) | (50) |
| C-cell, hyperplasia | 8 (16%) | 4 (8%) | 7 (14%) | 7 (14%) |
| Follicular cell, hyperplasia | 1 (2%) | 1 (2%) | | |
| **General Body System** | | | | |
| None | | | | |

**TABLE A5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Genital System** | | | | |
| Penis | | | (1) | |
| Necrosis | | | 1 (100%) | |
| Preputial gland | (50) | (50) | (49) | (50) |
| Hyperplasia | 2 (4%) | 3 (6%) | 3 (6%) | |
| Inflammation, suppurative | 4 (8%) | | 4 (8%) | |
| Prostate | (50) | (50) | (49) | (50) |
| Hyperplasia | 1 (2%) | 1 (2%) | | 1 (2%) |
| Inflammation, suppurative | 31 (62%) | 24 (48%) | 27 (55%) | 27 (54%) |
| Seminal vesicle | (50) | (50) | (49) | (50) |
| Dilatation | | 1 (2%) | | |
| Inflammation, suppurative | 1 (2%) | | | |
| Epithelium, hyperplasia | 1 (2%) | | | |
| Testes | (50) | (50) | (49) | (50) |
| Bilateral, interstitial cell, hyperplasia | | | 1 (2%) | 1 (2%) |
| Germinal epithelium, atrophy | 20 (40%) | 19 (38%) | 18 (37%) | 20 (40%) |
| Interstitial cell, hyperplasia | 4 (8%) | 3 (6%) | 7 (14%) | 7 (14%) |
| **Hematopoietic System** | | | | |
| Lymph node | (12) | (7) | (15) | (6) |
| Deep cervical, ectasia | | 1 (14%) | | |
| Deep cervical, hyperplasia, lymphoid | 1 (8%) | | | |
| Deep cervical, inflammation | | 1 (14%) | | |
| Deep cervical, inflammation, suppurative | | | | 1 (17%) |
| Pancreatic, ectasia | 1 (8%) | | | |
| Pancreatic, hemorrhage | | | 1 (7%) | |
| Pancreatic, pigmentation | | 1 (14%) | | |
| Lymph node, bronchial | (24) | (7) | (9) | (21) |
| Hemorrhage | | | 1 (11%) | |
| Hyperplasia, lymphoid | | | | 2 (10%) |
| Lymph node, mesenteric | (50) | (50) | (49) | (50) |
| Ectasia | | 1 (2%) | | |
| Fibrosis | | | | 1 (2%) |
| Lymph node, mediastinal | (38) | (41) | (46) | (45) |
| Angiectasis | | 1 (2%) | 1 (2%) | |
| Hyperplasia, lymphoid | 1 (3%) | 1 (2%) | | |
| Spleen | (50) | (50) | (49) | (50) |
| Accessory spleen | 2 (4%) | 3 (6%) | 4 (8%) | 1 (2%) |
| Fibrosis | 5 (10%) | 1 (2%) | 7 (14%) | 4 (8%) |
| Hemorrhage | 1 (2%) | | 1 (2%) | 3 (6%) |
| Necrosis | 1 (2%) | 2 (4%) | 5 (10%) | 1 (2%) |

**TABLE A5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Integumentary System** | | | | |
| Mammary gland | (50) | (50) | (49) | (50) |
| Galactocele | 3 (6%) | 2 (4%) | 2 (4%) | 1 (2%) |
| Metaplasia, squamous | | 1 (2%) | | |
| Epithelium, cyst, squamous | | | | 1 (2%) |
| Skin | (50) | (50) | (49) | (50) |
| Cyst epithelial inclusion | 3 (6%) | 5 (10%) | 3 (6%) | 1 (2%) |
| Hyperkeratosis | 3 (6%) | 1 (2%) | 6 (12%) | 1 (2%) |
| Inflammation, granulomatous | | | | 2 (4%) |
| Ulcer | 1 (2%) | | | 2 (4%) |
| Prepuce, ulcer | | | 1 (2%) | |
| Sebaceous gland, hyperplasia, squamous | 1 (2%) | | | |
| Subcutaneous tissue, hemorrhage | | | | 1 (2%) |
| **Musculoskeletal System** | | | | |
| Bone | (50) | (50) | (49) | (50) |
| Fibrous osteodystrophy | 1 (2%) | | | |
| Cranium, hemorrhage | | | | 1 (2%) |
| Skeletal muscle | | | (2) | (3) |
| Mineralization | | | | 1 (33%) |
| **Nervous System** | | | | |
| Brain | (50) | (50) | (49) | (50) |
| Compression | 7 (14%) | 4 (8%) | 5 (10%) | 3 (6%) |
| Gliosis | | | 1 (2%) | |
| Hemorrhage | 4 (8%) | 4 (8%) | 4 (8%) | 2 (4%) |

**TABLE A5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Respiratory System** | | | | |
| Larynx | (50) | (49) | (48) | (50) |
| Foreign body | 1 (2%) | 2 (4%) | 1 (2%) | 1 (2%) |
| Inflammation, chronic | 1 (2%) | | | 3 (6%) |
| Inflammation, suppurative | | 2 (4%) | 1 (2%) | |
| Epiglottis, hyperplasia | | 1 (2%) | 1 (2%) | 1 (2%) |
| Epiglottis, metaplasia, squamous | | | 1 (2%) | |
| Lung | (50) | (50) | (49) | (50) |
| Hemorrhage | 1 (2%) | 2 (4%) | 1 (2%) | 1 (2%) |
| Inflammation, chronic | 5 (10%) | 2 (4%) | 5 (10%) | 4 (8%) |
| Inflammation, suppurative | | | 1 (2%) | 2 (4%) |
| Necrosis, focal | 1 (2%) | | | |
| Alveolar epithelium, hyperplasia | 6 (12%) | 2 (4%) | 5 (10%) | 6 (12%) |
| Alveolar epithelium, metaplasia, squamous | 1 (2%) | | | 4 (8%) |
| Alveolus, foreign body | | | | 2 (4%) |
| Alveolus, infiltration cellular, histiocyte | 11 (22%) | 3 (6%) | 8 (16%) | 8 (16%) |
| Alveolus, proteinosis | | 1 (2%) | | |
| Artery, mineralization | | | 1 (2%) | |
| Artery, thrombosis | | | 1 (2%) | |
| Interstitium, fibrosis | 5 (10%) | 1 (2%) | 4 (8%) | 6 (12%) |
| Nose | (50) | (49) | (49) | (50) |
| Foreign body | 6 (12%) | 6 (12%) | 4 (8%) | 3 (6%) |
| Hemorrhage | | | | 1 (2%) |
| Inflammation, chronic | | | | 4 (8%) |
| Inflammation, suppurative | 6 (12%) | 10 (20%) | 11 (22%) | 4 (8%) |
| Glands, dilatation | 1 (2%) | 2 (4%) | 7 (14%) | 15 (30%) |
| Goblet cell, hyperplasia | 1 (2%) | 1 (2%) | 2 (4%) | 15 (30%) |
| Nasolacrimal duct, inflammation, suppurative | | 1 (2%) | | 1 (2%) |
| Olfactory epithelium, degeneration, hyaline | | 25 (51%) | 45 (92%) | 50 (100%) |
| Olfactory epithelium, hyperplasia, basal cell | | | | 1 (2%) |
| Respiratory epithelium, hyperplasia | 2 (4%) | 2 (4%) | 4 (8%) | 3 (6%) |
| Respiratory epithelium, metaplasia, squamous | | | 1 (2%) | |
| Pleura | (49) | (50) | (49) | (50) |
| Inflammation, chronic | 6 (12%) | 2 (4%) | 3 (6%) | 7 (14%) |
| Mesothelium, hyperplasia | | | | 2 (4%) |
| Trachea | (50) | (49) | (49) | (50) |
| Glands, cyst | | | 1 (2%) | |
| **Special Senses System** | | | | |
| Ear | | (1) | | (1) |
| Cyst | | 1 (100%) | | |
| Eye | (50) | (49) | (49) | (50) |
| Atrophy | | | | 1 (2%) |
| Hemorrhage | 1 (2%) | | | |
| Anterior chamber, inflammation, suppurative | | | 1 (2%) | |
| Anterior chamber, cornea, inflammation | | | | 1 (2%) |
| Anterior chamber, cornea, inflammation, suppurative | | | | 1 (2%) |
| Cornea, inflammation, suppurative | | | 1 (2%) | |

**TABLE A5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Urinary System** | | | | |
| Kidney | (50) | (50) | (49) | (50) |
| Infarct | | 1 (2%) | | |
| Nephropathy, chronic | 46 (92%) | 50 (100%) | 49 (100%) | 50 (100%) |
| Pigmentation | | | 1 (2%) | |
| Cortex, infarct | 4 (8%) | | | 2 (4%) |
| Cortex, renal tubule, accumulation, hyaline droplet | 1 (2%) | 2 (4%) | 9 (18%) | 17 (34%) |
| Cortex, renal tubule, hyperplasia | | 3 (6%) | 7 (14%) | 19 (38%) |
| Cortex, renal tubule, necrosis | | | 1 (2%) | |
| Papilla, mineralization | | 8 (16%) | 28 (57%) | 41 (82%) |
| Pelvis, dilatation | 1 (2%) | | | |
| Pelvis, inflammation, suppurative | | | 1 (2%) | |
| Pelvis, transitional epithelium, hyperplasia | 2 (4%) | 1 (2%) | 6 (12%) | 15 (30%) |
| Renal tubule, mineralization | 1 (2%) | | | |
| Renal tubule, pigmentation | 1 (2%) | | 2 (4%) | |
| Urethra | (1) | | (1) | (2) |
| Inflammation, suppurative | | | | 1 (50%) |
| Transitional epithelium, hyperplasia | 1 (100%) | | 1 (100%) | 2 (100%) |
| Urinary bladder | (50) | (49) | (49) | (50) |
| Hemorrhage | 1 (2%) | | | |
| Inflammation, chronic | 1 (2%) | | | |
| Inflammation, suppurative | 1 (2%) | | | |
| Necrosis | 1 (2%) | | | |
| Ulcer | 1 (2%) | | | |
| Transitional epithelium, hyperplasia | 3 (6%) | 1 (2%) | 3 (6%) | 6 (12%) |

# APPENDIX B
# SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER


| | | |
|---|---|---|
| TABLE B1 | Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 124 |
| TABLE B2 | Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 128 |
| TABLE B3 | Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 150 |
| TABLE B4 | Historical Incidence of Urinary Bladder Neoplasms in Control Female F344/N Rats . . . . | 153 |
| TABLE B5 | Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 154 |

**TABLE B1**
**Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Moribund | 14 | 12 | 20 | 11 |
| Natural deaths | 3 | 4 | 2 | 3 |
| Survivors | | | | |
| Terminal sacrifice | 33 | 34 | 28 | 36 |
| Animals examined microscopically | 50 | 50 | 50 | 50 |
| **Alimentary System** | | | | |
| Liver | (49) | (50) | (50) | (50) |
| Hepatocellular adenoma | 1 (2%) | | | 2 (4%) |
| Histiocytic sarcoma, metastatic, skin | | | | 1 (2%) |
| Mesentery | (17) | (23) | (10) | (17) |
| Carcinoma, metastatic, ovary | | | 1 (10%) | |
| **Cardiovascular System** | | | | |
| Heart | (50) | (50) | (50) | (50) |
| **Endocrine System** | | | | |
| Adrenal cortex | (49) | (50) | (50) | (50) |
| Adenoma | 2 (4%) | 2 (4%) | 1 (2%) | 4 (8%) |
| Carcinoma | | 2 (4%) | | 1 (2%) |
| Adrenal medulla | (49) | (50) | (50) | (50) |
| Pheochromocytoma malignant | | | | 1 (2%) |
| Pheochromocytoma benign | 2 (4%) | 1 (2%) | | |
| Islets, pancreatic | (49) | (50) | (50) | (50) |
| Adenoma | | 1 (2%) | 1 (2%) | 2 (4%) |
| Carcinoma | 1 (2%) | | | |
| Pituitary gland | (49) | (50) | (50) | (49) |
| Adenoma | 30 (61%) | 36 (72%) | 32 (64%) | 22 (45%) |
| Carcinoma, metastatic, Zymbal's gland | 1 (2%) | | | |
| Thyroid gland | (49) | (50) | (50) | (50) |
| C-cell, adenoma | 8 (16%) | 2 (4%) | 3 (6%) | 4 (8%) |
| C-cell, carcinoma | 2 (4%) | | | |
| Follicular cell, adenoma | | 1 (2%) | | |
| **General Body System** | | | | |
| None | | | | |

**TABLE B1**
**Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Genital System** | | | | |
| Clitoral gland | (50) | (50) | (50) | (50) |
| Adenoma | 1 (2% | | | |
| Carcinoma | 2 (4%) | 2 (4%) | 1 (2%) | |
| Sarcoma, metastatic, vagina | 1 (2%) | | | |
| Ovary | (50) | (50) | (50) | (50) |
| Cystadenocarcinoma | | 1 (2%) | 1 (2%) | |
| Granulosa cell tumor malignant | | | 1 (2%) | |
| Granulosa-theca tumor malignant | 1 (2%) | | | |
| Uterus | (50) | (50) | (50) | (50) |
| Leiomyosarcoma | 1 (2%) | | | |
| Polyp stromal | 5 (10%) | 7 (14%) | 11 (22%) | 6 (12%) |
| Sarcoma stromal | | | 1 (2%) | |
| Bilateral, polyp stromal | | | 1 (2%) | |
| Endometrium, adenoma | | 1 (2%) | | |
| Vagina | (1) | | | |
| Sarcoma | 1 (100%) | | | |
| **Hematopoietic System** | | | | |
| Lymph node | (5) | (3) | (3) | (6) |
| Lymph node, bronchial | (9) | (4) | (10) | (5) |
| Histiocytic sarcoma, metastatic, skin | | | | 1 (20%) |
| Squamous cell carcinoma, metastatic, lung | | | 1 (10%) | |
| Lymph node, mandibular | (1) | (2) | (2) | |
| Lymph node, mesenteric | (50) | (50) | (50) | (50) |
| Lymph node, mediastinal | (43) | (46) | (45) | (43) |
| Histiocytic sarcoma, metastatic, skin | | | | 1 (2%) |
| Squamous cell carcinoma, metastatic, lung | | | 2 (4%) | |
| Spleen | (49) | (50) | (50) | (50) |
| Thymus | (45) | (50) | (50) | (48) |
| **Integumentary System** | | | | |
| Mammary gland | (49) | (50) | (50) | (50) |
| Adenoma | | 2 (4%) | | |
| Carcinoma | 4 (8%) | 4 (8%) | 1 (2%) | 1 (2%) |
| Carcinoma, multiple | 1 (2%) | | | |
| Fibroadenoma | 18 (37%) | 21 (42%) | 17 (34%) | 20 (40%) |
| Fibroadenoma, multiple | 7 (14%) | 8 (16%) | 4 (8%) | 9 (18%) |
| Sarcoma, metastatic, vagina | 1 (2%) | | | |
| Skin | (50) | (50) | (50) | (50) |
| Squamous cell papilloma | | | | 1 (2%) |
| Eyelid, neural crest tumor | | | 1 (2%) | |
| Subcutaneous tissue, fibroma | 1 (2%) | | | |
| Subcutaneous tissue, fibrosarcoma | 1 (2%) | | | 1 (2%) |
| Subcutaneous tissue, fibrous histiocytoma | 1 (2%) | | | |
| Subcutaneous tissue, histiocytic sarcoma | | | | 1 (2%) |
| Subcutaneous tissue, lipoma | | | 1 (2%) | |
| Subcutaneous tissue, liposarcoma | 1 (2%) | | | |
| Subcutaneous tissue, sarcoma, metastatic vagina | 1 (2%) | | | |

**TABLE B1**
**Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Musculoskeletal System** | | | | |
| Skeletal muscle | (1) | | (2) | |
| Fibrous histiocytoma, metastatic, skin | 1 (100%) | | | |
| Squamous cell carcinoma, metastatic, lung | | | 1 (50%) | |
| **Nervous System** | | | | |
| Brain | (49) | (50) | (50) | (50) |
| Carcinoma, metastatic, Zymbal's gland | 1 (2%) | | | |
| Pineal gland, carcinoma | | | 1 (2%) | |
| **Respiratory System** | | | | |
| Lung | (50) | (50) | (50) | (50) |
| Carcinoma, metastatic, thyroid gland | 1 (2%) | | | |
| Carcinoma, metastatic, adrenal cortex | | 1 (2%) | | |
| Histiocytic sarcoma, metastatic, skin | | | | 1 (2%) |
| Sarcoma, metastatic, vagina | 1 (2%) | | | |
| Squamous cell carcinoma | | | 2 (4%) | |
| Alveolus, squamous cell carcinoma, metastatic, lung | | | 1 (2%) | |
| **Special Senses System** | | | | |
| Zymbal's gland | (42) | (44) | (43) | (46) |
| Carcinoma | 2 (5%) | 1 (2%) | 1 (2%) | |
| **Urinary System** | | | | |
| Kidney | (49) | (50) | (50) | (50) |
| Cortex, renal tubule, adenoma | | | | 1 (2%) |
| Urinary bladder | (49) | (50) | (50) | (50) |
| Transitional epithelium, papilloma | | | | 1 (2%) |
| **Systemic Lesions** | | | | |
| Multiple organs[b] | (50) | (50) | (50) | (50) |
| Histiocytic sarcoma | | | | 1 (2%) |
| Leukemia mononuclear | 24 (48%) | 24 (48% | 28 (56%) | 20 (40%) |

**TABLE B1**
**Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Neoplasm Summary** | | | | |
| Total animals with primary neoplasms[c] | 49 | 48 | 50 | 45 |
| Total primary neoplasms | 117 | 116 | 109 | 97 |
| Total animals with benign neoplasms | 41 | 45 | 42 | 41 |
| Total benign neoplasms | 75 | 82 | 71 | 72 |
| Total animals with malignant neoplasms | 33 | 27 | 32 | 23 |
| Total malignant neoplasms | 42 | 34 | 37 | 25 |
| Total animals with metastatic neoplasms | 4 | 1 | 3 | 1 |
| Total metastatic neoplasms | 8 | 1 | 6 | 4 |
| Total animals with uncertain neoplasms–benign or malignant | | | 1 | |
| Total uncertain neoplasms | | | 1 | |

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 1 7 1 | 2 8 4 | 3 8 0 | 4 1 5 | 5 3 7 | 5 5 8 | 5 8 7 | 5 9 3 | 6 2 5 | 6 4 2 | 6 7 0 | 6 8 4 | 6 8 7 | 7 0 2 | 7 0 8 | 7 1 5 | 7 1 8 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 4 5 | 1 3 9 | 1 0 4 | 1 1 8 | 1 0 3 | 1 1 6 | 1 3 1 | 1 4 2 | 1 4 1 | 1 0 6 | 1 1 1 | 1 4 0 | 1 0 5 | 1 0 2 | 1 4 6 | 1 3 5 | 1 3 2 | 1 2 9 | 1 3 0 | 1 3 8 | 1 4 3 | 1 4 8 | 1 0 7 | 1 0 8 | 1 0 9 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + |
| Intestine small, ileum | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular adenoma | | | | | | | | | | | | | | | | | | | | | | X | | | |
| Mesentery | | | | + | + | | + | | + | | | + | | | | | + | | | + | + | | + | | |
| Pancreas | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tongue | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tooth | | | | | | | | | | + | | | | | | | | | | | | | | | |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal medulla | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma benign | | | | | | | | | | | | | | X | | | | | | | | | | | |
| Islets, pancreatic | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | X | | | | | |
| Parathyroid gland | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary gland | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | X | X | | | X | | | | X | X | X | | X | X | | | X | | | X | |
| Carcinoma, metastatic, Zymbal's gland | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Thyroid gland | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | X | | | | | | | X | | | | X | | | | | X | | | X | |
| C-cell, carcinoma | | | | | | | | X | | | | | | | | | | | | | X | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tissue NOS | | | | | | | | | | | | | | | | | | | | | | | | | |

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 1 0 | 1 1 2 | 1 1 3 | 1 1 9 | 1 2 1 | 1 2 3 | 1 2 4 | 1 2 5 | 1 2 7 | 1 3 3 | 1 3 6 | 1 4 4 | 1 4 7 | 1 4 9 | 1 5 0 | 1 0 1 | 1 1 4 | 1 1 5 | 1 1 7 | 1 2 0 | 1 2 2 | 1 2 6 | 1 2 8 | 1 3 4 | 1 3 7 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Hepatocellular adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Mesentery | | | | + | | | + | | | + | + | | | | | | + | | | | + | + | | + | | 17 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Tongue | | | + | | | | | | | | | | | + | | | | | | | | | | | | 2 |
| Tooth | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | | | | | | | | | X | | | | | | | | | | | | | | | X | 2 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pheochromocytoma benign | | | | | | | | X | | | | | | | | | | | | | | | | | | 2 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | X | X | X | X | X | X | | X | | X | X | X | X | X | X | X | | | X | X | X | X | | X | X | 30 |
| Carcinoma, metastatic, Zymbal's gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| C-cell, adenoma | | | | | X | X | | | | | | | | | | | | | | | X | | | | | 8 |
| C-cell, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tissue NOS | | | | | | | | | | | + | | | | | | | | | | | | | | | 1 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 1 7 1 | 2 8 4 | 3 8 0 | 4 1 5 | 5 3 7 | 5 5 8 | 5 8 7 | 5 9 3 | 6 2 5 | 6 4 2 | 6 7 0 | 6 8 4 | 6 8 7 | 7 0 2 | 7 0 8 | 7 1 5 | 7 1 8 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 4 5 | 1 3 9 | 1 0 4 | 1 1 8 | 1 0 3 | 1 1 6 | 1 3 1 | 1 4 2 | 1 4 1 | 1 1 6 | 1 1 1 | 1 4 0 | 1 0 5 | 1 0 2 | 1 4 6 | 1 3 5 | 1 3 2 | 1 2 9 | 1 3 0 | 1 3 8 | 1 4 3 | 1 4 8 | 1 4 7 | 1 0 8 | 1 0 9 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Carcinoma | | | | | | | | | | | | | | X | | | | | | | | | | | |
| Sarcoma, metastatic, vagina | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Granulosa-theca tumor malignant | | | | | | | | | | | | X | | | | | | | | | | | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leiomyosarcoma | | | | | | | | | | | | X | | | | | | | | | | | | | |
| Polyp stromal | | | | | | | | | | | | | | | | | | | | | | | | | |
| Vagina | | | | | + | | | | | | | | | | | | | | | | | | | | |
| Sarcoma | | | | | X | | | | | | | | | | | | | | | | | | | | |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | + | + | | | | | | | | | | | | | + | | | | | | | | | |
| Lymph node, bronchial | M | M | M | + | M | M | + | + | M | M | M | M | M | M | + | M | + | + | M | M | M | M | M | M | M |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | + | + | + | + | + | M | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + |
| Spleen | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | + | A | + | + | M | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Carcinoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fibroadenoma | | | | | | X | | | | | | | | | | | | | X | X | | X | X | | |
| Fibroadenoma, multiple | | | | | | | | | | | | | | | X | | | X | | | | | | X | |
| Sarcoma, metastatic, vagina | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, fibroma | | | | | | | | | | | X | | | | | | | | | | | | | | |
| Subcutaneous tissue, fibrosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, fibrous histiocytoma | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Subcutaneous tissue, liposarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, sarcoma, metastatic, vagina | | | | | X | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skeletal muscle | | | | | | | | | | | | | + | | | | | | | | | | | | |
| Fibrous histiocytoma, metastatic, skin | | | | | | | | | | | | | X | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, Zymbal's gland | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Peripheral nerve | | | | | | | | | | | | + | | | | | | | | | | | | | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 1 0 | 1 1 2 | 1 1 3 | 1 1 9 | 1 2 1 | 1 2 3 | 1 2 4 | 1 2 5 | 1 2 7 | 1 3 3 | 1 3 6 | 1 4 4 | 1 4 7 | 1 4 9 | 1 5 0 | 1 0 1 | 1 1 4 | 1 1 5 | 1 1 7 | 1 2 0 | 1 2 2 | 1 2 6 | 1 2 8 | 1 3 4 | 1 3 7 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Carcinoma | | | | | | | X | | | | | | | | | | | | | | | | | | | | 2 |
| Sarcoma, metastatic, vagina | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Granulosa-theca tumor malignant | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Leiomyosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Polyp stromal | | X | | X | X | | | | | X | | | | | | | | | | | | | X | | | | 5 |
| Vagina | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node | | | | | | | | | | | | | | | | + | + | | | | | | | | | | 5 |
| Lymph node, bronchial | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | + | M | M | + | | 9 |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | | 1 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 50 |
| Lymph node, mediastinal | + | + | + | + | + | M | + | M | + | + | M | + | + | + | M | + | + | + | + | + | + | M | + | + | + | | 43 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 49 |
| Thymus | + | + | + | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | | 45 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 49 |
| Carcinoma | | | | | | X | X | | X | | | | | | | X | | | | | | | | | | 4 |
| Carcinoma, multiple | | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Fibroadenoma | | | X | X | X | | X | | | X | X | | X | | X | X | X | | | | | | X | X | X | | 18 |
| Fibroadenoma, multiple | | X | | | | | | | | | | | | | | | | X | | | X | X | | | | | 7 |
| Sarcoma, metastatic, vagina | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 50 |
| Subcutaneous tissue, fibroma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, fibrosarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, fibrous histiocytoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, liposarcoma | X | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, sarcoma, metastatic, vagina | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 50 |
| Skeletal muscle | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Fibrous histiocytoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 49 |
| Carcinoma, metastatic, Zymbal's gland | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Peripheral nerve | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 1 7 1 | 2 8 4 | 3 8 0 | 4 1 5 | 5 3 7 | 5 5 8 | 5 8 7 | 5 9 3 | 6 2 5 | 6 4 2 | 6 7 0 | 6 8 4 | 6 8 7 | 7 0 2 | 7 0 8 | 7 1 5 | 7 1 8 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 4 5 | 1 3 9 | 1 0 4 | 1 1 8 | 1 0 3 | 1 1 6 | 1 3 1 | 1 4 2 | 1 4 1 | 1 0 6 | 1 1 1 | 1 4 0 | 1 0 5 | 1 0 2 | 1 4 6 | 1 3 5 | 1 3 2 | 1 2 9 | 1 3 0 | 1 3 8 | 1 4 3 | 1 4 8 | 1 0 7 | 1 0 8 | 1 0 9 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, thyroid gland | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Sarcoma, metastatic, vagina | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Zymbal's gland | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | + | + | M | + | + |
| Carcinoma | | X | | X | | | | | | | | | | | | | | | | | | | | | |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leukemia mononuclear | | | X | | | | X | | | X | | X | X | X | X | X | X | X | | | X | X | | | X |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 1 0 | 1 1 2 | 1 1 3 | 1 1 9 | 1 2 1 | 1 2 3 | 1 2 4 | 1 2 5 | 1 2 7 | 1 3 3 | 1 3 6 | 1 4 4 | 1 4 7 | 1 4 9 | 1 5 0 | 1 0 1 | 1 1 4 | 1 1 5 | 1 1 7 | 1 2 0 | 1 2 2 | 1 2 6 | 1 2 8 | 1 3 4 | 1 3 7 | Total Tissues/ Tumors |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, thyroid gland | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, vagina | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | + | | | | | | | | | | | 1 |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Zymbal's gland | + | + | M | + | + | M | + | + | + | + | + | M | + | M | + | + | + | + | + | + | + | M | + | + | + | | 42 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Leukemia mononuclear | | | X | | | | | X | | | | | X | X | X | X | X | X | | | | X | X | X | | | 24 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 4 1 0 | 6 2 1 | 6 4 2 | 6 4 2 | 6 5 6 | 6 5 6 | 6 6 0 | 6 7 6 | 6 8 1 | 6 8 3 | 6 8 4 | 7 0 8 | 7 2 2 | 7 2 5 | 7 2 6 | 7 2 6 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 3 7 | 3 4 7 | 3 4 2 | 3 4 9 | 3 1 1 | 3 4 0 | 3 3 0 | 3 1 5 | 3 2 3 | 3 1 9 | 3 0 6 | 3 1 3 | 3 3 6 | 3 5 0 | 3 1 6 | 3 4 3 | 3 0 1 | 3 0 8 | 3 1 0 | 3 2 2 | 3 3 3 | 3 3 4 | 3 4 8 | 3 0 4 | 3 0 5 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | + | + | + | + | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, ileum | + | + | + | + | + | + | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mesentery | | + | | + | + | + | + | + | + | | | + | | | | | | | | | | + | | + | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Carcinoma | | | | X | | | | | | | | | | | | | | | | | | | | | |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma benign | | | | | | | | | | | | | | | | | | | | | | | | | |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | X | X | | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | | X | X | | | X | |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | | | | | | | | | | | | X | | X | | | | | | | |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | | | | | X | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tissue NOS | | | | + | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cystadenocarcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyp stromal | | | | | | | | | | | | | | | | | X | X | | | | X | | | |
| Endometrium, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 0 0 7 | 3 1 2 | 3 1 4 | 3 2 0 | 3 2 4 | 3 2 5 | 3 2 6 | 3 3 1 | 3 3 2 | 3 3 5 | 3 4 5 | 3 0 2 | 3 0 3 | 3 0 9 | 3 1 7 | 3 1 8 | 3 2 1 | 3 2 7 | 3 2 8 | 3 2 9 | 3 3 8 | 3 3 9 | 3 4 1 | 3 4 4 | 3 4 6 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mesentery | + | + | + | + | + | | | | | | | + | + | | | | + | | | | + | + | + | + | + | 23 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | X | X | | | | | | | | | | | | | | | | | 2 |
| Carcinoma | | | | | | X | | | | | | | | | | | | | | | | | | | | 2 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pheochromocytoma benign | X | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | X | | | | | | | | | | | | | 1 |
| Parathyroid gland | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | X | X | X | X | X | X | X | | X | | | X | | X | | X | X | | X | X | X | X | | | 36 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| C-cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tissue NOS | | | + | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | | X | | | | | | | | | | | | | | 2 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Cystadenocarcinoma | | | | | | | | | | | | | | | | | | | | | | | | | X | 1 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Polyp stromal | X | | X | | | | | | | | | | | | | | | | | | X | X | | | | 7 |
| Endometrium, adenoma | | | | | | | | | | | | | | | | | | | | | | | X | | | 1 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 4 1 0 | 6 2 1 | 6 4 2 | 6 4 2 | 6 5 6 | 6 5 6 | 6 6 0 | 6 7 6 | 6 8 1 | 6 8 3 | 6 8 4 | 7 0 8 | 7 2 2 | 7 2 5 | 7 2 6 | 7 2 6 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 3 7 | 3 4 7 | 3 4 2 | 3 4 9 | 3 1 1 | 3 4 0 | 3 3 0 | 3 1 5 | 3 2 3 | 3 1 9 | 3 0 6 | 3 1 3 | 3 3 6 | 3 5 0 | 3 1 6 | 3 4 3 | 3 0 1 | 3 0 8 | 3 1 0 | 3 2 2 | 3 2 3 | 3 3 4 | 3 4 8 | 3 4 4 | 3 0 5 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | | | | | | | | | | | | | | | | | + | | | | | |
| Lymph node, bronchial | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mandibular | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | + | + | + | + | + | + | + | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | X | | | | | |
| Carcinoma | | | | | X | | | | | X | | | | | | | | | | | | | | | |
| Fibroadenoma | | | X | | | | X | X | | | X | | X | | X | | X | X | X | | | X | X | X | |
| Fibroadenoma, multiple | | | | | X | | | | | | | | | | | X | | | | X | | | | | X |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, adrenal cortex | | | | X | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | + | | | + | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Zymbal's gland | + | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | M | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leukemia mononuclear | | | | X | X | | | X | | X | X | X | | | X | | X | | | X | X | | X | X | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 0 7 | 3 1 2 | 3 1 4 | 3 2 0 | 3 2 4 | 3 2 5 | 3 2 6 | 3 3 1 | 3 3 2 | 3 3 5 | 3 4 5 | 3 0 2 | 3 0 3 | 3 0 9 | 3 1 7 | 3 1 8 | 3 2 1 | 3 2 7 | 3 2 8 | 3 2 9 | 3 3 8 | 3 3 9 | 3 4 1 | 3 4 4 | 3 4 6 | Total Tissues/ Tumors |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | | + | | | | | | | | | + | | | | | | | | | | | | | | | 3 |
| Lymph node, bronchial | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | + | M | + | M | M | 4 |
| Lymph node, mandibular | M | M | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 2 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node, mediastinal | + | + | + | M | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | X | | | | | | | | | | | | | 2 |
| Carcinoma | | | X | | | | | | | | | | | | | | | | | | X | | | | | 4 |
| Fibroadenoma | | X | X | X | | | | X | | X | | X | | | X | | | | | X | | X | | | | 21 |
| Fibroadenoma, multiple | | | | | | | X | | X | | | | | | | | X | | X | | | | | | | 8 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, adrenal cortex | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Zymbal's gland | + | + | + | + | + | + | + | + | M | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | M | 44 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | X | | | | 1 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Leukemia mononuclear | X | X | | | | | | | X | X | X | X | | | | X | | X | X | X | X | X | | | | 24 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 471 | 507 | 509 | 523 | 528 | 559 | 576 | 593 | 610 | 617 | 634 | 637 | 646 | 646 | 670 | 682 | 692 | 698 | 698 | 709 | 712 | 712 | 730 | 730 | 730 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 550 | 526 | 517 | 518 | 528 | 516 | 545 | 536 | 534 | 511 | 515 | 505 | 512 | 543 | 506 | 525 | 520 | 510 | 520 | 532 | 513 | 527 | 529 | 529 | 538 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mesentery | | | + | + | | | | + | | | | | | | | | | | | | | | | | |
| Carcinoma, metastatic, ovary | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | X | X | X | | | | X | X | X | X | X | | X | | X | X | | X | X | X | |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cystadenocarcinoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Granulosa cell tumor malignant | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyp stromal | | | | | | X | | | | | | X | | | X | | | | X | | | | X | | |
| Sarcoma stromal | | | | | | | | | | | | | | | | | | | X | | | | | | |
| Bilateral, polyp stromal | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 5 0 8 | 5 1 4 | 5 1 9 | 5 2 1 | 5 2 3 | 5 2 4 | 5 3 0 | 5 3 7 | 5 3 9 | 5 4 0 | 5 4 1 | 5 4 2 | 5 4 4 | 5 4 6 | 5 4 7 | 5 4 9 | 5 0 1 | 5 0 3 | 5 0 4 | 5 0 7 | 5 2 2 | 5 2 3 | 5 3 3 | 5 3 5 | 5 4 8 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mesentery | + | + | | + | | | + | | | | + | | | | | | | | + | | | | | + | | 10 |
| Carcinoma, metastatic, ovary | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | X | | | | | | | | | | | | | | | | | | | | 1 |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | X | X | X | X | X | | X | X | | X | | | | X | X | | X | X | X | X | X | X | X | | X | 32 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| C-cell, adenoma | | | | | | | | | | X | | | | | | | | | | | | | | X | | 3 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | X | | | | 1 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Cystadenocarcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Granulosa cell tumor malignant | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Polyp stromal | X | | X | | | | | | | | | | | X | | X | | | X | | | | | X | | 11 |
| Sarcoma stromal | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Bilateral, polyp stromal | | | | | | | | | X | | | | | | | | | | | | | | | | | 1 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 471 | 507 | 509 | 523 | 528 | 559 | 576 | 593 | 610 | 617 | 634 | 637 | 646 | 646 | 670 | 682 | 692 | 698 | 698 | 709 | 712 | 712 | 730 | 730 | 730 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 550 | 526 | 517 | 518 | 528 | 516 | 545 | 536 | 534 | 511 | 515 | 505 | 512 | 543 | 506 | 525 | 502 | 510 | 520 | 523 | 513 | 527 | 509 | 529 | 538 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | + | | | | | | | | | + | | | | | | | | | | | | |
| Lymph node, bronchial | + | M | M | M | M | M | M | + | M | + | M | M | M | M | + | M | M | + | + | M | + | + | M | M | M |
| Squamous cell carcinoma, metastatic, lung | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | + | + |
| Squamous cell carcinoma, metastatic, lung | X | | | | | | | | | X | | | | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fibroadenoma | | | | | | | | | X | | | X | X | | X | X | X | | | X | X | X | | | X |
| Fibroadenoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Eyelid, neural crest tumor | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | X | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skeletal muscle | + | | | | | | | + | | | | | | | | | | | | | | | | | |
| Squamous cell carcinoma, metastatic, lung | X | | | | | | | | | | | | | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pineal gland, carcinoma | | | | | | | | | | | | | | | | | | | | | | X | | | |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Squamous cell carcinoma | X | | | | | | | | | X | | | | | | | | | | | | | | | |
| Alveolus, squamous cell carcinoma, metastatic, lung | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | + | + | + | + | + | + |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Zymbal's gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | M | + | + | + | + | M | M | + | + |
| Carcinoma | | | | | | | | | X | | | | | | | | | | | | | | | | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 5 0 8 | 5 1 4 | 5 1 9 | 5 2 1 | 5 2 3 | 5 2 4 | 5 3 0 | 5 3 7 | 5 3 9 | 5 4 0 | 5 4 1 | 5 4 2 | 5 4 4 | 5 4 6 | 5 4 7 | 5 4 9 | 5 0 1 | 5 0 3 | 5 0 4 | 5 0 7 | 5 2 2 | 5 2 1 | 5 3 3 | 5 3 5 | 5 4 8 | Total Tissues/ Tumors |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | | | | | | | | | | | | | | + | | | | | | | | | | | | 3 |
| Lymph node, bronchial | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | M | + | M | M | M | M | M | 10 |
| Squamous cell carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | + | M | M | 2 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node, mediastinal | + | M | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 45 |
| Squamous cell carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | X | | | | | | | | | | | | | | | | | | | 1 |
| Fibroadenoma | X | | | | X | | | | | | | X | | | | X | | | | | X | X | | X | | 17 |
| Fibroadenoma, multiple | | X | | | | | X | | | | | | | | X | | | | X | | | | | | | 4 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Eyelid, neural crest tumor | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Skeletal muscle | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Squamous cell carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pineal gland, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Respiratory system** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Squamous cell carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Alveolus, squamous cell carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Zymbal's gland | + | + | M | + | + | + | + | + | + | M | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | 43 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 471 | 507 | 509 | 523 | 528 | 529 | 576 | 593 | 610 | 617 | 634 | 637 | 646 | 646 | 670 | 682 | 692 | 698 | 698 | 709 | 712 | 712 | 730 | 730 | 730 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 55 0 | 52 6 | 51 7 | 51 8 | 52 8 | 51 6 | 54 5 | 53 6 | 53 4 | 51 1 | 51 5 | 50 5 | 51 2 | 54 3 | 50 6 | 52 5 | 50 2 | 51 0 | 52 0 | 53 2 | 51 3 | 52 7 | 50 9 | 52 9 | 53 8 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leukemia mononuclear | | X | X | X | | X | | X | | X | X | X | X | X | | | X | X | X | X | X | | | | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 5 0 8 | 5 1 4 | 5 1 9 | 5 2 1 | 5 2 3 | 5 2 4 | 5 3 0 | 5 3 7 | 5 3 9 | 5 4 0 | 5 4 1 | 5 4 2 | 5 4 4 | 5 4 6 | 5 4 7 | 5 4 9 | 5 0 1 | 5 0 3 | 5 0 4 | 5 0 7 | 5 2 2 | 5 3 1 | 5 3 3 | 5 3 5 | 5 4 8 | Total Tissues/ Tumors |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Leukemia mononuclear | X | X | X | X | X | X | | X | X | | X | | X | | | | | | | X | | X | | X | | 28 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 2 8 3 | 5 1 9 | 5 5 0 | 5 5 5 | 5 8 6 | 6 1 7 | 6 4 2 | 6 6 9 | 6 7 5 | 6 8 4 | 6 8 4 | 7 1 7 | 7 2 2 | 7 2 6 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 2 4 | 7 4 7 | 7 3 1 | 7 3 5 | 7 2 9 | 7 4 9 | 7 3 6 | 7 0 4 | 7 2 2 | 7 3 2 | 7 4 0 | 7 2 1 | 7 0 1 | 7 0 9 | 7 1 5 | 7 2 0 | 7 2 3 | 7 3 4 | 7 4 1 | 7 4 8 | 7 0 2 | 7 0 3 | 7 0 5 | 7 0 7 | 7 1 0 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | A | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | A | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | A | + | + | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | A | + | + | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | A | + | + | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, ileum | A | + | + | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular adenoma | | | | | | | | | | | | | | X | | | | | | | | | | |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | | | | | + | | | | + | | | | | + | | + | + | + | + | + | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tongue | | | | | | | | | | | | | + | | | | | | | | | | | |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | | + | | | + | + | + | + | + | + | + | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | X | | | | | | | | | | | | | | |
| Carcinoma | | | | | | | | | | | | | | | | | | | X | | | | | |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma malignant | | | | | | | | | | | | | | | X | | | | | | | | | |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid gland | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary gland | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | X | X | | X | X | | X | X | X | | | | X | | X | X | X | | | X |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| C-cell, adenoma | | | | | | | | X | | | | | | | | | | | | | | X | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyp stromal | | | | X | | | | | | | | | | X | | | | | | | X | | | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 1 1 3 | 7 1 1 4 | 7 2 2 6 | 7 2 2 7 | 7 3 3 8 | 7 4 4 3 | 7 5 5 0 | 7 0 0 6 | 7 0 0 8 | 7 1 1 1 | 7 1 1 2 | 7 1 1 6 | 7 1 1 7 | 7 1 1 8 | 7 1 1 9 | 7 2 2 5 | 7 2 2 8 | 7 3 3 0 | 7 3 3 3 | 7 3 3 7 | 7 3 3 9 | 7 4 4 2 | 7 4 4 4 | 7 4 4 5 | 7 4 4 6 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hepatocellular adenoma | | | | | | | | | | | | | | | | | | | | | | | | | X | 2 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| Mesentery | | | | | | | | | + | | | + | + | + | | + | | | + | | | + | | | + | 17 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Tongue | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | X | | | | | | | | X | | | | | | | | | | | X | | | | 4 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pheochromocytoma malignant | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | X | | | | | | | | | | | | X | | | | | | | | | | 2 |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | 48 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | | | X | | | X | | | | X | | X | X | | X | X | | | X | X | | | X | | 22 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| C-cell, adenoma | | | | | | | | | | | | | | | X | X | | | | | | | | | | 4 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Polyp stromal | | | | X | | | | X | | | | | | | | | | | | | | X | | | | 6 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 2 8 3 | 5 1 9 | 5 5 0 | 5 5 5 | 5 8 6 | 6 1 7 | 6 4 2 | 6 6 9 | 6 7 5 | 6 8 4 | 6 8 4 | 7 1 7 | 7 2 2 | 7 2 6 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 2 4 | 7 4 7 | 7 3 1 | 7 3 5 | 7 2 9 | 7 4 9 | 7 3 6 | 7 0 4 | 7 2 2 | 7 3 2 | 7 4 0 | 7 2 1 | 7 0 1 | 7 0 9 | 7 1 5 | 7 2 0 | 7 2 3 | 7 3 4 | 7 4 1 | 7 4 8 | 7 0 2 | 7 0 3 | 7 0 5 | 7 0 7 | 7 1 0 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | + | | | | | | | | | | + | | | | | | | | | + | | |
| Lymph node, bronchial | M | M | M | M | M | + | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | M | + | + | + | + | + | M | + | + | + | + | M | + | + | M | + | + | M | M | + | + | + | + | + | + |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | M | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fibroadenoma | | | | | | | X | | | X | | | | X | | | | X | X | | X | | | | |
| Fibroadenoma, multiple | | | | | | | | X | | | | X | X | | | | X | | | | | X | X | | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Squamous cell papilloma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, fibrosarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | |
| Subcutaneous tissue, histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | + | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lacrimal gland | | | | | | | | | | | | | | | | | + | | | | | | | | |
| Zymbal's gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | M | + | + | + |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 1 3 | 7 1 4 | 7 2 6 | 7 2 7 | 7 3 8 | 7 4 3 | 7 5 0 | 7 0 6 | 7 0 8 | 7 1 1 | 7 1 2 | 7 1 6 | 7 1 7 | 7 1 8 | 7 1 9 | 7 2 5 | 7 2 8 | 7 3 0 | 7 3 3 | 7 3 7 | 7 3 9 | 7 4 2 | 7 4 4 | 7 4 5 | 7 4 6 | Total Tissues/ Tumors |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | | | + | | | | | | | + | | + | | | | | | | | | | | | | | 6 |
| Lymph node, bronchial | M | + | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | + | M | M | M | M | M | M | M | 5 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| Lymph node, mandibular | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node, mediastinal | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | 43 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma | | | | | | | | | | | | X | | | | | | | | | | | | | | 1 |
| Fibroadenoma | | X | | X | | X | X | X | X | X | | X | X | | X | | | | | X | X | | X | | X | 20 |
| Fibroadenoma, multiple | | | X | | X | | | | | | | | | | | | X | | | | | | | | | 9 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, fibrosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, histiocytic sarcoma | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma, metastatic, skin | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pleura | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lacrimal gland | | | | | | | | | | | | + | | | | | | | | | | | | | | 2 |
| Zymbal's gland | + | + | + | M | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 2 8 3 | 5 1 9 | 5 5 0 | 5 5 5 | 5 8 6 | 6 1 7 | 6 4 2 | 6 6 9 | 6 7 5 | 6 8 4 | 6 8 4 | 7 1 7 | 7 2 2 | 7 2 6 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 2 4 | 7 4 7 | 7 3 1 | 7 3 5 | 7 2 9 | 7 4 9 | 7 3 6 | 7 0 4 | 7 0 2 | 7 3 2 | 7 4 0 | 7 2 1 | 7 0 1 | 7 0 9 | 7 1 5 | 7 2 0 | 7 2 3 | 7 3 4 | 7 4 1 | 7 4 8 | 7 0 2 | 7 0 3 | 7 0 5 | 7 0 7 | 7 1 0 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | X | | | | | |
| Urethra | | | | | | | | | | | | | | | | | + | | | | | | | | |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Transitional epithelium, papilloma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leukemia mononuclear | | X | X | X | | X | | X | | X | | | | X | | | X | | | | | X | X | | |

**TABLE B2**
**Individual Animal Tumor Pathology of Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 1 3 | 7 1 4 | 7 2 6 | 7 2 7 | 7 3 8 | 7 4 3 | 7 5 0 | 7 0 6 | 7 0 8 | 7 1 1 | 7 1 2 | 7 1 6 | 7 1 7 | 7 1 8 | 7 1 9 | 7 2 5 | 7 2 8 | 7 3 0 | 7 3 3 | 7 3 7 | 7 3 9 | 7 4 2 | 7 4 4 | 7 4 5 | 7 4 6 | Total Tissues/ Tumors |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Cortex, renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Urethra | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Transitional epithelium, papilloma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| Leukemia mononuclear | X | | X | | | X | | | | X | | X | X | | | X | X | | | | | | X | | X | 20 |

**TABLE B3**
**Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-Butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Adrenal Cortex: Adenoma** | | | | |
| Overall rate[a] | 2/49 (4%) | 2/50 (4%) | 1/50 (2%) | 4/50 (8%) |
| Adjusted rate[b] | 4.7% | 4.3% | 2.4% | 8.8% |
| Terminal rate[c] | 2/33 (6%) | 2/34 (6%) | 1/28 (4%) | 3/36 (8%) |
| First incidence (days) | 730 (T) | 730 (T) | 730 (T) | 684 |
| Poly-3 test[d] | P=0.196 | P=0.662N | P=0.504N | P=0.367 |
| **Clitoral Gland: Adenoma or Carcinoma** | | | | |
| Overall rate | 3/50 (6%) | 2/50 (4%) | 1/50 (2%) | 0/50 (0%) |
| Adjusted rate | 7.0% | 4.3% | 2.4% | 0.0% |
| Terminal rate | 2/33 (6%) | 2/34 (6%) | 1/28 (4%) | 0/36 (0%) |
| First incidence (days) | 702 | 730 (T) | 730 (T) | —[e] |
| Poly-3 test | P=0.100N | P=0.464N | P=0.312N | P=0.109N |
| **Mammary Gland: Fibroadenoma** | | | | |
| Overall rate | 25/50 (50%) | 29/50 (58%) | 21/50 (42%) | 29/50 (58%) |
| Adjusted rate | 57.7% | 60.8% | 47.9% | 63.0% |
| Terminal rate | 23/33 (70%) | 21/34 (62%) | 12/28 (43%) | 23/36 (64%) |
| First incidence (days) | 558 | 642 | 610 | 642 |
| Poly-3 test | P=0.321 | P=0.464 | P=0.236N | P=0.378 |
| **Mammary Gland: Fibroadenoma or Adenoma** | | | | |
| Overall rate | 25/50 (50%) | 30/50 (60%) | 21/50 (42%) | 29/50 (58%) |
| Adjusted rate | 57.7% | 62.9% | 47.9% | 63.0% |
| Terminal rate | 23/33 (70%) | 22/34 (65%) | 12/28 (43%) | 23/36 (64%) |
| First incidence (days) | 558 | 642 | 610 | 642 |
| Poly-3 test | P=0.360 | P=0.382 | P=0.236N | P=0.378 |
| **Mammary Gland: Carcinoma** | | | | |
| Overall rate | 5/50 (10%) | 4/50 (8%) | 1/50 (2%) | 1/50 (2%) |
| Adjusted rate | 11.7% | 8.5% | 2.4% | 2.2% |
| Terminal rate | 5/33 (15%) | 2/34 (6%) | 1/28 (4%) | 1/36 (3%) |
| First incidence (days) | 730 (T) | 656 | 730 (T) | 730 (T) |
| Poly-3 test | P=0.083N | P=0.442N | P=0.104N | P=0.089N |
| **Mammary Gland: Adenoma or Carcinoma** | | | | |
| Overall rate | 5/50 (10%) | 6/50 (12%) | 1/50 (2%) | 1/50 (2%) |
| Adjusted rate | 11.7% | 12.8% | 2.4% | 2.2% |
| Terminal rate | 5/33 (15%) | 4/34 (12%) | 1/28 (4%) | 1/36 (3%) |
| First incidence (days) | 730 (T) | 656 | 730 (T) | 730 (T) |
| Poly-3 test | P=0.045N | P=0.565 | P=0.104N | P=0.089N |
| **Mammary Gland: Fibroadenoma, Adenoma, or Carcinoma** | | | | |
| Overall rate | 27/50 (54%) | 32/50 (64%) | 21/50 (42%) | 29/50 (58%) |
| Adjusted rate | 62.3% | 66.8% | 47.9% | 63.0% |
| Terminal rate | 25/33 (76%) | 23/34 (68%) | 12/28 (43%) | 23/36 (64%) |
| First incidence (days) | 558 | 642 | 610 | 642 |
| Poly-3 test | P=0.540 | P=0.405 | P=0.120N | P=0.559 |
| **Pituitary Gland (Unspecified Site): Adenoma** | | | | |
| Overall rate | 30/49 (61%) | 36/50 (72%) | 32/50 (64%) | 22/49 (45%) |
| Adjusted rate | 67.4% | 72.5% | 70.1% | 47.1% |
| Terminal rate | 23/33 (70%) | 21/34 (62%) | 20/28 (71%) | 15/36 (42%) |
| First incidence (days) | 537 | 410 | 528 | 586 |
| Poly-3 test | P=0.003N | P=0.379 | P=0.482 | P=0.036N |

**TABLE B3**
**Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-Butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Skin (Subcutaneous Tissue): Fibroma, Fibrous Histiocytoma, or Fibrosarcoma** | | | | |
| Overall rate | 3/50 (6%) | 0/50 (0%) | 0/50 (0%) | 1/50 (2%) |
| Adjusted rate | 7.0% | 0.0% | 0.0% | 2.2% |
| Terminal rate | 1/33 (3%) | 0/34 (0%) | 0/28 (0%) | 0/36 (0%) |
| First incidence (days) | 670 | — | — | 684 |
| Poly-3 test | P=0.540N | P=0.106N | P=0.123N | P=0.287N |
| **Thyroid Gland (C-Cell): Adenoma** | | | | |
| Overall rate | 8/49 (16%) | 2/50 (4%) | 3/50 (6%) | 4/50 (8%) |
| Adjusted rate | 18.4% | 4.3% | 7.1% | 8.8% |
| Terminal rate | 5/33 (15%) | 1/34 (3%) | 2/28 (7%) | 3/36 (8%) |
| First incidence (days) | 537 | 726 | 593 | 669 |
| Poly-3 test | P=0.411N | P=0.034N | P=0.103N | P=0.154N |
| **Thyroid Gland (C-Cell): Adenoma or Carcinoma** | | | | |
| Overall rate | 9/49 (18%) | 2/50 (4%) | 3/50 (6%) | 4/50 (8%) |
| Adjusted rate | 20.5% | 4.3% | 7.1% | 8.8% |
| Terminal rate | 5/33 (15%) | 1/34 (3%) | 2/28 (7%) | 3/36 (8%) |
| First incidence (days) | 537 | 726 | 593 | 669 |
| Poly-3 test | P=0.335N | P=0.019N | P=0.065N | P=0.101N |
| **Uterus: Stromal Polyp or Stromal Sarcoma** | | | | |
| Overall rate | 5/50 (10%) | 7/50 (14%) | 12/50 (24%) | 6/50 (12%) |
| Adjusted rate | 11.7% | 15.1% | 27.8% | 13.1% |
| Terminal rate | 5/33 (15%) | 7/34 (21%) | 8/28 (29%) | 4/36 (11%) |
| First incidence (days) | 730 (T) | 730 (T) | 559 | 555 |
| Poly-3 test | P=0.453N | P=0.438 | P=0.052 | P=0.548 |
| **All Organs: Mononuclear Cell Leukemia** | | | | |
| Overall rate | 24/50 (48%) | 24/50 (48%) | 28/50 (56%) | 20/50 (40%) |
| Adjusted rate | 53.3% | 50.3% | 59.3% | 41.9% |
| Terminal rate | 15/33 (46%) | 17/34 (50%) | 13/28 (46%) | 13/36 (36%) |
| First incidence (days) | 380 | 642 | 507 | 519 |
| Poly-3 test | P=0.123N | P=0.469N | P=0.354 | P=0.184N |
| **All Organs: Benign Neoplasms** | | | | |
| Overall rate | 41/50 (82%) | 45/50 (90%) | 42/50 (84%) | 41/50 (82%) |
| Adjusted rate | 90.8% | 90.0% | 89.8% | 85.7% |
| Terminal rate | 31/33 (94%) | 29/34 (85%) | 26/28 (93%) | 30/36 (83%) |
| First incidence (days) | 537 | 410 | 528 | 555 |
| Poly-3 test | P=0.245N | P=0.586N | P=0.580N | P=0.317N |
| **All Organs: Malignant Neoplasms** | | | | |
| Overall rate | 33/50 (66%) | 27/50 (54%) | 32/50 (64%) | 23/50 (46%) |
| Adjusted rate | 69.0% | 56.6% | 66.0% | 48.1% |
| Terminal rate | 20/33 (61%) | 20/34 (59%) | 14/28 (50%) | 16/36 (44%) |
| First incidence (days) | 284 | 642 | 471 | 519 |
| Poly-3 test | P=0.040N | P=0.147N | P=0.465N | P=0.028N |

**TABLE B3**
**Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-Butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **All Organs: Benign or Malignant Neoplasms** | | | | |
| Overall rate | 49/50 (98%) | 48/50 (96%) | 50/50 (100%) | 45/50 (90%) |
| Adjusted rate | 100.0% | 96.0% | 100.0% | 91.7% |
| Terminal rate | 33/33 (100%) | 32/34 (94%) | 28/28 (100%) | 32/36 (89%) |
| First incidence (days) | 284 | 410 | 471 | 519 |
| Poly-3 test | P=0.028N | P=0.245N | P=1.000 | P=0.058N |

(T) Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, clitoral gland, pituitary gland, and thyroid gland; for other tissues, denominator is number of animals necropsied.
[b] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the chamber control incidence is the P value associated with the trend test. Beneath the exposed group incidence are the P values corresponding to pairwise comparisons between the chamber controls and that exposed group. The Poly-3 test accounts for the differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in an exposed group is indicated by **N**.
[e] Not applicable; no neoplasms in animal group

**TABLE B4**
**Historical Incidence of Urinary Bladder Neoplasms in Control Female F344/N Rats[a]**

| Study | Incidence in Controls | |
|---|---|---|
| | Carcinoma | Papilloma |
| **Historical Incidence: Inhalation Studies** | | |
| Decalin | 0/50 | 0/50 |
| Indium phosphide | 0/49 | 0/50 |
| Naphthalene | 0/48 | 1/48 |
| Propylene glycol mono-*t*-butyl ether | 0/49 | 0/49 |
| Stoddard solvent IIC | 0/49 | 1/49 |
| Vanadium pentoxide | 1/50 | 0/50 |
| **Overall Historical Incidence: Inhalation Studies** | | |
| Total (%) | 1/295 (0.3%) | 2/295 (0.7%) |
| Mean ± standard deviation | 0.3% ± 0.8% | 0.7% ± 1.1% |
| Range | 0%-2% | 0%-2% |
| **Overall Historical Incidence** | | |
| Total (%) | 1/1,104 (0.9%) | 5/1,104 (0.5%) |
| Mean ± standard deviation | 0.1% ± 0.5% | 0.5% ± 0.9% |
| Range | 0%-2% | 0%-2% |

[a] Data as of March 3, 2003

**TABLE B5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Moribund | 14 | 12 | 20 | 11 |
| Natural deaths | 3 | 4 | 2 | 3 |
| Survivors | | | | |
| Terminal sacrifice | 33 | 34 | 28 | 36 |
| Animals examined microscopically | 50 | 50 | 50 | 50 |
| **Alimentary System** | | | | |
| Liver | (49) | (50) | (50) | (50) |
| Angiectasis | 1 (2%) | | 3 (6%) | 1 (2%) |
| Basophilic focus | 39 (80%) | 45 (90%) | 43 (86%) | 40 (80%) |
| Clear cell focus | 12 (24%) | 13 (26%) | 11 (22%) | 27 (54%) |
| Eosinophilic focus | 1 (2%) | | | 1 (2%) |
| Fatty change | | 1 (2%) | | |
| Hepatodiaphragmatic nodule | 8 (16%) | 10 (20%) | 9 (18%) | 7 (14%) |
| Infarct | 1 (2%) | | | |
| Inflammation, granulomatous | 1 (2%) | | 1 (2%) | 2 (4%) |
| Necrosis | | 1 (2%) | 1 (2%) | 2 (4%) |
| Thrombosis | | | | 1 (2%) |
| Vacuolization cytoplasmic | 3 (6%) | 4 (8%) | 3 (6%) | |
| Bile duct, dilatation | 1 (2%) | | | |
| Serosa, hemorrhage | 1 (2%) | | | |
| Mesentery | (17) | (23) | (10) | (17) |
| Necrosis | 17 (100%) | 21 (91%) | 9 (90%) | 17 (100%) |
| Fat, hemorrhage | 1 (6%) | 1 (4%) | | |
| Pancreas | (49) | (50) | (50) | (50) |
| Cyst | | | 1 (2%) | |
| Necrosis | | 1 (2%) | | |
| Stomach, forestomach | (49) | (50) | (50) | (49) |
| Erosion | | | | 1 (2%) |
| Inflammation, suppurative | | | 1 (2%) | |
| Ulcer | | | 4 (8%) | |
| Stomach, glandular | (49) | (50) | (50) | (49) |
| Ulcer | 1 (2%) | | | |
| Epithelium, hyperplasia | | | | 1 (2%) |
| Tongue | (2) | | | (1) |
| Epithelium, hyperkeratosis | | | | 1 (100%) |
| Epithelium, hyperplasia | 1 (50%) | | | |
| Tooth | (1) | | | |
| Peridontal tissue, inflammation | 1 (100%) | | | |
| **Cardiovascular System** | | | | |
| Heart | (50) | (50) | (50) | (50) |
| Cardiomyopathy | | 3 (6%) | 1 (2%) | |
| Atrium, thrombosis | | 2 (4%) | | |
| Epicardium, inflammation, chronic | | | 1 (2%) | |
| Myocardium, degeneration | | | 1 (2%) | |
| Myocardium, necrosis | | | 1 (2%) | |

[a] Number of animals examined microscopically at the site and the number of animals with lesion

**TABLE B5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Endocrine System** | | | | |
| Adrenal cortex | (49) | (50) | (50) | (50) |
| Accessory adrenal cortical nodule | | | | 1 (2%) |
| Atrophy | | 1 (2%) | | |
| Degeneration, cystic | 1 (2%) | | | |
| Hemorrhage | | | 1 (2%) | |
| Hyperplasia | 2 (4%) | | 2 (4%) | 1 (2%) |
| Metaplasia, osseous | 1 (2%) | | | |
| Vacuolization cytoplasmic | 15 (31%) | 10 (20%) | 6 (12%) | 5 (10%) |
| Adrenal medulla | (49) | (50) | (50) | (50) |
| Hyperplasia | 1 (2%) | 1 (2%) | 2 (4%) | |
| Pituitary gland | (49) | (50) | (50) | (49) |
| Angiectasis | 4 (8%) | 4 (8%) | 1 (2%) | 4 (8%) |
| Cyst | | | | 1 (2%) |
| Hemorrhage | 1 (2%) | | 1 (2%) | |
| Hyperplasia | 3 (6%) | 6 (12%) | 3 (6%) | 3 (6%) |
| Pars intermedia, vacuolization cytoplasmic | | | | 1 (2%) |
| Thyroid gland | (49) | (50) | (50) | (50) |
| C-cell, hyperplasia | 9 (18%) | 8 (16%) | 7 (14%) | 5 (10%) |
| **General Body System** | | | | |
| None | | | | |
| **Genital System** | | | | |
| Clitoral gland | (50) | (50) | (50) | (50) |
| Cyst | 2 (4%) | 3 (6%) | 1 (2%) | 4 (8%) |
| Hyperplasia | 3 (6%) | 3 (6%) | 2 (4%) | 2 (4%) |
| Inflammation, chronic | | 1 (2%) | 2 (4%) | 1 (2%) |
| Ovary | (50) | (50) | (50) | (50) |
| Cyst | 6 (12%) | 5 (10%) | 3 (6%) | 8 (16%) |
| Hemorrhage | | | 1 (2%) | |
| Uterus | (50) | (50) | (50) | (50) |
| Decidual reaction | 1 (2%) | | | |
| Hemorrhage | 1 (2%) | | | 1 (2%) |
| Hemorrhage, chronic | 1 (2%) | | | |
| Necrosis | | | 1 (2%) | |
| Endometrium, hyperplasia | | | 1 (2%) | 2 (4%) |
| Endometrium, ulcer | | | | 1 (2%) |

**TABLE B5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Hematopoietic System** | | | | |
| Lymph node | (5) | (3) | (3) | (6) |
| Deep cervical, infiltration cellular, histiocyte | | | 1 (33%) | |
| Deep cervical, inflammation, chronic | 1 (20%) | | | |
| Lymph node, bronchial | (9) | (4) | (10) | (5) |
| Angiectasis | 1 (11%) | | | 1 (20%) |
| Infiltration cellular, histiocyte | | | 1 (10%) | |
| Lymph node, mandibular | (1) | (2) | (2) | |
| Ectasia | | 1 (50%) | 1 (50%) | |
| Lymph node, mesenteric | (50) | (50) | (50) | (50) |
| Fibrosis | | 1 (2%) | | |
| Hemorrhage | | 1 (2%) | | |
| Lymph node, mediastinal | (43) | (46) | (45) | (43) |
| Angiectasis | 3 (7%) | 1 (2%) | 1 (2%) | 2 (5%) |
| Fibrosis | | 1 (2%) | 1 (2%) | |
| Hemorrhage | | 1 (2%) | | |
| Infiltration cellular, histiocyte | 1 (2%) | 2 (4%) | 4 (9%) | |
| Inflammation, suppurative | | | 1 (2%) | |
| Pigmentation | 3 (7%) | 1 (2%) | | |
| Spleen | (49) | (50) | (50) | (50) |
| Accessory spleen | 1 (2%) | 2 (4%) | | |
| Degeneration | | 1 (2%) | | |
| Fibrosis | | | | 2 (4%) |
| Hematopoietic cell proliferation | | | | 1 (2%) |
| Hemorrhage | 1 (2%) | | | |
| Necrosis | | 1 (2%) | | 3 (6%) |
| **Integumentary System** | | | | |
| Mammary gland | (49) | (50) | (50) | (50) |
| Galactocele | | 7 (14%) | 2 (4%) | 1 (2%) |
| Skin | (50) | (50) | (50) | (50) |
| Cyst epithelial inclusion | | 1 (2%) | 1 (2%) | |
| Hyperkeratosis | | | 1 (2%) | |
| Inflammation, chronic | | 1 (2%) | 1 (2%) | 1 (2%) |
| Ulcer | 1 (2%) | | | 1 (2%) |
| Subcutaneous tissue, hemorrhage | | | | 1 (2%) |
| **Musculoskeletal System** | | | | |
| Bone | (50) | (50) | (50) | (50) |
| Fibrous osteodystrophy | | 1 (2%) | | |
| Maxilla, necrosis | 1 (2%) | | | |
| Metatarsal, fracture | | | | 1 (2%) |
| Tibia, osteopetrosis | | 1 (2%) | | |
| **Nervous System** | | | | |
| Brain | (49) | (50) | (50) | (50) |
| Compression | 5 (10%) | 9 (18%) | 8 (16%) | 4 (8%) |
| Hemorrhage | 4 (8%) | 3 (6%) | 6 (12%) | 2 (4%) |
| Hydrocephalus | | 1 (2%) | | |
| Medulla, gliosis, focal | | | 1 (2%) | |

**TABLE B5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Respiratory System** | | | | |
| Larynx | (49) | (50) | (50) | (50) |
| Foreign body | 1 (2%) | 1 (2%) | | |
| Inflammation, suppurative | 4 (8%) | 2 (4%) | 1 (2%) | 2 (4%) |
| Epiglottis, metaplasia, squamous | | | 1 (2%) | 2 (4%) |
| Respiratory epithelium, epiglottis, degeneration | | | 1 (2%) | |
| Lung | (50) | (50) | (50) | (50) |
| Foreign body | | | | 1 (2%) |
| Hemorrhage | 1 (2%) | 2 (4%) | | 1 (2%) |
| Inflammation, chronic | 9 (18%) | 2 (4%) | 7 (14%) | 6 (12%) |
| Metaplasia, osseous | | | 1 (2%) | |
| Thrombosis | 1 (2%) | | | |
| Alveolar epithelium, hyperplasia | 6 (12%) | 4 (8%) | 5 (10%) | 4 (8%) |
| Alveolus, infiltration cellular, histiocyte | 15 (30%) | 9 (18%) | 13 (26%) | 20 (40%) |
| Alveolus, proteinosis | 4 (8%) | | 3 (6%) | 2 (4%) |
| Bronchiole, hyperplasia | 1 (2%) | 1 (2%) | | |
| Interstitium, fibrosis | 4 (8%) | 1 (2%) | 4 (8%) | 2 (4%) |
| Mediastinum, inflammation, granulomatous | | | 1 (2%) | |
| Nose | (49) | (49) | (50) | (50) |
| Foreign body | 2 (4%) | 2 (4%) | 2 (4%) | |
| Inflammation, suppurative | 4 (8%) | 2 (4%) | 5 (10%) | |
| Glands, dilatation | | | | 4 (8%) |
| Goblet cell, hyperplasia | | | | 3 (6%) |
| Nasolacrimal duct, inflammation, suppurative | 1 (2%) | 1 (2%) | 4 (8%) | 1 (2%) |
| Olfactory epithelium, degeneration, hyaline | 10 (20%) | 22 (45%) | 48 (96%) | 50 (100%) |
| Respiratory epithelium, hyperplasia | 2 (4%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Pleura | (50) | (50) | (49) | (50) |
| Inflammation, chronic | 15 (30%) | 10 (20%) | 11 (22%) | 17 (34%) |
| **Special Senses System** | | | | |
| Eye | (49) | (50) | (50) | (50) |
| Atrophy | | | 2 (4%) | |
| Phthisis bulbi | 1 (2%) | | 1 (2%) | |
| Anterior chamber, sclera, inflammation, suppurative | | | 1 (2%) | |
| Cornea, edema | | | | 1 (2%) |
| Cornea, inflammation, chronic | | | 1 (2%) | 1 (2%) |
| Cornea, mineralization | | | | 10 (20%) |
| Cornea, necrosis | | | | 1 (2%) |
| Lens, cataract | 1 (2%) | 4 (8%) | 3 (6%) | 1 (2%) |
| Lens, mineralization | | 1 (2%) | | |
| Sclera, inflammation, suppurative | 1 (2%) | | | |
| Zymbal's gland | (42) | (44) | (43) | (46) |
| Cyst | | | 1 (2%) | |
| Hyperplasia | | | 1 (2%) | |

**TABLE B5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Urinary System** | | | | |
| Kidney | (49) | (50) | (50) | (50) |
| Inflammation, suppurative | | 2 (4%) | | |
| Nephropathy, chronic | 45 (92%) | 45 (90%) | 45 (90%) | 49 (98%) |
| Cortex, infarct | | | | 1 (2%) |
| Cortex, renal tubule, accumulation, hyaline droplet | 1 (2%) | 2 (4%) | | 1 (2%) |
| Cortex, renal tubule, hyperplasia | | | 1 (2%) | 1 (2%) |
| Pelvis, mineralization | 13 (27%) | 5 (10%) | 7 (14%) | 3 (6%) |
| Pelvis, transitional epithelium, hyperplasia | | 4 (8%) | | |
| Renal tubule, mineralization | | | 2 (4%) | |
| Urethra | | | | (1) |
| Transitional epithelium, hyperplasia | | | | 1 (100%) |
| Urinary bladder | (49) | (50) | (50) | (50) |
| Hemorrhage | 1 (2%) | | | |
| Mineralization | | | 1 (2%) | |
| Ulcer | | | 1 (2%) | |
| Transitional epithelium, hyperplasia | 1 (2%) | 1 (2%) | | |
| Transitional epithelium, mineralization | | | 1 (2%) | |

# APPENDIX C
# SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR INHALATION STUDY OF PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER


| | | |
|---|---|---|
| TABLE C1 | Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 161 |
| TABLE C2 | Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 166 |
| TABLE C3 | Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 192 |
| TABLE C4 | Historical Incidence of Liver Neoplasms in Control Male B6C3F$_1$ Mice . . . . . | 195 |
| TABLE C5 | Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 196 |

**TABLE C1**
**Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Moribund | 4 | 6 | 6 | 8 |
| Natural deaths | 11 | 4 | 4 | 5 |
| Survivors | | | | |
| Terminal sacrifice | 35 | 40 | 40 | 37 |
| Animals examined microscopically | 50 | 50 | 50 | 50 |
| **Alimentary System** | | | | |
| Gallbladder | (38) | (41) | (39) | (40) |
| Sarcoma, metastatic, mesentery | | | 1 (3%) | |
| Intestine large, cecum | (43) | (47) | (48) | (48) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (2%) | | | |
| Polyp adenomatous | | | | 1 (2%) |
| Intestine small, duodenum | (43) | (48) | (47) | (44) |
| Polyp adenomatous | | 2 (4%) | 1 (2%) | |
| Intestine small, jejunum | (42) | (47) | (47) | (45) |
| Carcinoma | 2 (5%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Polyp adenomatous | 1 (2%) | | 1 (2%) | 1 (2%) |
| Intestine small, ileum | (43) | (47) | (46) | (46) |
| Carcinoma | | | 1 (2%) | |
| Liver | (50) | (49) | (50) | (50) |
| Hemangiosarcoma | 2 (4%) | | 1 (2%) | 1 (2%) |
| Hepatoblastoma | | | 1 (2%) | 5 (10%) |
| Hepatocellular carcinoma | 8 (16%) | 7 (14%) | 11 (22%) | 9 (18%) |
| Hepatocellular carcinoma, multiple | 1 (2%) | 1 (2%) | 2 (4%) | 2 (4%) |
| Hepatocellular adenoma | 15 (30%) | 16 (33%) | 14 (28%) | 13 (26%) |
| Hepatocellular adenoma, multiple | 3 (6%) | 7 (14%) | 12 (24%) | 23 (46%) |
| Histiocytic sarcoma | | 1 (2%) | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (2%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (2%) | | | |
| Sarcoma, metastatic, mesentery | | | 1 (2%) | |
| Mesentery | (14) | (16) | (13) | (11) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (7%) | | | |
| Hemangiosarcoma | | 2 (13%) | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (7%) | | | |
| Sarcoma | | | 1 (8%) | |
| Pancreas | (48) | (49) | (50) | (50) |
| Osteosarcoma, metastatic, uncertain primary site | 1 (2%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (2%) | | | |
| Sarcoma, metastatic, mesentery | | | 1 (2%) | |
| Salivary glands | (50) | (50) | (50) | (50) |
| Stomach, forestomach | (48) | (49) | (50) | (50) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (2%) | | | |
| Mast cell tumor malignant, metastatic, bone marrow | | | 1 (2%) | |
| Epithelium, squamous cell carcinoma | | 1 (2%) | | |
| Epithelium, squamous cell papilloma | | | 1 (2%) | |
| Stomach, glandular | (46) | (48) | (50) | (48) |
| Mast cell tumor malignant, metastatic, bone marrow | | | 1 (2%) | |
| Sarcoma, metastatic, mesentery | | | 1 (2%) | |
| Tongue | | | | (1) |
| Squamous cell papilloma | | | | 1 (100%) |

**TABLE C1**
**Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Cardiovascular System** | | | | |
| Heart | (50) | (50) | (50) | (50) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (2%) | | | |
| Hemangiosarcoma | | 1 (2%) | | |
| **Endocrine System** | | | | |
| Adrenal cortex | (48) | (49) | (50) | (50) |
| Adenoma | | | | 1 (2%) |
| Carcinoma | | 1 (2%) | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (2%) | | | |
| Sarcoma, metastatic, mesentery | | | 1 (2%) | |
| Capsule, adenoma | | | | 1 (2%) |
| Subcapsular, adenoma | 1 (2%) | 1 (2%) | 1 (2%) | 2 (4%) |
| Subcapsular, carcinoma | | 1 (2%) | | |
| Adrenal medulla | (47) | (49) | (49) | (49) |
| Pheochromocytoma benign | | | 1 (2%) | |
| Islets, pancreatic | (48) | (49) | (50) | (50) |
| Adenoma | 2 (4%) | | | |
| Thyroid gland | (48) | (48) | (49) | (49) |
| Follicular cell, adenoma | 1 (2%) | | 1 (2%) | |
| Follicular cell, carcinoma | | | 1 (2%) | |
| **General Body System** | | | | |
| Peritoneum | (2) | | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (50%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (50%) | | | |
| **Genital System** | | | | |
| Epididymis | (50) | (50) | (50) | (50) |
| Prostate | (49) | (49) | (47) | (50) |
| Adenoma | 1 (2%) | | | |
| Seminal vesicle | (47) | (49) | (49) | (49) |
| Adenoma | | 1 (2%) | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (2%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (2%) | | | |
| Sarcoma, metastatic, mesentery | | | 1 (2%) | |
| Testes | (50) | (50) | (50) | (50) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (2%) | | | |
| Hemangioma | 1 (2%) | | | |
| Interstitial cell, adenoma | 2 (4%) | | 2 (4%) | |

**TABLE C1**
**Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Hematopoietic System** | | | | |
| Bone marrow | (49) | (49) | (50) | (50) |
| Mast cell tumor malignant | | | 1 (2%) | |
| Lymph node | (2) | (1) | (4) | (1) |
| Pancreatic, sarcoma, metastatic, lymph node, mesenteric | | | 1 (25%) | |
| Lymph node, bronchial | (32) | (36) | (36) | (35) |
| Osteosarcoma, metastatic, uncertain primary site | 1 (3%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (3%) | | | |
| Lymph node, mandibular | (28) | (38) | (30) | (25) |
| Lymph node, mesenteric | (48) | (49) | (49) | (50) |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (2%) | | | |
| Sarcoma, metastatic, mesentery | | | 1 (2%) | |
| Lymph node, mediastinal | (39) | (39) | (43) | (36) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (3%) | | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (3%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (3%) | | | |
| Spleen | (48) | (48) | (50) | (50) |
| Hemangiosarcoma | 2 (4%) | 1 (2%) | 1 (2%) | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (2%) | | | |
| Thymus | (40) | (41) | (39) | (40) |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (3%) | | | |
| **Integumentary System** | | | | |
| Skin | (49) | (50) | (50) | (50) |
| Subcutaneous tissue, fibrosarcoma | | 1 (2%) | | |
| Subcutaneous tissue, fibrous histiocytoma | | 2 (4%) | 2 (4%) | |
| Subcutaneous tissue, hemangioma | | | 1 (2%) | |
| Subcutaneous tissue, hemangiosarcoma | | | 1 (2%) | |
| Subcutaneous tissue, histiocytic sarcoma | | 1 (2%) | | |
| Subcutaneous tissue, lipoma | 1 (2%) | | | |
| Subcutaneous tissue, sarcoma | | 1 (2%) | | |
| **Musculoskeletal System** | | | | |
| None | | | | |
| **Nervous System** | | | | |
| None | | | | |

**TABLE C1**
**Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Respiratory System** | | | | |
| Lung | (50) | (50) | (50) | (50) |
| Alveolar/bronchiolar adenoma | 13 (26%) | 7 (14%) | | 7 (14%) |
| Alveolar/bronchiolar carcinoma | 6 (12%) | 3 (6%) | | 4 (8%) |
| Alveolar/bronchiolar carcinoma, multiple | | | 1 (2%) | |
| Carcinoma, metastatic, harderian gland | | | | 1 (2%) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (2%) | | | |
| Hepatoblastoma, metastatic, liver | | | 1 (2%) | |
| Hepatocellular carcinoma, metastatic, liver | 3 (6%) | 2 (4%) | 5 (10%) | 3 (6%) |
| Histiocytic sarcoma | | 1 (2%) | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (2%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (2%) | | | |
| Sarcoma, metastatic, mesentery | | | 1 (2%) | |
| Sarcoma, metastatic, skin | | 1 (2%) | | |
| Bronchiole, adenoma | | 1 (2%) | | |
| Pleura | (1) | | (1) | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (100%) | | | |
| **Special Senses System** | | | | |
| Harderian gland | (50) | (50) | (50) | (50) |
| Adenoma | 6 (12%) | 4 (8%) | 3 (6%) | 4 (8%) |
| Carcinoma | 1 (2%) | 1 (2%) | | 2 (4%) |
| Bilateral, adenoma | | | 1 (2%) | |
| **Urinary System** | | | | |
| Kidney | (50) | (49) | (50) | (50) |
| Carcinoma, metastatic, intestine small, jejunum | 1 (2%) | | | |
| Histiocytic sarcoma | | 1 (2%) | | |
| Osteosarcoma, metastatic, uncertain primary site | 1 (2%) | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | 1 (2%) | | | |
| Renal tubule, adenoma | 1 (2%) | | | |
| Renal tubule, carcinoma | 1 (2%) | | | |
| Urinary bladder | (48) | (48) | (49) | (50) |
| Transitional epithelium, papilloma | 1 (2%) | | | |
| **Systemic Lesions** | | | | |
| Multiple organs[b] | (50) | (50) | (50) | (50) |
| Histiocytic sarcoma | | 1 (2%) | | |
| Lymphoma malignant | 3 (6%) | 1 (2%) | 6 (12%) | 3 (6%) |

**TABLE C1**
**Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Neoplasm Summary** | | | | |
| Total animals with primary neoplasms[c] | 40 | 38 | 41 | 43 |
| Total primary neoplasms | 75 | 65 | 70 | 81 |
| Total animals with benign neoplasms | 30 | 28 | 30 | 39 |
| Total benign neoplasms | 49 | 39 | 39 | 54 |
| Total animals with malignant neoplasms | 20 | 20 | 26 | 18 |
| Total malignant neoplasms | 26 | 26 | 31 | 27 |
| Total animals with metastatic neoplasms | 6 | 3 | 7 | 4 |
| Total metastatic neoplasms | 33 | 3 | 17 | 4 |
| Total animals with malignant neoplasms–uncertain primary site | 2 | | | |

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 2 8 1 | 6 1 0 | 6 2 2 | 6 3 0 | 6 3 4 | 6 4 1 | 6 6 8 | 6 6 9 | 6 6 9 | 6 7 1 | 6 9 3 | 7 0 8 | 7 1 1 | 7 1 4 | 7 2 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 3 2 | 0 0 6 | 0 0 7 | 0 4 6 | 0 4 5 | 0 4 9 | 0 3 4 | 0 1 0 | 0 1 5 | 0 2 3 | 0 3 3 | 0 2 7 | 0 1 9 | 0 5 0 | 0 0 3 | 0 0 1 | 0 0 4 | 0 1 1 | 0 1 7 | 0 1 8 | 0 2 0 | 0 2 4 | 0 2 5 | 0 2 8 | 0 3 7 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | M | M | A | A | A | I | A | + | + | M | A | A | + | + | M | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | A | + | + | + | A | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | A | + | + | + | A | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | A | A | + | A | A | + | + | A | A | + | + | + | A | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | |
| Intestine small, duodenum | + | + | A | A | + | A | A | + | + | A | A | + | + | + | A | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | A | A | + | A | A | + | + | A | A | A | + | + | A | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | X | | | | | X | | | | | | |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | |
| Intestine small, ileum | + | + | A | A | + | A | A | + | + | A | A | + | + | + | A | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | X | | | | | X | | | | | | | | | | | | |
| Hepatocellular carcinoma | | | | X | X | | | | | X | | | | | | | | X | | X | | | | |
| Hepatocellular carcinoma, multiple | | | | | | | | | | | | | | | X | | | | | | | | | |
| Hepatocellular adenoma | | | X | | | X | | | | | X | | | | | | X | X | | | | | | X |
| Hepatocellular adenoma, multiple | | | | | | | | | | | | | X | X | | | | | | | | | | |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | | | + | | + | | | | | + | | | + | | | | + | | | | + |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | A | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | A | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | |
| Stomach, glandular | + | + | A | + | + | + | A | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | |

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 4 1 | 0 4 2 | 0 4 3 | 0 4 8 | 0 0 2 | 0 0 5 | 0 0 8 | 0 1 2 | 0 1 4 | 0 1 6 | 0 2 1 | 0 2 2 | 0 2 6 | 0 3 1 | 0 3 5 | 0 3 6 | 0 3 8 | 0 4 0 | 0 4 4 | 0 4 7 | 0 0 9 | 0 1 3 | 0 2 9 | 0 3 0 | 0 3 9 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | 38 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 43 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 43 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 42 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Polyp adenomatous | | | | | | | X | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 43 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Hepatocellular carcinoma | | | | | X | X | | | | | | | | | | X | | | | | | | | | | 8 |
| Hepatocellular carcinoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular adenoma | | | | | | X | X | X | X | X | | | | X | | | | | | X | X | | | | X | 15 |
| Hepatocellular adenoma, multiple | | | | X | | | | | | | | | | | | | | | | | | | | | | 3 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Mesentery | | | | + | + | | | | | + | | | | | + | | | | | + | | | + | + | + | 14 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 2 8 1 | 6 1 0 | 6 2 2 | 6 3 0 | 6 3 4 | 6 4 1 | 6 6 8 | 6 6 9 | 6 6 9 | 6 7 1 | 6 9 3 | 7 0 8 | 7 1 1 | 7 1 4 | 7 2 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 3 2 | 0 0 6 | 0 0 7 | 0 4 6 | 0 4 5 | 0 4 9 | 0 3 4 | 0 1 0 | 0 1 5 | 0 2 3 | 0 3 3 | 0 2 7 | 0 1 9 | 0 5 0 | 0 0 3 | 0 0 1 | 0 0 4 | 0 1 1 | 0 1 7 | 0 1 8 | 0 2 0 | 0 2 4 | 0 2 5 | 0 2 8 | 0 3 7 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | A | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Subcapsular, adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal medulla | + | + | A | + | + | + | + | + | + | A | + | + | I | + | + | + | + | + | + | + | + | + | + | + |
| Islets, pancreatic | + | + | A | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid gland | M | M | M | + | + | M | + | M | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pituitary gland | M | + | M | + | + | + | M | + | + | A | A | + | + | + | M | + | + | + | + | + | + | + | + | + |
| Thyroid gland | + | + | M | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | + | | | | + | | | | | | | | | | | | | | | | | | |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Prostate | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Seminal vesicle | + | + | + | + | + | + | A | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | |
| Hemangioma | | | | | | | | | | | | | | | | | | | | | | | | |
| Interstitial cell, adenoma | | | | | | | | | X | | | | | | | | | | | | | | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 729 | 729 | 729 | 729 | 730 | 700 | 730 | 700 | 700 | 730 | 700 | 730 | 700 | 730 | 730 | 730 | 730 | 700 | 730 | 730 | 700 | 731 | 731 | 731 | 731 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 04 1 | 04 2 | 04 3 | 04 8 | 00 2 | 00 5 | 00 8 | 01 2 | 01 4 | 01 6 | 02 1 | 02 2 | 02 6 | 03 1 | 03 5 | 03 6 | 03 8 | 04 0 | 04 4 | 04 7 | 04 9 | 01 3 | 02 9 | 03 0 | 03 9 | Total Tissues/ Tumors |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcapsular, adenoma | | | | | | | X | | | | | | | | | | | | | | | | | | | 1 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Adenoma | | | | | | | | | | | X | | | X | | | | | | | | | | | | 2 |
| Parathyroid gland | M | + | + | + | M | + | M | + | + | + | + | + | M | + | + | + | + | + | + | + | M | M | + | M | + | 37 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | 43 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Follicular cell, adenoma | | | | | | | X | | | | | | | | | | | | | | | | | | | 1 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hemangioma | | | | | | | | | | | | | | | | | | | X | | | | | | | 1 |
| Interstitial cell, adenoma | | | | | | | | | X | | | | | | | | | | | | | | | | | 2 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 2 8 1 | 6 1 0 | 6 2 2 | 6 3 0 | 6 3 4 | 6 4 1 | 6 6 8 | 6 6 9 | 6 6 9 | 6 7 1 | 6 9 3 | 7 0 8 | 7 1 1 | 7 1 4 | 7 2 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 3 2 | 0 0 6 | 0 0 7 | 0 4 6 | 0 4 5 | 0 4 9 | 0 3 4 | 0 1 0 | 0 1 5 | 0 2 3 | 0 3 3 | 0 2 7 | 0 1 9 | 0 5 0 | 0 0 3 | 0 0 1 | 0 1 4 | 0 1 1 | 0 1 7 | 0 1 8 | 0 2 0 | 0 2 4 | 0 2 5 | 0 2 8 | 0 3 7 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | | | | | | + | | | | | | | | | | | | | | | |
| Lymph node, bronchial | + | + | + | + | + | + | + | + | + | + | M | M | M | + | + | + | + | + | + | M | + | + | M | + | + |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mandibular | M | M | + | + | + | M | + | + | M | + | + | M | + | + | M | + | + | M | M | + | + | + | M | + | M |
| Lymph node, mesenteric | M | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mediastinal | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | M | M | + | + | + | + | + |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | + | + | A | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| Thymus | M | + | + | + | M | + | + | + | M | + | + | + | M | + | M | + | + | + | + | + | M | M | + | + | M |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | | | | | | | | X | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 4 1 | 0 4 2 | 0 4 3 | 0 4 8 | 0 0 2 | 0 0 5 | 0 0 8 | 0 1 2 | 0 1 4 | 0 1 6 | 0 2 1 | 0 2 2 | 0 2 6 | 0 3 1 | 0 3 5 | 0 3 6 | 0 3 8 | 0 4 0 | 0 4 4 | 0 4 7 | 0 0 9 | 0 1 3 | 0 2 9 | 0 3 0 | 0 3 9 | Total Tissues/ Tumors |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node | | | | | | | | | | | | | + | | | | | | | | | | | | | 2 |
| Lymph node, bronchial | + | M | M | M | + | + | M | + | M | M | + | M | + | M | M | M | M | + | M | + | + | M | + | + | + | 32 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mandibular | + | M | M | M | + | M | + | + | + | M | M | + | M | M | M | M | + | M | + | + | + | + | + | M | + | 28 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mediastinal | M | + | M | + | + | M | M | + | + | M | + | + | + | M | + | + | + | + | M | + | + | + | + | + | M | 39 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Hemangiosarcoma | | | | | | | | | | | | X | | | | | | | | | | | | | | 2 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thymus | M | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | 40 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | + | 49 |
| Subcutaneous tissue, lipoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 281 | 610 | 622 | 630 | 634 | 641 | 668 | 669 | 669 | 671 | 693 | 708 | 711 | 714 | 722 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 00332 | 00026 | 00007 | 00046 | 00445 | 00449 | 00343 | 00101 | 00115 | 00223 | 00337 | 00327 | 00119 | 00505 | 00303 | 00011 | 00414 | 00111 | 00177 | 00118 | 00220 | 00224 | 00225 | 00228 | 00337 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | X | | | | | | | X | | | | | | | | | | X | | | | | |
| Alveolar/bronchiolar carcinoma | | | | | | | | X | X | | | | | | | | | | | | | | | | |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | | | | X | | | | | | | | | | | X | | | X | | | | | | | |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | | | | | | + | | | | | | | | | | | | | | | | | | | |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | | |
| Trachea | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | A | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | X | | | | | | | X | | | | | | | | |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Zymbal's gland | M | M | + | + | + | M | + | + | M | M | M | + | + | M | I | + | + | M | + | + | + | + | + | + | + |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | X | | | | | | | | | | | | | | | | | | | |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Renal tubule, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Urinary bladder | + | + | A | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Transitional epithelium, papilloma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymphoma malignant | | | | | | | | | X | | | | | | | | | | | | | | | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 0 4 1 | 0 4 2 | 0 4 3 | 0 4 8 | 0 0 2 | 0 0 5 | 0 0 8 | 0 1 2 | 0 1 4 | 0 1 6 | 0 2 1 | 0 2 2 | 0 2 6 | 0 3 1 | 0 3 5 | 0 3 6 | 0 3 8 | 0 4 0 | 0 4 4 | 0 4 7 | 0 4 9 | 0 1 3 | 0 1 2 | 0 2 9 | 0 3 0 | 0 3 9 | Total Tissues/ Tumors |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar adenoma | | | | | X | X | | | X | | X | | | X | | | X | | | X | X | X | | X | | | 13 |
| Alveolar/bronchiolar carcinoma | X | | | | X | | | | X | | | | | | | | | | X | | | | | | | | 6 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | | 3 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pleura | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | X | X | | | | | | | | X | | | | X | | | | | | | | | | | | | 6 |
| Carcinoma | | | | | | | | | | | | | | | X | | | | | | | | | | | | 1 |
| Zymbal's gland | + | + | + | + | I | + | + | M | + | M | M | + | + | + | + | M | + | + | + | + | + | + | + | + | M | + | 35 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, intestine small, jejunum | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Osteosarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Plasma cell tumor malignant, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Renal tubule, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Renal tubule, carcinoma | | | | | X | | | | | | | | | | | | | | | | | | | | | | 1 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Transitional epithelium, papilloma | | | | | | | | | | X | | | | | | | | | | | | | | | | | 1 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymphoma malignant | | | | | | | | | | | | | X | | | | | | X | | | | | | | | 3 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 1 3 7 | 1 3 7 | 4 6 6 | 5 6 8 | 6 1 1 | 6 2 7 | 6 3 0 | 6 6 3 | 7 0 5 | 7 1 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 0 8 | 2 2 1 | 2 3 7 | 2 3 4 | 2 1 5 | 2 0 7 | 2 1 2 | 2 4 2 | 2 2 3 | 2 1 9 | 2 0 4 | 2 0 6 | 2 1 1 | 2 1 6 | 2 1 7 | 2 1 8 | 2 2 0 | 2 2 2 | 2 2 5 | 2 2 8 | 2 3 0 | 2 3 1 | 2 3 2 | 2 3 6 | 2 3 8 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | + | A | + | + | + | A | I | + | + | + | + | + | + | + | + | + | I | + | M | + | + | M | + | + |
| Intestine large, colon | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | A | + | + | + | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | X | | | |
| Intestine small, jejunum | + | + | A | + | + | + | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Intestine small, ileum | + | + | A | + | + | + | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular carcinoma | | | | | | | | | X | X | | | | | | | | | X | | | | | | |
| Hepatocellular carcinoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular adenoma | | | | | | | | | | X | | X | | | | X | | | X | | | X | X | | |
| Hepatocellular adenoma, multiple | | | | | | | | | X | | X | | | | | | | | | X | X | | | | |
| Histiocytic sarcoma | | | | X | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | | | | + | | | | + | + | | + | | + | | + | | | + | | | | |
| Hemangiosarcoma | | | | | | | | | | | | | | X | | | | | | | | | | | |
| Pancreas | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Epithelium, squamous cell carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Stomach, glandular | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | X | | | | | | |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Subcapsular, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcapsular, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal medulla | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Islets, pancreatic | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid gland | + | + | A | M | + | M | + | + | + | M | + | + | + | + | M | + | + | + | + | M | + | + | I | + | + |
| Pituitary gland | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + |
| Thyroid gland | + | + | A | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tissue NOS | | | | | | | | | | | | | | | | | | | | | | | + | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 729 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 24 00 | 20 01 | 20 02 | 20 05 | 20 09 | 21 13 | 22 24 | 22 27 | 22 29 | 23 39 | 24 41 | 24 43 | 24 44 | 24 46 | 24 47 | 24 49 | 25 00 | 20 03 | 21 10 | 21 14 | 22 26 | 23 23 | 23 35 | 24 45 | 24 48 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | I | + | + | + | + | 41 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Polyp adenomatous | | | | | | | | | | X | | | | | | | | | | | | | | | | 2 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Carcinoma | | | | | | | | | | | | | | | | | | X | | | | | | | | 1 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Hepatocellular carcinoma | | | X | | | | | X | | | | | | | X | | X | | | | | | | | | 7 |
| Hepatocellular carcinoma, multiple | | | | X | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular adenoma | X | X | X | | X | X | | X | | X | | X | | | | | | X | | | | | | | X | 16 |
| Hepatocellular adenoma, multiple | | | | | | | | | | | | | | | | | | | | X | | | X | X | | 7 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Mesentery | + | | | | | + | + | + | + | | | + | | | | | | | | + | | + | | | + | 16 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | X | | | | 2 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Epithelium, squamous cell carcinoma | | | | | | | | | | | X | | | | | | | | | | | | | | | 1 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcapsular, adenoma | | | | | X | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcapsular, carcinoma | | | | | | | | | | | X | | | | | | | | | | | | | | | 1 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Parathyroid gland | M | M | + | + | + | + | M | + | + | + | M | + | M | M | + | + | + | M | + | + | + | + | + | + | M | 35 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tissue NOS | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 1 3 7 | 1 3 7 | 4 6 6 | 5 6 8 | 6 1 1 | 6 2 7 | 6 3 0 | 6 6 3 | 7 0 5 | 7 1 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 0 8 | 2 2 1 | 2 3 7 | 2 3 4 | 2 1 5 | 2 0 7 | 2 1 2 | 2 4 2 | 2 2 3 | 2 1 9 | 2 0 4 | 2 0 6 | 2 1 1 | 2 1 6 | 2 1 7 | 2 1 8 | 2 2 0 | 2 2 2 | 2 2 5 | 2 3 8 | 2 3 0 | 2 3 1 | 2 3 2 | 2 3 6 | 2 3 8 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Prostate | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Seminal vesicle | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | X | | | | |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | A | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, bronchial | + | M | A | + | + | M | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + |
| Lymph node, mandibular | + | + | M | + | M | M | + | + | + | + | M | + | M | + | + | + | M | + | + | + | + | + | + | + | + | + |
| Lymph node, mesenteric | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | M | A | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | M | + | + | + | + | M | + | + |
| Spleen | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Thymus | + | + | A | M | + | + | M | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, fibrosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, fibrous histiocytoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, histiocytic sarcoma | | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, sarcoma | | | | | | X | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | | | | | | | X | X | | X | | | | | | | | | | | | | | |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Sarcoma, metastatic, skin | | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Bronchiole, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 729 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 24040 | 20001 | 20002 | 20005 | 20009 | 21013 | 22024 | 22027 | 22029 | 23039 | 24041 | 24043 | 24044 | 24046 | 24047 | 24049 | 25000 | 20003 | 21010 | 21104 | 22026 | 23033 | 23035 | 24045 | 24048 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node | | | | | | | | | | | | | | | | | | | | + | | | | | | 1 |
| Lymph node, bronchial | + | M | M | M | + | + | M | + | + | + | + | + | + | + | M | + | M | M | + | M | + | + | + | M | M | 36 |
| Lymph node, mandibular | + | + | + | M | + | M | + | + | + | + | + | + | M | + | M | M | M | + | + | + | + | + | + | + | + | 38 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node, mediastinal | + | + | + | + | + | M | + | M | + | + | M | + | + | M | + | + | M | + | + | + | + | + | + | M | + | 39 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thymus | + | + | + | M | M | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | 41 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Subcutaneous tissue, fibrosarcoma | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Subcutaneous tissue, fibrous histiocytoma | | | | | | | | | | | | | | | X | | | | | | | | | X | | 2 |
| Subcutaneous tissue, histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar adenoma | | | | | | | X | | X | | | | | | | X | | | | X | | | | | | 7 |
| Alveolar/bronchiolar carcinoma | | X | | | | | | | | X | | | | | | | | | | | | | | X | | 3 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | | | | | | | X | | | | | | | | | | | 2 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Bronchiole, adenoma | | | | | | | X | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 1 3 7 | 1 3 7 | 4 6 6 | 5 6 8 | 6 1 1 | 6 2 7 | 6 3 0 | 6 6 3 | 7 0 5 | 7 1 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 0 8 | 2 2 1 | 2 3 7 | 2 3 4 | 2 1 5 | 2 0 7 | 2 1 2 | 2 4 2 | 2 2 3 | 2 1 9 | 2 0 4 | 2 0 6 | 2 1 1 | 2 1 6 | 2 1 7 | 2 1 8 | 2 2 0 | 2 2 2 | 2 2 5 | 2 2 8 | 2 3 0 | 2 3 1 | 2 3 2 | 2 3 6 | 2 3 8 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | X | | | X | | | | | | X | | | | | | | | |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Zymbal's gland | + | M | M | + | M | + | + | + | + | M | M | M | + | + | + | + | + | + | + | + | + | M | + | M | + |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | X | | | | | | | | | | | | | | | | | | | | | |
| Urinary bladder | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | X | | | | | | | | | | | | | | | | | | | | | |
| Lymphoma malignant | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 2 4 0 | 2 0 1 | 2 0 2 | 2 0 5 | 2 0 9 | 2 1 3 | 2 2 4 | 2 2 7 | 2 2 9 | 2 3 9 | 2 4 1 | 2 4 3 | 2 4 4 | 2 4 6 | 2 4 7 | 2 4 9 | 2 5 0 | 2 0 3 | 2 1 0 | 2 1 4 | 2 2 6 | 2 3 3 | 2 3 5 | 2 4 5 | 2 4 8 | Total Tissues/ Tumors |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | X | | | | | | | | | | | | | | | 4 |
| Carcinoma | | X | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Zymbal's gland | + | + | + | + | M | M | M | M | + | + | + | + | + | + | + | M | M | + | + | + | + | + | + | M | + | | 35 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymphoma malignant | | | | | | | | | | | | | | | | | | | | X | | | | | | | 1 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 4 5 1 | 4 6 3 | 5 3 1 | 5 6 2 | 5 6 4 | 5 9 6 | 6 0 6 | 6 4 1 | 6 4 2 | 7 0 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 4 4 | 4 4 3 | 4 0 7 | 4 2 0 | 4 1 6 | 4 2 6 | 4 3 4 | 4 3 6 | 4 4 1 | 4 4 5 | 4 0 2 | 4 0 4 | 4 0 5 | 4 0 8 | 4 0 9 | 4 1 0 | 4 1 8 | 4 2 8 | 4 2 9 | 4 3 0 | 4 3 1 | 4 3 2 | 4 3 3 | 4 4 0 | 4 4 7 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | + | A | A | M | + | + | + | + | A | + | M | I | + | M | + | + | + | + | M | + | + | + | + | + |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Intestine large, colon | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | A | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | X | |
| Intestine small, jejunum | A | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | | |
| Intestine small, ileum | A | + | A | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | X | | | | | | | | | | | | | | |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Hepatoblastoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma | | | X | X | X | | | | X | X | | | | | X | | | | | | | | | | |
| Hepatocellular carcinoma, multiple | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular adenoma | | | | | | | | | X | X | | | | X | | | | | | | | | X | X | |
| Hepatocellular adenoma, multiple | | | | | | | | | | | X | | X | | X | | | X | | | | | | | |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | + | | | | | + | | | | + | | | | | + | | | | + | | | + | | | + |
| Sarcoma | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mast cell tumor malignant, metastatic, bone marrow | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epithelium, squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mast cell tumor malignant, metastatic, bone marrow | | | | | | | | | | | | | | | | | | | | | | | | | |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | | | | | | + | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 730 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 40 03 | 41 2 | 41 3 | 41 5 | 41 9 | 42 1 | 42 2 | 42 3 | 42 4 | 42 5 | 42 7 | 43 5 | 43 7 | 43 9 | 44 2 | 44 6 | 44 8 | 44 9 | 40 1 | 40 6 | 41 1 | 41 4 | 41 7 | 43 8 | 45 0 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | I | + | + | + | M | + | + | + | + | + | 39 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Carcinoma | | | X | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | X | | | | 1 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatoblastoma | | | X | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular carcinoma | | | | | | | | X | X | | | | X | | X | | | | | | | X | | | | | | 11 |
| Hepatocellular carcinoma, multiple | | | X | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Hepatocellular adenoma | | X | | | | | X | | | | | | | X | | | X | | | X | X | X | | X | X | | X | 14 |
| Hepatocellular adenoma, multiple | | | | X | | | | X | | X | X | X | X | | | X | | | | | | | | | | X | | 12 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Mesentery | | | | | + | + | | | + | | | | + | | | | + | | | | + | | | | | | | 13 |
| Sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mast cell tumor malignant, metastatic, bone marrow | X | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Epithelium, squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mast cell tumor malignant, metastatic, bone marrow | X | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 4 5 1 | 4 6 3 | 5 3 1 | 5 6 2 | 5 6 4 | 5 9 6 | 6 0 6 | 6 4 1 | 6 4 2 | 7 0 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 4 4 | 4 4 3 | 4 0 7 | 4 2 0 | 4 1 6 | 4 2 6 | 4 3 4 | 4 3 6 | 4 4 1 | 4 4 5 | 4 0 2 | 4 0 4 | 4 0 5 | 4 0 8 | 4 0 9 | 4 1 0 | 4 1 8 | 4 2 8 | 4 2 9 | 4 3 0 | 4 3 1 | 4 3 2 | 4 3 3 | 4 4 0 | 4 4 7 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcapsular, adenoma | | | | | | | | | | | | | | | | | | | X | | | | | | |
| Adrenal medulla | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma benign | | | | | | | | | | | | | | | | | | | | | | | | | |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid gland | + | + | M | + | + | M | + | + | + | M | + | M | + | + | + | + | + | + | M | M | + | + | + | + | M |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Follicular cell, carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Prostate | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Seminal vesicle | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Interstitial cell, adenoma | | | | | | | | | | | X | | | | | | | | | | | X | | | |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Mast cell tumor malignant | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node | + | | | | | | | + | | | | | | | | | | | | | | | | | |
| Pancreatic, sarcoma, metastatic, lymph node, mesenteric | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, bronchial | + | M | + | + | + | + | + | + | + | M | + | M | M | M | + | + | + | + | + | M | + | + | + | + | M |
| Lymph node, mandibular | M | + | M | + | M | + | M | + | + | M | + | + | M | + | M | M | + | + | + | + | M | + | M | + | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mediastinal | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + | M | + | + | + | + |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Thymus | M | M | M | + | M | + | M | + | M | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, fibrous histiocytoma | | | | | | | | | | | | | | | | | | | X | | | | | X | |
| Subcutaneous tissue, hemangioma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, hemangiosarcoma | | | | | | | | | | | | | X | | | | | | | | | | | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 0 0 3 | 4 0 1 2 | 4 1 1 3 | 4 1 1 5 | 4 1 1 9 | 4 2 2 1 | 4 2 2 2 | 4 2 2 3 | 4 2 2 4 | 4 2 2 5 | 4 2 2 7 | 4 2 3 5 | 4 3 3 7 | 4 3 3 9 | 4 4 4 2 | 4 4 4 6 | 4 4 4 8 | 4 4 4 9 | 4 4 0 1 | 4 4 0 6 | 4 4 1 1 | 4 4 1 4 | 4 4 1 7 | 4 4 3 8 | 4 4 5 0 | Total Tissues/ Tumors |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcapsular, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pheochromocytoma benign | | | | | | | | | | | | | | | | | | X | | | | | | | | 1 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Parathyroid gland | + | + | + | + | + | + | + | M | + | + | M | M | + | + | + | M | M | + | + | + | M | + | + | + | + | 37 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | 49 |
| Follicular cell, adenoma | | | | | | | | | | | | | | | | | X | | | | | | | | | 1 |
| Follicular cell, carcinoma | | | | | | | | | | | | X | | | | | | | | | | | | | | 1 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | I | + | + | + | + | + | + | + | 47 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Interstitial cell, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Mast cell tumor malignant | X | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node | | + | | | | | | | | | | | | | + | | | | | | | | | | | 4 |
| Pancreatic, sarcoma, metastatic, lymph node, mesenteric | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, bronchial | + | M | + | + | + | + | + | + | + | + | + | + | M | M | + | + | + | M | + | + | + | M | M | M | + | 36 |
| Lymph node, mandibular | M | + | + | + | M | + | M | + | + | M | M | M | + | M | + | + | M | + | + | + | + | + | M | + | + | 30 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mediastinal | + | + | + | + | M | + | + | + | + | M | + | M | + | + | + | + | + | + | + | + | M | + | + | + | + | 43 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | M | + | M | + | + | + | + | M | + | + | + | M | + | 39 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | 2 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Subcutaneous tissue, fibrous histiocytoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Subcutaneous tissue, hemangioma | | | | | | X | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 4 5 1 | 4 6 3 | 5 3 1 | 5 5 6 2 | 5 6 4 | 5 9 6 | 6 0 6 | 6 4 1 | 6 4 2 | 7 0 2 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 4 4 | 4 4 3 | 4 0 7 | 4 2 0 | 4 1 6 | 4 2 6 | 4 3 4 | 4 3 6 | 4 4 1 | 4 4 5 | 4 0 2 | 4 0 4 | 4 0 5 | 4 0 8 | 4 0 9 | 4 1 0 | 4 1 8 | 4 2 8 | 4 2 9 | 4 3 0 | 4 3 1 | 4 3 2 | 4 3 3 | 4 4 0 | 4 4 7 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar carcinoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatoblastoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | | X | | | | | | | X | | | | | | X | | | | | | | | | | | |
| Sarcoma, metastatic, mesentery | X | | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | | | | | | | | | | | | | | | | | | + | | | | | | | | |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | X | | | | | X | | | |
| Bilateral, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Zymbal's gland | + | + | M | M | M | + | M | + | + | M | + | + | M | + | M | + | M | + | + | + | + | + | + | + | + | + |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymphoma malignant | | | | | | | X | X | | | | | | | | | | X | | X | | | | | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 4 0 3 | 4 1 2 | 4 1 3 | 4 1 5 | 4 1 9 | 4 2 1 | 4 2 2 | 4 2 3 | 4 2 4 | 4 2 5 | 4 2 7 | 4 3 5 | 4 3 7 | 4 3 9 | 4 4 2 | 4 4 6 | 4 4 8 | 4 4 9 | 4 4 1 | 4 0 6 | 4 0 6 | 4 1 1 | 4 1 4 | 4 1 7 | 4 3 8 | 4 5 0 | Total Tissues/ Tumors |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar carcinoma, multiple | | | | | | | | | | | | | | | | | | | X | | | | | | | | 1 |
| Hepatoblastoma, metastatic, liver | | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular carcinoma, metastatic, liver | | | X | | | | | | X | | | | | | | | | | | | | | | | | | 5 |
| Sarcoma, metastatic, mesentery | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Pleura | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | | | X | | | | | | | | | | | | 3 |
| Bilateral, adenoma | | | | | | | | | | | | | | | | | | | | | | | | X | | | 1 |
| Zymbal's gland | + | + | + | + | + | + | + | + | M | M | M | + | M | + | + | + | + | M | + | + | M | + | + | + | + | + | 36 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymphoma malignant | | | | | | | | | | | X | | | | X | | | | | | | | | | | | 6 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 3 2 5 | 5 2 6 | 5 2 7 | 5 6 0 | 5 9 9 | 6 0 0 | 6 3 2 | 6 3 7 | 6 4 2 | 6 4 3 | 6 7 2 | 7 0 5 | 7 1 1 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 2 9 | 6 3 8 | 6 2 7 | 6 4 5 | 6 4 1 | 6 0 6 | 6 0 0 | 6 2 0 | 6 4 2 | 6 2 3 | 6 1 0 | 6 3 0 | 6 0 9 | 6 3 7 | 6 0 1 | 6 0 5 | 6 1 2 | 6 1 6 | 6 1 7 | 6 2 1 | 6 2 6 | 6 2 8 | 6 3 2 | 6 3 4 | 6 3 5 | 6 3 9 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | I | A | + | + | A | + | + | + | + | I | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | A | A | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | + | A | A | + | I | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + |
| Intestine large, cecum | + | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | | | X |
| Intestine small, duodenum | + | A | + | A | A | + | + | + | + | A | A | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | A | + | A | A | + | + | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Intestine small, ileum | + | A | + | A | A | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | X | | | | | | | | | | | | | |
| Hepatoblastoma | | | | | | | | | | | | | | | | | | | | | X | | X | | | |
| Hepatocellular carcinoma | | | | X | | | | X | X | | | X | X | | | | | | | | | | X | | | |
| Hepatocellular carcinoma, multiple | | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular adenoma | | | | | X | | X | | | X | | | | | | | | | X | | | | | | X | |
| Hepatocellular adenoma, multiple | | | X | | | | | | X | | | X | X | X | | | X | | X | X | X | | | | | X |
| Mesentery | | | + | | | | | | + | + | | | | | | | | | | | + | | + | | + | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tongue | | | | | | + | | | | | | | | | | | | | | | | | | | | |
| Squamous cell papilloma | | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | X | |
| Capsule, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcapsular, adenoma | | | | | | | | | | | | | X | | | | | | | | | | | | | |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | I | + | + |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 4 4 | 6 4 7 | 6 5 0 | 6 0 0 7 | 6 0 0 8 | 6 0 1 3 | 6 1 1 4 | 6 1 1 5 | 6 1 1 9 | 6 2 2 2 | 6 2 2 4 | 6 2 3 5 | 6 3 1 | 6 3 3 | 6 4 3 3 | 6 4 4 6 | 6 4 0 2 | 6 0 0 3 | 6 0 0 4 | 6 0 1 1 | 6 1 3 6 | 6 4 0 | 6 4 4 1 | 6 4 4 8 | 6 4 4 9 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | M | + | I | I | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | M | + | + | 40 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Polyp adenomatous | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 44 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 45 |
| Carcinoma | | | | | | | | | | | | | | X | | | | | | | | | | | | 1 |
| Polyp adenomatous | | | | | | | | | | | X | | | | | | | | | | | | | | | 1 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatoblastoma | | | X | | | | X | | | | | | | | | | | X | | | | | | | | 5 |
| Hepatocellular carcinoma | | | X | | | | | | | | | | | X | | | | X | | | | | | | | 9 |
| Hepatocellular carcinoma, multiple | | | | | | | X | | | | | | | | | | | | | | | | | | | 2 |
| Hepatocellular adenoma | X | X | X | | | | X | | | | | | X | | | X | X | X | | | | | | | | 13 |
| Hepatocellular adenoma, multiple | | | | X | | | | X | X | X | X | X | | | X | | | | X | X | X | | X | X | X | 23 |
| Mesentery | + | | | + | + | | | | | | | | + | | | | + | | | | | | | | | 11 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Tongue | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Capsule, adenoma | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcapsular, adenoma | | | | | | | | | | | | | | | | | | X | | | | | | | | 2 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Parathyroid gland | + | I | + | + | M | M | + | + | M | + | + | + | + | + | + | M | + | + | M | M | + | M | + | + | + | 40 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | + | 49 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 3 2 5 | 5 2 6 | 5 2 7 | 5 6 0 | 5 9 9 | 6 0 0 | 6 3 2 | 6 3 7 | 6 4 2 | 6 4 3 | 6 7 2 | 7 0 5 | 7 1 1 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 | 7 2 9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 2 9 | 6 3 8 | 6 2 7 | 6 4 5 | 6 1 8 | 6 0 6 | 6 0 2 | 6 4 2 | 6 2 3 | 6 1 0 | 6 3 0 | 6 0 9 | 6 3 7 | 6 0 1 | 6 0 5 | 6 1 2 | 6 1 6 | 6 1 7 | 6 2 1 | 6 2 6 | 6 2 8 | 6 3 2 | 6 3 4 | 6 3 5 | 6 3 9 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | | | | | | | | | | | |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, bronchial | M | M | + | + | + | + | + | + | + | M | M | + | M | + | M | + | + | M | + | + | M | + | M | M | + |
| Lymph node, mandibular | + | M | + | M | + | M | + | + | + | + | M | M | M | M | M | M | + | + | + | + | M | + | M | + | M |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | M | + | + | M | + | + | + | M | + | + | M | M | M | + | + | + | M | + | + | + | M | + | + | + | + |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Thymus | + | + | + | + | + | M | + | + | + | + | M | + | M | + | + | + | + | + | + | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | | | X | | | | X | | | | | | | | | | X | | | | | | |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | X | X | | | | | |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | | | | | | X | | X | X | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | X | | | | | | | | | | | | | | X | X | | | |
| Carcinoma | | | | | | | | | | | | | X | | | | | | | X | | | | | |
| Lacrimal gland | | | | | | | | + | | | | | | | | | | | | | | | | | |
| Zymbal's gland | M | + | M | M | M | M | + | M | + | + | M | M | + | + | + | + | + | M | M | M | M | + | + | M | M |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 4 4 4 | 6 4 4 7 | 6 5 0 | 6 0 0 7 | 6 0 0 8 | 6 1 1 3 | 6 1 1 4 | 6 1 1 5 | 6 1 1 9 | 6 2 2 2 | 6 2 2 4 | 6 2 2 5 | 6 3 1 | 6 3 3 3 | 6 4 3 3 | 6 4 4 6 | 6 0 2 | 6 0 0 3 | 6 0 4 | 6 1 1 | 6 3 1 6 | 6 4 4 0 | 6 4 4 1 | 6 4 4 8 | 6 4 4 9 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Coagulating gland | | | | | | | | | | | | | | | | | | | | | | | | + | | 1 |
| Epididymis | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Preputial gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Prostate | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Seminal vesicle | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Testes | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | | | | | + | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, bronchial | + | + | + | + | + | + | + | + | + | + | M | M | + | M | + | + | + | + | + | + | + | M | M | + | + | 35 |
| Lymph node, mandibular | + | M | M | + | M | M | + | M | + | + | + | + | M | + | + | M | M | + | M | + | M | M | M | M | + | 25 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node, mediastinal | M | + | + | + | + | + | + | + | + | M | + | + | + | + | M | + | + | + | + | M | + | M | M | + | + | 36 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Thymus | + | + | M | M | M | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | + | + | M | M | 40 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | M | M | M | M | M | M | M | M | + | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | 1 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar adenoma | X | | | X | | | | | | | | | | | | | | | X | | | X | | | | 7 |
| Alveolar/bronchiolar carcinoma | | X | | | | | | | | | X | | | | | | | | | | | | | | | 4 |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 3 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 4 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Lacrimal gland | | | | | | | | | | | | | | | | | + | | | | | | | | | 2 |
| Zymbal's gland | + | + | + | + | M | + | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | 32 |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 325 | 522 | 557 | 560 | 599 | 600 | 602 | 633 | 647 | 642 | 643 | 642 | 705 | 711 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 | 729 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 62 9 | 63 8 | 62 7 | 64 5 | 61 8 | 60 6 | 62 0 | 64 2 | 62 3 | 61 0 | 63 0 | 60 9 | 63 7 | 60 1 | 60 5 | 61 2 | 61 6 | 61 7 | 62 1 | 62 6 | 62 8 | 63 2 | 63 4 | 63 5 | 63 9 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymphoma malignant | | | | | | | | | | | | | | | | | | | | | | | | X | X | |

**TABLE C2**
**Individual Animal Tumor Pathology of Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 2 9 | 7 2 9 | 7 2 9 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 6 4 4 | 6 4 7 | 6 5 0 | 6 0 7 | 6 0 8 | 6 1 3 | 6 1 4 | 6 1 5 | 6 1 9 | 6 2 2 | 6 2 4 | 6 2 5 | 6 3 1 | 6 3 3 | 6 4 3 | 6 4 6 | 6 0 2 | 6 0 3 | 6 0 4 | 6 1 1 | 6 3 6 | 6 4 0 | 6 4 1 | 6 4 8 | 6 4 9 | Total Tissues/ Tumors |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymphoma malignant | | | | | X | | | | | | | | | | | | | | | | | | | | | 3 |

**TABLE C3**
**Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Adrenal Cortex: Adenoma** | | | | |
| Overall rate[a] | 1/48 (2%) | 1/49 (2%) | 1/50 (2%) | 4/50 (8%) |
| Adjusted rate[b] | 2.2% | 2.2% | 2.2% | 8.9% |
| Terminal rate[c] | 1/35 (3%) | 1/40 (3%) | 1/40 (3%) | 3/37 (8%) |
| First incidence (days) | 729 (T) | 729 (T) | 729 (T) | 711 |
| Poly-3 test[d] | P=0.057 | P=0.759N | P=0.758N | P=0.180 |
| **Harderian Gland: Adenoma** | | | | |
| Overall rate | 6/50 (12%) | 4/50 (8%) | 4/50 (8%) | 4/50 (8%) |
| Adjusted rate | 13.0% | 8.8% | 8.9% | 8.9% |
| Terminal rate | 5/35 (14%) | 3/40 (8%) | 4/40 (10%) | 3/37 (8%) |
| First incidence (days) | 671 | 663 | 729 (T) | 632 |
| Poly-3 test | P=0.440N | P=0.379N | P=0.383N | P=0.385N |
| **Harderian Gland: Adenoma or Carcinoma** | | | | |
| Overall rate | 7/50 (14%) | 5/50 (10%) | 4/50 (8%) | 6/50 (12%) |
| Adjusted rate | 15.2% | 11.0% | 8.9% | 13.3% |
| Terminal rate | 6/35 (17%) | 4/40 (10%) | 4/40 (10%) | 4/37 (11%) |
| First incidence (days) | 671 | 663 | 729 (T) | 632 |
| Poly-3 test | P=0.554 | P=0.390N | P=0.273N | P=0.518N |
| **Liver: Hepatocellular Adenoma** | | | | |
| Overall rate | 18/50 (36%) | 23/49 (47%) | 26/50 (52%) | 36/50 (72%) |
| Adjusted rate | 38.4% | 51.0% | 57.0% | 76.7% |
| Terminal rate | 13/35 (37%) | 21/40 (53%) | 24/40 (60%) | 29/37 (78%) |
| First incidence (days) | 622 | 705 | 642 | 527 |
| Poly-3 test | P<0.001 | P=0.154 | P=0.052 | P<0.001 |
| **Liver: Hepatocellular Carcinoma** | | | | |
| Overall rate | 9/50 (18%) | 8/49 (16%) | 13/50 (26%) | 11/50 (22%) |
| Adjusted rate | 19.2% | 17.7% | 27.1% | 23.7% |
| Terminal rate | 5/35 (14%) | 6/40 (15%) | 7/40 (18%) | 5/37 (14%) |
| First incidence (days) | 630 | 705 | 463 | 560 |
| Poly-3 test | P=0.348 | P=0.535N | P=0.253 | P=0.393 |
| **Liver: Hepatocellular Adenoma or Carcinoma** | | | | |
| Overall rate | 25/50 (50%) | 26/49 (53%) | 33/50 (66%) | 41/50 (82%) |
| Adjusted rate | 52.2% | 57.6% | 68.7% | 85.0% |
| Terminal rate | 16/35 (46%) | 24/40 (60%) | 27/40 (68%) | 31/37 (84%) |
| First incidence (days) | 622 | 705 | 463 | 527 |
| Poly-3 test | P<0.001 | P=0.375 | P=0.071 | P<0.001 |
| **Liver: Hepatoblastoma** | | | | |
| Overall rate | 0/50 (0%) | 0/49 (0%) | 1/50 (2%) | 5/50 (10%) |
| Adjusted rate | 0.0% | 0.0% | 2.2% | 11.2% |
| Terminal rate | 0/35 (0%) | 0/40 (0%) | 1/40 (3%) | 5/37 (14%) |
| First incidence (days) | —[e] | —[f] | 729 (T) | 729 (T) |
| Poly-3 test | P<0.001 | | P=0.497 | P=0.028 |
| **Liver: Hepatocellular Carcinoma or Hepatoblastoma** | | | | |
| Overall rate | 9/50 (18%) | 8/49 (16%) | 13/50 (26%) | 12/50 (24%) |
| Adjusted rate | 19.2% | 17.7% | 27.1% | 25.8% |
| Terminal rate | 5/35 (14%) | 6/40 (15%) | 7/40 (18%) | 6/37 (16%) |
| First incidence (days) | 630 | 705 | 463 | 560 |
| Poly-3 test | P=0.248 | P=0.535N | P=0.253 | P=0.303 |

**TABLE C3**
**Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma** | | | | |
| Overall rate | 25/50 (50%) | 26/49 (53%) | 33/50 (66%) | 41/50 (82%) |
| Adjusted rate | 52.2% | 57.6% | 68.7% | 85.0% |
| Terminal rate | 16/35 (46%) | 24/40 (60%) | 27/40 (68%) | 31/37 (84%) |
| First incidence (days) | 622 | 705 | 463 | 527 |
| Poly-3 test | P<0.001 | P=0.375 | P=0.071 | P<0.001 |
| **Lung: Alveolar/bronchiolar Adenoma** | | | | |
| Overall rate | 13/50 (26%) | 7/50 (14%) | 0/50 (0%) | 7/50 (14%) |
| Adjusted rate | 27.9% | 15.4% | 0.0% | 15.4% |
| Terminal rate | 11/35 (31%) | 5/40 (13%) | 0/40 (0%) | 5/37 (14%) |
| First incidence (days) | 622 | 705 | — | 599 |
| Poly-3 test | P=0.286N | P=0.114N | P<0.001N | P=0.113N |
| **Lung: Alveolar/bronchiolar Carcinoma** | | | | |
| Overall rate | 6/50 (12%) | 3/50 (6%) | 1/50 (2%) | 4/50 (8%) |
| Adjusted rate | 12.9% | 6.6% | 2.2% | 9.0% |
| Terminal rate | 4/35 (11%) | 3/40 (8%) | 1/40 (3%) | 4/37 (11%) |
| First incidence (days) | 669 | 729 (T) | 729 (T) | 729 (T) |
| Poly-3 test | P=0.569N | P=0.255N | P=0.060N | P=0.393N |
| **Lung: Alveolar/bronchiolar Adenoma or Carcinoma** | | | | |
| Overall rate | 17/50 (34%) | 10/50 (20%) | 1/50 (2%) | 10/50 (20%) |
| Adjusted rate | 36.2% | 22.0% | 2.2% | 22.0% |
| Terminal rate | 13/35 (37%) | 8/40 (20%) | 1/40 (3%) | 8/37 (22%) |
| First incidence (days) | 622 | 705 | 729 (T) | 599 |
| Poly-3 test | P=0.284N | P=0.102N | P<0.001N | P=0.100N |
| **Skin (Subcutaneous Tissue): Fibrosarcoma, Fibrous Histiocytoma, or Sarcoma** | | | | |
| Overall rate | 0/50 (0%) | 4/50 (8%) | 2/50 (4%) | 0/50 (0%) |
| Adjusted rate | 0.0% | 8.8% | 4.4% | 0.0% |
| Terminal rate | 0/35 (0%) | 3/40 (8%) | 2/40 (5%) | 0/37 (0%) |
| First incidence (days) | — | 627 | 729 (T) | — |
| Poly-3 test | P=0.196N | P=0.059 | P=0.233 | — |
| **All Organs: Hemangiosarcoma** | | | | |
| Overall rate | 3/50 (6%) | 3/50 (6%) | 2/50 (4%) | 1/50 (2%) |
| Adjusted rate | 6.5% | 6.6% | 4.4% | 2.2% |
| Terminal rate | 1/35 (3%) | 3/40 (8%) | 1/40 (3%) | 0/37 (0%) |
| First incidence (days) | 668 | 729 (T) | 606 | 711 |
| Poly-3 test | P=0.232N | P=0.652 | P=0.507N | P=0.317N |
| **All Organs: Hemangioma or Hemangiosarcoma** | | | | |
| Overall rate | 4/50 (8%) | 3/50 (6%) | 3/50 (6%) | 1/50 (2%) |
| Adjusted rate | 8.6% | 6.6% | 6.6% | 2.2% |
| Terminal rate | 2/35 (6%) | 3/40 (8%) | 2/40 (5%) | 0/37 (0%) |
| First incidence (days) | 668 | 729 (T) | 606 | 711 |
| Poly-3 test | P=0.164N | P=0.513N | P=0.508N | P=0.189N |
| **All Organs: Malignant Lymphoma** | | | | |
| Overall rate | 3/50 (6%) | 1/50 (2%) | 6/50 (12%) | 3/50 (6%) |
| Adjusted rate | 6.5% | 2.2% | 13.1% | 6.7% |
| Terminal rate | 2/35 (6%) | 1/40 (3%) | 4/40 (10%) | 3/37 (8%) |
| First incidence (days) | 669 | 729 (T) | 606 | 729 (T) |
| Poly-3 test | P=0.507 | P=0.313N | P=0.239 | P=0.647 |

**TABLE C3**
**Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **All Organs: Benign Neoplasms** | | | | |
| Overall rate | 30/50 (60%) | 28/50 (56%) | 30/50 (60%) | 39/50 (78%) |
| Adjusted rate | 63.3% | 61.4% | 65.8% | 82.3% |
| Terminal rate | 23/35 (66%) | 25/40 (63%) | 28/40 (70%) | 31/37 (84%) |
| First incidence (days) | 622 | 663 | 642 | 527 |
| Poly-3 test | P=0.009 | P=0.508N | P=0.487 | P=0.027 |
| **All Organs: Malignant Neoplasms** | | | | |
| Overall rate | 22/50 (44%) | 20/50 (40%) | 26/50 (52%) | 18/50 (36%) |
| Adjusted rate | 45.4% | 43.2% | 52.5% | 38.7% |
| Terminal rate | 11/35 (31%) | 16/40 (40%) | 17/40 (43%) | 12/37 (32%) |
| First incidence (days) | 610 | 568 | 451 | 560 |
| Poly-3 test | P=0.263N | P=0.499N | P=0.309 | P=0.326N |
| **All Organs: Benign or Malignant Neoplasms** | | | | |
| Overall rate | 41/50 (82%) | 38/50 (76%) | 41/50 (82%) | 43/50 (86%) |
| Adjusted rate | 83.6% | 81.7% | 82.8% | 89.1% |
| Terminal rate | 27/35 (77%) | 33/40 (83%) | 32/40 (80%) | 33/37 (89%) |
| First incidence (days) | 610 | 568 | 451 | 527 |
| Poly-3 test | P=0.199 | P=0.512N | P=0.563N | P=0.306 |

(T) Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, liver, and lung; for other tissues, denominator is number of animals necropsied.
[b] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the chamber control incidence is the P value associated with the trend test. Beneath the exposed group incidence are the P values corresponding to pairwise comparisons between the chamber controls and that exposed group. The Poly-3 test accounts for the differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in an exposed group is indicated by **N**.
[e] Not applicable; no neoplasms in animal group
[f] Value of statistic cannot be computed.

**TABLE C4**
**Historical Incidence of Liver Neoplasms in Control Male B6C3F$_1$ Mice[a]**

| Study | Incidence in Controls | | | | |
|---|---|---|---|---|---|
| | Hepatocelluar Adenoma | Hepatocellular Carcinoma | Hepatocellular Adenoma or Carcinoma | Hepatoblastoma | Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma |
| **Historical Incidence: Inhalation Studies** | | | | | |
| Decalin | 22/50 | 10/50 | 28/50 | 0/50 | 28/50 |
| Indium phosphide | 17/50 | 11/50 | 26/50 | 0/50 | 26/50 |
| Propylene glycol mono-*t*-butyl ether | 18/50 | 9/50 | 25/50 | 0/50 | 25/50 |
| Stoddard solvent IIC | 23/50 | 16/50 | 34/50 | 0/50 | 34/50 |
| Vanadium pentoxide | 15/50 | 14/50 | 26/50 | 0/50 | 26/50 |
| **Overall Historical Incidence: Inhalation Studies** | | | | | |
| Total (%) | 95/250 (38.0%) | 60/250 (24.0%) | 139/250 (55.6%) | 0/250 (0%) | 139/250 (55.6%) |
| Mean ± standard deviation | 38.0% ± 6.8% | 24.0% ± 5.8% | 55.6% ± 7.3% | | 55.6% ± 7.3% |
| Range | 30%-46% | 18%-32% | 50%-68% | | 50%-68% |
| **Overall Historical Incidence** | | | | | |
| Total (%) | 357/1,159 (30.8%) | 247/1,159 (21.3%) | 543/1,159 (46.9%) | 16/1,159 (1.4%) | 548/1,159 (47.3%) |
| Mean ± standard deviation | 32.2% ± 10.5% | 22.3% ± 8.7% | 48.9% ± 14.5% | 1.5% ± 2.6% | 49.3% ± 14.5% |
| Range | 12%-46% | 8%-46% | 20%-72% | 0%-10% | 20%-72% |

[a] Data as of March 3, 2003

**TABLE C5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Moribund | 4 | 6 | 6 | 8 |
| Natural deaths | 11 | 4 | 4 | 5 |
| Survivors | | | | |
| Terminal sacrifice | 35 | 40 | 40 | 37 |
| Animals examined microscopically | 50 | 50 | 50 | 50 |
| **Alimentary System** | | | | |
| Gallbladder | (38) | (41) | (39) | (40) |
| Degeneration, hyaline | | 1 (2%) | 2 (5%) | |
| Intestine large, colon | (46) | (48) | (48) | (47) |
| Serosa, inflammation, granulomatous | | 1 (2%) | | |
| Intestine large, rectum | (46) | (48) | (48) | (46) |
| Infiltration cellular, mixed cell | 1 (2%) | | | |
| Intestine large, cecum | (43) | (47) | (48) | (48) |
| Necrosis | 1 (2%) | 1 (2%) | | |
| Intestine small, jejunum | (42) | (47) | (47) | (45) |
| Infiltration cellular, mixed cell | 2 (5%) | | 2 (4%) | |
| Inflammation, granulomatous | 1 (2%) | 1 (2%) | | |
| Necrosis | | | 1 (2%) | |
| Epithelium, hyperplasia | 1 (2%) | | | |
| Intestine small, ileum | (43) | (47) | (46) | (46) |
| Infiltration cellular, mixed cell | 4 (9%) | 2 (4%) | 2 (4%) | 1 (2%) |
| Inflammation, acute | | | 1 (2%) | |
| Inflammation, chronic active | | 1 (2%) | 1 (2%) | |
| Necrosis | | | 1 (2%) | |
| Epithelium, hyperplasia | 1 (2%) | 1 (2%) | | |
| Liver | (50) | (49) | (50) | (50) |
| Basophilic focus | 6 (12%) | 11 (22%) | 16 (32%) | 4 (8%) |
| Clear cell focus | 20 (40%) | 18 (37%) | 16 (32%) | 17 (34%) |
| Eosinophilic focus | 9 (18%) | 14 (29%) | 11 (22%) | 29 (58%) |
| Fatty change | | 1 (2%) | | 2 (4%) |
| Hematopoietic cell proliferation | 1 (2%) | 1 (2%) | 1 (2%) | |
| Infarct | 2 (4%) | 1 (2%) | 1 (2%) | 3 (6%) |
| Inflammation, granulomatous | 9 (18%) | 12 (24%) | 11 (22%) | 3 (6%) |
| Mixed cell focus | | | | 4 (8%) |
| Tension lipidosis | 1 (2%) | 2 (4%) | 4 (8%) | 2 (4%) |
| Centrilobular, necrosis | 1 (2%) | 1 (2%) | 1 (2%) | |
| Hepatocyte, multinucleated | 27 (54%) | 23 (47%) | 24 (48%) | 46 (92%) |
| Mesentery | (14) | (16) | (13) | (11) |
| Inflammation, granulomatous | 2 (14%) | 1 (6%) | 4 (31%) | 1 (9%) |
| Artery, inflammation | | | 1 (8%) | 2 (18%) |
| Fat, necrosis | 10 (71%) | 14 (88%) | 7 (54%) | 7 (64%) |
| Pancreas | (48) | (49) | (50) | (50) |
| Atrophy | | 1 (2%) | | |
| Basophilic focus | | | | 1 (2%) |

[a] Number of animals examined microscopically at the site and the number of animals with lesion

**TABLE C5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Alimentary System** (continued) | | | | |
| Stomach, forestomach | (48) | (49) | (50) | (50) |
| Hyperkeratosis | | | 1 (2%) | |
| Hyperplasia, squamous | | | | 1 (2%) |
| Inflammation | 2 (4%) | 3 (6%) | 9 (18%) | 9 (18%) |
| Ulcer | | | | 1 (2%) |
| Artery, inflammation, chronic active | | | 1 (2%) | |
| Epithelium, hyperplasia, squamous | 2 (4%) | 5 (10%) | 9 (18%) | 7 (14%) |
| Epithelium, ulcer | 1 (2%) | 1 (2%) | 3 (6%) | 3 (6%) |
| Stomach, glandular | (46) | (48) | (50) | (48) |
| Hyperplasia | 1 (2%) | | | |
| Metaplasia, squamous | 1 (2%) | | | |
| Mineralization | 1 (2%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Necrosis | | 2 (4%) | 1 (2%) | |
| Tooth | (50) | (50) | (50) | (50) |
| Inflammation, chronic active | 3 (6%) | 5 (10%) | 4 (8%) | 15 (30%) |
| Malformation | 24 (48%) | 15 (30%) | 15 (30%) | 16 (32%) |
| **Cardiovascular System** | | | | |
| Heart | (50) | (50) | (50) | (50) |
| Cardiomyopathy | 9 (18%) | 8 (16%) | 11 (22%) | 7 (14%) |
| Mineralization | 1 (2%) | 1 (2%) | | |
| Necrosis | 2 (4%) | | | |
| Thrombosis | | | 1 (2%) | 1 (2%) |
| Artery, inflammation, chronic active | | | 3 (6%) | |
| **Endocrine System** | | | | |
| Adrenal cortex | (48) | (49) | (50) | (50) |
| Hyperplasia | 11 (23%) | 9 (18%) | 14 (28%) | 7 (14%) |
| Hypertrophy | 34 (71%) | 32 (65%) | 29 (58%) | 18 (36%) |
| Adrenal medulla | (47) | (49) | (49) | (49) |
| Hyperplasia | | 1 (2%) | 1 (2%) | 2 (4%) |
| Infiltration cellular, polymorphonuclear | | | 1 (2%) | |
| Islets, pancreatic | (48) | (49) | (50) | (50) |
| Hyperplasia | | 1 (2%) | | |
| Pituitary gland | (43) | (48) | (50) | (48) |
| Cyst | | 1 (2%) | | |
| Pars distalis, hyperplasia | | 1 (2%) | 4 (8%) | 1 (2%) |
| Thyroid gland | (48) | (48) | (49) | (49) |
| Follicular cell, hyperplasia | | | 1 (2%) | |
| **General Body System** | | | | |
| None | | | | |

**TABLE C5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Genital System** | | | | |
| Epididymis | (50) | (50) | (50) | (50) |
| Granuloma sperm | 1 (2%) | 1 (2%) | | |
| Inflammation, chronic | | 1 (2%) | | |
| Preputial gland | (50) | (50) | (50) | (50) |
| Ectasia | 2 (4%) | 1 (2%) | 1 (2%) | |
| Hyperplasia, squamous | 1 (2%) | | | 2 (4%) |
| Inflammation, chronic | | 2 (4%) | 2 (4%) | |
| Inflammation, suppurative | | 3 (6%) | 2 (4%) | 2 (4%) |
| Prostate | (49) | (49) | (47) | (50) |
| Inflammation, suppurative | | | 1 (2%) | |
| Artery, inflammation, chronic active | | 1 (2%) | 1 (2%) | |
| Seminal vesicle | (47) | (49) | (49) | (49) |
| Inflammation, chronic | | 2 (4%) | 1 (2%) | |
| Testes | (50) | (50) | (50) | (50) |
| Amyloid deposition | | 1 (2%) | | |
| Atrophy | | 1 (2%) | 1 (2%) | |
| Mineralization | 1 (2%) | | | |
| Germinal epithelium, degeneration | 1 (2%) | | | 1 (2%) |
| **Hematopoietic System** | | | | |
| Bone marrow | (49) | (49) | (50) | (50) |
| Thrombosis | | | | 1 (2%) |
| Lymph node, bronchial | (32) | (36) | (36) | (35) |
| Infiltration cellular, plasma cell | 1 (3%) | | | |
| Lymph node, mandibular | (28) | (38) | (30) | (25) |
| Infiltration cellular, plasma cell | | | | 1 (4%) |
| Lymph node, mesenteric | (48) | (49) | (49) | (50) |
| Angiectasis | | | 1 (2%) | |
| Infiltration cellular, plasma cell | 2 (4%) | 1 (2%) | 4 (8%) | |
| Infiltration cellular, mixed cell | 1 (2%) | | | |
| Pigmentation | | 1 (2%) | | |
| Lymph node, mediastinal | (39) | (39) | (43) | (36) |
| Inflammation, granulomatous | | 1 (3%) | | |
| Spleen | (48) | (48) | (50) | (50) |
| Angiectasis | | | | 1 (2%) |
| Hematopoietic cell proliferation | 4 (8%) | 2 (4%) | 2 (4%) | 2 (4%) |
| Hyperplasia, lymphoid | | | | 1 (2%) |
| Infiltration cellular, histiocyte | 1 (2%) | | | |
| **Integumentary System** | | | | |
| Skin | (49) | (50) | (50) | (50) |
| Infiltration cellular, mixed cell | | 1 (2%) | | |
| Inflammation, chronic active | 4 (8%) | 1 (2%) | 6 (12%) | 5 (10%) |
| Epidermis, hyperplasia | | | | 1 (2%) |
| Subcutaneous tissue, edema | 1 (2%) | | | |
| Subcutaneous tissue, hemorrhage | 1 (2%) | | | |

**TABLE C5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Musculoskeletal System** | | | | |
| Bone | (50) | (50) | (50) | (50) |
| Fibrous osteodystrophy | 1 (2%) | | | |
| **Nervous System** | | | | |
| Brain | (50) | (50) | (50) | (50) |
| Necrosis | 1 (2%) | | | |
| Artery, inflammation, chronic active | | | 1 (2%) | |
| **Respiratory System** | | | | |
| Larynx | (49) | (50) | (50) | (50) |
| Artery, inflammation, chronic active | | | 1 (2%) | |
| Lung | (50) | (50) | (50) | (50) |
| Hemorrhage | | 1 (2%) | | 1 (2%) |
| Inflammation, granulomatous | | 1 (2%) | | 1 (2%) |
| Inflammation, suppurative | | | 1 (2%) | |
| Mineralization | | 1 (2%) | | |
| Thrombosis | | 3 (6%) | | |
| Alveolar epithelium, hyperplasia | 6 (12%) | 4 (8%) | 4 (8%) | |
| Alveolus, infiltration cellular, histiocyte | 1 (2%) | | | 2 (4%) |
| Nose | (50) | (49) | (50) | (50) |
| Amyloid deposition | | 1 (2%) | | |
| Inflammation, suppurative | 5 (10%) | | 4 (8%) | 6 (12%) |
| Olfactory epithelium, atrophy | | | 1 (2%) | |
| Respiratory epithelium, metaplasia, squamous | | | | 1 (2%) |
| Respiratory epithelium, necrosis | | | 1 (2%) | 1 (2%) |
| Pleura | (1) | | (1) | |
| Necrosis, fatty | | | 1 (100%) | |
| Trachea | (48) | (48) | (50) | (50) |
| Degeneration, hyaline | | | 1 (2%) | |
| Inflammation, suppurative | | | 1 (2%) | |
| **Special Senses System** | | | | |
| Eye | (48) | (49) | (50) | (50) |
| Cornea, erosion | | | | 1 (2%) |
| Cornea, hyperplasia, squamous | 1 (2%) | | | 1 (2%) |
| Cornea, inflammation, chronic active | 1 (2%) | | 1 (2%) | 1 (2%) |
| Cornea, mineralization | | | | 3 (6%) |
| Harderian gland | (50) | (50) | (50) | (50) |
| Hyperplasia | 10 (20%) | 3 (6%) | 5 (10%) | 1 (2%) |
| Zymbal's gland | (35) | (35) | (36) | (32) |
| Hyperplasia | 1 (3%) | | | |

**TABLE C5**
**Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Urinary System** | | | | |
| Kidney | (50) | (49) | (50) | (50) |
| Amyloid deposition | | 1 (2%) | | |
| Cyst | 1 (2%) | 1 (2%) | 2 (4%) | |
| Infarct | 3 (6%) | 3 (6%) | 3 (6%) | 7 (14%) |
| Inflammation, chronic, suppurative | | 1 (2%) | | 1 (2%) |
| Metaplasia, osseous | 3 (6%) | 6 (12%) | 2 (4%) | |
| Mineralization | | 1 (2%) | | |
| Nephropathy | 41 (82%) | 40 (82%) | 44 (88%) | 36 (72%) |
| Artery, inflammation, chronic active | | | 2 (4%) | 1 (2%) |
| Papilla, inflammation, suppurative | | | 1 (2%) | |
| Pelvis, dilatation | | | 1 (2%) | 2 (4%) |
| Renal tubule, hyperplasia | 2 (4%) | | 1 (2%) | |
| Renal tubule, necrosis | 1 (2%) | | | |
| Transitional epithelium, hyperplasia | | | | 2 (4%) |
| Urinary bladder | (48) | (48) | (49) | (50) |
| Inflammation, chronic active | | | 1 (2%) | |
| Artery, inflammation, chronic active | | 1 (2%) | 1 (2%) | |

# APPENDIX D
# SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER


| | | |
|---|---|---|
| TABLE D1 | Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 202 |
| TABLE D2 | Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 206 |
| TABLE D3 | Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 230 |
| TABLE D4 | Historical Incidence of Liver Neoplasms in Control Female B6C3F$_1$ Mice . . . . . | 233 |
| TABLE D5 | Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . | 234 |

**TABLE D1**
**Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Accidental deaths | | 1 | | 1 |
| Moribund sacrifice | 8 | 10 | 6 | 4 |
| Natural deaths | 3 | 3 | 2 | 6 |
| Survivors | | | | |
| Died last week of study | | | 1 | 1 |
| Terminal sacrifice | 39 | 36 | 41 | 38 |
| Animals examined microscopically | 50 | 50 | 50 | 49 |
| **Alimentary System** | | | | |
| Gallbladder | (40) | (39) | (43) | (33) |
| Histiocytic sarcoma | | | 1 (2%) | |
| Intestine large, colon | (48) | (49) | (50) | (48) |
| Hepatocholangiocarcinoma, metastatic, liver | | | 1 (2%) | |
| Histiocytic sarcoma | | | 1 (2%) | |
| Intestine large, rectum | (48) | (49) | (50) | (48) |
| Hepatocholangiocarcinoma, metastatic, liver | | | 1 (2%) | |
| Intestine large, cecum | (49) | (48) | (49) | (46) |
| Histiocytic sarcoma | | | 1 (2%) | |
| Leiomyoma | | | | 1 (2%) |
| Intestine small, duodenum | (49) | (47) | (50) | (46) |
| Histiocytic sarcoma | | | 1 (2%) | |
| Intestine small, jejunum | (49) | (48) | (48) | (47) |
| Carcinoma | | | | 1 (2%) |
| Intestine small, ileum | (49) | (48) | (48) | (45) |
| Carcinoma | 1 (2%) | | | |
| Sarcoma, metastatic, skin | | 1 (2%) | | |
| Liver | (49) | (50) | (50) | (49) |
| Cholangioma | | | | 1 (2%) |
| Hemangioma | | | | 1 (2%) |
| Hemangiosarcoma | | 2 (4%) | | |
| Hepatoblastoma | | | | 2 (4%) |
| Hepatocellular carcinoma | 4 (8%) | 8 (16%) | 6 (12%) | 8 (16%) |
| Hepatocellular carcinoma, multiple | | | 1 (2%) | 2 (4%) |
| Hepatocellular adenoma | 8 (16%) | 8 (16%) | 7 (14%) | 5 (10%) |
| Hepatocellular adenoma, multiple | 6 (12%) | | 3 (6%) | 32 (65%) |
| Hepatocholangiocarcinoma | | | 1 (2%) | |
| Histiocytic sarcoma | 1 (2%) | | 1 (2%) | 1 (2%) |
| Mesentery | (17) | (21) | (13) | (2) |
| Hemangiosarcoma | 1 (6%) | | | |
| Hepatocholangiocarcinoma, metastatic, liver | | | 1 (8%) | |
| Pancreas | (49) | (50) | (50) | (48) |
| Hepatocholangiocarcinoma, metastatic, liver | | | 1 (2%) | |
| Histiocytic sarcoma | | | 1 (2%) | |
| Salivary glands | (50) | (50) | (50) | (49) |
| Stomach, forestomach | (49) | (50) | (50) | (48) |
| Histiocytic sarcoma | | | 1 (2%) | |
| Squamous cell papilloma | | | 1 (2%) | 1 (2%) |
| Stomach, glandular | (49) | (48) | (50) | (48) |
| Histiocytic sarcoma | | | 1 (2%) | |

**TABLE D1**
**Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Cardiovascular System** | | | | |
| Heart | (50) | (50) | (50) | (49) |
| Sarcoma, metastatic, uncertain primary site | | | 1 (2%) | |
| **Endocrine System** | | | | |
| Adrenal cortex | (49) | (50) | (50) | (48) |
| Carcinoma | 1 (2%) | | | |
| Hepatocellular carcinoma, metastatic, liver | | 1 (2%) | | |
| Adrenal medulla | (47) | (49) | (50) | (48) |
| Pheochromocytoma malignant | | 1 (2%) | | |
| Islets, pancreatic | (49) | (50) | (50) | (48) |
| Adenoma | 1 (2%) | | | |
| Pituitary gland | (48) | (49) | (47) | (46) |
| Pars distalis, adenoma | 9 (19%) | 11 (22%) | 12 (26%) | 8 (17%) |
| Pars intermedia, adenoma | | 1 (2%) | 1 (2%) | |
| **General Body System** | | | | |
| Peritoneum | | (1) | (2) | |
| Hepatocholangiocarcinoma, metastatic, liver | | | 1 (50%) | |
| Histiocytic sarcoma | | | 1 (50%) | |
| **Genital System** | | | | |
| Ovary | (50) | (49) | (49) | (48) |
| Carcinoma | | 1 (2%) | | |
| Cystadenoma | 2 (4%) | 1 (2%) | 3 (6%) | 1 (2%) |
| Histiocytic sarcoma | | | 1 (2%) | |
| Luteoma | 2 (4%) | | 1 (2%) | 1 (2%) |
| Uterus | (50) | (50) | (50) | (48) |
| Adenoma | 1 (2%) | | | |
| Hemangiosarcoma | | | 2 (4%) | |
| Histiocytic sarcoma | | | 1 (2%) | |
| Leiomyoma | | | 2 (4%) | |
| Leiomyosarcoma | | | | 1 (2%) |
| Polyp stromal | | 1 (2%) | 1 (2%) | |
| Sarcoma stromal | 1 (2%) | | | |

**TABLE D1**
**Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Hematopoietic System** | | | | |
| Bone marrow | (49) | (50) | (50) | (48) |
| Hemangiosarcoma | | 1 (2%) | | |
| Histiocytic sarcoma | | | | 1 (2%) |
| Lymph node | (4) | (8) | (6) | (2) |
| Lumbar, hemangiosarcoma | | | 1 (17%) | |
| Lymph node, bronchial | (45) | (34) | (44) | (42) |
| Histiocytic sarcoma | 1 (2%) | | | |
| Lymph node, mandibular | (44) | (45) | (45) | (34) |
| Histiocytic sarcoma | | | | 1 (3%) |
| Lymph node, mesenteric | (48) | (48) | (48) | (48) |
| Histiocytic sarcoma | | | 1 (2%) | 1 (2%) |
| Lymph node, mediastinal | (40) | (41) | (41) | (31) |
| Alveolar/bronchiolar carcinoma, metastatic, lung | | 1 (2%) | | |
| Hepatocholangiocarcinoma, metastatic, liver | | | 1 (2%) | |
| Histiocytic sarcoma | 1 (3%) | | 1 (2%) | |
| Spleen | (49) | (50) | (50) | (48) |
| Hemangiosarcoma | | 1 (2%) | | |
| Histiocytic sarcoma | 1 (2%) | | 1 (2%) | 1 (2%) |
| Thymus | (45) | (45) | (46) | (42) |
| Sarcoma, metastatic, uncertain primary site | | | 1 (2%) | |
| **Integumentary System** | | | | |
| Skin | (50) | (50) | (50) | (49) |
| Subcutaneous tissue, hemangiosarcoma | | 1 (2%) | | |
| Subcutaneous tissue, mast cell tumor benign | | 1 (2%) | | |
| Subcutaneous tissue, sarcoma | 1 (2%) | 7 (14%) | 1 (2%) | 2 (4%) |
| Subcutaneous tissue, sarcoma, multiple | | 1 (2%) | | |
| **Musculoskeletal System** | | | | |
| None | | | | |
| **Nervous System** | | | | |
| Brain | (50) | (50) | (50) | (49) |
| Histiocytic sarcoma | | | | 1 (2%) |

**TABLE D1**
**Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Respiratory System** | | | | |
| Larynx | (50) | (50) | (50) | (48) |
| Lung | (50) | (50) | (50) | (49) |
| Alveolar/bronchiolar adenoma | 2 (4%) | 2 (4%) | 2 (4%) | |
| Alveolar/bronchiolar carcinoma | 1 (2%) | 3 (6%) | | 1 (2%) |
| Alveolar/bronchiolar carcinoma, multiple | | | 1 (2%) | |
| Carcinoma, metastatic, harderian gland | | 1 (2%) | | 2 (4%) |
| Carcinoma, metastatic, ovary | | 1 (2%) | | |
| Hepatocellular carcinoma, metastatic, liver | 1 (2%) | 4 (8%) | 2 (4%) | 3 (6%) |
| Hepatocholangiocarcinoma, metastatic, liver | | | 1 (2%) | |
| Histiocytic sarcoma | 1 (2%) | | 1 (2%) | 1 (2%) |
| Sarcoma, metastatic, skin | | | 1 (2%) | |
| Sarcoma, metastatic, uncertain primary site | | | 1 (2%) | |
| Nose | (50) | (50) | (49) | (49) |
| Carcinoma, metastatic, harderian gland | | 1 (2%) | | |
| Pleura | | (1) | (1) | |
| Sarcoma, metastatic, uncertain primary site | | | 1 (100%) | |
| **Special Senses System** | | | | |
| Eye | (50) | (50) | (50) | (48) |
| Carcinoma, metastatic, harderian gland | | 1 (2%) | | 1 (2%) |
| Harderian gland | (50) | (50) | (50) | (49) |
| Adenoma | 3 (6%) | 4 (8%) | 5 (10%) | 3 (6%) |
| Carcinoma | | 2 (4%) | | 2 (4%) |
| Bilateral, adenoma | | | | 1 (2%) |
| **Urinary System** | | | | |
| Kidney | (49) | (50) | (50) | (48) |
| Histiocytic sarcoma | | | 1 (2%) | |
| Urinary bladder | (50) | (49) | (50) | (47) |
| Histiocytic sarcoma | | | 1 (2%) | |
| **Systemic Lesions** | | | | |
| Multiple organs[b] | (50) | (50) | (50) | (49) |
| Histiocytic sarcoma | 1 (2%) | | 1 (2%) | 1 (2%) |
| Lymphoma malignant | 13 (26%) | 15 (30%) | 10 (20%) | 7 (14%) |
| **Neoplasm Summary** | | | | |
| Total animals with primary neoplasms[c] | 37 | 39 | 36 | 47 |
| Total primary neoplasms | 58 | 72 | 62 | 82 |
| Total animals with benign neoplasms | 25 | 24 | 28 | 39 |
| Total benign neoplasms | 34 | 29 | 38 | 55 |
| Total animals with malignant neoplasms | 23 | 30 | 20 | 22 |
| Total malignant neoplasms | 24 | 43 | 24 | 27 |
| Total animals with metastatic neoplasms | 1 | 8 | 5 | 5 |
| Total metastatic neoplasms | 1 | 11 | 14 | 6 |
| Total animals with malignant neoplasms–uncertain primary site | | | 1 | |

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 5 8 8 | 6 2 4 | 6 3 8 | 6 5 3 | 6 8 0 | 6 8 0 | 6 8 3 | 6 9 1 | 7 0 1 | 7 0 5 | 7 2 5 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 0 0 6 | 1 0 1 8 | 1 0 3 7 | 1 0 3 5 | 1 0 1 9 | 1 0 1 3 8 | 1 0 0 2 | 1 0 1 3 | 1 0 1 0 9 | 1 0 2 5 | 1 0 2 7 | 1 0 1 3 | 1 0 1 1 | 1 0 1 2 | 1 0 2 9 | 1 0 2 9 | 1 0 3 0 | 1 0 3 3 | 1 0 3 9 | 1 0 4 5 | 1 0 4 8 | 1 0 1 | 1 0 1 4 | 1 0 4 7 | 1 0 1 6 | 1 0 1 7 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | M | + | + | + | A | I | + | A | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | + | I | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | I | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, ileum | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Liver | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular carcinoma | | X | | | | | | X | X | | | | | | | | | | | | | | | | |
| Hepatocellular adenoma | | | | | | | | | | | X | | | | | | | | | | X | X | | | |
| Hepatocellular adenoma, multiple | | | | | X | | | | | | | | | | | | X | | | X | | | | | |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mesentery | | | | | | + | | | | + | | + | | | + | + | | | + | | | + | | | |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Oral mucosa | | | | | | | | | | | + | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | X | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal medulla | + | I | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Islets, pancreatic | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Parathyroid gland | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | M | + | + | + | + | M | + |
| Pituitary gland | + | I | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars distalis, adenoma | | | | | | X | | | | | | | | | X | X | | | | | | X | | | X |
| Thyroid gland | + | + | + | I | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | |

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 2 2 1 | 1 2 2 2 | 1 2 2 6 | 1 2 2 8 | 1 3 3 2 | 1 3 3 4 | 1 3 3 6 | 1 4 4 1 | 1 4 4 3 | 1 4 4 6 | 1 4 4 7 | 1 4 4 9 | 1 4 0 5 | 1 4 0 8 | 1 4 1 0 | 1 4 1 4 | 1 4 1 5 | 1 4 2 0 | 1 4 2 3 | 1 4 2 4 | 1 4 3 1 | 1 4 3 4 | 1 4 4 0 | 1 4 4 2 | 1 4 4 4 | 1 4 5 0 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | + | + | + | + | + | + | + | I | M | M | + | + | + | + | + | + | + | + | + | + | + | + | M | M | 40 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Hepatocellular carcinoma | | | | | | | | | | | X | | | | | | | | | | | | | | | | 4 |
| Hepatocellular adenoma | | | | | | X | | | | X | | | | | | | X | X | | X | | | | | | | 8 |
| Hepatocellular adenoma, multiple | X | | X | | | | | | | | | | | | | X | | | | | | | | | | | 6 |
| Histiocytic sarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | | | 1 |
| Mesentery | + | + | | + | + | | | | + | + | | | | | + | + | | + | | | | | | | + | | 17 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Oral mucosa | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | 47 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Parathyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | M | + | + | + | M | + | + | I | + | | 43 |
| Pituitary gland | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 48 |
| Pars distalis, adenoma | | X | | X | | | | | X | | | | | | | | | | | X | | | | | | | 9 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | | 49 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 5 8 8 | 6 2 4 | 6 3 8 | 6 5 3 | 6 8 0 | 6 8 0 | 6 8 3 | 6 9 1 | 7 0 1 | 7 0 5 | 7 2 5 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 0 0 6 | 1 1 6 8 | 1 3 7 7 | 1 3 5 5 | 1 1 9 9 | 1 3 0 8 | 1 0 2 2 | 1 1 2 3 | 1 0 9 9 | 1 2 5 5 | 1 2 7 7 | 1 0 3 3 | 1 1 1 1 | 1 1 2 2 | 1 2 9 9 | 1 3 0 0 | 1 3 3 3 | 1 3 9 9 | 1 4 5 5 | 1 4 4 8 | 1 0 1 1 | 1 0 4 4 | 1 0 7 7 | 1 1 6 6 | 1 1 7 7 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | M | + | + | M | + | + | + | M | I | + | + | + | + | + | + | + | + | + | + | + | M |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cystadenoma | | | | | | | | | | | | | | X | | | | | | X | | | | | |
| Luteoma | | | | | | | | | | | | X | | | | | | | | | | | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | X | | | | | | | | | | | | | |
| Sarcoma stromal | | | | | | | | | | | | | | | | | | | X | | | | | | |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | | | | | | | | | | | | | | | | | | + | | | | |
| Lymph node, bronchial | + | + | + | M | + | + | + | + | + | + | + | + | M | + | + | + | + | + | M | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, mandibular | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | M | + | + | + | + | + | + |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | M | + | + | + | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thymus | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, sarcoma | | | | X | | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skeletal muscle | | | + | | | | | | | | | | | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Spinal cord | | | + | | | | + | | | | | | | | | | | | | | | | | | |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | X | | | | | | | | | | | | |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | X | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 2 1 | 1 2 2 | 1 2 6 | 1 2 8 | 1 3 2 | 1 3 4 | 1 3 6 | 1 4 1 | 1 4 3 | 1 4 6 | 1 4 7 | 1 4 9 | 1 0 5 | 1 0 8 | 1 1 0 | 1 1 4 | 1 1 5 | 1 2 0 | 1 2 3 | 1 2 4 | 1 3 1 | 1 4 0 | 1 4 2 | 1 4 4 | 1 5 0 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | I | + | I | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | 42 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Cystadenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Luteoma | | | X | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma stromal | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node | | | | | + | | | + | | | | | | + | | | | | | | | | | | | 4 |
| Lymph node, bronchial | + | + | M | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | 45 |
| Histiocytic sarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Lymph node, mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | M | + | M | + | 44 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | M | I | + | + | + | + | + | + | + | + | + | + | 48 |
| Lymph node, mediastinal | + | + | M | + | + | + | + | + | + | + | + | M | + | + | + | + | + | M | + | M | M | + | M | M | + | 40 |
| Histiocytic sarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Histiocytic sarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Thymus | + | + | + | + | I | + | + | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | M | + | 45 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Subcutaneous tissue, sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Skeletal muscle | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Spinal cord | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | | | | | | | | | X | | | | | 2 |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | X | | | | 1 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 5 8 8 | 6 2 4 | 6 3 8 | 6 5 3 | 6 8 0 | 6 8 0 | 6 8 3 | 6 9 1 | 7 0 1 | 7 0 5 | 7 2 5 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 0 6 | 1 1 8 | 1 3 7 | 1 3 5 | 1 1 9 | 1 3 8 | 1 0 2 | 1 1 3 | 1 0 9 | 1 2 5 | 1 2 7 | 1 0 3 | 1 1 1 | 1 1 2 | 1 2 9 | 1 3 0 | 1 3 3 | 1 3 9 | 1 4 5 | 1 4 8 | 1 0 1 | 1 0 4 | 1 0 7 | 1 1 6 | 1 1 7 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lacrimal gland | | | | + | | | | | | | | | | | | | | | | | | | | | |
| Zymbal's gland | + | + | M | + | M | + | + | + | M | + | + | + | + | M | M | + | M | M | + | + | M | + | M | + | + |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymphoma malignant | | | | | | X | | | | X | X | | X | | | | | X | | | X | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: Chamber Control**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 1 2 1 | 1 2 2 | 1 2 6 | 1 2 8 | 1 3 2 | 1 3 4 | 1 3 6 | 1 4 1 | 1 4 3 | 1 4 6 | 1 4 7 | 1 4 9 | 1 0 5 | 1 0 8 | 1 1 0 | 1 1 4 | 1 1 5 | 1 2 0 | 1 2 3 | 1 2 4 | 1 3 1 | 1 4 0 | 1 4 2 | 1 4 4 | 1 5 0 | Total Tissues/ Tumors |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | X | | | | | | | | | X | | | | | X | | | | | | | | | 3 |
| Lacrimal gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Zymbal's gland | + | M | + | M | M | + | I | M | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | 35 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Lymphoma malignant | X | | X | | | | | X | | | | | X | | X | X | | | | X | | | | | | 13 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 5 3 3 | 5 8 6 | 6 0 2 | 6 1 6 | 6 3 0 | 6 4 3 | 6 6 9 | 6 8 0 | 6 8 6 | 6 9 4 | 6 9 5 | 7 0 5 | 7 2 5 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 0 3 | 3 4 1 | 3 0 4 | 3 5 0 | 3 5 2 | 3 7 3 | 3 2 0 | 3 9 1 | 3 2 3 | 3 1 5 | 3 3 7 | 3 3 4 | 3 3 7 | 3 1 6 | 3 2 8 | 3 1 0 | 3 3 8 | 3 4 0 | 3 0 1 | 3 0 2 | 3 0 5 | 3 1 1 | 3 1 3 | 3 1 5 | 3 1 9 | 3 2 0 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | + | + | + | + | I | M | I | I | + | M | + | I | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, colon | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | + | + | + | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, duodenum | + | + | A | + | + | A | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, ileum | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma | | X | X | | | X | | X | X | | | | | | | X | | | | | | | | X | |
| Hepatocellular adenoma | | | X | | | | | | | | | | | | | | X | | | | | | | X | X |
| Mesentery | | + | | + | + | + | | + | | | + | + | + | + | | | + | | | + | | | + | | + | + |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, glandular | + | + | A | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | X | | | | | | | | | | | | | | | | |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pheochromocytoma malignant | | | | | | | | | | | X | | | | | | | | | | | | | | |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid gland | + | + | + | + | + | + | M | + | + | M | + | M | + | + | + | + | + | + | + | + | + | + | M | + | M |
| Pituitary gland | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars distalis, adenoma | | | | | | | X | | | | | X | | X | X | | X | X | | | | | | | |
| Pars intermedia, adenoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | + | | | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | M | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + |
| Ovary | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | X | | | | | | | | | | | | | | | | |
| Cystadenoma | | | | | | | | | | | | X | | | | | | | | | | | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Polyp stromal | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 2 4 | 3 2 5 | 3 2 9 | 3 3 0 | 3 3 6 | 3 3 9 | 3 4 3 | 3 4 5 | 3 4 6 | 3 0 6 | 3 0 7 | 3 0 8 | 3 1 2 | 3 1 4 | 3 1 8 | 3 2 2 | 3 2 6 | 3 3 1 | 3 3 2 | 3 3 3 | 3 4 2 | 3 4 4 | 3 4 7 | 3 4 8 | 3 4 9 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | M | + | + | + | I | + | + | + | + | + | + | M | + | + | + | + | I | + | I | + | + | + | + | 39 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Sarcoma, metastatic, skin | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | X | | | X | | | | | | | | | | | | | | | | | | | | 2 |
| Hepatocellular carcinoma | | | | | | | | | | | | | | | | | | X | | | | | | | | 8 |
| Hepatocellular adenoma | X | X | | | | | | | | | | | X | X | | | | | | | | | | | | 8 |
| Mesentery | + | | | + | | | | + | | | | | | | | + | | | | + | | + | + | | | 21 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | 49 |
| Pheochromocytoma malignant | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Parathyroid gland | + | + | + | + | + | M | + | + | + | + | + | + | + | + | M | + | M | + | + | + | + | M | + | + | + | 41 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pars distalis, adenoma | X | | X | | | | X | | | | | | | | X | | | | | | | | | | X | 11 |
| Pars intermedia, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | M | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | 43 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Cystadenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Polyp stromal | | X | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 5 3 3 | 5 8 6 | 6 0 2 | 6 1 6 | 6 3 0 | 6 4 3 | 6 6 9 | 6 8 0 | 6 8 6 | 6 9 4 | 6 9 5 | 7 0 5 | 7 2 5 | 7 3 0 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 0 3 | 3 4 1 | 3 0 4 | 3 5 0 | 3 2 7 | 3 2 3 | 3 0 9 | 3 2 1 | 3 3 5 | 3 1 7 | 3 3 4 | 3 3 7 | 3 1 6 | 3 2 8 | 3 1 0 | 3 3 8 | 3 4 0 | 3 0 1 | 3 0 2 | 3 0 5 | 3 1 1 | 3 1 3 | 3 1 5 | 3 1 9 | 3 2 0 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | | X | | | | | | | | | | |
| Lymph node | | | | | + | | | | | + | | | + | | | | | | | | | + | | |
| Lymph node, bronchial | M | M | + | + | M | + | + | + | + | + | + | + | + | M | + | M | + | + | + | + | + | M | I | + | M |
| Lymph node, mandibular | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | M | + | + | + | + | + | + |
| Lymph node, mesenteric | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mediastinal | + | + | + | + | + | + | M | + | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | M | + |
| Alveolar/bronchiolar carcinoma, metastatic, lung | | | | | | | | | | | | X | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | | X | | | | | | | | | | |
| Thymus | M | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, hemangiosarcoma | | | | | | | | | | | | | | X | | | | | | | | | | |
| Subcutaneous tissue, mast cell tumor benign | | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous tissue, sarcoma | X | | | | | | | | | X | X | | | | | | | | | | | X | X | |
| Subcutaneous tissue, sarcoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skeletal muscle | | | | + | | | | | | | | | | | | | | | | | | | | | |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Peripheral nerve | + | | | | | | | | | | | | | | | | | | | | | | | | |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | X | | | X | | | | | | | | | X | |
| Carcinoma, metastatic, harderian gland | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Carcinoma, metastatic, ovary | | | | | | | | | X | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | | X | | | | X | | X | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, harderian gland | | | | | X | | | | | | | | | | | | | | | | | | | | |
| Pleura | | | | | | | | | | + | | | | | | | | | | | | | | | |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 2 4 | 3 2 5 | 3 2 9 | 3 3 0 | 3 3 6 | 3 3 9 | 3 4 3 | 3 4 5 | 3 4 6 | 3 0 6 | 3 0 7 | 3 0 8 | 3 1 2 | 3 1 4 | 3 1 8 | 3 2 2 | 3 2 6 | 3 3 1 | 3 3 2 | 3 3 3 | 3 3 4 | 3 4 4 | 3 4 7 | 3 4 8 | 3 4 9 | Total Tissues/ Tumors |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node | + | + | | | | | | | | + | | | | | | | | I | | | | | + | | | 8 |
| Lymph node, bronchial | + | + | + | + | M | M | M | + | + | + | + | M | + | + | + | + | + | + | M | + | + | M | + | M | M | 34 |
| Lymph node, mandibular | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | M | + | I | + | + | + | + | + | + | + | 45 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | 48 |
| Lymph node, mediastinal | + | + | M | + | M | + | + | M | + | + | + | + | + | + | + | + | + | + | M | + | + | M | + | + | + | 41 |
| Alveolar/bronchiolar carcinoma, metastatic, lung | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | 45 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Subcutaneous tissue, hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, mast cell tumor benign | | | | | | | | | | X | | | | | | | | | | | | | | | | 1 |
| Subcutaneous tissue, sarcoma | | | | | | | | | | X | | | X | | | | | | | | | | | | | 7 |
| Subcutaneous tissue, sarcoma, multiple | | | | | | | | | | | | | | | | | | | | | | | X | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Skeletal muscle | | | + | | | | | | | | | | | | | | | | | | | | | | | 2 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Peripheral nerve | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | | | | | | | | | | X | | | | 2 |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 3 |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Carcinoma, metastatic, ovary | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | X | | | | | | | | 4 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pleura | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 553 | 586 | 602 | 616 | 630 | 643 | 669 | 680 | 686 | 694 | 695 | 705 | 725 | 730 | 731 | 731 | 732 | 732 | 732 | 732 | 732 | 732 | 732 | 732 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 30303 | 30411 | 30404 | 30550 | 30727 | 30223 | 30209 | 30221 | 30235 | 31137 | 33344 | 33747 | 31656 | 32488 | 31290 | 33813 | 33840 | 34001 | 30212 | 30025 | 31111 | 31135 | 31151 | 32090 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, harderian gland | | | | | X | | | | | | | | | | | | | | | | | | | |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | X | | | | | | | X | | | | | | | | | | | |
| Carcinoma | | | | | X | | | | | | | X | | | | | | | | | | | | |
| Lacrimal gland | | | | | | | | | | | | | | | | | | | | + | | | | |
| Zymbal's gland | + | M | + | + | + | + | + | M | M | M | M | + | + | M | M | + | M | + | + | + | + | M | + | + | + |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymphoma malignant | X | | | | | | | | | | | | X | | | X | | | | | X | X | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 75 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 3 2 4 | 3 2 5 | 3 2 9 | 3 3 0 | 3 3 6 | 3 3 9 | 3 4 3 | 3 4 5 | 3 4 6 | 3 0 6 | 3 0 7 | 3 0 8 | 3 1 2 | 3 1 4 | 3 1 8 | 3 2 2 | 3 2 6 | 3 3 1 | 3 3 2 | 3 3 3 | 3 4 2 | 3 4 4 | 3 4 7 | 3 4 8 | 3 4 9 | Total Tissues/ Tumors |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | X | | | X | | | | | | | | | | | 4 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Lacrimal gland | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Zymbal's gland | M | + | + | + | + | + | + | + | + | + | M | + | + | + | M | + | + | + | M | M | M | + | + | + | + | 35 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymphoma malignant | X | X | X | X | X | | | | X | X | | | | | | | | | X | | X | X | | | | 15 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 600 | 604 | 605 | 655 | 658 | 666 | 711 | 717 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 732 | 732 | 732 | 732 | 732 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 53707 | 50808 | 50401 | 52214 | 54493 | 53433 | 52327 | 52233 | 50003 | 50404 | 51018 | 51919 | 52020 | 52202 | 52208 | 53030 | 53308 | 54545 | 54646 | 55060 | 50202 | 50025 | 50026 | 51013 | 51114 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | M | + | + | I | + | M | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Intestine small, jejunum | + | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, ileum | + | + | + | A | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocellular carcinoma | X | | | | | | | | | | | X | | | | | | | | X | X | | | | |
| Hepatocellular carcinoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular adenoma | | | | | | | | | | X | | | | | | X | | | | X | | X | | | |
| Hepatocellular adenoma, multiple | | | | | | | | | | | | | X | | | | | X | | | | | | | |
| Hepatocholangiocarcinoma | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Mesentery | | + | | | + | | + | | | | | | | | + | + | + | + | + | | | + | | | |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Squamous cell papilloma | | | | | | | | | | | | | | | X | | | | | | | | | | |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Sarcoma, metastatic, uncertain primary site | | | X | | | | | | | | | | | | | | | | | | | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 5 1 1 6 | 5 2 1 | 5 2 2 9 | 5 3 1 | 5 3 2 | 5 3 3 4 | 5 3 5 | 5 4 2 | 5 4 3 | 5 4 4 | 5 4 4 7 | 5 4 8 | 5 0 1 | 5 0 7 | 5 0 9 | 5 1 0 | 5 1 1 | 5 1 2 | 5 1 5 | 5 1 7 | 5 2 5 | 5 2 6 | 5 3 6 | 5 3 9 | 5 4 0 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Gallbladder | + | + | + | + | + | + | + | + | I | + | + | + | I | + | + | + | I | + | + | + | + | + | + | + | + | 43 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hepatocellular carcinoma | | | | | | | X | | | | X | | | | | | | | | | | | | | | 6 |
| Hepatocellular carcinoma, multiple | | | | | | X | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular adenoma | | | | | | | | | | | | | | | X | | | | X | | X | | | | | 7 |
| Hepatocellular adenoma, multiple | | | | | | | | | | | | | | | | | X | | | | | | | | | 3 |
| Hepatocholangiocarcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Mesentery | | | | | | | | + | | | | | | | | + | | | | + | | | + | | | 13 |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Blood vessel | | | | | | | | | | | | | | | + | | + | | | | | | | | | 2 |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Sarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 6 0 0 | 6 0 4 | 6 0 5 | 6 0 5 | 6 0 5 | 6 0 6 | 7 0 1 | 7 0 1 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 | 7 0 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 5 3 0 7 | 5 0 8 | 5 0 4 1 | 5 2 4 | 5 4 9 | 5 3 3 | 5 2 7 | 5 2 3 | 5 0 3 | 5 0 4 | 5 1 8 | 5 1 9 | 5 2 0 | 5 2 2 | 5 2 8 | 5 3 0 | 5 3 8 | 5 4 5 | 5 4 6 | 5 5 0 | 5 0 2 | 5 0 5 | 5 0 6 | 5 1 3 | 5 1 4 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid gland | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | M | M | + |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | I | + | + | + | + | + | + | + | + | + |
| Pars distalis, adenoma | | | | X | | | | | | X | | | | | | | | | X | X | | | X | X | |
| Pars intermedia, adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | + | + | | | | | | | | | | | | | | | | | |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | + | + | + |
| Cystadenoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Luteoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Leiomyoma | | | | | | | | | X | | | | | | | | | | | | X | | | | |
| Polyp stromal | | | | | | | | | | | | | | | | | | X | | | | | | | |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node | | | | | | | | | | | | | | | | + | | | | | | | + | | |
| Lumbar, hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | X | | |
| Lymph node, bronchial | + | + | + | + | M | + | + | M | + | + | + | + | + | + | M | + | + | M | + | + | + | + | + | + | + |
| Lymph node, mandibular | + | + | + | + | + | + | + | M | M | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + |
| Lymph node, mesenteric | + | + | + | M | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Lymph node, mediastinal | M | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | M | + | M | + | M | + | + |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Thymus | + | M | + | + | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + |
| Sarcoma, metastatic, uncertain primary site | | | X | | | | | | | | | | | | | | | | | | | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 5 1 1 6 | 5 2 1 | 5 2 9 | 5 3 1 | 5 3 2 | 5 3 4 | 5 3 5 | 5 4 2 | 5 4 3 | 5 4 4 | 5 4 4 | 5 4 7 | 5 4 8 | 5 0 1 | 5 0 7 | 5 0 9 | 5 1 0 | 5 1 1 | 5 1 2 | 5 1 5 | 5 1 7 | 5 2 5 | 5 2 6 | 5 3 6 | 5 3 9 | 5 4 0 | Total Tissues/ Tumors |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Parathyroid gland | + | M | + | + | M | + | + | + | + | + | + | + | M | + | M | M | + | + | + | + | M | + | + | + | + | + | 40 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | 47 |
| Pars distalis, adenoma | | | | | | | X | X | X | | | X | | | | X | | | | | X | | | | | | 12 |
| Pars intermedia, adenoma | | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Peritoneum | | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Cystadenoma | | | | | | | | | | | | | | | | | | | X | X | | | | | | | 3 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Luteoma | | | | | | | | | | | | | | | | | | | | | | | X | | | | 1 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Hemangiosarcoma | | | | | | X | | | | | | | | | | | | | | | | | | X | | | 2 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Leiomyoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Polyp stromal | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lymph node | | | | | | | | | | | | + | | | | | | + | | | | + | | | + | | 6 |
| Lumbar, hemangiosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, bronchial | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | 44 |
| Lymph node, mandibular | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | M | + | + | + | + | + | + | + | 45 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mediastinal | + | + | + | + | + | + | M | + | + | M | M | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | 41 |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thymus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Sarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 600 | 604 | 605 | 605 | 605 | 606 | 711 | 711 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 | 733 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 53 07 | 50 08 | 54 01 | 52 44 | 54 09 | 53 33 | 52 07 | 52 23 | 50 03 | 50 04 | 51 18 | 51 19 | 52 02 | 52 22 | 52 28 | 53 03 | 53 38 | 54 45 | 54 46 | 55 00 | 50 02 | 50 05 | 50 06 | 51 13 | 51 14 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, sarcoma | | | | | | | | | | | | | | | | | X | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | | | | | | | | | | | | | |
| Alveolar/bronchiolar carcinoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | X | | | | | | | | | | | | | | | | | | | | | X | | | |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | X | | | | | | | | | | | | | | | | | | |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | X | | | | | | | | |
| Sarcoma, metastatic, uncertain primary site | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + |
| Pleura | | | + | | | | | | | | | | | | | | | | | | | | | | |
| Sarcoma, metastatic, uncertain primary site | | | X | | | | | | | | | | | | | | | | | | | | | | |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | X | | | X | | | | X | | | | | | | | | | | | | X | X | | | |
| Zymbal's gland | M | M | + | M | M | + | M | + | M | + | + | M | + | + | + | + | + | M | + | M | + | M | + | M | + |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | | |
| Lymphoma malignant | | | | | | | | | | | X | | X | | | X | | | | | X | X | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 300 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 5 1 6 | 5 2 1 | 5 2 9 | 5 3 1 | 5 3 2 | 5 3 4 | 5 3 5 | 5 4 2 | 5 4 3 | 5 4 4 | 5 4 7 | 5 4 8 | 5 0 1 | 5 0 7 | 5 0 9 | 5 1 0 | 5 1 1 | 5 1 2 | 5 1 5 | 5 1 7 | 5 2 5 | 5 2 6 | 5 3 6 | 5 3 9 | 5 4 0 | Total Tissues/ Tumors |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Subcutaneous tissue, sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Alveolar/bronchiolar adenoma | | | | | | | | | | | | | | X | | | | X | | | | | | | | 2 |
| Alveolar/bronchiolar carcinoma, multiple | | | | | | | | X | | | | | | | | | | | | | | | | | | 1 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Hepatocholangiocarcinoma, metastatic, liver | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, skin | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Pleura | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Sarcoma, metastatic, uncertain primary site | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | + | | | | | | | | | | | | | | | | 1 |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Adenoma | | | | | | | | | | | | | | | | | | | | | | | | | | 5 |
| Zymbal's gland | + | + | + | + | + | M | + | I | M | + | M | M | + | M | M | M | + | M | + | M | + | + | M | + | + | 28 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 50 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymphoma malignant | | | | X | | | | | | | X | | | X | | | | | | | X | | | X | | 10 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 4 4 0 | 5 0 1 | 5 1 9 | 5 8 5 | 6 3 2 | 6 6 6 | 6 8 1 | 6 9 4 | 7 2 2 | 7 2 2 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 1 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 1 9 | 7 2 8 | 7 3 1 | 7 2 5 | 7 4 1 | 7 3 2 | 7 5 0 | 7 1 6 | 7 1 8 | 7 4 6 | 7 0 5 | 7 0 7 | 7 0 9 | 7 2 1 | 7 2 6 | 7 3 0 | 7 3 4 | 7 3 6 | 7 3 7 | 7 4 4 | 7 0 2 | 7 0 3 | 7 1 7 | 7 2 0 |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Gallbladder | M | + | A | + | + | A | M | A | + | A | I | + | + | + | + | M | I | M | + | I | + | + | + | + |
| Intestine large, colon | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, rectum | + | + | + | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine large, cecum | + | + | A | + | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leiomyoma | | | | | | | | | | | | | | | | | | | X | | | | | |
| Intestine small, duodenum | + | + | A | + | + | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Intestine small, jejunum | + | + | A | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | X |
| Intestine small, ileum | + | + | A | + | + | A | A | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cholangioma | | | | | | | | | | | | | | | | | | | | | | | | |
| Hemangioma | | | | X | | | | | | | | | | | | | | | | | | | | |
| Hepatoblastoma | | | | | | | | | | | | | | | | | X | | | | | | | |
| Hepatocellular carcinoma | X | | | | | | | X | | | | | X | | | | | X | | X | | | X | |
| Hepatocellular carcinoma, multiple | | | X | | | | X | | | | | | | | | | | | | | | | | |
| Hepatocellular adenoma | | | | | X | | X | | | | | | | | | | | | | | | | | X |
| Hepatocellular adenoma, multiple | | | X | | | | | | X | X | | X | X | X | X | X | X | | X | | X | X | X | |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | | |
| Mesentery | | | | | | | + | | | | | | | | | | | | | | | | | |
| Pancreas | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Stomach, forestomach | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | | | | | | |
| Stomach, glandular | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adrenal medulla | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Islets, pancreatic | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Parathyroid gland | + | + | + | + | + | + | + | M | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + |
| Pituitary gland | + | + | A | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Pars distalis, adenoma | | | | | | | | | X | X | | | | | X | | | | | | X | | | |
| Thyroid gland | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 2 2 | 7 2 4 | 7 3 8 | 7 3 9 | 7 4 2 | 7 4 9 | 7 0 1 | 7 0 4 | 7 0 6 | 7 0 8 | 7 1 0 | 7 1 1 | 7 1 2 | 7 1 3 | 7 1 4 | 7 1 5 | 7 2 3 | 7 2 7 | 7 2 9 | 7 3 3 | 7 3 5 | 7 4 0 | 7 4 3 | 7 4 7 | 7 4 8 | Total Tissues/ Tumors |
| **Alimentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Gallbladder | + | I | + | I | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | M | M | + | + | + | 33 |
| Intestine large, colon | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, rectum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Intestine large, cecum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Leiomyoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, duodenum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Intestine small, jejunum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Intestine small, ileum | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 45 |
| Liver | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Cholangioma | | | | | X | | | | | | | | | | | | | | | | | | | | | 1 |
| Hemangioma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Hepatoblastoma | | | | | | | | | | | | | | | | | | | X | | | | | | | 2 |
| Hepatocellular carcinoma | | | | X | | | | | | | | | | | | | | | | | | X | | | | 8 |
| Hepatocellular carcinoma, multiple | | | | | | | | | | | | | | | | | | | | | | | | | | 2 |
| Hepatocellular adenoma | | | | | | | | | | | X | | | | | | | | | | X | | | | | 5 |
| Hepatocellular adenoma, multiple | X | X | X | X | X | X | X | | | | | X | | X | X | X | X | X | X | X | | X | X | X | X | 32 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Mesentery | | | | | | | | | | | | | | | | | | | + | | | | | | | 2 |
| Pancreas | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Salivary glands | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Stomach, forestomach | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Squamous cell papilloma | | | | | | | | | | | | | | | | | | | X | | | | | | | 1 |
| Stomach, glandular | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Tooth | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Cardiovascular System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Endocrine System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adrenal cortex | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Adrenal medulla | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Islets, pancreatic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Parathyroid gland | + | + | + | + | + | + | + | M | + | + | + | M | + | + | + | + | M | M | + | + | + | + | + | M | + | 42 |
| Pituitary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | 46 |
| Pars distalis, adenoma | | X | | | | | | X | | | | | | | X | | | | | | | | | | X | 8 |
| Thyroid gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| **General Body System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| None | | | | | | | | | | | | | | | | | | | | | | | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 440 | 501 | 519 | 585 | 632 | 666 | 681 | 694 | 722 | 722 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 732 | 732 | 732 | 732 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 719 | 728 | 731 | 725 | 741 | 732 | 750 | 761 | 718 | 746 | 705 | 700 | 709 | 722 | 726 | 730 | 734 | 736 | 737 | 744 | 802 | 803 | 717 | 720 |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | M | + | + | + | + |
| Ovary | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Cystadenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Luteoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Uterus | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Leiomyosarcoma | | | | | | | | | | | X | | | | | | | | | | | | | |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | | |
| Lymph node | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph node, bronchial | M | + | + | + | + | M | M | + | M | M | + | + | + | + | + | + | + | + | + | M | + | + | M | + |
| Lymph node, mandibular | M | M | + | + | M | M | + | M | M | + | + | + | + | + | M | M | + | + | + | + | + | + | M | M |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | | |
| Lymph node, mesenteric | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | | |
| Lymph node, mediastinal | M | M | + | + | + | + | M | + | M | + | M | + | M | + | + | M | + | + | + | M | M | + | + | + |
| Spleen | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | | |
| Thymus | M | + | + | M | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | M | M | + | + | + |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Subcutaneous tissue, sarcoma | | | | | | | | X | | | | | | | | | | | | | | | | |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | | |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | | | | | | | | | | | | |
| Hepatocellular carcinoma, metastatic, liver | | | X | | | | | | | | | | | | | | X | | | | | | | |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Trachea | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 2 2 | 7 2 4 | 7 3 8 | 7 3 9 | 7 4 2 | 7 4 9 | 7 0 1 | 7 0 4 | 7 0 6 | 7 0 8 | 7 1 0 | 7 1 1 | 7 1 2 | 7 1 3 | 7 1 4 | 7 1 5 | 7 2 3 | 7 2 7 | 7 2 9 | 7 3 3 | 7 3 5 | 7 4 0 | 7 4 3 | 7 4 7 | 7 4 8 | Total Tissues/ Tumors |
| **Genital System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Clitoral gland | + | + | + | + | + | + | + | + | + | M | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | 45 |
| Ovary | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Cystadenoma | | | | | | | | X | | | | | | | | | | | | | | | | | | 1 |
| Luteoma | | | | | | | | | | | X | | | | | | | | | | | | | | | 1 |
| Uterus | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Leiomyosarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Hematopoietic System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone marrow | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node | | | | | | | | | | | | | + | | | | | + | | | | | | | | 2 |
| Lymph node, bronchial | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 42 |
| Lymph node, mandibular | + | + | M | M | + | + | M | + | + | M | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | 34 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mesenteric | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymph node, mediastinal | + | M | M | M | M | + | + | + | + | + | + | + | + | M | + | M | M | + | + | M | M | + | + | + | + | 31 |
| Spleen | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Thymus | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | 42 |
| **Integumentary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Skin | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Subcutaneous tissue, sarcoma | | | | | | | | | X | | | | | | | | | | | | | | | | | 2 |
| **Musculoskeletal System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| **Nervous System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| **Respiratory System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Larynx | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Lung | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Alveolar/bronchiolar carcinoma | | | | | | | | | | | | | | | | | | | | | | | | X | | 1 |
| Carcinoma, metastatic, harderian gland | | | | | | | | | X | | | | | | | | | | | X | | | | | | 2 |
| Hepatocellular carcinoma, metastatic, liver | | | | | | X | | | | | | | | | | | | | | | | | | | | 3 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | 1 | | | | | | | | |
| Nose | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Trachea | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 440 | 501 | 519 | 585 | 632 | 666 | 681 | 694 | 722 | 722 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 731 | 732 | 732 | 732 | 732 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 719 | 728 | 731 | 725 | 741 | 732 | 750 | 716 | 718 | 746 | 705 | 707 | 709 | 721 | 726 | 730 | 734 | 736 | 737 | 744 | 802 | 803 | 720 |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | + | | | | | | | | | | | | | | | | | |
| Eye | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | | | | | | | | | | | |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Adenoma | | | | | | | | | | | | | | | X | | | | X | | | | |
| Carcinoma | | | | | | | | | | | | | | | | | | | | | | | |
| Bilateral, adenoma | | | | | | | | | | | | | | | | | | | | | | | |
| Zymbal's gland | M | M | M | + | + | M | + | + | M | + | + | + | + | + | + | + | + | M | M | + | + | + | + |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Urinary bladder | + | + | A | + | + | + | + | A | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | X | | | |
| Lymphoma malignant | | | | | | X | | | | X | | | | | | | | | | | | | |

**TABLE D2**
**Individual Animal Tumor Pathology of Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether: 1,200 ppm**

| Number of Days on Study | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 2 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | 7 3 3 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carcass ID Number** | 7 2 2 | 7 2 4 | 7 3 8 | 7 3 9 | 7 4 2 | 7 4 9 | 7 0 1 | 7 0 4 | 7 0 6 | 7 0 8 | 7 1 0 | 7 1 1 | 7 1 2 | 7 1 3 | 7 1 4 | 7 1 5 | 7 2 3 | 7 2 7 | 7 2 9 | 7 3 3 | 7 3 5 | 7 4 0 | 7 4 3 | 7 4 7 | 7 4 8 | Total Tissues/ Tumors |
| **Special Senses System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ear | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Eye | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Carcinoma, metastatic, harderian gland | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Harderian gland | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Adenoma | | | | | | | | | | | | | | | | | | | | X | | | | | | 3 |
| Carcinoma | | | | | | | | | X | | | | | | | | | | | X | | | | | | 2 |
| Bilateral, adenoma | | | | | | | | | | | | | | | X | | | | | | | | | | | 1 |
| Zymbal's gland | + | + | + | + | + | + | + | M | + | + | M | + | + | + | + | + | + | + | M | M | + | M | + | + | M | 36 |
| **Urinary System** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Kidney | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Urinary bladder | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 47 |
| **Systemic Lesions** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple organs | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Histiocytic sarcoma | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymphoma malignant | | | | | | | X | | | | | | X | | | | | X | X | | | | | X | | 7 |

**TABLE D3**
**Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Harderian Gland: Adenoma** | | | | |
| Overall rate[a] | 3/50 (6%) | 4/50 (8%) | 5/50 (10%) | 4/49 (8%) |
| Adjusted rate[b] | 6.3% | 8.6% | 10.2% | 8.8% |
| Terminal rate[c] | 3/39 (8%) | 2/36 (6%) | 2/42 (5%) | 4/39 (10%) |
| First incidence (days) | 731 (T) | 643 | 600 | 731 (T) |
| Poly-3 test[d] | P=0.503 | P=0.490 | P=0.371 | P=0.475 |
| **Harderian Gland: Adenoma or Carcinoma** | | | | |
| Overall rate | 3/50 (6%) | 6/50 (12%) | 5/50 (10%) | 5/49 (10%) |
| Adjusted rate | 6.3% | 12.7% | 10.2% | 11.0% |
| Terminal rate | 3/39 (8%) | 2/36 (6%) | 2/42 (5%) | 5/39 (13%) |
| First incidence (days) | 731 (T) | 630 | 600 | 731 (T) |
| Poly-3 test | P=0.460 | P=0.238 | P=0.371 | P=0.332 |
| **Liver: Hepatocellular Adenoma** | | | | |
| Overall rate | 14/49 (29%) | 8/50 (16%) | 10/50 (20%) | 37/49 (76%) |
| Adjusted rate | 29.8% | 17.1% | 20.8% | 79.3% |
| Terminal rate | 12/39 (31%) | 7/36 (19%) | 10/42 (24%) | 32/39 (82%) |
| First incidence (days) | 680 | 602 | 731 (T) | 519 |
| Poly-3 test | P<0.001 | P=0.112N | P=0.220N | P<0.001 |
| **Liver: Hepatocellular Carcinoma** | | | | |
| Overall rate | 4/49 (8%) | 8/50 (16%) | 7/50 (14%) | 10/49 (20%) |
| Adjusted rate | 8.4% | 16.7% | 14.4% | 21.2% |
| Terminal rate | 1/39 (3%) | 3/36 (8%) | 6/42 (14%) | 6/39 (15%) |
| First incidence (days) | 624 | 586 | 600 | 440 |
| Poly-3 test | P=0.109 | P=0.183 | P=0.275 | P=0.071 |
| **Liver: Hepatocellular Adenoma or Carcinoma** | | | | |
| Overall rate | 18/49 (37%) | 14/50 (28%) | 16/50 (32%) | 41/49 (84%) |
| Adjusted rate | 37.8% | 29.2% | 33.0% | 86.2% |
| Terminal rate | 13/39 (33%) | 9/36 (25%) | 15/42 (36%) | 34/39 (87%) |
| First incidence (days) | 624 | 586 | 600 | 440 |
| Poly-3 test | P<0.001 | P=0.249N | P=0.391N | P<0.001 |
| **Liver: Hepatocellular Carcinoma or Hepatoblastoma** | | | | |
| Overall rate | 4/49 (8%) | 8/50 (16%) | 7/50 (14%) | 12/49 (24%) |
| Adjusted rate | 8.4% | 16.7% | 14.4% | 25.4% |
| Terminal rate | 1/39 (3%) | 3/36 (8%) | 6/42 (14%) | 8/39 (21%) |
| First incidence (days) | 624 | 586 | 600 | 440 |
| Poly-3 test | P=0.031 | P=0.183 | P=0.275 | P=0.025 |
| **Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma** | | | | |
| Overall rate | 18/49 (37%) | 14/50 (28%) | 16/50 (32%) | 41/49 (84%) |
| Adjusted rate | 37.8% | 29.2% | 33.0% | 86.2% |
| Terminal rate | 13/39 (33%) | 9/36 (25%) | 15/42 (36%) | 34/39 (87%) |
| First incidence (days) | 624 | 586 | 600 | 440 |
| Poly-3 test | P<0.001 | P=0.249N | P=0.391N | P<0.001 |
| **Lung: Alveolar/bronchiolar Carcinoma** | | | | |
| Overall rate | 1/50 (2%) | 3/50 (6%) | 1/50 (2%) | 1/49 (2%) |
| Adjusted rate | 2.1% | 6.5% | 2.1% | 2.2% |
| Terminal rate | 1/39 (3%) | 2/36 (6%) | 1/42 (2%) | 1/39 (3%) |
| First incidence (days) | 731 (T) | 705 | 731 (T) | 731 (T) |
| Poly-3 test | P=0.454N | P=0.297 | P=0.758N | P=0.750 |

**TABLE D3**
**Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Lung: Alveolar/bronchiolar Adenoma or Carcinoma** | | | | |
| Overall rate | 3/50 (6%) | 5/50 (10%) | 3/50 (6%) | 1/49 (2%) |
| Adjusted rate | 6.3% | 10.7% | 6.3% | 2.2% |
| Terminal rate | 3/39 (8%) | 3/36 (8%) | 3/42 (7%) | 1/39 (3%) |
| First incidence (days) | 731 (T) | 630 | 731 (T) | 731 (T) |
| Poly-3 test | P=0.144N | P=0.348 | P=0.657N | P=0.322N |
| **Ovary: Cystadenoma** | | | | |
| Overall rate | 2/50 (4%) | 1/49 (2%) | 3/49 (6%) | 1/48 (2%) |
| Adjusted rate | 4.2% | 2.2% | 6.4% | 2.2% |
| Terminal rate | 2/39 (5%) | 0/36 (0%) | 3/41 (7%) | 1/39 (3%) |
| First incidence (days) | 731 (T) | 705 | 731 (T) | 731 (T) |
| Poly-3 test | P=0.475N | P=0.512N | P=0.495 | P=0.519N |
| **Pituitary Gland (Pars Distalis): Adenoma** | | | | |
| Overall rate | 9/48 (19%) | 11/49 (22%) | 12/47 (26%) | 8/46 (17%) |
| Adjusted rate | 19.5% | 23.8% | 26.5% | 18.5% |
| Terminal rate | 8/38 (21%) | 8/36 (22%) | 11/39 (28%) | 6/38 (16%) |
| First incidence (days) | 680 | 669 | 656 | 722 |
| Poly-3 test | P=0.386N | P=0.401 | P=0.294 | P=0.558N |
| **Skin (Subcutaneous Tissue): Sarcoma** | | | | |
| Overall rate | 1/50 (2%) | 8/50 (16%) | 1/50 (2%) | 2/49 (4%) |
| Adjusted rate | 2.1% | 16.9% | 2.1% | 4.4% |
| Terminal rate | 0/39 (0%) | 5/36 (14%) | 1/42 (2%) | 1/39 (3%) |
| First incidence (days) | 653 | 533 | 731 (T) | 694 |
| Poly-3 test | P=0.291N | P=0.015 | P=0.760N | P=0.483 |
| **All Organs: Hemangiosarcoma** | | | | |
| Overall rate | 1/50 (2%) | 3/50 (6%) | 3/50 (6%) | 0/49 (0%) |
| Adjusted rate | 2.1% | 6.5% | 6.3% | 0.0% |
| Terminal rate | 1/39 (3%) | 2/36 (6%) | 3/42 (7%) | 0/39 (0%) |
| First incidence (days) | 731 (T) | 730 | 731 (T) | —[e] |
| Poly-3 test | P=0.183N | P=0.296 | P=0.309 | P=0.509N |
| **All Organs: Hemangioma or Hemangiosarcoma** | | | | |
| Overall rate | 1/50 (2%) | 3/50 (6%) | 3/50 (6%) | 1/49 (2%) |
| Adjusted rate | 2.1% | 6.5% | 6.3% | 2.2% |
| Terminal rate | 1/39 (3%) | 2/36 (6%) | 3/42 (7%) | 0/39 (0%) |
| First incidence (days) | 731 (T) | 730 | 731 (T) | 585 |
| Poly-3 test | P=0.403N | P=0.296 | P=0.309 | P=0.753 |
| **All Organs: Malignant Lymphoma** | | | | |
| Overall rate | 13/50 (26%) | 15/50 (30%) | 10/50 (20%) | 7/49 (14%) |
| Adjusted rate | 27.2% | 31.9% | 20.8% | 15.3% |
| Terminal rate | 10/39 (26%) | 13/36 (36%) | 10/42 (24%) | 5/39 (13%) |
| First incidence (days) | 680 | 533 | 731 (T) | 666 |
| Poly-3 test | P=0.057N | P=0.389 | P=0.313N | P=0.126N |
| **All Organs: Benign Neoplasms** | | | | |
| Overall rate | 25/50 (50%) | 24/50 (48%) | 28/50 (56%) | 39/49 (80%) |
| Adjusted rate | 52.1% | 50.2% | 57.4% | 82.7% |
| Terminal rate | 22/39 (56%) | 17/36 (47%) | 25/42 (60%) | 33/39 (85%) |
| First incidence (days) | 680 | 602 | 600 | 519 |
| Poly-3 test | P<0.001 | P=0.505N | P=0.376 | P<0.001 |

**TABLE D3**
**Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **All Organs: Malignant Neoplasms** | | | | |
| Overall rate | 23/50 (46%) | 30/50 (60%) | 21/50 (42%) | 23/49 (47%) |
| Adjusted rate | 46.9% | 60.8% | 43.0% | 48.5% |
| Terminal rate | 15/39 (39%) | 18/36 (50%) | 17/42 (41%) | 17/39 (44%) |
| First incidence (days) | 624 | 533 | 600 | 440 |
| Poly-3 test | P=0.388N | P=0.119 | P=0.424N | P=0.521 |
| **All Organs: Benign or Malignant Neoplasms** | | | | |
| Overall rate | 37/50 (74%) | 39/50 (78%) | 37/50 (74%) | 47/49 (96%) |
| Adjusted rate | 75.5% | 78.6% | 75.3% | 97.3% |
| Terminal rate | 29/39 (74%) | 26/36 (72%) | 32/42 (76%) | 38/39 (97%) |
| First incidence (days) | 624 | 533 | 600 | 440 |
| Poly-3 test | P<0.001 | P=0.448 | P=0.582N | P<0.001 |

(T) Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for liver, lung, ovary, and pituitary gland; for other tissues, denominator is number of animals necropsied.
[b] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the chamber control incidence is the P value associated with the trend test. Beneath the exposed group incidence are the P values corresponding to pairwise comparisons between the chamber controls and that exposed group. The Poly-3 test accounts for the differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in an exposed group is indicated by **N**.
[e] Not applicable; no neoplasms in animal group

**TABLE D4**
**Historical Incidence of Liver Neoplasms in Control Female B6C3F$_1$ Mice[a]**

| Study | Incidence in Controls | | | |
|---|---|---|---|---|
| | Hepatocelluar Adenoma | Hepatocellular Carcinoma | Hepatocellular Adenoma or Carcinoma | Hepatoblastoma |
| **Historical Incidence: Inhalation Studies** | | | | |
| Decalin | 7/49 | 4/49 | 11/49 | 0/49 |
| Indium phosphide | 12/50 | 6/50 | 18/50 | 0/50 |
| Propylene glycol mono-*t*-butyl ether | 14/49 | 4/49 | 18/49 | 0/49 |
| Stoddard solvent IIC | 9/50 | 6/50 | 13/50 | 0/50 |
| Vanadium pentoxide | 6/50 | 6/50 | 12/50 | 0/50 |
| **Overall Historical Incidence: Inhalation Studies** | | | | |
| Total (%) | 48/248 (19.4%) | 26/248 (10.5%) | 72/248 (29.0%) | 0/248 (0%) |
| Mean ± standard deviation | 19.4% ± 6.9% | 10.5% ± 2.1% | 29.0% ± 6.8% | |
| Range | 12%-29% | 8%-12% | 22%-37% | |
| **Overall Historical Incidence:** | | | | |
| Total (%) | 179/1,152 (15.5%) | 87/1,152 (7.6%) | 250/1,152 (21.7%) | 0/1,152 (0%) |
| Mean ± standard deviation | 16.3% ± 6.6% | 8.1% ± 4.2% | 22.8% ± 9.4% | |
| Range | 6%-29% | 3%-16% | 8%-40% | |

[a] Data as of March 3, 2003

**TABLE D5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Disposition Summary** | | | | |
| Animals initially in study | 50 | 50 | 50 | 50 |
| Early deaths | | | | |
| Accidental deaths | | 1 | | 1 |
| Moribund | 8 | 10 | 6 | 4 |
| Natural deaths | 3 | 3 | 2 | 6 |
| Survivors | | | | |
| Died last week of study | | | 1 | 1 |
| Terminal sacrifice | 39 | 36 | 41 | 38 |
| Animals examined microscopically | 50 | 50 | 50 | 49 |
| **Alimentary System** | | | | |
| Gallbladder | (40) | (39) | (43) | (33) |
| Cyst | 1 (3%) | | | |
| Intestine large, colon | (48) | (49) | (50) | (48) |
| Infiltration cellular, mixed cell | | | | 1 (2%) |
| Intestine large, rectum | (48) | (49) | (50) | (48) |
| Necrosis | | | | 1 (2%) |
| Intestine large, cecum | (49) | (48) | (49) | (46) |
| Necrosis | | | 2 (4%) | |
| Intestine small, duodenum | (49) | (47) | (50) | (46) |
| Infiltration cellular, mixed cell | | | | 1 (2%) |
| Epithelium, hyperplasia | | | 1 (2%) | |
| Intestine small, jejunum | (49) | (48) | (48) | (47) |
| Infiltration cellular, mixed cell | | | 1 (2%) | |
| Inflammation, suppurative | | | | 1 (2%) |
| Necrosis | | | | 1 (2%) |
| Intestine small, ileum | (49) | (48) | (48) | (45) |
| Hyperplasia | 1 (2%) | | | |
| Infiltration cellular, mixed cell | 2 (4%) | 1 (2%) | 3 (6%) | 1 (2%) |
| Necrosis | | | | 2 (4%) |
| Epithelium, hyperplasia | 1 (2%) | | | |
| Liver | (49) | (50) | (50) | (49) |
| Angiectasis | | | 1 (2%) | |
| Basophilic focus | 3 (6%) | 4 (8%) | 4 (8%) | 2 (4%) |
| Clear cell focus | 4 (8%) | 4 (8%) | 6 (12%) | 5 (10%) |
| Eosinophilic focus | 11 (22%) | 10 (20%) | 9 (18%) | 27 (55%) |
| Fatty change | 2 (4%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Fatty change, focal | | 1 (2%) | | |
| Hematopoietic cell proliferation | | | 1 (2%) | |
| Infarct | | | 1 (2%) | |
| Inflammation, granulomatous | 23 (47%) | 9 (18%) | 17 (34%) | 12 (24%) |
| Tension lipidosis | 4 (8%) | 3 (6%) | 6 (12%) | 4 (8%) |
| Thrombosis | | | 1 (2%) | |
| Bile duct, cyst | 1 (2%) | | | |
| Bile duct, hyperplasia | | 1 (2%) | 1 (2%) | |
| Centrilobular, necrosis | | 3 (6%) | | |
| Hepatocyte, mitotic alteration | | 1 (2%) | | |
| Mesentery | (17) | (21) | (13) | (2) |
| Infiltration cellular, mast cell | 1 (6%) | | | |
| Fat, congestion | 1 (6%) | | | |
| Fat, necrosis | 14 (82%) | 19 (90%) | 12 (92%) | 2 (100%) |

[a] Number of animals examined microscopically at the site and the number of animals with lesion

**TABLE D5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Alimentary System** (continued) | | | | |
| Oral mucosa | (1) | | | |
| Inflammation | 1 (100%) | | | |
| Pancreas | (49) | (50) | (50) | (48) |
| Atrophy | 1 (2%) | | 2 (4%) | |
| Basophilic focus | 1 (2%) | 1 (2%) | 1 (2%) | |
| Duct, cyst | | | 1 (2%) | |
| Salivary glands | (50) | (50) | (50) | (49) |
| Atrophy | | | | 1 (2%) |
| Stomach, forestomach | (49) | (50) | (50) | (48) |
| Hyperplasia, squamous | 3 (6%) | 5 (10%) | 1 (2%) | 6 (13%) |
| Infiltration cellular, mast cell | | | 1 (2%) | |
| Infiltration cellular, mixed cell | 1 (2%) | | | |
| Inflammation | 2 (4%) | 5 (10%) | 2 (4%) | 6 (13%) |
| Ulcer | 2 (4%) | | 1 (2%) | 4 (8%) |
| Stomach, glandular | (49) | (48) | (50) | (48) |
| Mineralization | 2 (4%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Tooth | (50) | (50) | (50) | (49) |
| Inflammation, chronic active | 1 (2%) | 2 (4%) | 1 (2%) | 7 (14%) |
| Malformation | 1 (2%) | 1 (2%) | | |
| **Cardiovascular System** | | | | |
| Blood vessel | | | (2) | |
| Inflammation, chronic | | | 1 (50%) | |
| Heart | (50) | (50) | (50) | (49) |
| Cardiomyopathy | 5 (10%) | 4 (8%) | 8 (16%) | 3 (6%) |
| Inflammation, chronic | | 1 (2%) | | |
| Mineralization | 1 (2%) | 1 (2%) | | |
| Thrombosis | | | | 1 (2%) |
| Artery, inflammation, chronic active | 1 (2%) | | | |
| Endocardium, hyperplasia | | 1 (2%) | | |
| Valve, inflammation, suppurative | | 1 (2%) | | |
| **Endocrine System** | | | | |
| Adrenal cortex | (49) | (50) | (50) | (48) |
| Hyperplasia | 8 (16%) | 3 (6%) | 3 (6%) | 4 (8%) |
| Hypertrophy | 7 (14%) | 7 (14%) | 1 (2%) | 2 (4%) |
| Necrosis | 1 (2%) | 1 (2%) | | |
| Vacuolization cytoplasmic | | 3 (6%) | 3 (6%) | |
| Adrenal medulla | (47) | (49) | (50) | (48) |
| Hyperplasia | 2 (4%) | 4 (8%) | 1 (2%) | 3 (6%) |
| Hypertrophy | | | | 1 (2%) |
| Necrosis | 1 (2%) | | | |
| Islets, pancreatic | (49) | (50) | (50) | (48) |
| Hyperplasia | 1 (2%) | | | 1 (2%) |
| Pituitary gland | (48) | (49) | (47) | (46) |
| Pars distalis, angiectasis | 1 (2%) | | 1 (2%) | 1 (2%) |
| Pars distalis, hyperplasia | 16 (33%) | 11 (22%) | 16 (34%) | 11 (24%) |
| Thyroid gland | (49) | (50) | (50) | (48) |
| Follicular cell, hyperplasia | 2 (4%) | 1 (2%) | 3 (6%) | 1 (2%) |

**TABLE D5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **General Body System** | | | | |
| Peritoneum | | (1) | (2) | |
| Inflammation, chronic, suppurative | | 1 (100%) | | |
| **Genital System** | | | | |
| Clitoral gland | (42) | (43) | (48) | (45) |
| Inflammation, chronic | | 1 (2%) | | |
| Ovary | (50) | (49) | (49) | (48) |
| Angiectasis | 1 (2%) | 1 (2%) | | |
| Atrophy | | | | 1 (2%) |
| Cyst | 12 (24%) | 12 (24%) | 12 (24%) | 11 (23%) |
| Inflammation, chronic active | | 1 (2%) | | |
| Thrombosis | | | 1 (2%) | |
| Uterus | (50) | (50) | (50) | (48) |
| Angiectasis | 3 (6%) | 1 (2%) | 4 (8%) | 2 (4%) |
| Inflammation, suppurative | | 1 (2%) | 2 (4%) | 2 (4%) |
| Thrombosis | | 2 (4%) | | |
| Endometrium, fibrosis | 1 (2%) | | | |
| Endometrium, hyperplasia, cystic | 46 (92%) | 48 (96%) | 48 (96%) | 45 (94%) |
| **Hematopoietic System** | | | | |
| Bone marrow | (49) | (50) | (50) | (48) |
| Thrombosis | | | | 1 (2%) |
| Lymph node | (4) | (8) | (6) | (2) |
| Angiectasis | | 2 (25%) | | |
| Ectasia | | | 1 (17%) | |
| Lumbar, angiectasis | 1 (25%) | | | |
| Renal, angiectasis | 1 (25%) | | | |
| Renal, ectasia | 1 (25%) | | | |
| Lymph node, mandibular | (44) | (45) | (45) | (34) |
| Hyperplasia, lymphoid | | | | 1 (3%) |
| Infiltration cellular, plasma cell | | | | 1 (3%) |
| Lymph node, mesenteric | (48) | (48) | (48) | (48) |
| Angiectasis | 1 (2%) | 2 (4%) | 2 (4%) | 1 (2%) |
| Infiltration cellular, plasma cell | | 1 (2%) | | |
| Inflammation, granulomatous | | | 1 (2%) | |
| Inflammation, suppurative | | | | 1 (2%) |
| Lymph node, mediastinal | (40) | (41) | (41) | (31) |
| Hemorrhage | 1 (3%) | | | |
| Spleen | (49) | (50) | (50) | (48) |
| Fibrosis | | 1 (2%) | | |
| Hematopoietic cell proliferation | 4 (8%) | 4 (8%) | 2 (4%) | 3 (6%) |
| **Integumentary System** | | | | |
| Skin | (50) | (50) | (50) | (49) |
| Hyperplasia, squamous | 1 (2%) | | | |
| Infiltration cellular, mixed cell | 1 (2%) | 3 (6%) | 2 (4%) | |
| Inflammation, acute | | | | 1 (2%) |
| Inflammation, chronic active | | | | 1 (2%) |
| Subcutaneous tissue, inflammation, acute | | 1 (2%) | | |

**TABLE D5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Musculoskeletal System** | | | | |
| Bone | (50) | (50) | (50) | (49) |
| Synovial tissue, hyperplasia | | | 1 (2%) | |
| Skeletal muscle | (1) | (2) | | |
| Hemorrhage | 1 (100%) | | | |
| Inflammation, acute | | 1 (50%) | | |
| **Nervous System** | | | | |
| Brain | (50) | (50) | (50) | (49) |
| Meninges, infiltration cellular, mononuclear cell | 1 (2%) | | | |
| Spinal cord | (2) | | | |
| Hemorrhage | 1 (50%) | | | |
| **Respiratory System** | | | | |
| Larynx | (50) | (50) | (50) | (48) |
| Metaplasia, squamous | 1 (2%) | | | |
| Lung | (50) | (50) | (50) | (49) |
| Foreign body | | | 1 (2%) | |
| Inflammation, granulomatous | | | | 2 (4%) |
| Mineralization | | | 1 (2%) | |
| Thrombosis | 1 (2%) | | | 2 (4%) |
| Alveolar epithelium, hyperplasia | 3 (6%) | 2 (4%) | 4 (8%) | 3 (6%) |
| Alveolus, infiltration cellular, histiocyte | 2 (4%) | 1 (2%) | | 3 (6%) |
| Artery, inflammation, acute | | | | 2 (4%) |
| Nose | (50) | (50) | (49) | (49) |
| Inflammation, acute | | 1 (2%) | | |
| Inflammation, suppurative | 3 (6%) | | 1 (2%) | 1 (2%) |
| Respiratory epithelium, metaplasia, squamous | 2 (4%) | | | |
| Respiratory epithelium, necrosis | 2 (4%) | | | 1 (2%) |
| Pleura | | (1) | (1) | |
| Hyperplasia | | 1 (100%) | | |
| **Special Senses System** | | | | |
| Eye | (50) | (50) | (50) | (48) |
| Cataract | | | | 2 (4%) |
| Anterior chamber, inflammation, acute | 1 (2%) | | | 1 (2%) |
| Cornea, erosion | | | | 3 (6%) |
| Cornea, hyperplasia, squamous | 1 (2%) | 2 (4%) | | 2 (4%) |
| Cornea, inflammation, acute | | | | 1 (2%) |
| Cornea, inflammation, chronic active | 1 (2%) | 2 (4%) | | 4 (8%) |
| Cornea, mineralization | 1 (2%) | 2 (4%) | | 20 (42%) |
| Cornea, ulcer | | 1 (2%) | | 1 (2%) |
| Retrobulbar, inflammation, granulomatous | | | | 1 (2%) |
| Harderian gland | (50) | (50) | (50) | (49) |
| Hyperplasia | 3 (6%) | 3 (6%) | 4 (8%) | 4 (8%) |

**TABLE D5**
**Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|---|
| **Urinary System** | | | | |
| Kidney | (49) | (50) | (50) | (48) |
| Infarct | 1 (2%) | | 2 (4%) | 3 (6%) |
| Metaplasia, osseous | 2 (4%) | 1 (2%) | 1 (2%) | 1 (2%) |
| Nephropathy | 34 (69%) | 34 (68%) | 32 (64%) | 34 (71%) |
| Thrombosis | | | 1 (2%) | |
| Pelvis, dilatation | | | 1 (2%) | |
| Renal tubule, degeneration, hyaline | 1 (2%) | | | 1 (2%) |
| Renal tubule, necrosis | | | 1 (2%) | |
| Urinary bladder | (50) | (49) | (50) | (47) |
| Inflammation, acute | | | | 1 (2%) |
| Transitional epithelium, hyperplasia | 1 (2%) | | | |

# APPENDIX E
# GENETIC TOXICOLOGY

*SALMONELLA TYPHIMURIUM* MUTAGENICITY TEST PROTOCOL . . . . . 240
CHINESE HAMSTER OVARY CELL CYTOGENETICS PROTOCOLS . . . . . 240
MOUSE PERIPHERAL BLOOD MICRONUCLEUS TEST PROTOCOL . . . . . 241
EVALUATION PROTOCOL . . . . . 241
RESULTS . . . . . 242
TABLE E1 Mutagenicity of Propylene Glycol Mono-*t*-butyl Ether in *Salmonella typhimurium* . . . . . 243
TABLE E2 Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Propylene Glycol Mono-*t*-butyl Ether . . . . . 245
TABLE E3 Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by Propylene Glycol Mono-*t*-butyl Ether . . . . . 246
TABLE E4 Frequency of Micronuclei in Peripheral Blood Erythrocytes of Mice Following Treatment with Propylene Glycol Mono-*t*-butyl Ether by Inhalation for 3 Months . . . . . 247

# GENETIC TOXICOLOGY

## *Salmonella typhimurium* Mutagenicity Test Protocol

Testing was performed as reported by Zeiger *et al.* (1992). Propylene glycol mono-*t*-butyl ether was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). It was incubated with the *Salmonella typhimurium* tester strains TA97, TA98, TA100, TA1535, and TA1537 either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver) for 20 minutes at 37º C. Top agar supplemented with L-histidine and d-biotin was added, and the contents of the tubes were mixed and poured onto the surfaces of minimal glucose agar plates. Histidine-independent mutant colonies arising on these plates were counted following 2 days incubation at 37º C.

Each trial consisted of triplicate plates of concurrent positive and negative controls and of five doses of propylene glycol mono-*t*-butyl ether. In the absence of toxicity, 10,000 µg/plate was selected as the high dose. All positive trials were repeated under the conditions that elicited the positive response.

In this assay, a positive response is defined as a reproducible, dose-related increase in histidine-independent (revertant) colonies in any one strain/activation combination. An equivocal response is defined as an increase in revertants that is not dose related, is not reproducible, or is not of sufficient magnitude to support a determination of mutagenicity. A negative response is obtained when no increase in revertant colonies is observed following chemical treatment. There is no minimum percentage or fold increase required for a chemical to be judged positive or weakly positive.

## Chinese Hamster Ovary Cell Cytogenetics Protocols

Testing was performed as reported by Galloway *et al.* (1987). Propylene glycol mono-*t*-butyl ether was sent to the laboratory as a coded aliquot by Radian Corporation. It was tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCEs) and chromosomal aberrations (Abs), both in the presence and absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least three doses of propylene glycol mono-*t*-butyl ether; in the absence of toxicity, the high dose was limited to 5,000 µg/mL. A single flask per dose was used.

***Sister Chromatid Exchange Test***: In the SCE test without S9, CHO cells were incubated for 26 hours with propylene glycol mono-*t*-butyl ether in supplemented McCoy's 5A medium. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 26 hours, the medium containing propylene glycol mono-*t*-butyl ether was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with propylene glycol mono-*t*-butyl ether, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing serum and BrdU and no propylene glycol mono-*t*-butyl ether. Incubation proceeded for an additional 26 hours, with Colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9. All slides were scored blind and those from a single test were read by the same person. Fifty second-division metaphase cells were scored for frequency of SCEs/cell from each dose level.

Statistical analyses were conducted on the slopes of the dose-response curves and the individual dose points (Galloway *et al*., 1987). An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001. An increase of 20% or greater at any single dose was considered weak evidence of activity; increases at two or more doses resulted in a determination that the trial was positive. A highly significant trend ($P<0.005$), in the absence of any responses reaching 20% above background, led to a call of equivocal.

***Chromosomal Aberrations Test:*** In the Abs test without S9, cells were incubated in McCoy's 5A medium with propylene glycol mono-*t*-butyl ether for 10.7 hours; Colcemid was added and incubation continued for 2 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the Abs test with S9, cells were treated with propylene glycol mono-*t*-butyl ether and S9 for 2 hours, after which the treatment medium was removed and the cells incubated for 10 hours in fresh medium, with Colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9. The harvest time for the Abs test was based on the cell cycle information obtained in the SCE test.

Cells were selected for scoring on the basis of good morphology and completeness of karyotype ($21 \pm 2$ chromosomes). All slides were scored blind, and those from a single test were read by the same person. Two hundred first-division metaphase cells were scored at each dose level. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

Chromosomal aberration data are presented as percentage of cells with aberrations. To arrive at a statistical call for a trial, analyses were conducted on both the dose response curve and individual dose points. For a single trial, a statistically significant ($P \leq 0.05$) difference for one dose point and a significant trend ($P \leq 0.015$) were considered weak evidence for a positive response; significant differences for two or more doses indicated the trial was positive. A positive trend test in the absence of a statistically significant increase at any one dose resulted in an equivocal call (Galloway *et al.,* 1987). Ultimately, the trial calls were based on a consideration of the statistical analyses as well as the biological information available to the reviewers.

## Mouse Peripheral Blood Micronucleus Test Protocol

A detailed discussion of this assay is presented by MacGregor *et al.* (1990). At the end of the 3-month toxicity study, peripheral blood samples were obtained from male and female mice. Smears were immediately prepared and fixed in absolute methanol. The methanol-fixed slides were stained with acridine orange and coded. Slides were scanned to determine the frequency of micronuclei in 2,000 normochromatic erythrocytes (NCEs) in each of 10 animals per exposed group. In addition, the percentage of polychromatic erythrocytes (PCEs) was determined as a measure of bone marrow toxicity.

The results were tabulated as the mean of the pooled results from all animals within a treatment group plus or minus the standard error of the mean. The frequency of micronucleated cells among NCEs was analyzed by a statistical software package that tested for increasing trend over exposure groups with a one-tailed Cochran-Armitage trend test, followed by pairwise comparisons between each exposed group and the control group (ILS, 1990). In the presence of excess binomial variation, as detected by a binomial dispersion test, the binomial variance of the Cochran-Armitage test was adjusted upward in proportion to the excess variation. In the micronucleus test, an individual trial is considered positive if the trend test P value is less than or equal to 0.025 or if the P value for any single exposed group is less than or equal to 0.025 divided by the number of exposed groups. A final call of positive for micronucleus induction is preferably based on reproducibly positive trials (as noted above). Results of the 3-month study were accepted without repeat tests, because additional test data could not be obtained. Ultimately, the final call is determined by the scientific staff after considering the results of statistical analyses, the reproducibility of any effects observed, and the magnitudes of those effects.

## Evaluation Protocol

These are the basic guidelines for arriving at an overall assay result for assays performed by the National Toxicology Program. Statistical as well as biological factors are considered. For an individual assay, the statistical procedures for data analysis have been described in the preceding protocols. There have been instances, however, in which multiple aliquots of a chemical were tested in the same assay, and different results were obtained among

aliquots and/or among laboratories. Results from more than one aliquot or from more than one laboratory are not simply combined into an overall result. Rather, all the data are critically evaluated, particularly with regard to pertinent protocol variations, in determining the weight of evidence for an overall conclusion of chemical activity in an assay. In addition to multiple aliquots, the *in vitro* assays have another variable that must be considered in arriving at an overall test result. *In vitro* assays are conducted with and without exogenous metabolic activation. Results obtained in the absence of activation are not combined with results obtained in the presence of activation; each testing condition is evaluated separately. The summary table in the Abstract of this Technical Report presents a result that represents a scientific judgement of the overall evidence for activity of the chemical in an assay.

## RESULTS

Propylene glycol mono-*t*-butyl ether, tested over a concentration range of 100 to 10,000 µg/plate, was mutagenic in *S. typhimurium* strain TA97 in the absence of liver S9 activation enzymes; negative results were obtained with strain TA97 in the presence of rat or hamster liver S9 enzymes, and in strains TA98, TA100, and TA1535 with and without S9 (Table E1). Propylene glycol mono-*t*-butyl ether was also nonmutagenic in TA1537 in the absence of S9; it was not tested with S9. Propylene glycol mono-*t*-butyl ether did not induce SCEs (Table E2) or Abs (Table E3) in CHO cells, with or without S9. In these cytogenetic assays, propylene glycol mono-*t*-butyl ether was tested up to 5,000 µg/mL, the maximum concentration set by the assay protocol. Propylene glycol mono-*t*-butyl ether, administered for 3 months by inhalation over an exposure concentration range of 75 to 1,200 ppm, induced a small but significant increase in the frequency of micronucleated NCEs in peripheral blood of female mice; no increase in micronucleated NCEs was seen in male mice (Table E4). The percentages of PCEs in the exposed groups were similar to those of the chamber control groups.

**TABLE E1**
**Mutagenicity of Propylene Glycol Mono-*t*-butyl Ether in *Salmonella typhimurium*[a]**

| Strain | Dose (µg/plate) | Revertants/Plate[b] –S9 Trial 1 | –S9 Trial 2 | + 30% hamster S9 Trial 1 | + 30% rat S9 Trial 1 |
|---|---|---|---|---|---|
| **TA100** | 0 | 104 ± 5.7 | | 123 ± 8.7 | 121 ± 3.2 |
| | 100 | 91 ± 3.2 | | 116 ± 1.7 | 114 ± 3.2 |
| | 333 | 107 ± 1.3 | | 122 ± 2.8 | 122 ± 6.5 |
| | 1,000 | 98 ± 8.1 | | 139 ± 3.6 | 127 ± 1.5 |
| | 3,333 | 106 ± 4.9 | | 125 ± 6.7 | 116 ± 7.0 |
| | 10,000 | 103 ± 3.5 | | 121 ± 7.9 | 114 ± 2.4 |
| Trial summary | | Negative | | Negative | Negative |
| Positive control[c] | | 850 ± 31.7 | | 828 ± 40.1 | 907 ± 102.3 |
| **TA1535** | 0 | 10 ± 1.7 | | 11 ± 1.8 | 10 ± 1.8 |
| | 100 | 7 ± 0.9 | | 10 ± 1.2 | 13 ± 1.5 |
| | 333 | 7 ± 0.6 | | 8 ± 2.0 | 8 ± 0.6 |
| | 1,000 | 6 ± 0.3 | | 8 ± 1.2 | 6 ± 0.7 |
| | 3,333 | 7 ± 1.5 | | 10 ± 2.0 | 8 ± 1.0 |
| | 10,000 | 3 ± 0.6[d] | | 7 ± 1.2 | 9 ± 0.6 |
| Trial summary | | Negative | | Negative | Negative |
| Positive control | | 1,347 ± 22.8 | | 564 ± 16.1 | 246 ± 13.6 |
| **TA1537** | 0 | 9 ± 2.5 | | | |
| | 100 | 12 ± 0.9 | | | |
| | 333 | 12 ± 0.9 | | | |
| | 1,000 | 12 ± 1.9 | | | |
| | 3,333 | 11 ± 3.8 | | | |
| | 10,000 | 9 ± 2.8 | | | |
| Trial summary | | Negative | | | |
| Positive control | | 224 ± 10.0 | | | |
| **TA97** | 0 | 135 ± 3.8 | 149 ± 0.3 | 170 ± 4.2 | 157 ± 6.4 |
| | 100 | 123 ± 3.8 | 146 ± 8.4 | 189 ± 10.9 | 187 ± 4.9 |
| | 333 | 131 ± 8.3 | 163 ± 5.0 | 183 ± 8.7 | 180 ± 8.0 |
| | 1,000 | 150 ± 5.5 | 227 ± 22.3 | 179 ± 10.9 | 166 ± 5.2 |
| | 3,333 | 248 ± 18.3 | 247 ± 10.7 | 196 ± 10.2 | 154 ± 6.0 |
| | 10,000 | 325 ± 18.9 | 318 ± 26.6 | 167 ± 18.9 | 184 ± 2.8 |
| Trial summary | | Positive | Positive | Negative | Negative |
| Positive control | | 585 ± 23.1 | 467 ± 34.3 | 929 ± 27.2 | 959 ± 104.5 |

**TABLE E1**
**Mutagenicity of Propylene Glycol Mono-*t*-butyl Ether in *Salmonella typhimurium***

| Strain | Dose (µg/plate) | Revertants/Plate –S9 Trial 1 | –S9 Trial 2 | + 30% hamster S9 Trial 1 | + 30% rat S9 Trial 1 |
|---|---|---|---|---|---|
| **TA98** | 0 | 13 ± 0.3 | | 21 ± 2.3 | 16 ± 2.4 |
| | 100 | 14 ± 1.2 | | 17 ± 2.7 | 18 ± 3.3 |
| | 333 | 14 ± 0.7 | | 19 ± 2.6 | 18 ± 1.2 |
| | 1,000 | 15 ± 2.7 | | 18 ± 1.7 | 15 ± 1.2 |
| | 3,333 | 19 ± 2.9 | | 15 ± 1.9 | 15 ± 0.9 |
| | 10,000 | 7 ± 1.5[d] | | 19 ± 0.6 | 16 ± 0.7 |
| Trial summary | | Negative | | Negative | Negative |
| Positive control | | 460 ± 13.9 | | 905 ± 18.6 | 652 ± 23.5 |

[a] Study performed at SRI International. The detailed protocol is presented by Zeiger *et al*. (1992). 0 µg/plate was the solvent control.
[b] Revertants are presented as mean ± standard error from three plates.
[c] The positive controls in the absence of metabolic activation were sodium azide (TA100 and TA1535), 9-aminoacridine (TA97 and TA1537), and 4-nitro-*o*-phenylenediamine (TA98). The positive control for metabolic activation with all strains was 2-aminoanthracene.
[d] Slight toxicity

**TABLE E2**
**Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Propylene Glycol Mono-*t*-butyl Ether[a]**

| Compound | Dose (µg/mL) | Total Cells Scored | No. of Chromosomes | No. of SCEs | SCEs/ Chromosome | SCEs/ Cell | Hrs in BrdU | Relative Change of SCEs/ Chromosome[b] (%) |
|---|---|---|---|---|---|---|---|---|
| **–S9** | | | | | | | | |
| **Trial 1** | | | | | | | | |
| Summary: Negative | | | | | | | | |
| Dimethylsulfoxide[c] | | 50 | 1,049 | 383 | 0.36 | 7.7 | 26.0 | |
| Propylene glycol mono-*t*-butyl ether | 167 | 50 | 1,047 | 400 | 0.38 | 8.0 | 26.0 | 4.64 |
| | 500 | 50 | 1,049 | 369 | 0.35 | 7.4 | 26.0 | -3.65 |
| | 1,667 | 50 | 1,050 | 387 | 0.36 | 7.7 | 26.0 | 0.95 |
| | 5,000 | Cytostatic | | | | | 31.0 | |
| | | | | | P=0.588[d] | | | |
| Mitomycin-C[e] | 0.001 | 50 | 1,050 | 497 | 0.47 | 9.9 | 26.0 | 29.64 |
| | 0.004 | 10 | 210 | 217 | 1.03 | 21.7 | 26.0 | 183.03 |
| **+S9** | | | | | | | | |
| **Trial 1** | | | | | | | | |
| Summary: Negative | | | | | | | | |
| Dimethylsulfoxide | | 50 | 1,050 | 389 | 0.37 | 7.8 | 26.0 | |
| Propylene glycol mono-*t*-butyl ether | 500 | 50 | 1,050 | 387 | 0.36 | 7.7 | 26.0 | -0.51 |
| | 1,667 | 50 | 1,051 | 381 | 0.36 | 7.6 | 26.0 | -2.15 |
| | 5,000 | 50 | 1,049 | 392 | 0.37 | 7.8 | 26.0 | 0.87 |
| | | | | | P=0.486 | | | |
| Cyclophosphamide[e] | 0.125 | 50 | 1,049 | 498 | 0.47 | 10.0 | 26.0 | 28.14 |
| | 0.500 | 10 | 210 | 180 | 0.85 | 18.0 | 26.0 | 131.37 |

[a] Study was performed at SITEK Research Laboratories, Inc. The detailed protocol is presented by Galloway *et al.* (1987).
SCE=sister chromatid exchange; BrdU=bromodeoxyuridine
[b] SCEs/chromosome in treated cells versus SCEs/chromosome in solvent control cells
[c] Solvent control
[d] Significance of SCEs/chromosome tested by the linear regression trend test versus log of the dose
[e] Positive control

**TABLE E3**
**Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by Propylene Glycol Mono-*t*-butyl Ether[a]**

| Compound | Dose (µg/mL) | Total Cells Scored | Number of Aberrations | Aberrations/ Cell | Cells with Aberrations (%) |
|---|---|---|---|---|---|
| **–S9** | | | | | |
| **Trial 1** | | | | | |
| Harvest time: 12.7 hours | | | | | |
| Summary: Negative | | | | | |
| Dimethylsulfoxide[b] | | 200 | 3 | 0.02 | 1.5 |
| Propylene glycol mono-*t*-butyl ether | 1,081 | 200 | 0 | 0.00 | 0.0 |
| | 2,325 | 200 | 1 | 0.01 | 0.5 |
| | 5,000 | 200 | 1 | 0.01 | 0.5 |
| | | | | | P=0.842[c] |
| Mitomycin-C[d] | 0.40 | 25 | 11 | 0.44 | 36.0 |
| **+S9** | | | | | |
| **Trial 1** | | | | | |
| Harvest time: 12.0 hours | | | | | |
| Summary: Negative | | | | | |
| Dimethylsulfoxide | | 200 | 1 | 0.01 | 0.5 |
| Propylene glycol mono-*t*-butyl ether | 1,081 | 200 | 1 | 0.01 | 0.5 |
| | 2,325 | 200 | 2 | 0.01 | 1.0 |
| | 5,000 | 200 | 4 | 0.02 | 2.0 |
| | | | | | P=0.056 |
| Cyclophosphamide[d] | 20 | 25 | 14 | 0.56 | 40.0 |

[a] Study was performed at SITEK Research Laboratories, Inc. The detailed protocol is presented by Galloway *et al.* (1987).
[b] Solvent control
[c] Significance of percent cells with aberrations tested by the linear regression trend test versus log of the dose
[d] Positive control

**TABLE E4**
**Frequency of Micronuclei in Peripheral Blood Erythrocytes of Mice Following Treatment with Propylene Glycol Mono-*t*-butyl Ether by Inhalation for 3 Months[a]**

| Concentration (ppm) | Number of Mice with Erythrocytes Scored | Micronucleated NCEs/ 1,000 NCEs[b] | P Value[c] | PCEs (%) |
|---|---|---|---|---|
| **Male** | | | | |
| Chamber control | 10 | 1.05 ± 0.23 | | 2.2 |
| 75 | 10 | 0.95 ± 0.17 | 0.6241 | 2.3 |
| 150 | 10 | 1.25 ± 0.20 | 0.2776 | 2.2 |
| 300 | 10 | 1.00 ± 0.17 | 0.5621 | 2.4 |
| 600 | 10 | 0.55 ± 0.17 | 0.9615 | 1.9 |
| 1,200 | 10 | 1.10 ± 0.15 | 0.4394 | 2.1 |
| | | P=0.636[d] | | |
| **Female** | | | | |
| Chamber control | 10 | 0.70 ± 0.15 | | 1.5 |
| 75 | 10 | 0.95 ± 0.20 | 0.1919 | 1.9 |
| 150 | 10 | 0.75 ± 0.20 | 0.4263 | 1.5 |
| 300 | 10 | 0.60 ± 0.18 | 0.6526 | 1.7 |
| 600 | 10 | 1.00 ± 0.15 | 0.1516 | 1.6 |
| 1,200 | 10 | 1.25 ± 0.17 | 0.0390 | 1.3 |
| | | P=0.021 | | |

[a] Study was performed at SITEK Research Laboratories, Inc. The detailed protocol is presented by MacGregor *et al*. (1990).
NCE=normochromatic erythrocyte; PCE=polychromatic erythrocyte
[b] Mean ± standard error
[c] Pairwise comparison with the chamber controls, significant at P≤0.005 (ILS, 1990)
[d] Significance of micronucleated NCEs/1,000 NCEs tested by the one-tailed trend test, significant at P≤0.025 (ILS, 1990)

# APPENDIX F
# CLINICAL PATHOLOGY RESULTS


**TABLE F1** **Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether** . . . . . **250**

**TABLE F2** **Hematology Data for Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether** . . . . . **257**

**TABLE F1**
**Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Male** | | | | | | |
| Hematology | | | | | | |
| Day 3 | 10 | 10 | 10 | 10 | 10 | 10 |
| Day 23 | 10 | 9 | 10 | 10 | 10 | 10 |
| Week 14 | 10 | 10 | 10 | 10 | 10 | 10 |
| Hematocrit (%) | | | | | | |
| Day 3 | 45.2 ± 0.5 | 45.4 ± 0.4 | 44.6 ± 0.5 | 45.6 ± 0.4 | 44.4 ± 0.4 | 44.5 ± 0.5 |
| Day 23 | 47.0 ± 0.5 | 47.1 ± 0.5 | 45.9 ± 0.4 | 46.7 ± 0.3 | 46.1 ± 0.3 | 46.3 ± 0.4 |
| Week 14 | 45.5 ± 0.3 | 45.6 ± 0.2 | 44.9 ± 0.5 | 44.3 ± 0.4* | 44.6 ± 0.2* | 44.4 ± 0.3* |
| Packed cell volume (%) | | | | | | |
| Day 3 | 44.3 ± 0.5 | 44.0 ± 0.5 | 43.6 ± 0.6 | 44.7 ± 0.3 | 43.6 ± 0.6 | 44.0 ± 0.6 |
| Day 23 | 45.4 ± 0.5 | 45.5 ± 0.4 | 44.2 ± 0.4 | 45.4 ± 0.3 | 45.1 ± 0.3 | 44.8 ± 0.4 |
| Week 14 | 45.7 ± 0.3 | 45.3 ± 0.3 | 44.9 ± 0.4 | 44.0 ± 0.4** | 44.4 ± 0.2** | 44.3 ± 0.3** |
| Hemoglobin (g/dL) | | | | | | |
| Day 3 | 14.0 ± 0.1 | 13.9 ± 0.2 | 13.9 ± 0.2 | 14.3 ± 0.1 | 13.9 ± 0.1 | 13.6 ± 0.1 |
| Day 23 | 15.5 ± 0.2 | 15.5 ± 0.1 | 15.2 ± 0.1 | 15.4 ± 0.1 | 15.1 ± 0.1* | 14.7 ± 0.2** |
| Week 14 | 14.9 ± 0.1 | 14.8 ± 0.1 | 14.7 ± 0.1 | 14.5 ± 0.1* | 14.4 ± 0.1** | 14.5 ± 0.1** |
| Erythrocytes ($10^6$/µL) | | | | | | |
| Day 3 | 6.91 ± 0.10 | 6.78 ± 0.08 | 6.78 ± 0.11 | 6.97 ± 0.05 | 6.73 ± 0.09 | 6.82 ± 0.09 |
| Day 23 | 7.44 ± 0.10 | 7.43 ± 0.07 | 7.19 ± 0.09 | 7.44 ± 0.08 | 7.37 ± 0.07 | 7.25 ± 0.08 |
| Week 14 | 8.40 ± 0.06 | 8.32 ± 0.03 | 8.24 ± 0.08 | 8.09 ± 0.06** | 8.15 ± 0.04** | 8.11 ± 0.07** |
| Reticulocytes ($10^6$/µL) | | | | | | |
| Day 3 | 0.20 ± 0.03 | 0.20 ± 0.02 | 0.20 ± 0.03 | 0.20 ± 0.02 | 0.30 ± 0.02** | 0.26 ± 0.03* |
| Day 23 | 0.23 ± 0.01 | 0.28 ± 0.02* | 0.27 ± 0.01* | 0.25 ± 0.01 | 0.29 ± 0.01** | 0.29 ± 0.01** |
| Week 14 | 0.20 ± 0.01 | 0.22 ± 0.01 | 0.23 ± 0.01 | 0.20 ± 0.01 | 0.24 ± 0.01 | 0.22 ± 0.01 |
| Mean cell volume (fL) | | | | | | |
| Day 3 | 64.0 ± 0.4 | 64.9 ± 0.4 | 64.4 ± 0.4 | 64.1 ± 0.2 | 64.7 ± 0.2 | 64.5 ± 0.2 |
| Day 23 | 61.3 ± 0.2 | 61.1 ± 0.2 | 61.6 ± 0.3 | 61.1 ± 0.3 | 61.3 ± 0.3 | 61.8 ± 0.4 |
| Week 14 | 54.5 ± 0.2 | 54.3 ± 0.2 | 54.6 ± 0.2 | 54.4 ± 0.2 | 54.6 ± 0.2 | 54.7 ± 0.2 |
| Mean cell hemoglobin (pg) | | | | | | |
| Day 3 | 20.3 ± 0.1 | 20.5 ± 0.1 | 20.5 ± 0.1 | 20.5 ± 0.1 | 20.6 ± 0.1 | 20.0 ± 0.1 |
| Day 23 | 20.8 ± 0.1 | 20.8 ± 0.1 | 21.2 ± 0.1 | 20.8 ± 0.1 | 20.5 ± 0.1 | 20.3 ± 0.1* |
| Week 14 | 17.8 ± 0.1 | 17.9 ± 0.0 | 17.8 ± 0.1 | 17.9 ± 0.1 | 17.7 ± 0.1 | 17.9 ± 0.1 |
| Mean cell hemoglobin concentration (g/dL) | | | | | | |
| Day 3 | 31.7 ± 0.1 | 31.6 ± 0.2 | 31.9 ± 0.2 | 32.0 ± 0.2 | 31.8 ± 0.2 | 31.1 ± 0.2 |
| Day 23 | 34.0 ± 0.1 | 34.0 ± 0.2 | 34.4 ± 0.2 | 34.0 ± 0.1 | 33.4 ± 0.2* | 32.9 ± 0.1** |
| Week 14 | 32.7 ± 0.1 | 32.8 ± 0.1 | 32.7 ± 0.2 | 32.9 ± 0.2 | 32.5 ± 0.1 | 32.7 ± 0.1 |
| Platelets ($10^3$/µL) | | | | | | |
| Day 3 | 891.4 ± 19.3 | 882.1 ± 14.0 | 856.6 ± 18.4 | 841.7 ± 15.1 | 852.0 ± 15.2 | 854.3 ± 13.1 |
| Day 23 | 693.2 ± 16.6 | 724.4 ± 9.7 | 695.3 ± 12.2 | 700.0 ± 15.9 | 706.2 ± 10.8 | 726.1 ± 12.3 |
| Week 14 | 600.8 ± 10.2 | 626.5 ± 6.6 | 634.0 ± 10.5* | 622.2 ± 6.8 | 662.5 ± 9.1** | 690.2 ± 8.2** |
| Leukocytes ($10^3$/µL) | | | | | | |
| Day 3 | 7.44 ± 0.44 | 7.73 ± 0.37 | 7.49 ± 0.48 | 8.97 ± 0.56 | 7.65 ± 0.48 | 5.04 ± 0.24** |
| Day 23 | 10.84 ± 0.40 | 11.41 ± 0.48 | 11.30 ± 0.42 | 10.62 ± 0.48 | 10.46 ± 0.51 | 6.70 ± 0.33** |
| Week 14 | 6.58 ± 0.34 | 8.32 ± 0.32** | 9.17 ± 0.39** | 8.26 ± 0.38** | 8.03 ± 0.40** | 9.08 ± 0.25** |
| Segmented neutrophils ($10^3$/µL) | | | | | | |
| Day 3 | 0.82 ± 0.07 | 0.76 ± 0.08 | 0.87 ± 0.07 | 0.97 ± 0.07 | 0.84 ± 0.12 | 1.10 ± 0.10 |
| Day 23 | 0.82 ± 0.05 | 0.89 ± 0.11 | 0.78 ± 0.05 | 0.92 ± 0.09 | 0.96 ± 0.06 | 0.57 ± 0.05 |
| Week 14 | 1.44 ± 0.08 | 1.79 ± 0.08* | 1.97 ± 0.08** | 1.79 ± 0.08* | 1.70 ± 0.05 | 1.70 ± 0.08 |

**TABLE F1**
**Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Male** (continued) | | | | | | |
| Hematology (continued) | | | | | | |
| Day 3 | 10 | 10 | 10 | 10 | 10 | 10 |
| Day 23 | 10 | 9 | 10 | 10 | 10 | 10 |
| Week 14 | 10 | 10 | 10 | 10 | 10 | 10 |
| Lymphocytes ($10^3$/μL) | | | | | | |
| Day 3 | 6.08 ± 0.35 | 6.57 ± 0.38 | 6.48 ± 0.47 | 7.55 ± 0.51 | 6.48 ± 0.37 | 3.81 ± 0.17* |
| Day 23 | 9.64 ± 0.35 | 10.17 ± 0.44 | 10.20 ± 0.41 | 9.33 ± 0.44 | 9.15 ± 0.49 | 5.96 ± 0.29** |
| Week 14 | 4.70 ± 0.25 | 5.94 ± 0.24** | 6.54 ± 0.32** | 5.87 ± 0.34** | 5.75 ± 0.33** | 6.75 ± 0.22** |
| Monocytes ($10^3$/μL) | | | | | | |
| Day 3 | 0.52 ± 0.12 | 0.38 ± 0.06 | 0.14 ± 0.03** | 0.39 ± 0.08 | 0.29 ± 0.07 | 0.12 ± 0.02** |
| Day 23 | 0.31 ± 0.03 | 0.28 ± 0.04 | 0.27 ± 0.02 | 0.31 ± 0.03 | 0.28 ± 0.03 | 0.11 ± 0.02** |
| Week 14 | 0.39 ± 0.04 | 0.53 ± 0.04 | 0.61 ± 0.03** | 0.56 ± 0.03 | 0.53 ± 0.04 | 0.58 ± 0.02** |
| Basophils ($10^3$/μL) | | | | | | |
| Day 3 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 |
| Day 23 | 0.039 ± 0.004 | 0.036 ± 0.006 | 0.027 ± 0.009 | 0.036 ± 0.007 | 0.044 ± 0.005 | 0.042 ± 0.006 |
| Week 14 | 0.000 ± 0.000 | 0.007 ± 0.007 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 |
| Eosinophils ($10^3$/μL) | | | | | | |
| Day 3 | 0.03 ± 0.02 | 0.02 ± 0.02 | 0.00 ± 0.00 | 0.06 ± 0.03 | 0.04 ± 0.02 | 0.01 ± 0.01 |
| Day 23 | 0.03 ± 0.00 | 0.03 ± 0.00 | 0.03 ± 0.00 | 0.03 ± 0.00 | 0.03 ± 0.00 | 0.03 ± 0.00 |
| Week 14 | 0.05 ± 0.00 | 0.05 ± 0.00 | 0.05 ± 0.01 | 0.05 ± 0.00 | 0.05 ± 0.00 | 0.06 ± 0.01 |
| Clinical Chemistry | | | | | | |
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| Urea nitrogen (mg/dL) | | | | | | |
| Day 3 | 7.6 ± 0.3 | 6.6 ± 0.5 | 6.7 ± 0.5 | 7.2 ± 0.4 | 6.5 ± 0.3 | 8.2 ± 0.5 |
| Day 23 | 9.8 ± 0.4 | 9.3 ± 0.3 | 9.1 ± 0.4 | 8.5 ± 0.3 | 8.6 ± 0.3 | 8.8 ± 0.2 |
| Week 14 | 14.9 ± 0.6 | 14.1 ± 0.4 | 12.7 ± 0.4* | 13.0 ± 0.4 | 15.4 ± 0.4 | 14.0 ± 0.3 |
| Creatinine (mg/dL) | | | | | | |
| Day 3 | 0.66 ± 0.02 | 0.62 ± 0.01 | 0.67 ± 0.02 | 0.66 ± 0.02 | 0.71 ± 0.02 | 0.99 ± 0.05** |
| Day 23 | 0.71 ± 0.02 | 0.73 ± 0.02 | 0.68 ± 0.02 | 0.72 ± 0.02 | 0.69 ± 0.02 | 1.58 ± 0.11** |
| Week 14 | 0.85 ± 0.03 | 0.89 ± 0.02 | 0.85 ± 0.02 | 0.85 ± 0.02 | 0.91 ± 0.01 | 0.88 ± 0.03 |
| Total protein (g/dL) | | | | | | |
| Day 3 | 5.6 ± 0.1 | 5.5 ± 0.1 | 5.6 ± 0.1 | 5.7 ± 0.1 | 5.8 ± 0.1 | 5.8 ± 0.1* |
| Day 23 | 6.0 ± 0.1 | 6.1 ± 0.1 | 5.9 ± 0.1 | 6.1 ± 0.1 | 6.2 ± 0.1 | 6.3 ± 0.1* |
| Week 14 | 6.6 ± 0.1 | 6.7 ± 0.1 | 6.5 ± 0.1 | 6.6 ± 0.1 | 6.7 ± 0.1 | 7.1 ± 0.1** |
| Albumin (g/dL) | | | | | | |
| Day 3 | 3.8 ± 0.1 | 3.7 ± 0.1 | 3.6 ± 0.0 | 3.8 ± 0.1 | 3.9 ± 0.1 | 4.0 ± 0.1 |
| Day 23 | 4.0 ± 0.1 | 3.9 ± 0.1 | 4.0 ± 0.0 | 3.9 ± 0.1 | 4.1 ± 0.1 | 4.2 ± 0.1 |
| Week 14 | 4.0 ± 0.1 | 3.8 ± 0.1 | 3.9 ± 0.0 | 3.9 ± 0.1 | 3.9 ± 0.1 | 4.2 ± 0.1 |
| Globulin (g/dL) | | | | | | |
| Day 3 | 1.7 ± 0.1 | 1.8 ± 0.1 | 2.0 ± 0.1 | 1.9 ± 0.1 | 1.9 ± 0.1 | 1.8 ± 0.1 |
| Day 23 | 2.1 ± 0.1 | 2.1 ± 0.0 | 1.8 ± 0.1 | 2.1 ± 0.1 | 2.1 ± 0.1 | 2.2 ± 0.1 |
| Week 14 | 2.6 ± 0.2 | 2.9 ± 0.1 | 2.6 ± 0.1 | 2.8 ± 0.1 | 2.8 ± 0.1 | 2.9 ± 0.1 |
| Albumin/globulin ratio | | | | | | |
| Day 3 | 2.4 ± 0.2 | 2.1 ± 0.1 | 1.9 ± 0.1 | 2.0 ± 0.1 | 2.1 ± 0.1 | 2.4 ± 0.1 |
| Day 23 | 1.9 ± 0.1 | 1.9 ± 0.1 | 2.3 ± 0.1 | 1.9 ± 0.1 | 2.0 ± 0.1 | 2.0 ± 0.1 |
| Week 14 | 1.6 ± 0.1 | 1.3 ± 0.1 | 1.5 ± 0.1 | 1.4 ± 0.1 | 1.4 ± 0.1 | 1.4 ± 0.1 |

**TABLE F1**
**Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Male** (continued) | | | | | | |
| Clinical Chemistry (continued) | | | | | | |
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| Alanine aminotransferase (IU/L) | | | | | | |
| Day 3 | 65 ± 2 | 67 ± 2 | 65 ± 1 | 61 ± 2 | 66 ± 2 | 62 ± 2 |
| Day 23 | 46 ± 1 | 47 ± 2 | 42 ± 1* | 43 ± 1* | 39 ± 1** | 38 ± 1** |
| Week 14 | 69 ± 4 | 60 ± 2* | 50 ± 1** | 46 ± 2** | 52 ± 3** | 49 ± 1** |
| Alkaline phosphatase (IU/L) | | | | | | |
| Day 3 | 810 ± 15 | 861 ± 25 | 810 ± 20 | 760 ± 14 | 783 ± 14 | 645 ± 15** |
| Day 23 | 526 ± 14 | 530 ± 14 | 503 ± 12 | 493 ± 14 | 493 ± 13 | 444 ± 12** |
| Week 14 | 290 ± 10 | 289 ± 4 | 274 ± 6 | 279 ± 8 | 287 ± 8 | 280 ± 4 |
| Creatine kinase (IU/L) | | | | | | |
| Day 3 | 404 ± 45 | 440 ± 53 | 467 ± 52[b] | 415 ± 39 | 573 ± 67[c] | 466 ± 72 |
| Day 23 | 300 ± 25 | 410 ± 43[b] | 382 ± 38 | 410 ± 33[b] | 316 ± 30 | 291 ± 24 |
| Week 14 | 197 ± 17 | 176 ± 24 | 151 ± 20 | 182 ± 29 | 198 ± 28 | 180 ± 24 |
| Sorbitol dehydrogenase (IU/L) | | | | | | |
| Day 3 | 13 ± 0 | 10 ± 0** | 11 ± 1 | 11 ± 0 | 11 ± 1* | 12 ± 0 |
| Day 23 | 9 ± 1 | 10 ± 1 | 9 ± 1 | 8 ± 1 | 8 ± 0 | 9 ± 1 |
| Week 14 | 16 ± 1 | 16 ± 1 | 14 ± 1 | 13 ± 1 | 14 ± 1 | 14 ± 1 |
| Bile acids (µmol/L) | | | | | | |
| Day 3 | 25.9 ± 1.0 | 30.3 ± 1.2* | 37.7 ± 3.0** | 38.6 ± 1.1** | 50.1 ± 5.5** | 49.0 ± 6.1** |
| Day 23 | 33.8 ± 2.3 | 40.8 ± 4.3 | 36.2 ± 1.3 | 48.3 ± 5.7** | 47.1 ± 1.9** | 47.9 ± 1.4** |
| Week 14 | 35.0 ± 4.0 | 29.4 ± 1.3 | 28.5 ± 1.5 | 29.0 ± 0.9 | 34.1 ± 3.5 | 32.5 ± 4.7 |
| Urinalysis | | | | | | |
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| Volume (mL/16 hours) | 12.2 ± 1.8 | 19.0 ± 2.6 | 19.8 ± 3.1 | 13.9 ± 2.3 | 25.3 ± 3.7** | 26.8 ± 2.7** |
| Specific gravity | 1.017 ± 0.002 | 1.012 ± 0.002 | 1.014 ± 0.002 | 1.020 ± 0.003 | 1.013 ± 0.002 | 1.013 ± 0.001 |
| Creatinine (mg/dL) | 68.40 ± 8.90 | 50.10 ± 7.04 | 51.00 ± 9.19 | 71.40 ± 10.05 | 40.50 ± 6.12* | 34.00 ± 3.19** |
| Glucose (µg/mg creatinine) | 118 ± 5 | 153 ± 6* | 163 ± 12** | 156 ± 6* | 159 ± 8** | 149 ± 15 |
| Protein (µg/mg creatinine) | 964 ± 43 | 1,256 ± 81** | 1,266 ± 49** | 1,161 ± 44** | 1,293 ± 48** | 1,585 ± 61** |
| Alkaline phosphatase (mU/mg creatinine) | 259 ± 14 | 322 ± 17 | 293 ± 18 | 266 ± 15 | 288 ± 17 | 299 ± 19 |
| Aspartate aminotransferase (mU/mg creatinine) | 9 ± 0 | 52 ± 4** | 61 ± 3** | 59 ± 4** | 52 ± 3** | 78 ± 5** |
| Lactate dehydrogenase (mU/mg creatinine) | 39 ± 1 | 118 ± 15** | 121 ± 6** | 127 ± 6** | 124 ± 7** | 156 ± 9** |
| γ-Glutamyltransferase (U/mg creatinine) | 2.1 ± 0.1 | 2.2 ± 0.1 | 2.2 ± 0.1 | 2.0 ± 0.1 | 2.0 ± 0.1 | 1.8 ± 0.1 |
| *N*-acetyl-β-D-glucosaminidase (mU/mg creatinine) | 14 ± 1 | 23 ± 1** | 23 ± 1** | 22 ± 1** | 24 ± 1** | 27 ± 2** |

**TABLE F1**
**Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Female** | | | | | | |
| Hematology | | | | | | |
| Day 3 | 10 | 10 | 10 | 10 | 10 | 10 |
| Day 23 | 10 | 10 | 10 | 10 | 10 | 9 |
| Week 14 | 8 | 10 | 10 | 9 | 9 | 8 |
| Hematocrit (%) | | | | | | |
| Day 3 | 46.4 ± 0.4 | 46.0 ± 0.4 | 48.3 ± 0.7 | 46.0 ± 0.6 | 46.7 ± 0.5 | 44.9 ± 0.4 |
| Day 23 | 46.8 ± 0.2 | 46.5 ± 0.3 | 46.9 ± 0.3 | 46.7 ± 0.2 | 46.4 ± 0.3 | 45.3 ± 0.4 |
| Week 14 | 45.9 ± 0.4 | 45.3 ± 0.3 | 44.9 ± 0.3 | 45.8 ± 0.3 | 45.3 ± 0.5 | 45.6 ± 0.2 |
| Packed cell volume (%) | | | | | | |
| Day 3 | 45.8 ± 0.5 | 46.1 ± 0.6 | 47.7 ± 0.7 | 46.0 ± 0.7 | 46.0 ± 0.6 | 44.4 ± 0.4 |
| Day 23 | 46.1 ± 0.3 | 46.1 ± 0.3 | 46.9 ± 0.4 | 45.5 ± 0.3 | 45.5 ± 0.3 | 44.4 ± 0.4** |
| Week 14 | 46.0 ± 0.4 | 45.8 ± 0.3 | 45.2 ± 0.3 | 46.4 ± 0.4 | 46.0 ± 0.6 | 46.2 ± 0.2 |
| Hemoglobin (g/dL) | | | | | | |
| Day 3 | 14.7 ± 0.2 | 14.8 ± 0.1 | 15.3 ± 0.2 | 14.7 ± 0.2 | 14.7 ± 0.2 | 14.1 ± 0.1* |
| Day 23 | 15.7 ± 0.1 | 15.9 ± 0.1 | 16.0 ± 0.1 | 15.6 ± 0.1 | 15.5 ± 0.1 | 14.9 ± 0.1** |
| Week 14 | 15.3 ± 0.1 | 15.2 ± 0.1 | 15.1 ± 0.1 | 15.5 ± 0.1 | 15.2 ± 0.2 | 15.4 ± 0.1 |
| Erythrocytes ($10^6$/µL) | | | | | | |
| Day 3 | 7.19 ± 0.09 | 7.28 ± 0.10 | 7.48 ± 0.14 | 7.27 ± 0.14 | 7.22 ± 0.13 | 6.89 ± 0.07 |
| Day 23 | 7.49 ± 0.07 | 7.40 ± 0.07 | 7.54 ± 0.08 | 7.39 ± 0.07 | 7.35 ± 0.06 | 7.16 ± 0.08** |
| Week 14 | 8.02 ± 0.07 | 8.00 ± 0.06 | 7.91 ± 0.06 | 8.12 ± 0.07 | 8.00 ± 0.10 | 8.08 ± 0.05 |
| Reticulocytes ($10^6$/µL) | | | | | | |
| Day 3 | 0.13 ± 0.01 | 0.16 ± 0.01 | 0.14 ± 0.02 | 0.20 ± 0.03 | 0.12 ± 0.01 | 0.14 ± 0.02 |
| Day 23 | 0.25 ± 0.01 | 0.23 ± 0.01 | 0.24 ± 0.01 | 0.23 ± 0.01 | 0.22 ± 0.01 | 0.18 ± 0.01** |
| Week 14 | 0.24 ± 0.01 | 0.23 ± 0.01 | 0.21 ± 0.01 | 0.21 ± 0.01 | 0.21 ± 0.01 | 0.21 ± 0.01 |
| Mean cell volume (fL) | | | | | | |
| Day 3 | 63.8 ± 0.4 | 63.5 ± 0.3 | 63.7 ± 0.3 | 63.4 ± 0.4 | 63.7 ± 0.4 | 64.3 ± 0.3 |
| Day 23 | 61.6 ± 0.3 | 62.5 ± 0.3 | 62.1 ± 0.4 | 61.6 ± 0.4 | 62.0 ± 0.3 | 62.0 ± 0.3 |
| Week 14 | 57.6 ± 0.2 | 57.4 ± 0.2 | 57.0 ± 0.2 | 57.0 ± 0.2 | 57.6 ± 0.2 | 57.1 ± 0.2 |
| Mean cell hemoglobin (pg) | | | | | | |
| Day 3 | 20.5 ± 0.2 | 20.3 ± 0.1 | 20.5 ± 0.1 | 20.2 ± 0.1 | 20.4 ± 0.2 | 20.4 ± 0.1 |
| Day 23 | 21.0 ± 0.2 | 21.5 ± 0.1 | 21.3 ± 0.1 | 21.2 ± 0.2 | 21.2 ± 0.1 | 20.8 ± 0.1 |
| Week 14 | 19.1 ± 0.1 | 19.0 ± 0.1 | 19.1 ± 0.1 | 19.1 ± 0.1 | 19.1 ± 0.1 | 19.1 ± 0.1 |
| Mean cell hemoglobin concentration (g/dL) | | | | | | |
| Day 3 | 32.2 ± 0.2 | 32.1 ± 0.2 | 32.1 ± 0.1 | 31.8 ± 0.1 | 32.1 ± 0.2 | 31.7 ± 0.2 |
| Day 23 | 34.1 ± 0.2 | 34.5 ± 0.1 | 34.2 ± 0.1 | 34.3 ± 0.2 | 34.1 ± 0.1 | 33.5 ± 0.1* |
| Week 14 | 33.3 ± 0.2 | 33.2 ± 0.1 | 33.4 ± 0.1 | 33.4 ± 0.1 | 33.2 ± 0.2 | 33.5 ± 0.2 |
| Platelets ($10^3$/µL) | | | | | | |
| Day 3 | 826.8 ± 26.8 | 838.8 ± 31.4 | 801.6 ± 21.5 | 770.4 ± 14.9 | 817.4 ± 18.4 | 759.8 ± 17.5 |
| Day 23 | 641.7 ± 15.8 | 661.8 ± 7.5 | 635.3 ± 12.9 | 659.2 ± 14.5 | 644.7 ± 9.1 | 628.1 ± 18.1 |
| Week 14 | 620.5 ± 11.0 | 618.4 ± 12.6 | 605.8 ± 19.6 | 612.4 ± 18.3 | 632.9 ± 12.7 | 618.5 ± 27.9 |
| Leukocytes ($10^3$/µL) | | | | | | |
| Day 3 | 11.16 ± 0.78 | 11.83 ± 0.58 | 10.33 ± 0.61 | 10.27 ± 0.44 | 10.22 ± 0.32 | 5.59 ± 0.40** |
| Day 23 | 12.20 ± 0.41 | 13.28 ± 0.30 | 12.15 ± 0.62 | 12.01 ± 0.28 | 11.04 ± 0.40 | 7.56 ± 0.50** |
| Week 14 | 8.56 ± 0.48 | 7.28 ± 0.54 | 7.32 ± 0.53 | 6.66 ± 0.38 | 7.24 ± 0.64 | 6.24 ± 0.44* |
| Segmented neutrophils ($10^3$/µL) | | | | | | |
| Day 3 | 1.14 ± 0.14 | 0.84 ± 0.07 | 0.92 ± 0.15 | 0.94 ± 0.15 | 0.90 ± 0.10 | 0.83 ± 0.05 |
| Day 23 | 0.86 ± 0.08 | 0.98 ± 0.09 | 0.96 ± 0.09 | 0.89 ± 0.07 | 0.99 ± 0.08 | 0.80 ± 0.12 |
| Week 14 | 2.11 ± 0.15 | 1.76 ± 0.14 | 1.58 ± 0.16* | 1.47 ± 0.10** | 1.65 ± 0.17* | 1.31 ± 0.12** |

**TABLE F1**
**Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Female** (continued) | | | | | | |
| Hematology (continued) | | | | | | |
| Day 3 | 10 | 10 | 10 | 10 | 10 | 10 |
| Day 23 | 10 | 10 | 10 | 10 | 10 | 9 |
| Week 14 | 8 | 10 | 10 | 9 | 9 | 8 |
| Lymphocytes ($10^3$/μL) | | | | | | |
| Day 3 | 9.64 ± 0.70 | 10.71 ± 0.57 | 9.13 ± 0.56 | 8.81 ± 0.28 | 9.18 ± 0.34 | 4.69 ± 0.38** |
| Day 23 | 10.98 ± 0.36 | 11.91 ± 0.26 | 10.82 ± 0.57 | 10.76 ± 0.30 | 9.67 ± 0.36* | 6.55 ± 0.40** |
| Week 14 | 5.90 ± 0.35 | 5.05 ± 0.39 | 5.33 ± 0.35 | 4.79 ± 0.31 | 5.14 ± 0.46 | 4.60 ± 0.37 |
| Monocytes ($10^3$/μL) | | | | | | |
| Day 3 | 0.35 ± 0.08 | 0.18 ± 0.06 | 0.24 ± 0.04 | 0.43 ± 0.09 | 0.53 ± 0.03** | 0.04 ± 0.01** |
| Day 23 | 0.28 ± 0.04 | 0.32 ± 0.04 | 0.34 ± 0.08 | 0.28 ± 0.03 | 0.30 ± 0.02 | 0.13 ± 0.02* |
| Week 14 | 0.51 ± 0.04 | 0.41 ± 0.05 | 0.36 ± 0.05 | 0.36 ± 0.04 | 0.41 ± 0.05 | 0.29 ± 0.03** |
| Basophils ($10^3$/μL) | | | | | | |
| Day 3 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 |
| Day 23 | 0.035 ± 0.005 | 0.040 ± 0.006 | 0.051 ± 0.007 | 0.031 ± 0.004 | 0.034 ± 0.005 | 0.052 ± 0.008 |
| Week 14 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 |
| Eosinophils ($10^3$/μL) | | | | | | |
| Day 3 | 0.02 ± 0.02 | 0.09 ± 0.03 | 0.04 ± 0.02 | 0.10 ± 0.03 | 0.05 ± 0.02 | 0.02 ± 0.01 |
| Day 23 | 0.04 ± 0.01 | 0.05 ± 0.00 | 0.04 ± 0.00 | 0.05 ± 0.00 | 0.04 ± 0.00 | 0.03 ± 0.00* |
| Week 14 | 0.05 ± 0.01 | 0.06 ± 0.01 | 0.05 ± 0.01 | 0.03 ± 0.00 | 0.04 ± 0.01 | 0.04 ± 0.01 |
| Clinical Chemistry | | | | | | |
| Day 3 | 10 | 10 | 10 | 10 | 10 | 10 |
| Day 23 | 10 | 10 | 10 | 10 | 10 | 9 |
| Week 14 | 10 | 10 | 10 | 9 | 10 | 10 |
| Urea nitrogen (mg/dL) | | | | | | |
| Day 3 | 9.1 ± 0.4 | 8.1 ± 0.5 | 8.5 ± 0.4 | 8.5 ± 0.4 | 7.0 ± 0.4** | 9.0 ± 0.4 |
| Day 23 | 11.5 ± 0.5 | 11.0 ± 0.4 | 10.0 ± 0.3* | 9.3 ± 0.3** | 9.2 ± 0.4** | 7.6 ± 0.3** |
| Week 14 | 15.3 ± 0.4 | 14.9 ± 0.5 | 15.7 ± 0.6 | 15.7 ± 0.3 | 14.8 ± 0.5 | 15.2 ± 0.7 |
| Creatinine (mg/dL) | | | | | | |
| Day 3 | 0.64 ± 0.02[b] | 0.63 ± 0.02 | 0.69 ± 0.02 | 0.62 ± 0.01 | 0.66 ± 0.02 | 0.71 ± 0.02 |
| Day 23 | 0.72 ± 0.01 | 0.69 ± 0.01 | 0.76 ± 0.02 | 0.73 ± 0.02 | 0.72 ± 0.01 | 0.87 ± 0.02** |
| Week 14 | 0.79 ± 0.03 | 0.83 ± 0.03 | 0.81 ± 0.03 | 0.86 ± 0.03 | 0.78 ± 0.03 | 0.83 ± 0.03 |
| Total protein (g/dL) | | | | | | |
| Day 3 | 5.7 ± 0.1 | 5.6 ± 0.0 | 5.8 ± 0.0 | 5.6 ± 0.0 | 5.9 ± 0.1* | 5.8 ± 0.1 |
| Day 23 | 5.9 ± 0.1 | 6.0 ± 0.1 | 6.1 ± 0.1 | 6.1 ± 0.1 | 6.2 ± 0.1 | 6.0 ± 0.1 |
| Week 14 | 6.9 ± 0.1 | 6.9 ± 0.1 | 6.8 ± 0.1 | 6.9 ± 0.1 | 6.7 ± 0.1 | 7.3 ± 0.1 |
| Albumin (g/dL) | | | | | | |
| Day 3 | 3.8 ± 0.1 | 3.8 ± 0.1 | 3.9 ± 0.0 | 3.8 ± 0.1 | 3.9 ± 0.1 | 4.0 ± 0.1** |
| Day 23 | 4.1 ± 0.1 | 4.0 ± 0.1 | 4.1 ± 0.1 | 4.2 ± 0.1 | 4.3 ± 0.1 | 4.1 ± 0.1 |
| Week 14 | 4.6 ± 0.1 | 4.7 ± 0.1 | 4.4 ± 0.1 | 4.5 ± 0.1 | 4.4 ± 0.1 | 4.7 ± 0.1 |
| Globulin (g/dL) | | | | | | |
| Day 3 | 1.9 ± 0.1 | 1.8 ± 0.0 | 1.9 ± 0.0 | 1.8 ± 0.1 | 2.0 ± 0.1 | 1.8 ± 0.1 |
| Day 23 | 1.8 ± 0.1 | 2.0 ± 0.1 | 2.0 ± 0.1 | 1.9 ± 0.1 | 1.9 ± 0.1 | 1.9 ± 0.1 |
| Week 14 | 2.3 ± 0.1 | 2.2 ± 0.1 | 2.4 ± 0.1 | 2.4 ± 0.1 | 2.3 ± 0.1 | 2.6 ± 0.1* |

**TABLE F1**
**Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Female** (continued) | | | | | | |
| Clinical Chemistry (continued) | | | | | | |
| Day 3 | 10 | 10 | 10 | 10 | 10 | 10 |
| Day 23 | 10 | 10 | 10 | 10 | 10 | 9 |
| Week 14 | 10 | 10 | 10 | 9 | 10 | 10 |
| Albumin/globulin ratio | | | | | | |
| Day 3 | 2.1 ± 0.1 | 2.1 ± 0.1 | 2.1 ± 0.1 | 2.2 ± 0.2 | 2.0 ± 0.1 | 2.3 ± 0.1 |
| Day 23 | 2.4 ± 0.1 | 2.1 ± 0.1 | 2.1 ± 0.1 | 2.2 ± 0.1 | 2.3 ± 0.1 | 2.3 ± 0.1 |
| Week 14 | 2.0 ± 0.1 | 2.2 ± 0.1 | 1.8 ± 0.1 | 1.9 ± 0.0 | 1.9 ± 0.1 | 1.8 ± 0.1 |
| Alanine aminotransferase (IU/L) | | | | | | |
| Day 3 | 51 ± 3 | 47 ± 1 | 48 ± 1 | 46 ± 2 | 45 ± 2 | 49 ± 2 |
| Day 23 | 44 ± 1 | 42 ± 1 | 44 ± 1 | 40 ± 1* | 40 ± 1* | 35 ± 1** |
| Week 14 | 61 ± 4[b] | 58 ± 4 | 59 ± 4 | 69 ± 6 | 61 ± 6 | 55 ± 4 |
| Alkaline phosphatase (IU/L) | | | | | | |
| Day 3 | 619 ± 23 | 610 ± 13 | 610 ± 9 | 590 ± 14 | 586 ± 16 | 483 ± 10** |
| Day 23 | 377 ± 13 | 341 ± 9* | 352 ± 10 | 352 ± 10 | 350 ± 7 | 287 ± 7** |
| Week 14 | 240 ± 16 | 234 ± 15 | 248 ± 10 | 261 ± 10 | 254 ± 11 | 204 ± 5* |
| Creatine kinase (IU/L) | | | | | | |
| Day 3 | 461 ± 41[c] | 486 ± 91[b] | 524 ± 44[b] | 429 ± 40 | 437 ± 43 | 278 ± 24*[b] |
| Day 23 | 304 ± 39 | 355 ± 30 | 285 ± 29 | 374 ± 36 | 370 ± 46 | 362 ± 100 |
| Week 14 | 287 ± 25[b] | 351 ± 57 | 417 ± 68[c] | 226 ± 41[d] | 379 ± 71 | 335 ± 68[c] |
| Sorbitol dehydrogenase (IU/L) | | | | | | |
| Day 3 | 9 ± 1 | 11 ± 1 | 11 ± 1 | 11 ± 0* | 10 ± 0 | 11 ± 0 |
| Day 23 | 13 ± 1 | 11 ± 1 | 14 ± 1 | 12 ± 1 | 12 ± 1 | 11 ± 0 |
| Week 14 | 14 ± 1 | 12 ± 1 | 12 ± 1 | 14 ± 1 | 18 ± 4 | 13 ± 1 |
| Bile acids (μmol/L) | | | | | | |
| Day 3 | 21.5 ± 1.7 | 24.5 ± 1.9 | 32.6 ± 3.8** | 27.6 ± 1.8** | 32.3 ± 2.2** | 34.4 ± 2.8** |
| Day 23 | 29.6 ± 5.1 | 34.3 ± 6.6 | 35.4 ± 3.8 | 36.0 ± 5.3 | 34.1 ± 4.3 | 51.6 ± 10.7** |
| Week 14 | 32.7 ± 7.0 | 28.3 ± 4.3 | 36.6 ± 7.6 | 40.9 ± 6.1 | 38.1 ± 5.7 | 41.1 ± 4.7 |

**TABLE F1**
**Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Female** (continued) | | | | | | |
| Urinalysis | | | | | | |
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| Volume (mL/16 hours) | 12.0 ± 1.7 | 13.2 ± 1.6 | 10.4 ± 1.5 | 8.0 ± 1.1 | 13.8 ± 2.0 | 10.5 ± 1.9 |
| Specific gravity | 1.013 ± 0.002 | 1.012 ± 0.002 | 1.015 ± 0.002 | 1.020 ± 0.003* | 1.013 ± 0.002 | 1.023 ± 0.004* |
| Creatinine (mg/dL) | 45.00 ± 7.41 | 37.50 ± 4.61 | 44.80 ± 4.94 | 60.00 ± 9.69 | 35.00 ± 4.57 | 52.10 ± 9.44 |
| Glucose (µg/mg creatinine) | 106 ± 3 | 102 ± 4 | 106 ± 6 | 101 ± 3 | 93 ± 6 | 114 ± 4 |
| Protein (µg/mg creatinine) | 91 ± 4 | 158 ± 59 | 89 ± 3 | 94 ± 4 | 93 ± 8 | 105 ± 6 |
| Alkaline phosphatase (mU/mg creatinine) | 184 ± 10 | 172 ± 11 | 159 ± 11 | 177 ± 24 | 188 ± 11 | 186 ± 10 |
| Aspartate aminotransferase (mU/mg creatinine) | 2 ± 1 | 4 ± 1 | 2 ± 0 | 3 ± 0 | 3 ± 1 | 2 ± 0 |
| Lactate dehydrogenase/ (mU/mg creatinine) | 27 ± 3 | 31 ± 1 | 36 ± 2** | 42 ± 2** | 45 ± 2** | 60 ± 3** |
| γ-Glutamyltransferase (U/mg creatinine) | 0.9 ± 0.1 | 0.9 ± 0.1 | 0.8 ± 0.1 | 1.1 ± 0.2 | 1.2 ± 0.1 | 1.1 ± 0.1 |
| *N*-acetyl-β-D-glucosaminidase (U/mg creatinine) | 13 ± 0 | 13 ± 0 | 13 ± 0 | 13 ± 0 | 14 ± 0* | 15 ± 0** |

* Significantly different (P≤0.05) from the chamber control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error. Ratios were calculated and statistical tests were performed on unrounded data.
[b] n=9
[c] n=8
[d] n=6

**TABLE F2**
**Hematology Data for Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| **Male** | | | | | | |
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| Hematocrit (%) | 48.6 ± 0.4 | 50.4 ± 0.4** | 49.5 ± 0.5 | 50.4 ± 0.3** | 50.3 ± 0.4** | 50.7 ± 0.3** |
| Packed cell volume (mL/dL) | 47.5 ± 0.4 | 49.0 ± 0.3* | 48.6 ± 0.4 | 48.7 ± 0.2 | 48.7 ± 0.3 | 50.2 ± 0.5** |
| Hemoglobin (g/dL) | 15.8 ± 0.1 | 16.5 ± 0.1** | 16.1 ± 0.2* | 16.4 ± 0.1** | 16.5 ± 0.1** | 16.7 ± 0.1** |
| Erythrocytes ($10^6$/µL) | 9.80 ± 0.09 | 10.09 ± 0.05 | 10.02 ± 0.07 | 10.08 ± 0.05 | 10.06 ± 0.07 | 10.25 ± 0.11** |
| Reticulocytes ($10^6$/µL) | 0.19 ± 0.01 | 0.22 ± 0.01 | 0.23 ± 0.01 | 0.20 ± 0.01 | 0.23 ± 0.01 | 0.24 ± 0.01* |
| Mean cell volume (fL) | 48.6 ± 0.2 | 48.5 ± 0.2 | 48.5 ± 0.2 | 48.2 ± 0.1 | 48.5 ± 0.2 | 49.1 ± 0.2 |
| Mean cell hemoglobin (pg) | 16.1 ± 0.1 | 16.3 ± 0.1 | 16.1 ± 0.1 | 16.3 ± 0.1 | 16.4 ± 0.1 | 16.3 ± 0.1 |
| Mean cell hemoglobin concentration (g/dL) | 33.3 ± 0.2 | 33.7 ± 0.2 | 33.2 ± 0.2 | 33.8 ± 0.2 | 33.8 ± 0.2 | 33.3 ± 0.2 |
| Platelets ($10^3$/µL) | 771.7 ± 28.9 | 769.4 ± 25.7 | 797.4 ± 28.0 | 773.6 ± 38.0 | 790.8 ± 35.9 | 811.7 ± 26.2 |
| Leukocytes ($10^3$/µL) | 2.20 ± 0.21 | 2.82 ± 0.44 | 2.91 ± 0.41 | 2.98 ± 0.32 | 2.85 ± 0.31 | 3.06 ± 0.30 |
| Segmented neutrophils ($10^3$/µL) | 0.31 ± 0.05 | 0.36 ± 0.06 | 0.34 ± 0.06 | 0.39 ± 0.07 | 0.44 ± 0.05 | 0.47 ± 0.12 |
| Lymphocytes ($10^3$/µL) | 1.85 ± 0.18 | 2.42 ± 0.38 | 2.52 ± 0.37 | 2.59 ± 0.29 | 2.38 ± 0.27 | 2.54 ± 0.26 |
| Monocytes ($10^3$/µL) | 0.01 ± 0.01 | 0.01 ± 0.01 | 0.02 ± 0.01 | 0.03 ± 0.01 | 0.01 ± 0.01 | 0.01 ± 0.01 |
| Eosinophils ($10^3$/µL) | 0.02 ± 0.01 | 0.03 ± 0.01 | 0.04 ± 0.02 | 0.02 ± 0.01 | 0.02 ± 0.01 | 0.04 ± 0.01 |
| **Female** | | | | | | |
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| Hematocrit (%) | 48.0 ± 0.3 | 48.2 ± 0.3 | 47.6 ± 0.4 | 48.2 ± 0.6 | 47.6 ± 0.3 | 48.0 ± 0.4 |
| Packed cell volume (mL/dL) | 45.4 ± 0.3 | 45.8 ± 0.3 | 45.1 ± 0.3 | 46.0 ± 0.5 | 44.8 ± 0.3 | 45.6 ± 0.3 |
| Hemoglobin (g/dL) | 15.9 ± 0.1 | 15.8 ± 0.1 | 15.7 ± 0.1 | 16.0 ± 0.2 | 15.6 ± 0.1 | 15.8 ± 0.1 |
| Erythrocytes ($10^6$/µL) | 9.41 ± 0.03 | 9.46 ± 0.08 | 9.29 ± 0.06 | 9.47 ± 0.10 | 9.29 ± 0.08 | 9.44 ± 0.07 |
| Reticulocytes ($10^6$/µL) | 0.22 ± 0.01 | 0.23 ± 0.01 | 0.23 ± 0.01 | 0.27 ± 0.01* | 0.23 ± 0.01 | 0.21 ± 0.01 |
| Mean cell volume (fL) | 48.2 ± 0.2 | 48.4 ± 0.2 | 48.4 ± 0.2 | 48.5 ± 0.3 | 48.3 ± 0.2 | 48.3 ± 0.2 |
| Mean cell hemoglobin (pg) | 16.9 ± 0.1 | 16.7 ± 0.1 | 17.0 ± 0.1 | 16.8 ± 0.1 | 16.8 ± 0.1 | 16.8 ± 0.1 |
| Mean cell hemoglobin concentration (g/dL) | 35.0 ± 0.2 | 34.5 ± 0.2 | 34.9 ± 0.2 | 34.6 ± 0.2 | 34.9 ± 0.2 | 34.6 ± 0.1 |
| Platelets ($10^3$/µL) | 739.6 ± 42.5 | 761.1 ± 14.8 | 758.2 ± 30.9 | 784.6 ± 32.9 | 759.0 ± 35.3 | 801.7 ± 28.3 |
| Leukocytes ($10^3$/µL) | 3.47 ± 0.26 | 3.04 ± 0.28 | 3.31 ± 0.31 | 3.35 ± 0.29 | 2.94 ± 0.16 | 3.30 ± 0.26 |
| Segmented neutrophils ($10^3$/µL) | 0.39 ± 0.05 | 0.32 ± 0.03 | 0.41 ± 0.09 | 0.43 ± 0.05 | 0.42 ± 0.06 | 0.39 ± 0.05 |
| Lymphocytes ($10^3$/µL) | 3.05 ± 0.22 | 2.69 ± 0.27 | 2.87 ± 0.24 | 2.89 ± 0.27 | 2.47 ± 0.11 | 2.87 ± 0.24 |
| Monocytes ($10^3$/µL) | 0.02 ± 0.01 | 0.01 ± 0.01 | 0.01 ± 0.01 | 0.02 ± 0.01 | 0.01 ± 0.01 | 0.01 ± 0.01 |
| Eosinophils ($10^3$/µL) | 0.02 ± 0.01 | 0.02 ± 0.01 | 0.02 ± 0.01 | 0.02 ± 0.01 | 0.04 ± 0.02 | 0.03 ± 0.01 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error. Ratios were calculated and statistical tests were performed on unrounded data.

# APPENDIX G
# BIOMARKERS OF EXPOSURE

**TABLE G1 Urinary Biomarker Data for Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . 260**
**TABLE G2 Urinary Biomarker Data for Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . 261**

**TABLE G1**
**Urinary Biomarker Data for Rats in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|
| n | 10 | 10 | 10 |
| **Male** | | | |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine | | | |
| Week 2 | 113 ± 34 | 518 ± 128 | 1,850 ± 460 |
| Week 6 | 123 ± 18 | 588 ± 134 | 2,610 ± 990 |
| Week 14 | 83.0 ± 15.3 | 488 ± 87 | 1,900 ± 500 |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 1.50 ± 0.45 | 1.72 ± 0.43 | 1.54 ± 0.39 |
| Week 6 | 1.64 ± 0.24 | 1.96 ± 0.45 | 2.17 ± 0.83 |
| Week 14 | 1.11 ± 0.20▲■ | 1.63 ± 0.29▲ | 1.58 ± 0.42■ |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine | | | |
| Week 2 | 2,020 ± 180 | 8,100 ± 1,620 | 21,500 ± 1,700 |
| Week 6 | 1,810 ± 240 | 6,500 ± 870 | 22,800 ± 4,500 |
| Week 14 | 1,360 ± 150 | 5,310 ± 550 | 14,000 ± 1,800 |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 27.0 ± 2.3▲ | 27.0 ± 5.4■ | 17.9 ± 1.4▲■ |
| Week 6 | 24.1 ± 3.2▲ | 21.7 ± 2.9 | 19.0 ± 3.8▲ |
| Week 14 | 18.2 ± 2.1▲ | 17.7 ± 1.8■ | 11.7 ± 1.5▲■ |
| **Female** | | | |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine | | | |
| Week 2 | 46.7 ± 7.8 | 219 ± 68 | 1,720 ± 600 |
| Week 6 | 49.4 ± 8.9 | 240 ± 82 | 1,820 ± 390 |
| Week 14 | 46.0 ± 12.0 | 285 ± 51 | 2,380 ± 880 |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 0.622 ± 0.104▲ | 0.729 ± 0.226■ | 1.43 ± 0.50▲■ |
| Week 6 | 0.658 ± 0.119▲ | 0.799 ± 0.274■ | 1.52 ± 0.33▲■ |
| Week 14 | 0.614 ± 0.159▲ | 0.950 ± 0.170■ | 1.98 ± 0.73▲■ |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine | | | |
| Week 2 | 2,180 ± 170 | 7,850 ± 1,370 | 24,400 ± 3,700 |
| Week 6 | 2,110 ± 320 | 8,530 ± 1,660 | 24,500 ± 2,800 |
| Week 14 | 1,590 ± 400 | 8,100 ± 1,200 | 22,900 ± 4,600 |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 29.0 ± 2.3▲ | 26.2 ± 4.6■ | 20.4 ± 3.1▲■ |
| Week 6 | 28.1 ± 4.3▲ | 28.4 ± 5.5■ | 20.4 ± 2.4▲■ |
| Week 14 | 21.2 ± 5.4▲ | 27.0 ± 4.0▲■ | 19.2 ± 3.8■ |

[a] Data are presented as mean ± standard deviation; on each row, means sharing the same symbol (▲ or ■) are significantly different ($P \leq 0.05$) by the Tukey-Kramer test.

**TABLE G2**
**Urinary Biomarker Data for Mice in the 2-Year Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|
| n | 10 | 10 | 10 |
| **Male** | | | |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine | | | |
| Week 2 | 25.8 ± 6.3 | 89.3 ± 19.6 | 1,690 ± 610 |
| Week 6 | 27.7 ± 5.9 | 69.0 ± 26.0 | 1,170 ± 350 |
| Week 16 | 29.0 ± 3.4 | 122 ± 20 | 1,740 ± 350 |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 0.345 ± 0.084▲ | 0.298 ± 0.065■ | 1.41 ± 0.51▲■ |
| Week 6 | 0.370 ± 0.079▲ | 0.230 ± 0.087■ | 0.977 ± 0.289▲■ |
| Week 16 | 0.387 ± 0.045▲ | 0.406 ± 0.065■ | 1.45 ± 0.29▲■ |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine | | | |
| Week 2 | 2,280 ± 540 | 15,600 ± 2,400 | 49,700 ± 11,000 |
| Week 6 | 2,420 ± 680 | 10,600 ± 3,700 | 60,900 ± 11,900 |
| Week 16 | 2,310 ± 270 | 16,000 ± 1,700 | 76,000 ± 11,800 |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 30.4 ± 7.2▲ | 52.1 ± 8.1▲ | 41.4 ± 9.2▲ |
| Week 6 | 32.3 ± 9.0▲ | 35.4 ± 12.4■ | 50.8 ± 9.9▲■ |
| Week 16 | 30.8 ± 3.6▲ | 53.3 ± 5.7▲ | 63.3 ± 9.8▲ |
| **Female** | | | |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine | | | |
| Week 2 | 108 ± 34 | 814 ± 344 | 3,390 ± 1,760 |
| Week 6 | 140 ± 81 | 735 ± 309 | 2,180 ± 890 |
| Week 16 | 264 ± 83 | 964 ± 343 | 3,040 ± 1,420 |
| ng Propylene glycol mono-*t*-butyl ether sulfate/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 1.44 ± 0.46▲■ | 2.71 ± 1.15■ | 2.82 ± 1.47▲ |
| Week 6 | 1.87 ± 1.07[b] | 2.45 ± 1.03 | 1.82 ± 0.74 |
| Week 16 | 3.52 ± 1.11 | 3.21 ± 1.14 | 2.53 ± 1.19 |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine | | | |
| Week 2 | 2,000 ± 540 | 20,000 ± 7,200 | 41,500 ± 17,200 |
| Week 6 | 1,230 ± 770 | 8,930 ± 2,700 | 45,900 ± 21,600 |
| Week 16 | 2,200 ± 680 | 13,400 ± 4,300 | 44,900 ± 16,100 |
| ng Propylene glycol mono-*t*-butyl ether glucuronide/ µg creatinine per ppm propylene glycol mono-*t*-butyl ether | | | |
| Week 2 | 26.6 ± 7.2▲ | 66.4 ± 24.0▲■ | 34.6 ± 14.3■ |
| Week 6 | 16.4 ± 10.3▲ | 29.8 ± 9.0 | 38.2 ± 18.0▲ |
| Week 16 | 29.4 ± 9.0▲ | 44.7 ± 14.3▲ | 37.4 ± 13.4 |

[a] Data are presented as mean ± standard deviation; on each row, means sharing the same symbol (▲ or ■) are significantly different ($P \leq 0.05$) by the Tukey-Kramer test.
[b] n=9

# APPENDIX H
# RENAL TOXICITY RESULTS


TABLE H1 Renal Toxicity Data for Male F344/N Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . 264

TABLE H2 Renal Toxicity Data for Male NBR Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . 264

TABLE H3 Renal Toxicity Data for Male F344/N Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether . . . . . 265

**TABLE H1**
**Renal Toxicity Data for Male F344/N Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 5 | 5 | 5 | 5 | 5 | 5 |
| Cells labeled | 100.000 ± 3.619 | 98.800 ± 6.184 | 116.000 ± 9.143 | 110.000 ± 6.957 | 110.400 ± 7.139 | 143.800 ± 5.953** |
| Cells counted | 2,071.80 ± 13.34 | 2,182.80 ± 15.93 | 2,182.40 ± 55.17 | 2,110.80 ± 68.06 | 2,281.60 ± 65.80 | 2,177.80 ± 62.95 |
| Labeling index (%) | 4.829 ± 0.190 | 4.520 ± 0.256 | 5.301 ± 0.348 | 5.204 ± 0.252 | 4.834 ± 0.256 | 6.625 ± 0.331* |
| Soluble protein (g/dL) | 3.148 ± 0.090 | 3.114 ± 0.083 | 3.196 ± 0.055 | 3.238 ± 0.135 | 3.138 ± 0.152 | 3.310 ± 0.052 |
| α2u-Globulin (nmol/g kidney) | 123.940 ± 71.071 | 385.400 ± 156.912 | 265.200 ± 41.645 | 237.200 ± 49.292 | 355.800 ± 152.177 | 426.080 ± 223.424 |
| α2u-Globulin (ng/µg soluble protein) | 38.076 ± 22.233 | 113.040 ± 43.656 | 77.840 ± 12.658 | 68.720 ± 13.378 | 104.180 ± 43.971 | 121.480 ± 64.336 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Data are presented as mean ± standard error.

**TABLE H2**
**Renal Toxicity Data for Male NBR Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 5 | 5 | 5 | 5 | 5 | 5 |
| Cells labeled | 85.400 ± 6.969 | 80.600 ± 6.145 | 65.200 ± 9.281 | 84.400 ± 4.578 | 83.200 ± 5.161 | 93.600 ± 3.124 |
| Cells counted | 2,137.20 ± 41.28 | 2,128.40 ± 45.83 | 2,260.80 ± 40.03 | 2,184.00 ± 50.49 | 2,143.260 ± 71.70 | 2,142.40 ± 42.03 |
| Labeling index (%) | 3.979 ± 0.252 | 3.794 ± 0.310 | 2.880 ± 0.400 | 3.857 ± 0.140 | 3.869 ± 0.123 | 4.385 ± 0.219 |

[a] Data are presented as mean ± standard error.

**TABLE H3**
**Renal Toxicity Data for Male F344/N Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 5 | 5 | 5 | 5 | 5 | 5 |
| Cells labeled | | | | | | |
| Week 2 | 79.0 ± 2.8 | 80.0 ± 4.2 | 84.4 ± 4.5 | 74.2 ± 3.0 | 96.2 ± 4.3 | 122.4 ± 9.7 |
| Week 6 | 75.0 ± 2.4 | 66.2 ± 2.6 | 72.4 ± 5.4 | 84.6 ± 2.8 | 96.8 ± 1.4 | 109.6 ± 7.4 |
| Week 13 | 69.2 ± 4.3 | 83.2 ± 5.0 | 93.6 ± 3.2 | 87.4 ± 3.0 | 108.4 ± 9.2 | 148.0 ± 9.0 |
| Cells counted | | | | | | |
| Week 2 | 2,209.6 ± 90.7 | 2,199.6 ± 30.2 | 2,188.2 ± 48.1 | 2,158.4 ± 61.4 | 2,201.6 ± 60.1 | 2,216.6 ± 73.9 |
| Week 6 | 2,092.6 ± 22.4 | 2,091.4 ± 49.9 | 2,148.8 ± 38.2 | 2,187.0 ± 52.2 | 2,225.8 ± 28.3 | 2,213.6 ± 19.3 |
| Week 13 | 2,202.0 ± 52.1 | 2,200.4 ± 26.1 | 2,166.6 ± 48.7 | 2,147.2 ± 41.3 | 2,151.2 ± 28.0 | 2,238.4 ± 28.9 |
| Labeling index (%) | | | | | | |
| Week 2 | 3.6 ± 0.1 | 3.6 ± 0.2 | 3.9 ± 0.2 | 3.4 ± 0.1 | 4.4 ± 0.2* | 5.5 ± 0.4** |
| Week 6 | 3.6 ± 0.1 | 3.2 ± 0.1 | 3.4 ± 0.2 | 3.9 ± 0.1 | 4.3 ± 0.0* | 4.9 ± 0.3* |
| Week 13 | 3.2 ± 0.2 | 3.8 ± 0.2 | 4.3 ± 0.2** | 4.1 ± 0.2* | 5.0 ± 0.4** | 6.6 ± 0.4** |
| Soluble protein (g/dL) | | | | | | |
| Week 2 | 2.6 ± 0.1 | 2.2 ± 0.1 | 2.4 ± 0.1 | 2.2 ± 0.2 | 2.2 ± 0.1* | 1.9 ± 0.0** |
| Week 6 | 2.3 ± 0.2 | 2.4 ± 0.1 | 2.6 ± 0.1 | 2.9 ± 0.2* | 2.6 ± 0.1* | 2.7 ± 0.0* |
| Week 13 | 2.7 ± 0.1 | 2.9 ± 0.1 | 2.5 ± 0.1 | 3.2 ± 0.2 | 2.9 ± 0.1 | 2.6 ± 0.2 |
| α2u-Globulin (nmol/g kidney) | | | | | | |
| Week 2 | 21.5 ± 2.4 | 69.2 ± 25.2 | 126.3 ± 34.8 | 171.6 ± 46.0* | 332.6 ± 54.9** | 52.8 ± 15.2 |
| Week 6 | 160.1 ± 63.6 | 437.0 ± 78.9* | 505.6 ± 74.6* | 757.8 ± 120.1** | 670.2 ± 212.0** | 732.4 ± 77.4** |
| Week 13 | 319.0 ± 93.7 | 476.8 ± 73.9 | 525.8 ± 125.0 | 733.6 ± 71.2** | 553.4 ± 85.2* | 708.4 ± 159.1* |
| α2u-Globulin (ng/µg soluble protein) | | | | | | |
| Week 2 | 7.7 ± 0.9 | 28.0 ± 8.8* | 47.9 ± 12.7* | 71.4 ± 18.7** | 138.8 ± 21.4** | 25.6 ± 7.3** |
| Week 6 | 64.7 ± 25.4 | 167.8 ± 27.1* | 184.0 ± 25.5* | 249.2 ± 48.7** | 237.0 ± 73.5* | 250.0 ± 24.7** |
| Week 13 | 113.2 ± 37.0 | 153.0 ± 21.9 | 197.7 ± 44.0 | 218.2 ± 24.5* | 179.0 ± 25.0 | 254.0 ± 44.6* |

* Significantly different ($P \le 0.05$) from the chamber control group by Dunn's or Shirley's test.
** $P \le 0.01$
[a] Data are presented as mean ± standard error.

# APPENDIX I
# ORGAN WEIGHTS
# AND ORGAN-WEIGHT-TO-BODY-WEIGHT RATIOS


| | | |
|---|---|---|
| TABLE I1 | Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 268 |
| TABLE I2 | Organ Weights and Organ-Weight-to-Body-Weight Ratios for Male NBR Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 269 |
| TABLE I3 | Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 270 |
| TABLE I4 | Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 271 |
| TABLE I5 | Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 272 |

**TABLE I1**
**Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 5 | 5 | 5 | 5 | 5 | 5 |
| **Male** | | | | | | |
| Necropsy body wt | 219 ± 7 | 225 ± 4 | 217 ± 6 | 221 ± 4 | 222 ± 5 | 214 ± 5 |
| R. Kidney | | | | | | |
| Absolute | 0.750 ± 0.031 | 0.820 ± 0.016 | 0.772 ± 0.019 | 0.816 ± 0.028 | 0.854 ± 0.022* | 0.842 ± 0.030 |
| Relative | 3.420 ± 0.039 | 3.647 ± 0.084 | 3.569 ± 0.066 | 3.696 ± 0.086* | 3.848 ± 0.081** | 3.940 ± 0.059** |
| Liver | | | | | | |
| Absolute | 7.824 ± 0.669 | 8.644 ± 0.367 | 7.690 ± 0.322 | 8.610 ± 0.406 | 9.662 ± 0.361* | 10.938 ± 0.522** |
| Relative | 35.507 ± 2.104 | 38.575 ± 2.351 | 35.521 ± 1.158 | 38.966 ± 1.140 | 43.535 ± 1.540** | 51.271 ± 2.450** |
| Lung | | | | | | |
| Absolute | 1.160 ± 0.051 | 1.296 ± 0.070 | 1.234 ± 0.041 | 1.306 ± 0.060 | 1.312 ± 0.070 | 1.310 ± 0.077 |
| Relative | 5.289 ± 0.096 | 5.773 ± 0.354 | 5.705 ± 0.156 | 5.909 ± 0.187 | 5.909 ± 0.279 | 6.136 ± 0.347 |
| **Female** | | | | | | |
| Necropsy body wt | 147 ± 2 | 148 ± 3 | 145 ± 3 | 147 ± 3 | 144 ± 4 | 144 ± 4 |
| R. Kidney | | | | | | |
| Absolute | 0.554 ± 0.015 | 0.584 ± 0.014 | 0.580 ± 0.018 | 0.532 ± 0.015 | 0.568 ± 0.024 | 0.574 ± 0.023 |
| Relative | 3.762 ± 0.070 | 3.949 ± 0.094 | 4.015 ± 0.114 | 3.626 ± 0.129 | 3.951 ± 0.079 | 3.998 ± 0.088 |
| Liver | | | | | | |
| Absolute | 4.800 ± 0.162 | 5.236 ± 0.272 | 5.240 ± 0.166 | 4.990 ± 0.172 | 5.416 ± 0.264 | 6.034 ± 0.308** |
| Relative | 32.591 ± 0.841 | 35.338 ± 1.449 | 36.249 ± 0.824 | 33.909 ± 0.593 | 37.659 ± 1.081** | 41.957 ± 1.010** |
| Lung | | | | | | |
| Absolute | 0.922 ± 0.025 | 0.978 ± 0.013 | 0.932 ± 0.026 | 0.900 ± 0.017 | 0.892 ± 0.034 | 0.940 ± 0.026 |
| Relative | 6.262 ± 0.128 | 6.614 ± 0.112 | 6.456 ± 0.195 | 6.124 ± 0.060 | 6.206 ± 0.100 | 6.553 ± 0.058 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).

**TABLE I2**
**Organ Weights and Organ-Weight-to-Body-Weight Ratios for Male NBR Rats in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 5 | 5 | 5 | 5 | 5 | 5 |
| Necropsy body wt | 288 ± 4 | 284 ± 4 | 285 ± 9 | 283 ± 2 | 281 ± 5 | 281 ± 7 |
| R. Kidney | | | | | | |
| Absolute | 0.918 ± 0.027 | 0.934 ± 0.026 | 0.914 ± 0.036 | 0.930 ± 0.018 | 0.892 ± 0.012 | 0.938 ± 0.033 |
| Relative | 3.194 ± 0.097 | 3.288 ± 0.079 | 3.208 ± 0.072 | 3.286 ± 0.065 | 3.182 ± 0.054 | 3.338 ± 0.050 |
| Liver | | | | | | |
| Absolute | 9.550 ± 0.378 | 9.356 ± 0.388 | 9.026 ± 0.455 | 9.870 ± 0.365 | 10.504 ± 0.281 | 12.192 ± 0.841** |
| Relative | 33.290 ± 1.695 | 32.949 ± 1.362 | 31.643 ± 0.996 | 34.867 ± 1.223 | 37.425 ± 0.462 | 43.313 ± 2.234** |
| Lung | | | | | | |
| Absolute | 1.5321 ± 0.047 | 1.552 ± 0.057 | 1.474 ± 0.055 | 1.490 ± 0.051 | 1.398 ± 0.014 | 1.522 ± 0.036 |
| Relative | 5.334 ± 0.198 | 5.474 ± 0.251 | 5.172 ± 0.080 | 5.263 ± 0.165 | 4.991 ± 0.117 | 5.426 ± 0.121 |

** Significantly different ($P \leq 0.01$) from the chamber control group by Williams' or Dunnett's test

[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).

**TABLE I3**
**Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| **Male** | | | | | | |
| Necropsy body wt | 318 ± 4 | 330 ± 5 | 322 ± 4 | 326 ± 5 | 321 ± 5 | 341 ± 7* |
| Heart | | | | | | |
| Absolute | 0.887 ± 0.017 | 0.900 ± 0.016 | 0.889 ± 0.018 | 0.905 ± 0.013 | 0.891 ± 0.013 | 0.945 ± 0.019 |
| Relative | 2.785 ± 0.033 | 2.734 ± 0.047 | 2.761 ± 0.044 | 2.776 ± 0.041 | 2.775 ± 0.029 | 2.775 ± 0.021 |
| R. Kidney | | | | | | |
| Absolute | 0.938 ± 0.016 | 1.030 ± 0.023** | 1.068 ± 0.017** | 1.056 ± 0.027** | 1.050 ± 0.024** | 1.162 ± 0.033** |
| Relative | 2.946 ± 0.028 | 3.124 ± 0.035** | 3.317 ± 0.033** | 3.233 ± 0.052** | 3.266 ± 0.038** | 3.409 ± 0.049** |
| Liver | | | | | | |
| Absolute | 9.643 ± 0.236 | 10.532 ± 0.269* | 10.465 ± 0.285* | 11.079 ± 0.201** | 12.057 ± 0.297** | 14.104 ± 0.395** |
| Relative | 30.291 ± 0.658 | 31.964 ± 0.659 | 32.456 ± 0.521* | 33.959 ± 0.441** | 37.537 ± 0.785** | 41.380 ± 0.629** |
| Lung | | | | | | |
| Absolute | 1.720 ± 0.080 | 1.748 ± 0.084 | 1.621 ± 0.051 | 1.734 ± 0.045 | 1.642 ± 0.037 | 1.747 ± 0.029 |
| Relative | 5.401 ± 0.241 | 5.321 ± 0.284 | 5.030 ± 0.126 | 5.326 ± 0.171 | 5.111 ± 0.076 | 5.140 ± 0.096 |
| R. Testis | | | | | | |
| Absolute | 1.412 ± 0.021 | 1.386 ± 0.014 | 1.392 ± 0.015 | 1.435 ± 0.028 | 1.355 ± 0.029 | 1.481 ± 0.019 |
| Relative | 4.439 ± 0.069 | 4.212 ± 0.063 | 4.328 ± 0.059 | 4.400 ± 0.077 | 4.218 ± 0.066 | 4.362 ± 0.094 |
| Thymus | | | | | | |
| Absolute | 0.275 ± 0.007 | 0.289 ± 0.009 | 0.267 ± 0.008 | 0.271 ± 0.013 | 0.269 ± 0.007 | 0.292 ± 0.007 |
| Relative | 0.865 ± 0.023 | 0.877 ± 0.025 | 0.827 ± 0.017 | 0.829 ± 0.035 | 0.838 ± 0.026 | 0.859 ± 0.015 |
| **Female** | | | | | | |
| Necropsy body wt | 183 ± 4 | 185 ± 3 | 187 ± 5 | 191 ± 4 | 191 ± 4 | 190 ± 3 |
| Heart | | | | | | |
| Absolute | 0.604 ± 0.014 | 0.610 ± 0.010 | 0.612 ± 0.016 | 0.623 ± 0.008 | 0.636 ± 0.013 | 0.646 ± 0.011 |
| Relative | 3.308 ± 0.078 | 3.303 ± 0.058 | 3.276 ± 0.047 | 3.267 ± 0.046 | 3.328 ± 0.046 | 3.402 ± 0.052 |
| R. Kidney | | | | | | |
| Absolute | 0.613 ± 0.019 | 0.619 ± 0.013 | 0.632 ± 0.013 | 0.675 ± 0.014** | 0.684 ± 0.013** | 0.697 ± 0.021** |
| Relative | 3.350 ± 0.063 | 3.354 ± 0.083 | 3.388 ± 0.058 | 3.540 ± 0.081 | 3.581 ± 0.061* | 3.666 ± 0.088** |
| Liver | | | | | | |
| Absolute | 5.834 ± 0.211 | 5.988 ± 0.142 | 5.971 ± 0.263 | 6.129 ± 0.103 | 6.508 ± 0.118* | 7.497 ± 0.232** |
| Relative | 31.866 ± 0.803 | 32.444 ± 0.839 | 31.834 ± 0.754 | 32.114 ± 0.373 | 34.095 ± 0.683 | 39.436 ± 0.952** |
| Lung | | | | | | |
| Absolute | 1.037 ± 0.030 | 1.081 ± 0.027 | 1.098 ± 0.018 | 1.130 ± 0.020* | 1.114 ± 0.034* | 1.143 ± 0.032** |
| Relative | 5.670 ± 0.107 | 5.849 ± 0.123 | 5.887 ± 0.083 | 5.919 ± 0.065 | 5.826 ± 0.140 | 6.017 ± 0.155 |
| Thymus | | | | | | |
| Absolute | 0.222 ± 0.007 | 0.231 ± 0.007 | 0.233 ± 0.007 | 0.229 ± 0.008 | 0.243 ± 0.005 | 0.223 ± 0.005 |
| Relative | 1.212 ± 0.033 | 1.248 ± 0.031 | 1.254 ± 0.048 | 1.194 ± 0.029 | 1.275 ± 0.028 | 1.173 ± 0.023 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).

**TABLE I4**
**Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 2-Week Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether**[a]

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 5 | 5 | 5 | 5 | 5 | 5 |
| **Male** | | | | | | |
| Necropsy body wt | 26.1 ± 0.5 | 25.6 ± 0.5 | 25.6 ± 0.7 | 26.6 ± 0.6 | 26.1 ± 0.3 | 26.6 ± 0.4 |
| R. Kidney | | | | | | |
| Absolute | 0.214 ± 0.005 | 0.222 ± 0.004 | 0.232 ± 0.004 | 0.226 ± 0.005 | 0.230 ± 0.007 | 0.216 ± 0.004 |
| Relative | 8.197 ± 0.225 | 8.664 ± 0.114 | 9.079 ± 0.110** | 8.493 ± 0.136 | 8.802 ± 0.212 | 8.123 ± 0.203 |
| Liver | | | | | | |
| Absolute | 1.256 ± 0.044 | 1.290 ± 0.047 | 1.248 ± 0.053 | 1.370 ± 0.010 | 1.460 ± 0.035* | 1.770 ± 0.092** |
| Relative | 48.006 ± 0.911 | 50.251 ± 0.847 | 48.718 ± 1.050 | 51.548 ± 1.038 | 55.877 ± 0.897** | 66.411 ± 2.864** |
| Lung | | | | | | |
| Absolute | 0.198 ± 0.007 | 0.192 ± 0.006 | 0.176 ± 0.012 | 0.196 ± 0.006 | 0.190 ± 0.004 | 0.186 ± 0.007 |
| Relative | 7.574 ± 0.193 | 7.493 ± 0.214 | 6.889 ± 0.478 | 7.359 ± 0.107 | 7.280 ± 0.208 | 6.987 ± 0.230 |
| **Female** | | | | | | |
| Necropsy body wt | 21.9 ± 0.3 | 22.0 ± 0.4 | 22.4 ± 0.2 | 21.9 ± 0.4 | 22.0 ± 0.2 | 23.4 ± 0.4* |
| R. Kidney | | | | | | |
| Absolute | 0.156 ± 0.002 | 0.160 ± 0.007 | 0.164 ± 0.002 | 0.152 ± 0.004 | 0.160 ± 0.003 | 0.164 ± 0.002 |
| Relative | 7.118 ± 0.071 | 7.259 ± 0.253 | 7.320 ± 0.156 | 6.938 ± 0.091 | 7.283 ± 0.171 | 7.010 ± 0.073 |
| Liver | | | | | | |
| Absolute | 1.092 ± 0.030 | 1.096 ± 0.025 | 1.156 ± 0.031 | 1.216 ± 0.038* | 1.254 ± 0.025** | 1.468 ± 0.046** |
| Relative | 49.814 ± 1.076 | 49.766 ± 0.693 | 51.539 ± 1.017 | 55.510 ± 1.342** | 57.062 ± 1.136** | 62.690 ± 1.236** |
| Lung | | | | | | |
| Absolute | 0.186 ± 0.005 | 0.182 ± 0.006 | 0.186 ± 0.005 | 0.174 ± 0.005 | 0.174 ± 0.005 | 0.180 ± 0.008 |
| Relative | 8.486 ± 0.201 | 8.261 ± 0.186 | 8.304 ± 0.272 | 7.945 ± 0.192 | 7.921 ± 0.265 | 7.690 ± 0.327 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).

**TABLE I5**
**Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 75 ppm | 150 ppm | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| **Male** | | | | | | |
| Necropsy body wt | 37.1 ± 0.6 | 36.5 ± 1.0 | 34.7 ± 1.0 | 34.2 ± 0.9 | 36.1 ± 0.7 | 34.7 ± 0.7 |
| Heart | | | | | | |
| Absolute | 0.160 ± 0.004 | 0.163 ± 0.004 | 0.157 ± 0.004 | 0.150 ± 0.004 | 0.159 ± 0.004 | 0.153 ± 0.003 |
| Relative | 4.325 ± 0.130 | 4.487 ± 0.132 | 4.553 ± 0.137 | 4.396 ± 0.107 | 4.415 ± 0.107 | 4.416 ± 0.079 |
| R. Kidney | | | | | | |
| Absolute | 0.309 ± 0.007 | 0.304 ± 0.010 | 0.307 ± 0.007 | 0.295 ± 0.008 | 0.307 ± 0.008 | 0.291 ± 0.009 |
| Relative | 8.352 ± 0.231 | 8.347 ± 0.204 | 8.910 ± 0.263 | 8.642 ± 0.158 | 8.537 ± 0.275 | 8.380 ± 0.121 |
| Liver | | | | | | |
| Absolute | 1.551 ± 0.024 | 1.542 ± 0.047 | 1.538 ± 0.038 | 1.500 ± 0.039 | 1.673 ± 0.031* | 1.841 ± 0.053** |
| Relative | 41.921 ± 0.974 | 42.304 ± 0.681 | 44.486 ± 0.681* | 43.908 ± 0.520* | 46.441 ± 0.792** | 53.035 ± 0.852** |
| Lung | | | | | | |
| Absolute | 0.227 ± 0.005 | 0.233 ± 0.006 | 0.225 ± 0.005 | 0.219 ± 0.008 | 0.229 ± 0.003 | 0.220 ± 0.005 |
| Relative | 6.133 ± 0.154 | 6.413 ± 0.179 | 6.529 ± 0.184 | 6.409 ± 0.146 | 6.355 ± 0.067 | 6.345 ± 0.096 |
| R. Testis | | | | | | |
| Absolute | 0.111 ± 0.001 | 0.104 ± 0.003 | 0.111 ± 0.003 | 0.105 ± 0.003 | 0.107 ± 0.003 | 0.105 ± 0.003 |
| Relative | 3.001 ± 0.069 | 2.864 ± 0.081 | 3.210 ± 0.077 | 3.073 ± 0.078 | 2.976 ± 0.083 | 3.018 ± 0.081 |
| Thymus | | | | | | |
| Absolute | 0.037 ± 0.002 | 0.037 ± 0.002 | 0.031 ± 0.002 | 0.032 ± 0.001 | 0.035 ± 0.002 | 0.039 ± 0.001 |
| Relative | 0.995 ± 0.069 | 1.011 ± 0.066 | 0.906 ± 0.053 | 0.928 ± 0.028 | 0.957 ± 0.036 | 1.112 ± 0.036 |
| **Female** | | | | | | |
| Necropsy body wt | 28.7 ± 0.5 | 31.2 ± 1.0 | 30.2 ± 0.6 | 31.3 ± 0.8* | 30.9 ± 0.8 | 29.1 ± 0.7 |
| Heart | | | | | | |
| Absolute | 0.132 ± 0.002 | 0.134 ± 0.003 | 0.131 ± 0.002 | 0.134 ± 0.003 | 0.130 ± 0.003 | 0.128 ± 0.002 |
| Relative | 4.610 ± 0.057 | 4.312 ± 0.108 | 4.345 ± 0.061 | 4.292 ± 0.095 | 4.221 ± 0.093* | 4.415 ± 0.096 |
| R. Kidney | | | | | | |
| Absolute | 0.195 ± 0.003 | 0.203 ± 0.005 | 0.205 ± 0.003 | 0.201 ± 0.002 | 0.202 ± 0.002 | 0.201 ± 0.003 |
| Relative | 6.814 ± 0.131 | 6.523 ± 0.120 | 6.800 ± 0.080 | 6.446 ± 0.149 | 6.573 ± 0.153 | 6.930 ± 0.116 |
| Liver | | | | | | |
| Absolute | 1.314 ± 0.028 | 1.458 ± 0.055* | 1.440 ± 0.038* | 1.450 ± 0.030* | 1.553 ± 0.036** | 1.678 ± 0.045** |
| Relative | 45.837 ± 0.505 | 46.711 ± 1.018 | 47.714 ± 0.948 | 46.353 ± 0.485 | 50.393 ± 0.989** | 57.714 ± 0.742** |
| Lung | | | | | | |
| Absolute | 0.213 ± 0.003 | 0.226 ± 0.007 | 0.223 ± 0.004 | 0.220 ± 0.005 | 0.218 ± 0.004 | 0.214 ± 0.004 |
| Relative | 7.452 ± 0.173 | 7.284 ± 0.275 | 7.406 ± 0.177 | 7.057 ± 0.230 | 7.080 ± 0.146 | 7.397 ± 0.223 |
| Thymus | | | | | | |
| Absolute | 0.045 ± 0.002 | 0.050 ± 0.002 | 0.049 ± 0.002 | 0.049 ± 0.002 | 0.049 ± 0.002 | 0.050 ± 0.003 |
| Relative | 1.580 ± 0.052 | 1.604 ± 0.069 | 1.633 ± 0.064 | 1.557 ± 0.056 | 1.603 ± 0.069 | 1.725 ± 0.085 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).

# APPENDIX J
# REPRODUCTIVE TISSUE EVALUATIONS AND ESTROUS CYCLE CHARACTERIZATION


| | | |
|---|---|---|
| TABLE J1 | Summary of Reproductive Tissue Evaluations for Male Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 274 |
| TABLE J2 | Estrous Cycle Characterization for Female Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 274 |
| TABLE J3 | Summary of Reproductive Tissue Evaluations for Male Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 275 |
| TABLE J4 | Estrous Cycle Characterization for Female Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether | 275 |

**TABLE J1**
**Summary of Reproductive Tissue Evaluations for Male Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 |
| Weights (g) | | | | |
| Necropsy body wt | 318 ± 4 | 326 ± 5 | 321 ± 5 | 340 ± 6* |
| L. Cauda epididymis | 0.1839 ± 0.0035 | 0.1865 ± 0.0038 | 0.1707 ± 0.0066 | 0.1891 ± 0.0058 |
| L. Epididymis | 0.4525 ± 0.0107 | 0.4542 ± 0.0084 | 0.4359 ± 0.0072 | 0.4609 ± 0.0100 |
| L. Testis | 1.4773 ± 0.0281 | 1.4757 ± 0.0250 | 1.4166 ± 0.0301 | 1.5317 ± 0.0207 |
| Spermatid measurements | | | | |
| Spermatid heads ($10^7$/g testis) | 165.44 ± 5.67 | 146.71 ± 5.81 | 152.85 ± 8.49 | 143.50 ± 7.93* |
| Spermatid heads ($10^7$/testis) | 223.25 ± 8.85 | 197.13 ± 8.50 | 193.88 ± 9.68 | 193.63 ± 11.54 |
| Spermatid heads ($10^7$/g cauda epididymis) | 792.90 ± 39.12 | 775.20 ± 41.15 | 856.70 ± 58.67 | 788.80 ± 48.01 |
| Spermatid heads ($10^7$/cauda epididymis) | 145.24 ± 6.23 | 144.37 ± 7.92 | 147.26 ± 13.00 | 148.38 ± 9.16 |
| Epididymal spermatozoal measurements | | | | |
| Motility (%) | 89.43 ± 1.61 | 86.48 ± 1.29 | 84.39 ± 1.54 | 85.14 ± 1.76 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunnett's test (body weights) or by Dunn's test (spermatid measurements

[a] Data are presented as mean ± standard error. Differences from the chamber control group are not significant by Dunnett's test (tissue weights) or by Dunn's test (epididymal sperm motility measurements).

**TABLE J2**
**Estrous Cycle Characterization for Female Rats in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 |
| Necropsy body wt (g) | 183 ± 4 | 191 ± 4 | 191 ± 4 | 190 ± 3 |
| Estrous cycle length (days) | 4.95 ± 0.16 | 5.10 ± 0.27 | 4.70 ± 0.13 | 5.25 ± 0.17 |
| Estrous stages (% of cycle) | | | | |
| Diestrus | 46.7 | 49.2 | 45.8 | 45.0 |
| Proestrus | 10.0 | 10.8 | 9.2 | 10.0 |
| Estrus | 25.8 | 25.8 | 28.3 | 27.5 |
| Metestrus | 17.5 | 14.2 | 16.7 | 17.5 |

[a] Necropsy body weight and estrous cycle length data are presented as mean ± standard error. Differences from the chamber control group are not significant by Dunnett's test (body weight) or Dunn's test (estrous cycle length). By multivariate analysis of variance, exposed females do not differ significantly from the chamber control females in the relative length of time spent in the estrous stages.

**TABLE J3**
**Summary of Reproductive Tissue Evaluations for Male Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 |
| Weights (g) | | | | |
| Necropsy body wt | 37.1 ± 0.6 | 34.2 ± 0.9* | 36.1 ± 0.7 | 34.7 ± 0.7 |
| L. Cauda epididymis | 0.0177 ± 0.0015 | 0.0160 ± 0.0011 | 0.0169 ± 0.0010 | 0.0179 ± 0.0007 |
| L. Epididymis | 0.0559 ± 0.0027 | 0.0497 ± 0.0031 | 0.0493 ± 0.0025 | 0.0523 ± 0.0039 |
| L. Testis | 0.1081 ± 0.0014 | 0.1035 ± 0.0028 | 0.1073 ± 0.0031 | 0.0994 ± 0.0042 |
| Spermatid measurements | | | | |
| Spermatid heads ($10^7$/g testis) | 261.05 ± 12.26 | 238.77 ± 15.59 | 248.87 ± 7.75 | 236.39 ± 9.08 |
| Spermatid heads ($10^7$/testis) | 23.57 ± 0.99 | 20.99 ± 1.66 | 21.86 ± 1.05 | 19.85 ± 1.20 |
| Spermatid heads ($10^7$/g cauda epididymis) | 1,169.10 ± 113.92 | 1,198.60 ± 134.32 | 1,098.90 ± 68.48 | 954.70 ± 20.67 |
| Spermatid heads ($10^7$/cauda epididymis) | 19.34 ± 0.99 | 18.20 ± 1.10 | 18.19 ± 1.09 | 17.02 ± 0.49 |
| Epididymal spermatozoal measurements | | | | |
| Motility (%) | 82.88 ± 0.95 | 81.45 ± 1.11 | 79.54 ± 0.86 | 80.36 ± 0.60 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunnett's test
[a] Data are presented as mean ± standard error. Differences from the chamber control group are not significant by Dunnett's test (tissue weights) or by Dunn's test (spermatid epididymal sperm motility measurements).

**TABLE J4**
**Estrous Cycle Characterization for Female Mice in the 3-Month Inhalation Study of Propylene Glycol Mono-*t*-butyl Ether[a]**

| | Chamber Control | 300 ppm | 600 ppm | 1,200 ppm |
|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 |
| Necropsy body wt (g) | 28.7 ± 0.5 | 31.3 ± 0.8* | 30.9 ± 0.8 | 29.1 ± 0.7 |
| Estrous cycle length (days) | 4.05 ± 0.05 | 4.00 ± 0.00 | 4.15 ± 0.15 | 4.85 ± 0.41* |
| Estrous stages (% of cycle) | | | | |
| Diestrus | 28.3 | 26.7 | 28.3 | 34.2 |
| Proestrus | 20.0 | 23.3 | 23.3 | 16.7 |
| Estrus | 25.8 | 25.8 | 25.0 | 29.2 |
| Metestrus | 24.2 | 24.2 | 23.3 | 20.0 |
| Uncertain diagnoses | 1.7 | 0.0 | 0.0 | 0.0 |

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunnett's test (body weight) or by Dunn's test (estrous cycle length).
[a] Necropsy body weights and estrous cycle length data are presented as mean ± standard error. By multivariate analysis of variance, exposed females do not differ significantly from the chamber control females in the relative length of time spent in the estrous stages.

# APPENDIX K
# CHEMICAL CHARACTERIZATION AND GENERATION OF CHAMBER CONCENTRATIONS


PROCUREMENT AND CHARACTERIZATION OF PROPYLENE GLYCOL MONO-*t*-BUTYL ETHER . . . . . 278
VAPOR GENERATION AND EXPOSURE SYSTEM . . . . . 279
VAPOR CONCENTRATION MONITORING . . . . . 279
CHAMBER ATMOSPHERE CHARACTERIZATION . . . . . 280
TABLE K1 Gas Chromatography Systems Used in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether . . . . . 281
FIGURE K1 Infrared Absorption Spectrum of Propylene Glycol Mono-*t*-butyl Ether . . . . . 282
FIGURE K2 $^{1}$H-Nuclear Magnetic Resonance Spectrum of Propylene Glycol Mono-*t*-butyl Ether . . . . 283
Figure K3 $^{13}$C-Nuclear Magnetic Resonance Spectrum of Propylene Glycol Mono-*t*-butyl Ether . . . . 284
Figure K4 Mass Spectrum of Propylene Glycol Mono-*t*-butyl Ether . . . . . 285
Figure K5 Schematic of the Vapor Generation and Delivery System in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether . . . . . 286
TABLE K2 Summary of Chamber Concentrations in the 2-Week Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether . . . . . 287
TABLE K3 Summary of Chamber Concentrations in the 3-Month Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether . . . . . 287
TABLE K4 Summary of Chamber Concentrations in the 2-Year Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether . . . . . 288

# CHEMICAL CHARACTERIZATION AND GENERATION OF CHAMBER CONCENTRATIONS

## Procurement and Characterization of Propylene Glycol Mono-*t*-butyl Ether

Propylene glycol mono-*t*-butyl ether was obtained from Aldrich Chemical Company, Inc. (Milwaukee, WI), in three lots (00406CN, 00603PG, and 14301ER). For the 2-week and 3-month studies, lots 00406CN and 00603PG were combined and assigned a new lot number (8359-126-01). Lot 14301ER was used during the 2-year studies. Identity analyses of lot 14301ER were conducted by the analytical chemistry laboratory, Research Triangle Institute (Research Triangle Park, NC). Purity analyses of lots 8359-126-01 and 14301ER were conducted by the analytical chemistry laboratory and the study laboratory. Reports on analyses performed in support of the propylene glycol mono-*t*-butyl ether studies are on file at the National Institute of Environmental Health Sciences.

Lots 8359-126-01 and 14301ER, clear liquids, were identified as propylene glycol mono-*t*-butyl ether by Chemir/Polytech, Inc. (Maryland Heights, MO), using infrared, proton nuclear magnetic resonance (NMR), and carbon-13 NMR spectroscopy. Lot 14301ER was identified as propylene glycol mono-*t*-butyl ether by the analytical chemistry laboratory using infrared and proton NMR spectroscopy and gas chromatography/mass spectrometry (GC/MS) by system A (Table K1). Infrared, NMR, and mass spectra were consistent with the structure of propylene glycol mono-*t*-butyl ether. The infrared, proton NMR, carbon-13 NMR, and mass spectra are presented in Figures K1 through K4.

The purity of lot 8359-126-01 was determined by the study laboratory using GC by systems similar to systems B and C. The purity of lot 14301ER was determined by the analytical chemistry laboratory using GC by system D and by the study laboratory using GC by systems B and C. Elemental analyses of both lots were performed by Chemir/Polytech, Inc. The moisture content of lot 14301ER was determined by Chemir/Polytech, Inc. using Karl Fischer titration.

For lot 8359-126-01, elemental analyses for carbon, hydrogen, oxygen, nitrogen, and sulfur content were in good agreement with theoretical values for propylene glycol mono-*t*-butyl ether. GC by systems similar to systems B and C indicated one major peak and one impurity peak with an area of approximately 0.18% relative to a reference standard stored at -20° C. The overall purity of lot 8359-126-01 was determined to be greater than 99%.

For lot 14301ER, elemental analyses for carbon, hydrogen, oxygen, nitrogen, and sulfur content were in good agreement with theoretical values for propylene glycol mono-*t*-butyl ether. Karl Fischer water titration indicated a moisture content for lot 14301ER of 0.0512% ± 0.0137%. GC by system D conducted by the analytical chemistry laboratory indicated a purity of greater than 99%; one major peak, one impurity peak with an area of 0.13% of the total integrated area, and two impurity peaks each with areas of less than 0.1% of the total integrated area were detected. The largest impurity peak was identified as 1-*t*-butoxypropane by GC/MS using system A. GC by systems B and C conducted by the study laboratory indicated a purity of 102.7% ± 0.3% for lot 14301ER relative to a high-purity reference standard and one impurity with an area of 0.16% relative to the major peak area. The overall purity of lot 14301ER was determined to be greater than 99%.

Stability information provided by the manufacturer indicated that the bulk chemical is stable when stored under normal conditions in an enclosed container. To ensure stability, the bulk chemical was stored in the original metal or stainless steel drum shipping containers under nitrogen at room temperature. Stability was monitored by the study laboratory during the 2-week, 3-month, and 2-year studies with GC by systems B and C or similar systems. No degradation of the bulk chemical was detected.

## Vapor Generation and Exposure System

A diagram of the vapor generation and delivery system used in the studies is shown in Figure K5. Propylene glycol mono-*t*-butyl ether was pumped through a preheater and into the top of a heated glass column filled with glass beads. The glass beads increased the surface area for evaporation. Heated nitrogen entered the column from below and assisted in vaporizing the chemical while conveying it to a condenser column. The condensation that occurred in the condenser controlled the concentration of propylene glycol mono-*t*-butyl ether vapor produced by the generator. Condensate was collected in a waste flask at the bottom of the condenser column.

Adjusting the temperature of the condenser column controlled the vapor temperature leaving the top of the condenser column. The total output of the generator was determined from the metered nitrogen flow and the estimated propylene glycol mono-*t*-butyl ether vapor pressure at the temperature of the condenser column exit.

Because the vapor leaving the generator was above room temperature, it was transported to the exposure room at an elevated temperature to prevent condensation. In the exposure room, the vapor was mixed with heated air before entering a short vapor distribution manifold. The pressure in the distribution manifold was kept fixed to ensure constant flows through the manifold and into the chambers as the flow of vapor to another chamber was adjusted.

Electronically-actuated metering valves controlled flow to each chamber. In addition, a master exposure valve, mounted upstream of all chamber metering valves, diverted all vapor to the exposure chamber exhaust until the generation system was stable and exposures were ready to proceed. When the exposure started, the three-way valve was opened to allow the flow of vapor to reach the chamber metering valves. Each metering valve automatically opened, allowing vapor to flow through individual temperature-controlled delivery lines to each exposure chamber. The vapor was then injected into the chamber inlet duct where it was further diluted with conditioned chamber air to achieve the desired exposure concentration.

The study laboratory designed the inhalation exposure chamber (Harford Systems Division of Lab Products, Inc., Aberdeen, MD) so that uniform vapor concentrations could be maintained throughout the chamber with the catch pans in place. The total active mixing volume of each chamber was 1.7 $m^3$. A small particle detector (Type CN, Gardner Associates, Schenectady, NY) was used with and without animals in the exposure chambers to ensure that propylene glycol mono-*t*-butyl ether vapor, and not aerosol, was produced. The maximum attainable vapor concentration that could be generated without aerolization was 1,200 ppm, which was thus selected as the highest exposure concentration for the initial studies. No particle counts above the minimum resolvable level (approximately 200 particles/$cm^3$) were detected.

## Vapor Concentration Monitoring

Summaries of the chamber vapor concentrations are given in Tables K2 through K4. The propylene glycol mono-*t*-butyl ether concentrations in the exposure chambers were monitored by an on-line gas chromatograph (system E or a similar system). Samples were drawn from each exposure chamber approximately every 24 minutes using a 12-port stream select valve (VALCO Instruments Company, Houston, TX). The on-line chromatograph was checked throughout the day for instrument drift against an on-line standard of propylene glycol mono-*t*-butyl ether in nitrogen supplied by a diffusion tube standard generator (Model 360, Thermo Environmental Instruments, Franklin, MA). The on-line gas chromatograph was calibrated at least monthly by a comparison of chamber concentration data to data from grab samples, which were collected with charcoal sampling tubes (ORBO™-101, Supelco, Bellefonte, PA) extracted with ethyl acetate containing di(ethylene glycol) butyl ether as an internal standard, and analyzed by an off-line gas chromatograph (system B). The volumes of gas were sampled at a constant flow rate ensured by a calibrated critical orifice. The off-line gas chromatograph was calibrated with gravimetrically prepared standards of propylene glycol mono-*t*-butyl ether and the internal standard di(ethylene glycol) butyl ether in ethyl acetate.

## CHAMBER ATMOSPHERE CHARACTERIZATION

Buildup and decay rates for chamber vapor concentrations were determined with animals present in the chambers. At a chamber airflow rate of 15 air changes per hour, the theoretical value for the time to achieve 90% of the target concentration after the beginning of vapor generation ($T_{90}$) and the time for the chamber concentration to decay to 10% of the target concentration after vapor generation was terminated ($T_{10}$) was approximately 12.5 minutes. For rats and mice in the 2-week studies, $T_{90}$ values ranged from 9 to 15 minutes; $T_{10}$ values ranged from 9 to 17 minutes. For rats and mice in the 3-month studies, $T_{90}$ values ranged from 9 to 11 minutes; $T_{10}$ values ranged from 11 to 13 minutes. For rats and mice in the 2-year studies, $T_{90}$ values ranged from 8 to 12 minutes; $T_{10}$ values ranged from 11 to 18 minutes. A $T_{90}$ value of 12 minutes was selected for all studies.

The uniformity of propylene glycol mono-*t*-butyl ether vapor concentration with animals present was measured once during the 2-week studies, once during the 3-month studies, and approximately every 3 months during the 2-year studies. The vapor concentration was measured using the on-line chromatograph with the automatic 12-port sample valve disabled to allow continuous monitoring from a single input line. Samples were collected from twelve positions in each chamber. During the 2-week studies, excursions in chamber uniformity values (within-port variability was 9.3%) were observed in the 75 ppm exposure chambers; this variability was due to a faulty metering valve. Chamber concentration uniformity was maintained for all chambers other than the 75 ppm exposure chamber throughout the 2-week studies and for all chambers throughout the 3-month and 2-year studies.

The persistence of propylene glycol mono-*t*-butyl ether in the chamber after vapor delivery ended was determined by monitoring the concentration after shutoff of chemical to the chamber in the 1,200 ppm chamber in the 2-week, 3-month, and 2-year studies with animals present. In the 2-week studies, the concentration decreased to 1% of the target concentration within 19 minutes. In the 3-month studies, the concentration decreased to 1% of the target concentration within approximately 50 minutes. In the 2-year studies, the concentration decreased to 1% of the target concentration within 89 minutes for rats and 430 minutes for mice. The large difference in decay noted between the rat and mouse chambers suggested that the animal species affect the rate at which propylene glycol mono-*t*-butyl ether is cleared from the chamber environment.

The stability of propylene glycol mono-*t*-butyl ether in the distribution line, 75 and 1,200 ppm exposure chambers, and generator reservoir was monitored during the studies. Exposure chamber and distribution line samples were collected twice during the 2-week and 2-year studies with animals present and were analyzed with GC using systems B and C or similar systems. Commercial standards of potential degradation products and impurities were obtained from Supelco, Inc. (Bellefonte, PA). No evidence of degradation was detected, and no impurities were detected that were not present in the bulk material. Generator reservoir samples were collected twice during the 2-week and 3-month studies and were analyzed by GC using systems similar to systems B and D. No evidence of degradation of the test chemical in the generator reservoir was found. The results indicated that propylene glycol mono-*t*-butyl ether was stable for up to 157 days in the generator reservoir.

**TABLE K1**
**Gas Chromatography Systems Used in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether[a]**

| Detection System | Column | Carrier Gas | Oven Temperature Program |
|---|---|---|---|
| **System A** | | | |
| Mass spectrometry | HP 5MS, 30 m × 0.25 mm, 0.25-µm film (Hewlett-Packard, Palo Alto, CA) | Helium at 1.0 mL/minute | 35° C for 5 minutes, then 5° C/minute to 100° C, held for 22 minutes |
| **System B** | | | |
| Flame ionization | DB-5, 30 m × 0.53 mm, 1.5-µm film (J&W Scientific) | Helium at 6 psi | 60° C for 1 minute, then 16° C/minute to 200° C |
| **System C** | | | |
| Flame ionization | DB-5, 30 m × 0.25 mm, 1-µm film (J&W Scientific) | Helium at 24 psi | 50° C for 1 minute, then 8° C/minute to 260° C, held for 2 minutes |
| **System D** | | | |
| Flame ionization | DB-5, 30 m × 0.25 mm, 0.25-µm film (J&W Scientific Folsom, CA) | Helium at 1.0 mL/minute | 35° C for 5 minutes, then 5° C/minute to 100° C, held for 22 minutes |
| **System E** | | | |
| Flame ionization | Rtx-1, 15 m × 0.53 mm, 1.5-µm film (Restek, Bellefonte, PA) | Nitrogen at 25 mL/minute | 65° C isocratic |

[a] All gas chromatographs were manufactured by Hewlett-Packard (Palo Alto, CA).

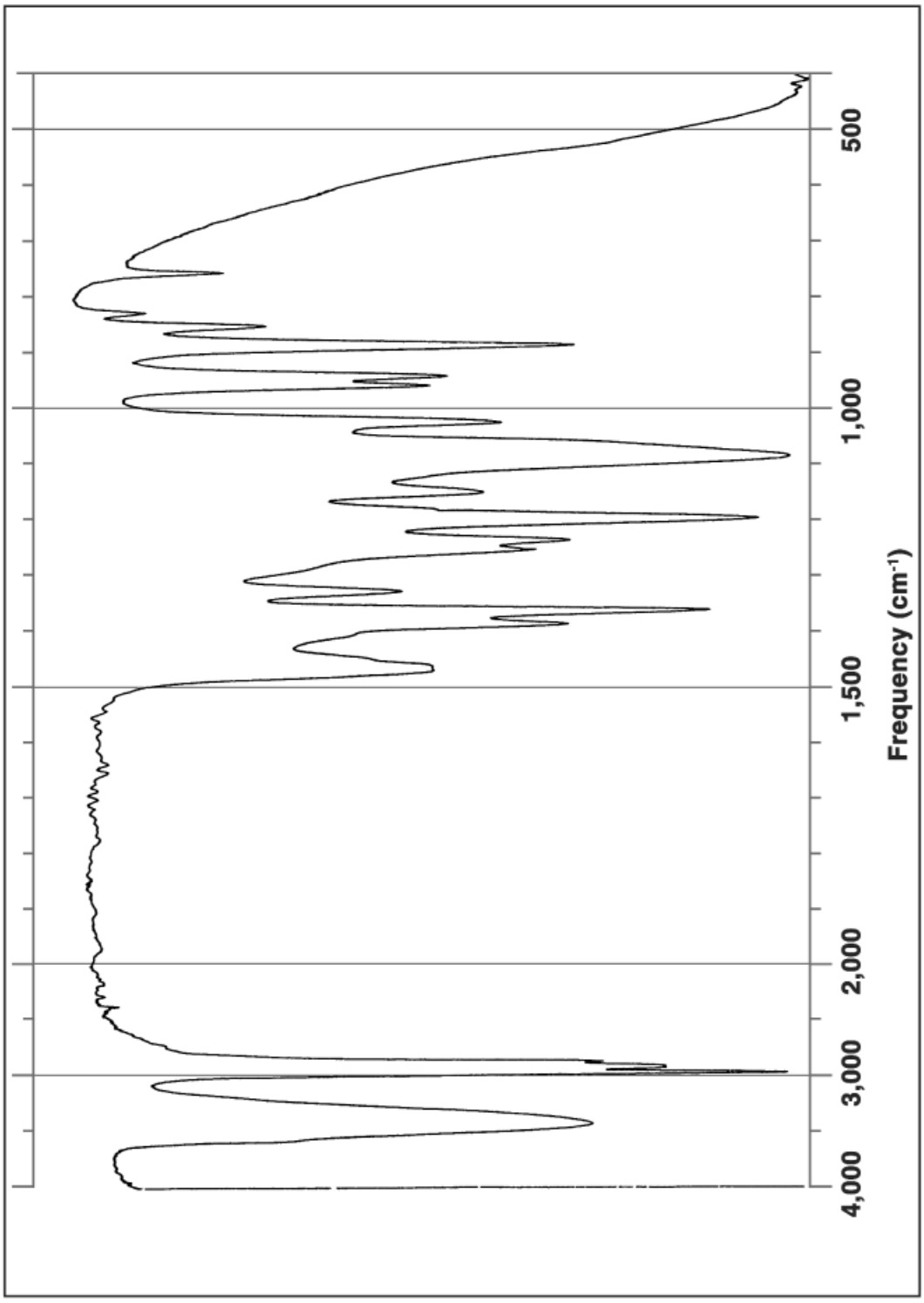


**FIGURE K1**
**Infrared Absorption Spectrum of Propylene Glycol Mono-*t*-butyl Ether**

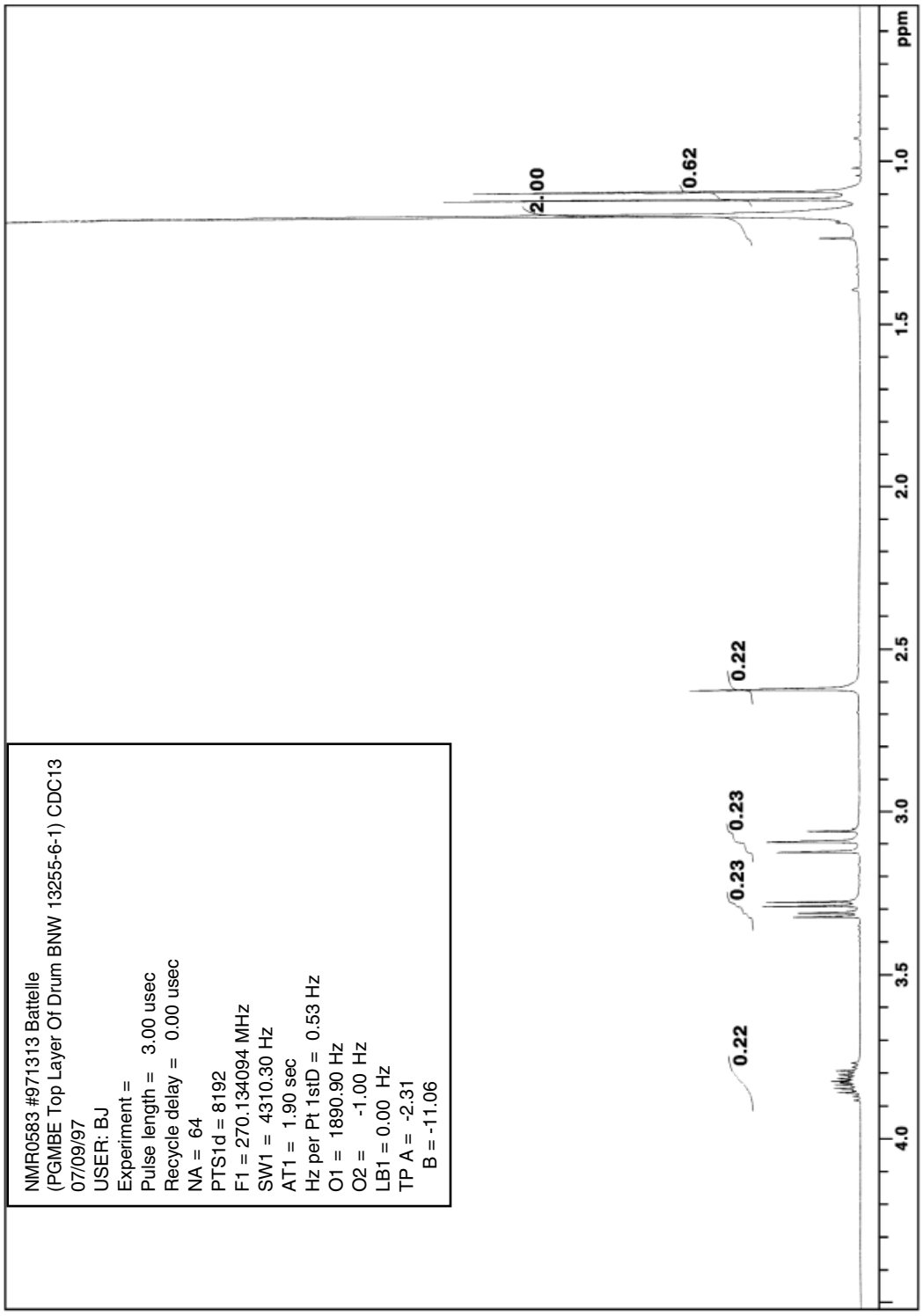


**FIGURE K2**
**$^{1}$H-Nuclear Magnetic Resonance Spectrum of Propylene Glycol Mono-*t*-butyl Ether**

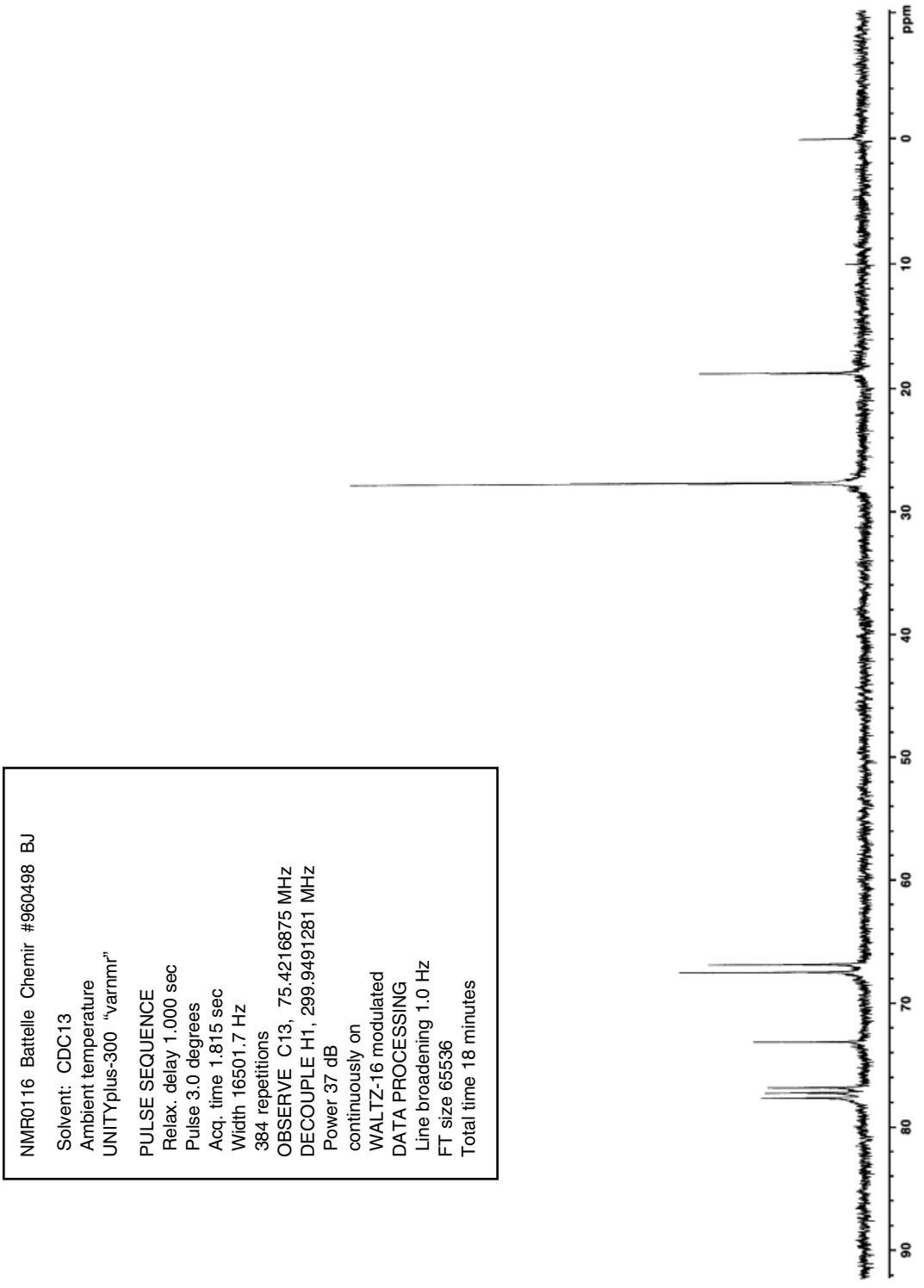


**FIGURE K3**
**$^{13}$C-Nuclear Magnetic Resonance Spectrum of Propylene Glycol Mono-*t*-butyl Ether**

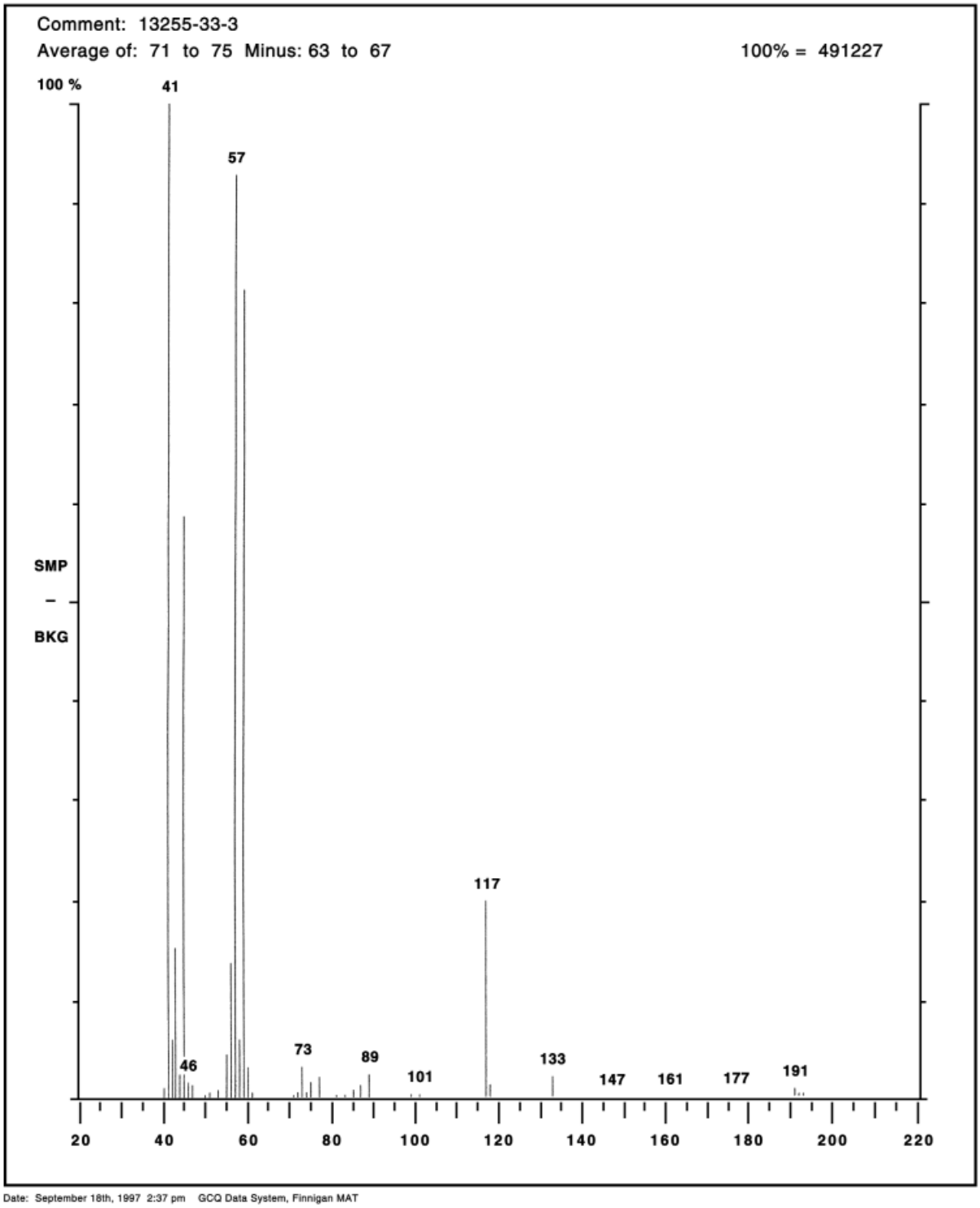


**FIGURE K4**
**Mass Spectrum of Propylene Glycol Mono-*t*-butyl Ether**

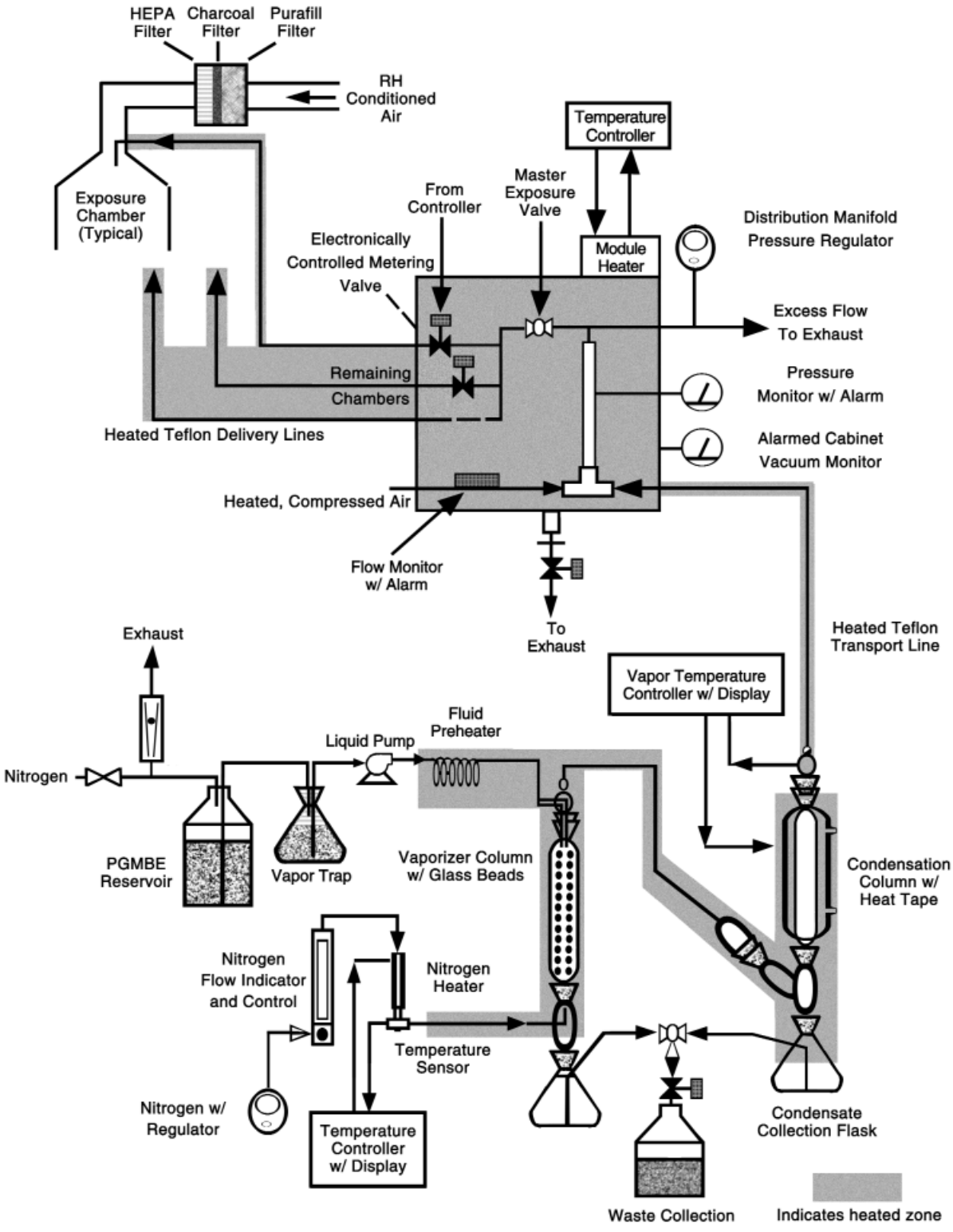


**FIGURE K5**
**Schematic of the Vapor Generation and Delivery System in the Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

**TABLE K2**
**Summary of Chamber Concentrations in the 2-Week Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| Target Concentration (ppm) | Total Number of Readings | Average Concentration[a] (ppm) |
|---|---|---|
| **Rat Chambers** | | |
| 75 | 196 | 72.5 ± 7.3 |
| 150 | 177 | 148 ± 6.2 |
| 300 | 188 | 297 ± 12 |
| 600 | 185 | 587 ± 25 |
| 1,200 | 192 | 1,170 ± 73 |
| **Mouse Chambers** | | |
| 75 | 213 | 72.3 ± 7.3 |
| 150 | 195 | 148 ± 6.0 |
| 300 | 206 | 297 ± 12 |
| 600 | 203 | 588 ± 24 |
| 1,200 | 210 | 1,170 ± 70 |

[a] Mean ± standard deviation

**TABLE K3**
**Summary of Chamber Concentrations in the 3-Month Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| Target Concentration (ppm) | Total Number of Readings | Average Concentration[a] (ppm) |
|---|---|---|
| **Rat Chambers** | | |
| 75 | 1,074 | 75.6 ± 4.2 |
| 150 | 1,068 | 148 ± 7.2 |
| 300 | 1,091 | 297 ± 10 |
| 600 | 1,100 | 599 ± 24 |
| 1,200 | 1,101 | 1,200 ± 38 |
| **Mouse Chambers** | | |
| 75 | 1,098 | 75.6 ± 4.1 |
| 150 | 1,085 | 148 ± 7.2 |
| 300 | 1,108 | 297 ± 10 |
| 600 | 1,117 | 599 ± 24 |
| 1,200 | 1,118 | 1,200 ± 38 |

[a] Mean ± standard deviation

**TABLE K4**
**Summary of Chamber Concentrations in the 2-Year Inhalation Studies of Propylene Glycol Mono-*t*-butyl Ether**

| Target Concentration (ppm) | Total Number of Readings | Average Concentration[a] (ppm) |
|---|---|---|
| **Rat Chambers** | | |
| 75 | 8,453 | 75.1 ± 3.3 |
| 300 | 8,495 | 301 ± 11 |
| 1,200 | 8,535 | 1,210 ± 50 |
| **Mouse Chambers** | | |
| 75 | 8,436 | 75.5 ± 3.2 |
| 300 | 8,452 | 301 ± 12 |
| 1,200 | 8,461 | 1,200 ± 48 |

[a] Mean ± standard deviation

# APPENDIX L
# INGREDIENTS, NUTRIENT COMPOSITION, AND CONTAMINANT LEVELS IN NTP-2000 RAT AND MOUSE RATION


| | | |
|---|---|---|
| TABLE L1 | Ingredients of NTP-2000 Rat and Mouse Ration | 290 |
| TABLE L2 | Vitamins and Minerals in NTP-2000 Rat and Mouse Ration | 290 |
| TABLE L3 | Nutrient Composition of NTP-2000 Rat and Mouse Ration | 291 |
| TABLE L4 | Contaminant Levels in NTP-2000 Rat and Mouse Ration | 292 |

**TABLE L1**
**Ingredients of NTP-2000 Rat and Mouse Ration**

| Ingredients | Percent by Weight |
|---|---|
| Ground hard winter wheat | 22.26 |
| Ground #2 yellow shelled corn | 22.18 |
| Wheat middlings | 15.0 |
| Oat hulls | 8.5 |
| Alfalfa meal (dehydrated, 17% protein) | 7.5 |
| Purified cellulose | 5.5 |
| Soybean meal (49% protein) | 5.0 |
| Fish meal (60% protein) | 4.0 |
| Corn oil (without preservatives) | 3.0 |
| Soy oil (without preservatives) | 3.0 |
| Dried brewer's yeast | 1.0 |
| Calcium carbonate (USP) | 0.9 |
| Vitamin premix[a] | 0.5 |
| Mineral premix[b] | 0.5 |
| Calcium phosphate, dibasic (USP) | 0.4 |
| Sodium chloride | 0.3 |
| Choline chloride (70% choline) | 0.26 |
| Methionine | 0.2 |

[a] Wheat middlings as carrier
[b] Calcium carbonate as carrier

**TABLE L2**
**Vitamins and Minerals in NTP-2000 Rat and Mouse Ration[a]**

| | Amount | Source |
|---|---|---|
| **Vitamins** | | |
| A | 4,000 IU | Stabilized vitamin A palmitate or acetate |
| D | 1,000 IU | D-activated animal sterol |
| K | 1.0 mg | Menadione sodium bisulfite complex |
| α-Tocopheryl acetate | 100 IU | |
| Niacin | 23 mg | |
| Folic acid | 1.1 mg | |
| *d*-Pantothenic acid | 10 mg | *d*-Calcium pantothenate |
| Riboflavin | 3.3 mg | |
| Thiamine | 4 mg | Thiamine mononitrate |
| $B_{12}$ | 52 µg | |
| Pyridoxine | 6.3 mg | Pyridoxine hydrochloride |
| Biotin | 0.2 mg | *d*-Biotin |
| **Minerals** | | |
| Magnesium | 514 mg | Magnesium oxide |
| Iron | 35 mg | Iron sulfate |
| Zinc | 12 mg | Zinc oxide |
| Manganese | 10 mg | Manganese oxide |
| Copper | 2.0 mg | Copper sulfate |
| Iodine | 0.2 mg | Calcium iodate |
| Chromium | 0.2 mg | Chromium acetate |

[a] Per kg of finished product

**TABLE L3**
**Nutrient Composition of NTP-2000 Rat and Mouse Ration**

| Nutrient | Mean ± Standard Deviation | Range | Number of Samples |
|---|---|---|---|
| Protein (% by weight) | 13.2 ± 0.38 | 12.5 – 14.0 | 24 |
| Crude fat (% by weight) | 8.1 ± 0.25 | 7.6 – 8.6 | 24 |
| Crude fiber (% by weight) | 9.3 ± 0.69 | 7.9 – 10.3 | 24 |
| Ash (% by weight) | 5.0 ± 0.18 | 4.7 – 5.4 | 24 |
| **Amino Acids (% of total diet)** | | | |
| Arginine | 0.731 ± 0.050 | 0.670 – 0.800 | 8 |
| Cystine | 0.224 ± 0.012 | 0.210 – 0.240 | 8 |
| Glycine | 0.684 ± 0.041 | 0.620 – 0.740 | 8 |
| Histidine | 0.333 ± 0.018 | 0.310 – 0.350 | 8 |
| Isoleucine | 0.524 ± 0.046 | 0.430 – 0.590 | 8 |
| Leucine | 1.061 ± 0.061 | 0.960 – 1.130 | 8 |
| Lysine | 0.708 ± 0.056 | 0.620 – 0.790 | 8 |
| Methionine | 0.401 ± 0.035 | 0.350 – 0.460 | 8 |
| Phenylalanine | 0.598 ± 0.036 | 0.540 – 0.640 | 8 |
| Threonine | 0.501 ± 0.051 | 0.430 – 0.590 | 8 |
| Tryptophan | 0.126 ± 0.014 | 0.110 – 0.150 | 8 |
| Tyrosine | 0.390 ± 0.056 | 0.280 – 0.460 | 8 |
| Valine | 0.640 ± 0.049 | 0.550 – 0.690 | 8 |
| **Essential Fatty Acids (% of total diet)** | | | |
| Linoleic | 3.97 ± 0.284 | 3.59 – 4.54 | 8 |
| Linolenic | 0.30 ± 0.042 | 0.21 – 0.35 | 8 |
| **Vitamins** | | | |
| Vitamin A (IU/kg) | 5,516 ± 1,175 | 3,280 – 7,790 | 24 |
| Vitamin D (IU/kg) | 1,000[a] | | |
| α-Tocopherol (ppm) | 82.2 ± 14.08 | 62.2 – 107.0 | 8 |
| Thiamine (ppm)[b] | 7.6 ± 0.95 | 6.1 – 9.3 | 24 |
| Riboflavin (ppm) | 5.6 ± 1.12 | 4.20 – 7.70 | 8 |
| Niacin (ppm) | 74.3 ± 5.94 | 66.4 – 85.8 | 8 |
| Pantothenic acid (ppm) | 22.5 ± 3.96 | 17.4 – 29.1 | 8 |
| Pyridoxine (ppm)[b] | 9.04 ± 2.37 | 6.4 – 12.4 | 8 |
| Folic acid (ppm) | 1.64 ± 0.38 | 1.26 – 2.32 | 8 |
| Biotin (ppm) | 0.333 ± 0.15 | 0.225 – 0.704 | 8 |
| Vitamin $B_{12}$ (ppb) | 68.7 ± 63.0 | 18.3 – 174.0 | 8 |
| Choline (ppm)[b] | 3,155 ± 325 | 2,700 – 3,790 | 8 |
| **Minerals** | | | |
| Calcium (%) | 0.970 ± 0.043 | 0.903 – 1.060 | 24 |
| Phosphorus (%) | 0.546 ± 0.025 | 0.498 – 0.590 | 24 |
| Potassium (%) | 0.659 ± 0.022 | 0.627 – 0.691 | 8 |
| Chloride (%) | 0.357 ± 0.027 | 0.300 – 0.392 | 8 |
| Sodium (%) | 0.189 ± 0.019 | 0.160 – 0.212 | 8 |
| Magnesium (%) | 0.199 ± 0.009 | 0.185 – 0.213 | 8 |
| Sulfur (%) | 0.178 ± 0.021 | 0.153 – 0.209 | 8 |
| Iron (ppm) | 160 ± 14.7 | 135 – 177 | 8 |
| Manganese (ppm) | 50.3 ± 4.82 | 42.1 – 56.0 | 8 |
| Zinc (ppm) | 50.7 ± 6.59 | 43.3 – 61.1 | 8 |
| Copper (ppm) | 6.29 ± 0.828 | 5.08 – 7.59 | 8 |
| Iodine (ppm) | 0.461 ± 0.187 | 0.233 – 0.843 | 8 |
| Chromium (ppm) | 0.542 ± 0.128 | 0.330 – 0.707 | 7 |
| Cobalt (ppm) | 0.23 ± 0.049 | 0.20 – 0.30 | 7 |

[a] From formulation
[b] As hydrochloride (thiamine and pyridoxine) or chloride (choline)

**TABLE L4**
**Contaminant Levels in NTP-2000 Rat and Mouse Ration[a]**

| Nutrient | Mean ± Standard Deviation[b] | Range | Number of Samples |
|---|---|---|---|
| **Contaminants** | | | |
| Arsenic (ppm) | 0.20 ± 0.136 | 0.10 – 0.50 | 24 |
| Cadmium (ppm) | 0.04 ± 0.006 | 0.04 – 0.07 | 24 |
| Lead (ppm) | 0.08 ± 0.038 | 0.06 – 0.25 | 24 |
| Mercury (ppm) | <0.02 | | 24 |
| Selenium (ppm) | 0.17 ± 0.033 | 0.13 – 0.28 | 24 |
| Aflatoxins (ppb) | <5.00 | | 24 |
| Nitrate nitrogen (ppm)[c] | 14.0 ± 7.33 | 9.04 – 39.6 | 24 |
| Nitrite nitrogen (ppm)[c] | <0.61 | | 24 |
| BHA (ppm)[d] | 1.1 ± 0.37 | 1.0 – 2.5 | 24 |
| BHT (ppm)[d] | 1.0 ± 0.14 | 1.0 – 1.7 | 24 |
| Aerobic plate count (CFU/g) | <10 | | 24 |
| Coliform (MPN/g) | 1.3 ± 0.6 | 0.0 – 3.0 | 24 |
| *Escherichia coli* (MPN/g) | <10 | | 24 |
| *Salmonella* (MPN/g) | Negative | | 24 |
| Total nitrosoamines (ppb)[e] | 5.1 ± 1.76 | 2.1 – 8.8 | 24 |
| *N*-Nitrosodimethylamine (ppb)[e] | 2.0 ± 0.91 | 1.1 – 5.1 | 24 |
| *N*-Nitrosopyrrolidine (ppb)[e] | 3.1 ± 1.3 | 1.0 – 5.6 | 24 |
| **Pesticides (ppm)** | | | |
| α-BHC | <0.01 | | 24 |
| β-BHC | <0.02 | | 24 |
| γ-BHC | <0.01 | | 24 |
| δ-BHC | <0.01 | | 24 |
| Heptachlor | <0.01 | | 24 |
| Aldrin | <0.01 | | 24 |
| Heptachlor epoxide | <0.01 | | 24 |
| DDE | <0.01 | | 24 |
| DDD | <0.01 | | 24 |
| DDT | <0.01 | | 24 |
| HCB | <0.01 | | 24 |
| Mirex | <0.01 | | 24 |
| Methoxychlor | <0.05 | | 24 |
| Dieldrin | <0.01 | | 24 |
| Endrin | <0.01 | | 24 |
| Telodrin | <0.01 | | 24 |
| Chlordane | <0.05 | | 24 |
| Toxaphene | <0.10 | | 24 |
| Estimated PCBs | <0.20 | | 24 |
| Ronnel | <0.01 | | 24 |
| Ethion | <0.02 | | 24 |
| Trithion | <0.05 | | 24 |
| Diazinon | <0.10 | | 24 |
| Methyl chlorpyrifos | 0.099 ± 0.087 | 0.020 – 0.368 | 24 |
| Methyl parathion | <0.02 | | 24 |
| Ethyl parathion | <0.02 | | 24 |
| Malathion | 0.221 ± 0.210 | 0.020 – 0.826 | 24 |
| Endosulfan I | <0.01 | | 24 |
| Endosulfan II | <0.01 | | 24 |
| Endosulfan sulfate | <0.03 | | 24 |

[a] All samples were irradiated. CFU=colony-forming units; MPN=most probable number; BHC=hexachlorocyclohexane or benzene hexachloride
[b] For values less than the limit of detection, the detection limit is given as the mean.
[c] Sources of contamination: alfalfa, grains, and fish meal
[d] Sources of contamination: soy oil and fish meal
[e] All values were corrected for percent recovery.

# APPENDIX M
# SENTINEL ANIMAL PROGRAM

METHODS . . . . . 294
RESULTS . . . . . 295

# SENTINEL ANIMAL PROGRAM

## METHODS

Rodents used in the Carcinogenesis Program of the National Toxicology Program are produced in optimally clean facilities to eliminate potential pathogens that may affect study results. The Sentinel Animal Program is part of the periodic monitoring of animal health that occurs during the toxicologic evaluation of chemical compounds. Under this program, the disease state of the rodents is monitored via serology on sera from extra (sentinel) animals in the study rooms. These animals and the study animals are subject to identical environmental conditions. The sentinel animals come from the same production source and weanling groups as the animals used for the studies of chemical compounds.

Serum samples were collected from randomly selected rats and mice during the 3-month and 2-year studies. Blood from each animal was collected and allowed to clot, and the serum was separated. Samples were processed appropriately and sent to Microbiological Associates, Inc. (Rockville, MD), for determination of antibody titers. The laboratory serology methods and viral agents for which testing was performed are tabulated below; the times at which blood was collected during the studies are also listed.

| Method and Test | Time of Analysis |
|---|---|
| **RATS** | |
| **3-Month Study** | |
| ELISA | |
| *Mycoplasma arthritidis* | Study termination |
| *Mycoplasma pulmonis* | Study termination |
| PVM (pneumonia virus of mice) | Study termination |
| RCV/SDA | |
| (rat coronavirus/sialodacryoadenitis virus) | Study termination |
| Sendai | Study termination |
| Hemagglutination Inhibition | |
| H-1 (Toolan's H-1 virus) | Study termination |
| KRV (Kilham rat virus) | Study termination |
| **2-Year Study** | |
| ELISA | |
| *M. arthritidis* | Study termination |
| *M. pulmonis* | Study termination |
| PVM | 6, 12, and 18 months, study termination |
| RCV/SDA | 6, 12, and 18 months, study termination |
| Sendai | 6, 12, and 18 months, study termination |
| Immunofluorescence Assay | |
| Parvovirus | 6, 12, and 18 months, study termination |

| Method and Test | Time of Analysis |
|---|---|
| **MICE** | |
| **3-Month Study** | |
| ELISA | |
| Ectromelia virus | Study termination |
| EDIM (epizootic diarrhea of infant mice) | Study termination |
| GDVII (mouse encephalomyelitis virus) | Study termination |
| LCM (lymphocytic choriomeningitis virus) | Study termination |
| MAd-Fl (mouse adenoma virus-FL) | Study termination |
| MHV (mouse hepatitis virus) | Study termination |
| *M. arthritidis* | Study termination |
| *M. pulmonis* | Study termination |
| PVM | Study termination |
| Reovirus 3 | Study termination |
| Sendai | Study termination |
| Immunofluorescence Assay | |
| GDVII | Study termination |
| MCMV *(*mouse cytomegalovirus) | Study termination |
| Hemagglutination Inhibition | |
| K (papovavirus) | Study termination |
| MVM (minute virus of mice) | Study termination |
| Polyoma virus | Study termination |
| **2-Year Study** | |
| ELISA | |
| Ectromelia virus | 6, 12, and 18 months, study termination |
| EDIM | 6, 12, and 18 months, study termination |
| GDVII | 6, 12, and 18 months, study termination |
| LCM | 6, 12, and 18 months, study termination |
| Mouse adenoma virus | 6, 12, and 18 months, study termination |
| MHV | 6, 12, and 18 months, study termination |
| *M. arthritidis* | Study termination |
| *M. pulmonis* | Study termination |
| PVM | 6, 12, and 18 months, study termination |
| Reovirus 3 | 6, 12, and 18 months, study termination |
| Sendai | 6, 12, and 18 months, study termination |
| Immunofluorescence Assay | |
| Mouse adenoma virus-FL | 6 and 12 months |
| MCMV | Study termination |
| Parvovirus | 6, 12, and 18 months, study termination |
| PVM | 6 months |

## RESULTS

For the 2-year studies in rats and mice, all serology tests were negative. At the end of the 3-month studies, one rat had a low level positive result for *M. arthritidis*. This was probably a false positive. ELISA frequently gives a positive test for *M. arthritidis* antibodies, but in many instances this positive test cannot be confirmed by other testing methods or culture. *M. arthritidis* is a weak pathogen that is rarely associated with lesions or other effects that might interfere with experimental studies in rodents.

# APPENDIX N
# SINGLE-EXPOSURE TOXICOKINETIC STUDIES IN F344/N RATS AND B6C3F$_1$ MICE


INTRODUCTION . . . . . 298
MATERIALS AND METHODS . . . . . 298
RESULTS AND DISCUSSION . . . . . 299
FIGURE N1 Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Male F344/N Rats after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation . . . . . 300
FIGURE N2 Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Female F344/N Rats after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation . . . . . 301
TABLE N1 Toxicokinetic Parameter Estimates in F344/N Rats after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation . . . . . 302
FIGURE N3 Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Male B6C3F$_1$ Mice after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation . . . . . 303
FIGURE N4 Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Female B6C3F$_1$ Mice after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation . . . . . 304
TABLE N2 Toxicokinetic Parameter Estimates in B6C3F$_1$ Mice after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation . . . . . 305

# SINGLE-EXPOSURE TOXICOKINETIC STUDIES IN F344/N RATS AND B6C3F$_1$ MICE

## INTRODUCTION

Single-administration inhalation toxicokinetic studies were designed to estimate toxicokinetic parameters relevant to the elimination of propylene glycol mono-*t*-butyl ether from blood in Fischer 344/N rats and B6C3F$_1$ mice. Male and female rats and mice received a single 6-hour whole-body inhalation exposure to target concentrations of 75, 300, and 1,200 ppm propylene glycol mono-*t*-butyl ether. Postexposure blood samples were analyzed for propylene glycol mono-*t*-butyl ether and the results were used to estimate toxicokinetic parameters of interest.

## MATERIALS AND METHODS

Propylene glycol mono-*t*-butyl ether (638 kg) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI), in two lots (00406CN and 00603PG) that were combined and assigned a new lot number (8359-126-01). This homogeneous composite lot was the same lot used in the 2-week and 3-month toxicology and carcinogenicity studies. Characterization of lot 8359-126-01 and the system for generation and monitoring the test article vapor are described in Appendix K.

Male and female F344/N rats (approximately 11 weeks old) with an average weight of 221 and 134 g, respectively, and male and female B6C3F$_1$ mice (approximately 12 weeks old) with an average weight of 29.3 and 23.7 g, respectively, received a single whole-body inhalation exposure to a target concentration of 75, 300, or 1,200 ppm propylene glycol mono-*t*-butyl ether for 6 hours plus $T_{90}$ (a $T_{90}$ value of 12 minutes was selected for all studies). During exposure, animals had access to tap water, but not to food.

Heparinized blood was collected from the retroorbital plexus (rats) or supraorbital sinus (mice) under 70% $CO_2$ (in room air) anesthesia after exposure. Each animal was bled twice, once from each eye. Rats from the 75 ppm group were bled at less than 5 minutes, and at 10, 20, 30, 45, 60, 90, and 120 minutes postexposure. Rats from the 300 and 1,200 ppm groups were bled at less than 5 minutes and at 10, 45, 90, 180, 300, 489, and 600 minutes postexposure. Mice from the 75 ppm group were bled at less than 5 minutes and at 10, 20, 30, 45, 60, 90, and 120 minutes postexposure. Mice from the 300 ppm group were bled at less than 5 minutes and at 10, 30, 45, 60, 90, 120, and 180 minutes postexposure. Mice from the 1,200 ppm group were bled at less than 5 minutes and at 10, 30, 60, 90, 120, 180, and 240 minutes postexposure. Samples were stored at -70°C until analysis.

Blood samples were thawed at room temperature. Aliquots of 100 uL (75 and 300 ppm) or 10 uL (1,200 ppm) of blood were diluted with 100 uL of 200 mM sulfuric acid (adjusted to pH 2 with sodium hydroxide) and 320 ng propylene glycol mono-*t*-butyl ether-$d_{15}$ (Cambridge Isotope laboratories, Andover, MA) added as an internal standard. The mixture was vortexed, 0.5 mL ethyl acetate was added, and the mixture was vortexed again and centrifuged. The organic layer was transferred to automated liquid sampler vials for analysis.

Determination of propylene glycol mono-*t*-butyl ether in blood was performed using a validated gas chromatography/mass spectrometry method. An HP-5973 mass-selective detector interfaced with an HP-6890 gas chromatograph was used (Hewlett-Packard, Palo Alto, CA). Separations were carried out on a fused silica capillary column (Stabilwax-DA; 30 m × 0.25 mm ID, 0.25-µm film; Restek, Bellefonte, PA). The column temperature was held at 50° C for 0.5 minutes, then increased to 250° C at 20° C per minute and held for 2 minutes. Amounts of propylene glycol mono-*t*-butyl ether were determined from calibration curves generated by addition of propylene glycol mono-*t*-butyl ether to blood from untreated animals.

Blood concentration versus time data were analyzed using a nonlinear least-squares fitting program (SAS PROC NLIN; SAS Institute, Inc., Cary, NC).

## Results and Discussion

Blood elimination profiles following 75 and 300 ppm exposures have the appearance typical of biexponential kinetics (Figures N1 to N4). However, at 1,200 ppm, elimination appears to be saturated and the data are better described by Michaelis-Menten kinetics (Figures N1 to N4; Tables N1and N2). Because of the difficulty of estimating terminal rate constants, area under the curve (AUC) data are best compared over the time period for which data were available for all groups, 0 to 90 minutes. The calculated initial blood concentration ($C_0$) normalized to the exposure concentration ($C_0$/exposure concentration) data and $AUC_{90}$/exposure concentration data clearly show the nonlinearity in elimination and dose between the 300 and 1,200 ppm exposures (Tables N1 and N2).

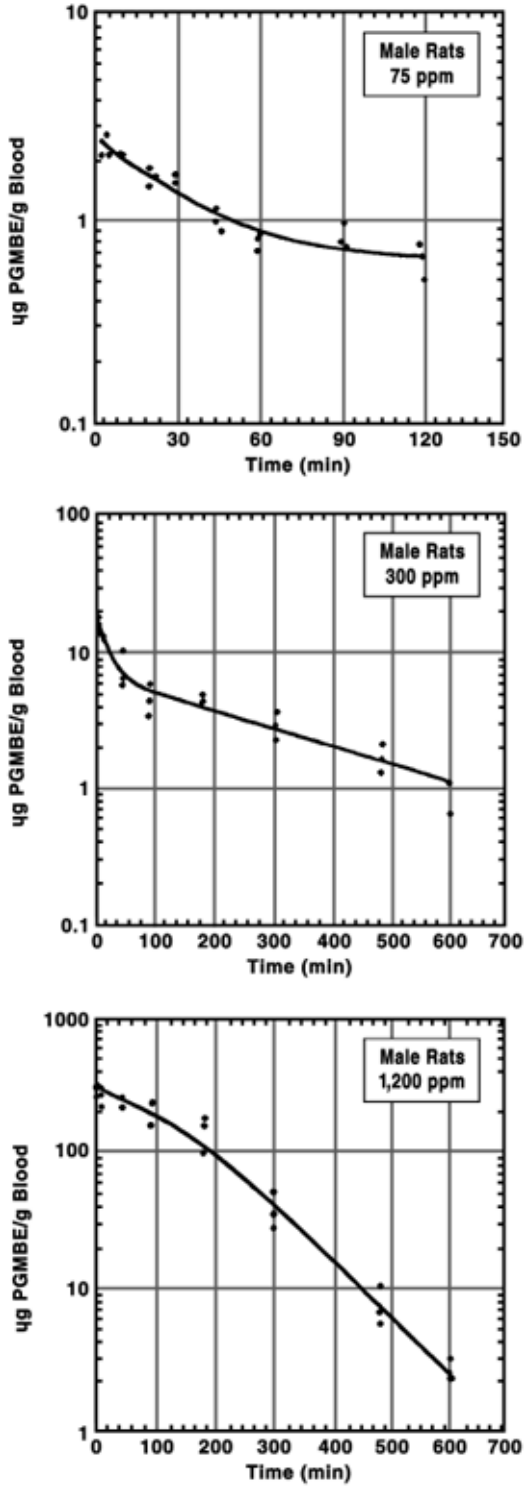


**Figure N1**
**Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Male F344/N Rats after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation**

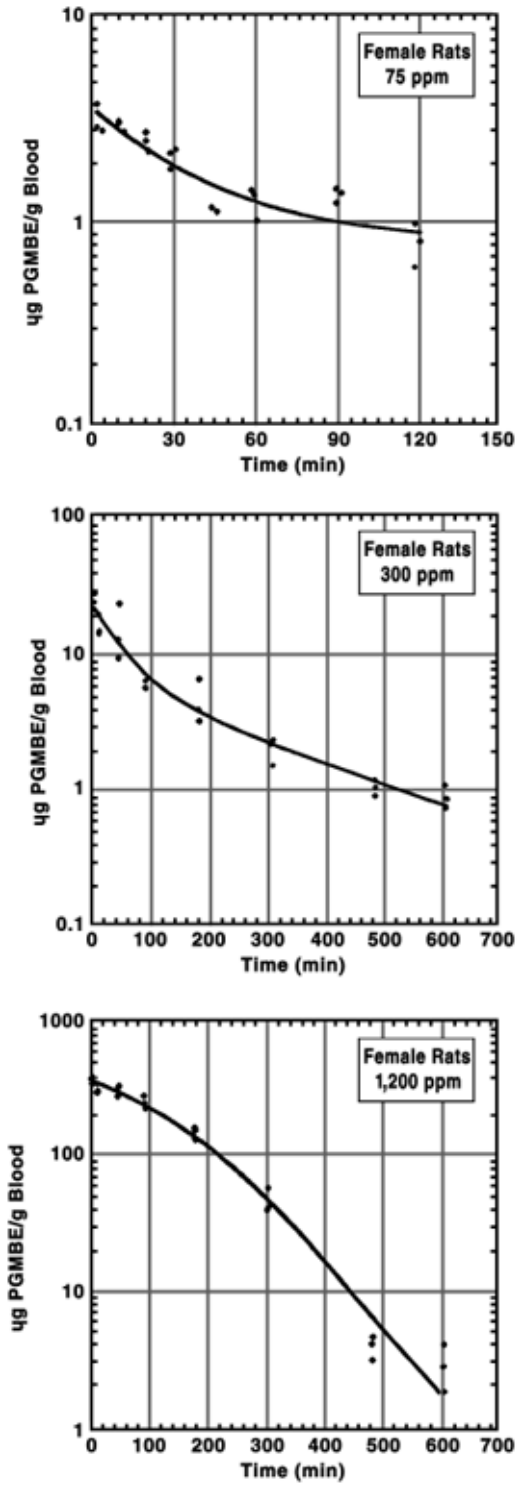


**FIGURE N2**
**Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Female F344/N Rats after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation**

**TABLE N1**
**Toxicokinetic Parameter Estimates in F344/N Rats after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation**

| Parameter[a] | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|
| **Male** | | | |
| $C_0$ (µg/g) | 2.71 ± 0.39 | 17.3 ± 2.7 | 311 ± 42 |
| $C_0$/exposure concentration (µg/g per ppm) | 0.0361 ± 0.0052 | 0.0577 ± 0.0090 | 0.259 ± 0.035 |
| $\alpha$ ($min^{-1}$) | 0.0353 ± 0.033 | 0.0459 ± 0.034 | |
| $t_{½}\alpha$ (min) | 19.6 ± 18 | 15.1 ± 11 | |
| $\beta$ ($min^{-1}$) | 0.00334 ± 0.0051 | 0.00301 ± 0.00095 | |
| $t_{½}\beta$ (min) | 207 ± 313 | 230 ± 72 | |
| $K_m$ (µg/g) | | | 274 ± 278 |
| $V_{max}$ (µg/g per min) | | | 2.78 ± 2.3 |
| $K_0$ ($min^{-1}$) | | | 0.0101 ± 0.0020 |
| Postexposure $AUC_\infty$ (µg•min/g) | 324 ± 261 | 2,529 ± 214 | 52,533 ± 4,867 |
| $AUC_\infty$/exposure concentration (µg•min/g per ppm) | 4.32 ± 3.5 | 8.43 ± 0.71 | 43.8 ± 4.1 |
| Postexposure $AUC_{90}$ (µg•min/g) | 114 ± 4.3 | 796 ± 104 | 22,136 ± 1,938 |
| $AUC_{90}$/exposure concentration (µg•min/g per ppm) | 1.52 ± 0.057 | 2.65 ± 0.35 | 18.4 ± 1.6 |
| **Female** | | | |
| $C_0$ (µg/g) | 3.75 ± 0.66 | 22.9 ± 4.7 | 368 ± 39 |
| $C_0$/exposure concentration (µg/g per ppm) | 0.0500 ± 0.00069 | 0.0763 ± 0.0157 | 0.307 ± 0.033 |
| $\alpha$ ($min^{-1}$) | 0.0353 ± 0.052 | 0.0205 ± 0.022 | |
| $t_{½}\alpha$ (min) | 19.7 ± 29 | 33.8 ± 36 | |
| $\beta$ ($min^{-1}$) | 0.00734 ± 0.0069 | 0.00362 ± 0.0039 | |
| $t_{½}\beta$ (min) | 94.4 ± 89 | 192 ± 208 | |
| $K_m$ (µg/g) | | | 202 ± 144 |
| $V_{max}$ (µg/g per min) | | | 2.44 ± 1.3 |
| $K_0$ ($min^{-1}$) | | | 0.0121 ± 0.0024 |
| Postexposure $AUC_\infty$ (µg•min/g) | 304 ± 96 | 2,773 ± 423 | 61,497 ± 2,795 |
| $AUC_\infty$/exposure concentration (µg•min/g per ppm) | 4.05 ± 1.3 | 9.24 ± 1.41 | 51.2 ± 2.3 |
| Postexposure $AUC_{90}$ (µg•min/g) | 166 ± 7.0 | 1,252 ± 299 | 27,579 ± 1,580 |
| $AUC_{90}$/exposure concentration (µg•min/g per ppm) | 2.21 ± 0.093 | 4.17 ± 1.0 | 23.0 ± 1.3 |

[a] Estimate ± 0.5 of the 95% confidence interval

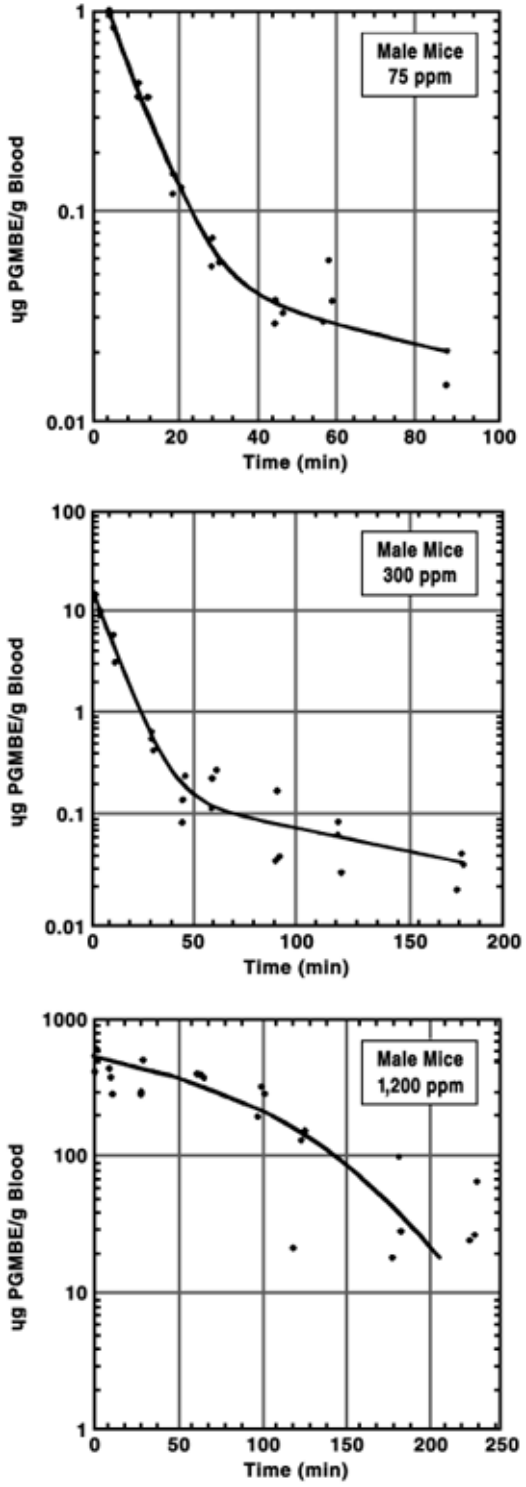


**FIGURE N3**
**Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Male B6C3F$_1$ Mice after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation**

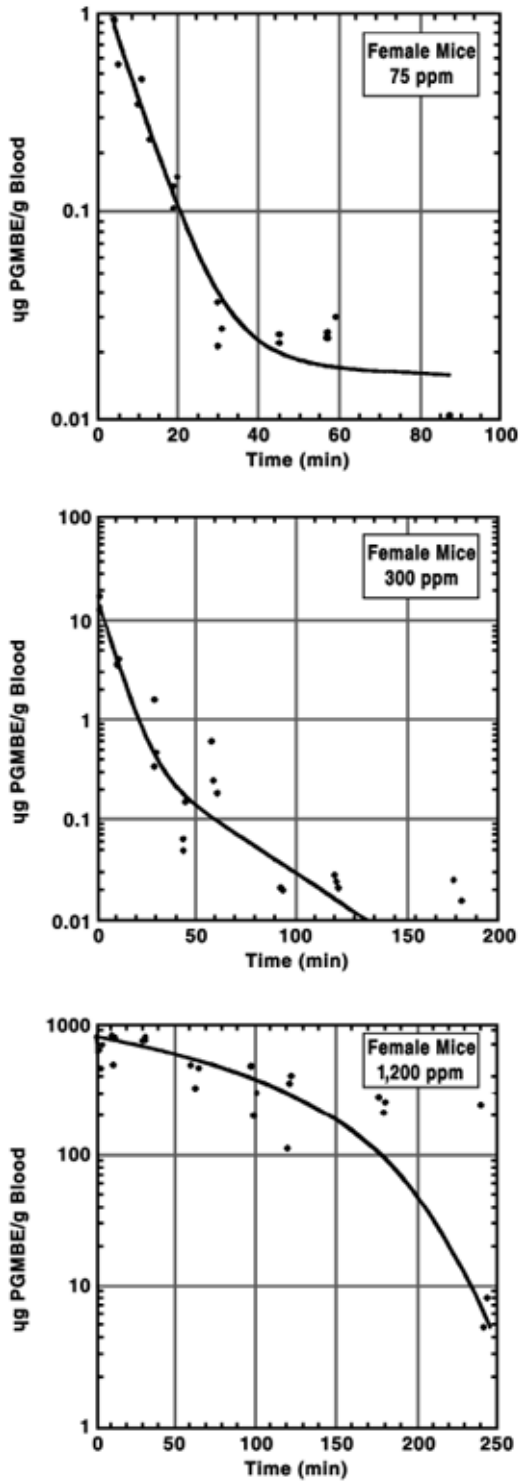


**Figure N4**
**Blood Concentrations of Propylene Glycol Mono-*t*-butyl Ether in Female B6C3F$_1$ Mice after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation**

**TABLE N2**
**Toxicokinetic Parameter Estimates in B6C3F$_1$ Mice after a Single 6-Hour Exposure to Propylene Glycol Mono-*t*-butyl Ether by Inhalation**

| Parameter[a] | 75 ppm | 300 ppm | 1,200 ppm |
|---|---|---|---|
| **Male** | | | |
| $C_0$ (µg/g) | 1.69 ± 0.22 | 15.5 ± 1.8 | 547 ± 128 |
| $C_0$/exposure concentration (µg/g per ppm) | 0.0225 ± 0.00029 | 0.0517 ± 0.0060 | 0.456 ± 0.11 |
| $\alpha$ (min$^{-1}$) | 0.141 ± 0.021 | 0.121 ± 0.020 | |
| $t_{½}\alpha$ (min) | 4.92 ± 0.74 | 5.72 ± 0.93 | |
| $\beta$ (min$^{-1}$) | 0.0111 ± 0.015 | 0.00917 ± 0.015 | |
| $t_{½}\beta$ (min) | 62.2 ± 81 | 75.6 ± 120 | |
| $K_m$ (µg/g) | | | 119 ± 287 |
| $V_{max}$ (µg/g per min) | | | 4.54 ± 4.8 |
| $K_0$ (min$^{-1}$) | | | 0.0381 ± 0.054 |
| Postexposure $AUC_\infty$ (µg•min/g) | 17.5 ± 3.2 | 169 ± 26 | 48,266 ± 5,250 |
| $AUC_\infty$/exposure concentration (µg•min/g per ppm) | 0.233 ± 0.042 | 0.563 ± 0.086 | 40.2 ± 4.4 |
| Postexposure $AUC_{90}$ (µg•min/g) | 15.6 ± 0.81 | 160 ± 26 | 36,333 ± 3,687 |
| $AUC_{90}$/exposure concentration (µg•min/g per ppm) | 0.207 ± 0.011 | 0.535 ± 0.087 | 30.3 ± 3.1 |
| **Female** | | | |
| $C_0$ (µg/g) | 1.49 ± 0.35 | 16.2 ± 3.1 | 800 ± 165 |
| $C_0$/exposure concentration (µg/g per ppm) | 0.0199 ± 0.0047 | 0.0540 ± 0.0106 | 0.667 ± 0.14 |
| $\alpha$ (min$^{-1}$) | 0.139 ± 0.035 | 0.148 ± 0.050 | |
| $t_{½}\alpha$ (min) | 4.99 ± 1.3 | 4.69 ± 1.6 | |
| $\beta$ (min$^{-1}$) | 0.00216 ± 0.041 | 0.0294 ± 0.049 | |
| $t_{½}\beta$ (min) | 320 ± 6,015 | 23.6 ± 39 | |
| $K_m$ (µg/g) | | | 77.7 ± 165 |
| $V_{max}$ (µg/g per min) | | | 4.84 ± 3.1 |
| $K_0$ (min$^{-1}$) | | | 0.0623 ± 0.098 |
| Postexposure $AUC_\infty$ (µg•min/g) | 15.4 ± 44 | 157 ± 26 | 88,137 ± 10,202 |
| $AUC_\infty$/exposure concentration (µg•min/g per ppm) | 0.205 ± 0.58 | 0.523 ± 0.086 | 73.4 ± 8.5 |
| Postexposure $AUC_{90}$ (µg•min/g) | 12.9 ± 1.6 | 155 ± 27 | 53,780 ± 5,050 |
| $AUC_{90}$/exposure concentration (µg•min/g per ppm) | 0.172 ± 0.021 | 0.515 ± 0.089 | 44.8 ± 4.2 |

[a] Estimate ± 0.5 of the 95% confidence interval (estimate ± 0.5 confidence interval); $C_0 = A_0 + B_0$

# National Toxicology Program Technical Reports

## Printed as of March 2004

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| Chemical | TR No. |
|---|---|
| Acetaminophen | 394 |
| Acetonitrile | 447 |
| Acrylonitrile | 506 |
| Agar | 230 |
| Allyl Glycidyl Ether | 376 |
| Allyl Isothiocyanate | 234 |
| Allyl Isovalerate | 253 |
| 1-Amino-2,4-Dibromoanthraquinone | 383 |
| 2-Amino-4-Nitrophenol | 339 |
| 2-Amino-5-Nitrophenol | 334 |
| 11-Aminoundecanoic Acid | 216 |
| *dl*-Amphetamine Sulfate | 387 |
| Ampicillin Trihydrate | 318 |
| Asbestos, Amosite (Hamsters) | 249 |
| Asbestos, Amosite (Rats) | 279 |
| Asbestos, Chrysotile (Hamsters) | 246 |
| Asbestos, Chrysotile (Rats) | 295 |
| Asbestos, Crocidolite | 280 |
| Asbestos, Tremolite | 277 |
| L-Ascorbic Acid | 247 |
| AZT and AZT/α-Interferon A/D | 469 |
| Barium Chloride Dihydrate | 432 |
| Benzaldehyde | 378 |
| Benzene | 289 |
| Benzethonium Chloride | 438 |
| Benzofuran | 370 |
| Benzyl Acetate (Gavage) | 250 |
| Benzyl Acetate (Feed) | 431 |
| Benzyl Alcohol | 343 |
| *o*-Benzyl-*p*-Chlorophenol (Gavage) | 424 |
| *o*-Benzyl-*p*-Chlorophenol (Mouse Skin) | 444 |
| 2-Biphenylamine Hydrochloride | 233 |
| 2,2-Bis(Bromomethyl)-1,3-Propanediol | 452 |
| Bis(2-Chloro-1-Methylethyl) Ether | 239 |
| Bisphenol A | 215 |
| Boric Acid | 324 |
| Bromodichloromethane | 321 |
| Bromoethane | 363 |
| 1,3-Butadiene | 288 |
| 1,3-Butadiene | 434 |
| *t*-Butyl Alcohol | 436 |
| Butyl Benzyl Phthalate | 213 |
| Butyl Benzyl Phthalate | 458 |
| *n*-Butyl Chloride | 312 |
| *t*-Butylhydroquinone | 459 |
| γ-Butyrolactone | 406 |
| Caprolactam | 214 |
| *d*-Carvone | 381 |
| Chloral Hydrate | 502 |
| Chloral Hydrate | 503 |
| Chlorinated and Chloraminated Water | 392 |
| Chlorendic Acid | 304 |
| Chlorinated Paraffins: $C_{23}$, 43% Chlorine | 305 |
| Chlorinated Paraffins: $C_{12}$, 60% Chlorine | 308 |
| Chlorinated Trisodium Phosphate | 294 |
| 2-Chloroacetophenone | 379 |
| *p*-Chloroaniline Hydrochloride | 351 |
| Chlorobenzene | 261 |
| Chlorodibromomethane | 282 |
| Chloroethane | 346 |
| 2-Chloroethanol | 275 |
| 3-Chloro-2-Methylpropene | 300 |
| Chloroprene | 467 |
| 1-Chloro-2-Propanol | 477 |
| Chlorpheniramine Maleate | 317 |
| C.I. Acid Orange 3 | 335 |
| C.I. Acid Orange 10 | 211 |
| C.I. Acid Red 14 | 220 |
| C.I. Acid Red 114 | 405 |
| C.I. Basic Red 9 Monohydrochloride | 285 |
| C.I. Direct Blue 15 | 397 |
| C.I. Direct Blue 218 | 430 |
| C.I. Disperse Blue 1 | 299 |
| C.I. Disperse Yellow 3 | 222 |
| C.I. Pigment Red 3 | 407 |
| C.I. Pigment Red 23 | 411 |
| C.I. Solvent Yellow 14 | 226 |
| *trans*-Cinnamaldehyde | 514 |
| Citral | 505 |
| Cobalt Sulfate Heptahydrate | 471 |
| Coconut Oil Acid Diethanolamine Condensate | 479 |
| Codeine | 455 |
| Comparative Initiation/Promotion Studies (Mouse Skin) | 441 |
| Corn Oil, Safflower Oil, and Tricaprylin | 426 |
| Coumarin | 422 |
| CS2 | 377 |
| Cytembena | 207 |
| D&C Red No. 9 | 225 |
| D&C Yellow No. 11 | 463 |
| Decabromodiphenyl Oxide | 309 |
| Diallyl Phthalate (Mice) | 242 |
| Diallyl Phthalate (Rats) | 284 |
| 4,4′-Diamino-2,2′-Stilbenedisulfonic Acid, Disodium Salt | 412 |
| 2,4-Diaminophenol Dihydrochloride | 401 |
| 1,2-Dibromo-3-Chloropropane | 206 |
| 1,2-Dibromoethane | 210 |
| 2,3-Dibromo-1-Propanol | 400 |
| 1,2-Dichlorobenzene (*o*-Dichlorobenzene) | 255 |
| 1,4-Dichlorobenzene (*p*-Dichlorobenzene) | 319 |
| *p,p′*-Dichlorodiphenyl sulfone | 501 |
| 2,4-Dichlorophenol | 353 |
| 2,6-Dichloro-*p*-Phenylenediamine | 219 |
| 1,2-Dichloropropane | 263 |
| 1,3-Dichloropropene (Telone II) | 269 |
| Dichlorvos | 342 |
| Dietary Restriction | 460 |
| Diethanolamine | 478 |
| Di(2-Ethylhexyl) Adipate | 212 |
| Di(2-Ethylhexyl) Phthalate | 217 |
| Diethyl Phthalate | 429 |
| Diglycidyl Resorcinol Ether | 257 |
| 3,4-Dihydrocoumarin | 423 |
| 1,2-Dihydro-2,2,4-Trimethylquinoline (Monomer) | 456 |
| Dimethoxane | 354 |
| 3,3′-Dimethoxybenzidine Dihydrochloride | 372 |
| N,N-Dimethylaniline | 360 |
| 3,3′-Dimethylbenzidine Dihydrochloride | 390 |
| Dimethyl Hydrogen Phosphite | 287 |
| Dimethyl Methylphosphonate | 323 |
| Dimethyl Morpholinophosphoramidate | 298 |
| Dimethylvinyl Chloride | 316 |
| Diphenhydramine Hydrochloride | 355 |
| 5,5-Diphenylhydantoin | 404 |
| Emodin | 493 |
| Ephedrine Sulfate | 307 |
| Epinephrine Hydrochloride | 380 |
| 1,2-Epoxybutane | 329 |
| Erythromycin Stearate | 338 |

| Chemical | TR No. |
|---|---|
| Ethyl Acrylate | 259 |
| Ethylbenzene | 466 |
| Ethylene Glycol | 413 |
| Ethylene Glycol Monobutyl Ether | 484 |
| Ethylene Oxide | 326 |
| Ethylene Thiourea | 388 |
| Eugenol | 223 |
| FD&C Yellow No. 6 | 208 |
| Fumonisin $B_1$ | 496 |
| Furan | 402 |
| Furfural | 382 |
| Furfuryl Alcohol | 482 |
| Furosemide | 356 |
| Gallium Arsenide | 492 |
| Geranyl Acetate | 252 |
| Glutaraldehyde | 490 |
| Glycidol | 374 |
| Guar Gum | 229 |
| Gum Arabic | 227 |
| HC Blue 1 | 271 |
| HC Blue 2 | 293 |
| HC Red 3 | 281 |
| HC Yellow 4 | 419 |
| Hexachlorocyclopentadiene | 437 |
| Hexachloroethane | 361 |
| 2,4-Hexadienal | 509 |
| 4-Hexylresorcinol | 330 |
| Hydrochlorothiazide | 357 |
| Hydroquinone | 366 |
| 8-Hydroxyquinoline | 276 |
| Indium Phosphide | 499 |
| Iodinated Glycerol | 340 |
| Isobutene | 487 |
| Isobutyl Nitrite | 448 |
| Isobutyraldehyde | 472 |
| Isophorone | 291 |
| Isoprene | 486 |
| Lauric Acid Diethanolamine Condensate | 480 |
| *d*-Limonene | 347 |
| Locust Bean Gum | 221 |
| 60-Hz Magnetic Fields | 488 |
| Magnetic Field Promotion | 489 |
| Malonaldehyde, Sodium Salt | 331 |
| Manganese Sulfate Monohydrate | 428 |
| D-Mannitol | 236 |
| Marine Diesel Fuel and JP-5 Navy Fuel | 310 |
| Melamine | 245 |
| 2-Mercaptobenzothiazole | 332 |
| Mercuric Chloride | 408 |
| Methacrylonitrile | 497 |
| 8-Methoxypsoralen | 359 |
| α-Methylbenzyl Alcohol | 369 |
| Methyl Bromide | 385 |
| Methyl Carbamate | 328 |
| Methyldopa Sesquihydrate | 348 |
| Methylene Chloride | 306 |
| 4,4′-Methylenedianiline Dihydrochloride | 248 |
| Methyleugenol | 491 |
| Methyl Methacrylate | 314 |
| N-Methylolacrylamide | 352 |
| Methylphenidate Hydrochloride | 439 |
| Mirex | 313 |
| Molybdenum Trioxide | 462 |
| Monochloroacetic Acid | 396 |
| Monuron | 266 |
| Nalidixic Acid | 368 |
| Naphthalene (Mice) | 410 |
| Naphthalene (Rats) | 500 |
| Nickel (II) Oxide | 451 |
| Nickel Sulfate Hexahydrate | 454 |
| Nickel Subsulfide | 453 |

| Chemical | TR No. |
|---|---|
| *p*-Nitroaniline | 418 |
| *o*-Nitroanisole | 416 |
| *p*-Nitrobenzoic Acid | 442 |
| Nitrofurantoin | 341 |
| Nitrofurazone | 337 |
| Nitromethane | 461 |
| *p*-Nitrophenol | 417 |
| *o*-Nitrotoluene | 504 |
| *p*-Nitrotoluene | 498 |
| Ochratoxin A | 358 |
| Oleic Acid Diethanolamine Condensate | 481 |
| Oxazepam (Mice) | 443 |
| Oxazepam (Rats) | 468 |
| Oxymetholone | 485 |
| Oxytetracycline Hydrochloride | 315 |
| Ozone and Ozone/NNK | 440 |
| Penicillin VK | 336 |
| Pentachloroanisole | 414 |
| Pentachloroethane | 232 |
| Pentachloronitrobenzene | 325 |
| Pentachlorophenol, Purified | 483 |
| Pentachlorophenol, Technical Grade | 349 |
| Pentaerythritol Tetranitrate | 365 |
| Phenolphthalein | 465 |
| Phenylbutazone | 367 |
| Phenylephrine Hydrochloride | 322 |
| N-Phenyl-2-Naphthylamine | 333 |
| *o*-Phenylphenol | 301 |
| Polybrominated Biphenyl Mixture (Firemaster FF-1) (Gavage) | 244 |
| Polybrominated Biphenyl Mixture (Firemaster FF-1) (Feed) | 398 |
| Polysorbate 80 (Glycol) | 415 |
| Polyvinyl Alcohol | 474 |
| Primidone | 476 |
| Probenecid | 395 |
| Promethazine Hydrochloride | 425 |
| Propylene | 272 |
| Propylene Glycol Mono-*t*-butyl Ether | 515 |
| 1,2-Propylene Oxide | 267 |
| Propyl Gallate | 240 |
| Pyridine | 470 |
| Quercetin | 409 |
| Riddelliine | 508 |
| Resorcinol | 403 |
| Rhodamine 6G | 364 |
| Rotenone | 320 |
| Roxarsone | 345 |
| Salicylazosulfapyridine | 457 |
| Scopolamine Hydrobromide Trihydrate | 445 |
| Sodium Azide | 389 |
| Sodium Fluoride | 393 |
| Sodium Nitrite | 495 |
| Sodium Xylenesulfonate | 464 |
| Stannous Chloride | 231 |
| Succinic Anhydride | 373 |
| Talc | 421 |
| Tara Gum | 224 |
| 2,3,7,8-Tetrachlorodibenzo-*p*-Dioxin (Dermal) | 201 |
| 2,3,7,8-Tetrachlorodibenzo-*p*-Dioxin (Gavage) | 209 |
| 1,1,1,2-Tetrachloroethane | 237 |
| Tetrachloroethylene | 311 |
| Tetracycline Hydrochloride | 344 |
| Tetrafluoroethylene | 450 |
| 1-Trans-Delta$^9$-Tetrahydrocannabinol | 446 |
| Tetrahydrofuran | 475 |
| Tetrakis(Hydroxymethyl)Phosphonium Sulfate | 296 |
| Tetrakis(Hydroxymethyl)Phosphonium Chloride | 296 |
| Tetranitromethane | 386 |
| Theophylline | 473 |
| 4,4-Thiobis(6-*t*-Butyl-*m*-Cresol) | 435 |
| Titanocene Dichloride | 399 |
| Toluene | 371 |

| Chemical | TR No. | Chemical | TR No. |
|---|---|---|---|
| 2,4- & 2,6-Toluene Diisocyanate | 251 | Turmeric Oleoresin (Curcumin) | 427 |
| Triamterene | 420 | Vanadium Pentoxide | 507 |
| Tribromomethane | 350 | 4-Vinylcyclohexene | 303 |
| Trichloroethylene | 243 | 4-Vinyl-1-Cyclohexene Diepoxide | 362 |
| Trichloroethylene | 273 | Vinylidene Chloride | 228 |
| 1,2,3-Trichloropropane | 384 | Vinyl Toluene | 375 |
| Tricresyl Phosphate | 433 | Xylenes (Mixed) | 327 |
| Triethanolamine | 449 | 2,6-Xylidine | 278 |
| Tris(2-Chloroethyl) Phosphate | 391 | Zearalenone | 235 |
| Tris(2-Ethylhexyl) Phosphate | 274 | Ziram | 238 |