NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF DIPROPYLENE GLYCOL

(CAS NO. 25265-71-8)

IN F344/N RATS AND B6C3F$_1$ MICE

(DRINKING WATER STUDIES)

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

June 2004

NTP TR 511

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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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SUMMARY

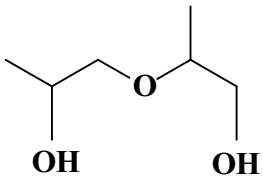
Background
Dipropylene glycol is found in antifreeze, air fresheners, cosmetic products, solvents, and plastics. We studied the effects of dipropylene glycol on male and female rats and mice to identify potential toxic or cancer-related hazards to humans.

Methods
We gave groups of 50 male and female mice drinking water containing dipropylene glycol at concentrations of 10,000, 20,000 or 40,000 parts per million (corresponding to 1%, 2%, or 4%) for two years. Male and female rats received concentrations of 2,500, 10,000, or 40,000 parts per million. Other groups received untreated water and were the control groups. Tissues from more than 40 sites were examined for every animal.

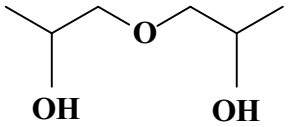
Results
The groups of animals receiving 40,000 ppm dipropylene glycol weighed less than the control animals. All the male rats receiving 40,000 ppm dipropylene glycol died before the end of the study, mainly because of kidney disease. All the other animal groups survived as well as the controls. No increases in tumor rates were seen in any of the groups of rats or mice.

Conclusions
We conclude that dipropylene glycol did not cause cancer in male or female rats or mice. Exposure to dipropylene glycol did increase the rate and severity of kidney nephropathy and inflammation of the liver and salivary gland in male rats and some atrophy of the epithelial tissue of the nose in male and female rats.

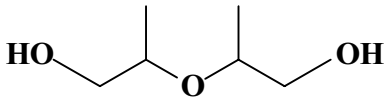
ABSTRACT



2-(2-Hydroxypropoxy)-1-propanol



1,1′-Oxybis(2-propanol)



2,2′-Oxybis(1-propanol)

DIPROPYLENE GLYCOL

CAS No. 25265-71-8

Chemical Formula: $C_6H_{14}O_3$ Molecular Weight: 134.18

Synonyms: Bis(2-hydroxypropyl) ether; 2,2′-dihydroxydipropyl ether; 2,2′-dihydroxyisopropyl ether; di-1,2-propylene glycol; dipropylene glycol (6CI); dipropyl glycol; oxybis-propanol; oxydipropanol; 1,1′-oxydi-2-propanol

Dipropylene glycol is a component of many widely used commercial products such as antifreeze, air fresheners, cosmetic products, solvents, and plastic. The National Cancer Institute nominated dipropylene glycol for carcinogenicity studies based on its high production volume and suspected widespread consumer and occupational exposure. Male and female F344/N rats and B6C3F$_1$ mice were exposed to dipropylene glycol (greater than 99% pure) in drinking water for 2 weeks, 3 months, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*.

2-Week Study in Rats

Groups of five male and five female F344/N rats were exposed to 0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm dipropylene glycol (equivalent to average daily doses of approximately 635, 1,450, 2,650, 5,850, or 13,000 mg dipropylene glycol/kg body weight to males and 850, 1,670, 2,860, 5,420, or 11,100 mg/kg to females) in drinking water for 2 weeks. All rats survived to the end of the study. Mean body weights of 80,000 ppm males and females were significantly less than those of the controls. Water consumption by exposed and control groups was generally similar. Liver and kidney weights of males and females generally increased with increasing exposure concentration. Focal fatty change occurred in the livers of all 80,000 ppm males.

2-Week Study in Mice

Groups of five male and five female B6C3F$_1$ mice were exposed to 0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm dipropylene glycol in drinking water for 2 weeks. Due to leaking water bottles, water consumption measurements were unreliable; therefore, the average daily dose of dipropylene glycol achieved for each exposure group was not calculated. All mice survived to the end of the study. The mean body weight gain of 80,000 ppm males was significantly less than that of the controls. Thinness, hypoactivity, and abnormal gait were observed in 80,000 ppm females. Liver weights of 80,000 ppm mice were significantly increased. There were no lesions attributed to dipropylene glycol exposure.

3-Month Study in Rats

Groups of 10 male and 10 female F344/N rats were exposed to 0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm dipropylene glycol (equivalent to average daily doses of approximately 425, 890, 1,840, 3,890, or 12,800 mg/kg to males and 460, 920, 1,690, 3,340, or 8,950 mg/kg to females) in drinking water for 3 months. All rats survived to the end of the study. Mean body weights of all exposed groups of males and 20,000 ppm or greater females were significantly less than those of the control groups. Water consumption by 80,000 ppm males and females increased during the second week of the study and was greater than that by controls for the remainder of the study. Hypoactivity and poor hair coats were observed in all 80,000 ppm males.

Hematology results indicated that exposure of rats to dipropylene glycol induced a minimal erythron decrease at week 14 in males and increases in serum alanine aminotransferase and sorbitol dehydrogenase activities and/or total bile acid concentrations that suggest a hepatic effect in males and females. Liver weights of rats receiving 10,000 ppm or greater and kidney weights of rats receiving 40,000 and 80,000 ppm were greater than those of the controls. Minimal to mild hypertrophy of the adrenal cortex occurred in all exposed groups of rats. The incidences of liver and kidney lesions were significantly increased in 20,000 ppm or greater males and 80,000 ppm females. Focal olfactory epithelial degeneration was present in all 80,000 ppm rats. Male rats in the 80,000 ppm group had small testes, preputial glands, seminal vesicles, and prostate glands. The left testis, cauda epididymis, and epididymis weights of 80,000 ppm males were significantly decreased. The incidences of testicular atrophy, epididymal hypospermia, preputial gland atrophy, and seminal vesicle depletion were generally increased in the 80,000 ppm group. Epididymal hypospermia consisted of decreases in epididymal sperm counts per cauda and spermatid heads per gram testis.

3-Month Study in Mice

Groups of 10 male and 10 female B6C3F$_1$ mice were exposed to 0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm dipropylene glycol (equivalent to average daily doses of approximately 715, 1,350, 2,620, 4,790, or 11,000 mg/kg to males and 1,230, 2,140, 4,020, 7,430, or 14,700 mg/kg to females) in drinking water for 3 months. Three males and one female exposed to 80,000 ppm and one 20,000 ppm female died during the study. Body weights of 10,000 ppm females were significantly greater than those of the controls. Water consumption by exposed males and females was generally less than that by the controls. Hypoactivity and dehydration were observed in 80,000 ppm males and females. Liver weights of 40,000 ppm males and 80,000 ppm males and females were significantly greater than those of the controls. The estrous cycle of 80,000 ppm females was significantly longer than that of the controls. Centrilobular hypertrophy of the liver occurred in 40,000 ppm males and 80,000 ppm males and females.

2-Year Study in Rats

Groups of 50 male and 50 female F344/N rats were exposed to 0, 2,500, 10,000, or 40,000 ppm dipropylene glycol (equivalent to average daily doses of approximately 115, 470, or 3,040 mg/kg to males and 140, 530, or 2,330 mg/kg to females) in drinking water for 2 years. Survival of 40,000 ppm males was significantly less than that of the control group. Mean body weights of 40,000 ppm males and females were less than those of the controls throughout the study. Water consumption by 40,000 ppm males was greater than that by the controls.

The incidences of nephropathy were significantly increased in 10,000 and 40,000 ppm males, and the severities were greater than that in the controls. Increased incidences of focal histiocytic and focal granulomatous inflammation of the liver in males, bile duct hyperplasia of the liver in males and females, olfactory epithelium degeneration of the nose in males and females, and olfactory epithelium atrophy and thrombosis of the nose in males were considered related to dipropylene glycol exposure. The incidence of minimal to mild suppurative inflammation of the salivary gland was significantly increased in 40,000 ppm males. There were no increased incidences of neoplasms that were attributed to exposure to dipropylene glycol.

2-Year Study in Mice

Groups of 50 male and 50 female B6C3F$_1$ mice were exposed to 0, 10,000, 20,000, or 40,000 ppm dipropylene glycol (equivalent to average daily doses of approximately 735, 1,220, or 2,390 mg/kg to males and 575, 1,040, or 1,950 mg/kg to females) in drinking water for 2 years. Survival of males and females was similar to that of the controls. Mean body weights of 40,000 ppm males were less than those of the controls throughout the

study, and mean body weights of 40,000 ppm females were less during the second year of the study. Water consumption by 40,000 ppm males was less than that by the controls. There were no increased incidences of neoplasms or nonneoplastic lesions that were attributed to exposure to dipropylene glycol.

Genetic Toxicology

Dipropylene glycol was not mutagenic in *S. typhimurium* strain TA97, TA98, TA100, or TA1535 with or without induced rat or hamster liver S9 enzymes.

Conclusions

Under the conditions of this 2-year drinking water study, there was *no evidence of carcinogenic activity** of dipropylene glycol in male or female F344/N rats exposed to 2,500, 10,000, or 40,000 ppm. There was *no evidence of carcinogenic activity* of dipropylene glycol in male or female $B6C3F_1$ mice exposed to 10,000, 20,000, or 40,000 ppm.

Exposure to dipropylene glycol in drinking water resulted in increased incidences and severities of nephropathy in male rats, increased incidences of focal histiocytic and focal granulomatous inflammation of the liver in male rats, increased incidences of suppurative inflammation of the salivary gland in male rats, increased incidences of bile duct hyperplasia in male and female rats, increased incidences of olfactory epithelial atrophy and thrombosis of the nose in male rats, and increased incidences of olfactory epithelial degeneration of the nose in male and female rats.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 11. A summary of the Technical Reports Review Subcommittee comments on this Technical Report appears on page 13.

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Dipropylene Glycol

	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Concentrations in drinking water	0, 2,500, 10,000, or 40,000 ppm	0, 2,500, 10,000, or 40,000 ppm	0, 10,000, 20,000, or 40,000 ppm	0, 10,000, 20,000, or 40,000 ppm
Body weights	40,000 ppm group less than the control group	40,000 ppm group less than the control group	40,000 ppm group less than the control group	40,000 ppm group less than the control group
Survival rates	23/50, 27/50, 27/50, 0/50	30/50, 31/50, 38/50, 31/50	40/50, 39/50, 35/50, 34/49	37/50, 38/50, 38/50, 33/50
Nonneoplastic effects	Kidney: nephropathy (41/47, 47/50, 50/50, 48/48); severity of nephropathy (2.1, 2.2, 2.8, 3.9) Liver: inflammation, focal, histiocytic (18/50, 27/50, 46/49, 48/48); inflammation, focal, granulomatous (22/50, 26/50, 42/49, 27/48); bile duct hyperplasia (34/50, 38/50, 43/49, 44/48) Nose: olfactory epithelium, atrophy (4/46, 3/50, 3/50, 34/49); olfactory epithelium, degeneration (0/46, 0/50, 0/50, 7/49); thrombosis (2/46, 5/50, 4/50, 9/49) Salivary Gland: suppurative inflammation (0/49, 1/49, 0/55, 22/50)	Liver: bile duct hyperplasia (2/50, 3/50, 7/50, 18/49) Nose: olfactory epithelium, degeneration (0/48, 0/48, 0/46, 9/49)	None	None
Neoplastic effects	None	None	None	None
Level of evidence of carcinogenic activity	No evidence	No evidence	No evidence	No evidence
Genetic toxicology				
Salmonella typhimurium gene mutations:	Negative in strains TA97, TA98, TA100, and TA1535 with and without S9			

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 Dipropylene Glycol 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 September 5, 2002, the draft Technical Report on the toxicology and carcinogenesis studies of dipropylene glycol received public review by the National Toxicology Program's Board of Scientific Counselors' Technical Reports Review Subcommittee. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. M. J. Hooth, NIEHS, introduced the toxicology and carcinogenesis studies of dipropylene glycol by discussing the uses of the chemical and the rationale for study, describing the experimental design, reporting on survival and body weight effects, commenting on compound-related neoplastic lesions in rats. The proposed conclusions for the 2-year studies were *no evidence of carcinogenic activity* of dipropylene glycol in male or female F344/N rats exposed to 2,500, 10,000, or 40,000 ppm and *no evidence of carcinogenic activity* of dipropylene glycol in male and female $B6C3F_1$ mice exposed to 10,000, 20,000, or 40,000 ppm.

Exposure to dipropylene glycol in drinking water resulted in increased incidences and severities of nephropathy in male rats, increased incidences of focal histiocytic and focal granulomatous inflammation of the liver in male rats, increased incidences of bile duct hyperplasia in male and female rats, and changes in the olfactory epithelium of the nose in male and female rats.

Dr. Thrall, the first principal reviewer, agreed with the proposed conclusions of the study. She felt the top dose for the male rats was excessive, particularly because the animals drank even larger quantities of water than the control group, and noted that all the animals in that group died of nephropathy. She also noted that dipropylene glycol was metabolized differently than ethylene glycol and that the metabolites of dipropylene glycol were generally much less toxic.

Dr. Klaunig, the second principal reviewer, agreed with the proposed conclusions but suggested that the changes noted in the olfactory epithelium be specified. He offered the generic comment that the precision of the subclassification of hepatocellular foci in NTP studies may be misleading.

Dr. Vore, the third principal reviewer, agreed with the proposed conclusions and inquired about the use and significance of the bile acid measures in the 3-month rat study.

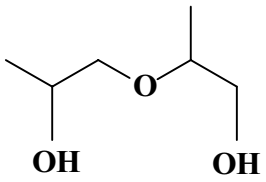
Dr. Hooth noted that there were no indications from the 3-month studies that the 40,000 ppm dose would produce overt toxicity. Dr. J.R. Hailey, NIEHS, described the sampling procedures for liver foci and indicated that they were used as a supplemental indicator of proliferative processes. Dr. G.S. Travlos, NIEHS, explained that bile acid measures were used as one of the biomarkers for hepatobiliary health and that the measures did contain some variability, so that some apparent decreases in rats in the 3-month study were within historical ranges.

Dr. Elwell inquired about a statement linking the adrenal gland changes observed in rats in the 3-month study to stress. He also asked about the characteristics of the nephropathy, which became lethal in the 2-year study, and about the cytoplasmic clefts in the liver and the significance of the salivary gland changes. Dr. R.A. Herbert, NIEHS, replied that while the adrenal gland changes appeared treatment related, the biological significance was unclear and stress was proposed as one possibility. He confirmed that the nephropathy was different from the normal rat kidney nephropathy, with greater incidences and severity of protein casts even after 3 months. While some histiocytic changes were seen in the livers of control animals, the clefts were observed only in dosed animals. Dr. Herbert also agreed that the salivary gland changes were worthy of mention.

Dr. M. Banton, representing Lyondell Chemical Company, Dow Chemical Company, and Huntsman Chemical Company, said that the top doses in the rodent studies were quite high and suggested that some of the effects in those groups could be attributable to substantially lower body weights rather than to chemical toxicity.

Dr. Thrall moved that the conclusions be accepted as written. Dr. Vore seconded the motion, which was accepted with nine affirmative votes and one abstention (Dr. Boekelheide).

INTRODUCTION



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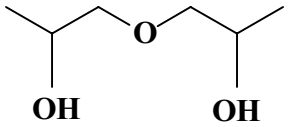
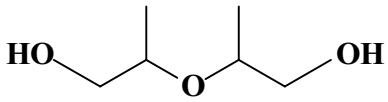


1,1′-Oxybis(2-propanol)



2,2′-Oxybis(1-propanol)

DIPROPYLENE GLYCOL

CAS No. 25265-71-8

Chemical Formula: $C_6H_{14}O_3$ Molecular Weight: 134.18

Synonyms: Bis(2-hydroxypropyl) ether; 2,2′-dihydroxydipropyl ether; 2,2′-dihydroxyisopropyl ether; di-1,2-propylene glycol; dipropylene glycol (6CI); dipropyl glycol; oxybis-propanol; oxydipropanol; 1,1′-oxydi-2-propanol

Chemical and Physical Properties

Dipropylene glycol is a colorless, odorless, slightly viscous liquid (*Patty's*, 2001). It has a boiling point of 231.9° C at 760 mm Hg, a vapor pressure of less than 0.01 mm Hg at 20° C, and a specific gravity of 1.0252 at 20° C. Dipropylene glycol is a combustible chemical with a flash point of 250° to 280° F in an open cup. It is miscible with water, methanol, and ether (Browning, 1965; HSDB, 2001). Dipropylene glycol (commercial or technical grade) is a mixture of three structural isomers: 2-(2-hydroxypropoxy)-1-propanol (CAS No. 106-62-7); 1,1′-oxybis(2-propanol) (CAS No. 110-98-5); and 2,2′-oxybis(1-propanol) (CAS No. 108-61-2). Dipropylene glycol is composed of these isomers at approximately 53%, 43%, and 4%, respectively (*Kirk-Othmer*, 1980). Because each structural isomer has two asymmetric carbons, in theory there are four possible stereochemical isomers per structure. However, due to symmetry, there are only 10 stereoisomers of dipropylene glycol.

Production, Use, and Human Exposure

Dipropylene glycol is prepared commercially during propylene glycol production from propylene oxide (*Patty's*, 2001). The total production capacity of dipropylene glycol in the United States by its five major producers was 131 million pounds in 1998 (ChemExpo, 2001). The United States domestic demand for dipropylene glycol in 1998 was 108 million pounds and was expected to increase to 125 million pounds by 2002, representing growth of 3% to 4% per year. Approximately 15 million pounds of dipropylene glycol are exported annually. Imports of dipropylene glycol to the United States are negligible.

The major uses of dipropylene glycol are in the manufacture of plasticizers (38% of production), polyester resins (23% of production), cosmetics and fragrances (10% of production), polyurethane polyols

(8% of production), and alkyd resins (7% of production) (ChemExpo, 2001). Miscellaneous uses of dipropylene glycol as a solvent in dyes, inks, and paints and as a functional fluid in hydraulic brake fluids and cutting oils account for 14% of its production. Dipropylene glycol is used in hair care and bath products, perfumes, facial makeup, deodorants, and skin care preparations at concentrations ranging from less than 0.1% to 50% (CIR, 1985). Opdyke (1978) reported concentrations of dipropylene glycol in cosmetic formulations ranging from 0.1% to 1.5% in soaps, 0.01% to 0.15% in detergents, 0.05% to 0.5% in creams and lotions, and 1.0% to 8.0% in perfumes. The Environmental Defense Scorecard (2001) web site lists 18 pesticide products that contain dipropylene glycol at concentrations ranging from 0.5% to 5.56% by mass. However, only two of these products maintain active registrations in the United States (CDPR, 2001).

The most probable routes of human exposure to dipropylene glycol are inhalation, dermal contact, and oral ingestion. Occupational exposure may occur through dermal contact or inhalation at sites where dipropylene glycol is produced or used. In 1989, the National Institute for Occupational Safety and Health reported that an estimated 218,354 workers are potentially exposed to dipropylene glycol in the United States (HSDB, 2001). Consumers are exposed through the use of household products that contain dipropylene glycol such as air and room fresheners, household cleaners, cosmetic formulations, auto paints, and antifreeze (Environmental Defense Scorecard, 2001). In addition, humans may be exposed to low levels of dipropylene glycol in contaminated groundwater and drinking water supplies (Lucas, 1984; BUA, 1996). Dipropylene glycol is listed as a drinking water contaminant in a survey of United States cities and locales including Pomona, Escondido, Lake Tahoe, and Orange County, CA; Dallas; Washington, DC; Cincinnati; Philadelphia; Miami; New Orleans; Ottumwa, IA; and Seattle (Lucas, 1984). Dipropylene glycol was detected at concentrations of 0.2 to 0.4 ng/L in 2 of 11 drinking water samples taken from seven United States cities (Lin *et al*., 1981).

Dipropylene glycol is not used in drugs, pharmaceuticals, or food because its toxicologic characteristics have not been clearly defined (*Patty's*, 2001). It is an indirect food additive approved by the Food and Drug Administration (FDA) for use as a component of adhesives used in packaging, transporting, or holding food (21 CFR 175.105) and in cross-linked polyester resins used as articles or components of articles intended for repeated use in contact with food (21 CFR 177.2420). It is also approved for use as a surface lubricant in the manufacture of metallic articles that contact food (21 CFR 178.3910) and as a defoaming agent used as a component of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food (21 CFR 176.200).

ABSORPTION, DISTRIBUTION, METABOLISM AND EXCRETION

Experimental Animals

Reports in the literature on the absorption, distribution, metabolism, or excretion of dipropylene glycol are limited. Dipropylene glycol is readily absorbed from the gastrointestinal tract (Hanzlik *et al*., 1939a). Although the exact metabolism of dipropylene glycol is unknown, it likely involves metabolic pathways identified for similar compounds such as diethylene glycol.

At least two studies concluded that cleavage of the ether linkage of diethylene glycol does not occur *in vivo*. Wiener and Richardson (1989) administered 1.1 g [1,2-^{14}C]-diethylene glycol/kg body weight to Wistar Furth rats by intragastric intubation or intravenous injection and followed its elimination and metabolism. After 6 hours, 28% to 34% of the administered dose was eliminated as unchanged diethylene glycol and 7% to 9% of the dose was excreted as a single metabolite, 2-(hydroxy) ethoxyacetic acid (HEAA). Similar results were reported by Mathews *et al*. (1991) in dogs and Fischer rats. Oral doses were well absorbed with approximately 80% excreted in the urine within 24 hours. Greater than half of the administered dose of radiolabeled diethylene glycol was excreted in the urine as unchanged parent, and 10% to 30% was excreted as HEAA. Ethylene glycol and the ethylene glycol metabolites, glycolic acid and oxalic acid, were not detected, indicating that diethylene glycol is not hydrolyzed to ethylene glycol (Wiener and Richardson, 1989; Mathews *et al*., 1991).

A metabolism study of tripropylene glycol was conducted in male F344 rats (Mendrala, 1995). Following a 48 mg/kg gavage dose of 84% radiochemically pure tripropylene glycol, about 21% of the administered radioactivity was exhaled as $^{14}CO_2$

within 24 hours. The majority (52%) of the radioactivity was excreted in urine. GC/MS analysis of the urine revealed that 13%, 8%, and 4% of the administered dose was either free or conjugated tripropylene-, dipropylene-, or propylene glycol, respectively. This study provides evidence that the ether linkage in a propylene glycol ether can be cleaved metabolically. However, the CO_2 and conjugated/free propylene glycol measured requires only the metabolism of tripropylene glycol to dipropylene glycol. The low radiochemical purity also makes interpretation of the data difficult. Based on this study, dipropylene glycol cleavage is likely, but the evidence is indirect and equivocal. If the ether linkage of dipropylene glycol were cleaved, propylene glycol and the analogous aldehyde/ketone would be formed and further metabolized to lactic or pyruvic acid. Lactic and pyruvic acids are normal constituents of the body and are used as sources of energy either through the production of glucose and glycogen or through the tricarboxylic acid cycle. Pyruvic acid can be further metabolized to carbon dioxide and water (LaKind *et al.*, 1999; *Patty's*, 2001).

Dipropylene glycol concentrations in blood of dogs decreased to nonmeasurable levels within approximately 24 hours after a single intragastric dose of 5 mL/kg (5.13 mg/kg) (Hanzlik *et al*., 1939a). Unlike propylene glycol, dipropylene glycol is not used by the liver or stored as glycogen (Hanzlik *et al*., 1939b; Newman *et al*., 1939). Absorption of dipropylene glycol from the gastrointestinal tract of dogs occurred very rapidly. There was a good correlation of blood dipropylene glycol concentrations following oral and intravenous administration of 2 mL/kg (2.05 mg/kg) to one dog (Hanzlik *et al*., 1939a).

Humans

No reports were found in the literature on the absorption, distribution, metabolism, or excretion of dipropylene glycol by humans.

TOXICITY

Experimental Animals

The ability to substitute one glycol for another commercially has raised questions about their comparative toxicities. Ethylene glycol administered orally or by inhalation has been shown to have adverse reproductive and developmental effects in rodents resulting in fetal toxicity and skeletal malformations. Ethylene glycol exposure is also associated with central nervous system and renal toxicity (LaKind *et al.*, 1999). In contrast, propylene glycol and dipropylene glycol are much less toxic than other low-molecular-weight glycols including ethylene glycol and diethylene glycol (Gosselin *et al*., 1984). Dipropylene glycol is not acutely toxic by oral, dermal, or inhalation exposure (Hanzlik *et al*., 1939a; Browning, 1965).

The acute oral LD_{50} value for dipropylene glycol in rats is approximately 15 g/kg (Hanzlik *et al*., 1939a; *Patty's*, 2001). The intraperitoneal LD_{50} value for dipropylene glycol in rats and mice is 10.3 mL/kg (10.56 g/kg) and 4.6 g/kg, respectively (Opdyke, 1978). The intravenous LD_{50} value for dipropylene glycol in rats and dogs is 5.8 g/kg and 11.5 mL/kg (11.79 g/kg), respectively (Hanzlik *et al*., 1939a; Shaffer *et al*., 1951). Central nervous system depression occurred in dogs after a single intravenous injection of 5.9 mL/kg (6.05 mg/kg) dipropylene glycol (Hanzlik *et al*., 1939a).

Dipropylene glycol is not acutely toxic by dermal exposure (Browning, 1965). No mortality occurred when dipropylene glycol was administered to the skin of rabbits at doses of 5 g/kg or 20 mL/kg (20.5 mg/kg) (Opdyke, 1978; *Kirk-Othmer*, 1980). A formulation containing 7.2% dipropylene glycol produced a cutaneous LD_{50} greater than 2 g/kg in rabbits (CIR, 1985).

Female albino mice developed slight renal tubule degeneration 1 to 4 days after administration of a single intraperitoneal injection of 4.5 g/kg dipropylene glycol (Karel *et al*., 1947). Cellular hyperplasia was noted in the spleen, intestinal mucosa, liver, and lymphoid tissue on days 5 to 7.

Two of ten rabbits given a single intravenous injection of 2 to 4 mL/kg (2.05 to 4.10 g/kg) dipropylene glycol died on the fourth day after treatment (Kesten *et al*., 1939). Kidney lesions were present in the two rabbits that died early and in three of the remaining eight animals terminated at intervals of 1 to 21 days. The lesions were characterized by extensive hydropic degeneration of the renal tubule epithelium. One of the animals with kidney lesions also had damage to the liver parenchyma.

Dipropylene glycol is only slightly irritating to the skin and eyes of rabbits. Ten applications of dipropylene glycol to the skin of rabbits in 12 days produced negligible irritation (*Patty's*, 2001). Dipropylene glycol was reported to cause only mild skin irritation in rabbits

exposed to 500 mg in a 24-hour dermal application test (CIR, 1985). In the eyes of rabbits, 510 mg undiluted dipropylene glycol caused irritation and a formulation containing 7.2% produced minimal transient eye irritation (CIR, 1985).

Repeated exposure of rats to dipropylene glycol at concentrations up to 5% in the drinking water did not result in adverse effects (Kesten *et al*., 1939). At very high doses (10% to 12%), dipropylene glycol produced lethality, kidney damage, and neurobehavioral changes in rats. No chemical-related effects were observed in seven rats given 1% or 5% dipropylene glycol in the drinking water for 33 to 77 days. However, 7 of 25 rats administered 10% dipropylene glycol in drinking water for 9 to 68 days died between exposure days 10 and 30. Five rats had kidney lesions described as hydropic degeneration of the renal tubule epithelium. Four of 18 rats examined at interim evaluations between days 9 and 68 also had kidney lesions.

Dipropylene glycol was administered to four dogs by gavage (Hanzlik *et al*., 1939a). One dog received six doses of 1.5 mL/kg for a total dose of 9 mL/kg (9.23 g/kg), two dogs received six doses of 2 mL/kg for a total dose of 12 mL/kg (12.30 g/kg), and one dog received four doses of 5 mL/kg for a total dose of 20 mL/kg (20.50 g/kg). Emesis and recovery were observed in one dog administered 12 mL/kg. No deaths or other signs of toxicity were observed in any of the dogs. The four dogs showed minimal evidence of liver damage at necropsy. Moderate degenerative changes occurred in the convoluted tubules in the kidneys of two dogs. Kidney changes were not significant in the other two dogs.

Administration of 12% dipropylene glycol in the diet to five female white rats for 15 weeks resulted in decreased running activity relative to controls and to rats administered 12% propylene glycol (van Winkle and Kennedy, 1940).

Chicks were fed a diet containing 5% dipropylene glycol for 27 days without adverse effects (Yoshida *et al*., 1969). The chicks were unable to use dipropylene glycol as an energy source.

Propylene glycol was administered in drinking water at a concentration of 5% to four female dogs for 5 to 9 months (van Winkle and Newman, 1941). The dogs were allowed to drink the mixture *ad libitum* twice daily during a 1-hour period. The average daily intake was 5.1 mL/kg (5.23 g/kg). Additionally, each of four male dogs was allowed to drink 600 mL 10% propylene glycol in drinking water daily for 5 to 6 months. The results indicated no impairment of hepatic or renal function in male or female dogs.

Humans

Dipropylene glycol does not produce allergic skin reactions or sensitization in humans (Opdyke, 1978). It did not produce irritation in human subjects after a 48-hour closed patch test when administered at a concentration of 20% in petrolatum.

Dipropylene glycol did not produce allergic skin reactions in 503 human volunteers with eczema tested for sensitivity to dipropylene glycol (Johansen *et al*., 1995). Patients were exposed to 10% dipropylene glycol for 2 days. Only one patient had a positive patch test reaction to dipropylene glycol.

In a 48-hour closed patch test using a shaving preparation containing 7.2% dipropylene glycol, mild irritation was observed in 6 of 101 subjects after the first exposure and in 8 of 101 subjects after repeating the application 2 weeks later (CIR, 1985; BUA, 1996). Repeated applications of the shaving preparation did not have a sensitizing effect in 50 volunteers treated occlusively for 24 or 48 hours, 3 times per week over a 3-week period. No photosensitizing properties could be detected after ultraviolet irradiation. Likewise, no effects were observed in 59 patients exposed to the shaving preparation for a 4-week period.

The repeated application of a 20% formulation of dipropylene glycol in petrolatum did not have a sensitizing effect on 25 human volunteers (BUA, 1996). Exposure to dipropylene glycol consisted of five consecutive treatments, each lasting 48 hours; another 48-hour repeat treatment occurred 1 to 14 days after the fifth consecutive treatment.

REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY

Experimental Animals

The National Toxicology Program conducted developmental toxicity studies of dipropylene glycol in rats and rabbits.

Dipropylene glycol did not cause fetal toxicity or teratogenicity when administered by gavage to timed pregnant Sprague-Dawley (CD®) rats (20 to 25 per group) at doses of 800, 2,000 or 5,000 mg/kg per day on days 6 to 15 of gestation (NTP, 1992a). Dams were necropsied on gestation day 20. One of 25 pregnant rats in the 2,000 mg/kg group and 2 of 22 pregnant rats in the 5,000 mg/kg group died before day 20. Reduced body weight gain, reduced feed consumption, and increased water consumption were observed in 5,000 mg/kg dams. Although maternal toxicity was observed in rats administered 2,000 or 5,000 mg/kg, developmental toxicity in the fetuses was not observed. Dipropylene glycol did not affect resorptions, fetal viability, fetal body weight, or fetal external, visceral, or skeletal alterations.

Dipropylene glycol was administered by gavage to groups of 24 pregnant New Zealand White® rabbits at doses of 200, 400, 800, or 1,200 mg/kg per day on days 6 to 19 of gestation (NTP, 1992b). Dams were necropsied on gestation day 30. There was no evidence of maternal toxicity, although mortality was seen in a preliminary study at 800 and 1,500 mg/kg per day. Dipropylene glycol exposure did not affect resorptions, fetal viability, fetal body weight, or fetal external, visceral, or skeletal alterations.

Reproductive studies have been conducted for the structural analogues tripropylene glycol and propylene glycol. Tripropylene glycol did not affect reproductive or developmental endpoints in Crj:CD rats administered doses up to 1,000 mg/kg per day by gavage; however, increased liver and kidney weights were observed in parental animals administered 1,000 mg/kg per day (OECD, 2001). Similarly, propylene glycol was not a reproductive or developmental toxicant in female mice. Propylene glycol was tested for reproductive effects in a continuous breeding study in Swiss (CD-1®) mice (Morrissey *et al*., 1989). It was administered to males and females at concentrations of 0%, 1%, 2.5%, or 5% in drinking water for 7 days premating and through 98 days of cohabitation. Estimated daily doses were 1.82, 4.8, and 10.1 g/kg per day, respectively. No adverse effects were found in the F_0, F_1, or F_2 generations or in their ability to reproduce. There were no significant differences between control and exposed groups with respect to mating index, fertility index, mean number of live pups per litter, sex of pups born alive, or mean live pup weight per litter.

In another reproductive study, 30 pregnant female Swiss (CD-1®) mice were administered single gavage doses of 10 g/kg propylene glycol per day on days 8 to 12 of gestation (Kavlock *et al*., 1987). The fertility rate, number of maternal deaths, number of resorptions, average litter size, birth weights, and pup postnatal weight gains of dosed mice were not significantly different from those of the controls.

Small increases in the numbers of fetal malformations were seen in mice injected subcutaneously with propylene glycol (Nomura, 1977). Twenty-one pregnant ICR/Jcl female mice (9 to 12 weeks old) were injected with 0.01 mg/g on day 9, 10, or 11 of gestation, the period of sensitivity to the induction of fetal deaths and malformations in this strain. The following malformations were noted in 5 of 226 living fetuses (2%): open eyelid (three fetuses), polydactyly (one fetus), and cleft palate (one fetus). However, three fetuses with malformations (open eyelid, polydactyly, and exencephalus) were also noted among 1,026 living fetuses in the untreated control group.

Humans

No reproductive or developmental toxicity studies of dipropylene glycol in humans were found in the literature.

CARCINOGENICITY

Experimental Animals

No carcinogenicity studies of dipropylene glycol in experimental animals were found in the literature. Substances that are structurally related to dipropylene glycol, including propylene glycol and polypropylene glycol, were not carcinogenic in rats or mice when administered orally, dermally, or by subcutaneous injection (CIR, 1994).

Gaunt *et al*. (1972) administered propylene glycol in feed to groups of 30 male and 30 female CD rats at concentrations of 0, 6,250, 12,500, 25,000, or 50,000 ppm for 104 weeks (approximately 0.2, 0.4, 0.9, or 1.7 g/kg per day to males and 0.3, 0.5, 1.0, or 2.1 g/kg per day to females). Propylene glycol had no effect on mortality, body weight gain, feed consumption, hematology, organ weights, or pathology. No increases in tumor incidences occurred in the exposed rats compared to the controls.

The potential carcinogenicity of propylene glycol was studied in female Swiss mice (Stenbäck and Shubik, 1974). Propylene glycol was applied to the shaved dorsal skin of 50 mice per group twice a week at concentrations of 10%, 50%, or 100%. Applications continued for the lifetime of the animals. Propylene glycol did not produce a statistically significant increase in tumor incidence compared to that in the untreated controls.

Compound-related lesions were not observed after chronic dietary administration of 2 to 5 g/kg propylene glycol to groups of five male and five female dogs for 104 weeks (Weil *et al.*, 1971).

Humans

No epidemiology studies of dipropylene glycol in humans were found in the literature.

Genetic Toxicity

No published data on the genetic toxicity of dipropylene glycol were found in the literature.

Study Rationale

Dipropylene glycol is a component of many widely used commercial products such as antifreeze, air fresheners, cosmetic products, solvents, and plastics. The National Cancer Institute nominated dipropylene glycol for carcinogenicity studies based on its high production volume and suspected widespread consumer and occupational exposure. The 2-week, 3-month, and 2-year studies were performed in male and female F344/N rats and $B6C3F_1$ mice to evaluate the toxicity and carcinogenicity of dipropylene glycol. Technical-grade dipropylene glycol was selected for testing because humans are exposed to the isomeric mixture. Drinking water was chosen as the route of exposure because dipropylene glycol was detected in drinking water at several locations across the United States and may enter groundwater following occupational and consumer use and disposal. This route of exposure was also selected because the FDA has approved the use of dipropylene glycol as an indirect food additive in adhesives and polymer resins intended for use in articles in repeated contact with food.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF DIPROPYLENE GLYCOL

Dipropylene glycol was obtained from Union Carbide Corporation (Berwyn, IL) in one lot (0365) for use in the 2-week and 3-month studies and from Aldrich Chemical Company, Inc. (Milwaukee, WI) in one lot (10626DN) for use in the 2-year studies. Identity, moisture content, purity, and stability analyses were conducted by the analytical chemistry laboratories (lot 0365: Midwest Research Institute, Kansas City, MO; lots 0365 and 10626DN: Research Triangle Institute, Research Triangle Park, NC). Identity and purity analyses were conducted by the study laboratories. Reports on analyses performed in support of the dipropylene glycol studies are on file at the National Institute of Environmental Health Sciences.

Both lots of the chemical, a clear, colorless liquid, were identified as dipropylene glycol by the analytical chemistry laboratories with boiling point and density determinations; infrared (IR), nuclear magnetic resonance (NMR), and ultraviolet/visible spectroscopy; and high- and low-resolution mass spectrometry (MS) and by the study laboratories with IR spectroscopy. For lot 0365, the observed boiling point of 231° C and density of 1.0202 g/mL were in agreement with the literature values (Lide, 1992). For lot 10626DN, an observed boiling point of 230° C and a density of 1.014 g/mL were in agreement with the literature values. The IR spectra from both lots were consistent with the structure of dipropylene glycol and literature references (*Aldrich*, 1981, 1985). The ultraviolet/visible spectra from both lots were consistent with the structure of dipropylene glycol. The NMR spectra were consistent with the structure of a mixture of dipropylene glycol isomers. The low-resolution MS spectrum was consistent with the structure of a 1-hydroxy isomer of dipropylene glycol (*NIST Standard Reference Database*). The observed mass of the high-resolution mass spectrometry base peak was within acceptable limits of the calculated mass. The IR and NMR spectra are presented in Figures I1 and I2. The moisture contents of lots 0365 and 10626DN were determined by the analytical chemistry laboratories using Karl Fischer titration. The purity of lot 0365 was determined by an analytical chemistry laboratory using elemental analyses, functional group titration, and thin layer chromatography (TLC). The study laboratories analyzed purity using gas chromatography (GC).

For lot 0365, Karl Fischer titration indicated 0.08% ± 0.01% water. Elemental analyses for carbon and hydrogen were in agreement with the theoretical values for dipropylene glycol. Functional group titration indicated a purity of approximately 99%. TLC indicated a major spot and no impurities. For lot 10626DN, Karl Fischer titration indicated 0.475% water. GC analyses by the study laboratories indicated four isomer peaks and no impurities.

Additional analyses were performed by an analytical chemistry laboratory to characterize the isomers of dipropylene glycol present in each lot using GC with flame ionization detection (FID), GC/MS, and GC/IR. GC/FID indicated nine major peaks representing three diastereomers of dipropylene glycol with a combined area of greater than 99% of the total peak area; all peaks identified in each lot of bulk chemical were associated with dipropylene glycol. All GC/MS spectra were consistent with the literature spectra for the three diastereomers of dipropylene glycol (*Wiley Mass Spectral Database*; *Kirk-Othmer*; 1980). GC/IR analyses confirmed the presence of the major functional groups and the chemical bonding expected for the diastereomers. The diastereomer ratios were determined to be 35:52:13 (lot 0365) and 29:53:18 (lot 10626DN) 1,1′-oxybis(2-propanol): 2-(2-hydroxypropoxy)-1-propanol: 2,2′-oxybis(1-propanol). Early purity analyses using GC, without the benefit of chiral column separations, resolved fewer peaks, but the peaks in all analyses were consistent with the structure of dipropylene glycol diastereomers and their enantiomers.

Accelerated stability studies of the bulk chemical were performed by the analytical chemistry laboratories using GC. These studies indicated that dipropylene glycol was stable as a bulk chemical for 2 weeks when stored protected from light at temperatures up to 60° C. The stability of lot 10626DN was monitored by the analytical

chemistry laboratory after approximately 18 months storage at room temperature using GC. No degradation of the bulk chemical was detected. To ensure stability, the bulk chemical was stored at room temperature, protected from light, in amber glass containers. Stability was monitored by the study laboratories during the 3-month and 2-year studies by GC. No degradation of the bulk chemical was detected.

Preparation and Analysis of Dose Formulations

The dose formulations used during the 2-week and 3-month studies were prepared at least every 2 weeks by mixing dipropylene glycol with deionized water (Table I2). Dose formulations were stored in carboys, protected from light, at room temperature for up to 2 weeks. Dose formulations used during the 2-year studies were prepared every 7 to 12 weeks by mixing dipropylene glycol with tap water (Table I2). Dose formulations were stored in stainless steel drums at room temperature.

Stability studies of a 0.8 mg/mL dipropylene glycol formulation (lot 0365) were conducted by the analytical chemistry laboratory using GC. Stability was confirmed for up to four weeks for dose formulations stored in sealed septum vials protected from light at 5° C or room temperature. Stability was also confirmed for up to 96 hours for dose formulations stored exposed to light in drinking water bottles fitted with Teflon®-lined septa and sipper tubes at room temperature.

Stability studies of a 2.5 mg/mL dipropylene glycol formulation (lot 10626DN) were conducted by the analytical chemistry laboratory using GC. Stability was confirmed for up to 32 days for dose formulations stored frozen, refrigerated, or at room temperature in sealed vials protected from light. Stability was also confirmed for dose formulations stored up to seven days exposed to light in drinking water bottles fitted with Teflon® cap liners and stainless steel sipper tubes at room temperature.

Periodic analyses of the dose formulations were conducted by the study laboratories using GC. During the 2-week studies, the dose formulations were analyzed twice (Table I3). Of the dose formulations analyzed, all 10 for rats and mice were within 10% of the target concentrations; of the animal room samples analyzed, all 20 were within 10% of the target concentrations. During the 3-month studies, the dose formulations were analyzed at the beginning, midpoint, and end of the studies; animal room samples of these dose formulations were also analyzed (Table I4). Of the dose formulations analyzed, all 30 samples for rats and mice were within 10% of the target concentrations; of the animal room samples analyzed, all 30 samples for rats and mice were within 10% of the target concentrations. During the 2-year studies, the dose formulations were analyzed approximately every nine weeks (Table I5). Of the dose formulations analyzed, all 33 dose formulations for rats and mice were within 10% of the target concentrations. Animal room samples were also analyzed periodically; 11 of 12 samples for rats and all for mice were within 10% of the target concentrations.

2-Week Studies

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Taconic Farms (Germantown, NY). On receipt, the rats and mice were 5 weeks old. Animals were quarantined for 13 (rats) or 14 (mice) days and were 7 weeks old on the first day of the studies. Groups of five male and five female rats and mice were exposed to 0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm dipropylene glycol in deionized drinking water. Feed and water were available *ad libitum*. Rats were housed five per cage, and mice were housed individually. Clinical findings were recorded daily. Water consumption was measured over a 24-hour period on days 5, 6 (mice), 7 (rats), and 10. The animals were weighed initially, on day 8, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 1.

Necropsies were performed on all rats and mice. The right kidney and liver were weighed. Histopathologic examinations were performed on all 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 dipropylene glycol 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 Farms (Germantown, NY). On receipt, the rats and mice were approximately 5 weeks old. Animals were quarantined for 11 or 12 (rats) or 13 or 14 (mice) days and were 6 (male rats) or 7 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. At the end of the studies, serologic analyses were performed on five male and five female control rats and mice using the protocols of the NTP Sentinel Animal Program (Appendix L).

Groups of 10 male and 10 female core study rats and mice and groups of 10 male and 10 female clinical pathology study rats were exposed to 0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm dipropylene glycol in deionized drinking water for 13 (mice) or 14 (rats) weeks. Feed and water were available *ad libitum*. Rats were housed five per cage, and mice were housed individually. Clinical findings were recorded weekly for core study rats and mice, and water consumption was measured over a 24-hour period once weekly. Core study animals were weighed initially, on day 8, weekly thereafter, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 1.

Blood was collected for hematology and clinical chemistry analyses from clinical pathology study rats on days 3 and 22 and from core study rats at study termination. At all time points, the rats were anesthetized with carbon dioxide and blood was collected from the retroorbital sinus. Blood for hematology determinations was placed in tubes containing EDTA as the anticolagulant. Automated hematocrit, erythrocyte, leukocyte and platelet counts, and hemoglobin concentration were determined using a Contraves 801 hematology analyzer (Contraves, Zürich, Switzerland). Differential leukocyte counts and erythrocyte and platelet morphologies were determined microscopically from blood smears stained with a modified Wright-Giemsa stain on a Hema-Tek® slide stainer (Miles Laboratory, Ames Division, Elkhart, IN). A Miller disc was used to determine reticulocyte counts from smears prepared with blood stained with new methylene blue. For clinical chemistry analyses, blood samples were placed into serum separator tubes. Serum chemistry parameters were determined using a Hitachi 737® or Hitachi 704® (bile acid concentrations and sorbitol dehydrogenase activities) chemistry analyzer (Boehringer Mannheim, Indianapolis, IN) with reagents provided by the manufacturer, except those for bile acid and sorbitol dehydrogenase determinations were provided by Sigma Chemical Co. (St. Louis, MO). The hematology and clinical chemistry parameters measured are listed in Table 1.

At the end of the 3-month studies, samples were collected for sperm count and motility and vaginal cytology evaluations from 10 male and 10 female core study rats and mice exposed to 0, 5,000, 20,000, or 80,000 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.

Necropsies were performed on all core study animals. The right kidney and liver 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. Complete histopathologic examinations were performed on core study animals in the control and 80,000 ppm groups. The liver of rats and mice, the adrenal gland, bone, kidney, nose, preputial gland, and testes of rats, and the spleen of male mice 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 0, 2,500 (rats only), 10,000, 20,000 (mice only), or 40,000 ppm dipropylene in drinking water for 104 or 105 weeks.

Source and Specification of Animals

Male and female F344/N rats and $B6C3F_1$ mice were obtained from Taconic Laboratory Animals and Services (Germantown, NY) for use in the 2-year studies. Rats were quarantined for 11 or 12 days and mice for 12 or 13 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 L).

Animal Maintenance

Male rats were housed two or three per cage, female rats and mice were housed five per cage, and male mice were housed individually. Feed and water were available *ad libitum*. Water consumption was measured over a 7-day period at 4-week intervals, beginning the first week of the study. Cages were changed once (male mice) or twice weekly; cages and racks were rotated every 2 weeks. Further details of animal maintenance are given in Table 1. Information on feed composition and contaminants is provided in Appendix K.

Clinical Examinations and Pathology

All animals were observed twice daily. Clinical findings were recorded on day 36, at 4-week intervals thereafter, and at the end of the studies. Body weights were recorded initially, on days 8 and 36, at 4-week intervals thereafter, and at necropsy.

Complete necropsies and microscopic examinations were performed on all 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. 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 nose of male and female rats; the adrenal gland, forestomach, kidney, liver, parathyroid gland, and pituitary gland of male rats; the liver of male and female mice; and the forestomach of female mice.

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).

TABLE 1
Experimental Design and Materials and Methods in the Drinking Water Studies of Dipropylene Glycol

2-Week Studies	3-Month Studies	2-Year Studies
Study Laboratory		
Arthur D. Little, Inc. (Cambridge, MA)	Arthur D. Little, Inc. (Cambridge, MA)	Battelle Columbus Operations (Columbus, OH)
Strain and Species		
F344/N rats $B6C3F_1$ mice	F344/N rats $B6C3F_1$ mice	F344/N rats $B6C3F_1$ mice
Animal Source		
Taconic Farms (Germantown, NY)	Taconic Farms (Germantown, NY)	Taconic Laboratory Animals and Services (Germantown, NY)
Time Held Before Studies		
Rats: 13 days Mice: 14 days	Rats: 11 days (males) or 12 days (females) Mice: 13 days (females) or 14 days (males)	Rats: 11 days (males) or 12 days (females) Mice: 12 days (females) or 13 days (males)
Average Age When Studies Began		
7 weeks	6 (male rats) or 7 weeks	6 weeks
Date of First Exposure		
Rats: March 21, 1990 Mice: March 22, 1990	Rats: July 9 (males) or 10 (females), 1990 Mice: July 11 (females) or 12 (males), 1990	Rats: March 31 (males) or April 1 (females), 1997 Mice: March 18 (females) or 19 (males), 1997
Duration of Exposure		
15 days	Rats: 14 weeks Mice: 13 weeks	Rats: 105 weeks Mice: 104 or 105 weeks
Date of Last Exposure and Necropsy		
Rats: April 4, 1990 Mice: April 5, 1990	Rats: October 11 or 12, 1990 Mice: October 9 or 10, 1990	Rats: March 29 or 30, 1999 (males) and March 30 or April 1, 1999 (females) Mice: March 17-19 (males) or 15-17 (females), 1999
Average Age at Necropsy		
9 weeks	20 weeks	Rats: 109 or 110 weeks Mice: 110 weeks
Size of Study Groups		
5 males and 5 females	10 males and 10 females	50 males and 50 females
Method of Distribution		
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		
Rats: 5 Mice: 1	Rats: 5 Mice: 1	Rats: 2 or 3 (males) or 5 (females) Mice: 1 (males) or 5 (females)
Method of Animal Identification		
Tail tattoo	Tail tattoo	Tail tattoo

TABLE 1
Experimental Design and Materials and Methods in the Drinking Water Studies of Dipropylene Glycol

2-Week Studies	3-Month Studies	2-Year Studies
Diet		
NIH-07 open formula pelleted diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*, changed weekly	Same as 2-week studies	Irradiated NTP-2000 open formula pelleted diet (Zeigler Brothers, Gardners, PA), available *ad libitum*, changed weekly
Water		
Charcoal-filtered deionized water via amber glass bottles with plastic Teflon®-lined caps and stainless steel sipper tubes, available *ad libitum* and changed twice weekly	Same as 2-week studies	Tap water (Columbus municipal supply) via amber glass bottles with plastic Teflon®-lined caps and stainless steel sipper tubes, available *ad libitum* and changed once weekly (male mice) or twice weekly
Cages		
Solid-bottom polycarbonate (rats: Lab Products, Inc., Maywood, NJ; mice: Allentown Caging, Allentown, NJ), changed twice weekly (rats) or once weekly (mice)	Same as 2-week studies	Solid-bottom polycarbonate (Lab Products, Inc., Maywood, NJ), changed once weekly (male mice) or twice weekly
Bedding		
Hardwood chips (Northeastern Products, Corp., Warrensburg, NY), changed twice weekly (rats) or once weekly (mice)	Same as 2-week studies	Sani-Chips® (P.J. Murphy Forest Products Corp., Montville, NJ), changed once weekly (male mice) or twice weekly
Cage Filters		
Reemay® spun-bounded polyester (Allentown Caging, Allentown, NJ), changed every 2 weeks	Same as 2-week studies	DuPont 2024 spun-bonded polyester (Snow Filtration Co., Cincinnati, OH), changed every 2 weeks
Racks		
Stainless steel (Allentown Caging, Allentown, NJ), changed every 2 weeks	Same as 2-week studies	Stainless steel (Lab Products, Inc., Maywood, NJ), changed and rotated every 2 weeks
Animal Room Environment		
Temperature: 72° ± 3° F Relative humidity: 50% ± 15% Room fluorescent light: 12 hours/day Room air changes: 10/hour	Temperature: 72° ± 3° F Relative humidity: 50% ± 15% Room fluorescent light: 12 hours/day Room air changes: 10/hour	Temperature: 72° ± 3° F Relative humidity: 50% ± 15% Room fluorescent light: 12 hours/day Room air changes: 10/hour
Exposure Concentrations		
0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm in drinking water	0, 5,000, 10,000, 20,000, 40,000, or 80,000 ppm in drinking water	Rats: 0, 2,500, 10,000, or 40,000 ppm in drinking water Mice: 0, 10,000, 20,000, or 40,000 ppm in drinking water
Type and Frequency of Observation		
Observed twice daily; animals were weighed initially, on day 8, and at the end of the studies; clinical findings were recorded daily. Water consumption was measured over a 24-hour period on days 5, 6 (mice), 7 (rats), and 10.	Observed twice daily; core study animals were weighed initially, on day 8, weekly thereafter, and at the end of the studies; clinical findings were recorded weekly. Water consumption was measured over a 24-hour period once weekly for core study animals.	Observed twice daily; animals were weighed initially, on days 8 and 36, monthly thereafter, and at the end of the studies. Clinical findings were recorded on day 36, monthly thereafter, and at the end of the studies. Water consumption was measured over a 7-day period at 4-week intervals, beginning the first week of the study.

TABLE 1
Experimental Design and Materials and Methods in the Drinking Water Studies of Dipropylene Glycol

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 the right kidney and liver.	Necropsies were performed on all core study animals. Organs weighed were the right kidney and liver.	Necropsies were performed on all animals.
Clinical Pathology		
None	Blood was collected from the retroorbital sinus of clinical pathology study rats on days 3 and 22 and from core study rats at the end of the studies for hematology and clinical chemistry analyses. ***Hematology:*** automated hematocrit; manual hematocrit; hemoglobin concentration; erythrocyte, reticulocyte, and platelet counts; erythrocyte and platelet morphology; mean cell volume; mean cell hemoglobin; mean cell hemoglobin concentration; leukocyte count and differentials ***Clinical chemistry:*** urea nitrogen, creatinine, total protein, albumin, alanine aminotransferase, alkaline phosphatase, creatine kinase, sorbitol dehydrogenase, and bile acids	None
Histopathology		
Histopathology was performed on the brain, kidney, liver, and testes and from all organs that showed evidence of gross lesions.	Complete histopathology was performed on 0 and 80,000 ppm core study animals. In addition to gross lesions and tissue masses, the following tissues were examined: adrenal gland, bone with marrow, brain, clitoral gland, esophagus, gallbladder (mice only), heart and aorta, large intestine (cecum, colon, and rectum), small intestine (duodenum, jejunum, and ileum), kidney, liver, lung and mainstem bronchi, lymph nodes (mandibular and mesenteric), 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. The liver of rats and mice, the adrenal gland, bone, kidney, nose, preputial gland, and testis of rats, and the spleen of male mice were examined to a no-effect level.	Complete histopathology was performed on all rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined: adrenal gland, bone with marrow, brain, clitoral gland, esophagus, gallbladder (mice only), heart and aorta, large intestine (cecum, colon, and rectum), small intestine (duodenum, jejunum, and ileum), kidney, larynx, liver, lung and mainstem bronchi, lymph nodes (mandibular and mesenteric), mammary gland (except male mice), 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.

TABLE 1
Experimental Design and Materials and Methods in the Drinking Water Studies of Dipropylene Glycol

2-Week Studies	3-Month Studies	2-Year Studies
Sperm Motility and Vaginal Cytology		
None	At the end of the studies, sperm samples were collected from male animals in the 0, 5,000, 20,000, and 80,000 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 up to 12 consecutive days prior to the end of the studies from females exposed to 0, 5,000, 20,000, or 80,000 ppm for vaginal cytology evaluations. The percentage of time spent in the various estrous cycle stages and estrous cycle length were evaluated.	None

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 or missing 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, A4, B1, B4, C1, C4, D1, and D4 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, body weight, hematology, and clinical chemistry data were analyzed with the parametric multiple comparison procedures of Dunnett (1955) and Williams (1971, 1972). Spermatid and epididymal spermatozoal data, which have typically skewed distributions, were analyzed using the nonparametric multiple comparison methods of Shirley (1977) 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.

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 and fat than the NIH-07 diet previously used in toxicity and carcinogenicity studies (Rao, 1996, 1997). The NTP historical database for studies that use the NTP-2000 diet contains all 16 studies (15 for male rats) completed up to the present. Based on the extensive NTP historical database established for the NIH-07 diet, route of administration was not considered to be a significant variable for spontaneous neoplasms for the vast majority of sites. Thus, in general, the historical database will include studies with various routes of administration. For certain types of neoplasms where variations have been observed depending on route of administration, only studies with similar routes of administration will be used 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 dipropylene glycol was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium*. The protocol for this study 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.

RESULTS

RATS

2-WEEK STUDY

All rats survived to the end of the study (Table 2). The final mean body weights and body weight gains of males and females exposed to 80,000 ppm were significantly less than those of the controls. Water consumption by exposed and control groups was generally similar; some measurements were inaccurate due to leaking water bottles. Drinking water concentrations of 5,000, 10,000, 20,000, 40,000, or 80,000 ppm resulted in average daily doses of approximately 635, 1,450, 2,650, 5,850, or 13,000 mg dipropylene glycol/kg body weight to males and 850, 1,670, 2,860, 5,420, or 11,100 mg/kg to females. Hypoactivity, piloerection, and perinasal staining (males only) were observed in some 80,000 ppm rats.

Liver and kidney weights of males and females generally increased with increasing exposure concentration (Table G1). Absolute and relative liver weights of 20,000 ppm and greater males and 40,000 and

TABLE 2
Survival, Body Weights, and Water Consumption of Rats in the 2-Week Drinking Water Study of Dipropylene Glycol

Concentration (ppm)	Survival[a]	Mean Body Weight[b] (g) Initial	Final	Change	Final Weight Relative to Controls (%)	Water Consumption[c] Day 7	Day 10
Male							
0	5/5	133 ± 3	198 ± 5	66 ± 2		21.4	21.4
5,000	5/5	130 ± 2	196 ± 3	66 ± 2	99	20.0	—[d]
10,000	5/5	128 ± 3	197 ± 4	69 ± 1	99	21.6	22.6
20,000	5/5	131 ± 4	199 ± 5	69 ± 1	99	23.4	19.4
40,000	5/5	128 ± 4	192 ± 4	64 ± 2	97	19.4	18.2
80,000	5/5	133 ± 3	158 ± 2**	24 ± 2**	79	20.0	22.8
Female							
0	5/5	107 ± 2	140 ± 2	33 ± 1		16.0	16.4
5,000	5/5	109 ± 3	142 ± 2	33 ± 1	102	—[d]	19.2
10,000	5/5	108 ± 2	142 ± 2	34 ± 2	102	18.2	16.8
20,000	5/5	107 ± 2	142 ± 2	35 ± 4	102	16.4	14.6
40,000	5/5	106 ± 3	136 ± 3	30 ± 1	97	14.0	13.4
80,000	5/5	106 ± 2	120 ± 3**	13 ± 1**	86	14.0	13.4

** Significantly different (P≤0.01) from the control group by Williams' or 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.
[c] Water consumption is expressed as grams per animal per day. Due to leaking bottles on day 5, water consumption was measured on day 7.
[d] Leaking bottles observed; data not included

80,000 ppm females were significantly greater than those of the controls. Absolute and relative kidney weights of 40,000 and 80,000 ppm males and relative kidney weights of 40,000 and 80,000 ppm females were significantly greater than those of the controls.

Microscopically, minimal focal fatty change was observed in the livers of some males exposed to 20,000 ppm or greater (0 ppm, 0/5, 5,000 ppm, 0/5; 10,000 ppm, 0/5; 20,000 ppm, 1/5; 40,000 ppm, 2/5; 80,000 ppm, 5/5). Fatty change consisted of multiple small, round, clear spaces within the cytoplasm of midzonal hepatocytes.

Exposure Concentration Selection Rationale: Based on the absence of evidence of significant toxicity and some recovery of body weight decreases in 80,000 ppm males and females during the second week of the study, the exposure concentrations selected for the 3-month drinking water study in rats were the same as those used for the 2-week study (0, 5,000, 10,000, 20,000, 40,000, and 80,000 ppm).

3-Month Study

All rats survived to the end of the study (Table 3). The final mean body weights and body weight gains of all exposed groups of males and 20,000 ppm or greater females were significantly less than those of the controls; the decreases were greatest in the 80,000 ppm groups. The final mean body weights for the 80,000 ppm males and females were 47% and 16% less than those of the controls, respectively. Water consumption by 80,000 ppm rats was significantly less than that by controls during the first week of the study; however, water consumption by 80,000 ppm rats increased during the second week of the study (data not presented) and was greater than that by controls for the remainder of the study. Drinking water concentrations of 5,000, 10,000, 20,000, 40,000, or 80,000 ppm resulted in average daily doses of approximately 425, 890, 1,840, 3,890, or 12,800 mg/kg to males and 460, 920, 1,690, 3,340, or 8,950 mg/kg to females. All 80,000 ppm males were hypoactive and had poor hair coats throughout most of the study, and some 80,000 ppm males and females excreted pale feces.

The hematology and clinical chemistry data for rats in the 3-month toxicity study of dipropylene glycol are listed in Table F1, and selected data are presented in Table 4. In exposed males, a minimal increase in the erythron, evidenced by increases (less than 10%) in hemoglobin concentrations and/or hematocrit values, occurred on days 3 and 22. Minimal increases in erythrocyte counts occurred in exposed males on day 3. The erythron increase occurred primarily in the 80,000 ppm group, but was also present in the 20,000 and 40,000 ppm groups. The erythron increase was transient and was accompanied by an exposure concentration-related increase in serum albumin and total protein concentrations, suggesting that these findings may have been related to dehydration. Initial decreased water intake in 10,000 ppm or greater males was consistent with an early, transient increase in the erythron and serum protein concentrations in exposed male rats.

Table 3
Survival, Body Weights, and Water Consumption of Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

Concentration (ppm)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Week 1	Week 13
Male							
0	10/10	121 ± 3	345 ± 7	225 ± 6		19.7	26.4
5,000	10/10	118 ± 3	319 ± 10*	201 ± 7*	92	20.2	28.4
10,000	10/10	118 ± 3	329 ± 4*	210 ± 5*	95	16.5	27.3
20,000	10/10	121 ± 3	323 ± 4*	202 ± 4**	94	17.3	23.4
40,000	10/10	121 ± 3	324 ± 5*	203 ± 5**	94	16.8	20.7
80,000	10/10	123 ± 3	184 ± 6**	60 ± 5**	53	12.1	32.2
Female							
0	10/10	103 ± 3	196 ± 3	93 ± 3		15.1	12.8
5,000	10/10	103 ± 2	194 ± 3	91 ± 2	99	14.7	13.6
10,000	10/10	102 ± 2	199 ± 3	98 ± 3	102	13.2	12.8
20,000	10/10	102 ± 2	188 ± 2*	86 ± 2*	96	12.6	11.9
40,000	10/10	104 ± 2	187 ± 2*	82 ± 2**	95	12.6	11.8
80,000	10/10	104 ± 2	165 ± 2**	62 ± 2**	84	8.2	16.4

* Significantly different ($P \leq 0.05$) from the control group by Williams' 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.
[c] Water consumption is expressed as grams per animal per day.

TABLE 4
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Male						
Hematology						
n						
Day 3	10	10	10	10	10	10
Day 22	10	9	9	10	8	10
Week 14	10	10	10	10	10	10
Automated hematocrit (%)						
Day 3	43.0 ± 0.6	43.4 ± 0.5	44.7 ± 0.9	45.1 ± 0.6	45.3 ± 1.1	46.3 ± 0.9**
Day 22	49.5 ± 0.5	49.2 ± 0.5	48.8 ± 0.5	50.3 ± 0.3	50.6 ± 0.3	51.6 ± 0.4**
Week 14	49.3 ± 0.8	48.7 ± 0.4	47.3 ± 0.6	45.0 ± 0.6**	45.7 ± 0.5**	51.3 ± 0.5
Manual hematocrit (%)						
Day 3	45.0 ± 0.6	44.9 ± 0.7	46.9 ± 1.0	46.4 ± 0.7	47.6 ± 1.0*	47.8 ± 0.6*
Day 22	47.3 ± 0.4	47.4 ± 0.6[b]	47.4 ± 0.6	48.4 ± 0.3	48.6 ± 0.2[c]	50.0 ± 0.3**
Week 14	48.6 ± 0.5	48.9 ± 0.3	47.2 ± 0.4	45.3 ± 0.6**	46.3 ± 0.4**	51.5 ± 0.4**
Hemoglobin (g/dL)						
Day 3	14.8 ± 0.2	15.0 ± 0.2	15.1 ± 0.3	15.3 ± 0.1	15.5 ± 0.3*	15.9 ± 0.2**
Day 22	16.1 ± 0.2	16.3 ± 0.1	15.9 ± 0.1	16.3 ± 0.1	16.5 ± 0.1	17.5 ± 0.1**
Week 14	16.4 ± 0.3	16.5 ± 0.1	15.8 ± 0.2	15.2 ± 0.2**	15.3 ± 0.2**	18.0 ± 0.2**
Erythrocytes (10^6/μL)						
Day 3	7.13 ± 0.06	7.22 ± 0.10	7.37 ± 0.12	7.40 ± 0.08*	7.36 ± 0.18	7.60 ± 0.09**
Day 22	8.18 ± 0.09	8.21 ± 0.06	7.97 ± 0.09	8.12 ± 0.08	7.95 ± 0.07	8.38 ± 0.07
Week 14	9.10 ± 0.13	8.94 ± 0.04	8.63 ± 0.10**	8.38 ± 0.11**	8.22 ± 0.09**	8.44 ± 0.11**
Reticulocytes (10^6/μL)						
Day 3	0.33 ± 0.01	0.33 ± 0.03	0.40 ± 0.03	0.32 ± 0.04	0.28 ± 0.02	0.37 ± 0.04
Day 22	0.19 ± 0.02	0.13 ± 0.02	0.22 ± 0.04	0.18 ± 0.02	0.19 ± 0.03	0.12 ± 0.01
Week 14	0.30 ± 0.04	0.28 ± 0.03	0.38 ± 0.03	0.33 ± 0.02	0.40 ± 0.04	0.21 ± 0.02
Mean cell volume (fL)						
Day 3	60.3 ± 0.4	60.2 ± 0.3	60.6 ± 0.5	61.0 ± 0.4	61.6 ± 0.4	60.8 ± 0.6
Day 22	60.6 ± 0.5	60.0 ± 0.5	61.3 ± 0.6	62.0 ± 0.5*	63.6 ± 0.4**	61.6 ± 0.4**
Week 14	54.1 ± 0.2	54.5 ± 0.3	54.8 ± 0.2	53.6 ± 0.3	55.6 ± 0.2**	60.9 ± 0.5**
Mean cell hemoglobin (pg)						
Day 3	20.7 ± 0.1	20.8 ± 0.1	20.5 ± 0.2	20.7 ± 0.1	21.1 ± 0.1	20.9 ± 0.1
Day 22	19.7 ± 0.1	19.9 ± 0.1	20.0 ± 0.2	20.1 ± 0.1*	20.7 ± 0.2**	20.9 ± 0.1**
Week 14	18.0 ± 0.2	18.5 ± 0.1	18.3 ± 0.1	18.1 ± 0.1	18.6 ± 0.1*	21.3 ± 0.2**
Mean cell hemoglobin concentration (g/dL)						
Day 3	34.4 ± 0.2	34.5 ± 0.2	33.8 ± 0.2	34.0 ± 0.2	34.3 ± 0.2	34.4 ± 0.4
Day 22	32.5 ± 0.3	33.1 ± 0.2	32.7 ± 0.3	32.5 ± 0.1	32.6 ± 0.2	34.0 ± 0.2**
Week 14	33.4 ± 0.3	33.9 ± 0.21	33.5 ± 0.2	33.8 ± 0.2	33.4 ± 0.1	34.9 ± 0.2**

TABLE 4
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Male (continued)						
Clinical Chemistry						
n						
Day 3	10	10	10	10	10	10
Day 22	10	10	9	10	9	10
Week 14	9	10	10	9	10	10
Albumin (g/dL)						
Day 3	4.1 ± 0.0	4.2 ± 0.1	4.2 ± 0.1	4.2 ± 0.1	4.3 ± 0.0	4.6 ± 0.2**
Day 22	4.7 ± 0.0	4.8 ± 0.1	4.8 ± 0.0	4.9 ± 0.1*	5.1 ± 0.1**	5.6 ± 0.1**
Week 14	5.2 ± 0.1	5.5 ± 0.1	5.6 ± 0.1	5.5 ± 0.1	5.6 ± 0.1	4.6 ± 0.2*
Total protein (g/dL)						
Day 3	5.5 ± 0.1	5.6 ± 0.1	5.6 ± 0.7	5.7 ± 0.1	5.8 ± 0.1	5.9 ± 0.1**
Day 22	5.9 ± 0.1	6.0 ± 0.1	6.1 ± 0.1	6.3 ± 0.1*	6.4 ± 0.1**	6.4 ± 0.1**
Week 14	7.1 ± 0.1	7.3 ± 0.1	7.6 ± 0.1	7.7 ± 0.2*	7.7 ± 0.1*	6.1 ± 0.1**
Alanine aminotransferase (IU/L)						
Day 3	46 ± 2	48 ± 2	49 ± 3	44 ± 2	41 ± 1	37 ± 2**
Day 22	43 ± 2	42 ± 1	42 ± 1	38 ± 1	45 ± 2	100 ± 7**
Week 14	78 ± 6	86 ± 7	77 ± 7	92 ± 13	158 ± 13**	116 ± 6**
Sorbitol dehydrogenase (IU/L)						
Day 3	16 ± 1	16 ± 1	17 ± 2	14 ± 1	15 ± 0	13 ± 1
Day 22	18 ± 2	17 ± 1	15 ± 2	19 ± 1	19 ± 1	20 ± 2
Week 14	24 ± 1	22 ± 1	22 ± 2	27 ± 4	46 ± 3**	38 ± 3**
Bile acids (µmol/L)						
Day 3	27.1 ± 6.8	30.8 ± 5.4	25.1 ± 4.6	23.6 ± 2.3	15.9 ± 3.1	11.6 ± 2.3*
Day 22	9.9 ± 3.8	12.3 ± 2.7	18.7 ± 3.3	10.9 ± 2.8	12.2 ± 2.8	12.4 ± 1.8
Week 14	3.8 ± 1.3	11.9 ± 2.7*	17.2 ± 3.6*	33.9 ± 10.1*	68.4 ± 17.2**	35.9 ± 5.4**
Creatinine (mg/dL)						
Day 3	0.56 ± 0.02	0.56 ± 0.02	0.60 ± 0.02	0.69 ± 0.01**	1.12 ± 0.04**	1.46 ± 0.05**
Day 22	0.53 ± 0.02	0.55 ± 0.02	0.56 ± 0.02	0.62 ± 0.02	0.86 ± 0.08**	2.75 ± 0.10**
Week 14	0.67 ± 0.02	0.70 ± 0.02	0.71 ± 0.01	0.70 ± 0.00	0.73 ± 0.02	2.42 ± 0.17**
Urea nitrogen (mg/dL)						
Day 3	19.9 ± 0.6	19.6 ± 0.7	19.6 ± 0.7	18.7 ± 0.7	16.6 ± 0.7**	15.5 ± 0.6**
Day 22	21.3 ± 0.9	21.7 ± 0.8	21.7 ± 0.5	21.8 ± 0.6	21.9 ± 1.2	19.7 ± 1.3
Week 14	25.4 ± 1.5	27.4 ± 0.8	26.1 ± 0.8	24.6 ± 0.6	25.6 ± 0.6	20.2 ± 1.5**

TABLE 4
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Female						
Clinical Chemistry						
n						
Day 3	10	10	10	10	10	10
Day 22	10	10	10	9	10	10
Week 14	10	10	10	10	10	10
Albumin (g/dL)						
Day 3	4.1 ± 0.1	4.1 ± 0.0	4.1 ± 0.1	4.2 ± 0.1	4.3 ± 0.1**	4.5 ± 0.1**
Day 22	4.6 ± 0.1	4.8 ± 0.0	4.8 ± 0.1	4.8 ± 0.1	5.1 ± 0.1**	5.5 ± 0.1**
Week 14	4.8 ± 0.1	4.9 ± 0.1	4.9 ± 0.1	5.2 ± 0.1**	5.3 ± 0.1**	5.6 ± 0.1**
Total protein (g/dL)						
Day 3	5.5 ± 0.1	5.6 ± 0.1	5.5 ± 0.1	5.7 ± 0.1	6.0 ± 0.1**	6.3 ± 0.1**
Day 22	5.9 ± 0.1	5.9 ± 0.1	5.9 ± 0.1	6.6 ± 0.1	6.3 ± 0.1**	6.6 ± 0.1**
Week 14	6.3 ± 0.1	6.4 ± 0.1	6.6 ± 0.1*	6.7 ± 0.1**	6.9 ± 0.1**	7.3 ± 0.1**
Alanine aminotransferase (IU/L)						
Day 3	41 ± 2	41 ± 1	41 ± 2	42 ± 1	38 ± 1	30 ± 1**
Day 22	37 ± 1	38 ± 1	37 ± 1	36 ± 1	37 ± 1	68 ± 9**
Week 14	40 ± 3	45 ± 2	42 ± 2	49 ± 4	46 ± 4	55 ± 5*
Sorbitol dehydrogenase (IU/L)						
Day 3	14 ± 1[c]	14 ± 1	13 ± 0	14 ± 1[c]	13 ± 1	14 ± 1[c]
Day 22	19 ± 1	19 ± 1	19 ± 2	19 ± 2	19 ± 0	25 ± 1**
Week 14	16 ± 1	17 ± 1	16 ± 1	18 ± 1	20 ± 2	27 ± 3**
Bile acids (µmol/L)						
Day 3	19.0 ± 2.6	26.3 ± 3.9	25.3 ± 3.6	13.1 ± 4.0[c]	9.5 ± 2.2	9.8 ± 3.1[c]
Day 22	6.9 ± 2.2	13.9 ± 4.1	15.2 ± 4.8	16.0 ± 4.7	10.9 ± 2.7	9.9 ± 2.2
Week 14	8.1 ± 1.8	15.9 ± 3.1	15.4 ± 2.6	28.2 ± 5.9**	36.3 ± 9.5**	18.0 ± 2.4**
Creatinine (mg/dL)						
Day 3	0.62 ± 0.02	0.61 ± 0.02	0.60 ± 0.00	0.65 ± 0.02	0.83 ± 0.03**	0.86 ± 0.05**
Day 22	0.58 ± 0.01	0.58 ± 0.01	0.59 ± 0.01	0.59 ± 0.01	0.68 ± 0.02	1.69 ± 0.11**
Week 14	0.70 ± 0.02	0.69 ± 0.01	0.68 ± 0.01	0.70 ± 0.02	0.73 ± 0.02	1.29 ± 0.07**
Urea nitrogen (mg/dL)						
Day 3	21.8 ± 1.0	22.0 ± 0.7	20.4 ± 0.7	19.2 ± 0.6*	18.9 ± 0.8**	17.9 ± 0.6**
Day 22	23.7 ± 0.8	24.5 ± 0.5	22.7 ± 0.5	22.1 ± 0.6	22.3 ± 1.0	21.2 ± 0.8*
Week 14	21.4 ± 1.1	20.7 ± 1.0	21.0 ± 0.7[c]	21.3 ± 0.9	20.8 ± 0.7	20.3 ± 0.5

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Mean ± standard error. Statistical tests were performed on unrounded data.
[b] n=10
[c] n=9

At the end of the study, the erythron increases in exposed males were replaced with small erythron decreases (less than 10%), evidenced by decreases in hematocrit values and/or erythrocyte counts. On day 22 and at week 14, the mean cell volumes were generally increased in 20,000 ppm or greater males; for the 80,000 ppm males at week 14, the increase was approximately 13% greater than that in controls. The increased mean cell volumes occurred in the absence of increased reticulocyte counts, suggesting that the increase in red cell size was related to altered erythrocyte production/maturation rather than increased production. An increased mean cell volume may result in an increase in hematocrit values. Thus, if the erythrocytes had been of normal size, the week 14

hematocrit value for 80,000 ppm males would have been lower than those reported in this study. The decreased erythron at week 14 may have been related to a suppressed erythropoiesis and, possibly, a dyserythropoiesis.

Transient exposure concentration-related increases in total leukocyte counts occurred in the male rats on day 3. The increase was attributed to increased lymphocyte counts and suggests that exposure resulted in transiently altered peripheral distribution of lymphocytes.

In female rats, there were no erythron or leukon alterations attributed to dipropylene glycol exposure. Exposure concentration-related increases in serum albumin and total protein concentrations occurred throughout the study. While the reason for the difference between the male and female hematological response was unknown, the increased serum albumin concentration was consistent with dehydration.

Dipropylene glycol exposure generally resulted in increases in serum alanine aminotransferase and sorbitol dehydrogenase activities and/or total bile acid concentrations in males and females on day 22 and at week 14. Biochemical alterations indicating hepatic injury or altered hepatic metabolism occurred primarily in 20,000 ppm or greater males and females.

There were increases in serum creatinine concentrations throughout the study in various exposed groups of males and females. The 80,000 ppm males had the most dramatic increase with creatinine concentrations that, depending on the time point, were approximately 2.5- to 5-fold greater than those in the controls. Along with serum urea nitrogen concentration, serum creatinine is used as a marker 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. There was microscopic evidence of kidney lesions that may have influenced the serum creatinine values, but the lesions were of minimal to mild severity and serum urea nitrogen concentrations were unaffected or decreased. There also was evidence of dehydration that could have influenced serum creatinine values. While there was evidence of hepatic injury or altered metabolism that may have affected serum urea nitrogen levels, it seems unlikely that dehydration resulting in a 2- to 5-fold increase in creatinine concentration would have had no effect on serum urea nitrogen concentration. Additionally, serum creatinine depends on muscle mass. At week 14, the 80,000 ppm males weighed approximately 50% of the control weight, so their serum creatinine concentrations should have been lower than the control values; their serum creatinine concentrations were approximately 3.5 times higher and urea nitrogen was slightly decreased. It has been demonstrated that numerous compounds, dubbed noncreatinine chromagens, 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 creatinine analysis resulting in erroneously high values.

To investigate the possibility of direct analytical method interference, dipropylene glycol was mixed with rat serum (final concentrations of 0.75 M, 1.8 mM, 0.18 mM, and 0.018 mM) and the mixtures were analyzed for creatinine concentration. Assuming uniform tissue distribution, a 1.8 mM blood concentration of dipropylene glycol was theorized for the 80,000 ppm animals. The addition of dipropylene glycol to rat serum, however, did not result in any alteration of creatinine concentration (data not shown). Thus, the parent compound did not interfere with the creatinine values. The biological significance of the increased serum creatinine was unknown.

Exposure to 10,000 ppm or greater caused significant increases in absolute and relative liver weights of males and females compared to those of the controls (Table G2). Concentrations of 40,000 ppm in males and 80,000 ppm in males and females caused significant increases in absolute kidney weights. Relative kidney weights of males and females generally increased with increasing exposure concentration; exposure to 20,000 ppm or greater in males and 40,000 ppm or greater in females caused significant increases in relative kidney weights.

The left testis, cauda epididymis, and epididymis weights; motility of epididymal spermatozoa; epididymal sperm counts per cauda; and spermatid heads per gram testis of 80,000 ppm males were significantly decreased (Table H1). No significant differences were noted in estrous cycle parameters between exposed and control females (Table H2).

At necropsy, all 80,000 ppm males were thin and had a noticeable lack of mesenteric fat. One or more foci and/or generalized discoloration were noted in the livers of eight males and three females exposed to 80,000 ppm.

Minimal to mild hypertrophy of the adrenal cortex occurred in all exposed groups of rats (Table 5).

TABLE 5
Incidences of Selected Nonneoplastic Lesions in Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Male						
Adrenal Cortex[a]	10	10	10	10	10	10
Hypertrophy[b]	0	7** (1.3)[c]	5* (1.0)	6** (1.0)	6** (1.5)	10** (2.2)
Liver	10	2	10	10	10	10
Atypical Focus, Multiple	0	0	0	0	0	8** (3.1)
Fatty Change	0	0	0	9** (1.0)	10** (2.2)	10** (2.8)
Kidney	10	10	10	10	10	10
Renal Tubule, Casts, Protein	0	0	3 (1.0)	4* (1.0)	10** (1.3)	10** (1.8)
Infiltration Cellular, Lymphocyte	1 (1.0)	1 (1.0)	1 (1.0)	2 (1.0)	6* (1.0)	4 (1.0)
Nose	10	0	0	0	10	10
Olfactory Epithelium, Degeneration, Focal	0				0	10** (3.1)
Testes	10	0	0	0	10	10
Atrophy	0				0	10** (3.3)
Epididymis	10	0	0	0	0	10
Hypospermia	0					6** (3.3)
Preputial Gland	10	0	0	0	10	10
Atrophy	0				0	5* (2.0)
Seminal Vesicle	10	0	0	0	0	10
Cellular Depletion	0					2 (2.5)
Female						
Adrenal Cortex	10	10	10	10	10	10
Hypertrophy	0	8** (1.3)	10** (1.6)	10** (1.4)	10** (1.7)	9** (1.1)
Liver	10	0	1	3	10	10
Atypical Focus	0		0	0	0	1 (2.0)
Fatty Change	0		0	0	0	10** (2.0)
Kidney	10	10	10	10	10	10
Renal Tubule, Casts, Protein	0	0	0	0	0	8** (1.0)
Renal Tubule, Regeneration	0	0	0	0	0	4* (1.0)
Nose	10	0	0	0	10	10
Olfactory Epithelium, Degeneration, Focal	0				0	10** (3.1)

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

Hypertrophy consisted of focal enlargement of cells in the zona fasciculata and zona reticularis. The cytoplasmic appearance of affected cells varied from homogenous to foamy to slightly vacuolated. The biological significance of this change is uncertain and may possibly be related to treatment; however, the incidence was not dose related.

In male rats exposed to 80,000 ppm, the incidence of foci of hepatocellular alteration, classified histologically as atypical hepatocellular foci, was significantly increased (Table 5). One 80,000 ppm female had an atypical hepatocellular focus. There were significant increases in the incidences of fatty change in 20,000 ppm or greater males and 80,000 ppm females; the severities of fatty change in males increased with increasing exposure concentration.

The finding of foci of hepatocellular alteration in this study was unusual. Spontaneous foci of hepatocellular alteration are seldom observed in age-matched controls in subchronic studies, in contrast to the high numbers of spontaneous foci observed in 15- to 24-month old rats in 2-year studies. In addition, the microscopic morphology of these foci differed somewhat from typical altered hepatocellular foci. Atypical hepatocellular foci were single or multiple variably sized discrete lesions that were mostly subcapsular (Plates 1, 2, and 3). They were well-demarcated from the surrounding unaffected hepatic parenchyma by the more deeply eosinophilic tinctorial quality of the affected hepatocytes. These foci were atypical in that several were expanded by one or more variably sized cystic spaces that contained varying amounts of blood. A thin fibrous capsule partially surrounded expanded foci and the larger cystic spaces within them. Focal compression of hepatocytes surrounding foci expanded by larger cystic spaces was also evident. While the typical lobular organization of the hepatocytes was generally evident, there were small focal areas within the foci in which the lobular pattern was not discernable. Scattered hepatocytes had cytoplasmic and nuclear pleomorphism, and low numbers of mitotic figures were evident. Fatty change characterized by multiple small, discrete cytoplasmic vacuoles primarily affected the centrilobular hepatocytes.

The incidences of minimal to mild renal tubule protein casts were significantly increased in 20,000 ppm or greater males and 80,000 ppm females (Table 5). The incidence of renal tubule regeneration was significantly increased in 80,000 ppm females. The incidences of minimal lymphocyte cellular infiltration were increased in male rats exposed to 40,000 ppm or 80,000 ppm. In general, these lesions were consistent with those considered early manifestations of chronic nephropathy commonly observed in aged rats in 2-year studies. However, the presence of protein casts and interstitial lymphocytic infiltration were more common manifestations of the exposure concentration-related effect in the kidney than was the presence of regenerative tubular epithelial hyperplasia. This contrasts with spontaneous nephropathy in which regeneration of the tubular epithelium is a more prominent and early manifestation of renal disease.

Moderate focal olfactory epithelial degeneration was observed in the nose of all 80,000 ppm males and females (Table 5). Degeneration affected the olfactory epithelium primarily in the dorsal meatus in Level II and, to a lesser extent, the olfactory epithelium in the ethmoid region (Level III). Large clear cytoplasmic vacuoles distorted many of the sustentacular cells in affected sites and the lamina propria appeared loose and edematous.

Chemical-related effects occurred in the genital system of 80,000 ppm males (Table 5). Male rats in the 80,000 ppm group had small testes, preputial glands, seminal vesicles, and prostate glands, and the incidences of testicular atrophy, epididymal hypospermia, preputial gland atrophy, and seminal vesicle cellular depletion were generally significantly increased. Testicular atrophy consisted of decreased numbers or almost total absence of spermatogenic and Sertoli cells in the seminiferous tubules. There was a concomitant decrease (hypospermia) or absence of spermatozoa (azoospermia) within the epididymis. Preputial gland atrophy consisted of decreases in the number and size of the acini.

Although the prostate glands and spleens of 80,000 ppm males were abnormally small, microscopic changes were not observed in these organs. The small sizes were considered to have resulted from the substantial body weight losses in this group.

Exposure Concentration Selection Rationale: Based on the markedly decreased body weights in males and females and the increased incidences of renal lesions and presence of atypical hepatocellular foci in males, 80,000 ppm was considered too high for use in a 2-year study. Therefore, the exposure concentrations selected

for the 2-year drinking water study were 0, 2,500, 10,000, and 40,000 ppm. Although the incidences of renal lesions were increased in 40,000 ppm males in the 3-month study, the severities were minimal, and the lesions were not considered a potential threat to the health of the rats during a 2-year study. A wider exposure concentration range (fourfold steps) was used for the 2-year study because increased absolute and relative liver weights occurred at concentrations as low as 10,000 ppm in the 3-month study.

2-YEAR STUDY

Survival

Estimates of 2-year survival probabilities for male and female rats are shown in Table 6 and in the Kaplan-Meier survival curves (Figure 1). Survival of 40,000 ppm males was significantly less than that of the control group. Survival of 40,000 ppm males declined steeply after week 58, and there were no survivors after week 98. Reduced survival was largely due to a high rate of moribund sacrifices that occurred between days 431 and 690; more than half of the sacrifices occurred between 18 and 24 months. Moribundity was probably caused by chronic nephropathy and subsequent renal insufficiency. Survival of males exposed to 2,500 or 10,000 ppm and all exposed groups of females was similar to that of the controls.

TABLE 6
Survival of Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Male				
Animals initially in study	50	50	50	50
Moribund	12	14	18	31
Natural deaths	15	9	5	19
Animals surviving to study termination	23	27	27	0
Percent probability of survival at end of study[a]	46	54	54	0
Mean survival (days)[b]	662	681	681	572
Survival analysis[c]	P<0.001	P=0.437N	P=0.507N	P<0.001
Female				
Animals initially in study	50	50	50	50
Accidental death[d]	0	0	0	1
Moribund	11	9	6	12
Natural deaths	9	10	6	6
Animals surviving to study termination	30	31	38[e]	31
Percent probability of survival at end of study	60	62	76	63
Mean survival (days)	683	685	702	692
Survival analysis	P=1.000N	P=1.000N	P=0.134N	P=0.889N

[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 control column, and the results of the life table pairwise comparisons (Cox, 1972) with the 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

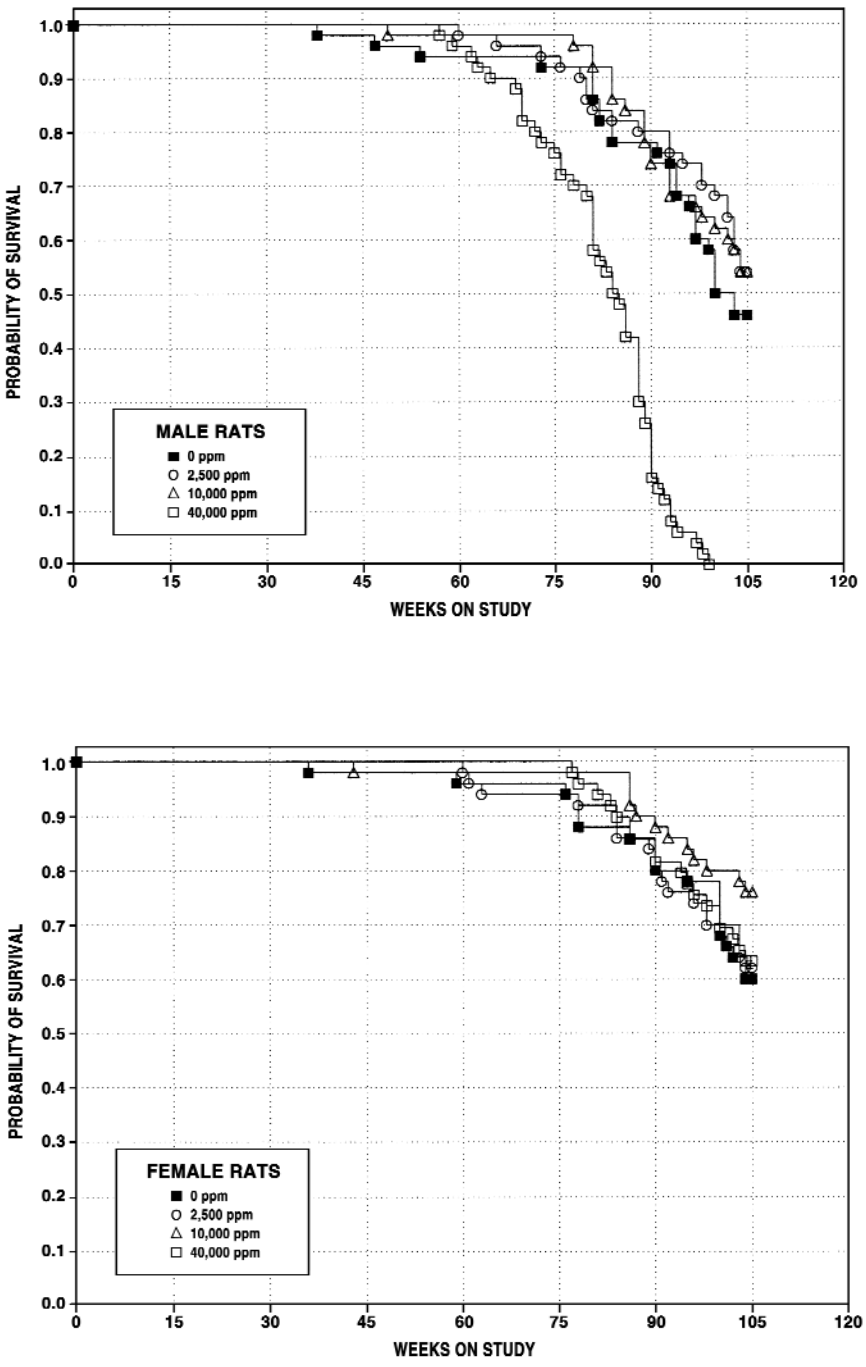


FIGURE 1
Kaplan-Meier Survival Curves for Male and Female Rats Exposed to Dipropylene Glycol in Drinking Water for 2 Years

Body Weights, Water and Compound Consumption, and Clinical Findings

Mean body weights of male and female rats exposed to 40,000 ppm were less than those of the controls throughout the study (Tables 7 and 8; Figure 2). By week 94, group mean body weights of male and female rats exposed to 40,000 ppm were 28% and 15% less than those of the controls. Mean body weights of 2,500 and 10,000 ppm males and females were similar to those of the controls throughout the study.

During the first week of the study, water consumption by males and females exposed to 40,000 ppm was less than that by controls (Tables J1 and J2); the decrease was attributed to taste aversion. However, water consumption by 40,000 ppm males increased after the first week of the study. From week 53 until the end of the study, water consumption by the 40,000 ppm males increased, resulting in an average consumption of 33.2 grams per day compared to 17.1 grams per day by the controls, suggesting renal insufficiency. Water consumption by males exposed to 2,500 or 10,000 ppm and all exposed groups of females was generally similar to that by the controls. Drinking water concentrations of 2,500, 10,000, or 40,000 ppm resulted in average daily doses of approximately 115, 470, or 3,040 mg/kg to males and 140, 530, or 2,330 mg/kg to females. Based on body weight, water consumption, and exposure concentration of dipropylene glycol, average daily doses for 2,500 and 10,000 ppm males and all exposed groups of females were proportional throughout the study. However, the average daily doses for male rats exposed to 40,000 ppm were greater than proportional and were attributed to increased water consumption.

Moribund rats were lethargic and thin, and several breathed abnormally. There were no other chemical-related clinical findings.

TABLE 7
Mean Body Weights and Survival of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		2,500 ppm			10,000 ppm			40,000 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	100	50	100	101	50	100	100	50	102	102	50
2	133	50	133	100	50	133	100	50	122	92	50
6	252	50	248	99	50	247	98	50	231	91	50
10	316	50	311	98	50	308	97	50	282	89	50
14	360	50	350	97	50	344	96	50	309	86	50
18	395	50	386	98	50	375	95	50	340	86	50
22	420	50	412	98	50	400	95	50	363	86	50
26	432	50	426	99	50	412	95	50	375	87	50
30	450	50	443	98	50	426	95	50	388	86	50
34	464	50	455	98	50	441	95	50	399	86	50
38	471	50	468	99	50	451	96	50	406	86	50
42	484	49	483	100	50	467	96	50	416	86	50
46	489	49	489	100	50	471	96	50	418	86	50
50	498	48	495	99	50	478	96	49	419	84	50
54	504	48	502	100	50	485	96	49	427	85	50
58	512	47	511	100	50	495	97	49	424	83	49
62	518	47	517	100	49	501	97	49	425	82	48
66	510	47	511	100	48	495	97	49	416	82	45
70	514	47	515	100	48	500	97	49	408	80	42
74	513	46	521	101	47	501	98	49	404	79	39
78	511	46	514	101	46	493	97	49	395	77	36
82	511	42	513	100	42	495	97	46	387	76	29
86	514	39	513	100	41	490	95	43	371	72	23
90	512	39	514	100	40	494	96	39	351	69	12
94	509	37	517	102	38	496	97	34	367	72	4
98	520	30	514	99	36	486	94	33	331	64	2
102	513	25	506	99	34	489	95	31			
Mean for weeks											
1-13	200		198	99		197	99		184	92	
14-52	446		441	99		427	96		383	86	
53-102	512		513	100		494	96		392	77	

TABLE 8
Mean Body Weights and Survival of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		2,500 ppm			10,000 ppm			40,000 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	94	50	94	100	50	93	99	50	93	99	50
2	112	50	112	101	50	112	100	50	105	94	50
6	162	50	161	99	50	160	99	50	152	94	50
10	184	50	181	98	50	180	98	50	165	90	50
14	195	50	194	100	50	193	99	50	179	92	50
18	209	50	206	99	50	204	98	50	187	90	50
22	218	50	216	99	50	215	98	50	196	90	50
26	222	50	219	99	50	219	99	50	199	89	50
30	232	50	228	98	50	227	98	50	203	88	50
34	241	50	235	98	50	236	98	50	208	87	50
38	245	49	244	100	50	245	100	50	214	87	50
42	254	49	252	99	50	255	100	50	218	86	50
46	267	49	264	99	50	263	98	49	224	84	50
50	279	49	275	98	50	275	98	49	231	83	50
54	288	49	283	98	50	285	99	49	244	85	50
58	299	49	293	98	50	295	99	49	251	84	50
62	307	48	298	97	48	305	99	49	260	85	50
66	313	48	303	97	47	310	99	49	263	84	50
70	320	48	311	97	47	317	99	49	271	85	50
74	328	48	320	98	47	324	99	49	278	85	50
78	328	46	315	96	47	325	99	49	274	84	48
82	337	44	321	95	46	328	97	49	285	85	46
86	337	44	325	96	43	332	98	49	289	86	44
90	342	42	328	96	41	336	98	45	288	84	42
94	348	40	335	96	38	342	98	43	297	85	39
98	351	39	339	97	36	348	99	41	295	84	37
102	351	33	347	99	35	352	101	40	301	86	34
Mean for weeks											
1-13	138		137	99		136	99		129	93	
14-52	236		233	99		233	99		206	87	
53-102	327		317	97		323	99		277	85	

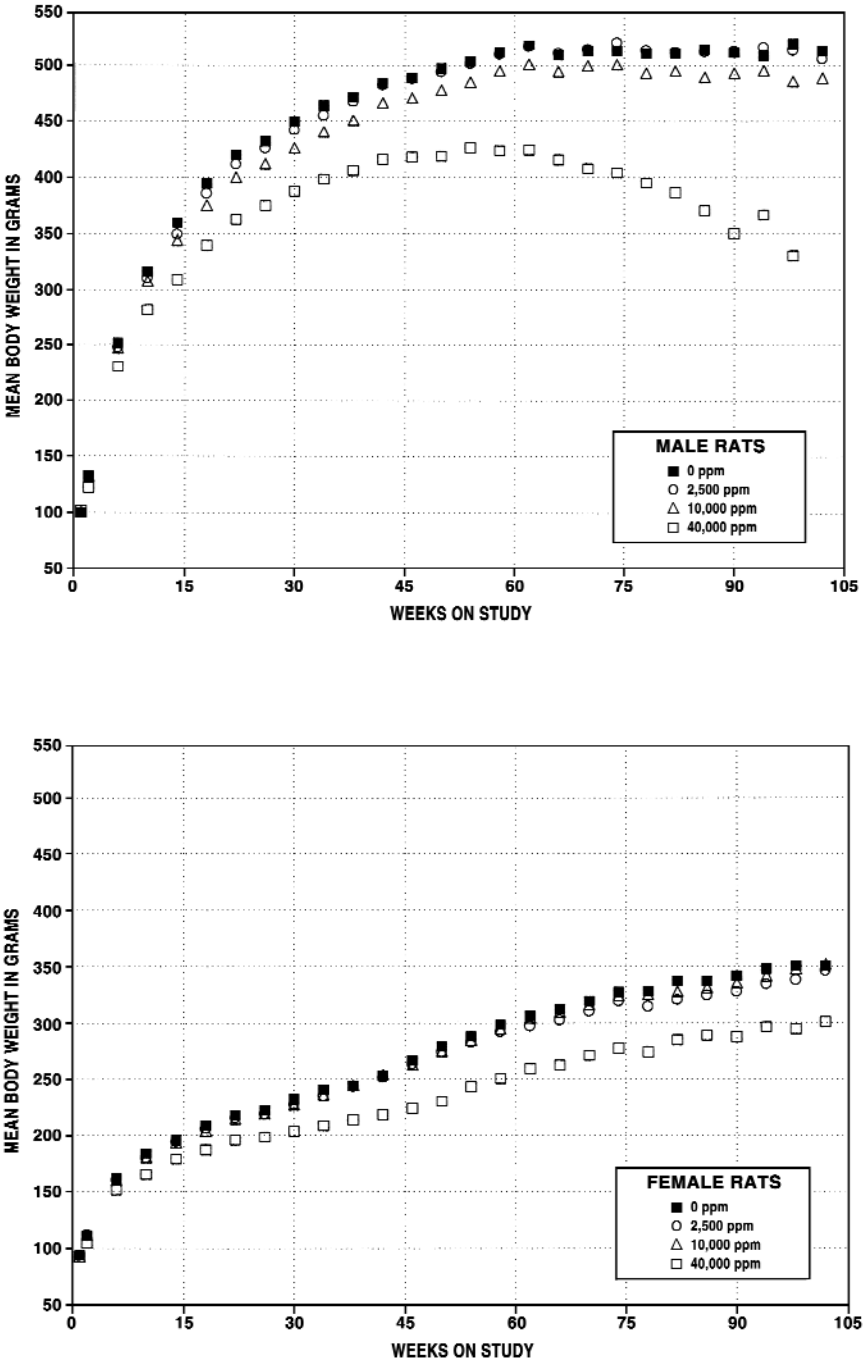


FIGURE 2
Growth Curves for Male and Female Rats Exposed to Dipropylene Glycol in Drinking Water for 2 Years

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 adrenal medulla, kidney, parathyroid gland, forestomach, heart, liver, nose, salivary gland, and mammary gland. 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.

Adrenal Medulla: The incidences of benign pheochromocytoma of the adrenal medulla in 2,500 and 10,000 ppm male rats were increased (0 ppm, 4/47; 2,500 ppm, 7/49; 10,000 ppm, 12/50; 40,000 ppm, 1/47; Table A3). The incidence in 10,000 ppm males was significantly greater than that in the controls and was at the upper end of the historical range in controls (all routes) given NTP-2000 diet [100/903 (11% ± 6%), range 3%-24%]. However, the incidence of benign or malignant pheochromocytoma (combined) in 10,000 ppm males was not significantly increased (9/47, 7/49, 13/50, 1/47; Table A3), indicating that the significant increase in the incidence of benign pheochromocytoma in 10,000 ppm males was not related to dipropylene glycol exposure. The incidence of benign or malignant pheochromocytoma (combined) in 40,000 ppm males was less than that in the controls. The biological significance of this effect is not clear but may have been related to the decreased survival in 40,000 ppm males. However, since most of the deaths occurred late in the study, mortality was unlikely to have completely masked an exposure-related effect.

Kidney: Although chronic nephropathy occurred in most male rats, including the controls, the incidences and severities in 10,000 and 40,000 ppm males were increased (Tables 9 and A4). Nephropathy was considered to be the cause of the debilitation that resulted in early moribund sacrifice of many 40,000 ppm males. Nephropathy is a common spontaneous age-related lesion in F344/N rats, particularly males, and occurs in virtually all male rats in NTP 2-year studies. Exacerbation of nephropathy is frequently observed as a treatment-related effect and is manifested as an increase in severity. The incidences of transitional epithelial hyperplasia in 10,000 and 40,000 ppm males were significantly increased. Transitional epithelial hyperplasia was generally mild in severity and consisted of focal papillary or nodular proliferation of the transitional epithelium lining the renal pelvis and was considered a component of chronic nephropathy.

The incidences of parathyroid gland hyperplasia (0 ppm, 0/45; 2,500 ppm, 4/48; 10,000 ppm, 1/49; 40,000 ppm, 5/50) and heart mineralization (0/50, 0/50, 0/50, 7/49) were significantly increased in 40,000 ppm males (Table A4). These lesions are considered to be secondary to chronic nephropathy. Chronic renal disease results in derangement of calcium metabolism and, consequently, a state of chronic hypocalcemia. Parathyroid gland hyperplasia results from sustained compensatory hyperfunction of the parathyroid gland with hypersecretion of parathyroid hormone in an effort to increase serum calcium levels. Increased intestinal absorption of calcium and mobilization of bone calcium due to high serum levels of parathyroid hormone leads to hypercalcemia and metastatic deposition of excess calcium in soft tissues such as the heart.

Nephropathy encompasses a spectrum of changes that include interstitial inflammation (chronic) and fibrosis; renal tubule degeneration, regeneration, dilatation, epithelial hyperplasia, and protein casts; renal tubule and glomerular basement membrane thickening and mineralization; and sclerotic glomeruli with dilated Bowman's spaces. In this study, the microscopic lesions of nephropathy were generally similar to the spontaneous lesions (Plates 4, 5, and 6). The lesions were characterized by interstitial fibrosis and inflammation, renal tubule epithelial necrosis, and dilated renal tubules containing protein casts. Many cortical tubules contained dense eosinophilic material, and some were surrounded by neutrophils. Many glomeruli were enlarged with thickened basement membranes and capsules. Brightly eosinophilic hyaline material was also increased in the cortical and medullary interstitium and the glomerular mesangium.

Liver: The incidences of minimal to mild focal granulomatous inflammation of the liver were significantly increased in 10,000 and 40,000 ppm males (Tables 9 and A4). Although the mean severities of granulomatous inflammation were not different from that in the controls, more animals in these groups had a severity grade of mild. The incidence of granulomatous inflammation in males exposed to 40,000 ppm was less than in males exposed to 10,000 ppm, which may have been due to early deaths. The incidence of granulomatous inflammation in female rats exposed to 10,000 ppm was slightly increased; however, this increase was not significant and

TABLE 9
Incidences of Nonneoplastic Lesions of the Kidney, Liver, and Nose in Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm		2,500 ppm		10,000 ppm		40,000 ppm	
Male								
Kidney[a]	47		50		50		48	
Nephropathy[b]	41	(2.1)[c]	47	(2.2)	50*	(2.8)	48*	(3.9)
Transitional Epithelium, Hyperplasia	1	(1.0)	3	(1.3)	7*	(1.3)	9**	(1.0)
Liver	50		50		49		48	
Inflammation, Focal, Granulomatous	22	(1.0)	26	(1.1)	42**	(1.5)	27*	(1.4)
Inflammation, Focal, Histiocytic	18	(1.1)	27	(1.2)	46**	(1.5)	48**	(2.9)
Bile Duct, Hyperplasia	34	(1.5)	38	(1.5)	43	(1.4)	44**	(1.4)
Basophilic Focus	24		35*		26		45**	
Clear Cell Focus	22		22		23		2**	
Centrilobular, Necrosis	15	(1.9)	11	(1.7)	12	(1.8)	3*	(2.7)
Nose	46		50		50		49	
Olfactory Epithelium, Atrophy	4	(1.3)	3	(1.3)	3	(1.0)	34**	(1.0)
Olfactory Epithelium, Degeneration	0		0		0		7**	(2.4)
Thrombosis	2	(3.0)	5	(2.4)	4	(2.0)	9**	(2.9)
Female								
Liver	50		50		50		49	
Inflammation, Focal, Granulomatous	30	(1.2)	33	(1.2)	37	(1.1)	26	(1.2)
Bile Duct, Hyperplasia	2	(1.5)	3	(1.0)	7	(1.1)	18**	(1.2)
Clear Cell Focus	10		16		20*		17	
Mixed Cell Focus	1		7*		7*		4	
Nose	48		48		46		49	
Olfactory Epithelium, Degeneration	0		0		0		9**	(2.4)

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

the severity was similar to that in the controls (Tables 9 and B4). Focal granulomatous inflammation was morphologically consistent with the spontaneous microgranulomatous lesions that are commonly observed in aged rats and considered to result from bacterial showering from the intestinal tract. This lesion occurred as small, randomly distributed foci predominantly composed of a mixture of small macrophages and lymphocytes with varying numbers of neutrophils (Plate 7). Larger foci tended to contain necrotic hepatocytes, minimal fibrosis, and slightly increased numbers of neutrophils.

There were exposure concentration-related increases in the incidences and severities of focal histiocytic inflammation in all exposed groups of male rats; the increases in the 10,000 and 40,000 ppm groups were significant. Focal histiocytic inflammation was also considered to be a spontaneous change, the morphology of which was clearly different from that of focal granulomatous inflammation. However, in control rats, foci of histiocytic inflammation were not as readily discernable as foci of granulomatous inflammation. The increased prominence and incidence of this lesion was considered

an exacerbation of a background change in exposed animals. Histiocytic inflammation consisted of individual or multifocal small clusters of large, irregularly oval to round histiocytic cells that were primarily portal, periportal, and centrilobular in distribution, but occasionally were randomly distributed throughout the parenchyma (Plate 8). In the controls, the histiocytes occurred primarily as scattered infiltrates of individual cells and rarely as clusters. The histiocytes had abundant foamy to lightly basophilic, homogenous to finely granular cytoplasm that frequently contained one to numerous, non-birefringent, irregularly elongate clear clefts (Plate 9). The numbers of cells with cytoplasmic clefts appeared to be prominently increased in the male rats exposed to 10,000 or 40,000 ppm. Occasionally, histocytes in the controls contained rare cleft-like structures that were not as prominent as those in treated animals. The contents of the clefts are unknown but, in the rats exposed to dipropylene glycol, some may have contained the tested material or its metabolized by-products. The cell nuclei were irregularly oval with lightly basophilic homogenous chromatin and indistinct nucleoli. Rare to frequent large syncytial cells with two or more nuclei were present; the nuclei were clustered or arranged individually around the periphery of the cell. The cytoplasm of some syncytial cells contained dense, homogenous, eosinophilic material that was usually centrally located.

The incidences of bile duct hyperplasia in 40,000 ppm males and females, basophilic foci in 2,500 and 40,000 ppm males, clear cell foci in 10,000 ppm females, and mixed cell foci in 2,500 and 10,000 ppm females were significantly greater than those in the controls. The incidences of clear cell foci and centrilobular necrosis in males exposed to 40,000 ppm were significantly less than those in the controls. The increased incidences of bile duct hyperplasia were considered related to dipropylene glycol exposure. Because the incidences of hepatocellular foci were variable and not exposure-concentration related, they were unlikely related to dipropylene glycol exposure.

Nose: The incidences of minimal to moderate olfactory epithelial atrophy in 40,000 ppm male rats and of minimal to moderate olfactory degeneration in 40,000 ppm male and female rats were significantly greater than those in the controls (Tables 9, A4, and B4). The incidence of mild to marked thrombosis in males exposed to 40,000 ppm was significantly increased. Olfactory epithelial atrophy was a segmental change that involved the dorsal meatus in Level II and occasionally Level III. The lesion was characterized by segmental disorganization and decreases in the height and number of layers of epithelial cells with occasional individual cell necrosis. Olfactory epithelial degeneration was morphologically similar to that observed in the 3-month study. Degeneration affected the olfactory epithelium primarily in the dorsal meatus in Level II and segments of the olfactory epithelium in the ethmoid region (Level III) of the nasal cavity. In affected segments of the epithelium, large clear cytoplasmic vacuoles distorted many of the sustentacular cells. The biological significance of these nasal lesions is not certain but could be related to metabolism of dipropylene glycol in the olfactory epithelium. The olfactory epithelium of rats has a moderately well-developed enzyme system that includes enzymes of the cytochrome P450 family that are capable of metabolizing xenobiotic chemicals.

Salivary Gland: The incidence of minimal to mild suppurative inflammation of the salivary gland was significantly increased in 40,000 ppm males [0 ppm, 0/49; 2,500 ppm, 1/49 (1.0); 10,000 ppm, 0/50; 40,000 ppm, 22/50 (1.8); Table A4]. The biological significance of this lesion is uncertain.

Mammary Gland: There was a significant decrease in the incidence of mammary gland fibroadenoma (36/50, 35/50, 30/50, 22/50) in 40,000 ppm females (Table B3). This decrease was likely associated with the decreased body weight in this exposure group, because the incidence of mammary gland fibroadenoma in female rats is significantly correlated with changes in body weight (Haseman, 1983; Rao *et al.*, 1987), and because the unusually high concurrent control value is outside the historical range for controls (all routes) given NTP-2000 diet [401/909 (42.1% ± 10.0%), range 28%-56%].

Forestomach: The incidences of forestomach ulceration (3/50, 5/50, 8/50, 10/49) and associated hyperplasia (0/50, 1/50, 3/50, 5/49) were increased in treated male rats. The biological significance of these changes in relation to exposure is uncertain.

MICE

2-WEEK STUDY

All mice survived to the end of the study (Table 10). Final mean body weights of male and female mice were similar to those of the controls. The mean body weight gain in male mice exposed to 80,000 ppm was significantly less than that of the controls. Due to leaking water bottles, water consumption measurements were considered abnormally high and nonphysiologic, particularly during the first week of the study (day 6). During the second week of the study (day 10), water consumption values for the male control mice appeared to be within normal range; however, values for the female controls continued to be somewhat higher than expected. Data during the second week of the study indicate decreased water consumption by 40,000 and 80,000 ppm males and females. Because the water consumption data were questionable, the average daily dose of dipropylene glycol for each exposure group was not calculated. Clinical findings in females exposed to 80,000 ppm included thinness, hypoactivity, and abnormal gait. There were no clinical findings in males.

Absolute and relative liver weights of male and female mice exposed to 80,000 ppm were significantly greater than those of the controls (Table G3). Relative kidney weights of 80,000 ppm females were significantly greater than those of the controls.

Minimal or mild centrilobular hepatocytomegaly was observed microscopically in the livers of 40,000 and 80,000 ppm male mice (0 ppm, 0/5; 5,000 ppm, 0/5; 10,000 ppm, 0/5; 20,000 ppm, 0/5; 40,000 ppm, 3/5;

TABLE 10
Survival, Body Weights, and Water Consumption of Mice in the 2-Week Drinking Water Study of Dipropylene Glycol

Concentration (ppm)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Day 6	Day 10
Male							
0	5/5	24.7 ± 0.4	27.9 ± 0.6	3.2 ± 0.2		12.4	4.2
5,000	5/5	24.9 ± 0.4	28.9 ± 0.4	4.0 ± 0.3	104	12.0	4.8
10,000	5/5	24.6 ± 0.5	27.9 ± 0.6	3.4 ± 0.1	100	11.4	3.8
20,000	5/5	24.7 ± 0.5	28.4 ± 0.6	3.7 ± 0.6	102	9.0	3.2
40,000	5/5	24.8 ± 0.4	27.7 ± 0.5	2.9 ± 0.3	99	9.2	2.6
80,000	5/5	25.0 ± 0.4	26.2 ± 0.6	1.2 ± 0.6**	94	11.0	2.4
Female							
0	5/5	19.8 ± 0.3	23.4 ± 0.4	3.6 ± 0.2		11.4	7.6
5,000	5/5	19.8 ± 0.5	22.9 ± 0.6	3.1 ± 0.1	98	16.5	8.2
10,000	5/5	19.8 ± 0.2	22.8 ± 0.4	3.1 ± 0.2	98	13.0	5.6
20,000	5/5	19.9 ± 0.4	23.2 ± 0.6	3.2 ± 0.4	99	18.3	9.6
40,000	5/5	19.9 ± 0.5	23.6 ± 0.5	3.8 ± 0.5	101	8.6	3.4
80,000	5/5	19.9 ± 0.4	22.8 ± 0.9	2.9 ± 0.6	97	14.3	4.2

** Significantly different ($P \leq 0.01$) from the control group by Williams' test
[a] Number of animals surviving at 2 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error.
[c] Water consumption is expressed as grams per animal per day. Due to leaking bottles on day 5, water consumption was measured on day 6.

80,000 ppm, 5/5). Hepatocellular hypertrophy often occurs in the liver following exposure to xenobiotics and most likely reflects hepatic enzyme induction or increased metabolic activity. Centrilobular cytoplasmic alteration was observed in 20,000 ppm males and 40,000 and 80,000 ppm males and females (males: 0/5, 0/5, 0/5, 3/5, 5/5, 4/5; females: 0/5, 0/5, 0/5, 0/5, 3/5, 5/5). The cytoplasm of affected hepatocytes had a homogenous eosinophilic tinctorial quality rather than the finely vacuolated or granular cytoplasmic appearance observed in the controls and may reflect hepatocellular glycogen depletion or enzyme induction.

Exposure Concentration Selection Rationale: Based on the absence of mortality or significant toxicity and similar final mean body weights in the 80,000 ppm groups compared to controls, the exposure concentrations selected for the 3-month drinking water study in mice were the same as those used in the 2-week study (0, 5,000, 10,000, 20,000, 40,000, and 80,000 ppm).

3-Month Study

Three males and one female exposed to 80,000 ppm dipropylene glycol died of apparent dehydration during the second week of the study (Table 11). One 20,000 ppm female died during week 5 of apparent hypothermia in a wet cage. Final mean body weights and body weight gains of exposed males were not significantly different from those of the controls. The final mean body weight and body weight gain of 10,000 ppm females were significantly greater than those of the controls. Water consumption by exposed males and females was generally less than that by controls during the first few weeks of the study. Decreased water consumption was less evident during the middle of the study (data not presented), but the decrease recurred in the last 2 to 3 weeks of the study. During week 12, water consumption by female controls was slightly increased, resulting in an apparent comparative decrease in water consumption by the exposed groups. Drinking water concentrations of 5,000, 10,000, 20,000, 40,000, or 80,000 ppm resulted in average daily doses of approximately 715, 1,350, 2,620, 4,790, or 11,000 mg/kg to males and 1,230, 2,140, 4,020, 7,430, or 14,700 mg/kg to females. Pale feces were observed in some 10,000 ppm or greater males and some females exposed to 5,000, 10,000, 20,000, or 80,000 ppm. Hypoactivity and dehydration were observed in 80,000 ppm mice.

Absolute liver weights of 10,000 ppm and greater males and 40,000 and 80,000 ppm females were significantly greater than those of the controls (Table G4). Relative liver weights of 40,000 and 80,000 ppm males and 80,000 ppm females were significantly greater than those of the controls. The estrous cycle of 80,000 ppm females

Table 11
Survival, Body Weights, and Water Consumption of Mice in the 3-Month Drinking Water Study of Dipropylene Glycol

Concentration (ppm)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Week 1	Week 12
Male							
0	10/10	25.4 ± 0.4	38.0 ± 0.7	12.6 ± 0.6		4.9	4.7
5,000	10/10	25.8 ± 0.3	40.7 ± 0.9	14.9 ± 0.7	107	4.4	3.9
10,000	10/10	25.8 ± 0.3	40.7 ± 0.7	15.0 ± 0.6	107	4.0	3.6
20,000	10/10	25.9 ± 0.2	39.6 ± 0.9	13.7 ± 0.7	104	3.4	4.1
40,000	10/10	25.9 ± 0.3	40.5 ± 0.9	14.6 ± 0.7	106	3.2	3.8
80,000	7/10[d]	25.1 ± 0.3	38.5 ± 0.6	13.4 ± 0.7	101	1.1	4.6
Female							
0	10/10	20.5 ± 0.2	31.7 ± 0.9	11.2 ± 0.8		6.3	7.4
5,000	10/10	20.1 ± 0.3	33.2 ± 0.9	13.0 ± 1.0	105	4.9	5.3
10,000	10/10	20.5 ± 0.3	35.5 ± 1.2*	15.0 ± 1.1*	112	4.5	5.6
20,000	9/10[e]	20.9 ± 0.2	33.8 ± 1.0	13.1 ± 1.0	107	3.2	4.9
40,000	10/10	20.1 ± 0.2	34.4 ± 0.8	14.3 ± 0.7	109	2.8	5.0
80,000	9/10[d]	19.8 ± 0.3	34.1 ± 1.0	14.3 ± 0.9	108	3.0	4.5

* Significantly different ($P \leq 0.05$) from the control group by 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.
[c] Water consumption is expressed as grams per animal per day.
[d] Week of deaths: 2
[e] Week of death: 5

was significantly longer than that of the controls (Table H4). There were no significant differences in sperm motility parameters between exposed and control males (Table H3).

Necropsy findings included small spleens in 80,000 ppm males that died early. There were significant increases in the incidences of minimal to mild centrilobular hypertrophy of the liver in 40,000 and 80,000 ppm males and 80,000 ppm females [males: 0 ppm, 0/10; 20,000 ppm, 1/1 (1.0); 40,000 ppm, 9/10 (1.0); 80,000 ppm, 7/10 (1.6); females: 0/10, 0/1, 0/10, 9/10 (1.1)]. Centrilobular hypertrophy consisted of increased size of primarily centrilobular hepatocytes, however, in some animals hypertrophic cells were observed in mid-zonal areas.

Exposure Concentration Selection Rationale: Based on increased mortality in males and females exposed to 80,000 ppm dipropylene glycol, the concentrations selected for the 2-year drinking water study in mice were 0, 10,000, 20,000, and 40,000 ppm.

2-YEAR STUDY

Survival

Estimates of 2-year survival probabilities for male and female mice are shown in Table 12 and in the Kaplan-Meier survival curves (Figure 3). Survival of male and female mice was similar to that of the controls. Four accidental deaths that occurred in the 40,000 ppm female group were attributed to hypothermia after the entire contents of a leaking water bottle spilled out into the cage.

TABLE 12
Survival of Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Male				
Animals initially in study	50	50	50	50
Missing[a]	0	0	0	1
Moribund	3	3	5	9
Natural deaths	7	8	10	6
Animals surviving to study termination	40[e]	39	35	34
Percent probability of survival at end of study[b]	80	78	70	69
Mean survival (days)[c]	704	686	700	675
Survival analysis[d]	P=0.204	P=0.921	P=0.382	P=0.292
Female				
Animals initially in study	50	50	50	50
Accidental deaths[a]	0	0	0	4
Moribund	2	1	4	6
Natural deaths	11	11	8	7
Animals surviving to study termination	37	38	38	33[e]
Percent probability of survival at end of study	74	76	76	73
Mean survival (days)	699	706	688	652
Survival analysis	P=0.702	P=0.989N	P=1.000N	P=0.873

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

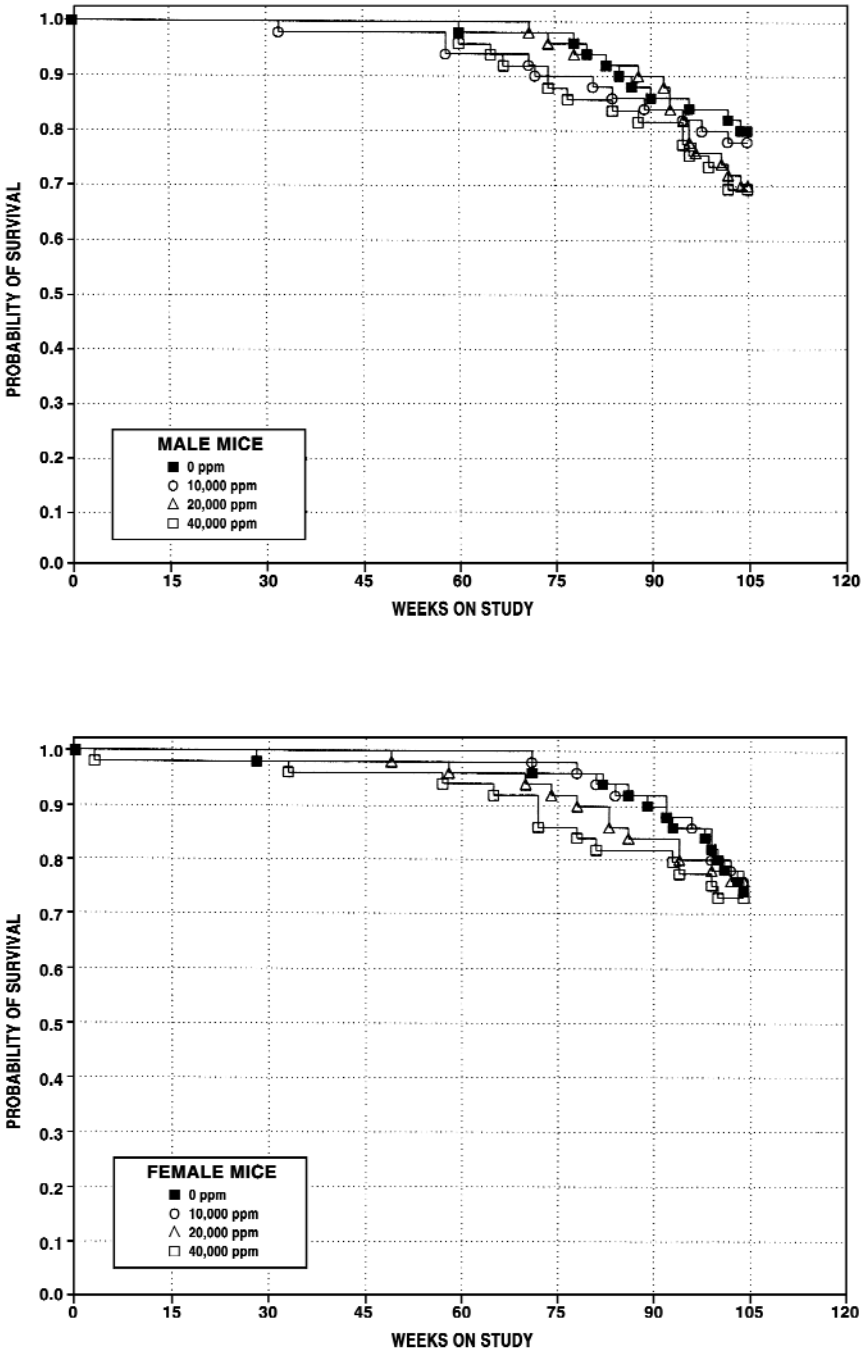


FIGURE 3
Kaplan-Meier Survival Curves for Male and Female Mice Exposed to Dipropylene Glycol in Drinking Water for 2 Years

Body Weights, Water and Compound Consumption, and Clinical Findings

Mean body weights of 40,000 ppm male mice were less than those of the controls throughout the study; mean body weights of females exposed to 40,000 ppm were less than those of the controls during the second year of the study (Figure 4; Tables 13 and 14). At study termination, mean body weights of male and female mice exposed to 40,000 ppm were approximately 23% and 14% less than those of the controls, respectively.

Water consumption by male and female mice exposed to 20,000 or 40,000 ppm was less than that by the controls during the first 2 (females) or 6 (males) weeks of the study, presumably due to taste aversion (Tables J3 and J4). However, water consumption by the 20,000 ppm males and females was similar to that by the controls by week 6 (females) or 10 (males). Water consumption by 40,000 ppm males remained less than that by the controls for the remainder of the study, whereas that by 40,000 ppm females was similar to that by the controls by week 18. Drinking water concentrations of 10,000, 20,000, or 40,000 ppm resulted in average daily doses of approximately 735, 1,220, or 2,390 mg/kg to males and 575, 1,040, or 1,950 mg/kg to females. There were no clinical findings related to dipropylene glycol exposure.

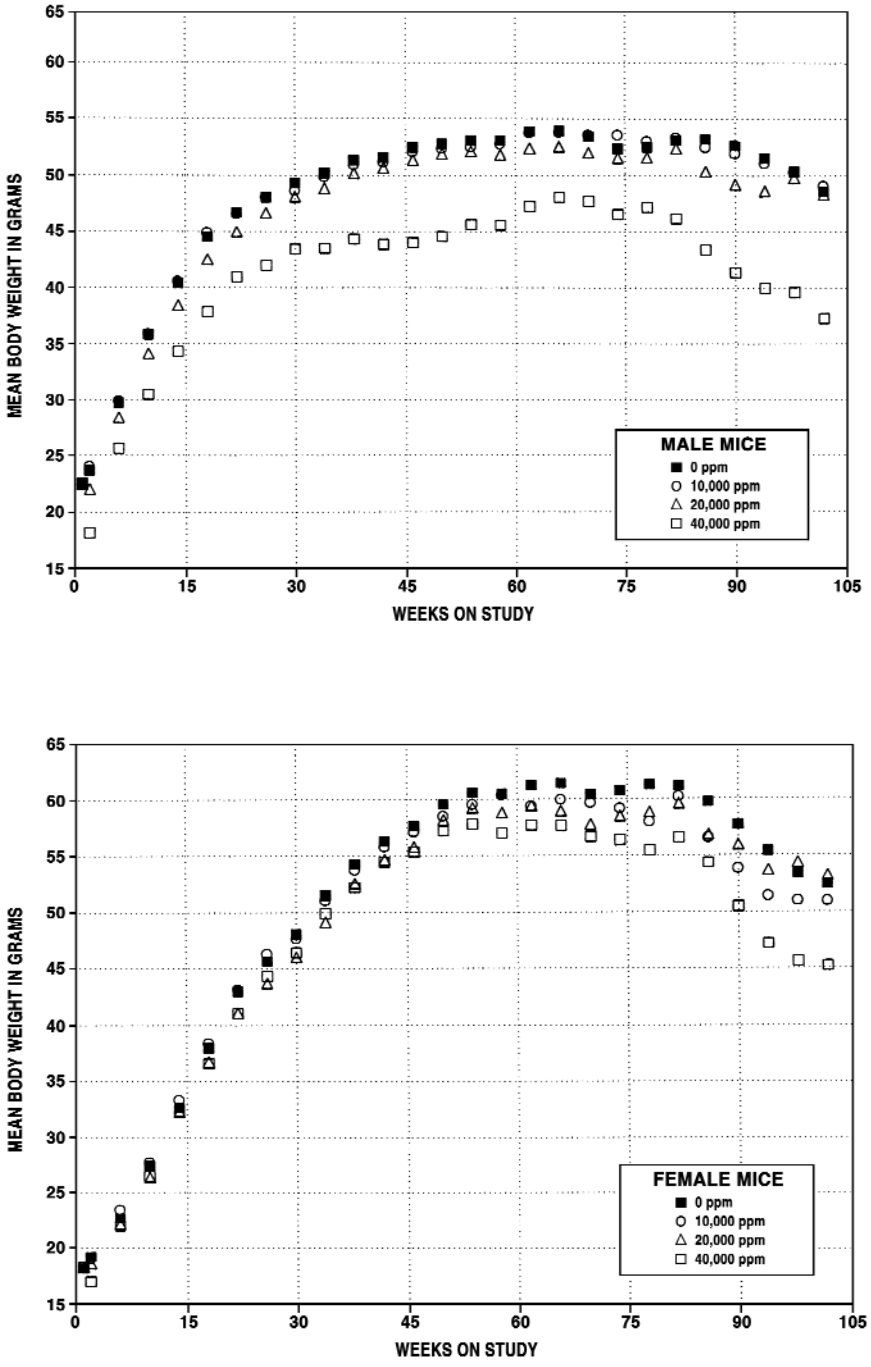


FIGURE 4
Growth Curves for Male and Female Mice Exposed to Dipropylene Glycol in Drinking Water for 2 Years

TABLE 13
Mean Body Weights and Survival of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		10,000 ppm			20,000 ppm			40,000 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	22.5	50	22.6	100	50	22.5	100	50	22.6	100	50
2	23.7	50	24.1	102	50	22.1	93	50	18.2	77	50
6	29.7	50	29.9	101	50	28.5	96	50	25.6	86	50
10	35.8	50	35.9	100	50	34.2	96	50	30.5	85	50
14	40.4	50	40.6	101	50	38.5	95	50	34.3	85	50
18	44.6	50	45.0	101	50	42.5	95	50	37.9	85	50
22	46.7	50	46.6	100	50	45.0	96	50	41.0	88	50
26	48.1	50	48.1	100	50	46.7	97	50	42.0	87	50
30	49.3	50	48.7	99	50	48.2	98	50	43.5	88	50
34	50.2	50	49.9	99	49	48.9	97	50	43.5	87	50
38	51.3	50	50.9	99	49	50.2	98	50	44.3	86	50
42	51.6	50	51.2	99	49	50.6	98	50	43.9	85	50
46	52.5	50	52.1	99	49	51.4	98	50	44.0	84	50
50	52.8	50	52.4	99	49	51.9	98	50	44.6	85	50
54	53.1	50	52.5	99	49	52.1	98	50	45.7	86	49
58	53.1	50	52.8	99	49	51.8	98	50	45.6	86	49
62	53.9	49	53.8	100	47	52.4	97	50	47.3	88	47
66	53.9	49	53.8	100	47	52.5	97	50	48.1	89	46
70	53.5	49	53.6	100	47	52.0	97	50	47.8	89	45
74	52.4	49	53.6	102	45	51.6	99	49	46.6	89	45
78	52.5	49	53.0	101	45	51.6	98	48	47.2	90	42
82	53.1	47	53.4	101	44	52.4	99	47	46.2	87	42
86	53.2	45	52.5	99	43	50.4	95	46	43.4	82	41
90	52.6	44	52.0	99	42	49.3	94	45	41.4	79	40
94	51.5	43	51.1	99	42	48.7	95	42	40.0	78	40
98	50.3	42	50.4	100	41	49.8	99	38	39.6	79	37
102	48.6	42	49.1	101	40	48.4	100	37	37.3	77	36
Mean for weeks											
1-13	27.9		28.1	101		26.8	96		24.2	87	
14-52	48.8		48.6	100		47.4	97		41.9	86	
53-102	52.4		52.4	100		51.0	97		44.3	85	

TABLE 14
Mean Body Weights and Survival of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		10,000 ppm			20,000 ppm			40,000 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	18.2	50	18.3	101	50	18.3	101	50	18.3	101	50
2	19.2	50	19.1	100	50	18.6	97	50	17.0	89	50
6	22.7	50	23.5	104	50	22.2	98	50	22.0	97	49
10	27.4	50	27.8	102	50	26.4	96	50	26.4	96	49
14	32.7	50	33.3	102	50	32.3	99	50	32.4	99	49
18	38.0	50	38.4	101	50	36.8	97	50	36.6	96	49
22	43.0	50	43.2	101	50	41.1	96	50	41.1	96	49
26	45.7	50	46.3	101	50	43.7	96	50	44.3	97	49
30	48.1	49	47.7	99	50	46.1	96	50	46.5	97	49
34	51.5	49	51.1	99	50	49.2	96	50	49.9	97	48
38	54.3	49	53.8	99	50	52.6	97	50	52.2	96	48
42	56.3	49	55.9	99	50	54.7	97	50	54.5	97	48
46	57.7	49	57.2	99	50	55.8	97	50	55.4	96	48
50	59.6	49	58.5	98	50	58.2	98	49	57.2	96	48
54	60.6	49	59.6	98	50	59.2	98	49	57.8	95	48
58	60.5	49	60.4	100	50	58.8	97	49	57.0	94	47
62	61.3	49	59.4	97	50	59.5	97	48	57.7	94	47
66	61.4	49	60.0	98	50	59.0	96	48	57.7	94	46
70	60.4	49	59.7	99	50	57.8	96	47	56.7	94	46
74	60.7	48	59.2	98	49	58.5	96	47	56.4	93	43
78	61.3	48	58.0	95	49	58.8	96	46	55.5	91	43
82	61.1	48	60.2	99	47	59.6	98	45	56.6	93	37
86	59.7	47	56.6	95	46	56.9	95	43	54.4	91	37
90	57.7	45	53.9	93	46	55.9	97	42	50.5	88	37
94	55.4	43	51.4	93	44	53.7	97	42	47.2	85	36
98	53.4	43	51.0	96	43	54.4	102	40	45.7	86	35
102	52.4	39	51.0	97	40	53.2	102	38	45.2	86	33
Mean for weeks											
1-13	21.9		22.2	101		21.4	98		20.9	95	
14-52	48.7		48.5	100		47.1	97		47.0	97	
53-102	58.9		57.0	97		57.3	97		53.7	91	

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, lung, and adrenal gland. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group are presented in Appendix C for male mice and Appendix D for female mice.

Liver: The incidence of hepatocellular adenoma in male mice exposed to 40,000 ppm was significantly less than that in the controls (0 ppm, 17/50; 10,000 ppm, 17/50; 20,000 ppm, 20/50; 40,000 ppm, 6/49; Table C3) and was at the lower end of the historical range for controls (all routes) given the NTP-2000 diet [290/959 (32% ± 10%), range 12%-46%]. However, the incidence of hepatocellular carcinoma was slightly increased in the 40,000 ppm males (14/50, 10/50, 11/50, 16/49) such that the overall incidences of hepatocellular adenoma or carcinoma (combined) were similar in all groups (29/50, 25/50, 28/50, 21/49). The decrease in the incidence of hepatocellular adenoma was most likely related to the decrease in body weight observed in the 40,000 ppm group; the incidences of hepatocellular neoplasms in mice have been shown to be correlated with changes in body weight (Haseman, 1983; Rao *et al.*, 1987).

Lung: The incidences of alveolar/bronchiolar adenoma (3/50, 9/50, 5/50, 4/49) and alveolar/bronchiolar adenoma or carcinoma (combined) (6/50, 14/50, 13/50, 8/49) in 10,000 ppm males were greater than those in the controls (Table C3). The incidences were not exposure concentration related and were within the historical ranges for controls (all routes) given NTP-2000 diet [alveolar/bronchiolar adenoma: 160/959 (17% ± 7%), range 4%-26%; alveolar/bronchiolar adenoma or carcinoma (combined): 244/959 (26% ± 10%), range 12%-44%] and were not considered to be related to dipropylene glycol exposure.

Adrenal Gland: There were exposure concentration-related decreases in the incidences of focal hyperplasia (0 ppm, 7/50; 10,000 ppm, 4/50; 20,000 ppm, 1/50; 40,000 ppm, 0/49) and focal hypertrophy (28/50, 24/50, 23/50, 15/49) of the adrenal cortex in exposed males (Table C4). The incidences of focal hyperplasia in 20,000 and 40,000 ppm males and focal hypertrophy in 40,000 ppm males were significantly less than those in the controls. The incidences of these changes occurred at a variable rate, and it is uncertain if the decreases were exposure related.

GENETIC TOXICOLOGY

Dipropylene glycol (100 to 10,000 µg/plate) was not mutagenic in *Salmonella typhimurium* strain TA97, TA98, TA100, or TA1535 with or without rat or hamster liver S9 enzymes (Table E1).

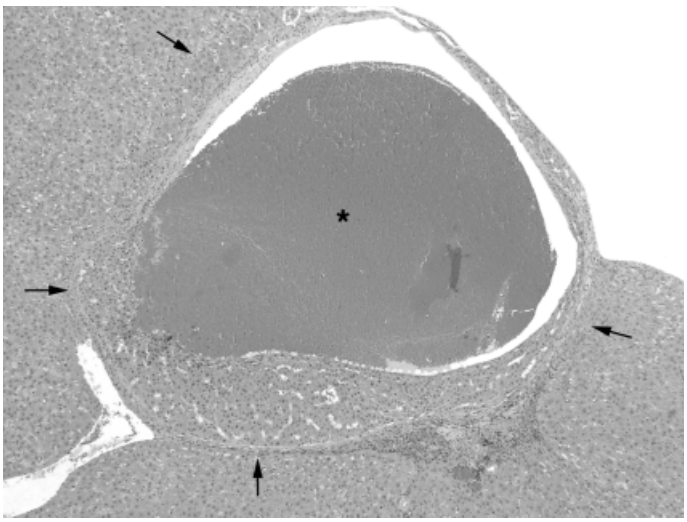


PLATE 1
Atypical hepatocellular focus (arrows) in a male rat exposed to 80,000 ppm dipropylene glycol in drinking water for 3 months. Focus is well demarcated from the surrounding hepatic parenchyma. Note large blood filled cystic space within the focus (asterisk). H&E; 4x

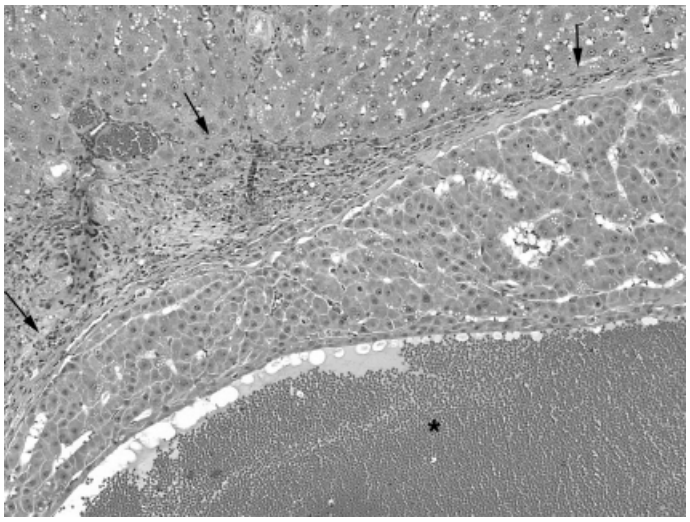


PLATE 2
Higher magnification of Plate 1. Note fibrous capsule (arrows) bordering the focus and blood filled cystic space (asterisk) within the lesion. H&E; 10x

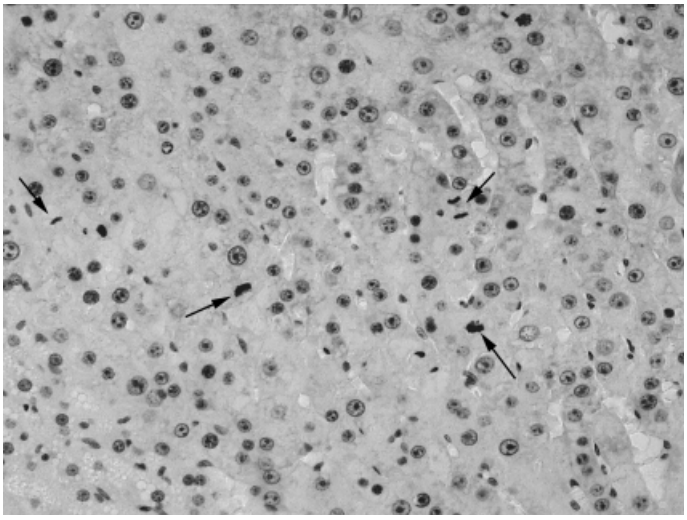


PLATE 3
Details of atypical focus of hepatocellular alteration in a male rat exposed to 80,000 ppm dipropylene glycol in drinking water for 3 months. Note mitotic figures (arrows) and variation in nuclear size. H&E; 20x

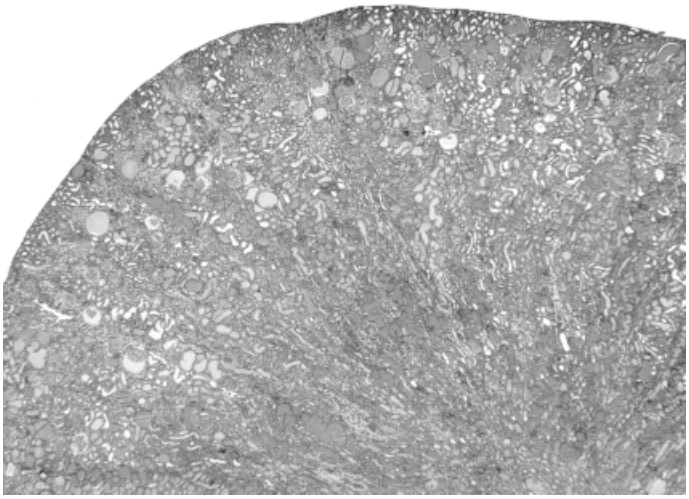


PLATE 4
Nephropathy in a male rat exposed to 40,000 ppm dipropylene glycol in drinking water for 2 years. There is generalized effacement of the renal architecture affecting cortical and medullary tubules, glomeruli and the interstitium. H&E; 4x

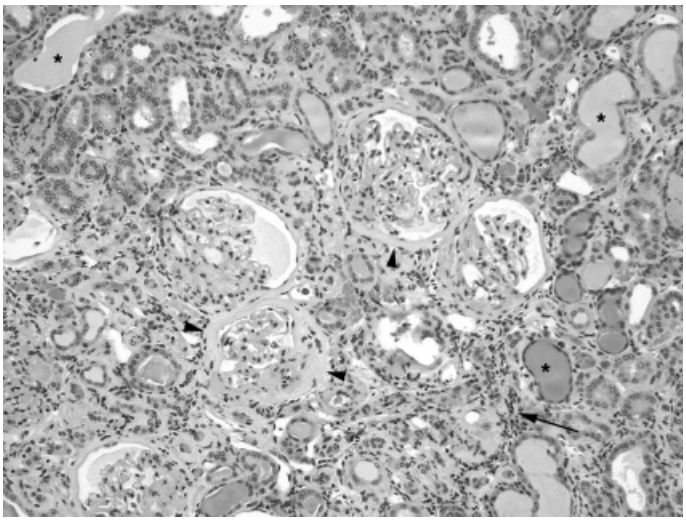


PLATE 5
Higher magnification of renal cortex in Plate 4. Note interstitial fibrosis with infiltrates of inflammatory cells (arrow), glomeruli with capsular and basement membrane thickening (arrowheads), and atrophic, dilated renal tubules (asterisks) many of which contain protein casts. H&E; 10x

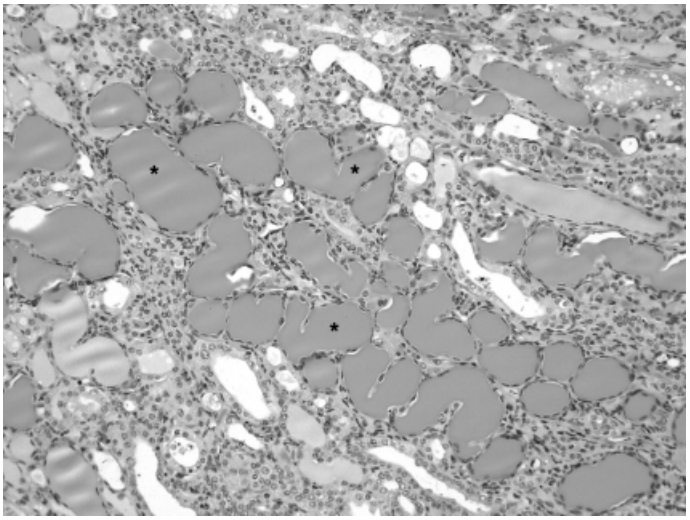


PLATE 6
Higher magnification of renal medulla in Plate 4. Note markedly dilated renal medullary tubules (asterisks) which contain protein casts. H&E; 10x

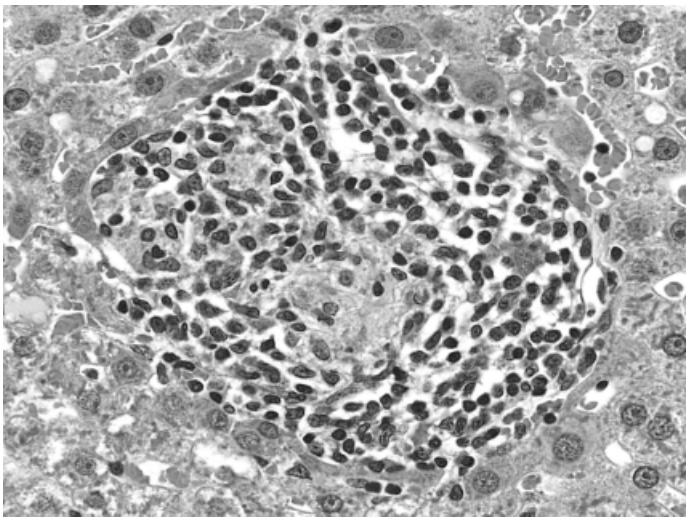


PLATE 7
Focal granulomatous inflammation in the liver of a male rat exposed to 10,000 ppm dipropylene glycol in drinking water for 2 years. The focus is composed primarily of macrophages and low numbers of lymphocytes. H&E; 40x

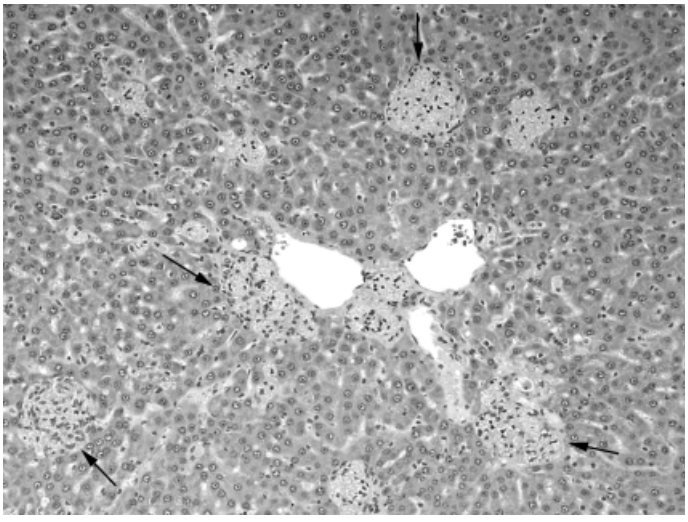


PLATE 8
Multiple randomly distributed foci of histiocytic inflammation (arrows) in the liver of a male rat exposed to 40,000 ppm dipropylene glycol in drinking water for 2 years. H&E; 20x

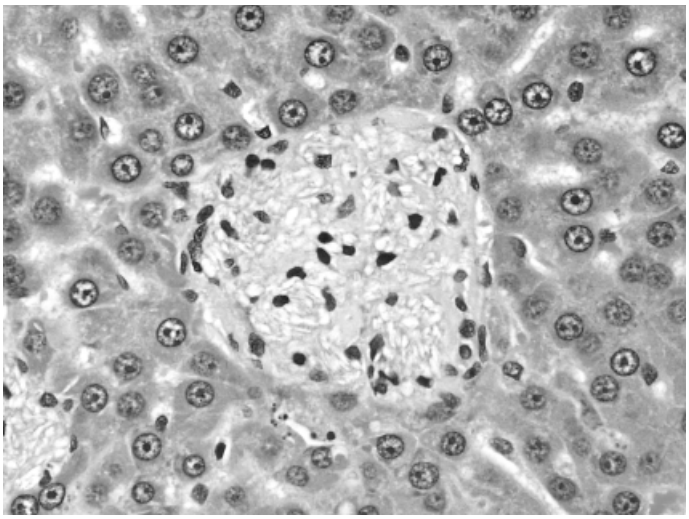


PLATE 9
Higher magnification of Plate 8. The focus is composed of clustered large macrophages that have foamy cytoplasm with numerous clear cleft-like spaces. H&E; 40×

DISCUSSION AND CONCLUSIONS

Dipropylene glycol is a component of many widely used commercial products such as antifreeze, air fresheners, cosmetic products, solvents and plastic. Toxicity and carcinogenicity studies of dipropylene glycol were performed because of suspected widespread consumer and occupational exposure based on the high production volume of dipropylene glycol.

Although consumers may be exposed to dipropylene glycol through the use of cosmetic products, the dermal route of exposure was not chosen for toxicity studies because the chemical is unlikely to be absorbed through the skin. Oral ingestion was considered to be a potentially significant route of human exposure because dipropylene glycol is approved for use as an indirect food additive in materials that are in repeated contact with food. Because dipropylene glycol was detected in drinking water supplies in United States cities (Lin *et al*., 1981), drinking water was selected as the route of exposure for the current studies.

There were no exposure-related deaths in the 2-week or 3-month rat studies. Absolute and relative kidney weights of 40,000 and 80,000 ppm males were significantly greater than those of the controls. In the 3-month rat study, early manifestations of chronic nephropathy, including the presence of renal tubule protein casts and lymphocyte infiltration, occurred in 80,000 ppm males. Absolute and relative liver weights were increased in male and female rats exposed to 10,000 ppm or greater. Hepatotoxicity in the 40,000 and 80,000 ppm groups was evident at week 14 based on elevated serum alanine aminotransferase and sorbitol dehydrogenase activities and total bile acid concentrations.

In the 3-month rat study, chemical-related effects occurred in the genital system of 80,000 ppm males. Male rats in this group had small testes, preputial glands, seminal vesicles, and prostate glands. Epididymal sperm counts and sperm motility of the 80,000 ppm males were also significantly decreased. Although the final mean body weight of 80,000 ppm males was 53% that of the controls, it is likely that the reproductive changes were caused by dipropylene glycol exposure rather than being a secondary effect of decreased body weight gain. Chapin *et al.* (1993) demonstrated that the Sprague-Dawley rat is largely resistant to adverse reproductive changes caused by body weight reductions up to 70% of control body weight. Following feed restriction in Sprague-Dawley rats for up to 17 weeks, the absolute weights of the prostate gland and seminal vesicles were decreased, but there was no decrease in the absolute weights of the testis or epididymis. There was a small decrease in the percentage of motile sperm, but there were no changes in sperm counts or morphology. Other studies have looked at more severe body weight reductions over 4 or 8 weeks, but found that testis weight was not affected until feed intake was approximately 15% to 25% of control feed levels and mean body weights were approximately 30% to 50% that of controls (Oishi *et al.*, 1979; Eng *et al.*, 1987).

Although chemical-related reproductive changes were observed in 80,000 ppm male F344/N rats in the 3-month study, dipropylene glycol was not a developmental toxicant when administered by gavage to Sprague-Dawley rats (CD®) at doses up to 5,000 mg/kg per day on days 6 through 15 of gestation or New Zealand White® rabbits at doses up to 1,200 mg/kg per day on days 6 through 19 of gestation (NTP 1992a,b). In contrast, ethylene glycol and diethylene glycol, two structurally related compounds, were reproductive toxicants in Swiss (CD-1®) mice when administered in the drinking water. Ethylene glycol at 1% (1,700 mg/kg per day) in drinking water caused a decrease in the number of litters per pair, in the mean litter size, and in live pup weight. In addition, 1% ethylene glycol induced rib, sternebrae, vertebrae, and facial bone abnormalities including cleft lip in F_1 pups (Lamb *et al.*, 1985). In a subsequent study using 1.5% ethylene glycol (2,800 mg/kg per day) in drinking water, reproductive parameters including testis weight, epididymis weight, and sperm motility were reduced in F_1 male rats (NTP, 1986). Facial structural abnormalities were also seen in this study at 1% and 1.5% ethylene glycol. The developmental toxicity of ethylene glycol was confirmed in a teratology study in rats and mice (Price *et al.*, 1985). Diethylene glycol at 3.5% (6,125 mg/kg per day) in

drinking water was a reproductive toxicant in mice based on reductions in the number of litters per pair and in the mean litter size (NTP, 1984; Williams *et al*., 1990).

In the 2-year rat study, the survival of 40,000 ppm males was significantly less than that of the control group. Increased mortality in this exposure group was not predicted by the 3-month study results. Reduced survival was largely due to a high rate of moribund sacrifices that were caused by chronic progressive nephropathy and subsequent renal insufficiency. From week 53 until the end of the study, water consumption by the 40,000 ppm males increased, resulting in an average consumption of 33.2 grams per day compared to 17.1 grams per day by the controls and suggesting renal insufficiency. Survival of 40,000 ppm males declined steeply after week 58 and may have affected the ability to detect late developing neoplasms.

Dipropylene glycol-related nonneoplastic lesions were found in the kidney, liver, and nose. There was an exposure concentration-related increase in the severity of chronic nephropathy in male rats. Male rats exposed to dipropylene glycol had an increased incidence of randomly distributed focal granulomatous and focal histiocytic inflammation in the liver. Lesions of similar morphology are recognized as common background changes in aged rats in 2-year studies. While the cause of these lesions in rats was not readily apparent, the increased incidences in this study were considered an exacerbation of background changes that may be related to dipropylene glycol administration. The presence of syncytial cells and cholesterol clefts in some of the histiocytic lesions suggest the presence of some indigestible material (possibly the test material or metabolized byproducts), which may have served as the inflammatory stimulus. Olfactory epithelial atrophy in male rats and olfactory epithelial degeneration in male and female rats may have been related to enzymatic metabolism of diproplyene glycol in the olfactory epithelium.

In the 2-week mouse study, no mortality was observed in male or female mice and final mean body weights in the exposed groups were similar to those of the controls. Therefore, the concentrations selected for the 3-month mouse study were the same as those used in the 2-week study.

In the 3-month study, three males and one female exposed to 80,000 ppm dipropylene glycol died of dehydration during the second week of the study. A dose related decrease in water consumption was observed in male and female mice during week 1 and clinical signs of dehydration were observed during week 2. Due to the increased mortality in 80,000 ppm males and females, the highest exposure concentration chosen for the 2-year studies was 40,000 ppm.

In the 2-year mouse study, no compound-related neoplasms or nonneoplastic lesions were observed in male or female mice exposed to 10,000, 20,000 or 40,000 ppm dipropylene glycol. Although minimal toxicity occurred, the 2-year mouse study was considered adequate to evaluate the toxicity and carcinogenicity of dipropylene glycol because significant body weight reductions occurred in 40,000 ppm male and female mice. Available evidence indicated that mice are less susceptible than rats to dipropylene glycol toxicity. Liver, kidney, and reproductive effects seen in rats were either absent or less severe in mice exposed to similar concentrations of dipropylene glycol in drinking water. The mechanisms responsible for this apparent species difference in toxicity are unknown.

Overall, these results suggest that even though dipropylene glycol is structurally related to ethylene glycol and diethylene glycol, it is minimally toxic to rodents. The differences in toxicity might be due to differences in metabolism. Ethylene glycol is metabolized to glycolic and glyoxylic acids resulting in acidosis; further oxidation of glyoxylic acid to oxalic acid leads to formation of insoluble calcium oxylate in the kidney causing renal failure (LaKind *et al*., 1999). Metabolism studies suggest that the ether bonds in diethylene glycol are not broken, suggesting that the parent chemical or metabolite that retains the ether bond is responsible for its toxicity (Wiener and Richardson, 1989; Mathews *et al*., 1991). The biotransformation of dipropylene glycol has not been determined in rodents. If the ether linkage of dipropylene glycol were cleaved, propylene glycol and the analogous aldehyde would be formed, and either would be further metabolized to lactic and pyruvic acids, which are normal biochemical intermediates (LaKind *et al*., 1999). Alternatively, it is likely that dipropylene glycol or metabolites with intact ether bonds are excreted in urine and are inherently less toxic than their structural analogues.

CONCLUSIONS

Under the conditions of this 2-year drinking water study, there was *no evidence of carcinogenic activity** of dipropylene glycol in male or female F344/N rats

exposed to 2,500, 10,000, or 40,000 ppm. There was *no evidence of carcinogenic activity* of dipropylene glycol in male or female B6C3F$_1$ mice exposed to 10,000, 20,000, or 40,000 ppm.

Exposure to dipropylene glycol in drinking water resulted in increased incidences and severities of nephropathy in male rats, increased incidences of focal histiocytic and focal granulomatous inflammation of the liver in male rats, increased incidences of suppurative inflammation of the salivary gland in male rats, increased incidences of bile duct hyperplasia in male and female rats, increased incidences of olfactory epithelial atrophy and thrombosis of the nose in male rats, and increased incidences of olfactory epithelial degeneration of the nose in male and female rats.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 11. A summary of the Technical Reports Review Subcommittee comments on this Technical Report appears on page 13.

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APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF DIPROPYLENE GLYCOL

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TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	12	14	18	31
Natural deaths	15	9	5	19
Survivors				
Terminal sacrifice	23	27	27	
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(41)	(49)	(48)	(43)
Polyp adenomatous		1 (2%)		
Intestine large, cecum	(38)	(46)	(47)	(35)
Intestine small, duodenum	(39)	(49)	(49)	(42)
Intestine small, jejunum	(37)	(45)	(48)	(39)
Carcinoma			1 (2%)	
Leiomyoma		1 (2%)		
Intestine small, ileum	(37)	(42)	(47)	(36)
Polyp adenomatous		1 (2%)		
Liver	(50)	(50)	(49)	(48)
Hepatocellular adenoma				1 (2%)
Sarcoma, metastatic, skin			1 (2%)	
Mesentery	(14)	(11)	(6)	(4)
Oral mucosa	(1)			(2)
Pharyngeal, squamous cell papilloma				1 (50%)
Pancreas	(44)	(49)	(50)	(47)
Adenoma		1 (2%)		1 (2%)
Carcinoma	1 (2%)			
Fibrosarcoma, metastatic, tissue NOS		1 (2%)		
Mixed tumor benign	2 (5%)			
Salivary glands	(49)	(49)	(50)	(50)
Carcinoma		1 (2%)		
Sarcoma		1 (2%)	3 (6%)	
Schwannoma malignant		2 (4%)		
Stomach, forestomach	(50)	(50)	(50)	(49)
Stomach, glandular	(46)	(49)	(50)	(48)
Tongue		(1)	(1)	
Squamous cell papilloma		1 (100%)	1 (100%)	
Cardiovascular System				
Heart	(50)	(50)	(50)	(49)
Sarcoma, metastatic, skin	1 (2%)		1 (2%)	
Schwannoma benign	2 (4%)	3 (6%)	1 (2%)	

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Endocrine System				
Adrenal cortex	(47)	(49)	(50)	(48)
Adenoma		2 (4%)		
Carcinoma				1 (2%)
Pheochromocytoma malignant, metastatic, adrenal medulla	1 (2%)			
Sarcoma, metastatic, skin	1 (2%)			
Adrenal medulla	(47)	(49)	(50)	(47)
Ganglioneuroma	1 (2%)			
Pheochromocytoma malignant	5 (11%)		2 (4%)	
Pheochromocytoma complex		1 (2%)		
Pheochromocytoma benign	4 (9%)	7 (14%)	11 (22%)	1 (2%)
Bilateral, pheochromocytoma benign			1 (2%)	
Islets, pancreatic	(44)	(48)	(50)	(47)
Adenoma	2 (5%)	3 (6%)		
Carcinoma		4 (8%)		2 (4%)
Parathyroid gland	(45)	(48)	(49)	(50)
Adenoma	1 (2%)	2 (4%)		
Pituitary gland	(47)	(49)	(50)	(49)
Pars distalis, adenoma	15 (32%)	21 (43%)	18 (36%)	7 (14%)
Pars distalis, carcinoma			1 (2%)	
Pars intermedia, adenoma		1 (2%)		
Thyroid gland	(42)	(47)	(48)	(47)
C-cell, adenoma	4 (10%)	4 (9%)	6 (13%)	
C-cell, carcinoma	2 (5%)	3 (6%)	2 (4%)	
Follicular cell, adenoma	1 (2%)	1 (2%)		
General Body System				
Peritoneum	(3)	(2)	(2)	
Tissue NOS		(1)		(1)
Fibrosarcoma		1 (100%)		
Genital System				
Epididymis	(50)	(50)	(50)	(49)
Preputial gland	(50)	(47)	(50)	(50)
Adenoma	3 (6%)	1 (2%)	3 (6%)	1 (2%)
Carcinoma	3 (6%)	1 (2%)	1 (2%)	
Sarcoma	1 (2%)			
Bilateral, carcinoma			1 (2%)	
Prostate	(48)	(50)	(50)	(50)
Adenoma	1 (2%)	1 (2%)	2 (4%)	
Hemangiosarcoma		1 (2%)		
Seminal vesicle	(43)	(48)	(49)	(46)
Testes	(50)	(50)	(50)	(50)
Bilateral, interstitial cell, adenoma	39 (78%)	41 (82%)	41 (82%)	44 (88%)
Interstitial cell, adenoma	6 (12%)	4 (8%)	2 (4%)	4 (8%)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Hematopoietic System				
Bone marrow	(46)	(48)	(50)	(48)
Pheochromocytoma malignant, metastatic, adrenal medulla	1 (2%)			
Lymph node	(18)	(14)	(21)	(9)
Deep cervical, carcinoma, metastatic, thyroid gland		1 (7%)		
Mediastinal, carcinoma, metastatic, thyroid gland		1 (7%)		
Lymph node, mandibular	(13)	(16)	(14)	(11)
Carcinoma, metastatic, Zymbal's gland		1 (6%)		
Lymph node, mesenteric	(44)	(48)	(49)	(47)
Spleen	(43)	(50)	(49)	(47)
Thymus	(39)	(48)	(43)	(41)
Thymoma benign			1 (2%)	
Integumentary System				
Mammary gland	(48)	(41)	(47)	(44)
Fibroadenoma	1 (2%)	6 (15%)	1 (2%)	
Fibroadenoma, multiple		1 (2%)		
Skin	(48)	(48)	(49)	(49)
Keratoacanthoma	1 (2%)	2 (4%)	4 (8%)	
Keratoacanthoma, multiple		1 (2%)		
Squamous cell carcinoma		2 (4%)		
Sebaceous gland, adenoma	1 (2%)	1 (2%)		
Subcutaneous tissue, fibroma	6 (13%)	5 (10%)	3 (6%)	1 (2%)
Subcutaneous tissue, lipoma	1 (2%)	1 (2%)		
Subcutaneous tissue, sarcoma	3 (6%)		5 (10%)	
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma			1 (2%)	1 (2%)
Nervous System				
Brain	(50)	(50)	(50)	(50)
Granular cell tumor benign		1 (2%)		
Sarcoma	1 (2%)			
Peripheral nerve	(1)			(1)
Sarcoma	1 (100%)			
Spinal cord			(1)	(1)
Osteosarcoma, metastatic, bone			1 (100%)	

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Respiratory System				
Lung	(50)	(49)	(50)	(49)
Alveolar/bronchiolar adenoma	2 (4%)	3 (6%)		1 (2%)
Alveolar/bronchiolar carcinoma	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Carcinoma, metastatic, pituitary gland			1 (2%)	
Carcinoma, metastatic, preputial gland	1 (2%)			
Carcinoma, metastatic, thyroid gland		1 (2%)		
Carcinoma, metastatic, Zymbal's gland	1 (2%)	1 (2%)		
Osteosarcoma, metastatic, bone			1 (2%)	1 (2%)
Pheochromocytoma malignant, metastatic, adrenal medulla	1 (2%)			
Sarcoma, metastatic, salivary glands		1 (2%)	1 (2%)	
Sarcoma, metastatic, skin	1 (2%)		1 (2%)	
Squamous cell carcinoma, metastatic, oral mucosa				1 (2%)
Nose	(46)	(50)	(50)	(49)
Trachea	(43)	(49)	(49)	(47)
Special Senses System				
Zymbal's gland	(3)	(2)	(1)	(1)
Carcinoma	3 (100%)	2 (100%)	1 (100%)	1 (100%)
Urinary System				
Kidney	(47)	(50)	(50)	(48)
Lipoma			2 (4%)	
Sarcoma, metastatic, skin	1 (2%)			
Stromal nephroma	1 (2%)			
Renal tubule, adenoma	1 (2%)			
Renal tubule, carcinoma		1 (2%)		
Urinary bladder	(46)	(50)	(49)	(49)
Sarcoma	1 (2%)			
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Leukemia mononuclear	16 (32%)	20 (40%)	22 (44%)	5 (10%)
Lymphoma malignant	1 (2%)		1 (2%)	
Mesothelioma benign	1 (2%)			
Mesothelioma malignant	6 (12%)	2 (4%)	2 (4%)	2 (4%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	49	50	50	50
Total primary neoplasms	141	161	142	75
Total animals with benign neoplasms	47	49	50	49
Total benign neoplasms	95	117	97	62
Total animals with malignant neoplasms	35	34	35	12
Total malignant neoplasms	46	44	45	13
Total animals with metastatic neoplasms	3	4	4	2
Total metastatic neoplasms	9	7	7	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 A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	261	232	361	511	516	564	565	586	596	682	684	636	645	653	663	655	667	673	676	679	687	697	699	698	698
Carcass ID Number	03707	03010	00112	01155	01177	04744	01400	01101	01166	10949	04003	02303	03505	00353	01919	04227	02727	02244	03343	01518	03232	01414	02848	04606	04848
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	A	+	+	+	+	+	A	+	+	A	+	+	+	+	A	A	A	A	+	+	+	+
Intestine large, rectum	+	A	+	A	+	+	+	+	+	A	+	A	A	+	+	+	+	A	A	+	A	+	+	+	+
Intestine large, cecum	A	A	+	A	+	+	+	+	A	A	+	A	A	+	+	+	+	A	A	A	A	+	+	+	+
Intestine small, duodenum	A	A	+	A	+	+	+	+	A	A	+	+	A	+	+	+	+	A	A	A	A	+	+	+	+
Intestine small, jejunum	A	A	+	A	+	+	+	+	A	A	+	A	A	+	+	+	+	A	A	A	A	A	+	+	+
Intestine small, ileum	A	A	+	A	+	+	+	+	A	A	+	A	A	+	+	+	+	A	A	A	A	A	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery			+	+	+				+							+	+		+		+				+
Oral mucosa																									
Pancreas	+	+	+	A	+	+	+	+	+	A	+	A	A	+	+	+	+	A	A	+	+	+	+	+	+
Carcinoma																									
Mixed tumor benign											X												X		
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	A	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Tooth																									
Cardiovascular System																									
Blood vessel																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin				X																					
Schwannoma benign							X															X			
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	A	+	+	+	+
Pheochromocytoma malignant, metastatic, adrenal medulla																									
Sarcoma, metastatic, skin				X																					
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	A	+	+	+	+
Ganglioneuroma																									
Pheochromocytoma malignant				X																					
Pheochromocytoma benign																						X			X
Islets, pancreatic	+	+	+	A	+	+	+	+	+	A	+	A	A	+	+	+	+	A	A	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	M	+	M	+	+	+	+
Adenoma																									
Pituitary gland	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Pars distalis, adenoma										X					X	X					X			X	X
Thyroid gland	A	A	+	A	+	+	+	+	+	A	+	+	A	+	+	+	+	A	+	A	+	+	+	+	+
C-cell, adenoma								X							X				X						
C-cell, carcinoma									X																
Follicular cell, adenoma																			X						
General Body System																									
Peritoneum																			+		+				

+: 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 Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	7 1 7	7 1 8	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	
Carcass ID Number	0 2 9	0 2 6	0 0 4	0 0 5	0 0 7	0 0 8	0 2 0	0 2 1	0 2 2	0 2 5	0 3 1	0 3 8	0 3 9	0 4 1	0 4 5	0 4 6	0 4 9	0 5 0	0 0 1	0 0 2	0 1 3	0 1 3	0 3 4	0 3 6	0 4 3	0 4 7	Total Tissues/ Tumors
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Intestine large, rectum	A	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	40
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Intestine small, duodenum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	37
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	37
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery	+			+	+															+		+					14
Oral mucosa																		+									1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Carcinoma																					X						1
Mixed tumor benign																											2
Salivary glands	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Tooth								+																			1
Cardiovascular System																											
Blood vessel																					+						1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skin																											1
Schwannoma benign																											2
Endocrine System																											
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pheochromocytoma malignant, metastatic, adrenal medulla																			X								1
Sarcoma, metastatic, skin																											1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Ganglioneuroma			X																								1
Pheochromocytoma malignant	X						X			X									X								5
Pheochromocytoma benign		X																				X					4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Adenoma			X	X																							2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenoma								X																			1
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma			X	X			X		X		X					X	X			X					X		15
Thyroid gland	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
C-cell, adenoma															X												4
C-cell, carcinoma																X											2
Follicular cell, adenoma																											1
General Body System																											
Peritoneum																										+	3

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	262161	303273	376136	511145	516174	566444	576455	586681	596891	508292	588434	603666	645355	663033	665539	665424	676673	677363	677696	678999	689777	699778	699868	699868
Carcass ID Number	03707	03310	00122	01155	01177	04744	01740	01101	01616	03109	04400	02233	03535	03053	01919	04242	02727	02244	03343	01818	03232	01424	02848	00646	04048
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																X				X					
Carcinoma				X				X																	
Sarcoma																									X
Prostate	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Adenoma																			X						
Seminal vesicle	A	+	+	+	+	+	+	+	A	A	+	A	+	+	+	+	+	A	+	+	A	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma				X	X	X		X	X		X	X	X	X	X	X	X		X	X	X	X	X		
Interstitial cell, adenoma							X											X							X
Hematopoietic System																									
Bone marrow	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	A	A	+	+	+	+	+	+
Pheochromocytoma malignant, metastatic, adrenal medulla																									
Lymph node					+			+			+		+	+			+			+		+	+		+
Lymph node, mandibular	M	M	M	M	+	+	M	+	M	M	M	M	A	M	M	M	M	M	M	M	M	+	M	+	M
Lymph node, mesenteric	+	A	+	A	+	+	+	+	+	A	+	+	A	+	+	+	+	M	M	+	+	+	+	+	+
Spleen	+	A	+	A	+	+	+	+	A	A	+	A	+	+	+	+	+	A	+	+	A	+	+	+	+
Thymus	+	A	+	+	M	+	+	+	+	I	+	+	M	+	M	+	+	A	+	+	+	M	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Fibroadenoma																									
Skin	I	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Sebaceous gland, adenoma																									
Subcutaneous tissue, fibroma									X												X		X		
Subcutaneous tissue, lipoma																									
Subcutaneous tissue, sarcoma				X																		X			
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma											X														
Peripheral nerve		+																							
Sarcoma		X																							

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	7 1 7	7 1 8	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	
Carcass ID Number	0 2 9	0 2 6	0 0 4	0 0 5	0 0 7	0 0 8	0 2 0	0 2 1	0 2 2	0 2 5	0 3 1	0 3 8	0 3 9	0 4 1	0 4 5	0 4 6	0 4 9	0 5 0	0 1	0 0	0 1 2	0 1 3	0 3 4	0 3 6	0 4 3	0 4 7	Total Tissues/ Tumors
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma								X																			3
Carcinoma										X																	3
Sarcoma																											1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																											1
Seminal vesicle	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
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	X		39
Interstitial cell, adenoma						X													X	X							6
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Pheochromocytoma malignant, metastatic, adrenal medulla																			X								1
Lymph node	+					+	+		+				+			+								+		+	18
Lymph node, mandibular	+	M	M	M	M	M	+	+	M	M	M	M	+	+	M	M	M	M	+	M	M	+	M	+	M		13
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Thymus	+	M	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+		39
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	48
Fibroadenoma			X																								1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Keratoacanthoma													X														1
Sebaceous gland, adenoma																					X						1
Subcutaneous tissue, fibroma			X				X		X																		6
Subcutaneous tissue, lipoma																		X									1
Subcutaneous tissue, sarcoma		X																									3
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																											1
Peripheral nerve																											1
Sarcoma																											1

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	261	323	376	511	564	564	565	568	569	582	584	636	645	653	653	654	667	673	676	679	687	697	697	698	698
Carcass ID Number	037	030	012	015	017	044	010	011	016	009	040	023	035	003	019	042	027	024	033	018	032	014	028	006	048
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma													X												
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, preputial gland				X																					
Carcinoma, metastatic, Zymbal's gland						X																			
Pheochromocytoma malignant, metastatic, adrenal medulla																									
Sarcoma, metastatic, skin				X																					
Nose	A	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Trachea	A	A	+	A	+	+	+	+	A	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Special Senses System																									
Eye										+															
Zymbal's gland			+			+																		+	
Carcinoma			X			X																		X	
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Sarcoma, metastatic, skin				X																					
Stromal nephroma																									
Renal tubule, adenoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	A	+	A	+	+	+	+	+
Sarcoma												X													
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X		X	X					X	X			X			X		X			X
Lymphoma malignant											X														
Mesothelioma benign																									
Mesothelioma malignant									X							X			X		X				

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	7 1 7	7 1 8	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	
Carcass ID Number	0 2 9	0 2 6	0 0 4	0 0 5	0 0 7	0 0 8	0 2 0	0 2 1	0 2 2	0 2 5	0 3 1	0 3 8	0 3 9	0 4 1	0 4 5	0 4 6	0 4 9	0 5 0	0 0 1	0 0 2	0 1 3	0 3 4	0 3 6	0 3 3	0 4 4	0 4 7	Total Tissues/ Tumors
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																X											2
Alveolar/bronchiolar carcinoma																		X									1
Carcinoma, metastatic, preputial gland																											1
Carcinoma, metastatic, Zymbal's gland																											1
Pheochromocytoma malignant, metastatic, adrenal medulla																				X							1
Sarcoma, metastatic, skin																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Special Senses System																											
Eye															+												2
Zymbal's gland																											3
Carcinoma																											3
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Sarcoma, metastatic, skin																											1
Stromal nephroma																				X							1
Renal tubule, adenoma							X																				1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Sarcoma																											1
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X			X		X	X						X											X		X	16
Lymphoma malignant																											1
Mesothelioma benign																X											1
Mesothelioma malignant																X										X	6

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	4 1 7	4 5 6	5 0 5	5 2 8	5 5 0	5 5 4	5 5 8	5 6 4	5 8 6	6 1 4	6 4 9	6 4 9	6 6 1	6 8 0	6 8 4	6 9 8	7 0 9	7 1 1	7 1 6	7 1 7	7 2 1	7 2 6	7 2 8	7 2 9	7 2 9
Carcass ID Number	0 5 5	0 6 8	0 8 5	0 9 2	0 6 3	0 8 8	0 8 1	0 7 4	0 8 9	0 9 4	0 5 9	0 7 2	0 7 3	0 5 8	0 9 1	0 6 6	0 5 4	0 5 9	0 9 0	0 9 6	0 7 8	0 6 2	0 9 8	0 5 1	0 5 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp adenomatous																			X						
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+
Leiomyoma																									
Intestine small, ileum	A	+	+	+	A	A	+	+	+	+	+	+	+	A	+	+	+	+	A	A	A	+	A	+	+
Polyp adenomatous																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery						+		+			+	+			+	+							+		
Pancreas	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Fibrosarcoma, metastatic, tissue NOS				X																					
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Carcinoma																									
Sarcoma										X															
Schwannoma malignant			X						X																
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Squamous cell papilloma																									
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma benign																									X
Endocrine System																									
Adrenal cortex	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																X									
Adrenal medulla	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma complex																									
Pheochromocytoma benign																		X		X			X		
Islets, pancreatic	+	+	+	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma												X													
Carcinoma																	X								X
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Adenoma											X														
Pituitary gland	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X		X						X						X	X	X			X	X	X			
Pars intermedia, adenoma																		X							
Thyroid gland	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+
C-cell, adenoma												X						X							
C-cell, carcinoma																				X					
Follicular cell, adenoma																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	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	730	
Carcass ID Number	05 57	06 61	06 64	06 65	07 00	07 01	07 75	07 76	07 77	07 79	08 82	08 83	08 86	08 87	09 07	10 10	05 03	05 56	06 00	06 67	06 69	08 80	08 84	09 03	09 05	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Polyp adenomatous																										1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Leiomyoma																	X									1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Polyp adenomatous																							X			1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery		+	+															+						+		11
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma													X													1
Fibrosarcoma, metastatic, tissue NOS																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma															X											1
Sarcoma																										1
Schwannoma malignant																										2
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue							+																			1
Squamous cell papilloma							X																			1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma benign									X													X				3
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																			X							2
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma complex																					X					1
Pheochromocytoma benign										X		X	X								X					7
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma				X	X																					3
Carcinoma															X								X			4
Parathyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma							X																			2
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma		X	X	X	X		X	X			X				X			X		X		X			X	21
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
C-cell, adenoma				X															X							4
C-cell, carcinoma	X																	X								3
Follicular cell, adenoma																								X		1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	4 1 7	4 5 6	5 0 5	5 2 8	5 5 0	5 5 4	5 5 8	5 6 4	5 8 6	6 1 4	6 4 9	6 4 9	6 6 1	6 8 0	6 8 4	6 9 8	7 0 9	7 1 1	7 1 6	7 1 7	7 2 1	7 2 6	7 2 8	7 2 9	7 2 9
Carcass ID Number	0 5 5	0 6 8	0 8 5	0 9 2	0 6 3	0 8 8	0 8 1	0 7 4	0 8 9	0 9 4	0 5 9	0 7 2	0 7 3	0 5 8	0 9 1	0 6 6	0 5 4	0 5 9	0 9 0	0 9 6	0 7 8	0 6 2	0 9 8	0 5 1	0 5 2
General Body System																									
Peritoneum						+		+																	
Tissue NOS				+																					
Fibrosarcoma				X																					
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	M	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Adenoma									X																
Carcinoma		X																							
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Hemangiosarcoma																						X			
Seminal vesicle	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma					X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Interstitial cell, adenoma				X															X						
Hematopoietic System																									
Bone marrow	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Lymph node					+					+	+	+	+		+			+		+				+	
Deep cervical, carcinoma, metastatic, thyroid gland																									
Mediastinal, carcinoma, metastatic, thyroid gland																									
Lymph node, mandibular	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	+	+	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	M	+	M	+	M	M	+	+	+	+	+	+	+	+	M	+	+	M	M	+	+	+	+	+
Fibroadenoma																								X	
Fibroadenoma, multiple																									X
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma						X																			
Keratoacanthoma, multiple																									
Squamous cell carcinoma																									
Sebaceous gland, adenoma																									
Subcutaneous tissue, fibroma								X																X	
Subcutaneous tissue, lipoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granular cell tumor benign						X																			

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	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	730	
Carcass ID Number	05571	06611	06644	06655	07070	07711	07755	07766	07777	07799	08072	08383	08636	08677	09197	10010	10553	10563	10600	10667	10699	10804	10843	10904	10953	Total Tissues/ Tumors
General Body System																										
Peritoneum																										2
Tissue NOS																										1
Fibrosarcoma																										1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																										1
Carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																								X		1
Hemangiosarcoma																										1
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
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	41
Interstitial cell, adenoma									X															X		4
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node	+				+					+							+				+					14
Deep cervical, carcinoma, metastatic, thyroid gland	X																									1
Mediastinal, carcinoma, metastatic, thyroid gland	X																									1
Lymph node, mandibular	M	+	M	M	M	+	M	M	M	+	M	+	M	M	M	+	M	M	+	M	+	M	+	+	M	16
Carcinoma, metastatic, Zymbal's gland																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	41
Fibroadenoma			X	X			X			X									X							6
Fibroadenoma, multiple																										1
Skin	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	48
Keratoacanthoma																					X					2
Keratoacanthoma, multiple													X													1
Squamous cell carcinoma					X							X														2
Sebaceous gland, adenoma																									X	1
Subcutaneous tissue, fibroma							X			X		X														5
Subcutaneous tissue, lipoma											X															1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granular cell tumor benign																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	4 1 7	4 5 6	5 0 5	5 2 8	5 5 0	5 5 4	5 5 8	5 6 4	5 8 6	6 1 4	6 4 9	6 4 9	6 6 1	6 8 0	6 8 4	6 9 8	7 0 9	7 1 1	7 1 6	7 1 7	7 2 1	7 2 6	7 2 8	7 2 9	7 2 9
Carcass ID Number	0 5 5	0 6 8	0 8 5	0 9 2	0 6 3	0 8 8	0 8 1	0 7 4	0 8 9	0 9 4	0 5 9	0 7 2	0 7 3	0 5 8	0 9 1	0 6 6	0 5 4	0 9 9	0 9 0	0 9 6	0 7 8	0 6 2	0 9 8	0 5 1	0 5 2
Respiratory System																									
Lung	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma									X														X		
Alveolar/bronchiolar carcinoma																		X				X			
Carcinoma, metastatic, thyroid gland																									
Carcinoma, metastatic, Zymbal's gland																X									
Sarcoma, metastatic, salivary glands										X															
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye							+																		
Zymbal's gland							+									+									
Carcinoma							X									X									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, carcinoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					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 Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	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	730	
Carcass ID Number	05 57	06 61	06 64	06 65	07 70	07 71	07 75	07 76	07 77	07 79	08 82	08 83	08 86	08 87	09 07	10 05	10 53	10 56	10 60	10 67	10 69	10 80	10 84	10 93	10 95	Total Tissues/ Tumors
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma									X																	3
Alveolar/bronchiolar carcinoma																										2
Carcinoma, metastatic, thyroid gland	X																									1
Carcinoma, metastatic, Zymbal's gland																										1
Sarcoma, metastatic, salivary glands																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																											
Eye				+																						2
Zymbal's gland																										2
Carcinoma																										2
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, carcinoma											X															1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear					X					X					X		X		X		X				X	20
Mesothelioma malignant																										2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	3 4 0	5 4 3	5 6 2	5 6 4	5 8 3	5 8 4	5 8 6	5 9 8	6 1 7	6 1 9	6 2 3	6 2 7	6 2 7	6 4 7	6 4 9	6 4 9	6 7 4	6 8 2	6 9 8	7 1 2	7 1 8	7 2 5	7 2 6	7 2 9	7 2 9
Carcass ID Number	1 2 1	1 2 6	1 4 3	1 0 2	1 2 2	1 1 1	1 3 0	1 1 5	1 2 9	1 3 1	1 2 7	1 0 9	1 1 9	1 1 7	1 4 7	1 4 9	1 4 1	1 1 4	1 0 4	1 1 3	1 3 9	1 0 7	1 0 1	1 0 3	1 1 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																							X		
Intestine small, ileum	A	+	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Liver	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin																					X				
Mesentery	+																			+					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma												X										X			
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Squamous cell papilloma																									
Tooth																									
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin																					X				
Schwannoma benign																				X					
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant	X																								
Pheochromocytoma benign	X				X					X													X		
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X		X	X			X		X		X	X								X	X		
Pars distalis, carcinoma		X																							
Thyroid gland	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma			X						X						X										
C-cell, carcinoma																							X		
General Body System																									
Peritoneum																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	729	729	729	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	11 18	12 20	12 23	12 24	12 25	12 28	13 32	13 34	13 35	13 37	14 40	14 42	14 44	14 45	10 05	10 06	10 08	11 10	11 16	13 33	13 36	13 38	14 46	14 48	15 50	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic, skin																										1
Mesentery	+								+							+			+							6
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																				X						3
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue																		+								1
Squamous cell papilloma																		X								1
Tooth					+	+																	+			3
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skin																										1
Schwannoma benign																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant										X																2
Pheochromocytoma benign				X	X		X		X			X			X					X						11
Bilateral, pheochromocytoma benign						X																				1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X								X			X	X				X	X		X		X	X	18
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C-cell, adenoma				X									X					X								6
C-cell, carcinoma																						X				2
General Body System																										
Peritoneum	+																		+							2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	3 4 0	5 4 3	5 6 2	5 6 4	5 8 3	5 8 4	5 8 6	5 9 8	6 1 7	6 1 9	6 2 3	6 2 7	6 2 7	6 4 7	6 4 9	6 4 9	6 7 4	6 8 2	6 9 8	7 1 2	7 1 8	7 2 5	7 2 6	7 2 9	7 2 9
Carcass ID Number	1 2 1	1 2 6	1 4 3	1 0 2	1 2 2	1 1 1	1 3 0	1 1 5	1 2 9	1 3 1	1 2 7	1 0 9	1 1 9	1 1 7	1 4 7	1 4 9	1 4 1	1 1 4	1 0 4	1 1 3	1 3 9	1 0 7	1 0 1	1 0 3	1 1 2
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									X
Carcinoma																					X				
Bilateral, carcinoma													X												
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Seminal vesicle	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma			X	X			X	X		X		X			X	X	X	X	X	X	X	X	X	X	X
Interstitial cell, adenoma						X																			
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node						+	+						+		+	+	+	+	+	+		+	+	+	+
Lymph node, mandibular	M	M	+	M	M	M	+	M	M	+	M	M	M	M	+	M	M	+	M	M	M	+	+	M	M
Lymph node, mesenteric	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	A	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	M	M	+	+	+	+	+	+	+
Thymoma benign																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma		X																							
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																	X				X				
Subcutaneous tissue, fibroma																					X				
Subcutaneous tissue, sarcoma																					X				X
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma				X																					
Skeletal muscle																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal cord				+																					
Osteosarcoma, metastatic, bone				X																					

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	729	729	729	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	11 18	12 20	12 23	12 24	12 25	12 28	13 32	13 34	13 35	13 37	14 40	14 42	14 44	14 45	10 05	10 06	10 08	11 10	11 16	13 33	13 36	13 38	14 46	14 48	15 50	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma							X	X																		3
Carcinoma																										1
Bilateral, carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X			X																					2
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
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	X	X	X	41
Interstitial cell, adenoma		X																								2
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+		+		+	+				+		+			+										+	21
Lymph node, mandibular	M	M	M	M	+	M	M	+	M	M	+	+	M	+	M	M	M	M	M	+	M	M	M	M	+	14
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	43
Thymoma benign																X										1
Integumentary System																										
Mammary gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Fibroadenoma																										1
Skin	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Keratoacanthoma						X				X							X									4
Subcutaneous tissue, fibroma					X																					3
Subcutaneous tissue, sarcoma										X				X							X					5
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle																							+			1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spinal cord																										1
Osteosarcoma, metastatic, bone																										1

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	340	543	562	564	583	584	586	598	617	619	623	627	627	647	649	649	674	682	698	712	718	725	726	729	729
Carcass ID Number	121	126	143	102	122	111	130	115	129	131	127	109	119	117	147	149	141	114	104	113	139	107	101	103	112
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma					X																				
Carcinoma, metastatic, pituitary gland		X																							
Osteosarcoma, metastatic, bone				X																					
Sarcoma, metastatic, salivary glands												X													
Sarcoma, metastatic, skin																					X				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pleura										+	+														
Trachea	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye						+																			+
Zymbal's gland																				+					
Carcinoma																				X					
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lipoma																	X								
Urinary bladder	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X	X						X		X	X	X	X	X		X		X	X	
Lymphoma malignant																									
Mesothelioma malignant																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	729	729	729	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	11 18	12 20	12 23	12 24	12 25	12 28	13 32	13 34	13 35	13 37	14 40	14 42	14 44	14 45	10 55	10 56	10 68	11 10	11 16	13 33	13 36	13 38	14 46	14 48	15 50	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma												X														2
Carcinoma, metastatic, pituitary gland																										1
Osteosarcoma, metastatic, bone																										1
Sarcoma, metastatic, salivary glands																										1
Sarcoma, metastatic, skin																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pleura																										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Eye																								+		3
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lipoma														X												2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear			X	X	X					X		X			X	X	X		X	X					X	22
Lymphoma malignant																		X								1
Mesothelioma malignant	X																		X							2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	3 9 8	4 0 8	4 3 1	4 3 8	4 4 9	4 8 3	4 8 4	4 8 4	4 8 4	5 0 2	5 0 7	5 2 5	5 2 9	5 3 2	5 4 3	5 5 4	5 6 1	5 6 4	5 6 4	5 6 4	5 6 5	5 7 4	5 7 8	5 8 4	5 8 6
Carcass ID Number	1 8 8 7	1 9 9 8	1 8 8 0	1 8 8 2	1 7 7 4	2 0 2 0	1 5 1	1 6 1 8	1 9 9 5	1 6 6 7	1 9 0	1 6 6 2	1 7 7 6	1 7 7 0	1 8 8 9	1 8 8 8	1 9 9 9	1 9 6 0	1 7 1	1 8 1 4	1 8 7 8	1 9 9 6	1 8 8 5	1 9 7 7	1 5 5 3
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	A	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+
Intestine large, rectum	+	I	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+
Intestine large, cecum	A	+	+	+	+	A	A	A	A	+	+	A	+	A	+	A	+	+	A	+	+	+	A	+	+
Intestine small, duodenum	A	+	+	+	+	+	A	M	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	+	A	A	M	+	+	+	A	+	A	+	+	+	+	+	+	+	+	A	+	+
Intestine small, ileum	A	+	+	+	+	A	A	A	+	+	+	A	+	A	+	A	+	+	A	+	+	+	A	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma												X													
Mesentery																									
Oral mucosa																									
Pharyngeal, squamous cell papilloma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel	+																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma														X											
Adrenal medulla	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																				X					
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X																X						
Thyroid gland	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
Tissue NOS																	+								
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma									X																
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	A	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	X	X
Interstitial cell, adenoma																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	5 8 9	5 9 6	5 9 8	5 9 8	6 1 0	6 1 0	6 1 3	6 1 3	6 1 4	6 1 4	6 1 7	6 1 9	6 2 4	6 2 7	6 2 7	6 2 7	6 2 9	6 3 1	6 4 0	6 4 5	6 4 7	6 5 3	6 7 3	6 8 2	6 9 0	
Carcass ID Number	1 7 7 9	1 5 9 9	1 5 5 2	1 6 6 6	1 5 6 7	1 6 6 4	1 6 6 1	1 6 6 9	1 1 5 6	1 6 6 3	1 1 9 2	1 1 5 5	1 1 9 3	1 1 7 7	1 1 8 1	1 1 9 1	1 1 5 8	1 1 8 3	1 1 7 3	1 1 5 4	1 1 8 6	1 1 7 5	1 1 9 4	1 1 7 2	1 1 6 5	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	43
Intestine large, rectum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	44
Intestine large, cecum	+	A	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	A	A	+	+	+	+	+	+	35
Intestine small, duodenum	+	A	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	42
Intestine small, jejunum	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	39
Intestine small, ileum	+	A	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	A	A	+	+	+	+	+	+	36
Liver	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hepatocellular adenoma																										1
Mesentery				+				+								+						+				4
Oral mucosa		+								+																2
Pharyngeal, squamous cell papilloma		X																								1
Pancreas	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																							X			1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cardiovascular System																										
Blood vessel																							+			2
Heart	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endocrine System																										
Adrenal cortex	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma																										1
Adrenal medulla	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pheochromocytoma benign										X																1
Islets, pancreatic	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Carcinoma																								X		2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma									X				X		X	X							X			7
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	47
General Body System																										
Tissue NOS																										1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
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	44
Interstitial cell, adenoma		X					X		X							X										4

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	3 9 8	4 0 8	4 3 1	4 3 8	4 4 9	4 8 3	4 8 4	4 8 4	4 8 4	5 0 2	5 0 7	5 2 5	5 2 9	5 3 2	5 4 3	5 5 4	5 6 1	5 6 4	5 6 4	5 6 4	5 6 5	5 7 4	5 7 8	5 8 4	5 8 6
Carcass ID Number	1 8 7	1 9 8	1 8 0	1 8 2	1 7 4	2 0 0	1 5 1	1 6 8	1 9 5	1 6 7	1 9 0	1 6 2	1 7 6	1 7 0	1 8 9	1 8 8	1 9 9	1 9 6	1 7 1	1 8 4	1 8 8	1 7 9	1 9 6	1 8 5	1 9 7	1 5 3
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymph node		+		+				+																+	
Lymph node, mandibular	M	M	+	M	M	M	M	M	M	+	M	M	M	M	M	M	M	+	M	M	M	+	+	+	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+
Integumentary System																									
Mammary gland	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I
Subcutaneous tissue, fibroma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																									
Skeletal muscle																+									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve																				+					
Spinal cord																				+					
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma				X																					
Alveolar/bronchiolar carcinoma																									
Osteosarcoma, metastatic, bone																									
Squamous cell carcinoma, metastatic, oral mucosa																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									
Zymbal's gland				+																					
Carcinoma				X																					
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X																							
Mesothelioma malignant																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	5 8 9	5 9 6	5 9 8	5 9 8	6 1 0	6 1 0	6 1 3	6 1 3	6 1 4	6 1 4	6 1 7	6 1 9	6 2 4	6 2 7	6 2 7	6 2 7	6 2 9	6 3 1	6 4 0	6 4 5	6 4 7	6 5 3	6 7 3	6 8 2	6 9 0	
Carcass ID Number	1 7 7 9	1 5 9 9	1 5 5 2	1 6 6 6	1 5 6 7	1 6 6 4	1 6 6 1	1 6 6 9	1 5 9 6	1 6 6 3	1 6 9 2	1 5 5 5	1 5 9 3	1 7 7 7	1 8 1 1	1 9 1 1	1 5 8 8	1 8 3 3	1 7 3 3	1 5 4 4	1 8 4 6	1 7 5 5	1 9 4 4	1 7 2 2	1 6 6 5	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node			+					+											+			+	+			9
Lymph node, mandibular	M	M	M	M	+	M	M	+	M	M	M	M	+	+	M	M	M	M	+	M	M	M	M	M	M	11
Lymph node, mesenteric	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	47
Spleen	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thymus	M	+	M	+	M	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	M	+	+	M	41
Integumentary System																										
Mammary gland	+	M	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Subcutaneous tissue, fibroma																									X	1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																			A	X						1
Skeletal muscle																				+						2
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma																										1
Alveolar/bronchiolar carcinoma											X															1
Osteosarcoma, metastatic, bone																				X						1
Squamous cell carcinoma, metastatic, oral mucosa										X																1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Special Senses System																										
Eye															+											1
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear			X					X											X			X				5
Mesothelioma malignant						X		X																		2

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	4/47 (9%)	7/49 (14%)[e]	12/50 (24%)	1/47 (2%)
Adjusted rate[b]	10.6%	16.6%	27.3%	4.1%
Terminal rate[c]	1/23 (4%)	4/27 (15%)	8/27 (30%)	0/0
First incidence (days)	697	711	340	614
Poly-3 test[d]	P=0.308N	P=0.323	P=0.049	P=0.339N
Adrenal Medulla: Malignant Pheochromocytoma				
Overall rate	5/47 (11%)	0/49 (0%)	2/50 (4%)	0/47 (0%)
Adjusted rate	13.1%	0.0%	4.7%	0.0%
Terminal rate	3/23 (13%)	0/27 (0%)	1/27 (4%)	0/0
First incidence (days)	511	—[f]	340	—
Poly-3 test	P=0.161N	P=0.023N	P=0.170N	P=0.094N
Adrenal Medulla: Benign, Complex, or Malignant Pheochromocytoma				
Overall rate	9/47 (19%)	7/49 (14%)	13/50 (26%)	1/47 (2%)
Adjusted rate	23.3%	16.6%	29.6%	4.1%
Terminal rate	4/23 (17%)	4/27 (15%)	9/27 (33%)	0/0
First incidence (days)	511	711	340	614
Poly-3 test	P=0.121N	P=0.317N	P=0.346	P=0.050N
Heart: Benign Schwannoma				
Overall rate	2/50 (4%)	3/50 (6%)	1/50 (2%)	0/49 (0%)
Adjusted rate	4.9%	7.1%	2.4%	0.0%
Terminal rate	0/23 (0%)	3/27 (11%)	0/27 (0%)	0/0
First incidence (days)	565	729 (T)	712	—
Poly-3 test	P=0.198N	P=0.520	P=0.486N	P=0.361N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	2/50 (4%)	3/49 (6%)	0/50 (0%)	1/49 (2%)
Adjusted rate	5.0%	7.1%	0.0%	3.9%
Terminal rate	1/23 (4%)	2/27 (7%)	0/27 (0%)	0/0
First incidence (days)	645	586	—	438
Poly-3 test	P=0.422N	P=0.525	P=0.227N	P=0.652N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	3/50 (6%)	5/49 (10%)	2/50 (4%)	2/49 (4%)
Adjusted rate	7.5%	11.8%	4.7%	7.8%
Terminal rate	2/23 (9%)	2/27 (7%)	1/27 (4%)	0/0
First incidence (days)	645	586	583	438
Poly-3 test	P=0.474N	P=0.387	P=0.474N	P=0.660
Mammary Gland: Fibroadenoma				
Overall rate	1/50 (2%)	7/50 (14%)	1/50 (2%)	0/50 (0%)
Adjusted rate	2.5%	16.5%	2.3%	0.0%
Terminal rate	1/23 (4%)	7/27 (26%)	0/27 (0%)	0/0
First incidence (days)	729 (T)	729 (T)	543	—
Poly-3 test	P=0.106N	P=0.036	P=0.746N	P=0.588N
Pancreas: Benign Mixed Tumor				
Overall rate	2/44 (5%)	0/49 (0%)	0/50 (0%)	0/47 (0%)
Adjusted rate	5.5%	0.0%	0.0%	0.0%
Terminal rate	0/23 (0%)	0/27 (0%)	0/27 (0%)	0/0
First incidence (days)	584	—	—	—
Poly-3 test	P=0.309N	P=0.207N	P=0.207N	P=0.346N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Pancreatic Islets: Adenoma				
Overall rate	2/44 (5%)	3/48 (6%)	0/50 (0%)	0/47 (0%)
Adjusted rate	5.5%	7.2%	0.0%	0.0%
Terminal rate	2/23 (9%)	2/27 (7%)	0/27 (0%)	0/0
First incidence (days)	729 (T)	649	—	—
Poly-3 test	P=0.145N	P=0.567	P=0.203N	P=0.342N
Pancreatic Islets: Carcinoma				
Overall rate	0/44 (0%)	4/48 (8%)	0/50 (0%)	2/47 (4%)
Adjusted rate	0.0%	9.6%	0.0%	8.2%
Terminal rate	0/23 (0%)	3/27 (11%)	0/27 (0%)	0/0
First incidence (days)	—	709	—	564
Poly-3 test	P=0.409	P=0.079	—[g]	P=0.163
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	2/44 (5%)	7/48 (15%)	0/50 (0%)	2/47 (4%)
Adjusted rate	5.5%	16.7%	0.0%	8.2%
Terminal rate	2/23 (9%)	5/27 (19%)	0/27 (0%)	0/0
First incidence (days)	729 (T)	649	—	564
Poly-3 test	P=0.379N	P=0.117	P=0.203N	P=0.545
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	15/47 (32%)	21/49 (43%)	18/50 (36%)	7/49 (14%)
Adjusted rate	37.5%	47.3%	39.9%	25.2%
Terminal rate	9/23 (39%)	12/27 (44%)	9/27 (33%)	0/0
First incidence (days)	582	417	562	431
Poly-3 test	P=0.100N	P=0.242	P=0.497	P=0.209N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rate	15/47 (32%)	21/49 (43%)	19/50 (38%)	7/49 (14%)
Adjusted rate	37.5%	47.3%	41.6%	25.2%
Terminal rate	9/23 (39%)	12/27 (44%)	9/27 (33%)	0/0
First incidence (days)	582	417	543	431
Poly-3 test	P=0.104N	P=0.242	P=0.433	P=0.209N
Preputial Gland: Adenoma				
Overall rate	3/50 (6%)	1/47 (2%)	3/50 (6%)	1/50 (2%)
Adjusted rate	7.4%	2.4%	7.1%	3.9%
Terminal rate	1/23 (4%)	0/27 (0%)	3/27 (11%)	0/0
First incidence (days)	654	586	729 (T)	484
Poly-3 test	P=0.543N	P=0.297N	P=0.644N	P=0.475N
Preputial Gland: Carcinoma				
Overall rate	3/50 (6%)	1/47 (2%)	2/50 (4%)	0/50 (0%)
Adjusted rate	7.3%	2.4%	4.7%	0.0%
Terminal rate	1/23 (4%)	0/27 (0%)	0/27 (0%)	0/0
First incidence (days)	511	456	627	—
Poly-3 test	P=0.258N	P=0.301N	P=0.484N	P=0.230N
Preputial Gland: Adenoma or Carcinoma				
Overall rate	6/50 (12%)	2/47 (4%)	5/50 (10%)	1/50 (2%)
Adjusted rate	14.4%	4.8%	11.8%	3.9%
Terminal rate	2/23 (9%)	0/27 (0%)	3/27 (11%)	0/0
First incidence (days)	511	456	627	484
Poly-3 test	P=0.284N	P=0.128N	P=0.484N	P=0.175N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Salivary Glands: Sarcoma				
Overall rate	0/49 (0%)	1/49 (2%)	3/50 (6%)	0/50 (0%)
Adjusted rate	0.0%	2.4%	7.1%	0.0%
Terminal rate	0/23 (0%)	0/27 (0%)	1/27 (4%)	0/0
First incidence (days)	—	614	627	—
Poly-3 test	P=0.646N	P=0.514	P=0.134	—
Skin: Keratoacanthoma				
Overall rate	1/50 (2%)	3/50 (6%)	4/50 (8%)	0/50 (0%)
Adjusted rate	2.5%	7.0%	9.4%	0.0%
Terminal rate	1/23 (4%)	2/27 (7%)	2/27 (7%)	0/0
First incidence (days)	729 (T)	554	674	—
Poly-3 test	P=0.378N	P=0.332	P=0.196	P=0.588N
Skin: Keratoacanthoma or Squamous Cell Carcinoma				
Overall rate	1/50 (2%)	5/50 (10%)	4/50 (8%)	0/50 (0%)
Adjusted rate	2.5%	11.6%	9.4%	0.0%
Terminal rate	1/23 (4%)	4/27 (15%)	2/27 (7%)	0/0
First incidence (days)	729 (T)	554	674	—
Poly-3 test	P=0.262N	P=0.118	P=0.196	P=0.588N
Skin (Subcutaneous Tissue): Fibroma				
Overall rate	6/50 (12%)	5/50 (10%)	3/50 (6%)	1/50 (2%)
Adjusted rate	14.7%	11.6%	7.1%	4.0%
Terminal rate	3/23 (13%)	4/27 (15%)	2/27 (7%)	0/0
First incidence (days)	569	564	718	690
Poly-3 test	P=0.143N	P=0.462N	P=0.223N	P=0.175N
Skin (Subcutaneous Tissue): Sarcoma				
Overall rate	3/50 (6%)	0/50 (0%)	5/50 (10%)	0/50 (0%)
Adjusted rate	7.4%	0.0%	11.9%	0.0%
Terminal rate	0/23 (0%)	0/27 (0%)	4/27 (15%)	0/0
First incidence (days)	511	—	718	—
Poly-3 test	P=0.425N	P=0.111N	P=0.374	P=0.228N
Skin (Subcutaneous Tissue): Fibroma or Sarcoma				
Overall rate	9/50 (18%)	5/50 (10%)	7/50 (14%)	1/50 (2%)
Adjusted rate	21.7%	11.6%	16.6%	4.0%
Terminal rate	3/23 (13%)	4/27 (15%)	6/27 (22%)	0/0
First incidence (days)	511	564	718	690
Poly-3 test	P=0.107N	P=0.171N	P=0.378N	P=0.058N
Testes: Adenoma				
Overall rate	45/50 (90%)	45/50 (90%)	43/50 (86%)	48/50 (96%)
Adjusted rate	96.5%	94.2%	92.3%	99.2%
Terminal rate	23/23 (100%)	25/27 (93%)	27/27 (100%)	0/0
First incidence (days)	511	528	562	398
Poly-3 test	P=0.145	P=0.488N	P=0.297N	P=0.385
Thyroid Gland (C-Cell): Adenoma				
Overall rate	4/42 (10%)	4/47 (9%)	6/48 (13%)	0/47 (0%)
Adjusted rate	10.9%	9.9%	14.1%	0.0%
Terminal rate	1/23 (4%)	2/27 (7%)	3/27 (11%)	0/0
First incidence (days)	568	649	562	—
Poly-3 test	P=0.175N	P=0.590N	P=0.466	P=0.138N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Thyroid Gland (C-Cell): Carcinoma				
Overall rate	2/42 (5%)	3/47 (6%)	2/48 (4%)	0/47 (0%)
Adjusted rate	5.5%	7.5%	4.8%	0.0%
Terminal rate	1/23 (4%)	2/27 (7%)	1/27 (4%)	0/0
First incidence (days)	569	717	726	—
Poly-3 test	P=0.222N	P=0.547	P=0.646N	P=0.341N
Thyroid Gland (C-Cell): Adenoma or Carcinoma				
Overall rate	6/42 (14%)	7/47 (15%)	8/48 (17%)	0/47 (0%)
Adjusted rate	16.1%	17.3%	18.8%	0.0%
Terminal rate	2/23 (9%)	4/27 (15%)	4/27 (15%)	0/0
First incidence (days)	568	649	562	—
Poly-3 test	P=0.077N	P=0.566	P=0.494	P=0.059N
Zymbal's Gland: Carcinoma				
Overall rate	3/50 (6%)	2/50 (4%)	1/50 (2%)	1/50 (2%)
Adjusted rate	7.2%	4.6%	2.4%	3.9%
Terminal rate	0/23 (0%)	0/27 (0%)	0/27 (0%)	0/0
First incidence (days)	376	558	712	438
Poly-3 test	P=0.423N	P=0.482N	P=0.298N	P=0.484N
All Organs: Mononuclear Cell Leukemia				
Overall rate	16/50 (32%)	20/50 (40%)	22/50 (44%)	5/50 (10%)
Adjusted rate	37.4%	44.5%	49.3%	18.2%
Terminal rate	6/23 (26%)	8/27 (30%)	12/27 (44%)	0/0
First incidence (days)	564	550	584	408
Poly-3 test	P=0.055N	P=0.320	P=0.176	P=0.075N
All Organs: Malignant Mesothelioma				
Overall rate	6/50 (12%)	2/50 (4%)	2/50 (4%)	2/50 (4%)
Adjusted rate	14.6%	4.6%	4.8%	7.7%
Terminal rate	2/23 (9%)	0/27 (0%)	2/27 (7%)	0/0
First incidence (days)	569	554	729 (T)	610
Poly-3 test	P=0.412N	P=0.113N	P=0.123N	P=0.328N
All Organs: Benign or Malignant Mesothelioma				
Overall rate	6/50 (12%)	2/50 (4%)	2/50 (4%)	2/50 (4%)
Adjusted rate	14.6%	4.6%	4.8%	7.7%
Terminal rate	2/23 (9%)	0/27 (0%)	2/27 (7%)	0/0
First incidence (days)	569	554	729 (T)	610
Poly-3 test	P=0.412N	P=0.113N	P=0.123N	P=0.328N
All Organs: Benign Neoplasms				
Overall rate	47/50 (94%)	49/50 (98%)	50/50 (100%)	49/50 (98%)
Adjusted rate	99.4%	99.5%	100.0%	99.6%
Terminal rate	23/23 (100%)	27/27 (100%)	27/27 (100%)	0/0
First incidence (days)	511	417	340	398
Poly-3 test	P=0.993	P=0.999	P=1.000	P=1.000
All Organs: Malignant Neoplasms				
Overall rate	35/50 (70%)	34/50 (68%)	35/50 (70%)	13/50 (26%)
Adjusted rate	72.8%	69.2%	73.6%	41.8%
Terminal rate	12/23 (52%)	14/27 (52%)	18/27 (67%)	0/0
First incidence (days)	323	456	340	408
Poly-3 test	P=0.004N	P=0.434N	P=0.559	P=0.003N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
All Organs: Benign or Malignant Neoplasms				
Overall rate	49/50 (98%)	50/50 (100%)	50/50 (100%)	50/50 (100%)
Adjusted rate	99.9%	100.0%	100.0%	100.0%
Terminal rate	23/23 (100%)	27/27 (100%)	27/27 (100%)	0/0
First incidence (days)	323	417	340	398
Poly-3 test	P=1.000	P=1.000	P=1.000	P=1.000

(T) Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, heart, lung, pancreas, pancreatic islets, pituitary gland, preputial gland, salivary 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 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 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 exposure group is indicated by **N**.
[e] A complex pheochromocytoma also occurred in an animal that had a benign pheochromocytoma.
[f] Not applicable; no neoplasms in animal group
[g] Value of statistic cannot be computed.

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	12	14	18	31
Natural deaths	15	9	5	19
Survivors				
Terminal sacrifice	23	27	27	
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(41)	(49)	(48)	(43)
Parasite metazoan	4 (10%)	1 (2%)	3 (6%)	
Ulcer		1 (2%)		1 (2%)
Intestine large, rectum	(40)	(50)	(48)	(44)
Parasite metazoan	6 (15%)	3 (6%)	6 (13%)	
Intestine large, cecum	(38)	(46)	(47)	(35)
Inflammation, acute			1 (2%)	
Ulcer		1 (2%)	1 (2%)	
Intestine small, duodenum	(39)	(49)	(49)	(42)
Necrosis				1 (2%)
Intestine small, ileum	(37)	(42)	(47)	(36)
Necrosis				1 (3%)
Liver	(50)	(50)	(49)	(48)
Angiectasis				2 (4%)
Basophilic focus	24 (48%)	35 (70%)	26 (53%)	45 (94%)
Clear cell focus	22 (44%)	22 (44%)	23 (47%)	2 (4%)
Degeneration, cystic	4 (8%)	3 (6%)	6 (12%)	2 (4%)
Eosinophilic focus	1 (2%)		2 (4%)	
Fatty change	6 (12%)	5 (10%)	3 (6%)	5 (10%)
Hepatodiaphragmatic nodule	3 (6%)	5 (10%)	4 (8%)	5 (10%)
Inflammation, focal, granulomatous	22 (44%)	26 (52%)	42 (86%)	27 (56%)
Inflammation, focal, histiocytic	18 (36%)	27 (54%)	46 (94%)	48 (100%)
Mixed cell focus		2 (4%)	2 (4%)	2 (4%)
Regeneration	3 (6%)			
Thrombosis	1 (2%)		1 (2%)	
Vacuolization cytoplasmic, focal		1 (2%)		
Bile duct, hyperplasia	34 (68%)	38 (76%)	43 (88%)	44 (92%)
Centrilobular, necrosis	15 (30%)	11 (22%)	12 (24%)	3 (6%)
Mesentery	(14)	(11)	(6)	(4)
Fat, inflammation	1 (7%)			
Fat, necrosis	12 (86%)	9 (82%)	5 (83%)	4 (100%)
Oral mucosa	(1)			(2)
Pharyngeal, hyperplasia				1 (50%)
Pharyngeal, necrosis	1 (100%)			
Pancreas	(44)	(49)	(50)	(47)
Atrophy	17 (39%)	20 (41%)	12 (24%)	9 (19%)
Basophilic focus	1 (2%)	2 (4%)	2 (4%)	
Hyperplasia	7 (16%)	6 (12%)	4 (8%)	5 (11%)
Thrombosis		1 (2%)		
Artery, inflammation	1 (2%)			

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

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Alimentary System (continued)				
Salivary glands	(49)	(49)	(50)	(50)
Atrophy	1 (2%)	5 (10%)		
Basophilic focus	1 (2%)	1 (2%)	1 (2%)	
Inflammation, suppurative		1 (2%)		22 (44%)
Stomach, forestomach	(50)	(50)	(50)	(49)
Cyst				1 (2%)
Hyperkeratosis		1 (2%)		
Hyperplasia, basal cell			1 (2%)	2 (4%)
Hyperplasia, diffuse, squamous	2 (4%)		1 (2%)	1 (2%)
Hyperplasia, squamous		1 (2%)	3 (6%)	5 (10%)
Inflammation, chronic			1 (2%)	
Inflammation, suppurative				1 (2%)
Ulcer	3 (6%)	5 (10%)	8 (16%)	10 (20%)
Stomach, glandular	(46)	(49)	(50)	(48)
Cyst, squamous				1 (2%)
Metaplasia		1 (2%)		
Mineralization		1 (2%)		2 (4%)
Necrosis	5 (11%)	7 (14%)	2 (4%)	5 (10%)
Tooth	(1)		(3)	
Inflammation, chronic active	1 (100%)		3 (100%)	
Cardiovascular System				
Blood vessel	(1)	(1)		(2)
Inflammation, granulomatous	1 (100%)			
Aorta, mineralization				1 (50%)
Heart	(50)	(50)	(50)	(49)
Cardiomyopathy	41 (82%)	42 (84%)	43 (86%)	22 (45%)
Hemorrhage	1 (2%)			
Mineralization				7 (14%)
Necrosis			1 (2%)	
Atrium, thrombosis		5 (10%)	2 (4%)	
Valve, inflammation, acute				1 (2%)
Endocrine System				
Adrenal cortex	(47)	(49)	(50)	(48)
Degeneration, cystic	1 (2%)			
Hyperplasia	15 (32%)	22 (45%)	26 (52%)	8 (17%)
Hypertrophy	5 (11%)	4 (8%)	6 (12%)	5 (10%)
Inflammation, granulomatous		1 (2%)		
Necrosis	1 (2%)	4 (8%)	1 (2%)	
Vacuolization cytoplasmic			1 (2%)	
Adrenal medulla	(47)	(49)	(50)	(47)
Hyperplasia	23 (49%)	23 (47%)	24 (48%)	4 (9%)
Necrosis	1 (2%)			1 (2%)
Islets, pancreatic	(44)	(48)	(50)	(47)
Hyperplasia			2 (4%)	
Parathyroid gland	(45)	(48)	(49)	(50)
Hyperplasia		4 (8%)	1 (2%)	5 (10%)
Pituitary gland	(47)	(49)	(50)	(49)
Angiectasis	1 (2%)			1 (2%)
Cyst		4 (8%)	1 (2%)	
Pars distalis, hyperplasia	9 (19%)	16 (33%)	16 (32%)	6 (12%)

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Endocrine System (continued)				
Thyroid gland	(42)	(47)	(48)	(47)
C-cell, hyperplasia	24 (57%)	26 (55%)	31 (65%)	3 (6%)
Follicular cell, hyperplasia	1 (2%)	1 (2%)	1 (2%)	2 (4%)
General Body System				
None				
Genital System				
Epididymis	(50)	(50)	(50)	(49)
Granuloma sperm				1 (2%)
Preputial gland	(50)	(47)	(50)	(50)
Cyst				2 (4%)
Hyperplasia	1 (2%)	3 (6%)	3 (6%)	1 (2%)
Inflammation, chronic active		1 (2%)		1 (2%)
Prostate	(48)	(50)	(50)	(50)
Hyperplasia	11 (23%)	11 (22%)	10 (20%)	5 (10%)
Inflammation, chronic active	8 (17%)	8 (16%)	12 (24%)	
Seminal vesicle	(43)	(48)	(49)	(46)
Inflammation, chronic active		2 (4%)		
Testes	(50)	(50)	(50)	(50)
Atrophy	2 (4%)	4 (8%)	1 (2%)	3 (6%)
Interstitial cell, hyperplasia	3 (6%)	2 (4%)	2 (4%)	1 (2%)
Hematopoietic System				
Bone marrow	(46)	(48)	(50)	(48)
Inflammation, granulomatous			1 (2%)	
Lymph node	(18)	(14)	(21)	(9)
Bronchial, ectasia			1 (5%)	
Mediastinal, ectasia	2 (11%)		1 (5%)	2 (22%)
Mediastinal, hemorrhage				1 (11%)
Mediastinal, hyperplasia			1 (5%)	
Mediastinal, infiltration cellular, plasma cell			1 (5%)	
Mediastinal, inflammation, granulomatous				1 (11%)
Lymph node, mesenteric	(44)	(48)	(49)	(47)
Inflammation, granulomatous		1 (2%)		
Spleen	(43)	(50)	(49)	(47)
Atrophy	1 (2%)			
Congestion	1 (2%)			
Fibrosis	6 (14%)	5 (10%)	4 (8%)	2 (4%)
Hematopoietic cell proliferation	2 (5%)	5 (10%)	2 (4%)	
Hemorrhage	2 (5%)			
Hyperplasia, focal, lymphoid	4 (9%)	4 (8%)	9 (18%)	2 (4%)
Necrosis		3 (6%)	2 (4%)	
Thymus	(39)	(48)	(43)	(41)
Atrophy		1 (2%)	1 (2%)	
Hemorrhage	1 (3%)			

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Integumentary System				
Mammary gland	(48)	(41)	(47)	(44)
Galactocele	1 (2%)		1 (2%)	
Skin	(48)	(48)	(49)	(49)
Cyst	1 (2%)			
Foreign body		1 (2%)		
Hyperkeratosis	1 (2%)	4 (8%)		
Hyperplasia, basal cell		1 (2%)		
Inflammation, chronic active	1 (2%)	1 (2%)		
Prepuce, inflammation, suppurative		1 (2%)		
Subcutaneous tissue, hemorrhage				1 (2%)
Musculoskeletal System				
Skeletal muscle			(1)	(2)
Cyst, squamous			1 (100%)	
Mineralization				1 (50%)
Nervous System				
Brain	(50)	(50)	(50)	(50)
Gliosis			1 (2%)	
Necrosis		1 (2%)	1 (2%)	
Respiratory System				
Lung	(50)	(49)	(50)	(49)
Foreign body		1 (2%)		
Hemorrhage	1 (2%)			
Infiltration cellular, histiocyte	32 (64%)	35 (71%)	39 (78%)	34 (69%)
Inflammation, chronic active	3 (6%)	2 (4%)	4 (8%)	1 (2%)
Inflammation, suppurative			1 (2%)	
Metaplasia, squamous	1 (2%)	1 (2%)	3 (6%)	
Mineralization		1 (2%)		1 (2%)
Thrombosis		2 (4%)	1 (2%)	3 (6%)
Alveolar epithelium, hyperplasia	11 (22%)	18 (37%)	10 (20%)	5 (10%)
Mediastinum, necrosis, fatty	1 (2%)			
Nose	(46)	(50)	(50)	(49)
Foreign body		2 (4%)		
Inflammation, suppurative	11 (24%)	17 (34%)	15 (30%)	6 (12%)
Thrombosis	2 (4%)	5 (10%)	4 (8%)	9 (18%)
Goblet cell, respiratory epithelium, hyperplasia		1 (2%)		
Olfactory epithelium, atrophy	4 (9%)	3 (6%)	3 (6%)	34 (69%)
Olfactory epithelium, degeneration				7 (14%)
Olfactory epithelium, metaplasia	4 (9%)	1 (2%)		2 (4%)
Respiratory epithelium, hyperplasia				1 (2%)
Pleura			(2)	
Inflammation, chronic			1 (50%)	
Inflammation, suppurative			1 (50%)	

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Special Senses System				
Eye	(2)	(2)	(3)	(1)
Cataract	2 (100%)	1 (50%)	2 (67%)	1 (100%)
Degeneration			1 (33%)	
Cornea, inflammation, suppurative		1 (50%)		
Cornea, mineralization		1 (50%)		
Retina, atrophy	1 (50%)	1 (50%)	2 (67%)	1 (100%)
Urinary System				
Kidney	(47)	(50)	(50)	(48)
Cyst			3 (6%)	
Hydronephrosis		1 (2%)		1 (2%)
Infarct	3 (6%)	6 (12%)	3 (6%)	2 (4%)
Metaplasia, osseous		1 (2%)		
Mineralization		2 (4%)	1 (2%)	2 (4%)
Nephropathy	41 (87%)	47 (94%)	50 (100%)	48 (100%)
Pigmentation	1 (2%)	2 (4%)	1 (2%)	
Papilla, necrosis		1 (2%)		
Renal tubule, accumulation, hyaline droplet			2 (4%)	
Transitional epithelium, hyperplasia	1 (2%)	3 (6%)	7 (14%)	9 (19%)
Urinary bladder	(46)	(50)	(49)	(49)
Hemorrhage		1 (2%)		
Inflammation, chronic active		1 (2%)		
Inflammation, suppurative			1 (2%)	
Mineralization				1 (2%)
Necrosis				1 (2%)

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF DIPROPYLENE GLYCOL

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TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental death				1
Moribund	11	9	6	12
Natural deaths	9	10	6	6
Survivors				
Died last week of study			1	
Terminal sacrifice	30	31	37	31
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(48)	(47)	(48)	(46)
Intestine large, rectum	(48)	(47)	(49)	(46)
Sarcoma, metastatic, mesentery			1 (2%)	
Sarcoma, metastatic, skin		1 (2%)		
Intestine large, cecum	(46)	(43)	(47)	(45)
Intestine small, duodenum	(47)	(46)	(47)	(47)
Intestine small, jejunum	(45)	(44)	(47)	(44)
Leiomyoma		1 (2%)		
Intestine small, ileum	(44)	(41)	(47)	(45)
Liver	(50)	(50)	(50)	(49)
Histiocytic sarcoma			2 (4%)	
Sarcoma, metastatic, mesentery				1 (2%)
Sarcoma, metastatic, skin		1 (2%)	1 (2%)	
Sarcoma, metastatic, skeletal muscle		1 (2%)		
Schwannoma malignant, metastatic, heart		1 (2%)		
Mesentery	(15)	(13)	(13)	(11)
Histiocytic sarcoma			1 (8%)	
Sarcoma			1 (8%)	2 (18%)
Sarcoma, metastatic, ovary	1 (7%)			
Sarcoma, metastatic, skeletal muscle		1 (8%)		
Pancreas	(47)	(48)	(48)	(48)
Adenoma	1 (2%)			
Histiocytic sarcoma			1 (2%)	
Sarcoma, metastatic, mesentery				1 (2%)
Sarcoma, metastatic, ovary	1 (2%)			
Salivary glands	(49)	(50)	(50)	(50)
Sarcoma		1 (2%)		
Stomach, forestomach	(50)	(49)	(50)	(48)
Histiocytic sarcoma			1 (2%)	
Sarcoma, metastatic, mesentery				1 (2%)
Squamous cell carcinoma				1 (2%)
Squamous cell papilloma	2 (4%)	1 (2%)		
Stomach, glandular	(49)	(47)	(49)	(47)
Tongue	(1)		(1)	(1)
Squamous cell carcinoma	1 (100%)			1 (100%)
Squamous cell papilloma			1 (100%)	
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Hemangiosarcoma				1 (2%)
Schwannoma benign		2 (4%)	4 (8%)	1 (2%)
Schwannoma malignant		1 (2%)		

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Endocrine System				
Adrenal cortex	(49)	(47)	(47)	(47)
Adenoma	1 (2%)		1 (2%)	
Adrenal medulla	(49)	(47)	(46)	(47)
Pheochromocytoma malignant	2 (4%)			
Pheochromocytoma benign		3 (6%)	1 (2%)	
Islets, pancreatic	(47)	(48)	(48)	(48)
Adenoma		1 (2%)		
Pituitary gland	(48)	(45)	(50)	(47)
Pars distalis, adenoma	20 (42%)	18 (40%)	20 (40%)	13 (28%)
Pars distalis, carcinoma	1 (2%)		1 (2%)	
Thyroid gland	(45)	(45)	(46)	(46)
Bilateral, C-cell, adenoma	1 (2%)			
C-cell, adenoma	5 (11%)	8 (18%)	3 (7%)	3 (7%)
C-cell, carcinoma	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Follicular cell, carcinoma	1 (2%)		1 (2%)	
General Body System				
Peritoneum				(1)
Sarcoma, metastatic, mesentery				1 (100%)
Genital System				
Clitoral gland	(48)	(44)	(48)	(48)
Adenoma	6 (13%)	8 (18%)	4 (8%)	4 (8%)
Carcinoma	4 (8%)	5 (11%)	2 (4%)	1 (2%)
Sarcoma			1 (2%)	
Bilateral, adenoma		1 (2%)		
Bilateral, carcinoma	1 (2%)			
Ovary	(50)	(50)	(49)	(48)
Histiocytic sarcoma			1 (2%)	
Sarcoma	1 (2%)			
Sarcoma, metastatic, mesentery				1 (2%)
Sarcoma, metastatic, skeletal muscle		1 (2%)		
Uterus	(50)	(48)	(50)	(49)
Adenoma	1 (2%)			1 (2%)
Carcinoma			1 (2%)	
Polyp stromal	8 (16%)	10 (21%)	6 (12%)	11 (22%)
Polyp stromal, multiple		2 (4%)		1 (2%)
Sarcoma, metastatic, ovary	1 (2%)			
Sarcoma stromal	1 (2%)		2 (4%)	
Vagina		(1)		
Sarcoma, metastatic, skeletal muscle		1 (100%)		
Hematopoietic System				
Bone marrow	(48)	(47)	(48)	(47)
Lymph node	(15)	(11)	(8)	(14)
Mediastinal, histiocytic sarcoma			1 (13%)	
Lymph node, mandibular	(18)	(12)	(14)	(14)
Lymph node, mesenteric	(49)	(47)	(49)	(48)
Histiocytic sarcoma			1 (2%)	
Sarcoma, metastatic, ovary	1 (2%)			

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Hematopoietic System (continued)				
Spleen	(48)	(48)	(49)	(48)
Histiocytic sarcoma			1 (2%)	
Sarcoma, metastatic, ovary	1 (2%)			
Sarcoma, metastatic, skin		1 (2%)		
Sarcoma, metastatic, skeletal muscle		1 (2%)		
Thymus	(48)	(49)	(48)	(39)
Thymoma benign	1 (2%)			
Integumentary System				
Mammary gland	(50)	(49)	(50)	(49)
Carcinoma	4 (8%)	4 (8%)	2 (4%)	2 (4%)
Fibroadenoma	20 (40%)	24 (49%)	14 (28%)	19 (39%)
Fibroadenoma, multiple	16 (32%)	11 (22%)	16 (32%)	3 (6%)
Sarcoma		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Trichoepithelioma		1 (2%)		
Subcutaneous tissue, fibroma	1 (2%)			
Subcutaneous tissue, histiocytic sarcoma			1 (2%)	
Subcutaneous tissue, sarcoma		2 (4%)	2 (4%)	
Subcutaneous tissue, schwannoma malignant		1 (2%)		
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma			1 (2%)	
Skeletal muscle	(1)	(1)		
Sarcoma		1 (100%)		
Nervous System				
Brain	(50)	(50)	(50)	(50)
Osteosarcoma, metastatic, bone			1 (2%)	
Respiratory System				
Lung	(50)	(50)	(50)	(49)
Alveolar/bronchiolar adenoma		2 (4%)		
Alveolar/bronchiolar carcinoma	1 (2%)	1 (2%)	1 (2%)	
Carcinoma, metastatic, mammary gland			1 (2%)	
Histiocytic sarcoma			1 (2%)	
Sarcoma, metastatic, skin		1 (2%)	1 (2%)	
Sarcoma, metastatic, skeletal muscle		1 (2%)		
Mediastinum, sarcoma, metastatic, skeletal muscle		1 (2%)		
Mediastinum, schwannoma malignant, metastatic, heart		1 (2%)		
Nose	(48)	(48)	(46)	(49)
Pleura				(1)
Sarcoma, metastatic, mesentery				1 (100%)
Special Senses System				
None				

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Urinary System				
Kidney	(49)	(49)	(49)	(47)
Hemangiosarcoma				1 (2%)
Histiocytic sarcoma			1 (2%)	
Mesenchymal tumor malignant				1 (2%)
Sarcoma, metastatic, skeletal muscle		1 (2%)		
Urinary bladder	(50)	(48)	(48)	(46)
Sarcoma, metastatic, skin		1 (2%)		
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma			2 (4%)	
Leukemia mononuclear	10 (20%)	10 (20%)	4 (8%)	13 (26%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	50	49	46	46
Total primary neoplasms	111	121	93	80
Total animals with benign neoplasms	44	45	40	36
Total benign neoplasms	83	93	70	56
Total animals with malignant neoplasms	25	24	20	21
Total malignant neoplasms	28	28	23	24
Total animals with metastatic neoplasms	1	3	4	2
Total metastatic neoplasms	5	15	5	6

[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 Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	2 4 7	4 1 3	5 2 7	5 4 0	5 4 2	5 4 3	5 9 6	6 2 4	6 2 6	6 2 6	6 5 9	6 9 6	6 9 7	6 9 7	6 9 7	6 9 7	7 0 2	7 0 9	7 2 4	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 1 1 7	2 1 1 5	2 3 3 8	2 0 0 8	2 0 4 7	2 3 3 5	2 2 5 4	2 2 2 7	2 2 2 9	2 4 3 3	2 1 1 1	2 4 1 4	2 0 0 9	2 1 1 9	2 3 3 7	2 4 4 0	2 3 0 1	2 5 1 0	2 1 0 0	2 4 0 5	2 0 1 1	2 0 0 4	2 0 0 6	2 2 1 1	2 2 1 3
Alimentary System																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	A	A	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine small, jejunum	+	+	+	A	+	A	+	+	+	+	A	+	+	+	+	+	+	A	A	+	+	+	+	+
Intestine small, ileum	+	+	+	A	+	A	+	A	+	+	A	+	+	+	+	+	+	A	A	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery				+							+		+			+			+	+			+	+	
Sarcoma, metastatic, ovary				X																				
Pancreas	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+
Adenoma																						X		
Sarcoma, metastatic, ovary				X																				
Salivary glands	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma	X																							
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																								
Squamous cell carcinoma																								
Tooth	+							+	+												+			
Cardiovascular System																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																								
Adrenal cortex	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
Adrenal medulla	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																	X			X				
Islets, pancreatic	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Pars distalis, adenoma		X									X		X			X				X	X	X		X	
Pars distalis, carcinoma					X																			
Thyroid gland	+	+	+	+	+	A	+	A	+	+	M	+	+	+	+	+	+	A	A	+	+	+	+	+
Bilateral, C-cell, adenoma																								
C-cell, adenoma									X															
C-cell, carcinoma																								
Follicular cell, carcinoma																								
General Body System																								
None																								

+: 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 Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	729	729	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	230	233	202	216	218	225	226	234	248	249	203	205	207	212	213	214	220	222	228	232	236	239	241	242	246	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery									+	+		+				+		+	+			+				15
Sarcoma, metastatic, ovary																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																										1
Sarcoma, metastatic, ovary																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																						X				2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue																						+				1
Squamous cell carcinoma																						X				1
Tooth											+	+														6
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma				X																						1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																										2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma			X	X			X	X	X			X		X				X		X		X	X	X		20
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Bilateral, C-cell, adenoma												X														1
C-cell, adenoma											X								X	X		X				5
C-cell, carcinoma																									X	1
Follicular cell, carcinoma																							X			1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	2 4 7	4 1 3	5 2 7	5 4 0	5 4 2	5 4 3	5 9 6	6 2 4	6 2 6	6 2 6	6 5 9	6 9 6	6 9 7	6 9 7	6 9 7	6 9 7	7 0 2	7 0 9	7 2 4	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 1 7	2 1 5	2 3 8	2 0 8	2 0 4 7	2 3 5	2 2 4	2 2 7	2 2 9	2 4 3	2 1 1	2 4 1 4	2 0 9	2 1 9	2 3 7	2 4 0	2 3 1	2 5 0	2 1 0	2 4 5	2 0 1	2 0 0 4	2 0 0 6	2 2 1	2 2 3
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																							X		
Carcinoma																									
Bilateral, carcinoma									X																
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma				X																					
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Polyp stromal																			X	X					
Sarcoma, metastatic, ovary				X																					
Sarcoma stromal																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Lymph node	+					+	+					+			+	+	+	+	+						
Lymph node, mandibular	M	M	+	M	+	+	M	+	+	M	M	+	M	M	M	M	M	M	M	+	M	M	+	+	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Sarcoma, metastatic, ovary				X																					
Spleen	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Sarcoma, metastatic, ovary				X																					
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																						X			
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma					X																		X		
Fibroadenoma	X							X			X			X	X	X									X
Fibroadenoma, multiple			X							X			X					X	X				X	X	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle								+																	
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Nose	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Special Senses System																									
Eye								+																	
Harderian gland								+																	
Lacrimal gland																						+			

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	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 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	
Carcass ID Number	2 3 0	2 3 3	2 0 2	2 1 6	2 1 8	2 2 5	2 2 6	2 3 4	2 4 8	2 4 9	2 0 3	2 0 5	2 0 7	2 1 2	2 1 3	2 1 4	2 2 0	2 2 2	2 2 8	2 3 2	2 3 6	2 3 9	2 4 1	2 4 2	2 4 6	Total Tissues/ Tumors
Genital System																											
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma		X		X						X							X			X						6
Carcinoma				X									X					X							X	4
Bilateral, carcinoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																		X								1
Polyp stromal							X		X		X				X								X		X	8
Sarcoma, metastatic, ovary																										1
Sarcoma stromal																					X					1
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node	+										+		+	+	+							+				15
Lymph node, mandibular	M	M	M	M	+	+	+	M	+	+	+	M	+	+	M	M	M	M	M	M	M	M	M	M	+	18
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic, ovary																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, ovary																										1
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	48
Thymoma benign																										1
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma			X															X								4
Fibroadenoma	X	X	X	X	X	X				X				X			X		X	X	X		X			20
Fibroadenoma, multiple							X				X	X	X			X		X				X		X	X	16
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibroma								X																		1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma								X																		1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Special Senses System																											
Eye	+																									2
Harderian gland																										1
Lacrimal gland																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	2 4 7	4 1 3	5 2 7	5 4 0	5 4 2	5 4 3	5 9 6	6 2 4	6 2 6	6 2 6	6 5 9	6 9 6	6 9 7	6 9 7	6 9 7	6 9 7	7 0 2	7 0 9	7 2 4	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 1 7	2 1 5	2 3 8	2 0 8	2 4 7	2 3 5	2 2 4	2 2 7	2 2 9	2 4 3	2 1 1	2 4 4	2 0 9	2 1 9	2 3 7	2 4 0	2 3 1	2 5 0	2 1 0	2 4 5	2 0 1	2 0 4	2 0 6	2 2 1	2 2 3	
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Ureter	+																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear						X	X					X				X		X							X	

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	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 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	
Carcass ID Number	2 3 0	2 3 3	2 0 2	2 1 6	2 1 8	2 2 5	2 2 6	2 3 4	2 4 8	2 4 9	2 0 3	2 0 5	2 0 7	2 1 2	2 1 3	2 1 4	2 2 0	2 2 2	2 2 8	2 3 2	2 3 6	2 3 9	2 4 1	2 4 2	2 4 6	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Ureter																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X										X	X		X												10

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	4 1 7	4 2 5	4 3 5	5 4 2	5 5 8	5 8 5	5 8 5	6 2 2	6 2 4	6 2 6	6 3 4	6 4 1	6 6 8	6 8 0	6 8 3	7 1 7	7 1 7	7 2 1	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 7 9	2 8 4	2 5 2	2 8 3	2 5 5	2 6 0	2 8 7	2 7 3	2 9 2	3 0 0	2 6 5	2 8 8	2 5 9	2 6 3	2 7 6	2 5 7	2 6 8	2 6 7	2 6 6	2 5 3	2 6 4	2 6 7	2 7 8	2 9 1	2 9 6
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	M	+
Intestine large, rectum	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Sarcoma, metastatic, skin															X										
Intestine large, cecum	A	A	+	+	+	+	+	+	A	+	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	A	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	+	+	A	+	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+
Leiomyoma																									
Intestine small, ileum	A	A	A	A	+	+	+	+	A	+	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin															X										
Sarcoma, metastatic, skeletal muscle									X																
Schwannoma malignant, metastatic, heart												X													
Mesentery	+			+	+				+										+		+		+		
Sarcoma, metastatic, skeletal muscle									X																
Pancreas	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma																									
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Squamous cell papilloma																									X
Stomach, glandular	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+
Tooth															+										
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma benign											X														
Schwannoma malignant												X													
Endocrine System																									
Adrenal cortex	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Adrenal medulla	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Pheochromocytoma benign								X																	
Islets, pancreatic	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Adenoma																	X								
Parathyroid gland	+	+	+	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	A	+	+	+	+	+	+	+	+	+	+	I	+	A	+	+	A	A	+	+	+	+	+	+	+
Pars distalis, adenoma				X			X	X	X				X		X	X			X		X				
Thyroid gland	A	+	+	+	+	+	+	+	A	+	A	+	+	A	+	+	A	+	+	+	+	+	+	+	+
C-cell, adenoma																		X	X		X				
C-cell, carcinoma																								X	
General Body System																									
None																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	729	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	29 98	25 51	25 56	25 58	27 70	27 72	28 80	28 82	28 85	29 00	29 03	29 37	29 99	25 54	26 61	26 62	26 69	27 71	27 74	27 75	28 81	28 86	28 89	29 94	29 95	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Sarcoma, metastatic, skin																										1
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Leiomyoma														X												1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skin																										1
Sarcoma, metastatic, skeletal muscle																										1
Schwannoma malignant, metastatic, heart																										1
Mesentery		+	+								+						+	+		+						13
Sarcoma, metastatic, skeletal muscle																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																				X						1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Tooth																			+							2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma benign																	X									2
Schwannoma malignant																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pheochromocytoma benign				X		X																				3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Pars distalis, adenoma							X	X		X		X	X				X	X			X		X			18
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
C-cell, adenoma							X				X												X	X	X	8
C-cell, carcinoma																										1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	4 1 7	4 2 5	4 3 5	5 4 2	5 8 5	5 8 5	5 8 5	6 2 2	6 2 4	6 2 6	6 3 4	6 4 1	6 6 8	6 8 0	6 8 3	7 1 7	7 1 7	7 2 1	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 7 9	2 8 4	2 5 2	2 8 3	2 5 5	2 6 0	2 8 7	2 7 3	2 9 2	3 0 0	2 6 5	2 8 8	2 5 9	2 6 3	2 7 6	2 5 7	2 6 8	2 7 7	2 6 6	2 5 3	2 6 4	2 6 7	2 7 8	2 9 1	2 9 6
Genital System																									
Clitoral gland	+	+	M	+	+	+	+	+	A	+	+	+	+	+	M	M	M	+	+	+	+	M	+	+	+
Adenoma							X																X		
Carcinoma																			X		X				
Bilateral, adenoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skeletal muscle									X																
Uterus	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Polyp stromal					X		X				X								X		X		X		
Polyp stromal, multiple												X													
Vagina									+																
Sarcoma, metastatic, skeletal muscle									X																
Hematopoietic System																									
Bone marrow	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Lymph node			+	+	+	+					+										+				
Lymph node, mandibular	M	+	M	+	+	M	M	M	M	M	+	M	M	M	M	+	M	M	M	M	M	M	M	M	M
Lymph node, mesenteric	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+
Sarcoma, metastatic, skin															X										
Sarcoma, metastatic, skeletal muscle									X																
Thymus	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Fibroadenoma							X							X		X	X			X		X	X		X
Fibroadenoma, multiple										X					X			X	X					X	
Sarcoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trichoepithelioma																									
Subcutaneous tissue, sarcoma															X										X
Subcutaneous tissue, schwannoma malignant																X									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle									+																
Sarcoma									X																
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	729	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	29 98	25 01	25 16	25 58	27 70	27 72	28 00	28 02	28 85	29 00	29 03	29 97	29 99	25 54	26 61	26 62	26 69	27 11	27 74	27 75	28 81	28 86	28 89	29 04	29 05	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Adenoma				X					X			X	X	X					X							8
Carcinoma			X													X	X									5
Bilateral, adenoma																			X							1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skeletal muscle																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Polyp stromal														X	X								X	X		10
Polyp stromal, multiple										X																2
Vagina																										1
Sarcoma, metastatic, skeletal muscle																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node							+					+							+			+		+		11
Lymph node, mandibular	M	M	M	M	M	+	M	M	M	+	M	M	M	M	+	+	M	+	M	M	M	M	M	+	+	12
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, skin																										1
Sarcoma, metastatic, skeletal muscle																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma		X			X			X									X									4
Fibroadenoma			X	X	X	X	X	X		X	X	X	X	X	X	X		X		X				X		24
Fibroadenoma, multiple	X																		X		X	X	X		X	11
Sarcoma																					X					1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trichoepithelioma																						X				1
Subcutaneous tissue, sarcoma																										2
Subcutaneous tissue, schwannoma malignant																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Sarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 ppm

Number of Days on Study	4 1 7	4 2 5	4 3 5	5 4 2	5 5 5	5 8 5	5 8 5	6 2 2	6 2 4	6 2 6	6 3 4	6 4 1	6 6 8	6 8 0	6 8 3	7 1 7	7 1 7	7 2 1	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	2 7 9	2 8 4	2 5 2	2 8 3	2 5 5	2 6 0	2 8 7	2 7 3	2 9 2	3 0 0	2 6 5	2 8 8	2 5 9	2 6 3	2 7 6	2 5 7	2 6 8	2 7 7	2 6 6	2 5 3	2 6 4	2 6 7	2 7 8	2 9 1	2 9 6
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Sarcoma, metastatic, skin															X										
Sarcoma, metastatic, skeletal muscle									X																
Mediastinum, sarcoma, metastatic, skeletal muscle									X																
Mediastinum, schwannoma malignant, metastatic, heart												X													
Nose	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																+									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Sarcoma, metastatic, skeletal muscle									X																
Urinary bladder	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Sarcoma, metastatic, skin															X										
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X		X	X	X	X					X										X				

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 2,500 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 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	
Carcass ID Number	2 9 8	2 5 1	2 5 6	2 5 8	2 7 0	2 7 2	2 8 0	2 8 2	2 8 5	2 9 0	2 9 3	2 9 7	2 9 9	2 5 4	2 6 1	2 6 2	2 6 9	2 7 1	2 7 4	2 7 5	2 8 1	2 8 6	2 8 9	2 9 4	2 9 5	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																X	X									2
Alveolar/bronchiolar carcinoma																				X						1
Sarcoma, metastatic, skin																										1
Sarcoma, metastatic, skeletal muscle																										1
Mediastinum, sarcoma, metastatic, skeletal muscle																										1
Mediastinum, schwannoma malignant, metastatic, heart																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Special Senses System																										
Eye																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic, skeletal muscle																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, skin																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear			X											X										X		10

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	29 5	59 7	59 8	60 0	60 0 4	62 7	63 8	66 5	66 7	68 1	71 7	72 5	72 9	72 9	72 9	72 9	72 9	73 0	73 0	73 0	73 0	73 0	73 0	73 0
Carcass ID Number	32 29	32 28	31 13	32 00	33 01	35 10	33 08	34 41	32 16	34 02	34 40	34 08	30 04	30 06	31 00	33 44	34 46	44 09	30 01	30 03	30 07	31 14	31 16	31 17	31 18
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, mesentery							X																		
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				X																					
Sarcoma, metastatic, skin								X																	
Mesentery	+	+		+			+		+	+		+					+								+
Histiocytic sarcoma				X																					
Sarcoma							X																		
Pancreas	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Stomach, glandular	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																		+							
Squamous cell papilloma																		X							
Tooth																					+				
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma benign																									
Endocrine System																									
Adrenal cortex	A	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Adrenal medulla	A	+	+	A	+	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign												X													
Islets, pancreatic	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X	X						X		X					X	X	X	X			X	X	
Pars distalis, carcinoma		X																							
Thyroid gland	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma			X																		X				
C-cell, carcinoma																									
Follicular cell, carcinoma																				X					
General Body System																									
None																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 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 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	
Carcass ID Number	3 1 1 9	3 2 5 5	3 2 7 7	3 3 3 3	3 3 5 5	3 3 6 6	3 3 7 7	3 3 9 9	3 4 3 3	3 4 4 7	3 0 2 2	3 0 0 5	3 0 8 8	3 0 9 9	3 1 1 1	3 1 1 2	3 1 5 5	3 2 1 1	3 2 2 2	3 2 3 3	3 2 4 4	3 3 0 0	3 3 2 2	3 3 4 4	3 4 4 5	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic, mesentery																										1
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																				X						2
Sarcoma, metastatic, skin																										1
Mesentery															+		+			+					+	13
Histiocytic sarcoma																										1
Sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue																										1
Squamous cell papilloma																										1
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma benign						X			X		X						X									4
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma				X																						1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X	X		X						X			X						X	X			X	X	X	20
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
C-cell, adenoma	X																									3
C-cell, carcinoma									X					X												2
Follicular cell, carcinoma																										1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	2 9 5	5 9 7	5 9 8	6 0 0	6 0 4	6 2 7	6 3 8	6 6 5	6 6 7	6 8 1	7 1 7	7 2 5	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	3 2 9	3 2 8	3 1 3	3 2 0	3 3 1	3 5 0	3 3 8	3 4 1	3 2 6	3 4 2	3 4 4 0	3 4 8	3 0 4	3 0 6	3 1 0	3 3 4	3 4 6	3 4 9	3 0 1	3 0 3	3 0 7	3 1 4	3 1 6	3 1 7	3 1 8
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Adenoma																								X	
Carcinoma														X				X							
Sarcoma																									
Ovary	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma															X										
Polyp stromal				X						X												X		X	X
Sarcoma stromal					X															X					
Hematopoietic System																									
Bone marrow	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+			+		+	+																	+	
Mediastinal, histiocytic sarcoma				X																					
Lymph node, mandibular	M	+	M	M	+	M	M	M	M	+	M	M	M	M	M	M	M	+	+	M	+	+	M	M	+
Lymph node, mesenteric	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Spleen	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Thymus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma															X										
Fibroadenoma											X			X							X	X	X	X	X
Fibroadenoma, multiple		X						X				X			X		X		X	X					
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, histiocytic sarcoma				X																					
Subcutaneous tissue, sarcoma								X																	
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma									X																
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone									X																
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, mammary gland															X										
Histiocytic sarcoma				X																					
Sarcoma, metastatic, skin								X																	
Nose	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 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 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	
Carcass ID Number	3 1 9	3 2 5	3 2 7	3 3 3	3 3 5	3 3 6	3 3 7	3 3 9	3 4 3	3 4 7	3 0 2	3 0 5	3 0 8	3 0 9	3 1 1	3 1 2	3 1 5	3 2 1	3 2 2	3 2 3	3 2 4	3 3 0	3 3 2	3 4 4	3 4 5	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma							X	X															X			4
Carcinoma																										2
Sarcoma											X															1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Polyp stromal																									X	6
Sarcoma stromal																										2
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node		+					+				+															8
Mediastinal, histiocytic sarcoma																										1
Lymph node, mandibular	M	M	M	M	+	+	M	M	+	M	M	+	M	M	M	M	M	M	M	M	M	+	+	M	M	14
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Thymus	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma		X																								2
Fibroadenoma						X	X	X	X		X				X			X								14
Fibroadenoma, multiple	X	X	X									X				X			X	X		X		X		16
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, histiocytic sarcoma																										1
Subcutaneous tissue, sarcoma								X																		2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic, bone																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma																		X								1
Carcinoma, metastatic, mammary gland																										1
Histiocytic sarcoma																										1
Sarcoma, metastatic, skin																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	2 9 5	5 9 7	5 9 8	6 0 0	6 0 4	6 2 7	6 3 8	6 6 5	6 6 7	6 8 1	7 1 7	7 2 5	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	3 2 9	3 2 8	3 1 3	3 2 0	3 3 1	3 5 0	3 3 8	3 4 1	3 2 6	3 4 2	3 4 0	3 4 4	3 4 8	3 0 4	3 0 6	3 1 0	3 3 4	3 4 6	3 4 9	3 0 1	3 0 3	3 0 7	3 1 4	3 1 6	3 1 7	3 1 8
Special Senses System																									
Eye			+																						
Urinary System																									
Kidney	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Urinary bladder	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Leukemia mononuclear	X					X																			

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	31 19	32 25	32 27	33 33	33 35	33 36	33 37	33 39	34 43	44 47	00 02	00 25	00 28	09 09	11 11	11 12	11 25	12 11	12 12	12 23	23 24	30 40	33 32	44 44	44 45	Total Tissues/ Tumors
Special Senses System																											
Eye																	+										2
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																					X						2
Leukemia mononuclear		X					X																				4

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	5 3 3	5 3 6	5 4 2	5 6 4	5 7 7	5 8 2	5 9 7	5 9 7	6 2 6	6 2 6	6 5 2	6 5 9	6 6 8	6 8 1	6 9 4	6 9 4	7 1 1	7 1 8	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	3 7 8	3 7 9	3 7 2	3 9 5	3 8 3	3 8 5	3 8 0	3 8 7	3 6 3	3 8 6	3 9 7	3 6 6	3 5 4	3 6 7	3 5 9	3 9 6	3 7 3	3 5 7	3 9 8	3 5 1	3 6 5	3 6 9	3 7 4	3 7 7	3 9 3
Alimentary System																									
Esophagus	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine large, rectum	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	A	+	+	+	+	A	A	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	A	+	A	+	+	+	+	A	A	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	A	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, mesentery																X									
Mesentery	+						+					+	+	+		+									+
Sarcoma	X															X									
Pancreas	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, mesentery																X									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, mesentery																X									
Squamous cell carcinoma																									
Stomach, glandular	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue				+																					
Squamous cell carcinoma				X																					
Tooth																									
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Schwannoma benign																									
Endocrine System																									
Adrenal cortex	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma					X					X						X			X				X		X
Thyroid gland	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+
C-cell, adenoma														X					X						
C-cell, carcinoma																								X	
General Body System																									
Peritoneum	+																								
Sarcoma, metastatic, mesentery	X																								
Genital System																									
Clitoral gland	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																			X						
Carcinoma			X																						
Ovary	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, mesentery	X																								

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	729	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	
Carcass ID Number	40 00	35 05	35 56	36 61	36 62	36 64	37 00	37 76	38 01	38 12	38 88	39 00	39 01	39 12	39 99	35 23	35 38	36 04	36 68	37 11	37 75	38 44	38 94	39 44	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic, mesentery																										1
Mesentery								+	+											+	+					11
Sarcoma																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, mesentery																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, mesentery																										1
Squamous cell carcinoma																			X							1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Tongue																										1
Squamous cell carcinoma																										1
Tooth									+																	1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma		X																								1
Schwannoma benign																								X		1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma		X	X			X		X	X		X			X												13
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
C-cell, adenoma																			X							3
C-cell, carcinoma																										1
General Body System																										
Peritoneum																										1
Sarcoma, metastatic, mesentery																										1
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	48
Adenoma						X			X	X																4
Carcinoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, mesentery																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	5 3 3	5 3 6	5 4 2	5 6 4	5 7 7	5 8 2	5 9 7	5 9 7	6 2 6	6 2 6	6 5 2	6 5 9	6 6 8	6 8 1	6 9 4	6 9 4	7 1 1	7 1 8	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	3 7 8	3 7 9	3 7 2	3 9 5	3 8 3	3 8 5	3 8 0	3 8 7	3 6 3	3 8 6	3 9 7	3 6 6	3 5 4	3 6 7	3 5 9	3 9 6	3 7 3	3 5 7	3 9 8	3 5 1	3 6 5	3 6 9	3 7 4	3 7 7	3 9 3
Genital System (continued)																									
Uterus	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Polyp stromal		X	X														X		X	X					
Polyp stromal, multiple									X																
Hematopoietic System																									
Bone marrow	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node								+					+	+	+				+						
Lymph node, mandibular	M	M	M	M	M	A	+	M	M	+	+	M	M	+	M	+	M	+	+	M	M	+	M	+	M
Lymph node, mesenteric	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	M	+	+	M	M	A	+	M	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma														X											
Fibroadenoma									X	X				X	X	X	X	X	X	X	X				
Fibroadenoma, multiple																									X
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pleura																+									
Sarcoma, metastatic, mesentery																X									
Trachea	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye														+						+					
Urinary System																									
Kidney	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma								X																	
Mesenchymal tumor malignant																									
Urinary bladder	A	I	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X	X	X		X	X	X	X	X				X						

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	729	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	
Carcass ID Number	40 00	35 05	35 06	36 01	36 02	36 04	37 00	37 06	38 01	38 02	38 08	39 00	39 01	39 02	39 09	35 02	35 03	35 08	36 00	36 08	37 11	37 15	38 04	38 09	39 04	Total Tissues/ Tumors
Genital System (continued)																										
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma															X											1
Polyp stromal	X											X		X		X						X			X	11
Polyp stromal, multiple																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node													+		+	+	+	+			+	+	+	+		14
Lymph node, mandibular	+	M	M	M	M	M	M	M	M	M	M	M	M	M	+	+	+	M	M	+	M	M	M	M	M	14
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thymus	+	+	+	M	+	+	M	+	M	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	39
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma					X																					2
Fibroadenoma			X					X	X		X				X				X	X	X		X			19
Fibroadenoma, multiple				X													X									3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pleura																										1
Sarcoma, metastatic, mesentery																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Special Senses System																										
Eye																		+								3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Hemangiosarcoma																										1
Mesenchymal tumor malignant		X																								1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear													X		X							X	X			13

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	0/49 (0%)	3/47 (6%)	1/46 (2%)	0/47 (0%)
Adjusted rate[b]	0.0%	7.2%	2.3%	0.0%
Terminal rate[c]	0/30 (0%)	2/31 (7%)	0/38 (0%)	0/31 (0%)
First incidence (days)	—[e]	622	725	—
Poly-3 test[d]	P=0.263N	P=0.113	P=0.505	—[f]
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rate	2/49 (4%)	3/47 (6%)	1/46 (2%)	0/47 (0%)
Adjusted rate	4.7%	7.2%	2.3%	0.0%
Terminal rate	0/30 (0%)	2/31 (7%)	0/38 (0%)	0/31 (0%)
First incidence (days)	702	622	725	—
Poly-3 test	P=0.118N	P=0.487	P=0.492N	P=0.241N
Clitoral Gland: Adenoma				
Overall rate	6/48 (13%)	9/44 (20%)	4/48 (8%)	4/48 (8%)
Adjusted rate	14.5%	23.1%	9.1%	9.5%
Terminal rate	6/29 (21%)	8/30 (27%)	4/37 (11%)	3/30 (10%)
First incidence (days)	729 (T)	585	729 (T)	725
Poly-3 test	P=0.164N	P=0.240	P=0.330N	P=0.357N
Clitoral Gland: Carcinoma				
Overall rate	5/48 (10%)	5/44 (11%)	2/48 (4%)	1/48 (2%)
Adjusted rate	12.0%	13.0%	4.5%	2.3%
Terminal rate	4/29 (14%)	4/30 (13%)	2/37 (5%)	0/30 (0%)
First incidence (days)	626	725	729 (T)	542
Poly-3 test	P=0.059N	P=0.578	P=0.194N	P=0.095N
Clitoral Gland: Adenoma or Carcinoma				
Overall rate	10/48 (21%)	14/44 (32%)	6/48 (13%)	5/48 (10%)
Adjusted rate	23.9%	35.9%	13.6%	11.7%
Terminal rate	9/29 (31%)	12/30 (40%)	6/37 (16%)	3/30 (10%)
First incidence (days)	626	585	729 (T)	542
Poly-3 test	P=0.027N	P=0.172	P=0.170N	P=0.116N
Heart: Benign Schwannoma				
Overall rate	0/50 (0%)	2/50 (4%)	4/50 (8%)	1/50 (2%)
Adjusted rate	0.0%	4.6%	8.7%	2.3%
Terminal rate	0/30 (0%)	1/31 (3%)	4/38 (11%)	1/31 (3%)
First incidence (days)	—	634	729 (T)	729 (T)
Poly-3 test	P=0.573N	P=0.238	P=0.068	P=0.502
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	1/50 (2%)	3/50 (6%)	1/50 (2%)	0/49 (0%)
Adjusted rate	2.3%	7.0%	2.2%	0.0%
Terminal rate	1/30 (3%)	3/31 (10%)	1/38 (3%)	0/31 (0%)
First incidence (days)	729 (T)	729 (T)	729 (T)	—
Poly-3 test	P=0.175N	P=0.304	P=0.747N	P=0.500N
Mammary Gland: Fibroadenoma				
Overall rate	36/50 (72%)	35/50 (70%)	30/50 (60%)	22/50 (44%)
Adjusted rate	77.7%	78.8%	64.3%	48.9%
Terminal rate	25/30 (83%)	27/31 (87%)	26/38 (68%)	14/31 (45%)
First incidence (days)	247	585	597	626
Poly-3 test	P<0.001N	P=0.551	P=0.107N	P=0.002N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Mammary Gland: Carcinoma				
Overall rate	4/50 (8%)	4/50 (8%)	2/50 (4%)	2/50 (4%)
Adjusted rate	9.1%	9.3%	4.4%	4.6%
Terminal rate	3/30 (10%)	4/31 (13%)	2/38 (5%)	1/31 (3%)
First incidence (days)	542	729 (T)	729 (T)	681
Poly-3 test	P=0.273N	P=0.635	P=0.315N	P=0.336N
Mammary Gland: Fibroadenoma or Carcinoma				
Overall rate	37/50 (74%)	37/50 (74%)	30/50 (60%)	23/50 (46%)
Adjusted rate	78.8%	83.3%	64.3%	51.1%
Terminal rate	25/30 (83%)	29/31 (94%)	26/38 (68%)	15/31 (48%)
First incidence (days)	247	585	597	626
Poly-3 test	P<0.001N	P=0.379	P=0.083N	P=0.003N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	20/48 (42%)	18/45 (40%)	20/50 (40%)	13/47 (28%)
Adjusted rate	46.4%	43.1%	42.6%	30.2%
Terminal rate	15/30 (50%)	10/31 (32%)	16/38 (42%)	9/31 (29%)
First incidence (days)	413	542	598	577
Poly-3 test	P=0.068N	P=0.466N	P=0.439N	P=0.089N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rate	21/48 (44%)	18/45 (40%)	21/50 (42%)	13/47 (28%)
Adjusted rate	48.1%	43.1%	44.3%	30.2%
Terminal rate	15/30 (50%)	10/31 (32%)	16/38 (42%)	9/31 (29%)
First incidence (days)	413	542	597	577
Poly-3 test	P=0.054N	P=0.404N	P=0.440N	P=0.065N
Thyroid Gland (C-Cell): Adenoma				
Overall rate	6/45 (13%)	8/45 (18%)	3/46 (7%)	3/46 (7%)
Adjusted rate	15.1%	20.1%	6.8%	7.3%
Terminal rate	5/30 (17%)	6/31 (19%)	2/38 (5%)	1/31 (3%)
First incidence (days)	626	721	598	681
Poly-3 test	P=0.117N	P=0.385	P=0.192N	P=0.223N
Thyroid Gland (C-Cell): Adenoma or Carcinoma				
Overall rate	7/45 (16%)	9/45 (20%)	5/46 (11%)	4/46 (9%)
Adjusted rate	17.6%	22.6%	11.3%	9.7%
Terminal rate	6/30 (20%)	7/31 (23%)	4/38 (11%)	2/31 (7%)
First incidence (days)	626	721	598	681
Poly-3 test	P=0.128N	P=0.390	P=0.307N	P=0.238N
Uterus: Stromal Polyp				
Overall rate	8/50 (16%)	12/50 (24%)	6/50 (12%)	12/50 (24%)
Adjusted rate	18.5%	26.9%	12.9%	26.5%
Terminal rate	6/30 (20%)	7/31 (23%)	4/38 (11%)	7/31 (23%)
First incidence (days)	724	585	600	536
Poly-3 test	P=0.281	P=0.249	P=0.330N	P=0.260
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rate	9/50 (18%)	12/50 (24%)	8/50 (16%)	12/50 (24%)
Adjusted rate	20.8%	26.9%	17.1%	26.5%
Terminal rate	7/30 (23%)	7/31 (23%)	5/38 (13%)	7/31 (23%)
First incidence (days)	724	585	600	536
Poly-3 test	P=0.367	P=0.340	P=0.425N	P=0.354

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
All Organs: Mononuclear Cell Leukemia				
Overall rate	10/50 (20%)	10/50 (20%)	4/50 (8%)	13/50 (26%)
Adjusted rate	22.5%	21.5%	8.5%	28.2%
Terminal rate	5/30 (17%)	4/31 (13%)	2/38 (5%)	4/31 (13%)
First incidence (days)	543	417	295	597
Poly-3 test	P=0.166	P=0.556N	P=0.056N	P=0.348
All Organs: Benign Neoplasms				
Overall rate	44/50 (88%)	45/50 (90%)	40/50 (80%)	36/50 (72%)
Adjusted rate	92.6%	95.5%	83.8%	77.1%
Terminal rate	30/30 (100%)	30/31 (97%)	33/38 (87%)	25/31 (81%)
First incidence (days)	247	542	597	536
Poly-3 test	P=0.003N	P=0.417	P=0.137N	P=0.021N
All Organs: Malignant Neoplasms				
Overall rate	25/50 (50%)	24/50 (48%)	20/50 (40%)	21/50 (42%)
Adjusted rate	54.1%	50.6%	40.6%	43.8%
Terminal rate	15/30 (50%)	13/31 (42%)	12/38 (32%)	8/31 (26%)
First incidence (days)	540	417	295	533
Poly-3 test	P=0.245N	P=0.445N	P=0.130N	P=0.212N
All Organs: Benign or Malignant Neoplasms				
Overall rate	50/50 (100%)	49/50 (98%)	46/50 (92%)	46/50 (92%)
Adjusted rate	100.0%	99.6%	92.0%	92.9%
Terminal rate	30/30 (100%)	31/31 (100%)	34/38 (90%)	28/31 (90%)
First incidence (days)	247	417	295	533
Poly-3 test	P=0.061N	P=1.000N	P=0.061N	P=0.075N

(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, heart, lung, 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 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 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 exposure group is indicated by **N**.
[e] Not applicable; no neoplasms in animal group
[f] Value of statistic cannot be computed.

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental death				1
Moribund	11	9	6	12
Natural deaths	9	10	6	6
Survivors				
Died last week of study			1	
Terminal sacrifice	30	31	37	31
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(48)	(47)	(48)	(46)
Parasite metazoan	4 (8%)	4 (9%)	1 (2%)	2 (4%)
Intestine large, rectum	(48)	(47)	(49)	(46)
Parasite metazoan	7 (15%)	5 (11%)	13 (27%)	3 (7%)
Intestine small, ileum	(44)	(41)	(47)	(45)
Necrosis				1 (2%)
Liver	(50)	(50)	(50)	(49)
Angiectasis		2 (4%)		
Basophilic focus	46 (92%)	46 (92%)	49 (98%)	46 (94%)
Clear cell focus	10 (20%)	16 (32%)	20 (40%)	17 (35%)
Eosinophilic focus			1 (2%)	4 (8%)
Fatty change	6 (12%)	9 (18%)	6 (12%)	4 (8%)
Hepatodiaphragmatic nodule	4 (8%)	7 (14%)	6 (12%)	6 (12%)
Inflammation, focal, granulomatous	30 (60%)	33 (66%)	37 (74%)	26 (53%)
Inflammation, focal, histiocytic	39 (78%)	37 (74%)	36 (72%)	28 (57%)
Mixed cell focus	1 (2%)	7 (14%)	7 (14%)	4 (8%)
Necrosis		1 (2%)		
Tension lipidosis		1 (2%)		
Bile duct, hyperplasia	2 (4%)	3 (6%)	7 (14%)	18 (37%)
Centrilobular, necrosis	6 (12%)	8 (16%)	2 (4%)	6 (12%)
Mesentery	(15)	(13)	(13)	(11)
Fat, hemorrhage		1 (8%)		
Fat, necrosis	14 (93%)	13 (100%)	11 (85%)	8 (73%)
Pancreas	(47)	(48)	(48)	(48)
Atrophy	7 (15%)	10 (21%)	6 (13%)	10 (21%)
Basophilic focus	3 (6%)	2 (4%)	3 (6%)	3 (6%)
Hyperplasia	2 (4%)	1 (2%)	4 (8%)	3 (6%)
Salivary glands	(49)	(50)	(50)	(50)
Atrophy	3 (6%)	4 (8%)	3 (6%)	1 (2%)
Basophilic focus	1 (2%)	3 (6%)	5 (10%)	
Inflammation, suppurative		1 (2%)	1 (2%)	1 (2%)
Stomach, forestomach	(50)	(49)	(50)	(48)
Foreign body	1 (2%)			
Hyperplasia, squamous	4 (8%)	3 (6%)	3 (6%)	2 (4%)
Inflammation, granulomatous	1 (2%)			
Ulcer	2 (4%)	6 (12%)	2 (4%)	1 (2%)

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

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Alimentary System (continued)				
Stomach, glandular	(49)	(47)	(49)	(47)
Hypertrophy, focal		1 (2%)		
Inflammation, chronic		1 (2%)		
Mineralization	1 (2%)	1 (2%)		1 (2%)
Necrosis	3 (6%)	2 (4%)	2 (4%)	4 (9%)
Neuroendocrine cell, hyperplasia		1 (2%)		
Tooth	(6)	(2)	(1)	(1)
Inflammation, chronic active	6 (100%)	2 (100%)	1 (100%)	1 (100%)
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	33 (66%)	42 (84%)	32 (64%)	26 (52%)
Atrium, thrombosis		2 (4%)		1 (2%)
Endocrine System				
Adrenal cortex	(49)	(47)	(47)	(47)
Angiectasis		1 (2%)	1 (2%)	
Atrophy		1 (2%)		
Degeneration, cystic	5 (10%)	2 (4%)		
Hyperplasia	18 (37%)	24 (51%)	25 (53%)	13 (28%)
Hypertrophy	11 (22%)	14 (30%)	12 (26%)	9 (19%)
Necrosis	1 (2%)	2 (4%)		2 (4%)
Thrombosis	1 (2%)			
Adrenal medulla	(49)	(47)	(46)	(47)
Hyperplasia	12 (24%)	8 (17%)	10 (22%)	7 (15%)
Necrosis				2 (4%)
Parathyroid gland	(49)	(47)	(47)	(49)
Hyperplasia				2 (4%)
Pituitary gland	(48)	(45)	(50)	(47)
Angiectasis			3 (6%)	2 (4%)
Cyst		1 (2%)		1 (2%)
Pars distalis, hyperplasia	19 (40%)	15 (33%)	22 (44%)	19 (40%)
Thyroid gland	(45)	(45)	(46)	(46)
C-cell, hyperplasia	36 (80%)	36 (80%)	38 (83%)	28 (61%)
Follicular cell, hyperplasia		1 (2%)		
General Body System				
None				

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Genital System				
Clitoral gland	(48)	(44)	(48)	(48)
Hyperplasia	5 (10%)	2 (5%)	3 (6%)	3 (6%)
Inflammation, chronic active	2 (4%)			1 (2%)
Ovary	(50)	(50)	(49)	(48)
Cyst	4 (8%)	6 (12%)	7 (14%)	8 (17%)
Inflammation, granulomatous				1 (2%)
Interstitial cell, hyperplasia			1 (2%)	
Uterus	(50)	(48)	(50)	(49)
Hydrometra	1 (2%)			
Hyperplasia, cystic	1 (2%)		1 (2%)	1 (2%)
Thrombosis	1 (2%)			
Hematopoietic System				
Lymph node	(15)	(11)	(8)	(14)
Deep cervical, ectasia			2 (25%)	
Deep cervical, hyperplasia				1 (7%)
Iliac, inflammation, suppurative	1 (7%)			
Mediastinal, ectasia		1 (9%)		1 (7%)
Mediastinal, hemorrhage	1 (7%)			
Mediastinal, hyperplasia	1 (7%)			
Mediastinal, infiltration cellular, plasma cell		1 (9%)		1 (7%)
Pancreatic, inflammation, granulomatous	1 (7%)			
Lymph node, mesenteric	(49)	(47)	(49)	(48)
Ectasia		1 (2%)		
Spleen	(48)	(48)	(49)	(48)
Accessory spleen			1 (2%)	
Hematopoietic cell proliferation	7 (15%)	7 (15%)	4 (8%)	2 (4%)
Hemorrhage	1 (2%)			1 (2%)
Inflammation, granulomatous		1 (2%)	1 (2%)	3 (6%)
Necrosis	1 (2%)	1 (2%)	1 (2%)	
Integumentary System				
Mammary gland	(50)	(49)	(50)	(49)
Galactocele	3 (6%)	3 (6%)	1 (2%)	1 (2%)
Inflammation, chronic		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Inflammation, chronic active				2 (4%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Inflammation, chronic active	1 (2%)			
Osteopetrosis	1 (2%)	3 (6%)	1 (2%)	1 (2%)
Skeletal muscle	(1)	(1)		
Inflammation, suppurative	1 (100%)			

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Nervous System				
Brain	(50)	(50)	(50)	(50)
Gliosis		1 (2%)		
Inflammation, suppurative	1 (2%)			
Necrosis				1 (2%)
Meninges, fibrosis			1 (2%)	
Respiratory System				
Lung	(50)	(50)	(50)	(49)
Cyst, squamous			1 (2%)	
Infiltration cellular, histiocyte	46 (92%)	47 (94%)	46 (92%)	45 (92%)
Inflammation, chronic active	8 (16%)	4 (8%)	8 (16%)	11 (22%)
Metaplasia, osseous		1 (2%)		
Metaplasia, squamous			1 (2%)	
Thrombosis	1 (2%)			
Alveolar epithelium, hyperplasia	11 (22%)	15 (30%)	17 (34%)	8 (16%)
Bronchiole, hyperplasia	1 (2%)	2 (4%)	3 (6%)	2 (4%)
Nose	(48)	(48)	(46)	(49)
Inflammation, suppurative	10 (21%)	5 (10%)	7 (15%)	4 (8%)
Thrombosis	1 (2%)	4 (8%)		3 (6%)
Olfactory epithelium, atrophy			1 (2%)	
Olfactory epithelium, degeneration				9 (18%)
Olfactory epithelium, metaplasia			1 (2%)	1 (2%)
Olfactory epithelium, metaplasia, squamous			1 (2%)	
Respiratory epithelium, accumulation, hyaline droplet	40 (83%)	36 (75%)	37 (80%)	46 (94%)
Respiratory epithelium, hyperplasia			1 (2%)	
Respiratory epithelium, metaplasia, squamous	1 (2%)			
Special Senses System				
Eye	(2)	(1)	(2)	(3)
Cataract	2 (100%)		2 (100%)	1 (33%)
Degeneration				2 (67%)
Inflammation, chronic active		1 (100%)		
Cornea, inflammation, suppurative	1 (50%)			
Retina, atrophy	2 (100%)		1 (50%)	2 (67%)
Harderian gland	(1)			
Inflammation, suppurative	1 (100%)			

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	2,500 ppm	10,000 ppm	40,000 ppm
Urinary System				
Kidney	(49)	(49)	(49)	(47)
Cyst			1 (2%)	
Hydronephrosis		1 (2%)		
Infarct	3 (6%)	2 (4%)	1 (2%)	4 (9%)
Inflammation, suppurative	1 (2%)	1 (2%)		
Mineralization	1 (2%)			
Nephropathy	43 (88%)	45 (92%)	47 (96%)	46 (98%)
Pelvis, inflammation, acute		1 (2%)	1 (2%)	
Renal tubule, hypertrophy	1 (2%)			
Transitional epithelium, hyperplasia		1 (2%)	1 (2%)	1 (2%)
Ureter	(1)			
Inflammation, suppurative	1 (100%)			
Urinary bladder	(50)	(48)	(48)	(46)
Transitional epithelium, hyperplasia				1 (2%)

APPENDIX C
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF DIPROPYLENE GLYCOL

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TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	3	3	5	9
Natural deaths	7	8	10	6
Survivors				
Died last week of study	1			
Terminal sacrifice	39	39	35	34
Missing				1
Animals examined microscopically	50	50	50	49
Alimentary System				
Intestine large, cecum	(50)	(50)	(50)	(49)
Carcinoma				1 (2%)
Intestine small, duodenum	(50)	(49)	(50)	(49)
Hemangioma	1 (2%)			
Polyp adenomatous	1 (2%)	2 (4%)		
Intestine small, jejunum	(50)	(50)	(50)	(49)
Carcinoma	1 (2%)	2 (4%)	3 (6%)	
Polyp adenomatous	1 (2%)	1 (2%)		
Liver	(50)	(50)	(50)	(49)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Hemangioma	1 (2%)	1 (2%)	2 (4%)	
Hemangiosarcoma		3 (6%)	1 (2%)	2 (4%)
Hepatoblastoma			4 (8%)	1 (2%)
Hepatocellular carcinoma	11 (22%)	7 (14%)	8 (16%)	9 (18%)
Hepatocellular carcinoma, multiple	3 (6%)	3 (6%)	3 (6%)	7 (14%)
Hepatocellular adenoma	10 (20%)	14 (28%)	14 (28%)	4 (8%)
Hepatocellular adenoma, multiple	7 (14%)	3 (6%)	6 (12%)	2 (4%)
Hepatocholangiocarcinoma			1 (2%)	
Histiocytic sarcoma		1 (2%)		
Mesentery	(8)	(10)	(1)	
Pancreas	(50)	(50)	(50)	(49)
Stomach, forestomach	(50)	(50)	(50)	(49)
Squamous cell carcinoma	1 (2%)			
Cardiovascular System				
Heart	(50)	(50)	(50)	(49)
Sarcoma, metastatic, skeletal muscle			1 (2%)	
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(49)
Adrenal medulla	(50)	(49)	(50)	(49)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Islets, pancreatic	(50)	(50)	(50)	(49)
Adenoma			1 (2%)	
Pituitary gland	(49)	(48)	(49)	(49)
Pars intermedia, adenoma	1 (2%)			
Thyroid gland	(50)	(50)	(50)	(49)
Follicle, adenoma		1 (2%)		

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
General Body System				
None				
Genital System				
Epididymis	(50)	(50)	(50)	(49)
Preputial gland	(50)	(50)	(50)	(49)
Hemangiosarcoma		1 (2%)		
Seminal vesicle	(50)	(50)	(50)	(49)
Testes	(50)	(50)	(50)	(49)
Interstitial cell, adenoma	3 (6%)			1 (2%)
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(49)
Histiocytic sarcoma		1 (2%)		
Lymph node	(1)			
Mediastinal, hepatocellular carcinoma, metastatic, liver	1 (100%)			
Lymph node, mesenteric	(48)	(50)	(49)	(48)
Carcinoma, metastatic, intestine large, cecum				1 (2%)
Spleen	(50)	(50)	(50)	(49)
Hemangiosarcoma			1 (2%)	1 (2%)
Histiocytic sarcoma		1 (2%)		
Thymus	(46)	(45)	(47)	(44)
Histiocytic sarcoma		1 (2%)		
Integumentary System				
Skin	(50)	(50)	(50)	(49)
Pinna, ear, neural crest tumor	1 (2%)	1 (2%)		
Musculoskeletal System				
Skeletal muscle	(1)		(1)	(1)
Hepatoblastoma, metastatic, liver				1 (100%)
Sarcoma			1 (100%)	
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(49)
Alveolar/bronchiolar adenoma	3 (6%)	9 (18%)	4 (8%)	4 (8%)
Alveolar/bronchiolar adenoma, multiple			1 (2%)	
Alveolar/bronchiolar carcinoma	1 (2%)	3 (6%)	6 (12%)	4 (8%)
Alveolar/bronchiolar carcinoma, multiple	2 (4%)	2 (4%)	2 (4%)	
Carcinoma, metastatic, harderian gland	1 (2%)			
Hepatoblastoma, metastatic, liver				1 (2%)
Hepatocellular carcinoma, metastatic, liver	6 (12%)	6 (12%)	2 (4%)	4 (8%)
Histiocytic sarcoma		1 (2%)		
Nose	(50)	(50)	(50)	(49)
Glands, carcinoma				1 (2%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Special Senses System				
Harderian gland	(3)	(3)	(4)	(1)
Adenoma	2 (67%)	3 (100%)	4 (100%)	1 (100%)
Carcinoma	1 (33%)			
Urinary System				
Kidney	(50)	(50)	(50)	(49)
Sarcoma, metastatic, skeletal muscle			1 (2%)	
Renal tubule, adenoma	1 (2%)			
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(49)
Histiocytic sarcoma		1 (2%)		
Lymphoma malignant	1 (2%)			
Mesothelioma malignant	1 (2%)			
Neoplasm Summary				
Total animals with primary neoplasms[c]	39	37	39	33
Total primary neoplasms	54	57	62	38
Total animals with benign neoplasms	27	23	26	11
Total benign neoplasms	31	34	32	12
Total animals with malignant neoplasms	19	19	26	25
Total malignant neoplasms	22	22	30	26
Total animals with metastatic neoplasms	7	6	3	6
Total metastatic neoplasms	8	6	6	7
Total Animals with uncertain neoplasms-benign or malignant	1	1		
Total uncertain neoplasms	1	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 C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	41 46	45 46	55 56	57 55	59 52	60 63	62 99	66 66	70 68	72 24	72 29	72 99	72 99	72 99	72 99	72 99	72 99	72 99	72 99	72 99	72 99	73 30	73 00	73 00	73 00	73 00
Carcass ID Number	04 43	00 21	01 17	04 40	02 09	01 98	01 13	02 32	01 66	03 44	00 01	00 77	01 11	02 33	02 25	03 11	03 36	03 88	04 46	05 00	00 02	00 06	00 09	01 02	01 14
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																										
Polyp adenomatous																										
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma															X											
Polyp adenomatous																							X			
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																										
Hepatocellular carcinoma	X	X		X	X	X		X	X	X														X		
Hepatocellular carcinoma, multiple							X																			
Hepatocellular adenoma					X									X	X			X								
Hepatocellular adenoma, multiple																			X	X	X				X	
Mesentery													+								+				+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth			+	+							+		+			+	+	+	+	+		+	+		+	
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	M	+	+	M	+	+	M	+	+	M	+	+	M	+	M	+	M	+	+	M	+	+
Pituitary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars intermedia, adenoma									X																	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																										
Peritoneum																										

+: 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 Drinking Water Study of Dipropylene Glycol: 0 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 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	
Carcass ID Number	0 1 5	0 2 4	0 2 7	0 3 0	0 3 2	0 3 3	0 3 5	0 3 7	0 4 2	0 4 4	0 0 3	0 0 4	0 0 5	0 0 8	0 1 0	0 1 9	0 2 0	0 2 6	0 2 8	0 3 9	0 4 1	0 4 5	0 4 7	0 4 8	0 4 9	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																X										1
Polyp adenomatous							X																			1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Polyp adenomatous																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma									X																	1
Hepatocellular carcinoma																				X			X			11
Hepatocellular carcinoma, multiple					X																X					3
Hepatocellular adenoma		X		X		X		X					X	X												10
Hepatocellular adenoma, multiple					X						X						X									7
Mesentery								+		+		+		+								+				8
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma															X											1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth	+				+	+	+		+	+			+		+	+	+	+				+		+	+	26
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	M	M	+	+	+	+	+	M	+	+	+	M	+	+	+	M	+	+	+	+	+	36
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
Peritoneum		+																								1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	4 1 6	5 4 6	5 5 6	5 7 5	5 9 2	6 0 3	6 2 9	6 6 6	7 0 8	7 2 4	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
Carcass ID Number	0 4 3	0 2 1	0 1 7	0 4 0	0 2 9	0 1 8	0 1 3	0 2 2	0 1 6	0 3 4	0 0 1	0 0 7	0 1 1	0 2 3	0 2 5	0 3 1	0 3 6	0 3 8	0 4 6	0 5 0	0 0 2	0 0 6	0 0 9	0 1 2	0 1 4
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma									X																
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node										+															
Mediastinal, hepatocellular carcinoma, metastatic, liver										X															
Lymph node, mandibular	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	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
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pinna, ear, neural crest tumor														X											
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma							X																		
Alveolar/bronchiolar carcinoma															X										
Alveolar/bronchiolar carcinoma, multiple																									
Carcinoma, metastatic, harderian gland																									
Hepatocellular carcinoma, metastatic, liver	X					X		X	X	X															
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland													+												
Adenoma													X												
Carcinoma																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 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 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	
Carcass ID Number	0 1 5	0 2 4	0 2 7	0 3 0	0 3 2	0 3 3	0 3 5	0 3 7	0 4 2	0 4 4	0 3 3	0 0 4	0 0 5	0 1 8	0 1 0	0 1 9	0 2 0	0 2 6	0 2 8	0 3 9	0 4 1	0 4 5	0 4 7	0 4 8	0 4 9	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell, adenoma												X												X		3
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node																										1
Mediastinal, hepatocellular carcinoma, metastatic, liver																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
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	3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pinna, ear, neural crest tumor																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	49
Skeletal muscle										+																1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma									X					X												3
Alveolar/bronchiolar carcinoma																										1
Alveolar/bronchiolar carcinoma, multiple																				X					X	2
Carcinoma, metastatic, harderian gland										X																1
Hepatocellular carcinoma, metastatic, liver																							X			6
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland										+					+											3
Adenoma															X											2
Carcinoma										X																1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	4 1 6	5 4 6	5 5 6	5 7 5	5 9 2	6 0 3	6 2 9	6 6 6	7 0 8	7 2 4	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 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 4 3	0 2 1	0 1 7	0 4 0	0 2 9	0 1 8	0 1 3	0 2 2	0 1 6	0 3 4	0 0 1	0 0 7	0 1 1	0 2 3	0 2 5	0 3 1	0 3 6	0 3 8	0 4 6	0 5 0	0 0 2	0 0 6	0 0 9	0 1 2	0 1 4
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																									
Urethra							+																		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant																									
Mesothelioma malignant																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 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 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	
Carcass ID Number	0 1 5	0 2 4	0 2 7	0 3 0	0 3 2	0 3 3	0 3 5	0 3 7	0 4 2	0 4 4	0 0 3	0 0 4	0 0 5	0 0 8	0 1 0	0 1 9	0 2 0	0 2 6	0 2 8	0 3 9	0 4 1	0 4 5	0 4 7	0 4 8	0 4 9	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenoma											X															1
Urethra																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant																	X									1
Mesothelioma malignant										X																1

Table C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	224	405	405	491	501	561	588	619	661	686	710	729	729	729	729	729	729	730	730	730	730	730	730	730	730
Carcass ID Number	077	072	093	086	051	087	060	098	092	067	054	055	056	059	079	082	094	052	066	071	073	075	080	081	083
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp adenomatous																									
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Polyp adenomatous																									
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Hemangiosarcoma																							X		
Hepatocellular carcinoma					X	X																		X	X
Hepatocellular carcinoma, multiple								X	X	X															
Hepatocellular adenoma																		X	X			X	X		
Hepatocellular adenoma, multiple																									X
Histiocytic sarcoma			X																						
Mesentery	+										+						+	+							
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth				+			+				+	+			+							+	+		+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Pituitary gland	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicle, adenoma																									
General Body System																									
None																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	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	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	
Carcass ID Number	0 8 4	0 8 9	0 9 6	0 9 7	0 5 3	0 5 7	0 5 8	0 6 1	0 6 2	0 6 3	0 6 4	0 6 5	0 6 8	0 6 9	0 7 0	0 7 4	0 7 6	0 7 8	0 8 5	0 8 8	0 9 0	0 9 1	0 9 5	0 9 9	1 0 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Polyp adenomatous				X		X																				2
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma									X					X												2
Polyp adenomatous												X														1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																							X			1
Hemangiosarcoma																		X	X							3
Hepatocellular carcinoma					X												X							X		7
Hepatocellular carcinoma, multiple																										3
Hepatocellular adenoma		X		X						X						X		X		X	X	X	X	X		14
Hepatocellular adenoma, multiple											X	X														3
Histiocytic sarcoma																										1
Mesentery				+	+						+	+	+												+	10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth		+			+	+	+	+		+		+				+		+	+	+	+			+	+	22
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	45
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicle, adenoma																				X						1
General Body System																										
None																										

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	224	205	405	491	501	561	588	619	661	686	710	729	729	729	729	729	729	730	730	730	730	730	730	730	730
Carcass ID Number	07707	07702	07903	08806	08501	08817	08960	09108	09902	06607	05504	05505	05506	05509	07709	08202	08904	09502	09626	09701	09713	09735	09800	09801	09803
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma			X																						
Lymph node, mandibular	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma			X																						
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma			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
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pinna, ear, neural crest tumor																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																				X					
Alveolar/bronchiolar carcinoma																									
Alveolar/bronchiolar carcinoma, multiple									X																
Hepatocellular carcinoma, metastatic, liver					X			X	X	X														X	
Histiocytic sarcoma			X																						
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye											+														
Harderian gland											+														
Adenoma											X														

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	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	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	
Carcass ID Number	0 8 4	0 8 9	0 9 6	0 9 7	0 5 3	0 5 7	0 5 8	0 6 1	0 6 2	0 6 3	0 6 4	0 6 5	0 6 8	0 6 9	0 7 0	0 7 4	0 7 6	0 7 8	0 8 5	0 8 8	0 9 0	0 9 1	0 9 5	0 9 9	1 0 0	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																				X						1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	M	+	M	+	M	+	+	+	+	+	+	+	+	45
Histiocytic sarcoma																										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	3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pinna, ear, neural crest tumor					X																					1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X		X			X						X					X		X	X	X				9
Alveolar/bronchiolar carcinoma	X							X									X									3
Alveolar/bronchiolar carcinoma, multiple																								X		2
Hepatocellular carcinoma, metastatic, liver																	X									6
Histiocytic sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye			+																							2
Harderian gland		+	+																							3
Adenoma		X	X																							3

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	2	4	4	4	5	5	5	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	2	0	0	9	0	6	8	1	6	8	1	2	2	2	2	2	2	3	3	3	3	3	3	3	3	3
	4	5	5	1	1	1	8	9	1	6	0	9	9	9	9	9	9	0	0	0	0	0	0	0	0	0
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	7	9	8	5	8	6	9	9	6	5	5	5	5	7	8	9	5	6	7	7	7	8	8	8	8
	7	2	3	6	1	7	0	8	2	7	4	5	6	9	9	2	4	2	6	1	3	5	0	1	3	
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma			X																							

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	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	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	
Carcass ID Number	0 8 4	0 8 9	0 9 6	0 9 7	0 5 3	0 5 7	0 5 8	0 6 1	0 6 2	0 6 3	0 6 4	0 6 5	0 6 8	0 6 9	0 7 0	0 7 4	0 7 6	0 7 8	0 8 5	0 8 8	0 9 0	0 9 1	0 9 5	0 9 9	1 0 0	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	4 9 4	5 1 8	5 4 2	5 7 5	6 1 6	6 4 0	6 4 5	6 4 5	6 6 1	6 6 6	6 7 2	6 7 6	7 0 6	7 0 8	7 2 7	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
Carcass ID Number	1 1 3	1 0 4	1 1 1	1 4 1	1 3 5	1 0 2	1 3 1	1 4 6	1 1 5	1 4 2	1 1 2	1 1 9	1 0 9	1 4 9	1 4 5	1 0 7	1 0 8	1 2 4	1 2 5	1 2 6	1 2 8	1 4 8	1 0 1	1 0 3	1 0 5
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																							X		
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung	X																								
Hemangioma																		X							
Hemangiosarcoma															X										
Hepatoblastoma					X		X	X			X														
Hepatocellular carcinoma						X							X					X	X						
Hepatocellular carcinoma, multiple					X			X		X															
Hepatocellular adenoma			X				X									X	X	X		X					
Hepatocellular adenoma, multiple											X														X
Hepatocholangiocarcinoma	X																								
Mesentery															+										
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth				+		+	+	+	+			+		+		+				+			+	+	
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skeletal muscle	X																								
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung	X																								
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma							X																		
Parathyroid gland	+	M	M	+	M	+	M	+	M	+	M	+	+	+	+	M	M	+	+	+	+	+	+	+	M
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 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 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	
Carcass ID Number	1 1 1 6	1 1 1 7	1 1 1 8	1 2 2 1	1 2 2 3	1 2 2 9	1 3 2 2	1 3 3 3	1 3 3 4	1 3 3 7	1 3 3 8	1 4 4 4	1 4 4 7	1 5 0 0	1 0 0 6	1 1 0 0	1 1 1 4	1 2 4 0	1 2 2 2	1 2 2 7	1 3 0 0	1 3 3 6	1 3 3 9	1 4 4 0	1 4 4 3	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma					X										X											3
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Hemangioma																	X									2
Hemangiosarcoma																										1
Hepatoblastoma																										4
Hepatocellular carcinoma																X		X	X						X	8
Hepatocellular carcinoma, multiple																										3
Hepatocellular adenoma				X	X				X	X		X								X	X			X		14
Hepatocellular adenoma, multiple							X				X							X	X							6
Hepatocholangiocarcinoma																										1
Mesentery																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth	+		+	+	+	+		+	+					+							+					20
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skeletal muscle																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Parathyroid gland	+	+	M	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	37
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	4 9 4	5 1 8	5 4 2	5 7 5	6 1 6	6 4 0	6 4 5	6 4 5	6 6 1	6 6 6	6 6 2	6 7 6	7 0 6	7 0 8	7 2 7	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
Carcass ID Number	1 1 0 3	1 0 4	1 1 1	1 4 1	1 3 5	1 0 2	1 3 1	1 4 6	1 1 5	1 4 2	1 1 2	1 1 9	1 0 9	1 4 9	1 4 5	1 0 7	1 0 8	1 2 4	1 2 5	1 2 6	1 2 8	1 4 8	1 0 1	1 0 3	1 0 5
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
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
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+																								
Sarcoma	X																								
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma			X			X																			
Alveolar/bronchiolar adenoma, multiple													X												
Alveolar/bronchiolar carcinoma														X						X					
Alveolar/bronchiolar carcinoma, multiple	X	X																							
Hepatocellular carcinoma, metastatic, liver					X																				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									+
Harderian gland																									+
Adenoma																									X
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skeletal muscle	X																								
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 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 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	
Carcass ID Number	1 1 1 6	1 1 1 7	1 1 1 8	1 2 2 1	1 2 2 3	1 2 2 9	1 3 3 2	1 3 3 3	1 3 3 4	1 3 3 7	1 3 3 8	1 3 4 4	1 4 4 7	1 5 0	1 0 6	1 1 0	1 1 4	1 2 0	1 2 2	1 2 7	1 3 0	1 3 6	1 3 9	1 4 0	1 4 3	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma			X																							1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
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	3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Sarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X											X													4
Alveolar/bronchiolar adenoma, multiple																										1
Alveolar/bronchiolar carcinoma	X						X					X									X					6
Alveolar/bronchiolar carcinoma, multiple																										2
Hepatocellular carcinoma, metastatic, liver																		X								2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye																										1
Harderian gland		+													+		+									4
Adenoma		X													X		X									4
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skeletal muscle																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	4 1 6	4 1 6	4 5 1	4 6 4	5 1 3	5 1 5	5 3 3	5 8 2	6 1 0	6 6 1	6 6 1	6 6 8	6 8 8	7 0 8	7 1 0	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
Carcass ID Number	1 7 7 6	1 8 4	1 6 3	1 7 4	1 7 3	1 8 0	1 8 3	1 8 9	1 8 5	1 9 2	1 9 5	1 8 7	1 6 9	1 9 9	1 7 9	1 5 5	1 5 7	1 6 0	1 6 1	1 8 1	1 8 8	1 9 1	1 5 6	1 5 9
Alimentary System																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																								
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																								
Hepatoblastoma												X												
Hepatocellular carcinoma						X		X		X				X		X			X					
Hepatocellular carcinoma, multiple			X				X					X	X		X					X				
Hepatocellular adenoma				X							X						X		X					
Hepatocellular adenoma, multiple																		X						
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth												+					+	+				+		
Cardiovascular System																								
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																								
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	M	M	+	+	+	+	+	M	+	M	M	M	+	+	+	M	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																								
None																								
Genital System																								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma																								

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 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 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	
Carcass ID Number	1 6 6 2	1 6 6 4	1 6 6 5	1 6 6 6	1 6 6 7	1 6 6 8	1 7 1	1 7 7 2	1 8 2	1 8 6	1 9 0	1 9 7	2 0 0	1 5 1	1 5 2	1 5 3	1 5 4	1 5 8	1 7 5	1 7 7	1 7 8	1 9 3	1 9 4	1 9 6	1 9 8	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma		X																								1
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma			X			X																				2
Hepatoblastoma																										1
Hepatocellular carcinoma							X										X						X			9
Hepatocellular carcinoma, multiple	X																									7
Hepatocellular adenoma																										4
Hepatocellular adenoma, multiple																						X				2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth						+												+				+				7
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid gland	+	+	+	+	+	+	M	+	M	+	M	+	+	M	+	+	+	+	M	M	M	M	+	+	M	33
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Interstitial cell, adenoma													X													1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	4 1 6	4 1 6	4 5 1	4 6 4	5 1 3	5 1 5	5 3 3	5 8 2	6 1 0	6 6 1	6 6 1	6 6 8	6 8 8	7 0 8	7 1 0	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
Carcass ID Number	1 7 7 6	1 8 4	1 6 3	1 7 4	1 7 3	1 8 0	1 8 3	1 8 9	1 8 5	1 9 2	1 9 5	1 8 7	1 6 9	1 9 9	1 7 9	1 5 5	1 5 7	1 6 0	1 6 1	1 8 1	1 8 8	1 9 1	1 5 6	1 5 9
Hematopoietic System																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Lymph node, mesenteric	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, intestine large, cecum																								
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma									X															
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
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle												+												
Hepatoblastoma, metastatic, liver												X												
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve									+															
Spinal cord									+															
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																	X			X		X		
Alveolar/bronchiolar carcinoma																								
Hepatoblastoma, metastatic, liver												X												
Hepatocellular carcinoma, metastatic, liver														X		X				X				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glands, carcinoma				X																				
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Harderian gland																					+			
Adenoma																					X			
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 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 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	
Carcass ID Number	1 6 2	1 6 4	1 6 5	1 6 6	1 6 7	1 6 8	1 7 1	1 7 2	1 8 2	1 8 6	1 9 0	1 9 7	2 0 0	1 5 1	1 5 2	1 5 3	1 5 4	1 5 8	1 7 5	1 7 7	1 7 8	1 9 3	1 9 4	1 9 6	1 9 8	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, intestine large, cecum		X																								1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	44
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	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skeletal muscle																										1
Hepatoblastoma, metastatic, liver																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma										X																4
Alveolar/bronchiolar carcinoma									X									X			X			X		4
Hepatoblastoma, metastatic, liver																										1
Hepatocellular carcinoma, metastatic, liver	X																									4
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Glands, carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Harderian gland																										1
Adenoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Harderian Gland: Adenoma				
Overall rate[a]	2/50 (4%)	3/50 (6%)	4/50 (8%)	1/49 (2%)
Adjusted rate[b]	4.4%	6.8%	8.9%	2.4%
Terminal rate[c]	2/40 (5%)	2/39 (5%)	4/35 (11%)	1/34 (3%)
First incidence (days)	729 (T)	710	729 (T)	729 (T)
Poly-3 test[d]	P=0.416N	P=0.482	P=0.329	P=0.531N
Harderian Gland: Adenoma or Carcinoma				
Overall rate	3/50 (6%)	3/50 (6%)	4/50 (8%)	1/49 (2%)
Adjusted rate	6.5%	6.8%	8.9%	2.4%
Terminal rate	3/40 (8%)	2/39 (5%)	4/35 (11%)	1/34 (3%)
First incidence (days)	729 (T)	710	729 (T)	729 (T)
Poly-3 test	P=0.285N	P=0.644	P=0.490	P=0.338N
Small Intestine (Duodenum or Jejunum): Adenomatous Polyp				
Overall rate	2/50 (4%)	3/50 (6%)	0/50 (0%)	0/49 (0%)
Adjusted rate	4.4%	6.8%	0.0%	0.0%
Terminal rate	2/40 (5%)	3/39 (8%)	0/35 (0%)	0/34 (0%)
First incidence (days)	729 (T)	729 (T)	—[e]	—
Poly-3 test	P=0.079N	P=0.481	P=0.241N	P=0.258N
Small Intestine (Jejunum): Carcinoma				
Overall rate	1/50 (2%)	2/50 (4%)	3/50 (6%)	0/49 (0%)
Adjusted rate	2.2%	4.5%	6.7%	0.0%
Terminal rate	1/40 (3%)	2/39 (5%)	3/35 (9%)	0/34 (0%)
First incidence (days)	729 (T)	729 (T)	729 (T)	—
Poly-3 test	P=0.375N	P=0.486	P=0.299	P=0.518N
Liver: Hemangiosarcoma				
Overall rate	0/50 (0%)	3/50 (6%)	1/50 (2%)	2/49 (4%)
Adjusted rate	0.0%	6.8%	2.2%	4.8%
Terminal rate	0/40 (0%)	3/39 (8%)	0/35 (0%)	2/34 (6%)
First incidence (days)	—	729 (T)	727	729 (T)
Poly-3 test	P=0.299	P=0.111	P=0.497	P=0.218
Liver: Hepatocellular Adenoma				
Overall rate	17/50 (34%)	17/50 (34%)	20/50 (40%)	6/49 (12%)
Adjusted rate	36.6%	38.6%	43.2%	14.0%
Terminal rate	16/40 (40%)	17/39 (44%)	17/35 (49%)	4/34 (12%)
First incidence (days)	592	729 (T)	542	464
Poly-3 test	P=0.011N	P=0.511	P=0.330	P=0.012N
Liver: Hepatocellular Carcinoma				
Overall rate	14/50 (28%)	10/50 (20%)	11/50 (22%)	16/49 (33%)
Adjusted rate	28.3%	21.7%	23.7%	35.3%
Terminal rate	5/40 (13%)	5/39 (13%)	6/35 (17%)	7/34 (21%)
First incidence (days)	416	501	616	451
Poly-3 test	P=0.200	P=0.306N	P=0.388N	P=0.306
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	29/50 (58%)	25/50 (50%)	28/50 (56%)	21/49 (43%)
Adjusted rate	58.7%	54.2%	58.8%	45.4%
Terminal rate	20/40 (50%)	20/39 (51%)	20/35 (57%)	10/34 (29%)
First incidence (days)	416	501	542	451
Poly-3 test	P=0.126N	P=0.408N	P=0.576	P=0.135N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Liver: Hepatoblastoma				
Overall rate	0/50 (0%)	0/50 (0%)	4/50 (8%)	1/49 (2%)
Adjusted rate	0.0%	0.0%	8.6%	2.4%
Terminal rate	0/40 (0%)	0/39 (0%)	0/35 (0%)	0/34 (0%)
First incidence (days)	—	—[f]	616	668
Poly-3 test	P=0.207		P=0.061	P=0.483
Liver: Hepatocellular Carcinoma or Hepatoblastoma				
Overall rate	14/50 (28%)	10/50 (20%)	13/50 (26%)	16/49 (33%)
Adjusted rate	28.3%	21.7%	27.7%	35.3%
Terminal rate	5/40 (13%)	5/39 (13%)	6/35 (17%)	7/34 (21%)
First incidence (days)	416	501	616	451
Poly-3 test	P=0.186	P=0.306N	P=0.561N	P=0.306
Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma				
Overall rate	29/50 (58%)	25/50 (50%)	28/50 (56%)	21/49 (43%)
Adjusted rate	58.7%	54.2%	58.8%	45.4%
Terminal rate	20/40 (50%)	20/39 (51%)	20/35 (57%)	10/34 (29%)
First incidence (days)	416	501	542	451
Poly-3 test	P=0.126N	P=0.408N	P=0.576	P=0.135N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	3/50 (6%)	9/50 (18%)	5/50 (10%)	4/49 (8%)
Adjusted rate	6.5%	20.4%	10.8%	9.5%
Terminal rate	2/40 (5%)	9/39 (23%)	2/35 (6%)	4/34 (12%)
First incidence (days)	629	729 (T)	542	729 (T)
Poly-3 test	P=0.526N	P=0.048	P=0.355	P=0.447
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	3/50 (6%)	5/50 (10%)	8/50 (16%)	4/49 (8%)
Adjusted rate	6.5%	11.3%	17.2%	9.5%
Terminal rate	3/40 (8%)	4/39 (10%)	5/35 (14%)	4/34 (12%)
First incidence (days)	729 (T)	661	494	729 (T)
Poly-3 test	P=0.366	P=0.337	P=0.102	P=0.451
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	6/50 (12%)	14/50 (28%)	13/50 (26%)	8/49 (16%)
Adjusted rate	13.0%	31.6%	27.3%	19.1%
Terminal rate	5/40 (13%)	13/39 (33%)	7/35 (20%)	8/34 (24%)
First incidence (days)	629	661	494	729 (T)
Poly-3 test	P=0.422	P=0.028	P=0.068	P=0.312
Testes: Adenoma				
Overall rate	3/50 (6%)	0/50 (0%)	0/50 (0%)	1/49 (2%)
Adjusted rate	6.5%	0.0%	0.0%	2.4%
Terminal rate	2/40 (5%)	0/39 (0%)	0/35 (0%)	1/34 (3%)
First incidence (days)	708	—	—	729 (T)
Poly-3 test	P=0.243N	P=0.127N	P=0.122N	P=0.339N
All Organs: Hemangiosarcoma				
Overall rate	0/50 (0%)	4/50 (8%)	2/50 (4%)	3/49 (6%)
Adjusted rate	0.0%	9.1%	4.4%	7.1%
Terminal rate	0/40 (0%)	4/39 (10%)	1/35 (3%)	2/34 (6%)
First incidence (days)	—	729 (T)	727	610
Poly-3 test	P=0.193	P=0.055	P=0.233	P=0.105

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	2/50 (4%)	5/50 (10%)	4/50 (8%)	3/49 (6%)
Adjusted rate	4.4%	11.3%	8.9%	7.1%
Terminal rate	2/40 (5%)	5/39 (13%)	3/35 (9%)	2/34 (6%)
First incidence (days)	729 (T)	729 (T)	727	610
Poly-3 test	P=0.486	P=0.200	P=0.329	P=0.464
All Organs: Benign Neoplasms				
Overall rate	27/50 (54%)	23/50 (46%)	26/50 (52%)	11/49 (22%)
Adjusted rate	57.6%	52.1%	55.7%	25.6%
Terminal rate	24/40 (60%)	22/39 (56%)	21/35 (60%)	9/34 (27%)
First incidence (days)	592	710	542	464
Poly-3 test	P<0.001N	P=0.372N	P=0.509N	P<0.001N
All Organs: Malignant Neoplasms				
Overall rate	19/50 (38%)	19/50 (38%)	26/50 (52%)	25/49 (51%)
Adjusted rate	38.4%	40.5%	53.7%	53.8%
Terminal rate	10/40 (25%)	13/39 (33%)	15/35 (43%)	14/34 (41%)
First incidence (days)	416	405	494	451
Poly-3 test	P=0.050	P=0.502	P=0.094	P=0.095
All Organs: Benign or Malignant Neoplasms				
Overall rate	39/50 (78%)	37/50 (74%)	39/50 (78%)	33/49 (67%)
Adjusted rate	78.9%	78.7%	79.5%	70.6%
Terminal rate	30/40 (75%)	30/39 (77%)	27/35 (77%)	21/34 (62%)
First incidence (days)	416	405	494	451
Poly-3 test	P=0.187N	P=0.589N	P=0.567	P=0.242N

(T) Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for liver, lung, and testes; 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 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 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 exposure group is indicated by **N**.
[e] Not applicable; no neoplasms in animal group
[f] Value of statistic cannot be computed.

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	3	3	5	9
Natural deaths	7	8	10	6
Survivors				
Died last week of study	1			
Terminal sacrifice	39	39	35	34
Missing				1
Animals examined microscopically	50	50	50	49
Alimentary System				
Esophagus	(50)	(50)	(50)	(49)
Inflammation, granulomatous	1 (2%)			
Gallbladder	(48)	(48)	(49)	(48)
Epithelium, cyst		1 (2%)		2 (4%)
Epithelium, cytoplasmic alteration	2 (4%)	1 (2%)		
Epithelium, mineralization			1 (2%)	
Intestine large, colon	(50)	(50)	(50)	(49)
Inflammation, suppurative	1 (2%)			
Serosa, inflammation, granulomatous		1 (2%)		
Intestine large, rectum	(50)	(50)	(50)	(49)
Epithelium, hyperplasia, focal	1 (2%)			
Intestine large, cecum	(50)	(50)	(50)	(49)
Ulcer		1 (2%)		
Intestine small, duodenum	(50)	(49)	(50)	(49)
Cyst				1 (2%)
Necrosis, focal	1 (2%)			
Epithelium, hyperplasia, focal				1 (2%)
Intestine small, jejunum	(50)	(50)	(50)	(49)
Hyperplasia				1 (2%)
Ulcer			1 (2%)	
Epithelium, hyperplasia, focal			1 (2%)	
Peyer's patch, hyperplasia, lymphoid	1 (2%)	1 (2%)	3 (6%)	
Peyer's patch, infiltration cellular, plasma cell			1 (2%)	
Liver	(50)	(50)	(50)	(49)
Angiectasis, focal			2 (4%)	1 (2%)
Basophilic focus	2 (4%)	1 (2%)		3 (6%)
Clear cell focus	26 (52%)	24 (48%)	31 (62%)	12 (24%)
Eosinophilic focus	15 (30%)	28 (56%)	18 (36%)	11 (22%)
Fibrosis, focal			1 (2%)	
Hepatodiaphragmatic nodule	1 (2%)			
Infiltration cellular, polymorphonuclear	1 (2%)			
Inflammation, chronic	23 (46%)	21 (42%)	20 (40%)	20 (41%)
Mixed cell focus	15 (30%)	20 (40%)	21 (42%)	7 (14%)
Necrosis, focal	7 (14%)	5 (10%)	5 (10%)	5 (10%)
Vacuolization cytoplasmic, focal	3 (6%)	3 (6%)	4 (8%)	2 (4%)
Serosa, fibrosis				1 (2%)
Mesentery	(8)	(10)	(1)	
Artery, inflammation, chronic		1 (10%)		
Fat, necrosis	7 (88%)	9 (90%)	1 (100%)	

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

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Alimentary System (continued)				
Pancreas	(50)	(50)	(50)	(49)
Fibrosis	1 (2%)			
Inflammation, chronic		1 (2%)		
Acinus, atrophy, focal	1 (2%)			
Duct, cyst				1 (2%)
Salivary glands	(50)	(50)	(50)	(49)
Atrophy, focal				1 (2%)
Stomach, forestomach	(50)	(50)	(50)	(49)
Hyperplasia, squamous	2 (4%)		1 (2%)	3 (6%)
Inflammation, focal, suppurative	2 (4%)			
Ulcer			2 (4%)	2 (4%)
Stomach, glandular	(50)	(50)	(50)	(49)
Infiltration cellular, lymphocyte			1 (2%)	
Inflammation, chronic	3 (6%)			
Mineralization, focal		3 (6%)		2 (4%)
Epithelium, hyperplasia, focal			2 (4%)	
Epithelium, inflammation, focal, suppurative		1 (2%)		
Tooth	(26)	(22)	(20)	(7)
Malformation	26 (100%)	22 (100%)	20 (100%)	7 (100%)
Cardiovascular System				
Blood vessel	(50)	(50)	(50)	(49)
Aorta, inflammation, chronic	1 (2%)			
Pulmonary artery, mineralization		1 (2%)		
Heart	(50)	(50)	(50)	(49)
Cardiomyopathy	3 (6%)		1 (2%)	
Artery, inflammation, chronic	1 (2%)	1 (2%)		
Myocardium, inflammation, chronic active, focal	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Myocardium, mineralization	2 (4%)		1 (2%)	
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(49)
Hyperplasia, focal	7 (14%)	4 (8%)	1 (2%)	
Hypertrophy, focal	28 (56%)	24 (48%)	23 (46%)	15 (31%)
Necrosis			1 (2%)	
Subcapsular, hyperplasia	47 (94%)	46 (92%)	44 (88%)	42 (86%)
Zona fasciculata, zona reticularis, vacuolization cytoplasmic	1 (2%)			
Adrenal medulla	(50)	(49)	(50)	(49)
Hyperplasia, focal		2 (4%)		
Islets, pancreatic	(50)	(50)	(50)	(49)
Hyperplasia	40 (80%)	41 (82%)	39 (78%)	43 (88%)
Pituitary gland	(49)	(48)	(49)	(49)
Pars distalis, hyperplasia, focal	3 (6%)	3 (6%)	2 (4%)	1 (2%)
Thyroid gland	(50)	(50)	(50)	(49)
Inflammation, granulomatous		1 (2%)		
Follicle, cyst	1 (2%)			1 (2%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
General Body System				
Peritoneum	(1)			
Inflammation, chronic	1 (100%)			
Genital System				
Epididymis	(50)	(50)	(50)	(49)
Atrophy				1 (2%)
Granuloma sperm	2 (4%)	1 (2%)		1 (2%)
Inflammation, chronic	1 (2%)			
Syncytial alteration	1 (2%)			
Preputial gland	(50)	(50)	(50)	(49)
Cyst	30 (60%)	32 (64%)	34 (68%)	34 (69%)
Cytoplasmic alteration			1 (2%)	
Inflammation, chronic	1 (2%)			2 (4%)
Inflammation, suppurative	5 (10%)	3 (6%)		
Bilateral, cyst	1 (2%)			
Prostate, NOS	(50)	(50)	(50)	(49)
Atrophy				1 (2%)
Inflammation, suppurative	1 (2%)			
Seminal vesicle	(50)	(50)	(50)	(49)
Atrophy				2 (4%)
Cyst		4 (8%)		1 (2%)
Fibrosis			1 (2%)	
Hyperplasia	1 (2%)	1 (2%)	2 (4%)	
Inflammation, chronic		1 (2%)		
Testes	(50)	(50)	(50)	(49)
Inflammation, granulomatous			1 (2%)	
Germinal epithelium, atrophy				1 (2%)
Interstitial cell, hyperplasia, focal	1 (2%)	2 (4%)		
Hematopoietic System				
Lymph node, mandibular	(47)	(49)	(48)	(47)
Hyperplasia, lymphoid	1 (2%)			
Infiltration cellular, megakaryocyte	1 (2%)			
Infiltration cellular, plasma cell		1 (2%)		
Lymph node, mesenteric	(48)	(50)	(49)	(48)
Hematopoietic cell proliferation	1 (2%)			
Hyperplasia, lymphoid			1 (2%)	
Infiltration cellular, plasma cell		1 (2%)		1 (2%)
Infiltration cellular, histiocyte				1 (2%)
Inflammation, granulomatous			1 (2%)	
Spleen	(50)	(50)	(50)	(49)
Hematopoietic cell proliferation	15 (30%)	17 (34%)	14 (28%)	12 (24%)
Lymphoid follicle, atrophy	11 (22%)	12 (24%)	11 (22%)	13 (27%)
Lymphoid follicle, hyperplasia	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Thymus	(46)	(45)	(47)	(44)
Hyperplasia, lymphoid		1 (2%)		
Integumentary System				
Skin	(50)	(50)	(50)	(49)
Hyperkeratosis				1 (2%)
Ulcer		1 (2%)	1 (2%)	

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Musculoskeletal System				
Bone	(49)	(50)	(50)	(49)
Fibrosis	2 (4%)			
Nervous System				
Brain	(50)	(50)	(50)	(49)
Hemorrhage		1 (2%)		
Peripheral nerve				(1)
Axon, degeneration				1 (100%)
Respiratory System				
Lung	(50)	(50)	(50)	(49)
Inflammation, chronic, focal		1 (2%)	1 (2%)	1 (2%)
Inflammation, granulomatous		1 (2%)	1 (2%)	1 (2%)
Metaplasia, focal, osseous			2 (4%)	1 (2%)
Thrombosis	1 (2%)		1 (2%)	
Alveolar epithelium, hyperplasia, focal	3 (6%)	3 (6%)	4 (8%)	3 (6%)
Artery, mineralization				1 (2%)
Nose	(50)	(50)	(50)	(49)
Hyperostosis	1 (2%)			
Inflammation, suppurative			1 (2%)	
Special Senses System				
Eye		(2)	(1)	
Cornea, degeneration		1 (50%)		
Cornea, inflammation, chronic			1 (100%)	
Cornea, inflammation, suppurative		1 (50%)		
Urinary System				
Kidney	(50)	(50)	(50)	(49)
Glomerulosclerosis			1 (2%)	
Hydronephrosis		2 (4%)	1 (2%)	
Infarct	7 (14%)	14 (28%)	10 (20%)	9 (18%)
Inflammation, acute	1 (2%)			
Inflammation, chronic, focal			1 (2%)	1 (2%)
Metaplasia, osseous	3 (6%)			
Nephropathy	38 (76%)	37 (74%)	34 (68%)	36 (73%)
Papilla, necrosis	2 (4%)			
Renal tubule, cyst	2 (4%)	1 (2%)	2 (4%)	
Renal tubule, degeneration			1 (2%)	
Renal tubule, hyperplasia, focal	3 (6%)	4 (8%)	2 (4%)	2 (4%)
Renal tubule, vacuolization cytoplasmic			1 (2%)	
Urethra	(1)			
Inflammation, suppurative	1 (100%)			
Urinary bladder	(50)	(50)	(50)	(48)
Inflammation, suppurative	1 (2%)			
Transitional epithelium, hyperplasia, focal			1 (2%)	

APPENDIX D
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF DIPROPYLENE GLYCOL

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TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental deaths				4
Moribund	2	1	4	6
Natural deaths	11	11	8	7
Survivors				
Died last week of study				1
Terminal sacrifice	37	38	38	32
Animals examined microscopically	50	50	50	50
Alimentary System				
Esophagus	(50)	(50)	(49)	(49)
Intestine large, colon	(50)	(50)	(50)	(50)
Leiomyoma	1 (2%)			
Polyp adenomatous, multiple				1 (2%)
Intestine small, duodenum	(50)	(50)	(50)	(50)
Polyp adenomatous		1 (2%)	1 (2%)	
Intestine small, jejunum	(50)	(50)	(50)	(50)
Leiomyosarcoma		1 (2%)		
Sarcoma NOS			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Hemangioma	1 (2%)		1 (2%)	1 (2%)
Hemangiosarcoma	2 (4%)			
Hepatoblastoma			1 (2%)	
Hepatocellular carcinoma	6 (12%)	2 (4%)	1 (2%)	2 (4%)
Hepatocellular carcinoma, multiple	1 (2%)		1 (2%)	
Hepatocellular adenoma	7 (14%)	11 (22%)	11 (22%)	10 (20%)
Hepatocellular adenoma, multiple	4 (8%)	3 (6%)	1 (2%)	1 (2%)
Histiocytic sarcoma			1 (2%)	1 (2%)
Sarcoma, metastatic, mesentery		1 (2%)	1 (2%)	
Mesentery	(11)	(18)	(13)	(14)
Carcinoma NOS			1 (8%)	
Fibrosarcoma			1 (8%)	
Fibrosarcoma, metastatic, bone		1 (6%)		
Liposarcoma		1 (6%)		
Sarcoma			1 (8%)	
Sarcoma NOS		2 (11%)		
Pancreas	(50)	(50)	(50)	(50)
Sarcoma, metastatic, mesentery		1 (2%)		
Stomach, forestomach	(50)	(50)	(50)	(50)
Squamous cell carcinoma		1 (2%)		
Squamous cell papilloma	2 (4%)			1 (2%)
Stomach, glandular	(50)	(50)	(50)	(50)
Tongue	(1)			
Squamous cell carcinoma	1 (100%)			
Cardiovascular System				
Heart	(50)	(50)	(49)	(50)
Carcinoma, metastatic, tissue NOS	1 (2%)			

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Endocrine System				
Adrenal cortex	(50)	(50)	(49)	(50)
Adrenal medulla	(50)	(49)	(49)	(50)
Pheochromocytoma malignant			1 (2%)	
Pheochromocytoma benign			1 (2%)	1 (2%)
Islets, pancreatic	(50)	(50)	(50)	(50)
Adenoma	2 (4%)			1 (2%)
Pituitary gland	(49)	(49)	(49)	(49)
Pars distalis, adenoma	1 (2%)	3 (6%)	3 (6%)	3 (6%)
Pars intermedia, carcinoma				1 (2%)
Thyroid gland	(49)	(48)	(49)	(48)
C-cell, carcinoma				1 (2%)
Follicle, adenoma		1 (2%)		1 (2%)
General Body System				
None				
Genital System				
Clitoral gland	(48)	(49)	(49)	(50)
Ovary	(50)	(50)	(50)	(50)
Cystadenoma		2 (4%)	2 (4%)	1 (2%)
Granulosa cell tumor benign	1 (2%)			
Histiocytic sarcoma			1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Deciduoma benign				1 (2%)
Polyp stromal			1 (2%)	
Hematopoietic System				
Bone marrow	(50)	(49)	(50)	(50)
Hemangiosarcoma		1 (2%)		
Histiocytic sarcoma			1 (2%)	
Lymph node	(5)	(3)	(1)	(2)
Mediastinal, sarcoma, metastatic, mesentery		1 (33%)		
Pancreatic, sarcoma, metastatic, mesentery		1 (33%)		
Lymph node, mandibular	(48)	(45)	(48)	(48)
Carcinoma, metastatic, harderian gland		1 (2%)		
Lymph node, mesenteric	(48)	(48)	(49)	(49)
Hemangioma				1 (2%)
Histiocytic sarcoma			1 (2%)	
Sarcoma, metastatic, mesentery			1 (2%)	
Sarcoma NOS			1 (2%)	
Spleen	(50)	(50)	(50)	(50)
Hemangiosarcoma	1 (2%)			
Histiocytic sarcoma			1 (2%)	
Thymus	(49)	(49)	(48)	(50)
Carcinoma, metastatic, tissue NOS	1 (2%)			
Hemangioma	1 (2%)		1 (2%)	

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Integumentary System				
Mammary gland	(50)	(50)	(50)	(49)
Adenoma	1 (2%)			
Carcinoma	1 (2%)	1 (2%)		1 (2%)
Skin	(50)	(50)	(50)	(50)
Subcutaneous tissue, sarcoma	3 (6%)	7 (14%)	2 (4%)	3 (6%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Fibrosarcoma		1 (2%)		
Skeletal muscle	(2)			
Sarcoma	1 (50%)			
Sarcoma NOS	1 (50%)			
Nervous System				
Brain	(50)	(49)	(49)	(50)
Respiratory System				
Lung	(50)	(50)	(49)	(50)
Alveolar/bronchiolar adenoma	2 (4%)		4 (8%)	1 (2%)
Alveolar/bronchiolar carcinoma	2 (4%)	2 (4%)	2 (4%)	2 (4%)
Carcinoma, metastatic, harderian gland		1 (2%)		
Carcinoma, metastatic, mesentery			1 (2%)	
Carcinoma, metastatic, tissue NOS	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	2 (4%)	1 (2%)	1 (2%)	
Histiocytic sarcoma			1 (2%)	1 (2%)
Sarcoma, metastatic, skin			2 (4%)	
Squamous cell carcinoma, metastatic, stomach, forestomach		1 (2%)		
Mediastinum, hemangiosarcoma	1 (2%)			
Special Senses System				
Harderian gland	(1)	(3)	(2)	(4)
Adenoma	1 (100%)	2 (67%)	2 (100%)	3 (75%)
Carcinoma		1 (33%)		
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Sarcoma, metastatic, mesentery		1 (2%)		
Renal tubule, adenoma		1 (2%)		
Urinary bladder	(50)	(49)	(49)	(50)
Sarcoma, metastatic, skin			1 (2%)	

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma			1 (2%)	1 (2%)
Lymphoma malignant	5 (10%)	2 (4%)	2 (4%)	4 (8%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	32	35	30	29
Total primary neoplasms	49	46	44	42
Total animals with benign neoplasms	22	24	22	21
Total benign neoplasms	24	24	28	27
Total animals with malignant neoplasms	18	18	14	14
Total malignant neoplasms	25	22	15	15
Total animals with metastatic neoplasms	3	6	4	
Total metastatic neoplasms	5	10	7	
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 D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	1 9 3	4 9 7	5 7 0	5 9 9	6 2 1	6 4 1	6 5 1	6 8 3	6 9 3	6 9 9	7 0 4	7 2 1	7 2 5	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	2 1 5	2 3 9	2 3 6	2 2 6	2 4 9	2 0 4	2 0 3	2 1 2	2 4 7	2 4 5	2 4 3	2 5 0	2 4 8	2 0 2	2 0 7	2 0 8	2 0 9	2 1 0	2 1 6	2 1 7	2 2 2	2 2 4	2 2 9	2 3 0	2 3 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																									
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Hemangiosarcoma																				X					
Hepatocellular carcinoma					X												X								
Hepatocellular carcinoma, multiple												X													
Hepatocellular adenoma										X							X	X	X						
Hepatocellular adenoma, multiple									X							X									
Mesentery			+								+			+	+		+		+					+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue		+																							
Squamous cell carcinoma		X																							
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, tissue NOS												X													
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X								
Parathyroid gland	+	+	+	M	+	+	+	M	+	M	+	M	+	+	+	+	+	+	M	+	M	+	+	+	M
Pituitary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Thyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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 Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	
Carcass ID Number	24 1	20 1	20 5	21 1	21 4	21 8	21 9	22 0	22 1	22 3	22 5	22 8	23 1	23 4	23 5	23 7	23 8	24 2	24 4	20 6	21 3	22 7	23 3	24 0	24 6	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyoma							X																			1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma			X																							1
Hemangiosarcoma										X																2
Hepatocellular carcinoma		X	X						X								X									6
Hepatocellular carcinoma, multiple																										1
Hepatocellular adenoma	X													X						X						7
Hepatocellular adenoma, multiple							X																X			4
Mesentery							+		+													+				11
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma										X																2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue																										1
Squamous cell carcinoma																										1
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, tissue NOS																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																	X									2
Parathyroid gland	+	+	+	M	+	+	+	+	+	M	M	+	M	+	+	+	+	+	M	M	M	+	+	+	M	35
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma								X																		1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	1 9 3	4 9 7	5 7 0	5 9 9	6 2 1	6 4 1	6 5 1	6 8 3	6 9 3	6 9 9	7 0 4	7 2 1	7 2 5	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	2 1 5	2 3 9	2 3 6	2 2 6	2 4 9	2 0 4	2 0 3	2 1 2	2 4 7	2 4 5	2 4 3	2 5 0	2 4 8	2 0 2	2 0 7	2 0 8	2 0 9	2 1 0	2 1 6	2 1 7	2 2 2	2 2 4	2 2 9	2 3 0	2 3 2
Genital System																									
Clitoral gland	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor benign																				X					
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node											+		+						+						
Lymph node, mandibular	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma					X																				
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, tissue NOS												X													
Hemangioma																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma													X												
Carcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, sarcoma			X			X																			
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle						+																			
Sarcoma																									
Sarcoma NOS						X																			
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve						+																			
Spinal cord						+																			
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma															X										
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, tissue NOS												X													
Hepatocellular carcinoma, metastatic, liver																	X								
Mediastinum, hemangiosarcoma					X																				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	
Carcass ID Number	24 1	20 1	20 5	21 1	21 4	21 8	21 9	22 0	22 1	22 3	22 5	22 8	23 1	23 4	23 5	23 7	23 8	24 2	24 4	20 6	21 3	21 7	23 3	24 0	24 6	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granulosa cell tumor benign																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node									+											+						5
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, tissue NOS																										1
Hemangioma																X										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Carcinoma											X															1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, sarcoma																X										3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																+										2
Sarcoma																X										1
Sarcoma NOS																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X																								2
Alveolar/bronchiolar carcinoma		X																							X	2
Carcinoma, metastatic, tissue NOS																										1
Hepatocellular carcinoma, metastatic, liver									X																	2
Mediastinum, hemangiosarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	1 9 3	4 9 7	5 7 0	5 9 9	6 2 1	6 4 1	6 5 1	6 8 3	6 9 3	6 9 9	7 0 4	7 2 1	7 2 5	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	2 1 5	2 3 9	2 3 6	2 2 6	2 4 9	2 0 4	2 0 3	2 1 2	2 4 7	2 4 5	2 4 3	2 5 0	2 4 8	2 0 2	2 0 7	2 0 8	2 0 9	2 1 0	2 1 6	2 1 7	2 2 2	2 2 4	2 2 9	2 3 0	2 3 2
Special Senses System																										
Eye																										
Harderian gland																										
Adenoma																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant	X												X						X							

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 0 ppm

Number of Days on Study	7 2 8	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 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	2 4 1	2 0 1	2 0 5	2 1 1	2 1 4	2 1 8	2 1 9	2 2 0	2 2 1	2 2 3	2 2 5	2 2 8	2 3 1	2 3 4	2 3 5	2 3 7	2 3 8	2 4 2	2 4 4	2 4 6	2 0 1	2 1 3	2 2 7	2 3 3	2 4 0	2 4 6	Total Tissues/ Tumors
Special Senses System																											
Eye																							+				1
Harderian gland																							+				1
Adenoma																							X				1
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant									X	X																	5

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	4 9 4	5 4 3	5 6 1	5 8 5	6 4 1	6 4 3	6 7 1	6 8 7	6 8 9	6 9 3	7 1 1	7 2 6	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	2 7 0	2 9 3	2 7 7	2 7 8	2 8 5	2 5 5	2 5 4	2 5 6	2 5 2	2 7 5	2 6 2	2 8 3	2 5 3	2 5 9	2 6 1	2 6 4	2 6 7	2 6 8	2 6 9	2 7 1	2 7 2	2 7 4	2 7 9	2 8 1	2 8 7
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polp adenomatous																								X	
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma			X																						
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																									
Hepatocellular adenoma								X	X				X												
Hepatocellular adenoma, multiple															X						X				
Sarcoma, metastatic, mesentery										X															
Mesentery	+	+	+			+				+				+		+		+		+	+		+	+	+
Fibrosarcoma, metastatic, bone																			X						
Liposarcoma																									
Sarcoma NOS						X				X															
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, mesentery						X																			
Salivary glands	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma											X														
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	M	M	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																				X					
Thyroid gland	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicle, adenoma																X									
General Body System																									
None																									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	
Carcass ID Number	29494	29496	29497	25577	26060	26066	27373	27676	28282	28484	28686	28889	28989	29090	29292	29929	25191	25518	26363	26655	26805	29091	29515	29780	30080	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp adenomatous																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma				X																X						2
Hepatocellular adenoma		X	X		X	X				X	X			X						X						11
Hepatocellular adenoma, multiple															X											3
Sarcoma, metastatic, mesentery																										1
Mesentery				+		+				+										+						18
Fibrosarcoma, metastatic, bone																										1
Liposarcoma																				X						1
Sarcoma NOS																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, mesentery																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	M	M	+	+	39
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma							X															X				3
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Follicle, adenoma																										1
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	4 9 4	5 4 3	5 6 1	5 8 5	6 4 1	6 4 3	6 7 1	6 8 7	6 8 9	6 9 3	7 1 1	7 2 6	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	2 7 0	2 9 3	2 7 7	2 7 8	2 8 5	2 5 5	2 5 4	2 5 6	2 5 2	2 7 5	2 6 2	2 8 3	2 5 3	2 5 9	2 6 1	2 6 4	2 6 7	2 6 8	2 6 9	2 7 1	2 7 2	2 7 4	2 7 9	2 8 1	2 8 7
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph node						+	+																		
Mediastinal, sarcoma, metastatic, mesentery						X																			
Pancreatic, sarcoma, metastatic, mesentery						X																			
Lymph node, mandibular	+	+	M	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Carcinoma, metastatic, harderian gland													X												
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, sarcoma			X		X			X	X			X				X									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																			X						
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, harderian gland													X												
Hepatocellular carcinoma, metastatic, liver																									
Squamous cell carcinoma, metastatic, stomach, forestomach											X														
Nose	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland					+								+												
Adenoma					X																				
Carcinoma													X												

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	
Carcass ID Number	29494	29496	29497	25577	26060	26066	27073	27076	28082	28484	28686	28889	29089	29090	29092	29929	25191	25818	26363	26655	26880	29091	29515	29780	30030	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma	X																						X			2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																				X						1
Lymph node													+													3
Mediastinal, sarcoma, metastatic, mesentery																										1
Pancreatic, sarcoma, metastatic, mesentery																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	45
Carcinoma, metastatic, harderian gland																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma				X																						1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, sarcoma																X										7
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma																	X					X				2
Carcinoma, metastatic, harderian gland																										1
Hepatocellular carcinoma, metastatic, liver																				X						1
Squamous cell carcinoma, metastatic, stomach, forestomach																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Harderian gland																		+								3
Adenoma																		X								2
Carcinoma																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	4 9 4	5 4 3	5 6 1	5 8 5	6 4 1	6 4 3	6 7 1	6 8 7	6 8 9	6 9 3	7 1 1	7 2 6	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	2 7 0	2 9 3	2 7 7	2 7 8	2 8 5	2 5 5	2 5 4	2 5 6	2 5 2	2 7 5	2 6 2	2 8 3	2 5 3	2 5 9	2 6 1	2 6 4	2 6 7	2 6 8	2 6 9	2 7 1	2 7 2	2 7 4	2 7 9	2 8 1	2 8 7
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, mesentery										X															
Renal tubule, adenoma																		X							
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant							X																		

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 10,000 ppm

Number of Days on Study	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	
Carcass ID Number	29 94	29 96	29 97	25 77	26 00	26 06	27 03	27 76	28 02	28 04	28 06	28 88	28 89	29 00	29 02	29 99	25 11	25 18	26 03	26 05	26 80	29 01	29 15	29 80	30 00	Total Tissues/ Tumors
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, mesentery																											1
Renal tubule, adenoma																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	49
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant													X														2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	3 4 0	4 0 6	4 8 4	5 1 5	5 4 3	5 7 6	5 7 6	5 9 9	6 5 4	6 5 4	6 9 3	7 0 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	3 0 4	3 4 3	3 2 6	3 0 7	3 2 7	3 1 3	3 5 0	3 2 0	3 0 8	3 3 9	3 4 2	3 2 5	3 0 2	3 0 3	3 0 9	3 1 0	3 1 2	3 1 7	3 2 1	3 2 4	3 2 8	3 2 9	3 3 0	3 3 1	3 3 4
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp adenomatous															X										
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma NOS						X																			
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma													X												
Hepatoblastoma											X														
Hepatocellular carcinoma																									
Hepatocellular carcinoma, multiple																									
Hepatocellular adenoma																X									X
Hepatocellular adenoma, multiple																									
Histiocytic sarcoma																									
Sarcoma, metastatic, mesentery								X																	
Mesentery				+				+	+	+	+							+						+	+
Carcinoma NOS																									
Fibrosarcoma																									
Sarcoma								X																	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																								X	
Pheochromocytoma benign											X														
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma															X							X			
Thyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	728	728	728	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	
Carcass ID Number	33 37	34 40	34 45	34 46	34 47	34 49	30 01	30 05	30 06	31 14	31 18	31 19	32 03	33 32	33 33	33 38	34 01	34 14	34 48	31 11	31 15	31 16	32 02	33 25	33 36	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polp adenomatous																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma NOS																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Hepatoblastoma																										1
Hepatocellular carcinoma												X														1
Hepatocellular carcinoma, multiple														X												1
Hepatocellular adenoma		X		X					X		X		X	X				X			X		X			11
Hepatocellular adenoma, multiple																X										1
Histiocytic sarcoma	X																									1
Sarcoma, metastatic, mesentery																										1
Mesentery				+					+					+					+				+			13
Carcinoma NOS														X												1
Fibrosarcoma				X																						1
Sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																										1
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma																							X			3
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	3 4 0	4 0 6	4 8 4	5 1 5	5 4 3	5 7 6	5 7 6	5 9 9	6 5 4	6 5 4	6 9 3	7 0 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	3 0 4	3 4 3	3 2 6	3 0 7	3 2 7	3 1 3	3 5 0	3 2 0	3 0 8	3 3 9	3 4 2	3 2 5	3 0 2	3 0 3	3 0 9	3 1 0	3 1 2	3 1 7	3 2 1	3 2 4	3 2 8	3 2 9	3 3 0	3 3 1	3 3 4
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma																							X		
Histiocytic sarcoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Lymph node			+																						
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Sarcoma, metastatic, mesentery								X																	
Sarcoma NOS						X																			
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Thymus	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, sarcoma							X			X															
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma							X								X										X
Alveolar/bronchiolar carcinoma									X																
Carcinoma, metastatic, mesentery																									
Hepatocellular carcinoma, metastatic, liver																									
Histiocytic sarcoma																									
Sarcoma, metastatic, skin							X			X															
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																									
Adenoma																									

Table D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	728	728	728	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	
Carcass ID Number	337	340	345	346	347	349	301	305	306	314	318	319	323	332	333	338	341	344	348	311	315	316	322	335	336	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma					X																					2
Histiocytic sarcoma	X																									1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal	X																									1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma	X																									1
Lymph node																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma	X																									1
Sarcoma, metastatic, mesentery																										1
Sarcoma NOS																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma	X																									1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hemangioma															X											1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, sarcoma																										2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma					X																					4
Alveolar/bronchiolar carcinoma			X																							2
Carcinoma, metastatic, mesentery														X												1
Hepatocellular carcinoma, metastatic, liver														X												1
Histiocytic sarcoma	X																									1
Sarcoma, metastatic, skin																										2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Harderian gland											+									+						2
Adenoma											X									X						2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	3 4 0	4 0 6	4 8 4	5 1 5	5 4 3	5 7 6	5 7 6	5 9 9	6 5 4	6 5 4	6 9 3	7 0 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	3 0 4	3 4 3	3 2 6	3 0 7	3 2 7	3 1 3	3 5 0	3 2 0	3 0 8	3 3 9	3 4 2	3 2 5	3 0 2	3 0 3	3 0 9	3 1 0	3 1 2	3 1 7	3 2 1	3 2 4	3 2 8	3 2 9	3 3 0	3 3 1	3 3 4
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin							X																	
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																								
Lymphoma malignant												X												

Table D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 20,000 ppm

Number of Days on Study	728	728	728	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	
Carcass ID Number	337	340	345	346	347	349	301	305	306	314	318	319	323	332	333	338	341	344	348	311	315	316	322	335	336	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic, skin																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma	X																									1
Lymphoma malignant																							X			2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	0202	2208	3395	4522	5011	5011	5044	5422	5422	5422	5422	5422	5422	5645	6467	6545	6883	6983	7228	7228	7228	7228	7228	7228	7228	7228
Carcass ID Number	3722	3766	3822	3667	3551	3554	3552	3616	3662	3663	3664	3665	3665	3858	3558	3773	3883	3884	3557	3606	3675	3799	3808	3881	3910	3992
Alimentary System																										
Esophagus	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp adenomatous, multiple			X																							
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																										X
Hepatocellular carcinoma											X															
Hepatocellular adenoma										X										X		X		X		X
Hepatocellular adenoma, multiple																										
Histiocytic sarcoma																	X									
Mesentery				+	+											+	+		+						+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth			+																							
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign			X																							
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma			X																							
Parathyroid gland	M	M	+	+	M	+	+	+	M	M	+	+	M	M	+	M	M	+	+	+	M	+	+	M	+	
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma															X					X	X					
Pars intermedia, carcinoma			X																							
Thyroid gland	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, carcinoma			X																							
Follicle, adenoma																										
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	
Carcass ID Number	39 96	39 99	40 00	35 03	35 56	35 59	36 66	36 68	36 69	37 01	37 74	38 46	38 67	38 79	39 01	39 13	39 34	39 45	39 57	35 05	37 00	37 73	37 78	38 88	39 08	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polp adenomatous, multiple																										1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Hepatocellular carcinoma																				X						2
Hepatocellular adenoma			X						X				X			X					X					10
Hepatocellular adenoma, multiple																		X								1
Histiocytic sarcoma																										1
Mesentery			+		+			+			+					+	+					+			+	14
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma		X																								1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										1
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Parathyroid gland	+	M	+	M	+	+	+	+	+	M	+	+	+	+	M	M	M	+	+	M	+	+	+	M	M	30
Pituitary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma																										3
Pars intermedia, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C-cell, carcinoma																										1
Follicle, adenoma								X																		1
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma																							X			1

Table D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	020	228	395	452	501	501	504	542	542	542	542	542	565	647	654	687	698	728	728	728	728	728	728	728	728
Carcass ID Number	372	376	382	367	351	354	352	361	362	363	364	365	385	358	377	383	384	357	360	375	379	380	381	390	392
Genital System (continued)																									
Oviduct																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Deciduoma benign									X																
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node																							+		
Lymph node, mandibular	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma							X																		
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, sarcoma													X					X							
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																			X						
Alveolar/bronchiolar carcinoma																				X					
Histiocytic sarcoma																X									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									+
Harderian gland																						+			+
Adenoma																						X			X
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Lymphoma malignant																	X						X		

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol: 40,000 ppm

Number of Days on Study	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	
Carcass ID Number	39 96	39 99	40 00	35 03	35 36	35 69	36 66	36 68	36 69	37 01	37 74	38 46	38 67	38 89	39 01	39 13	39 34	39 45	39 57	35 50	37 00	37 73	37 78	38 88	39 08	Total Tissues/ Tumors
Genital System (continued)																										
Oviduct											+															1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Deciduoma benign																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node																									+	2
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangioma																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma			X																							1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, sarcoma										X																3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Alveolar/bronchiolar carcinoma																					X					2
Histiocytic sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Eye																						+				2
Harderian gland										+												+				4
Adenoma										X																3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant											X														X	4

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Harderian Gland: Adenoma				
Overall rate[a]	1/50 (2%)	2/50 (4%)	2/50 (4%)	3/50 (6%)
Adjusted rate[b]	2.2%	4.3%	4.5%	7.5%
Terminal rate[c]	1/37 (3%)	1/38 (3%)	2/38 (5%)	3/33 (9%)
First incidence (days)	728 (T)	641	728 (T)	728 (T)
Poly-3 test[d]	P=0.184	P=0.506	P=0.487	P=0.259
Harderian Gland: Adenoma or Carcinoma				
Overall rate	1/50 (2%)	3/50 (6%)	2/50 (4%)	3/50 (6%)
Adjusted rate	2.2%	6.4%	4.5%	7.5%
Terminal rate	1/37 (3%)	2/38 (5%)	2/38 (5%)	3/33 (9%)
First incidence (days)	728 (T)	641	728 (T)	728 (T)
Poly-3 test	P=0.242	P=0.312	P=0.487	P=0.259
Liver: Hepatocellular Adenoma				
Overall rate	11/50 (22%)	14/50 (28%)	12/50 (24%)	11/50 (22%)
Adjusted rate	23.9%	30.0%	27.2%	27.0%
Terminal rate	9/37 (24%)	12/38 (32%)	12/38 (32%)	10/33 (30%)
First incidence (days)	693	687	728 (T)	542
Poly-3 test	P=0.468	P=0.333	P=0.452	P=0.464
Liver: Hepatocellular Carcinoma				
Overall rate	7/50 (14%)	2/50 (4%)	2/50 (4%)	2/50 (4%)
Adjusted rate	15.1%	4.3%	4.5%	4.9%
Terminal rate	5/37 (14%)	2/38 (5%)	2/38 (5%)	1/33 (3%)
First incidence (days)	621	728 (T)	728 (T)	542
Poly-3 test	P=0.081N	P=0.078N	P=0.090N	P=0.113N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	17/50 (34%)	15/50 (30%)	13/50 (26%)	13/50 (26%)
Adjusted rate	36.6%	32.2%	29.5%	31.5%
Terminal rate	13/37 (35%)	13/38 (34%)	13/38 (34%)	11/33 (33%)
First incidence (days)	621	687	728 (T)	542
Poly-3 test	P=0.345N	P=0.409N	P=0.310N	P=0.392N
Liver: Hepatocellular Carcinoma or Hepatoblastoma				
Overall rate	7/50 (14%)	2/50 (4%)	3/50 (6%)	2/50 (4%)
Adjusted rate	15.1%	4.3%	6.8%	4.9%
Terminal rate	5/37 (14%)	2/38 (5%)	2/38 (5%)	1/33 (3%)
First incidence (days)	621	728 (T)	693	542
Poly-3 test	P=0.101N	P=0.078N	P=0.175N	P=0.113N
Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma				
Overall rate	17/50 (34%)	15/50 (30%)	14/50 (28%)	13/50 (26%)
Adjusted rate	36.6%	32.2%	31.6%	31.5%
Terminal rate	13/37 (35%)	13/38 (34%)	13/38 (34%)	11/33 (33%)
First incidence (days)	621	687	693	542
Poly-3 test	P=0.360N	P=0.409N	P=0.392N	P=0.392N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	2/50 (4%)	0/50 (0%)	4/49 (8%)	1/50 (2%)
Adjusted rate	4.4%	0.0%	9.1%	2.5%
Terminal rate	2/37 (5%)	0/38 (0%)	3/38 (8%)	1/33 (3%)
First incidence (days)	728 (T)	—[e]	576	728 (T)
Poly-3 test	P=0.543	P=0.235N	P=0.319	P=0.546N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	3/50 (6%)	2/50 (4%)	6/49 (12%)	3/50 (6%)
Adjusted rate	6.6%	4.3%	13.5%	7.5%
Terminal rate	3/37 (8%)	2/38 (5%)	4/38 (11%)	3/33 (9%)
First incidence (days)	728 (T)	728 (T)	576	728 (T)
Poly-3 test	P=0.359	P=0.495N	P=0.226	P=0.599
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	1/49 (2%)	3/49 (6%)	3/49 (6%)	3/49 (6%)
Adjusted rate	2.2%	6.6%	6.9%	7.6%
Terminal rate	1/37 (3%)	3/38 (8%)	3/38 (8%)	2/32 (6%)
First incidence (days)	728 (T)	728 (T)	728 (T)	654
Poly-3 test	P=0.218	P=0.303	P=0.287	P=0.253
Skin (Subcutaneous Tissue): Sarcoma				
Overall rate	3/50 (6%)	7/50 (14%)	2/50 (4%)	3/50 (6%)
Adjusted rate	6.4%	14.7%	4.5%	7.4%
Terminal rate	1/37 (3%)	2/38 (5%)	0/38 (0%)	2/33 (6%)
First incidence (days)	570	561	576	565
Poly-3 test	P=0.417N	P=0.165	P=0.518N	P=0.597
All Organs: Hemangiosarcoma				
Overall rate	3/50 (6%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
Adjusted rate	6.5%	2.2%	0.0%	0.0%
Terminal rate	2/37 (5%)	1/38 (3%)	0/38 (0%)	0/33 (0%)
First incidence (days)	621	728 (T)	—	—
Poly-3 test	P=0.046N	P=0.304N	P=0.127N	P=0.146N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	5/50 (10%)	1/50 (2%)	2/50 (4%)	2/50 (4%)
Adjusted rate	10.8%	2.2%	4.5%	4.9%
Terminal rate	4/37 (11%)	1/38 (3%)	2/38 (5%)	1/33 (3%)
First incidence (days)	621	728 (T)	728 (T)	504
Poly-3 test	P=0.253N	P=0.101N	P=0.235N	P=0.270N
All Organs: Malignant Lymphoma				
Overall rate	5/50 (10%)	2/50 (4%)	2/50 (4%)	4/50 (8%)
Adjusted rate	10.7%	4.3%	4.5%	10.0%
Terminal rate	3/37 (8%)	1/38 (3%)	1/38 (3%)	3/33 (9%)
First incidence (days)	193	671	708	698
Poly-3 test	P=0.568	P=0.219N	P=0.240N	P=0.594N
All Organs: Benign Neoplasms				
Overall rate	22/50 (44%)	24/50 (48%)	22/50 (44%)	21/50 (42%)
Adjusted rate	47.7%	51.1%	49.2%	48.8%
Terminal rate	19/37 (51%)	21/38 (55%)	20/38 (53%)	16/33 (49%)
First incidence (days)	693	641	576	395
Poly-3 test	P=0.534	P=0.453	P=0.530	P=0.545
All Organs: Malignant Neoplasms				
Overall rate	18/50 (36%)	18/50 (36%)	14/50 (28%)	14/50 (28%)
Adjusted rate	36.9%	37.3%	30.2%	33.1%
Terminal rate	11/37 (30%)	9/38 (24%)	7/38 (18%)	9/33 (27%)
First incidence (days)	193	561	576	395
Poly-3 test	P=0.331N	P=0.567	P=0.318N	P=0.435N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
All Organs: Benign or Malignant Neoplasms				
Overall rate	32/50 (64%)	35/50 (70%)	30/50 (60%)	29/50 (58%)
Adjusted rate	65.3%	72.5%	64.7%	65.2%
Terminal rate	23/37 (62%)	26/38 (68%)	23/38 (61%)	20/33 (61%)
First incidence (days)	193	561	576	395
Poly-3 test	P=0.435N	P=0.289	P=0.563N	P=0.584N

(T) Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for liver, lung, 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 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 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 exposure group is indicated by **N**.
[e] Not applicable; no neoplasms in animal group

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental deaths				4
Moribund	2	1	4	6
Natural deaths	11	11	8	7
Survivors				
Died last week of study				1
Terminal sacrifice	37	38	38	32
Animals examined microscopically	50	50	50	50
Alimentary System				
Esophagus	(50)	(50)	(49)	(49)
Ulcer				1 (2%)
Gallbladder	(50)	(50)	(49)	(50)
Epithelium, cyst	5 (10%)	1 (2%)	1 (2%)	1 (2%)
Epithelium, cytoplasmic alteration	1 (2%)			
Intestine small, jejunum	(50)	(50)	(50)	(50)
Epithelium, hyperplasia, focal	1 (2%)			
Muscularis, inflammation, chronic			1 (2%)	
Peyer's patch, hyperplasia, lymphoid			2 (4%)	2 (4%)
Peyer's patch, inflammation, acute	1 (2%)			1 (2%)
Serosa, fibrosis			1 (2%)	
Intestine small, ileum	(50)	(50)	(50)	(50)
Epithelium, inflammation, chronic			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Angiectasis			1 (2%)	
Angiectasis, focal	3 (6%)	1 (2%)	2 (4%)	1 (2%)
Basophilic focus	2 (4%)		1 (2%)	1 (2%)
Clear cell focus	5 (10%)	5 (10%)	2 (4%)	8 (16%)
Eosinophilic focus	21 (42%)	13 (26%)	16 (32%)	17 (34%)
Hepatodiaphragmatic nodule				1 (2%)
Infiltration cellular, lymphocyte	30 (60%)	39 (78%)	35 (70%)	30 (60%)
Inflammation, chronic	36 (72%)	33 (66%)	35 (70%)	34 (68%)
Inflammation, focal, suppurative			1 (2%)	
Mixed cell focus	14 (28%)	19 (38%)	21 (42%)	15 (30%)
Necrosis, focal	2 (4%)	2 (4%)	2 (4%)	1 (2%)
Vacuolization cytoplasmic, focal	4 (8%)	10 (20%)	9 (18%)	10 (20%)
Sinusoid, amyloid deposition			1 (2%)	
Mesentery	(11)	(18)	(13)	(14)
Artery, inflammation, chronic				1 (7%)
Fat, necrosis	11 (100%)	13 (72%)	11 (85%)	13 (93%)
Vein, thrombosis		1 (6%)		
Pancreas	(50)	(50)	(50)	(50)
Inflammation, granulomatous			1 (2%)	
Acinus, atrophy			1 (2%)	1 (2%)
Acinus, vacuolization cytoplasmic, focal	1 (2%)			
Duct, cyst				1 (2%)
Salivary glands	(49)	(49)	(49)	(49)
Atrophy			1 (2%)	

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

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Alimentary System (continued)				
Stomach, forestomach	(50)	(50)	(50)	(50)
Hemorrhage				1 (2%)
Hyperplasia, squamous	4 (8%)	1 (2%)	1 (2%)	2 (4%)
Inflammation, focal, suppurative				1 (2%)
Ulcer	3 (6%)		1 (2%)	1 (2%)
Epithelium, cyst			1 (2%)	
Stomach, glandular	(50)	(50)	(50)	(50)
Infiltration cellular, lymphocyte		1 (2%)		
Inflammation, chronic	1 (2%)	1 (2%)	1 (2%)	
Mineralization, focal	4 (8%)	2 (4%)	5 (10%)	
Ulcer		1 (2%)		2 (4%)
Tooth				(1)
Malformation				1 (100%)
Cardiovascular System				
Blood vessel	(50)	(50)	(50)	(50)
Aorta, inflammation, chronic				2 (4%)
Aorta, mineralization	1 (2%)	3 (6%)		
Heart	(50)	(50)	(49)	(50)
Cardiomyopathy	1 (2%)			
Artery, inflammation, chronic	1 (2%)			1 (2%)
Epicardium, inflammation, chronic active		1 (2%)		
Myocardium, inflammation, chronic active, focal	2 (4%)			1 (2%)
Myocardium, mineralization	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Valve, inflammation, chronic			1 (2%)	
Endocrine System				
Adrenal cortex	(50)	(50)	(49)	(50)
Hematopoietic cell proliferation		1 (2%)		
Hyperplasia, focal	1 (2%)	1 (2%)	2 (4%)	
Hypertrophy, focal	3 (6%)	3 (6%)	2 (4%)	1 (2%)
Subcapsular, hyperplasia	48 (96%)	49 (98%)	49 (100%)	48 (96%)
Adrenal medulla	(50)	(49)	(49)	(50)
Hyperplasia, focal	1 (2%)		1 (2%)	
Islets, pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	31 (62%)	29 (58%)	29 (58%)	33 (66%)
Pituitary gland	(49)	(49)	(49)	(49)
Angiectasis	1 (2%)			
Pars distalis, hyperplasia, focal	6 (12%)	8 (16%)	6 (12%)	5 (10%)
Thyroid gland	(49)	(48)	(49)	(48)
Inflammation, granulomatous	1 (2%)	1 (2%)		2 (4%)
Follicle, cyst	1 (2%)			
General Body System				
None				

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Genital System				
Clitoral gland	(48)	(49)	(49)	(50)
Cyst				1 (2%)
Hyperplasia				1 (2%)
Inflammation, granulomatous		1 (2%)		
Ovary	(50)	(50)	(50)	(50)
Angiectasis	3 (6%)		5 (10%)	2 (4%)
Cyst	12 (24%)	11 (22%)	15 (30%)	14 (28%)
Hemorrhage	2 (4%)			
Periovarian tissue, infiltration cellular, lymphocyte		1 (2%)		
Oviduct				(1)
Cyst				1 (100%)
Uterus	(50)	(50)	(50)	(50)
Angiectasis		1 (2%)	2 (4%)	1 (2%)
Inflammation, chronic active	1 (2%)			
Endometrium, hyperplasia, cystic	38 (76%)	38 (76%)	39 (78%)	39 (78%)
Hematopoietic System				
Bone marrow	(50)	(49)	(50)	(50)
Fibrosis		1 (2%)		
Necrosis, acute, focal	1 (2%)			
Vacuolization cytoplasmic, focal	1 (2%)			
Lymph node	(5)	(3)	(1)	(2)
Lumbar, hematopoietic cell proliferation	1 (20%)			
Lumbar, infiltration cellular, plasma cell	2 (40%)			
Lumbar, infiltration cellular, histiocyte	1 (20%)			
Mediastinal, congestion			1 (100%)	
Mediastinal, hyperplasia, lymphoid			1 (100%)	
Mediastinal, infiltration cellular, plasma cell	1 (20%)			
Mediastinal, infiltration cellular, histiocyte	1 (20%)			
Mediastinal, pigmentation, hemosiderin	1 (20%)			
Pancreatic, inflammation, granulomatous			1 (100%)	
Renal, hyperplasia, lymphoid			1 (100%)	
Lymph node, mandibular	(48)	(45)	(48)	(48)
Hematopoietic cell proliferation			1 (2%)	
Hyperplasia, lymphoid	1 (2%)	1 (2%)		
Lymph node, mesenteric	(48)	(48)	(49)	(49)
Hyperplasia, lymphoid		1 (2%)		2 (4%)
Infiltration cellular, plasma cell		1 (2%)		
Infiltration cellular, histiocyte		1 (2%)		
Inflammation, granulomatous	2 (4%)		1 (2%)	
Spleen	(50)	(50)	(50)	(50)
Hematopoietic cell proliferation	29 (58%)	24 (48%)	25 (50%)	24 (48%)
Inflammation, granulomatous		1 (2%)		
Capsule, fibrosis, focal			1 (2%)	
Lymphoid follicle, amyloid deposition			1 (2%)	
Lymphoid follicle, atrophy	12 (24%)	10 (20%)	10 (20%)	12 (24%)
Lymphoid follicle, hyperplasia	7 (14%)	8 (16%)	6 (12%)	7 (14%)
Thymus	(49)	(49)	(48)	(50)
Hyperplasia, lymphoid	5 (10%)	1 (2%)	4 (8%)	1 (2%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Integumentary System				
Mammary gland	(50)	(50)	(50)	(49)
Hyperplasia		1 (2%)		1 (2%)
Duct, hyperplasia, squamous	1 (2%)			
Skin	(50)	(50)	(50)	(50)
Ulcer			1 (2%)	
Epidermis, cyst			1 (2%)	
Epidermis, hyperplasia, focal			1 (2%)	
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Fibrosis	4 (8%)	4 (8%)	4 (8%)	
Nervous System				
Brain	(50)	(49)	(49)	(50)
Hydrocephalus				2 (4%)
Necrosis, acute, focal			1 (2%)	
Artery, meninges, inflammation, chronic				1 (2%)
Hypothalamus, compression		1 (2%)		2 (4%)
Peripheral nerve	(1)			
Sciatic, axon, degeneration	1 (100%)			
Spinal cord	(1)			
Axon, degeneration	1 (100%)			
Respiratory System				
Lung	(50)	(50)	(49)	(50)
Congestion				1 (2%)
Hemorrhage, focal	1 (2%)	1 (2%)		
Inflammation, chronic, focal	3 (6%)	2 (4%)	4 (8%)	2 (4%)
Inflammation, granulomatous	1 (2%)	3 (6%)		2 (4%)
Thrombosis	3 (6%)			
Alveolar epithelium, hyperplasia, focal	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Artery, inflammation, chronic	1 (2%)			
Artery, mineralization		1 (2%)		
Bronchus, foreign body				4 (8%)
Bronchus, inflammation, acute	1 (2%)			4 (8%)
Nose	(50)	(49)	(50)	(50)
Inflammation, acute				3 (6%)
Inflammation, suppurative	1 (2%)			1 (2%)
Necrosis, focal	1 (2%)			
Glands, cyst	1 (2%)			

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

	0 ppm	10,000 ppm	20,000 ppm	40,000 ppm
Special Senses System				
Eye	(1)			(2)
Atrophy				1 (50%)
Degeneration				1 (50%)
Cornea, inflammation, chronic	1 (100%)			
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Hydronephrosis			2 (4%)	
Infarct	4 (8%)	7 (14%)	9 (18%)	8 (16%)
Inflammation, focal, suppurative			1 (2%)	
Metaplasia, osseous	1 (2%)	3 (6%)		
Nephropathy	12 (24%)	8 (16%)	15 (30%)	12 (24%)
Artery, inflammation, chronic	1 (2%)		1 (2%)	
Papilla, necrosis			1 (2%)	
Renal tubule, hyperplasia, focal		1 (2%)		
Renal tubule, vacuolization cytoplasmic				1 (2%)
Urinary bladder	(50)	(49)	(49)	(50)
Hemorrhage	1 (2%)			
Inflammation, acute	1 (2%)			

APPENDIX E
GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST PROTOCOL 214
RESULTS 214
TABLE E1 Mutagenicity of Dipropylene Glycol in *Salmonella typhimurium* 215

GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST PROTOCOL

Testing was performed as reported by Zeiger *et al.* (1987). Dipropylene glycol 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, and TA1535 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 37° 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 incubation for 2 days at 37° C.

Each trial consisted of triplicate plates of concurrent positive and negative controls and five doses of dipropylene glycol. In the absence of toxicity, 10,000 µg/plate was selected as the high dose. All trials were repeated at the same or higher S9 percentage.

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.

RESULTS

Dipropylene glycol (100 to 10,000 µg/plate) was not mutagenic in *S. typhimurium* strain TA97, TA98, TA100, or TA1535 with or without rat or hamster liver S9 enzymes (Table E1).

TABLE E1
Mutagenicity of Dipropylene Glycol in *Salmonella typhimurium*[a]

Strain	Dose (µg/plate)	Revertants/Plate[b]					
		−S9		+hamster S9		+rat S9	
		Trial 1	Trial 2	10%	30%	10%	30%
TA100	0	165 ± 1.7	112 ± 9.7	121 ± 2.4	159 ± 4.2	112 ± 10.1	191 ± 11.0
	100	156 ± 3.5	99 ± 4.1	128 ± 5.4	161 ± 11.3	123 ± 2.2	185 ± 14.0
	333	170 ± 5.8	115 ± 7.1	132 ± 4.6	173 ± 7.4	141 ± 2.6	182 ± 13.2
	1,000	162 ± 4.0	118 ± 13.9	122 ± 8.5	193 ± 9.8	111 ± 7.7	170 ± 7.5
	3,333	178 ± 3.1	116 ± 5.0	125 ± 3.7	168 ± 8.3	121 ± 1.2	202 ± 24.2
	10,000	177 ± 6.2	121 ± 8.8	109 ± 5.5	170 ± 4.9	103 ± 8.5	190 ± 7.0
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control[c]		343 ± 17.0	430 ± 3.6	335 ± 3.6	446 ± 7.8	963 ± 7.3	950 ± 12.2
TA1535	0	6 ± 3.0	8 ± 1.3	10 ± 2.2	17 ± 1.0	10 ± 0.9	17 ± 3.2
	100	9 ± 0.9	10 ± 0.6	12 ± 1.3	14 ± 1.0	12 ± 2.2	17 ± 1.3
	333	10 ± 0.7	12 ± 1.8	9 ± 0.6	22 ± 3.1	11 ± 1.2	19 ± 2.8
	1,000	13 ± 2.5	11 ± 2.6	12 ± 2.8	15 ± 2.0	10 ± 0.7	19 ± 3.5
	3,333	11 ± 1.3	9 ± 1.3	13 ± 2.7	20 ± 1.5	12 ± 0.6	16 ± 2.0
	10,000	13 ± 1.2	10 ± 1.3	12 ± 2.4	21 ± 3.6	9 ± 2.1	16 ± 1.5
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		206 ± 12.1	296 ± 4.7	62 ± 4.5	99 ± 18.6	190 ± 15.4	157 ± 6.4
TA97	0	153 ± 11.7	95 ± 1.9	193 ± 5.3	195 ± 5.2	193 ± 3.0	239 ± 1.5
	100	173 ± 4.4	92 ± 7.3	204 ± 2.5	217 ± 3.1	201 ± 12.2	219 ± 13.9
	333	156 ± 6.7	91 ± 5.7	204 ± 10.1	205 ± 9.6	186 ± 6.0	244 ± 12.4
	1,000	157 ± 1.5	93 ± 6.4	208 ± 15.0	212 ± 10.1	185 ± 2.0	236 ± 15.2
	3,333	171 ± 19.1	98 ± 3.5	179 ± 10.6	216 ± 2.2	204 ± 7.6	226 ± 5.4
	10,000	179 ± 14.2	98 ± 12.1	196 ± 9.7	197 ± 7.0	188 ± 5.6	240 ± 11.6
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		972 ± 62.5	457 ± 56.2	1,818 ± 28.2	921 ± 85.2	1,562 ± 152.5	564 ± 14.6

		−S9		+hamster S9			+rat S9	
		Trial 1	Trial 2	10%	10%	30%	10%	30%
TA98	0	19 ± 2.6	20 ± 3.9	19 ± 5.8	17 ± 0.3	28 ± 2.4	33 ± 2.2	18 ± 1.7
	100	22 ± 1.9	23 ± 0.3	18 ± 2.6	18 ± 3.5	30 ± 3.5	24 ± 4.2	26 ± 1.7
	333	17 ± 2.7	19 ± 1.5	18 ± 4.3	17 ± 2.6	27 ± 5.2	19 ± 0.9	24 ± 0.0
	1,000	17 ± 2.3	15 ± 1.5	28 ± 4.1	13 ± 1.3	26 ± 1.5	26 ± 3.4	26 ± 0.7
	3,333	22 ± 1.5	21 ± 1.7	28 ± 0.9	16 ± 0.9	19 ± 2.7	22 ± 3.2	25 ± 3.2
	10,000	19 ± 1.2	19 ± 2.6	32 ± 4.7	13 ± 3.8	20 ± 5.2	27 ± 3.0	21 ± 1.8
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative	Negative
Positive control		435 ± 4.2	318 ± 2.3	258 ± 9.1	377 ± 8.5	361 ± 9.9	206 ± 2.3	407 ± 22.9

[a] Study was performed at Microbiological Associates, Inc. The detailed protocol is presented by Zeiger *et al*. (1987). 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 4-nitro-*o*-phenylenediamine (TA98). The positive control for metabolic activation with all strains was 2-aminoanthracene.

APPENDIX F
CLINICAL PATHOLOGY RESULTS

TABLE F1 Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol 218

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Male						
Hematology						
n						
Day 3	10	10	10	10	10	10
Day 22	10	9	9	10	8	10
Week 14	10	10	10	10	10	10
Automated hematocrit (%)						
Day 3	43.0 ± 0.6	43.4 ± 0.5	44.7 ± 0.9	45.1 ± 0.6	45.3 ± 1.1	46.3 ± 0.9**
Day 22	49.5 ± 0.5	49.2 ± 0.5	48.8 ± 0.5	50.3 ± 0.3	50.6 ± 0.3	51.6 ± 0.4**
Week 14	49.3 ± 0.8	48.7 ± 0.4	47.3 ± 0.6	45.0 ± 0.6**	45.7 ± 0.5**	51.3 ± 0.5
Manual hematocrit (%)						
Day 3	45.0 ± 0.6	44.9 ± 0.7	46.9 ± 1.0	46.4 ± 0.7	47.6 ± 1.0*	47.8 ± 0.6*
Day 22	47.3 ± 0.4	47.4 ± 0.6[b]	47.4 ± 0.6	48.4 ± 0.3	48.6 ± 0.2[c]	50.0 ± 0.3**
Week 14	48.6 ± 0.5	48.9 ± 0.3	47.2 ± 0.4	45.3 ± 0.6**	46.3 ± 0.4**	51.5 ± 0.4**
Hemoglobin (g/dL)						
Day 3	14.8 ± 0.2	15.0 ± 0.2	15.1 ± 0.3	15.3 ± 0.1	15.5 ± 0.3*	15.9 ± 0.2**
Day 22	16.1 ± 0.2	16.3 ± 0.1	15.9 ± 0.1	16.3 ± 0.1	16.5 ± 0.1	17.5 ± 0.1**
Week 14	16.4 ± 0.3	16.5 ± 0.1	15.8 ± 0.2	15.2 ± 0.2**	15.3 ± 0.2**	18.0 ± 0.2**
Erythrocytes (10^6/µL)						
Day 3	7.13 ± 0.06	7.22 ± 0.10	7.37 ± 0.12	7.40 ± 0.08*	7.36 ± 0.18	7.60 ± 0.09**
Day 22	8.18 ± 0.09	8.21 ± 0.06	7.97 ± 0.09	8.12 ± 0.08	7.95 ± 0.07	8.38 ± 0.07
Week 14	9.10 ± 0.13	8.94 ± 0.04	8.63 ± 0.10**	8.38 ± 0.11**	8.22 ± 0.09**	8.44 ± 0.11**
Reticulocytes (10^6/µL)						
Day 3	0.33 ± 0.01	0.33 ± 0.03	0.40 ± 0.03	0.32 ± 0.04	0.28 ± 0.02	0.37 ± 0.04
Day 22	0.19 ± 0.02	0.13 ± 0.02	0.22 ± 0.04	0.18 ± 0.02	0.19 ± 0.03	0.12 ± 0.01
Week 14	0.30 ± 0.04	0.28 ± 0.03	0.38 ± 0.03	0.33 ± 0.02	0.40 ± 0.04	0.21 ± 0.02
Nucleated erythrocytes/100 leukocytes						
Day 3	0.70 ± 0.42	0.40 ± 0.22	0.10 ± 0.10	0.30 ± 0.15	0.10 ± 0.10	0.60 ± 0.31
Day 22	0.00 ± 0.00	0.22 ± 0.22	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.40 ± 0.27
Week 14	0.20 ± 0.20	0.00 ± 0.00	0.40 ± 0.40	0.10 ± 0.10	0.00 ± 0.00	0.10 ± 0.10
Mean cell volume (fL)						
Day 3	60.3 ± 0.4	60.2 ± 0.3	60.6 ± 0.5	61.0 ± 0.4	61.6 ± 0.4	60.8 ± 0.6
Day 22	60.6 ± 0.5	60.0 ± 0.5	61.3 ± 0.6	62.0 ± 0.5*	63.6 ± 0.4**	61.6 ± 0.4**
Week 14	54.1 ± 0.2	54.5 ± 0.3	54.8 ± 0.2	53.6 ± 0.3	55.6 ± 0.2**	60.9 ± 0.5**
Mean cell hemoglobin (pg)						
Day 3	20.7 ± 0.1	20.8 ± 0.1	20.5 ± 0.2	20.7 ± 0.1	21.1 ± 0.1	20.9 ± 0.1
Day 22	19.7 ± 0.1	19.9 ± 0.1	20.0 ± 0.2	20.1 ± 0.1*	20.7 ± 0.2**	20.9 ± 0.1**
Week 14	18.0 ± 0.2	18.5 ± 0.1	18.3 ± 0.1	18.1 ± 0.1	18.6 ± 0.1*	21.3 ± 0.2**
Mean cell hemoglobin concentration (g/dL)						
Day 3	34.4 ± 0.2	34.5 ± 0.2	33.8 ± 0.2	34.0 ± 0.2	34.3 ± 0.2	34.4 ± 0.4
Day 22	32.5 ± 0.3	33.1 ± 0.2	32.7 ± 0.3	32.5 ± 0.1	32.6 ± 0.2	34.0 ± 0.2**
Week 14	33.4 ± 0.3	33.9 ± 0.21	33.5 ± 0.2	33.8 ± 0.2	33.4 ± 0.1	34.9 ± 0.2**
Platelets (10^3/µL)						
Day 3	679.7 ± 21.8	678.2 ± 18.6	713.3 ± 19.7	693.4 ± 12.4	735.0 ± 17.9*	776.3 ± 14.2**
Day 22	659.4 ± 16.9	692.0 ± 8.9	719.2 ± 27.9	766.4 ± 17.7**	752.4 ± 15.4**	517.1 ± 12.3**
Week 14	568.7 ± 22.8	628.9 ± 40.9	683.1 ± 23.2**	741.8 ± 10.1**	706.1 ± 18.0**	475.6 ± 11.8*
Leukocytes (10^3/µL)						
Day 3	6.25 ± 0.33	7.04 ± 0.39	6.90 ± 0.32	7.55 ± 0.38*	8.73 ± 0.30**	10.72 ± 0.40**
Day 22	7.62 ± 0.39	8.10 ± 0.40	7.33 ± 0.66	8.34 ± 0.58	8.00 ± 0.54	7.09 ± 0.38
Week 14	8.82 ± 0.45[c]	8.62 ± 0.38	9.82 ± 0.50	10.29 ± 0.53	12.19 ± 0.36**	8.02 ± 0.59
Segmented neutrophils (10^3/µL)						
Day 3	0.56 ± 0.05	0.70 ± 0.08	0.60 ± 0.05	0.66 ± 0.05	0.58 ± 0.07	0.34 ± 0.05
Day 22	0.97 ± 0.12	0.92 ± 0.11	0.66 ± 0.11	1.14 ± 0.06	0.78 ± 0.08	0.49 ± 0.05**
Week 14	1.42 ± 0.16[c]	1.15 ± 0.12	1.25 ± 0.12	0.94 ± 0.14	1.48 ± 0.26	1.08 ± 0.13

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Male (continued)						
Hematology (continued)						
n						
Day 3	10	10	10	10	10	10
Day 22	10	9	9	10	8	10
Week 14	10	10	10	10	10	10
Bands ($10^3/\mu L$)						
Day 3	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Day 22	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Week 14	0.00 ± 0.00[c]	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Lymphocytes ($10^3/\mu L$)						
Day 3	5.61 ± 0.31	6.27 ± 0.41	6.25 ± 0.34	6.78 ± 0.40*	8.02 ± 0.30**	10.31 ± 0.43**
Day 22	6.40 ± 0.36	6.96 ± 0.35	6.54 ± 0.59	6.92 ± 0.52	7.00 ± 0.55	6.50 ± 0.36
Week 14	7.31 ± 0.47[c]	7.35 ± 0.38	8.46 ± 0.45	9.30 ± 0.48*	10.38 ± 0.45**	6.82 ± 0.54
Monocytes ($10^3/\mu L$)						
Day 3	0.08 ± 0.02	0.06 ± 0.02	0.05 ± 0.02	0.10 ± 0.03	0.11 ± 0.05	0.06 ± 0.04
Day 22	0.21 ± 0.06	0.20 ± 0.04	0.13 ± 0.05	0.26 ± 0.05	0.26 ± 0.06	0.12 ± 0.05
Week 14	0.06 ± 0.02[c]	0.12 ± 0.04	0.07 ± 0.03	0.02 ± 0.01	0.14 ± 0.04	0.10 ± 0.03
Basophils ($10^3/\mu L$)						
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 22	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
Week 14	0.000 ± 0.000[c]	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
Eosinophils ($10^3/\mu L$)						
Day 3	0.02 ± 0.01	0.04 ± 0.02	0.02 ± 0.01	0.04 ± 0.03	0.02 ± 0.01	0.02 ± 0.01
Day 22	0.08 ± 0.03	0.04 ± 0.03	0.01 ± 0.01	0.05 ± 0.02	0.01 ± 0.01	0.00 ± 0.00*
Week 14	0.04 ± 0.03[c]	0.05 ± 0.03	0.03 ± 0.02	0.03 ± 0.02	0.04 ± 0.02	0.02 ± 0.02
Clinical Chemistry						
n						
Day 3	10	10	10	10	10	10
Day 22	10	10	9	10	9	10
Week 14	9	10	10	9	10	10
Urea nitrogen (mg/dL)						
Day 3	19.9 ± 0.6	19.6 ± 0.7	19.6 ± 0.7	18.7 ± 0.7	16.6 ± 0.7**	15.5 ± 0.6**
Day 22	21.3 ± 0.9	21.7 ± 0.8	21.7 ± 0.5	21.8 ± 0.6	21.9 ± 1.2	19.7 ± 1.3
Week 14	25.4 ± 1.5	27.4 ± 0.8	26.1 ± 0.8	24.6 ± 0.6	25.6 ± 0.6	20.2 ± 1.5**
Creatinine (mg/dL)						
Day 3	0.56 ± 0.02	0.56 ± 0.02	0.60 ± 0.02	0.69 ± 0.01**	1.12 ± 0.04**	1.46 ± 0.05**
Day 22	0.53 ± 0.02	0.55 ± 0.02	0.56 ± 0.02	0.62 ± 0.02	0.86 ± 0.08**	2.75 ± 0.10**
Week 14	0.67 ± 0.02	0.70 ± 0.02	0.71 ± 0.01	0.70 ± 0.00	0.73 ± 0.02	2.42 ± 0.17**
Total protein (g/dL)						
Day 3	5.5 ± 0.1	5.6 ± 0.1	5.6 ± 0.7	5.7 ± 0.1	5.8 ± 0.1	5.9 ± 0.1**
Day 22	5.9 ± 0.1	6.0 ± 0.1	6.1 ± 0.1	6.3 ± 0.1*	6.4 ± 0.1**	6.4 ± 0.1**
Week 14	7.1 ± 0.1	7.3 ± 0.1	7.6 ± 0.1	7.7 ± 0.2*	7.7 ± 0.1*	6.1 ± 0.1**
Albumin (g/dL)						
Day 3	4.1 ± 0.0	4.2 ± 0.1	4.2 ± 0.1	4.2 ± 0.1	4.3 ± 0.0	4.6 ± 0.2**
Day 22	4.7 ± 0.0	4.8 ± 0.1	4.8 ± 0.0	4.9 ± 0.1*	5.1 ± 0.1**	5.6 ± 0.1**
Week 14	5.2 ± 0.1	5.5 ± 0.1	5.6 ± 0.1	5.5 ± 0.1	5.6 ± 0.1	4.6 ± 0.2*
Alanine aminotransferase (IU/L)						
Day 3	46 ± 2	48 ± 2	49 ± 3	44 ± 2	41 ± 1	37 ± 2**
Day 22	43 ± 2	42 ± 1	42 ± 1	38 ± 1	45 ± 2	100 ± 7**
Week 14	78 ± 6	86 ± 7	77 ± 7	92 ± 13	158 ± 13**	116 ± 6**

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Male (continued)						
Clinical Chemistry (continued)						
n						
Day 3	10	10	10	10	10	10
Day 22	10	10	9	10	9	10
Week 14	9	10	10	9	10	10
Alkaline phosphatase (IU/L)						
Day 3	1,549 ± 44	1,586 ± 29	1,624 ± 71	1,547 ± 46	1,538 ± 43	1,407 ± 38
Day 22	997 ± 32	998 ± 18	1,005 ± 20	962 ± 27	926 ± 25	795 ± 21**
Week 14	571 ± 24	674 ± 13**	605 ± 26	589 ± 18	774 ± 31**	579 ± 15
Creatine kinase (IU/L)						
Day 3	219 ± 14	251 ± 27	241 ± 15	218 ± 14	242 ± 28	244 ± 19
Day 22	252 ± 16	256 ± 24	210 ± 15	216 ± 13	214 ± 20	231 ± 23
Week 14	167 ± 22	182 ± 28	152 ± 20	205 ± 27	206 ± 43	170 ± 10
Sorbitol dehydrogenase (IU/L)						
Day 3	16 ± 1	16 ± 1	17 ± 2	14 ± 1	15 ± 0	13 ± 1
Day 22	18 ± 2	17 ± 1	15 ± 2	19 ± 1	19 ± 1	20 ± 2
Week 14	24 ± 1	22 ± 1	22 ± 2	27 ± 4	46 ± 3**	38 ± 3**
Bile acids (µmol/L)						
Day 3	27.1 ± 6.8	30.8 ± 5.4	25.1 ± 4.6	23.6 ± 2.3	15.9 ± 3.1	11.6 ± 2.3*
Day 22	9.9 ± 3.8	12.3 ± 2.7	18.7 ± 3.3	10.9 ± 2.8	12.2 ± 2.8	12.4 ± 1.8
Week 14	3.8 ± 1.3	11.9 ± 2.7*	17.2 ± 3.6*	33.9 ± 10.1*	68.4 ± 17.2**	35.9 ± 5.4**
Female						
Hematology						
n						
Day 3	9	10	10	10	10	10
Day 22	10	10	10	9	10	10
Week 14	10	10	10	10	10	10
Automated hematocrit (%)						
Day 3	46.9 ± 1.2	45.0 ± 0.8	45.6 ± 0.5	47.3 ± 1.4	46.1 ± 0.7	48.6 ± 0.8
Day 22	48.5 ± 0.5	47.5 ± 0.4	48.9 ± 0.4	48.1 ± 0.2	48.7 ± 0.6	49.8 ± 0.4
Week 14	46.4 ± 0.5	46.1 ± 0.6	47.1 ± 0.4	46.7 ± 0.6	47.2 ± 0.5	47.5 ± 0.6
Manual hematocrit (%)						
Day 3	47.6 ± 0.9[b]	47.7 ± 2.0	46.8 ± 0.8	48.1 ± 1.3	46.9 ± 1.0	49.9 ± 0.5
Day 22	48.0 ± 0.6	47.4 ± 0.5	48.0 ± 0.5	47.8 ± 0.3	49.3 ± 0.6	50.2 ± 0.5**
Week 14	46.2 ± 0.5	45.7 ± 0.6	46.2 ± 0.4	46.2 ± 0.5	46.5 ± 0.5	47.0 ± 0.4
Hemoglobin (g/dL)						
Day 3	16.2 ± 0.3	15.5 ± 0.3	15.7 ± 0.1	16.1 ± 0.4	15.9 ± 0.2	16.7 ± 0.2
Day 22	16.4 ± 0.1	16.1 ± 0.1	16.5 ± 0.1	16.4 ± 0.1	16.4 ± 0.2	16.9 ± 0.1*
Week 14	15.8 ± 0.1	15.7 ± 0.2	16.0 ± 0.2	16.1 ± 0.1	15.9 ± 0.1	16.1 ± 0.2
Erythrocytes (10^6/µL)						
Day 3	7.89 ± 0.18	7.47 ± 0.14	7.62 ± 0.10	7.82 ± 0.17	7.65 ± 0.12	8.17 ± 0.14
Day 22	8.24 ± 0.09	8.09 ± 0.05	8.26 ± 0.08	8.19 ± 0.05	8.19 ± 0.08	8.43 ± 0.05
Week 14	8.17 ± 0.08	8.11 ± 0.09	8.24 ± 0.05	8.21 ± 0.08	8.26 ± 0.06	8.25 ± 0.08
Reticulocytes (10^6/µL)						
Day 3	0.35 ± 0.03	0.30 ± 0.03	0.37 ± 0.05	0.37 ± 0.04	0.40 ± 0.03	0.31 ± 0.03
Day 22	0.18 ± 0.04	0.13 ± 0.01	0.14 ± 0.02	0.13 ± 0.02	0.18 ± 0.02	0.19 ± 0.02
Week 14	0.22 ± 0.03	0.21 ± 0.02	0.22 ± 0.02	0.22 ± 0.02	0.21 ± 0.01	0.19 ± 0.03

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Female (continued)						
Hematology (continued)						
n						
Day 3	9	10	10	10	10	10
Day 22	10	10	10	9	10	10
Week 14	10	10	10	10	10	10
Nucleated erythrocytes/100 leukocytes						
Day 3	0.00 ± 0.00	0.10 ± 0.10	0.00 ± 0.00	0.00 ± 0.00	0.10 ± 0.10	0.10 ± 0.10
Day 22	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.20 ± 0.20	0.10 ± 0.10
Week 14	0.00 ± 0.00	0.10 ± 0.10	0.00 ± 0.00	0.40 ± 0.22	0.20 ± 0.13	0.10 ± 0.10
Mean cell volume (fL)						
Day 3	59.4 ± 0.5	60.3 ± 0.2	59.9 ± 0.4	60.4 ± 0.7	60.3 ± 0.2	59.5 ± 0.2
Day 22	58.9 ± 0.4	58.8 ± 0.4	59.2 ± 0.3	58.8 ± 0.3	59.4 ± 0.3	59.1 ± 0.2
Week 14	56.8 ± 0.2	56.9 ± 0.2	57.2 ± 0.2	56.9 ± 0.3	57.1 ± 0.3	57.5 ± 0.4
Mean cell hemoglobin (pg)						
Day 3	20.5 ± 0.2	20.7 ± 0.1	20.6 ± 0.2	20.7 ± 0.1	20.8 ± 0.1	20.4 ± 0.1
Day 22	19.9 ± 0.1	19.9 ± 0.1	20.0 ± 0.1	20.0 ± 0.1	20.0 ± 0.1	20.0 ± 0.1
Week 14	19.3 ± 0.1	19.4 ± 0.2	19.4 ± 0.1	19.6 ± 0.1	19.2 ± 0.2	19.5 ± 0.1
Mean cell hemoglobin concentration (g/dL)						
Day 3	34.5 ± 0.3	34.4 ± 0.3	34.3 ± 0.2	34.3 ± 0.4	34.5 ± 0.2	34.3 ± 0.2
Day 22	33.8 ± 0.1	33.9 ± 0.1	33.7 ± 0.2	34.0 ± 0.1	33.6 ± 0.2	33.9 ± 0.1
Week 14	34.1 ± 0.2	34.1 ± 0.3	33.9 ± 0.2	34.4 ± 0.2	33.6 ± 0.2	33.9 ± 0.2
Platelets (10^3/µL)						
Day 3	677.8 ± 20.1	712.2 ± 8.0	732.7 ± 23.7	707.3 ± 16.8	756.8 ± 19.9*	741.8 ± 18.9
Day 22	574.4 ± 10.7	596.2 ± 9.9	579.2 ± 10.7	604.3 ± 16.0	629.6 ± 14.0*	556.9 ± 17.1
Week 14	660.6 ± 16.0	727.6 ± 55.7	700.4 ± 17.9	679.7 ± 22.8	718.1 ± 25.0	672.3 ± 11.6
Leukocytes (10^3/µL)						
Day 3	8.82 ± 0.46	8.84 ± 0.22	8.36 ± 0.29	8.16 ± 0.51	9.74 ± 0.50	9.75 ± 0.51
Day 22	9.57 ± 0.79	8.90 ± 0.41	8.26 ± 0.38	8.41 ± 0.43	8.36 ± 0.35	9.00 ± 0.66
Week 14	6.30 ± 0.21	6.62 ± 0.39	7.89 ± 0.49*	6.62 ± 0.32	6.28 ± 0.28	6.58 ± 0.37
Segmented neutrophils (10^3/µL)						
Day 3	0.58 ± 0.07	0.69 ± 0.11	0.50 ± 0.05	0.58 ± 0.08	0.61 ± 0.10	0.58 ± 0.10
Day 22	0.86 ± 0.09	0.81 ± 0.11	0.66 ± 0.10	0.81 ± 0.12	0.61 ± 0.12	0.44 ± 0.05**
Week 14	1.21 ± 0.15	1.27 ± 0.22	1.59 ± 0.42	1.09 ± 0.09	0.76 ± 0.06	0.68 ± 0.09
Bands (10^3/µL)						
Day 3	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Day 22	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Week 14	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Lymphocytes (10^3/µL)						
Day 3	8.16 ± 0.43	7.99 ± 0.21	7.72 ± 0.32	7.47 ± 0.44	9.02 ± 0.45	9.05 ± 0.48
Day 22	8.43 ± 0.80	7.80 ± 0.41	7.31 ± 0.35	7.29 ± 0.33	7.54 ± 0.36	8.27 ± 0.69
Week 14	4.95 ± 0.22	5.27 ± 0.21	6.23 ± 0.31*	5.46 ± 0.32	5.46 ± 0.30	5.86 ± 0.35
Monocytes (10^3/µL)						
Day 3	0.07 ± 0.02	0.11 ± 0.05	0.13 ± 0.02	0.09 ± 0.03	0.08 ± 0.02	0.09 ± 0.04
Day 22	0.24 ± 0.02	0.26 ± 0.05	0.24 ± 0.03	0.22 ± 0.04	0.17 ± 0.04	0.25 ± 0.03
Week 14	0.06 ± 0.02	0.04 ± 0.02	0.06 ± 0.02	0.05 ± 0.02	0.04 ± 0.02	0.03 ± 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 22	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
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	0.04 ± 0.02	0.08 ± 0.03	0.05 ± 0.02	0.04 ± 0.02	0.02 ± 0.01	0.04 ± 0.02
Day 22	0.09 ± 0.03	0.07 ± 0.02	0.05 ± 0.02	0.11 ± 0.04	0.04 ± 0.02	0.02 ± 0.01
Week 14	0.10 ± 0.04	0.05 ± 0.02	0.05 ± 0.03	0.05 ± 0.02	0.03 ± 0.02	0.03 ± 0.02

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Female (continued)						
Clinical Chemistry						
n						
Day 3	10	10	10	10	10	10
Day 22	10	10	10	9	10	10
Week 14	10	10	10	10	10	10
Urea nitrogen (mg/dL)						
Day 3	21.8 ± 1.0	22.0 ± 0.7	20.4 ± 0.7	19.2 ± 0.6*	18.9 ± 0.8**	17.9 ± 0.6**
Day 22	23.7 ± 0.8	24.5 ± 0.5	22.7 ± 0.5	22.1 ± 0.6	22.3 ± 1.0	21.2 ± 0.8*
Week 14	21.4 ± 1.1	20.7 ± 1.0	21.0 ± 0.7[c]	21.3 ± 0.9	20.8 ± 0.7	20.3 ± 0.5
Creatinine (mg/dL)						
Day 3	0.62 ± 0.02	0.61 ± 0.02	0.60 ± 0.00	0.65 ± 0.02	0.83 ± 0.03**	0.86 ± 0.05**
Day 22	0.58 ± 0.01	0.58 ± 0.01	0.59 ± 0.01	0.59 ± 0.01	0.68 ± 0.02	1.69 ± 0.11**
Week 14	0.70 ± 0.02	0.69 ± 0.01	0.68 ± 0.01	0.70 ± 0.02	0.73 ± 0.02	1.29 ± 0.07**
Total protein (g/dL)						
Day 3	5.5 ± 0.1	5.6 ± 0.1	5.5 ± 0.1	5.7 ± 0.1	6.0 ± 0.1**	6.3 ± 0.1**
Day 22	5.9 ± 0.1	5.9 ± 0.1	5.9 ± 0.1	6.6 ± 0.1	6.3 ± 0.1**	6.6 ± 0.1**
Week 14	6.3 ± 0.1	6.4 ± 0.1	6.6 ± 0.1*	6.7 ± 0.1**	6.9 ± 0.1**	7.3 ± 0.1**
Albumin (g/dL)						
Day 3	4.1 ± 0.1	4.1 ± 0.0	4.1 ± 0.1	4.2 ± 0.1	4.3 ± 0.1**	4.5 ± 0.1**
Day 22	4.6 ± 0.1	4.8 ± 0.0	4.8 ± 0.1	4.8 ± 0.1	5.1 ± 0.1**	5.5 ± 0.1**
Week 14	4.8 ± 0.1	4.9 ± 0.1	4.9 ± 0.1	5.2 ± 0.1**	5.3 ± 0.1**	5.6 ± 0.1**
Alanine aminotransferase (IU/L)						
Day 3	41 ± 2	41 ± 1	41 ± 2	42 ± 1	38 ± 1	30 ± 1**
Day 22	37 ± 1	38 ± 1	37 ± 1	36 ± 1	37 ± 1	68 ± 9**
Week 14	40 ± 3	45 ± 2	42 ± 2	49 ± 4	46 ± 4	55 ± 5*
Alkaline phosphatase (IU/L)						
Day 3	1,315 ± 41	1,326 ± 19	1,297 ± 41	1,313 ± 44	1,308 ± 35	1,191 ± 32
Day 22	910 ± 23	904 ± 20	861 ± 19	846 ± 22*	826 ± 11**	781 ± 27**
Week 14	463 ± 9	488 ± 28	478 ± 20	420 ± 13	437 ± 22	495 ± 20
Creatine kinase (IU/L)						
Day 3	253 ± 17	229 ± 9	251 ± 14	269 ± 16	306 ± 22*	306 ± 13*
Day 22	184 ± 13	188 ± 12	202 ± 17	216 ± 10	248 ± 23*	196 ± 15
Week 14	120 ± 8	133 ± 16	149 ± 18	130 ± 8	153 ± 18	130 ± 14
Sorbitol dehydrogenase (IU/L)						
Day 3	14 ± 1[c]	14 ± 1	13 ± 0	14 ± 1[c]	13 ± 1	14 ± 1[c]
Day 22	19 ± 1	19 ± 1	19 ± 2	19 ± 2	19 ± 0	25 ± 1**
Week 14	16 ± 1	17 ± 1	16 ± 1	18 ± 1	20 ± 2	27 ± 3**
Bile acids (μmol/L)						
Day 3	19.0 ± 2.6	26.3 ± 3.9	25.3 ± 3.6	13.1 ± 4.0[c]	9.5 ± 2.2	9.8 ± 3.1[c]
Day 22	6.9 ± 2.2	13.9 ± 4.1	15.2 ± 4.8	16.0 ± 4.7	10.9 ± 2.7	9.9 ± 2.2
Week 14	8.1 ± 1.8	15.9 ± 3.1	15.4 ± 2.6	28.2 ± 5.9**	36.3 ± 9.5**	18.0 ± 2.4**

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Mean ± standard error. Statistical tests were performed on unrounded data.
[b] n=10
[c] n=9

APPENDIX G
ORGAN WEIGHTS
AND ORGAN-WEIGHT-TO-BODY-WEIGHT RATIOS

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TABLE G1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 2-Week Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
n	5	5	5	5	5	5
Male						
Necropsy body wt	194 ± 5	192 ± 3	194 ± 5	195 ± 4	190 ± 4	157 ± 2**
R. Kidney						
Absolute	0.902 ± 0.019	0.912 ± 0.024	0.926 ± 0.037	0.990 ± 0.040	1.054 ± 0.021**	1.206 ± 0.034**
Relative	4.644 ± 0.091	4.756 ± 0.173	4.773 ± 0.100	5.069 ± 0.158	5.567 ± 0.151**	7.680 ± 0.194**
Liver						
Absolute	10.066 ± 0.475	10.580 ± 0.490	11.062 ± 0.457	12.290 ± 0.494**	14.788 ± 0.610**	15.692 ± 0.338**
Relative	51.668 ± 1.384	55.011 ± 1.940	57.011 ± 1.294	62.868 ± 1.284**	77.957 ± 2.559**	99.933 ± 1.961**
Female						
Necropsy body wt	138 ± 2	141 ± 2	141 ± 2	139 ± 2	134 ± 3	121 ± 3**
R. Kidney						
Absolute	0.678 ± 0.027	0.692 ± 0.018	0.696 ± 0.022	0.706 ± 0.007	0.716 ± 0.020	0.766 ± 0.010
Relative	4.900 ± 0.143	4.903 ± 0.080	4.949 ± 0.117	5.101 ± 0.118	5.328 ± 0.103*	6.351 ± 0.165**
Liver						
Absolute	6.716 ± 0.259	7.034 ± 0.163	6.976 ± 0.159	6.948 ± 0.240	7.378 ± 0.118*	9.244 ± 0.134**
Relative	48.519 ± 1.178	49.865 ± 0.936	49.601 ± 0.426	50.136 ± 1.542	54.937 ± 0.481**	76.545 ± 0.700**

* Significantly different ($P \leq 0.05$) from the control group by Williams' 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 G2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
n	10	10	10	10	10	10
Male						
Necropsy body wt	360 ± 7	340 ± 10	345 ± 4	341 ± 4*	334 ± 5**	184 ± 6**
R. Kidney						
Absolute	1.217 ± 0.034	1.164 ± 0.039	1.235 ± 0.021	1.281 ± 0.028	1.473 ± 0.041**	1.431 ± 0.037**
Relative	3.381 ± 0.058	3.419 ± 0.036	3.580 ± 0.065	3.758 ± 0.048**	4.406 ± 0.100**	7.811 ± 0.164**
Liver						
Absolute	12.859 ± 0.437	13.529 ± 0.710	15.813 ± 0.369**	16.384 ± 0.443**	19.602 ± 0.410**	15.831 ± 0.315**
Relative	35.724 ± 0.881	39.568 ± 1.199*	45.802 ± 0.873**	48.095 ± 1.092**	58.745 ± 1.526**	86.536 ± 1.892**
Female						
Necropsy body wt	200 ± 3	197 ± 3	203 ± 4	190 ± 2*	189 ± 2*	168 ± 2**
R. Kidney						
Absolute	0.817 ± 0.043	0.771 ± 0.017	0.892 ± 0.036	0.807 ± 0.041	0.887 ± 0.014	1.043 ± 0.031**
Relative	4.104 ± 0.235	3.922 ± 0.072	4.426 ± 0.250	4.232 ± 0.197	4.691 ± 0.100*	6.191 ± 0.156**
Liver						
Absolute	6.871 ± 0.155	7.148 ± 0.243	7.963 ± 0.139**	7.658 ± 0.164**	8.353 ± 0.171**	11.871 ± 0.372**
Relative	34.448 ± 0.763	36.305 ± 0.894	39.335 ± 0.851**	40.203 ± 0.680**	44.113 ± 0.778**	70.516 ± 2.185**

* Significantly different ($P \leq 0.05$) from the control group by Williams' 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 G3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 2-Week Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
n	5	5	5	5	5	5
Male						
Necropsy body wt	27.3 ± 0.6	28.2 ± 0.5	27.4 ± 0.5	27.8 ± 0.6	27.1 ± 0.6	25.9 ± 0.5
R. Kidney						
Absolute	0.270 ± 0.003	0.292 ± 0.004	0.282 ± 0.012	0.300 ± 0.008	0.286 ± 0.009	0.280 ± 0.008
Relative	9.926 ± 0.269	10.361 ± 0.236	10.280 ± 0.342	10.797 ± 0.266	10.564 ± 0.169	10.827 ± 0.251
Liver						
Absolute	1.566 ± 0.0.47	1.694 ± 0.029	1.622 ± 0.077	1.636 ± 0.048	1.602 ± 0.064	1.818 ± 0.067*
Relative	57.421 ± 0.817	60.053 ± 0.879	59.105 ± 1.907	58.835 ± 1.025	59.115 ± 1.327	70.252 ± 1.816**
Female						
Necropsy body wt	22.7 ± 0.4	22.4 ± 0.6	22.2 ± 0.4	22.5 ± 0.5	23.0 ± 0.5	22.5 ± 0.8
R. Kidney						
Absolute	0.196 ± 0.005	0.194 ± 0.009	0.198 ± 0.006	0.206 ± 0.004	0.216 ± 0.005	0.216 ± 0.009
Relative	8.636 ± 0.177	8.635 ± 0.212	8.918 ± 0.335	9.151 ± 0.089	9.431 ± 0.354	9.623 ± 0.464*
Liver						
Absolute	1.340 ± 0.046	1.302 ± 0.056	1.304 ± 0.055	1.400 ± 0.061	1.454 ± 0.057	1.606 ± 0.078**
Relative	58.971 ± 1.077	58.009 ± 1.509	58.553 ± 1.568	62.048 ± 1.421	63.267 ± 1.571	71.350 ± 2.615**

* Significantly different ($P \leq 0.05$) from the 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 G4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	10,000 ppm	20,000 ppm	40,000 ppm	80,000 ppm
Male						
n	9	10	10	10	10	7
Necropsy body wt	38.0 ± 0.7	40.7 ± 0.9	40.7 ± 0.7	39.6 ± 0.9	40.5 ± 0.9	38.5 ± 0.6
R. Kidney						
Absolute	0.373 ± 0.021	0.364 ± 0.015	0.434 ± 0.023	0.424 ± 0.031	0.416 ± 0.017	0.366 ± 0.004
Relative	9.745 ± 0.477	8.955 ± 0.356	10.723 ± 0.715	10.728 ± 0.757	10.324 ± 0.496	9.522 ± 0.180
Liver						
Absolute	1.964 ± 0.095	1.984 ± 0.032	2.266 ± 0.031*	2.090 ± 0.074*	2.364 ± 0.062**	2.689 ± 0.082**
Relative	51.320 ± 2.099	48.855 ± 0.885	55.696 ± 0.836	52.716 ± 1.281	58.437 ± 1.115**	69.949 ± 2.107**
Female						
n	10	10	10	9	10	9
Necropsy body wt	31.7 ± 0.9	33.2 ± 0.9	35.5 ± 1.2*	33.8 ± 1.0	34.4 ± 0.8	34.1 ± 1.0
R. Kidney						
Absolute	0.248 ± 0.005	0.243 ± 0.006	0.258 ± 0.009	0.274 ± 0.015	0.275 ± 0.015	0.274 ± 0.017
Relative	7.884 ± 0.282	7.350 ± 0.187	7.309 ± 0.256	8.121 ± 0.371	8.027 ± 0.451	8.109 ± 0.609
Liver						
Absolute	1.765 ± 0.046	1.794 ± 0.039	1.884 ± 0.059	1.822 ± 0.042	2.017 ± 0.090**	2.464 ± 0.054**
Relative	55.874 ± 1.384	54.190 ± 0.788	53.207 ± 1.016	54.029 ± 1.130	58.527 ± 1.790	72.398 ± 1.352**

* Significantly different ($P \leq 0.05$) from the 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 H
REPRODUCTIVE TISSUE EVALUATIONS AND ESTROUS CYCLE CHARACTERIZATION

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TABLE H1
Summary of Reproductive Tissue Evaluations for Male Rats in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	20,000 ppm	80,000 ppm
n	10	10	10	10
Weights (g)				
Necropsy body wt	360 ± 7	340 ± 10	341 ± 4	184 ± 6**
L. Cauda epididymis	0.2022 ± 0.0047	0.1860 ± 0.0072	0.2011 ± 0.0061	0.0803 ± 0.0059**
L. Epididymis	0.5011 ± 0.0093	0.4658 ± 0.0157	0.4869 ± 0.0085	0.2580 ± 0.0208**
L. Testis	1.5390 ± 0.0195	1.4793 ± 0.0363	1.5620 ± 0.0240	0.7334 ± 0.0700**[b]
Spermatid measurements				
Spermatid heads (10^7/g testis)	10.24 ± 0.51	9.58 ± 0.36	9.87 ± 0.54	5.40 ± 0.90**[b]
Spermatid heads (10^7/testis)	15.71 ± 0.70	14.15 ± 0.58	15.33 ± 0.71	3.90 ± 0.91**
Spermatid count (mean/10^{-4} mL suspension)	78.55 ± 3.48	70.75 ± 2.91	76.65 ± 3.53	19.48 ± 4.56**
Epididymal spermatozoal measurements				
Motility (%)	74.84 ± 2.70	74.33 ± 2.53	75.74 ± 2.48	45.91 ± 9.45*
Concentration (10^6/g cauda epididymal tissue)	347 ± 26	407 ± 56	298 ± 42	20 ± 6**

* Significantly different (P≤0.05) from the control group by Dunn's test
** Significantly different (P≤0.01) from the control group by Williams' test (necropsy body weight, tissue weights) or Shirley's test (spermatid measurements and epididymal spermatozoal concentration).
[a] Data are presented as mean ± standard error.
[b] n=9

TABLE H2
Estrous Cycle Characterization for Female Rats in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	20,000 ppm	80,000 ppm
n	10	10	10	10
Necropsy body wt	200 ± 3	197 ± 3	190 ± 2*	168 ± 2**
Estrous cycle length (days)	4.95 ± 0.22	5.00 ± 0.08	5.05 ± 0.12	5.50 ± 0.26
Estrous stages (% of cycle)				
Diestrus	35.8	30.8	36.7	41.7
Proestrus	18.3	20.0	11.7	16.7
Estrus	24.2	27.5	25.0	21.7
Metestrus	20.0	17.5	19.2	15.8
Uncertain diagnoses	1.7	4.2	7.5	4.2

* Significantly different (P≤0.05) from the control group by Williams' test
** P≤0.01
[a] Necropsy body weight and estrous cycle length data are presented as mean ± standard error. Differences from the control group for estrous cycle length are not significant by Dunn's test. By multivariate analysis of variance, exposed females do not differ significantly from the control females in the relative length of time spent in the estrous stages.

TABLE H3
Summary of Reproductive Tissue Evaluations for Male Mice in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	20,000 ppm	80,000 ppm
n	10	10	10	7
Weights (g)				
Necropsy body wt	38.0 ± 0.7	41.0 ± 1.1*	39.6 ± 0.8	38.5 ± 0.6
L. Cauda epididymis	0.0270 ± 0.0033	0.0290 ± 0.0038	0.0290 ± 0.0043	0.0257 ± 0.0030
L. Epididymis	0.0590 ± 0.0018	0.0600 ± 0.0067	0.0670 ± 0.0042	0.0643 ± 0.0048
L. Testis	0.1310 ± 0.0031	0.1230 ± 0.0082	0.1290 ± 0.0028	0.1243 ± 0.0057
Spermatid measurements				
Spermatid heads (10^7/g testis)	15.19 ± 0.67	18.08 ± 2.16	15.91 ± 0.91	18.17 ± 1.51
Spermatid heads (10^7/testis)	1.99 ± 0.10	2.09 ± 0.12	2.04 ± 0.11	2.23 ± 0.16
Spermatid count (mean/10^{-4} mL suspension)	62.13 ± 3.10	65.28 ± 3.80	63.85 ± 3.34	69.79 ± 5.07
Epididymal spermatozoal measurements				
Motility (%)	74.04 ± 2.41	73.60 ± 2.06	72.24 ± 2.30	56.83 ± 10.51
Concentration (10^6/g cauda epididymal tissue)	464 ± 98	487 ± 67	466 ± 131	395 ± 67

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

TABLE H4
Estrous Cycle Characterization for Female Mice in the 3-Month Drinking Water Study of Dipropylene Glycol[a]

	0 ppm	5,000 ppm	20,000 ppm	80,000 ppm
n	10	10	9	9
Necropsy body wt	31.7 ± 0.9	33.2 ± 0.9	33.8 ± 1.0	34.1 ± 1.0
Estrous cycle length (days)	4.05 ± 0.05	4.10 ± 0.10	4.28 ± 0.15	4.56 ± 0.18*
Estrous stages (% of cycle)				
Diestrus	30.0	26.7	33.3	33.3
Proestrus	20.0	20.0	17.6	16.7
Estrus	30.0	30.0	29.6	34.3
Metestrus	20.0	23.3	19.4	15.7

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

APPENDIX I
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

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CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

Procurement and Characterization of Dipropylene Glycol

Dipropylene glycol was obtained from Union Carbide Corporation (Berwyn, IL) in one lot (0365) for use in the 2-week and 3-month studies and from Aldrich Chemical Company, Inc. (Milwaukee, WI) in one lot (10626DN) for use in the 2-year studies. Identity, moisture content, purity, and stability analyses were conducted by the analytical chemistry laboratories (lot 0365: Midwest Research Institute, Kansas City, MO; lots 0365 and 10626DN: Research Triangle Institute, Research Triangle Park, NC). Identity and purity analyses were conducted by the study laboratories. Reports on analyses performed in support of the dipropylene glycol studies are on file at the National Institute of Environmental Health Sciences.

Both lots of the chemical, a clear, colorless liquid, were identified as dipropylene glycol by the analytical chemistry laboratories with boiling point and density determinations; infrared (IR), nuclear magnetic resonance (NMR), and ultraviolet/visible spectroscopy; and high- and low-resolution mass spectrometry (MS) and by the study laboratories with IR spectroscopy. For lot 0365, the observed boiling point of 231° C and density of 1.0202 g/mL were in agreement with the literature values (Lide, 1992). For lot 10626DN, an observed boiling point of 230° C and a density of 1.014 g/mL were consistent with the literature values. The IR spectra from both lots were consistent with a structure of dipropylene glycol and literature references (*Aldrich*, 1981, 1985). The ultraviolet/visible spectra from both lots were consistent with the structure of dipropylene glycol. The NMR spectra were consistent with the structure of a mixture of dipropylene glycol isomers. The low-resolution MS spectrum was consistent with the structure of a 1-hydroxy isomer of dipropylene glycol (*NIST Standard Reference Database*). The observed mass of the high-resolution mass spectrometry base peak was within acceptable limits of the calculated mass. The IR and NMR spectra for lot 0365 are presented in Figures I1 and I2.

The moisture contents of lots 0365 and 10626DN were determined by the analytical chemistry laboratories using Karl Fischer titration. The purity of lot 0365 was determined by an analytical chemistry laboratory using elemental analyses, functional group titration, and thin layer chromatography (TLC). For functional group titration, an excess of acetylating reagent was added to dipropylene glycol samples; unreacted acetylating reagent was hydrolyzed and titrated with alcoholic potassium hydroxide. The titration was monitored potentiometrically with a combination pH/mV electrode filled with 3 M potassium chloride. TLC was performed using Silica Gel 60A K6F plates and two solvent systems: 1) 100% methanol and 2) ethyl acetate:isooctane (95:5). The plates were examined using 254 nm ultraviolet light and a spray of potassium dichromate in aqueous sulfuric acid. Resorcinol was used as a reference standard. The study laboratories analyzed purity using gas chromatography (GC) by systems A (lot 0365) and B (lot 10626DN).

For lot 0365, Karl Fischer titration indicated 0.08% ± 0.01% water. Elemental analyses for carbon and hydrogen were in agreement with the theoretical values for dipropylene glycol. Functional group titration indicated a purity of approximately 99%. TLC indicated a major spot and no impurities for both solvent systems. For lot 10626DN, Karl Fischer titration indicated 0.475% water. GC analyses by the study laboratories indicated four isomer peaks and no impurities.

Additional analyses were performed by an analytical chemistry laboratory to characterize the isomers of dipropylene glycol present in each lot using GC with flame ionization detection (FID), GC/MS, and GC/IR. GC/FID (system C) indicated nine major peaks representing three diastereomers of dipropylene glycol with a combined area of greater than 99% of the total peak area; all peaks identified in each lot of bulk chemical were associated with dipropylene glycol. All GC/MS (system C) spectra were consistent with the literature spectra for the three diastereomers of dipropylene glycol (*Wiley Mass Spectral Database*; *Kirk-Othmer*; 1980). GC/IR (system D) analyses confirmed the presence of the major functional groups and the chemical bonding expected for

the diastereomers. The diasteriomer ratios were determined to be 35:52:13 (lot 0365) and 29:53:18 (lot 10626DN) 1,1′-oxybis(2-propanol):2-(2-hydroxypropoxy)-1-propanol:2,2′-oxybis(1-propanol). Early purity analyses using GC, without the benefit of chiral column separations, resolved fewer peaks, but the peaks in all analyses were consistent with the structure of dipropylene glycol diastereomers and their enantiomers. The overall purity of each lot was determined to be greater than 99%.

Accelerated stability studies of the bulk chemical were performed by the analytical chemistry laboratories. Stability studies of lot 0365 were performed by an analytical chemistry laboratory using GC by system A. Stability studies of lot 10626DN were performed by the analytical chemistry laboratory using system E. These studies indicated that dipropylene glycol was stable as a bulk chemical for 2 weeks when stored protected from light at temperatures up to 60° C. The stability of lot 10626DN was monitored by the analytical chemistry laboratory after approximately 18 months storage at room temperature using GC by system F. No degradation of the bulk chemical was detected. To ensure stability, the bulk chemical was stored at room temperature, protected from light, in amber glass containers. Stability was monitored by the study laboratories during the 3-month and 2-year studies by GC using system A (3-month studies) and system B (2-year studies). No degradation of the bulk chemical was detected.

Preparation and Analysis of Dose Formulations

The dose formulations used during the 2-week and 3-month studies were prepared at least every 2 weeks by mixing dipropylene glycol with deionized water (Table I2). Dose formulations were stored in carboys, protected from light, at room temperature for up to 2 weeks. Dose formulations used during the 2-year studies were prepared every 7 to 12 weeks by mixing dipropylene glycol with tap water (Table I2). Dose formulations were stored in stainless steel drums at room temperature.

Stability studies of a 0.8 mg/mL dipropylene glycol formulation (lot 0365) were conducted by the analytical chemistry laboratory using GC by system G. Stability was confirmed for up to four weeks for dose formulations stored in sealed septum vials protected from light at 5° C or room temperature. Stability was also confirmed for up to 96 hours for dose formulations stored exposed to light in drinking water bottles fitted with Teflon®-lined septa and sipper tubes at room temperature.

Stability studies of a 2.5 mg/mL dipropylene glycol formulation (lot 10626DN) were conducted by an analytical chemistry laboratory using GC by system H. Stability was confirmed for up to 32 days for dose formulations stored frozen, refrigerated, or at room temperature in sealed vials protected from light. Stability was also confirmed for dose formulations stored up to seven days exposed to light in drinking water bottles fitted with Teflon® cap liners and stainless steel sipper tubes at room temperature.

Periodic analyses of the dose formulations were conducted by the study laboratory using GC by systems similar to system G for the 2-week and 3-month studies. Analyses of dose formulations used in the 2-year studies were conducted by the study laboratory using GC by system B. During the 2-week studies, the dose formulations were analyzed twice (Table I3). Of the dose formulations analyzed, all 10 for rats and mice were within 10% of the target concentrations; of the animal room samples analyzed, all 20 were within 10% of the target concentrations. During the 3-month studies, the dose formulations were analyzed at the beginning, midpoint, and end of the studies; animal room samples of these dose formulations were also analyzed (Table I4). Of the dose formulations analyzed, all 30 samples for rats and mice were within 10% of the target concentrations; of the animal room samples analyzed, all 30 samples for rats and mice were within 10% of the target concentrations. During the 2-year studies, the dose formulations were analyzed approximately every nine weeks (Table I5). Of the dose formulations analyzed, all 33 dose formulations for rats and mice were within 10% of the target concentrations. Animal room samples were also analyzed periodically; 11 of 12 samples for rats and all for mice were within 10% of the target concentrations.

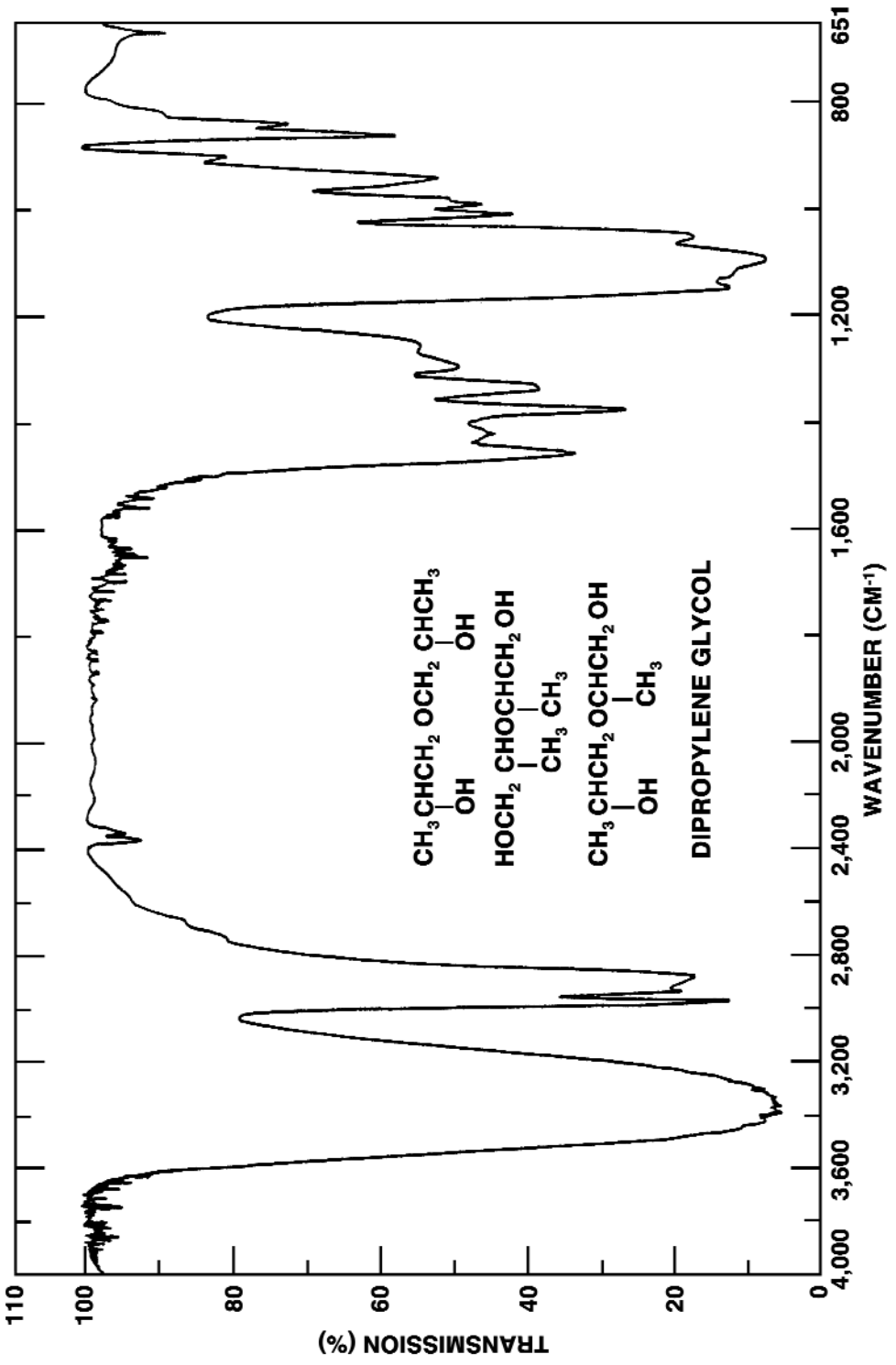

FIGURE I1
Infrared Absorption Spectrum of Dipropylene Glycol

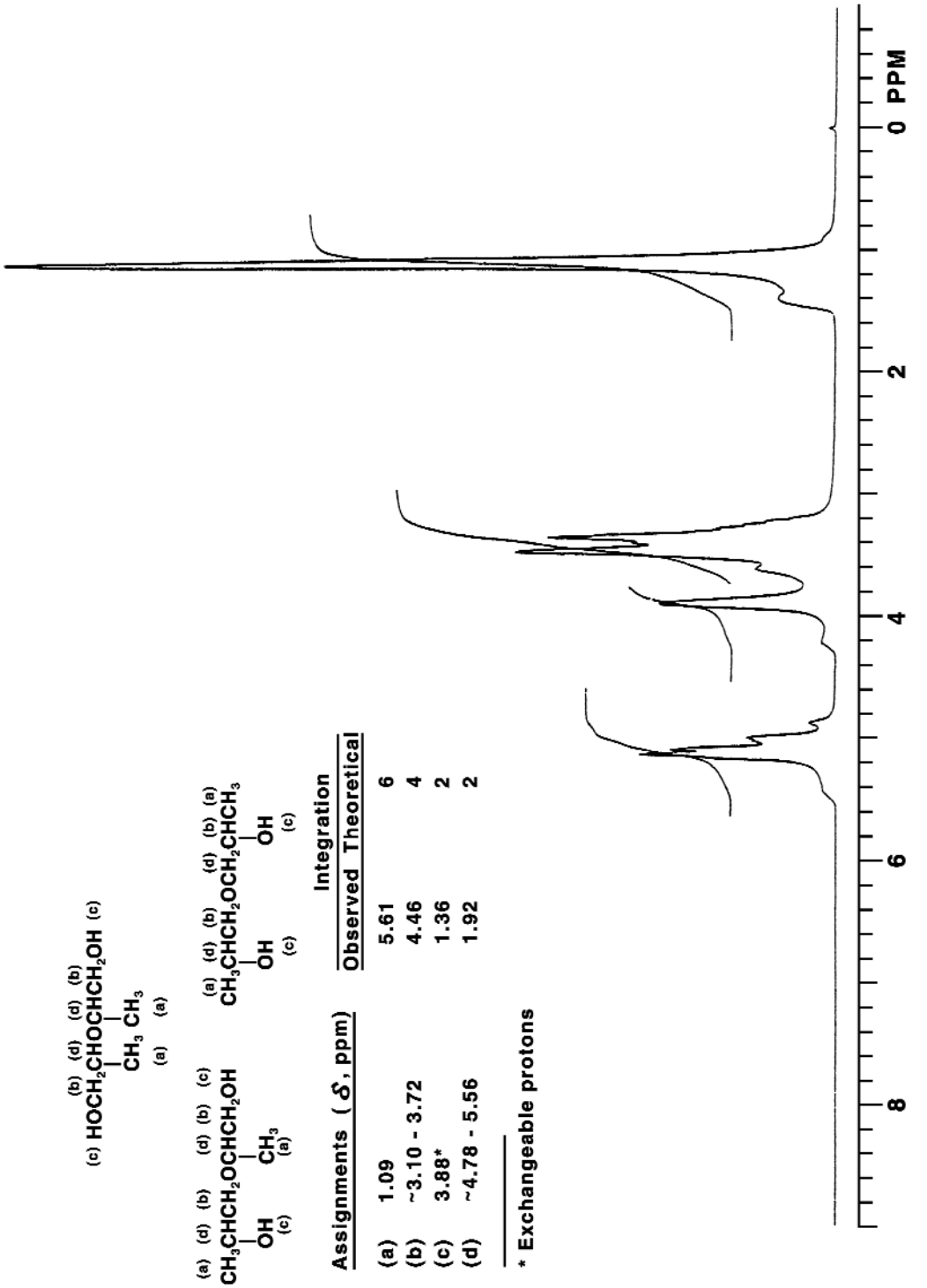

FIGURE I2
Nuclear Magnetic Resonance Spectrum of Dipropylene Glycol

TABLE I1
Gas Chromatography Systems Used in the Drinking Water Studies of Dipropylene Glycol[a]

Detection System	Column	Carrier Gas	Oven Temperature Program
System A			
Flame ionization	DB-5, 30 m × 0.53 mm, 1.5-µm film (J&W Scientific, Folsom, CA)	Helium at 10 mL/minute	50° C for 1 minute, then 10° C/minute to 150° C, held for 1 minute
System B			
Flame ionization	RTX-5 fused silica, 15 m × 0.53 mm, 0.5-µm film (Restek, Bellefonte, PA)	Helium at 5 mL/minute	50° C for 2 minutes, then 8° C/minute to 200° C
System C			
Flame ionization or mass spectrometry with electron impact ionization	Cyclodex-B, 30 m × 0.25 mm, 0.25-µm film (J&W Scientific)	Helium at 1.2 mL/minute	100° C for 15 minutes, then 1° C/minute to 115° C, then 8.5° C/minute to 200° C
System D			
Infrared	Cyclodex-B, 30 m × 0.25 mm, 0.25-µm film (J&W Scientific)	Helium with argon (1%) at 1 mL/minute	100° C for 15 minutes, then 1° C/minute to 115° C, then 8.5° C/minute to 200° C
System E			
Flame ionization	Supelco Nukol, 30 m × 0.25 mm, 0.25-µm film (Supelco, Bellefonte, PA)	Nitrogen at 1 mL/minute	110° C for 5 minutes, 5° C/minute to 200° C, held for 2 minutes
System F			
Flame ionization	Supelco Nukol, 30 m × 0.25 mm, 0.25-µm film (Supelco)	Helium at 1.4 mL/minute	110° C to 185° C at 5° C/minute, held for 25 minutes
System G			
Flame ionization	DB-5, 30 m × 0.53 mm, 1.5-µm film (J&W Scientific)	Helium at 10 mL/minute	Isothermal at 70° C
System H			
Flame ionization	Supelco Nukol, 30 m × 0.25 mm, 0.25-µm film, (Supelco)	Helium at 1.4 mL/minute	Isothermal at 140° C

[a] Gas chromatographs were manufactured by Varian, Inc. (Palo Alto, CA) (systems D and G) and Hewlett-Packard (Palo Alto, CA) (systems A, B, C, E, F, and H).

TABLE I2
Preparation and Storage of Dose Formulations in the Drinking Water Studies of Dipropylene Glycol

2-Week Studies	3-Month Studies	2-Year Studies
Preparation		
Dipropylene glycol was added to deionized water, mixed by swirling gently, and diluted further with deionized water. Dose formulations were prepared at the beginning of the studies and during the second week of the studies.	Dipropylene glycol was added to deionized water, mixed by swirling gently, diluted further with deionized water, and then mixed with a mechanical stirrer. Dose formulations were prepared approximately every 2 weeks.	Dipropylene glycol was added to tap water and mixed with a mechanical stirrer for approximately 5 minutes, then further diluted and stirred for an additional 5 minutes. Dose formulations were prepared approximately every 7 to 12 weeks.
Chemical Lot Number		
Lot 0365	Lot 0365	Lot 10626DN
Maximum Storage Time		
2 weeks	2 weeks	37 days
Storage Conditions		
Stored protected from light at room temperature	Stored in amber carboys, protected from light at room temperature	Stored in stainless steel drums at room temperature
Study Laboratory		
Arthur D. Little (Cambridge, MA)	Arthur D. Little (Cambridge, MA)	Battelle Columbus Operations (Columbus, OH)

TABLE I3
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Week Drinking Water Studies of Dipropylene Glycol

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration[a] (mg/mL)	Difference from Target (%)
Rats				
March 15, 1990	March 16, 1990	5	5.01	0
		10	10.02	0
		20	19.26	–4
		40	39.60	–1
		80	81.36	+2
	April 11-12,1990[b]	5	5.24	+5
		10	9.96	0
		20	20.18	+1
		40	40.08	0
		80	82.48	+3
March 28, 1990	March 28, 1990	5	5.46	+9
		10	10.66	+7
		20	21.24	+6
		40	43.04	+8
		80	85.12	+6
	April 11-12, 1990[b]	5	5.15	+3
		10	10.01	0
		20	20.32	+2
		40	40.64	+2
		80	85.20	+7
Mice				
March 15, 1990	March 16, 1990	5	5.01	0
		10	10.02	0
		20	19.26	–4
		40	39.60	–1
		80	81.36	+2
	April 11-12, 1990[b]	5	5.30	+6
		10	10.03	0
		20	20.00	0
		40	40.72	+2
		80	86.00	+8
March 28, 1990	March 28, 1990	5	5.46	+9
		10	10.66	+7
		20	21.24	+6
		40	43.04	+8
		80	85.12	+6
	April 11-12, 1990[b]	5	5.06	+1
		10	10.08	+1
		20	20.10	+1
		40	40.84	+2
		80	84.00	+5

[a] Results of duplicate analyses. 5 mg/mL=5,000 ppm; 10 mg/mL=10,000 ppm; 20 mg/mL=20,000 ppm; 40 mg/mL=40,000 ppm; 80 mg/mL=80,000 ppm
[b] Animal room samples

TABLE I4
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 3-Month Drinking Water Studies of Dipropylene Glycol

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration[a] (mg/mL)	Difference from Target (%)
Rats				
July 5, 1990	July 6, 1990	5	4.98	0
		10	9.96	0
		20	20.02	0
		40	40.08	0
		80	80.48	+1
	July 24, 1990[b]	5	5.02	0
		10	10.03	0
		20	19.82	–1
		40	40.32	+1
		80	80.24	0
August 23, 1990	August 23, 1990	5	5.18	+4
		10	10.13	+1
		20	21.06	+5
		40	41.40	+4
		80	85.84	+7
	September 14, 1990[b]	5	5.00	0
		10	9.86	–1
		20	19.82	–1
		40	40.12	0
		80	82.24	+3
October 4, 1990	October 4, 1990	5	5.16	+3
		10	10.43	+4
		20	20.74	+4
		40	41.52	+4
		80	85.72	+7
	October 11, 1990[b]	5	5.11	+2
		10	10.06	+1
		20	20.16	+1
		40	39.80	0
		80	81.36	+2

TABLE I4
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 3-Month Drinking Water Studies of Dipropylene Glycol

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration (mg/mL)	Difference from Target (%)
Mice				
July 5, 1990	July 6, 1990	5	4.98	0
		10	9.96	0
		20	20.02	0
		40	40.08	0
		80	80.48	+1
	July 24, 1990[b]	5	5.12	+2
		10	10.05	+1
		20	19.94	0
		40	38.64	–3
		80	80.24	0
August 23, 1990	August 23, 1990	5	5.18	+4
		10	10.13	+1
		20	21.06	+5
		40	41.40	+4
		80	85.84	+7
	September 14, 1990[b]	5	4.87	–3
		10	9.42	–6
		20	19.62	–2
		40	38.36	–4
		80	80.00	0
October 4, 1990	October 4, 1990	5	5.16	+3
		10	10.43	+4
		20	20.74	+4
		40	41.52	+4
		80	85.72	+7
	October 11, 1990[b]	5	4.86	–3
		10	10.00	0
		20	20.12	+1
		40	39.76	–1
		80	81.68	+2

[a] Results of duplicate analyses. 5 mg/mL=5,000 ppm; 10 mg/mL=10,000 ppm; 20 mg/mL=20,000 ppm; 40 mg/mL=40,000 ppm; 80 mg/mL=80,000 ppm
[b] Animal room samples

TABLE I5
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Dipropylene Glycol

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration[a] (mg/mL)	Difference from Target (%)
Rats				
March 10, 1997	March 10-11, 1997	0.25	0.2608	+4
		1	1.025	+3
		4	3.976	–1
	April 16-17, 1997[b]	0.25	0.2526	+1
		1	0.3477[c]	–65
		4	3.934	–2
May 5, 1997	May 6, 1997	0.25	0.2513	+1
		1	0.9798	–2
		4	3.835	–4
July 28, 1997	July 29-30, 1997	0.25	0.2551	+2
		1	1.015	+2
		4	3.886	–3
September 22, 1997	September 23-24, 1997	0.25	0.2490	0
		1	1.035	+4
		4	4.150	+4
	October 24-27, 1997[b]	0.25	0.2561	+2
		1	0.997	0
		4	4.033	+1
December 15, 1997	December 16, 1997	0.25	0.2305	–8
		1	1.048	+5
		4	4.224	+6
February 9, 1998	February 11-12, 1998	0.25	0.2413	–4
		1	1.024	+2
		4	4.098	+2
May 4, 1998	May 5-6, 1998	0.25	0.2576	+3
		1	1.013	+1
		4	3.982	0
	June 10-11, 1998[b]	0.25	0.2398	–4
		1	1.017	+2
		4	4.006	0
June 29, 1998	July 1, 1998	0.25	0.2596	+4
		1	1.019	+2
		4	4.042	+1
September 21, 1998	September 23-24, 1998	0.25	0.2625	+5
		1	1.039	+4
		4	4.057	+1

TABLE I5
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Dipropylene Glycol

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration (mg/mL)	Difference from Target (%)
Rats (continued)				
November 16, 1998	November 16-17, 1998	0.25	0.2416	–3
		1	1.062	+6
		4	4.308	+8
	December 22-23, 1998[b]	0.25	0.2372	–5
		1	1.049	+5
		4	4.312	+8
January 12, 1999	January 12-13, 1999	0.25	0.2509	0
		1	1.038	+4
		4	4.057	+1
Mice				
March 10, 1997	March 10-11, 1997	1	1.025	+3
		2	2.162	+8
		4	3.976	–1
	April 16-17, 1997[b]	1	0.9942	–1
		2	2.087	+4
		4	3.875	–3
May 5, 1997	May 6, 1997	1	0.9798	–2
		2	2.056	+3
		4	3.835	–4
July 28, 1997	July 29-30, 1997	1	1.015	+2
		2	1.799	–10
		4	3.886	–3
September 22, 1997	September 23-24, 1997	1	1.035	+4
		2	1.948	–3
		4	4.150	+4
	October 24-27, 1997[b]	1	1.013	+1
		2	1.989	–1
		4	4.125	+3
December 15, 1997	December 16, 1997	1	1.048	+5
		2	2.160	+8
		4	4.224	+6
February 9, 1998	February 11-12, 1998	1	1.024	+2
		2	1.974	–1
		4	4.098	+2

TABLE I5
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Dipropylene Glycol

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration (mg/mL)	Difference from Target (%)
Mice (continued)				
May 4, 1998	May 5-6, 1998	1	1.013	+1
		2	1.893	–5
		4	3.982	–1
	June 10-11, 1998[b]	1	1.022	+2
		2	1.922	–4
		4	4.057	+1
June 29, 1998	July 1, 1998	1	1.019	+2
		2	1.949	–3
		4	4.042	+1
September 21, 1998	September 23-24, 1998	1	1.039	+4
		2	1.986	–1
		4	4.057	+1
November 16, 1998	November 16-17, 1998	1	1.062	+6
		2	2.124	+6
		4	4.308	+8
	December 22-23, 1998[b]	1	1.049	+5
		2	2.145	+7
		4	4.373	+9
January 12, 1999	January 12-13, 1999	1	1.038	+4
		2	2.040	+2
		4	4.057	+1

[a] Results of single analyses; a second sample was analyzed to confirm the results. 2.5 mg/mL=2,500 ppm; 10 mg/mL=10,000 ppm; 20 mg/mL=20,000 ppm; 40 mg/mL=40,000 ppm
[b] Animal room samples
[c] Concentration of the repeat analysis was 0.3528 mg/mL.

APPENDIX J
WATER AND COMPOUND CONSUMPTION IN THE 2-YEAR DRINKING WATER STUDIES OF DIPROPYLENE GLYCOL

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TABLE J1
Water and Compound Consumption by Male Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		2,500 ppm			10,000 ppm			40,000 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose (mg/kg)[b]	Water (g/day)	Body Weight (g)	Dose (mg/kg)	Water (g/day)	Body Weight (g)	Dose (mg/kg)
1	16.2	100	16.3	100	406	15.9	100	1,588	9.4	102	3,680
2	16.4	133	16.5	133	311	16.8	133	1,269	15.7	122	5,155
6	19.8	252	19.1	248	192	20.4	247	824	21.2	231	3,684
10	17.9	316	17.5	311	141	18.7	308	608	19.0	282	2,696
14	17.5	360	17.4	350	124	17.4	344	506	17.5	309	2,263
18	18.3	395	17.7	386	114	17.2	375	457	18.9	340	2,227
22	19.1	420	18.6	412	113	18.6	400	466	21.2	363	2,339
26	19.3	432	19.2	426	112	17.9	412	436	21.9	375	2,338
30	18.6	450	18.6	443	105	18.7	426	439	21.8	388	2,249
34	18.1	464	19.3	455	106	19.0	441	432	22.6	399	2,267
38	17.0	471	17.1	468	91	16.4	451	363	20.9	406	2,057
42	17.7	484	17.7	483	92	18.1	467	387	22.6	416	2,177
46	16.5	489	17.2	489	88	17.4	471	370	21.9	418	2,100
50	17.4	498	17.6	495	89	18.3	478	384	27.0	419	2,576
54	17.9	504	17.7	502	88	18.2	485	376	28.7	427	2,690
58	16.4	512	17.0	511	83	16.9	495	342	26.9	424	2,537
62	17.6	518	17.8	517	86	18.0	501	359	30.1	425	2,836
66	16.9	510	17.4	511	85	17.8	495	359	31.0	416	2,980
70	17.2	514	16.8	515	82	17.1	500	342	29.3	408	2,877
74	16.4	513	16.1	521	77	16.9	501	338	35.0	404	3,465
78	16.5	511	16.1	514	79	16.1	493	327	36.3	395	3,671
82	16.9	511	16.5	513	80	16.3	495	329	34.6	387	3,583
86	16.7	514	16.9	513	83	17.2	490	352	37.7	371	4,061
90	17.2	512	17.4	514	85	16.9	494	343	29.9	351	3,409
94	16.0	509	16.7	517	81	16.8	496	339	43.0	367	4,685
98	18.5	520	18.0	514	88	17.9	486	369	35.9	331	4,340
102	18.1	513	16.2	506	80	18.7	489	382			
Mean for weeks											
1-13	17.6	200	17.3	198	263	18.0	197	1,072	16.3	184	3,804
14-52	17.9	446	18.0	441	103	17.9	427	424	21.6	383	2,259
53-102	17.1	512	17.0	513	83	17.3	494	350	33.2	392	3,428

[a] Grams of drinking water consumed per animal per day
[b] Milligrams of dipropylene glycol consumed per kilogram body weight per day

TABLE J2
Water and Compound Consumption by Female Rats in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		2,500 ppm			10,000 ppm			40,000 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose (mg/kg)[b]	Water (g/day)	Body Weight (g)	Dose (mg/kg)	Water (g/day)	Body Weight (g)	Dose (mg/kg)
1	14.2	94	14.3	94	380	13.8	93	1,490	8.3	93	3,570
2	13.2	112	13.5	112	300	13.2	112	1,182	12.2	105	4,635
6	14.4	162	14.3	161	222	13.9	160	866	12.9	152	3,392
10	13.2	184	14.0	181	194	12.9	180	718	11.6	165	2,817
14	12.6	195	12.6	194	163	11.2	193	580	10.9	179	2,431
18	12.9	209	12.6	206	153	11.7	204	575	11.1	187	2,382
22	13.1	218	12.9	216	150	12.6	215	586	11.5	196	2,343
26	13.1	222	12.7	219	145	11.9	219	542	11.2	199	2,263
30	12.7	232	12.5	228	137	11.9	227	522	12.1	203	2,383
34	13.1	241	13.6	235	145	13.3	236	564	13.3	208	2,557
38	11.9	245	12.2	244	126	12.0	245	489	12.5	214	2,339
42	12.2	254	12.3	252	122	12.0	255	472	12.5	218	2,299
46	12.5	267	12.5	264	119	12.4	263	473	12.6	224	2,238
50	13.6	279	13.7	275	125	12.9	275	469	13.1	231	2,277
54	12.2	288	12.9	283	114	12.4	285	437	13.6	244	2,231
58	12.0	299	12.4	293	106	12.0	295	406	13.2	251	2,105
62	11.8	307	11.8	298	99	11.8	305	389	12.6	260	1,938
66	12.4	313	12.7	303	105	12.6	310	405	13.1	263	1,996
70	12.9	320	13.6	311	109	12.6	317	398	13.9	271	2,043
74	11.8	328	12.8	320	100	12.2	324	375	13.3	278	1,917
78	11.7	328	12.7	315	101	12.4	325	381	13.7	274	2,002
82	12.5	337	12.5	321	98	13.1	328	398	13.1	285	1,840
86	12.7	337	13.8	325	106	13.1	332	396	13.8	289	1,916
90	13.2	342	12.9	328	99	13.4	336	400	14.5	288	2,011
94	13.7	348	13.8	335	103	13.3	342	389	14.6	297	1,963
98	13.8	351	14.5	339	107	14.1	348	406	15.1	295	2,049
102	14.4	351	14.8	347	107	13.7	352	390	14.3	301	1,896
Mean for weeks											
1-13	13.8	138	14.0	137	274	13.5	136	1,064	11.2	129	3,603
14-52	12.8	236	12.8	233	138	12.2	233	527	12.1	206	2,351
53-102	12.7	327	13.2	317	104	12.8	323	398	13.8	277	1,993

[a] Grams of drinking water consumed per animal per day
[b] Milligrams of dipropylene glycol consumed per kilogram body weight per day

TABLE J3
Water and Compound Consumption by Male Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		10,000 ppm			20,000 ppm			40,000 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose (mg/kg)[b]	Water (g/day)	Body Weight (g)	Dose (mg/kg)	Water (g/day)	Body Weight (g)	Dose (mg/kg)
2	3.4	23.7	3.4	24.1	1,423	1.9	22.1	1,743	1.1	18.2	2,322
6	3.2	29.7	3.0	29.9	995	2.3	28.5	1,638	2.0	25.6	3,088
10	2.9	35.8	2.7	35.9	749	2.3	34.2	1,344	1.9	30.5	2,495
14	2.9	40.4	2.8	40.6	690	2.6	38.5	1,342	2.2	34.3	2,604
18	3.0	44.6	2.9	45.0	655	2.5	42.5	1,175	2.3	37.9	2,472
22	3.1	46.7	2.9	46.6	631	2.6	45.0	1,162	2.5	41.0	2,446
26	3.4	48.1	3.3	48.1	676	2.9	46.7	1,230	2.5	42.0	2,415
30	3.3	49.3	3.0	48.7	611	2.7	48.2	1,110	2.4	43.5	2,245
34	3.7	50.2	3.4	49.9	686	3.0	48.9	1,227	2.5	43.5	2,298
38	3.7	51.3	3.3	50.9	643	2.9	50.2	1,139	2.4	44.3	2,137
42	3.8	51.6	3.3	51.2	652	2.9	50.6	1,127	2.3	43.9	2,071
46	4.0	52.5	3.5	52.1	665	3.0	51.4	1,160	2.5	44.0	2,244
50	4.0	52.8	3.5	52.4	666	2.8	51.9	1,089	2.3	44.6	2,033
54	4.3	53.1	3.6	52.5	686	3.1	52.1	1,188	2.6	45.7	2,307
58	4.3	53.1	3.7	52.8	701	3.0	51.8	1,155	2.6	45.6	2,318
62	4.4	53.9	3.7	53.8	680	2.9	52.4	1,122	2.7	47.3	2,306
66	4.4	53.9	4.1	53.8	753	3.2	52.5	1,208	3.0	48.1	2,529
70	4.2	53.5	3.8	53.6	702	3.0	52.0	1,150	3.0	47.8	2,501
74	4.3	52.4	3.7	53.6	693	2.8	51.6	1,099	3.0	46.6	2,595
78	4.4	52.5	3.9	53.0	739	3.0	51.6	1,149	2.9	47.2	2,424
82	4.5	53.1	3.7	53.4	699	3.0	52.4	1,142	3.0	46.2	2,578
86	4.5	53.2	3.8	52.5	730	3.0	50.4	1,180	2.4	43.4	2,256
90	4.5	52.6	3.7	52.0	706	2.8	49.3	1,156	2.0	41.4	1,947
94	4.2	51.5	3.9	51.1	757	3.1	48.7	1,254	2.6	40.0	2,602
98	4.1	50.3	3.6	50.4	705	2.9	49.8	1,161	2.5	39.6	2,479
102	4.3	48.6	3.6	49.1	729	3.1	48.4	1,293	2.3	37.3	2,464
Mean for weeks											
2-13	3.2	29.7	3.0	30.0	1,056	2.2	28.2	1,575	1.6	24.8	2,635
14-52	3.5	48.7	3.2	48.6	657	2.8	47.4	1,176	2.4	41.9	2,296
53-102	4.3	52.4	3.7	52.4	714	3.0	51.0	1,174	2.7	44.3	2,408

[a] Grams of drinking water consumed per animal per day
[b] Milligrams of dipropylene glycol consumed per kilogram body weight per day

TABLE J4
Water and Compound Consumption by Female Mice in the 2-Year Drinking Water Study of Dipropylene Glycol

Weeks on Study	0 ppm		10,000 ppm			20,000 ppm			40,000 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose (mg/kg)[b]	Water (g/day)	Body Weight (g)	Dose (mg/kg)	Water (g/day)	Body Weight (g)	Dose (mg/kg)
1	3.0	18.2	2.8	18.3	1,549	2.0	18.3	2,139	1.1	18.3	2,316
2	2.8	19.2	2.7	19.1	1,432	2.0	18.6	2,140	1.3	17.0	2,968
6	2.6	22.7	2.7	23.5	1,152	2.3	22.2	2,039	1.9	22.0	3,479
10	2.6	27.4	2.5	27.8	904	2.2	26.4	1,669	2.0	26.4	3,058
14	3.0	32.7	2.5	33.3	756	2.4	32.3	1,467	2.2	32.4	2,766
18	2.5	38.0	2.5	38.4	651	2.3	36.8	1,231	2.3	36.6	2,468
22	2.5	43.0	2.9	43.2	683	2.8	41.1	1,377	2.3	41.1	2,191
26	2.5	45.7	2.4	46.3	518	2.2	43.7	1,015	2.4	44.3	2,143
30	2.5	48.1	2.5	47.7	520	2.4	46.1	1,025	2.5	46.5	2,118
34	2.5	51.5	2.4	51.1	476	2.3	49.2	935	2.6	49.9	2,086
38	2.4	54.3	2.4	53.8	446	2.3	52.6	886	2.4	52.2	1,811
42	2.4	56.3	2.4	55.9	430	2.7	54.7	972	2.5	54.5	1,822
46	2.2	57.7	2.7	57.2	472	2.1	55.8	747	2.0	55.4	1,479
50	2.3	59.6	2.2	58.5	369	2.1	58.2	710	2.1	57.2	1,490
54	2.5	60.6	2.2	59.6	378	2.2	59.2	748	2.2	57.8	1,531
58	2.7	60.5	2.5	60.4	410	2.3	58.8	774	2.3	57.0	1,629
62	2.5	61.3	2.6	59.4	431	2.2	59.5	731	2.2	57.7	1,496
66	2.5	61.4	2.4	60.0	397	2.3	59.0	776	2.3	57.7	1,586
70	2.5	60.4	2.3	59.7	389	2.1	57.8	735	2.0	56.7	1,445
74	4.2	60.7	2.8	59.2	472	2.5	58.5	867	3.1	56.4	2,163
78	2.5	61.3	2.1	58.0	369	1.9	58.8	653	1.9	55.5	1,370
82	2.5	61.1	2.3	60.2	390	2.6	59.6	859	2.7	56.6	1,930
86	2.8	59.7	2.6	56.6	464	2.2	56.9	779	2.3	54.4	1,684
90	2.9	57.7	2.4	53.9	449	2.5	55.9	884	2.0	50.5	1,596
94	3.4	55.4	2.5	51.4	487	2.5	53.7	916	1.8	47.2	1,506
98	3.5	53.4	2.4	51.0	467	2.4	54.4	882	1.7	45.7	1,517
102	3.7	52.4	2.6	51.0	518	2.5	53.2	957	2.0	45.2	1,746
Mean for weeks											
1-13	2.8	21.9	2.7	22.2	1,259	2.1	21.4	1,997	1.6	20.9	2,955
14-52	2.5	48.7	2.5	48.5	532	2.3	47.1	1,037	2.3	47.0	2,037
53-102	2.9	58.9	2.5	57.0	432	2.3	57.3	812	2.2	53.7	1,631

[a] Grams of drinking water consumed per animal per day
[b] Milligrams of dipropylene glycol consumed per kilogram body weight per day

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

TABLE K1 Ingredients of NTP-2000 Rat and Mouse Ration 254
TABLE K2 Vitamins and Minerals in NTP-2000 Rat and Mouse Ration 254
TABLE K3 Nutrient Composition of NTP-2000 Rat and Mouse Ration 255
TABLE K4 Contaminant Levels in NTP-2000 Rat and Mouse Ration 256

TABLE K1
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 K2
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 K3
Nutrient Composition of NTP-2000 Rat and Mouse Ration

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	13.1 ± 0.36	12.5 – 13.8	24
Crude fat (% by weight)	8.1 ± 0.25	7.6 – 8.4	24
Crude fiber (% by weight)	9.5 ± 0.59	8.0 – 10.3	24
Ash (% by weight)	5.0 ± 0.15	4.7 – 5.3	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)	5,189 ± 1,145	3,280 – 7,420	24
Vitamin D (IU/kg)	1,000[a]		
α-Tocopherol (ppm)	82.2 ± 14.08	62.2 – 107.0	8
Thiamine (ppm)[b]	7.5 ± 0.94	6.0 – 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 (as chloride) (ppm)	3,155 ± 325	2,700 – 3,790	8
Minerals			
Calcium (%)	0.969 ± 0.040	0.905 – 1.050	24
Phosphorus (%)	0.544 ± 0.024	0.496 – 0.580	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

TABLE K4
Contaminant Levels in NTP-2000 Rat and Mouse Ration[a]

	Mean ± Standard Deviation[b]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.22 ± 0.143	0.10 – 0.50	24
Cadmium (ppm)	0.04 ± 0.012	0.04 – 0.10	24
Lead (ppm)	0.08 ± 0.020	0.06 – 0.15	24
Mercury (ppm)	<0.02		24
Selenium (ppm)	0.16 ± 0.028	0.11 – 0.23	24
Aflatoxins (ppb)	<5.00		24
Nitrate nitrogen (ppm)[c]	16.4 ± 8.11	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 – 1.6	24
Aerobic plate count (CFU/g)	10 ± 1.0	10 – 15	24
Coliform (MPN/g)	0.1 ± 0.6	0 – 3	24
Escherichia coli (MPN/g)	<10		24
Salmonella (MPN/g)	Negative		24
Total nitrosoamines (ppb)[e]	5.5 ± 3.77	2.1 – 20.9	24
N-Nitrosodimethylamine (ppb)[e]	2.1 ± 1.31	1.0 – 6.4	24
N-Nitrosopyrrolidine (ppb)[e]	3.5 ± 2.7	1.0 – 14.5	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	0.107 ± 0.088	0.020 – 0.368	24
Methyl parathion	<0.02		24
Ethyl parathion	<0.02		24
Malathion	0.322 ± 0.571	0.020 – 2.810	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 L
SENTINEL ANIMAL PROGRAM

METHODS 258
TABLE L1 Murine Virus Antibody Determinations for Rats and Mice in the 3-Month and 2-Year Drinking Water Studies of Dipropylene Glycol 260

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. The samples were processed appropriately and sent to Microbiological Associates, Inc. (Bethesda, 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	
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	
Mycoplasma arthritidis	Study termination
Mycoplasma pulmonis	Study termination
PVM	1, 6, 12, and 18 months, study termination
RCV/SDA	1, 6, 12, and 18 months, study termination
Sendai	1, 6, 12, and 18 months, study termination
Immunofluorescence Assay	
Parvovirus	6, 12, and 18 months, study termination
Hemagglutination Inhibition	
H-1	1 month
KRV	1 month

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
Mouse adenoma virus-FL	Study termination
MHV (mouse hepatitis virus)	Study termination
PVM	Study termination
Reovirus 3	Study termination
Sendai	Study termination
Immunofluorescence Assay	
EDIM	Study termination
Reovirus 3	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	1, 6, 12, and 18 months, study termination
EDIM	1, 6, 12, and 18 months, study termination
GDVII	1, 6, 12, and 18 months, study termination
LCM	1, 6, 12, and 18 months, study termination
Mouse adenoma virus-FL	1, 6, 12, and 18 months, study termination
MHV	1, 6, 12, and 18 months, study termination
M. arthritidis	Study termination
M. pulmonis	Study termination
PVM	1, 6, 12, and 18 months, study termination
Reovirus 3	1, 6, 12, and 18 months, study termination
Sendai	1, 6, 12, and 18 months, study termination
Immunofluorescence Assay	
MCMV (mouse cytomegalovirus)	Study termination
Parvovirus	12 and 18 months, study termination
Hemagglutination Inhibition	
K	1 and 6 months
MVM	1 and 6 months
Polyoma virus	1 and 6 months

Results of serology tests are presented in Table L1.

TABLE L1
Murine Virus Antibody Determinations for Rats and Mice in the 3-Month and 2-Year Drinking Water Studies of Dipropylene Glycol

Interval	Incidence of Antibody in Sentinel Animals	Positive Serologic Reaction for
3-Month Studies		
Rats		
Study termination	0/10	None positive
Mice		
Study termination	3/10	Reovirus 3
2-Year Studies		
Rats		
1 Month	0/10	None positive
6 Months	0/10	None positive
12 Months	0/10	None positive
18 Months	0/10	None positive
Study termination	0/10	None positive
Mice		
1 Month	0/10	None positive
6 Months	0/10	None positive
12 Months	0/10	None positive
18 Months	0/9	None positive
Study termination	0/10	None positive

National Toxicology Program Technical Reports

Printed as of June 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
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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
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3,4-Dihydrocoumarin	423
1,2-Dihydro-2,2,4-Trimethylquinoline (Monomer)	456
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3,3′-Dimethoxybenzidine Dihydrochloride	372
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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
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Ethylbenzene	466
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Furfural	382
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Glutaraldehyde	490
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HC Blue 2	293
HC Red 3	281
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Hexachloroethane	361
2,4-Hexadienal	509
4-Hexylresorcinol	330
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Hydroquinone	366
8-Hydroxyquinoline	276
Indium Phosphide	499
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8-Methoxypsoralen	359
α-Methylbenzyl Alcohol	369
Methyl Bromide	385
Methyl Carbamate	328
Methyldopa Sesquihydrate	348
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Methyleugenol	491
Methyl Methacrylate	314
N-Methylolacrylamide	352
Methylphenidate Hydrochloride	439
Mirex	313
Molybdenum Trioxide	462
Monochloroacetic Acid	396
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Nickel (II) Oxide	451
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Nitrofurazone	337
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2,4- & 2,6-Toluene Diisocyanate	251	Vanadium Pentoxide	507
Triamterene	420	4-Vinylcyclohexene	303
Tribromomethane	350	4-Vinyl-1-Cyclohexene Diepoxide	362
Trichloroethylene	243	Vinylidene Chloride	228
Trichloroethylene	273	Vinyl Toluene	375
1,2,3-Trichloropropane	384	Xylenes (Mixed)	327
Tricresyl Phosphate	433	2,6-Xylidine	278
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Triethanolamine	518	Ziram	238
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