NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF 1-CHLORO-2-PROPANOL
(TECHNICAL GRADE)

(CAS NO. 127-00-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(DRINKING WATER STUDIES)

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

September 1998

NTP TR 477

NIH Publication No. 98-3967

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. 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.

Listings of all published NTP reports and ongoing studies are available from NTP Central Data Management, NIEHS, P.O. Box 12233, MD E1-02, Research Triangle Park, NC 27709 (919-541-3419). The Abstracts and other study information for 2-year studies are also available at the NTP's World Wide Web site: http://ntp-server.niehs.nih.gov.

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CONTENTS

ABSTRACT 5

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY 9

TECHNICAL REPORTS REVIEW SUBCOMMITTEE 10

SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS 11

INTRODUCTION 13

MATERIALS AND METHODS 19

RESULTS 31

DISCUSSION AND CONCLUSIONS 57

REFERENCES 61

APPENDIX A Summary of Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 67

APPENDIX B Summary of Lesions in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 99

APPENDIX C Summary of Lesions in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 131

APPENDIX D Summary of Lesions in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 161

APPENDIX E Genetic Toxicology 199

APPENDIX F Continuous Breeding Study in Sprague-Dawley Rats 211

APPENDIX G Hematology, Clinical Chemistry, and Urinalysis Results 223

APPENDIX H Organ Weights and Organ-Weight-to-Body-Weight Ratios 229

APPENDIX I Reproductive Tissue Evaluations and Estrous Cycle Characterization 235

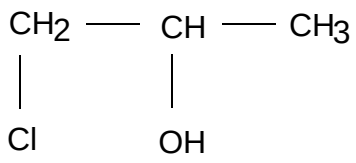
APPENDIX J Chemical Characterization and Dose Formulation Studies 239

APPENDIX K Water and Compound Consumption in the 2-Year Drinking Water Studies of 1-Chloro-2-propanol 251

APPENDIX L Ingredients, Nutrient Composition, and Contaminant Levels in NIH-07 Rat and Mouse Ration 257

APPENDIX M Sentinel Animal Program 261

ABSTRACT



TECHNICAL GRADE 1-CHLORO-2-PROPANOL

(~ 75% 1-CHLORO-2-PROPANOL; ~ 25% 2-CHLORO-1-PROPANOL)

CAS No. 127-00-4

Chemical Formula: C_3H_7ClO Molecular Weight: 94.54

Synonyms: Chlorohydrin, 1-chloro-2-hydroxypropane, 1-chloroisopropyl alcohol, propylene-∝-chlorohydrin, *sec*-propylene chlorohydrin

1-Chloro-2-propanol and its positional isomer, 2-chloro-1-propanol, are used as chemical intermediates for the manufacture of propylene oxide, a starting material for production of polyurethane polyols and propylene glycol. The National Cancer Institute nominated 1-chloro-2-propanol for study because of potential for human exposure due to its residues in various foods that are fumigated with ethylene oxide or propylene oxide. Male and female F344/N rats and $B6C3F_1$ mice were exposed to technical grade 1-chloro-2-propanol (75% to 76% 1-chloro-2-propanol; 24% to 25% 2-chloro-1-propanol) in drinking water for 14 days, 14 weeks, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, *Drosophila melanogaster*, and mouse peripheral blood erythrocytes. Continuous breeding studies were conducted in Sprague-Dawley rats.

14-Day Study in Rats

Groups of 10 male and 10 female F344/N rats were administered 1-chloro-2-propanol in drinking water at concentrations of 0, 100, 330, 1,000, 3,300, or 10,000 ppm for 14 days. Two 10,000 ppm females died before the end of the study. The final mean body weights and body weight gains of 3,300 and 10,000 ppm rats were significantly less than those of the controls; rats in the 10,000 ppm groups lost weight. Water consumption by the 3,300 and 10,000 ppm groups was significantly less than that by the controls throughout the study. The thymus weights of 10,000 ppm rats were significantly less than those of the controls. Exposure to 1-chloro-2-propanol caused cytoplasmic alteration and degeneration of the acinar cells and fatty change in the pancreas, atrophy of the bone marrow, and atrophy and hematopoiesis of the spleen in males and females.

14-Day Study in Mice

Groups of 10 male and 10 female $B6C3F_1$ mice were administered 1-chloro-2-propanol in drinking water at concentrations of 0, 100, 330, 1,000, 3,300, or 10,000 ppm for 14 days. One male mouse in the 10,000 ppm group died before the end of the study. Mean body weight gains of 10,000 ppm mice were significantly less than those of the controls. Water consumption by 3,300 and 10,000 ppm males and females was significantly less than that by the controls throughout the study. Liver weights of 1,000, 3,300, or 10,000 ppm males and females were significantly greater and thymus weights of 10,000 ppm mice were significantly less than those of the controls. Exposure

to 1-chloro-2-propanol caused hepatocellular vacuolization, cytoplasmic alteration and degeneration of the pancreas acinar cells, and atrophy of the spleen in males and females.

14-Week Study in Rats

Groups of 10 male and 10 female F344/N rats were administered 1-chloro-2-propanol at concentrations of 0, 33, 100, 330, 1,000, or 3,300 ppm (equivalent to average daily doses of approximately 5, 10, 35, 100, or 220 mg/kg) for 14 weeks. All rats survived to the end of the study. Mean body weight gains of 3,300 ppm rats were significantly less than those of the controls. Water consumption by the 3,300 ppm male and female rats was significantly less than that by the controls. A minimal to mild anemia was observed in exposed female rats. The cauda epididymis and epididymis weights of 3,300 ppm males were significantly less than those of the controls. The percentage of abnormal sperm in 3,300 ppm males and the concentration of epididymal sperm in 330 ppm males were significantly increased compared to the controls. Kidney and liver weights of males and females exposed to 100 ppm or more were generally greater than those of the controls. The incidences of acinar cell degeneration and fatty change of the pancreas in 1,000 and 3,300 ppm rats, hepatocytic metaplasia of the pancreatic islets in 3,300 ppm females, cytoplasmic vacuolization of the liver in 100, 1,000 and 3,300 ppm males, and renal tubule epithelium regeneration in 3,300 ppm females were increased compared to the controls.

14-Week Study in Mice

Groups of 10 male and 10 female B6C3F$_1$ mice were administered 1-chloro-2-propanol in drinking water at concentrations of 0, 33, 100, 330, 1,000, or 3,300 ppm (equivalent to average daily doses of approximately 5, 15, 50, 170, or 340 mg/kg to males and 7, 20, 70, 260, or 420 mg/kg to females) for 14 weeks. One 330 ppm male died before the end of the study. Mean body weight gains of exposed groups were similar to those of the controls. A minimal anemia was observed in 3,300 ppm males. The right epididymis weight of 3,300 ppm males was significantly greater than that of the controls. Kidney weights of 3,300 ppm mice, liver weights of 1,000 ppm males and of all exposed groups of females, and thymus weights of 1,000 and 3,300 ppm females were greater than those of the controls. The incidences of pancreatic acinar cell degeneration and fatty change in 3,300 ppm males and females and cytoplasmic vacuolization of the liver in all groups of exposed females were significantly increased compared to the controls. The severities of renal tubule cytoplasmic vacuolization were greater in 1,000 and 3,300 ppm males than in the controls.

2-Year Study in Rats

Groups of 50 male and 50 female F344/N rats were administered drinking water containing 0, 150, 325, or 650 ppm 1-chloro-2-propanol (equivalent to average daily doses of approximately 15, 30, or 65 mg/kg during the first several months of the study and 8, 17, or 34 mg/kg for the remainder of the 2-year study) for up to 105 weeks. Survival of all exposed groups was similar to that of the controls. Mean body weights of exposed rats were generally similar to those of the controls throughout most of the study. Water consumption by all exposed groups was similar to that by the controls. No treatment-related neoplasms or nonneoplastic lesions were observed in this study.

2-Year Study in Mice

Groups of 50 male and 50 female B6C3F$_1$ mice were administered drinking water containing 0, 250, 500, or 1,000 ppm 1-chloro-2-propanol (equivalent to average daily doses of approximately 45, 75, or 150 mg/kg to males and 60, 105, or 210 mg/kg to females during the first several months of the study and 25, 50, or 100 mg/kg for the remainder of the 2-year study) for up to 105 weeks. Survival of all exposed groups was similar to that of the controls. The mean body weights of all exposed mice were generally similar to those of the controls throughout the study. Water consumption by all exposed groups was similar to that by the controls. No treatment-related neoplasms or nonneoplastic lesions were observed in this study.

Genetic Toxicology

1-Chloro-2-propanol is a demonstrated mutagen *in vitro*. It was weakly mutagenic in *S. typhimurium* strain TA100 in the presence of hamster or rat liver S9 activation enzymes and was positive, with and without S9, in TA1535. No mutagenic activity was detected in strains TA97, TA98, and TA1537, with or without S9. In cytogenetic tests with Chinese hamster ovary cells, 1-chloro-2-propanol induced high levels of sister

chromatid exchanges and chromosomal aberrations in the presence and the absence of S9. The marked ability of 1-chloro-2-propanol to induce chromosomal effects *in vitro* was not seen *in vivo*. Positive results were obtained in a test in *D. melanogaster* for induction of sex-linked recessive lethal mutations in germ cells of males administered 1-chloro-2-propanol via injection; however, negative results were obtained when males were administered 1-chloro-2-propanol in feed. A subsequent germ cell reciprocal translocation test in *D. melanogaster* yielded negative results. Further, no induction of micronucleated erythrocytes was observed in peripheral blood of male and female mice administered 1-chloro-2-propanol via drinking water for 14 weeks.

CONCLUSIONS

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity** of technical grade 1-chloro-2-propanol in male or female F344/N rats exposed to 150, 325, or 650 ppm. There was *no evidence of carcinogenic activity* of technical grade 1-chloro-2-propanol in male or female $B6C3F_1$ mice exposed to 250, 500, or 1,000 ppm.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 9. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 11.

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of 1-Chloro-2-propanol

	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Concentrations	0, 150, 325, or 650 ppm	0, 150, 325, or 650 ppm	0, 250, 500, or 1,000 ppm	0, 250, 500, or 1,000 ppm
Body weights	Exposed groups similar to control group	Exposed groups similar to control group	Exposed groups similar to control group	Exposed groups similar to control group
Survival rates	20/50, 23/50, 24/50, 23/50	25/50, 33/50, 30/50, 31/50	40/50, 44/50, 29/50, 39/50	32/50, 32/50, 36/50, 32/50
Nonneoplastic effects	None	None	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:	Positive or equivocal with S9 in strain TA100; positive with and without S9 in strain TA1535; negative with and without S9 in strains TA97, TA98, and TA1537			
Sister chromatid exchanges				
Cultured Chinese hamster ovary cells *in vitro*:	Positive with and without S9			
Chromosomal aberrations				
Cultured Chinese hamster ovary cells *in vitro*:	Positive with and without S9			
Sex-linked recessive lethal mutations				
Drosophila melanogaster:	Positive when administered via injection, negative when administered via feed			
Reciprocal translocations				
Drosophila melanogaster:	Negative			
Micronucleated erythrocytes				
Mouse peripheral blood *in vivo*:	Negative			

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.

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 1-chloro-2-propanol on 10 December 1997 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 10 December 1997, the draft Technical Report on the toxicology and carcinogenesis studies of 1-chloro-2-propanol (technical grade) received public review by the National Toxicology Program's Board of Scientific Counselors' Technical Reports Review Subcommittee. The meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. J.K. Dunnick, NIEHS, introduced the toxicology and carcinogenesis studies of 1-chloro-2-propanol by discussing the uses of the chemical and the rationale for study, describing the experimental design, reporting on any survival and body weight effects, and commenting on compound-related neoplastic and nonneoplastic lesions in rats and mice. The proposed conclusions for the 2-year studies were *no evidence of carcinogenic activity* in male or female F344/N rats or $B6C3F_1$ mice.

Dr. Chatman, a principal reviewer, agreed with the proposed conclusions. She noted that the pancreas was a target tissue in the 14-week studies, and in light of epidemiologic reports of higher rates of pancreatic cancer in humans working in the chlorohydrin industry, she asked if the top doses should have been higher in the 2-year studies. Dr. Chatman asked why inhalation was not the preferred route of exposure. Dr. Dunnick responded that the chemical was administered orally because of concern about its being present in fumigated foods.

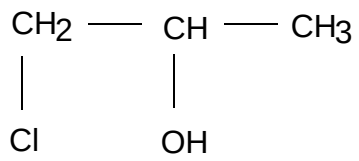
Dr. J. Russo, the second principal reviewer, agreed with the proposed conclusions. He commented on the significant decrease in drinking water consumption in exposed animals in the 14-week studies and asked whether this could be due to some type of hypothalamic damage. Dr. Dunnick said water consumption was decreased more in the 14-day studies than in the 14-week studies, and by 13 weeks, decreases in water consumption were much less as animals adapted to the taste of the chemical. Dr. Chatman inquired whether exposure concentrations were monitored in view of the decrease in water consumption. Dr. Dunnick said analyses were performed on the drinking water bottles and on the dose preparations, and, in general, concentrations were within targeted amounts.

Dr. Bus, the third principal reviewer, agreed with the proposed conclusions.

Dr. Goldsworthy also thought that the high doses may have been below maximal tolerated doses. Dr. J.R. Hailey, NIEHS, said that the 2-year study doses were based on the significant pancreatic lesions in the 14-week studies. Dr. Bus commented that based on the results of the 14-week studies, the doses for the 2-year studies were chosen properly. Dr. Cullen asked whether the pancreatic lesions in the 14-week studies were metaplastic and if the size of the pancreas had changed. Dr. Hailey replied that there was no change in size although there was apoptosis of acinar cells and replacement by adipocytes (fat cells). Dr. Chatman urged the NTP to pursue the evaluation of possible pancreatic effects in view of a possible association with increased pancreatic cancer in the workplace.

Dr. Chatman moved that the Technical Report on 1-chloro-2-propanol (technical grade) be accepted with the conclusions as written for male and female rats and mice, *no evidence of carcinogenic activity*. Dr. Goldsworthy seconded the motion, which was accepted unanimously with seven votes.

INTRODUCTION



TECHNICAL GRADE 1-CHLORO-2-PROPANOL

(~ 75% 1-CHLORO-2-PROPANOL; ~ 25% 2-CHLORO-1-PROPANOL)

CAS No. 127-00-4

Chemical Formula: C_3H_7ClO Molecular Weight: 94.54

Synonyms: Chlorohydrin, 1-chloro-2-hydroxypropane, 1-chloroisopropyl alcohol, propylene-∝-chlorohydrin, *sec*-propylene chlorohydrin

CHEMICAL AND PHYSICAL PROPERTIES

1-Chloro-2-propanol and 2-chloro-1-propanol are the isomers of propylene chlorohydrin. The chemical and physical properties of the two isomers are summarized in Table 1.

PRODUCTION, USE, AND HUMAN EXPOSURE

Propylene chlorohydrins, organic compounds containing chlorine and hydroxyl groups, are unknown as natural products; they are manufactured by the reaction of propylene with hypochlorous acid. The production of a mixture of 1-chloro-2-propanol and 2-chloro-1-propanol in the United States in 1976 was estimated to be greater than 8.1×10^8 kg or 1.78 billion pounds (USEPA, 1977).

The chlorine in propylene chlorohydrins is labile; it dehydrohalogenates readily through an intermediate epoxide, which then hydrolyzes to glycols (*Kirk-Othmer*, 1985). Propylene chlorohydrins are used commercially as chemical intermediates in the manufacture of propylene oxide, a starting material for the production of polyurethane polyols and propylene glycol. Approximately half of the propylene oxide produced in the United States in 1979 was from propylene chlorohydrins. Prior to 1969, all propylene oxide and most ethylene oxide produced in the United States were manufactured using propylene chlorohydrins (USEPA, 1977; SRI, 1980).

Propylene chlorohydrins have been identified as potential air pollutants from chemical manufacturing plants (USEPA, 1976). However, no threshold limit values have been set for workplace air in the United States, no occupational standard for exposure to propylene chlorohydrins has been established by the Occupational Safety and Health Administration (OSHA), and no allowable limits for water or soil have been determined by the U.S. Environmental Protection Agency.

Propylene chlorohydrins are generated from the hydrolysis of epichlorohydrin, a widely used chemical intermediate (Carr and Rosenkranz, 1978), and 1-chloro-2-propanol has been identified in the headspace above a soil sample contaminated with

TABLE 1
Summary of the Chemical and Physical Properties of Isomers of Propylene Chlorohydrin[a]

Property	1-Chloro-2-propanol (*sec*-propylene chlorohydrin) CAS No. 127-00-4	2-Chloro-1-propanol (propylene chlorohydrin) CAS No. 78-89-70
Molecular weight	94.54	94.54
Form	Colorless liquid	Colorless liquid, pleasant odor
Boiling point	126° to 127° C	133° to 134° C
Flash point	52° C	52° C
Density	1.115 at 20° C	1.103 at 20° C
Solubility[b]	Water, alcohol, diethyl ether	Water, alcohol, diethyl ether
Refractive index	1.4392 at 20° C	1.4362 at 20° C
Vapor pressure	4.9 mm Hg at 20° C	—

[a] *Merck Index*, 1989
[b] Lide, 1992

degradation products of burned polyurethane foam used for thermal insulation (Schulting and Wils, 1977).

Propylene chlorohydrins are found in a broad spectrum of foodstuffs, including powdered and flaked foods, cereals, dried fruits, spices, cocoa, flour, and egg powder, that have been fumigated or cold sterilized with propylene oxide (Ragelis *et al.*, 1966; Fishbein, 1969). Under conditions necessary for effective sterilization, propylene oxide reacts with naturally occurring inorganic chlorides in foods, forming propylene chlorohydrins (Wesley *et al.*, 1965). Concentrations of 1-chloro-2-propanol ranging from 4 ppm in cocoa to 47 ppm in glazed citron have been measured in foods fumigated with propylene oxide (Ragelis *et al.*, 1968). Only 5 ppm propylene chlorohydrins are permitted as a food additive in modified food starch (*Fed. Regist.*, 1969).

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Experimental Animals

Data from limited metabolism studies indicate that propylene chlorohydrins are partly excreted in the conjugated form in the urine of laboratory animals. Following oral administration of 140 mg/kg 2-chloro-1-propanol to rabbits, 11% of the dose was excreted in the urine as its glucuronic acid conjugate (Williams, 1959). In a study of the metabolism of 1-halogenopropanes (Barnsley, 1966), 1-chloro-2-propanol (0.5 mL) was administered as a 3.3% (w/v) solution in arachis oil. 2-Hydroxypropylmercapturic acid (*N*-acetyl-*S*-(2-hydroxypropyl)-L-cysteine) was identified as a urinary metabolite of 1-chloro-2-propanol in the urine of male rats (strain not specified) 24 hours after a single subcutaneous injection. Jones and Gibson (1980) conducted *in vitro* studies of the metabolism of 1,2-dichloropropane using the methods of Barnsley (1966), proposed 1-chloro-2-propanol as an intermediate metabolite to explain the presence of the *N*-acetyl-*S*-(2-hydroxypropyl)-cysteine found in the urine of male rats injected subcutaneously with 1,2-dichloropropane. Jones and Gibson (1980) also conducted *in vivo* studies in male Sprague-Dawley rats. Following subcutaneous injection of 100 mg [^{36}Cl]-1-chloro-2-propanol to a single rat, 4% of the administered radiolabel was excreted unchanged in the expired air. In addition, two major urinary metabolites identified in rats dosed orally with 1-chloro-2-propanol (100 mg/kg per day for 4 days) were *N*-acetyl-*S*-(2-hydroxypropyl)-cysteine and β-chlorolactate.

The disposition of 1-chloro-2-propanol was studied in male F344/N rats (aged 11 to 13 weeks) exposed by nose-only inhalation to approximately 8 or 80 ppm [^{14}C]-1-chloro-2-propanol for 6 hours (Bond *et al.*, 1988). The two major routes of ^{14}C elimination were urinary and respiratory, which together accounted for about 80% of the total radiolabel recovered 70 hours after the end of the 6-hour exposure. At both exposure concentrations, most of the radiolabel was eliminated in urine during the first day after exposure. Half-lives for elimination were 3.9 hours for breath and 5 hours for urine. The results indicated that

metabolism of 1-chloro-2-propanol was rapid and related linearly to the inhaled exposure concentration. Following inhalation, 1-chloro-2-propanol was widely distributed to tissues, rapidly metabolized, and eliminated. One hour after the end of the 6-hour exposure period, the kidney, liver, trachea, and nasal turbinates of 8 ppm rats contained 30 to 50 nmol ^{14}C/g tissue, and those of 80 ppm rats contained 200 to 350 nmol ^{14}C/g tissue; other tissues contained less than 150 nmol ^{14}C/g tissue. The tissue elimination of ^{14}C was biphasic at both exposure concentrations, with a short-term elimination half-life of 1 to 4 hours and a long-term elimination half-life of 40 to 126 hours. No evidence of unmetabolized 1-chloro-2-propanol was seen in the tissues examined. Biliary excretion was a major route of elimination of 1-chloro-2-propanol; approximately 30% of the administered radiolabel was excreted in the bile within 10 hours. Three hours after exposure of rats to 80 ppm, two major metabolites were detected in the urine and three major metabolites were detected in liver. In both cases, one of these metabolites was identified as *N*-acetyl-*S*-(hydroxypropyl)-cysteine and/or *S*-(2-hydroxypropyl)-cysteine, which is consistent with data obtained by Barnsley (1966) and Jones and Gibson (1980). These metabolites appear to be derived from the conjugation of 1-chloro-2-propanol with glutathione. Bond *et al*. (1988) also investigated whether the exhaled radiolabeled CO_2 was derived from the second and/or third carbon atoms using 1-chloro-2-propanol labeled with ^{14}C either at both carbons or only at the second carbon atom. Less $^{14}CO_2$ was detected in rats exposed to [2-^{14}C]-1-chloro-2-propanol than in rats exposed to [2,3-^{14}C]-1-chloro-2-propanol, indicating that the second and third carbon atoms are both metabolized, at least in part, to CO_2.

Humans

No information on the absorption, distribution, metabolism, or excretion of 1-chloro-2-propanol in humans was found in the literature.

TOXICITY

Experimental Animals

The acute oral (gavage) LD_{50} for a commercial grade of propylene chlorohydrins was 0.22 mL/kg in Carworth-Wistar rats (4 to 5 weeks of age) and 0.72 g/kg in guinea pigs; narcosis was observed in rats and guinea pigs at LD_{50} doses and greater (Smyth *et al*., 1941, 1969). Data from the Food and Drug Administration indicated an acute oral LD_{50} of 217 mg/kg for propylene chlorohydrins in the rat (strain not specified) (FAO, 1974). The acute oral LD_{50} for 1-chloro-2-propanol in rats was 0.1 to 0.3 g/kg (*Patty's*, 1982). Dogs (number not specified) survived an oral dose of 150 mg propylene chlorohydrin/kg (FAO, 1974). At 200 mg/kg, one of seven treated dogs died; single doses of 250 mg/kg or greater were lethal to all six dogs in each group. The dermal LD_{50} for propylene chlorohydrin (24-hour plastic-covered contact on clipped skin) was 0.48 mL/kg in male New Zealand rabbits (Smyth *et al*., 1969).

No skin irritation was observed in a single New Zealand rabbit 24 hours after the uncovered topical application of 0.01 mL (approximately 10 mg) neat propylene chlorohydrins to the clipped skin of the abdomen (Smyth *et al*., 1969). Severe (grade 8 on a scale of 1 to 10) corneal injury resulted from instillation of 0.005 mL (approximately 5 mg) neat propylene chlorohydrins or an excess of a 40% solution in propylene glycol into the eye of albino rabbits (Carpenter and Smyth, 1946).

Inhalation of 500 ppm commercial propylene chlorohydrins resulted in the death of one of six rats after a 4-hour exposure period (Smyth *et al*., 1969). In an inhalation study by Bond *et al*. (1988), there were no overt acute toxic effects of 1-chloro-2-propanol at exposure concentrations up to 80 ppm.

In an inhalation study by Gage (1970) using Alderley-Park specific-pathogen-free rats, exposure of two male and two female rats to a vapor concentration of 1,000 ppm 1-chloro-2-propanol for two 6-hour periods at a 3-day interval resulted in lethargy after the first exposure and the death of one rat after the second exposure. In the animal that died, necropsy findings included a pale liver and edematous, congested lungs; histopathology findings included swollen, vacuolated hepatocytes with nuclear degeneration and pulmonary interstitial inflammation. Following fifteen 6-hour exposures of two male and two female rats to 250 ppm, lethargy, irregular weight gain, and congestion and perivascular edema of the lungs were observed. Fifteen 6-hour exposures to 100 ppm resulted in no findings of toxicity in four male and four female rats; however, histopathologic findings included congestion and perivascular edema of the

lungs. No toxic or histopathologic effects were observed in four males or four females following fourteen 6-hour exposures to 30 ppm 1-chloro-2-propanol.

Humans

No information on toxicity in humans was reported in the literature.

CARCINOGENICITY

Experimental Animals

The carcinogenicity of 1-chloro-2-propanol was evaluated in a bioassay system involving induction of pulmonary adenomas in strain A mice (Theiss *et al*., 1979). Groups of 10 male and 10 female mice were given intraperitoneal injections of 1-chloro-2-propanol in tricaprylin three times per week (total of 24 injections) at concentrations of 0.53, 1.06, or 2.12 mmol/kg. Twenty-four weeks after the first injection, the number of adenomas on the lung surface was counted. No statistically significant differences in the average number of lung neoplasms per mouse were observed between treated and control mice.

Humans

Several studies in the literature examined mortality in men assigned to a chlorohydrin unit that produced ethylene chlorohydrin and/or propylene chlorohydrin from 1925 and 1957. Greenberg *et al*. (1990) reported statistically significant excess mortality due to pancreatic cancer and leukemia in men assigned to the chlorohydrin unit for 2 years or more during the period from 1925 through 1957; six deaths due to pancreatic cancer (0.7 expected) and three deaths due to leukemia (0.4 expected) occurred. A fourth death due to leukemia occurred in a man assigned to the chlorohydrin unit for less than 2 years. Nine of the ten decedents worked in the chlorohydrin unit between 1935 and 1945. The six men who died from pancreatic cancer were first assigned to the chlorohydrin unit between 1929 and 1944; their cumulative duration of assignments ranged from 2 to 30 years and averaged 12 years, and they died between 26 and 48 years after their first chlorohydrin assignment. The four men who died from leukemia were first assigned to the chlorohydrin unit prior to 1937; the average duration of their assignments was 9 years and ranged from less than 1 to 16 years. They died between 18 to 39 years after their first chlorohydrin assignment. Significant trends with duration of assignment to the chlorohydrin unit were found for both cancers. The authors concluded that the observed excesses of pancreatic cancer and leukemia were primarily associated with the production of ethylene chlorohydrin and/or propylene chlorohydrins although quantitative measurements of exposure were not available.

A second retrospective study was conducted at the same chemical plant to verify the previous findings of cancer excesses among 278 men with a mean duration of assignment to the chlorohydrin unit of 5.9 years and mean duration of follow-up of 36.5 years (Benson and Teta, 1993). During 1979 through 1988, two additional deaths from pancreatic cancer (0.9 expected) were reported, bringing the total to 8 observed versus 1.6 deaths expected. There were no additional deaths from leukemia, but the three- to fourfold increase in risk for lymphopoietic cancers persisted due to new cases of non-Hodgkin's lymphoma and multiple myeloma. Increases in risk were seen for total cancer, pancreatic cancer, all lymphatic and hematopoietic cancers, and leukemia with increasing durations of assignment to the chlorohydrin unit. The data were insufficient to conclusively identify the causative agent or combination of agents. However, the authors suggested that high exposure to ethylene dichloride, perhaps in combination with other chlorinated hydrocarbons, was the most likely agent. IARC has found insufficient epidemiological studies for ethylene dichloride, bischloro ethylene, ethylene chlorohydrin, and propylene chlorohydrin to determine the carcinogenic potential to humans (IARC, 1979).

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Experimental Animals

Administration of gavage doses of 8, 20, 50, or 125 mg propylene chlorohydrin/kg body weight per day to groups of five female rats on gestation days 6 to 15 had no effect on maternal growth or the growth and survival of fetuses (Exxon Chemical Company, 1980). There was a slight decrease in embryo survival in the 8 and 125 mg/kg groups, and two fetuses (dose level not specified) showed gross malformations. The investigators concluded that propylene chlorohydrin may be a weak teratogen.

Humans

No information on the reproductive or developmental toxicity in humans was reported in the literature.

GENETIC TOXICITY

1-Chloro-2-propanol (both 97% pure and 70% technical grade) was mutagenic in *Salmonella typhimurium* strains TA100 and TA1535, with and without induced S9 metabolic activation enzymes; no mutagenicity was detected in strains TA97, TA98, and TA1537, which revert via a frameshift mechanism (Carr and Rosenkranz, 1978; Pfeiffer and Dunkelberg, 1980; Zeiger *et al.*, 1987). The chemical was also positive in the *Escherichia coli* pol A assay for DNA damage (Hyman *et al.*, 1980). 1-Chloro-2-propanol (technical grade) induced sex-linked recessive lethal mutations in germ cells of male *Drosophila melanogaster* when administered by injection; however, results of a subsequent test for induction of reciprocal translocations in germ cells of male *D. melanogaster* were negative (Foureman *et al.*, 1994).

A mixture (proportions not stated) of 2-chloro-1-propanol and 1-chloro-2-propanol was tested for mutagenicity in *S. typhimurium*, and positive results were reported with strains TA100 and TA1535 in the absence of S9 (Pfeiffer and Dunkelberg, 1980). Biles and Piper (1983) confirmed this response in *S. typhimurium* with a 75:25 mixture of 1-chloro-2-propanol:2-chloro-1-propanol and further reported that addition of S9 enhanced the mutagenic response. In addition, they reported positive results with this mixture in the L5178Y mouse lymphoma assay, with and without S9. Finally, these authors reported that this mixture in doses of 10, 31, and 100 mg/kg per day for 5 days induced significant dose-related increases in chromosomal aberrations, consisting mainly of chromatid breaks, in rat bone marrow cells.

STUDY RATIONALE

The National Cancer Institute nominated 1-chloro-2-propanol and 2-chloro-1-propanol for carcinogenesis evaluation because these chemicals may be present in food fumigated with propylene oxide. The pure chemicals were not available and, therefore, technical grade 1-chloro-2-propanol (approximately 75% 1-chloro-2-propanol and 25% 2-chloro-1-propanol) was evaluated in the NTP studies. Drinking water was selected as the route of administration because human exposure may occur by the oral route.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF 1-CHLORO-2-PROPANOL

Technical grade 1-chloro-2-propanol (approximately 75% 1-chloro-2-propanol and 25% 2-chloro-1-propanol) was obtained from Eastman Kodak Laboratory Chemicals (Rochester, NY) in one lot (B15). Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO) (Appendix J). Reports on analyses performed in support of the 1-chloro-2-propanol studies are on file at the National Institute of Environmental Health Sciences.

The major component of the test chemical, a clear, colorless liquid, was identified as 1-chloro-2-propanol by infrared, ultraviolet/visible, and nuclear magnetic resonance spectroscopy. The purity of lot B15 was determined by elemental analyses, Karl Fischer water analysis, free acid titration, and gas chromatography. Elemental analyses for carbon, chlorine, and hydrogen were in agreement with the theoretical values for 1-chloro-2-propanol. Karl Fischer water analysis indicated 0.62% ± 0.02% water. Free acid titration indicated a hydrochloric acid content of 1,149 ± 2 ppm, equivalent to 0.0315 ± 0.0001 mEq of acid per gram of sample. Gas chromatography using one system indicated two major peaks and two impurities with a combined area of 0.47% relative to the total major peak area. Gas chromatography using another system indicated two major peaks and three impurities with a combined area of 0.67% relative to the total major peak area. No additional impurities with areas of 0.1% or greater relative to the major peak were detected using either system. The second major peak represents 2-chloro-1-propanol, a positional isomer of 1-chloro-2-propanol. The concentrations of 1-chloro-2-propanol and 2-chloro-1-propanol were estimated to be approximately 75% to 76% and 24% to 25%, respectively.

Stability studies of the bulk chemical were performed by the analytical chemistry laboratory using gas chromatography. These studies indicated that 1-chloro-2-propanol was stable as a bulk chemical for 2 weeks when stored protected from light at temperatures up to 60° C. To ensure stability, the bulk chemical was stored at 5.5° C (14-day and 14-week studies) or 1° to 8° C (2-year studies) protected from light in sealed glass containers. Stability was monitored during the 14-week studies using gas chromatography and free acid titration and during the 14-day and 2-year studies using gas chromatography. No degradation of the bulk chemical was detected.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared twice during the 14-day studies, every 2 weeks in the 14-week studies, and approximately every 2 weeks in the 2-year studies by mixing 1-chloro-2-propanol with ultraviolet light-treated, deionized water for the 14-day and 14-week studies and with deionized water for the 2-year studies (Table J1). The dose formulations were stored in closed bottles in the dark at room temperature prior to use. In the animal rooms, the drinking water bottles were changed twice per week.

Periodic analyses of the dose formulations of 1-chloro-2-propanol were conducted at the study laboratory using gas chromatography. During the 14-day studies, dose formulations were analyzed once per week (Table J2). Dose formulations were analyzed at the beginning, midpoint, and end of the 14-week studies (Table J3). During the 2-year studies, dose formulations were analyzed approximately every 8 weeks (Table J4). Through the 14-day, 14-week, and 2-year studies, all but one of the 149 dose formulations analyzed was within 10% of the target concentration; that formulation was remixed. Similarly, all but one of 54 animal room

samples was within 10% of target concentration. One 250 ppm animal room sample was outside of specifications and this was attributed to technical error; the dose was contaminated with a 650 ppm rat dose formulation. Results of periodic referee analyses performed by the analytical chemistry laboratory agreed with the results obtained by the study laboratory for the 14-week studies (Table J5).

14-Day 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 4 weeks old. Animals were quarantined for 11 to 14 days and were 6 weeks old on the first day of the studies. Groups of 10 male and 10 female rats and mice were exposed to 1-chloro-2-propanol at concentrations of 0, 100, 333, 1,000, 3,300, or 10,000 ppm in 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 for rats and mice. Water consumption was recorded weekly. The animals were weighed initially, weekly, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 2.

A necropsy was performed on all rats and mice. The brain, heart, right kidney, liver, lung, right testis, and thymus were weighed. Complete histopathologic examinations were performed on 0 and 10,000 ppm rats and mice. Additionally, the following tissues were examined to a no-effect level: bone marrow, pancreas, spleen, and uterus of rats and liver, pancreas, spleen, and thymus of mice. Table 2 lists the tissues and organs examined.

14-Week Studies

The 14-week studies were conducted to evaluate the cumulative toxic effects of repeated exposure to 1-chloro-2-propanol 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 4 weeks old. Animals were quarantined for 11 to 12 days and were 6 weeks old on the first day of the studies. Before initiation of the studies, 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 sentinel mice using the protocols of the NTP Sentinel Animal Program (Appendix M).

Groups of 10 male and 10 female rats and mice were given drinking water containing 1-chloro-2-propanol at concentrations of 0, 33, 100, 330, 1,000, or 3,300 ppm. Groups of 10 male and 10 female rats exposed to the same concentrations were designated as special study animals for clinical pathology evaluations. Feed and water were available *ad libitum*. Rats were housed five per cage, and mice were housed individually. Clinical findings were recorded weekly for rats and mice. Water consumption was recorded weekly. The animals were weighed initially, weekly, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 2.

On days 3, 15, and 45, clinical chemistry evaluations were performed for all male and female rats designated for special studies. At study termination, hematology and clinical chemistry evaluations were performed for all special study rats. Starting on day 14 and the day prior to study termination, timed urine collections were performed for all special study rats for urine chemistry evaluations. Hematology evaluations were performed for all core study mice at the end of the study. At all time points, rats and mice were anesthetized with a CO_2/O_2 mixture and blood was drawn from the retroorbital sinus. Blood for hematology determinations was placed in tubes containing potassium EDTA as the anticoagulant; blood for clinical chemistry analyses was placed in tubes without anticoagulant, allowed to clot at room temperature, and centrifuged, and the serum was separated. For urinalysis studies, rats were placed individually into metabolism cages for a 16-hour urine collection. During urine collection, containers were kept chilled with ice to minimize evaporation and suppress bacterial growth. Animals had access to food and water during the urine collection period. Table 2 lists the hematology, clinical chemistry, and urinalysis parameters evaluated.

Hematology determinations including erythrocyte and leukocyte counts, hemoglobin concentration, hematocrit, mean cell volume, mean cell hemoglobin, and mean cell hemoglobin concentration were performed on a Coulter Hematology Analyzer, Model S560 (Coulter Electronics, Hialeah, FL). Platelet counts were determined with a Baker Series 810 Whole Blood Platelet Analyzer (Serono-Baker Diagnostics, Allentown, PA). Leukocyte differential and nucleated erythrocyte counts and morphologic evaluation of blood cells were determined by light microscopic examination of blood films stained with Romanowsky stain. Blood smears stained with brilliant cresyl blue were examined microscopically for the quantitative determination of reticulocytes. Clinical chemistry and urinalysis evaluations were performed on a Gemini Miniature Centrifugal Analyzer (Electronucleonics, Inc., Fairfield, NJ) using commercially available reagents. Urine specific gravity was determined by refractometry; urine volume was a calculated value based on measurements of mass and specific gravity.

At the end of the 14-week studies, samples were collected for sperm morphology and vaginal cytology evaluations on rats and mice exposed to 0, 33, 330, and 3,300 ppm. The parameters evaluated are listed in Table 2. Methods used were those described in the NTP's sperm morphology and vaginal cytology evaluations protocol (NTP, 1985a). For 7 consecutive days prior to the 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 morphology, count, and motility. The right testis and right 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 right 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. Four sperm morphology slides were prepared for each animal evaluated. An aliquot of killed sperm suspension was stained in a test tube, spread on a microscope slide under a coverslip, and examined.

A necropsy was performed on all animals. The brain, heart, right kidney, liver, lung, right testis, and thymus were weighed. Tissues for microscopic examination were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 4 to 6 µm, and stained with hematoxylin and eosin. A complete histopathologic examination was performed on 0 and 3,300 ppm rats and mice. In addition, the kidney of mice, the liver of male rats and male and female mice, and the pancreas of rats and mice were examined in 33, 100, 330, and 1,000 ppm groups. Table 2 lists the tissues and organs routinely examined.

2-Year Studies

Study Design

Groups of 50 male and 50 female rats were given drinking water containing 1-chloro-2-propanol at concentrations of 0, 150, 325, or 650 ppm. Groups of 50 male and 50 female mice were exposed to 1-chloro-2-propanol in drinking water at concentrations of 0, 250, 500, or 1,000 ppm.

Source and Specification of Animals

Male and female F344/N rats and $B6C3F_1$ mice were obtained from Taconic Farms (Germantown, NY) for use in the 2-year studies. Rats and mice were quarantined for 12 to 15 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 7 weeks old at the beginning of the studies. The health of the animals was monitored during the studies according to the protocols of the NTP Sentinel Animal Program (Appendix M).

Animal Maintenance

Rats were housed five per cage, and mice were housed individually. Feed and water were available *ad libitum*. Water consumption was measured approximately monthly. Cages were changed three times per week for male rats, two times per week for female rats, and once per week for mice, and racks were rotated once every two weeks. Further details of animal maintenance are given in Table 2. Information on feed composition and contaminants is provided in Appendix L.

Clinical Examinations and Pathology

All animals were observed twice daily. Clinical findings were recorded monthly, except for an additional observation at week 6 for male mice. Body weights were recorded initially, weekly for 14 weeks, monthly thereafter, and at the end of the studies.

A complete necropsy and microscopic examination 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 (i.e., adrenal gland, kidney, ovary), samples from each organ were examined. Tissues examined microscopically are listed in Table 2.

Microscopic evaluations were completed by the study laboratory pathologist, and the pathology data were entered into the Toxicology Data Management System. The microscopic 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 mammary gland, pancreas (for acinar cell atrophy), and pituitary gland of rats, the liver, lung, and mesentery lymph nodes of male and female mice, and the pituitary gland pars distalis (for hyperplasia) 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 diagnosis 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 2
Experimental Design and Materials and Methods in the Drinking Water Studies of 1-Chloro-2-propanol

14-Day Studies	14-Week Studies	2-Year Studies
Study Laboratory		
SRI International (Menlo Park, CA)	SRI International (Menlo Park, CA)	TSI Mason Laboratories (Worcester, MA)
Strain and Species		
Rats: F344/N	Rats: F344/N	Rats: F344/N
Mice: $B6C3F_1$	Mice: $B6C3F_1$	Mice: $B6C3F_1$
Animal Source		
Taconic Farms (Germantown, NY)	Taconic Farms (Germantown, NY)	Taconic Farms (Germantown, NY)
Time Held Before Studies		
Rats: 11 days (males) or 12 days (females)	Rats: 11 days (males) or 12 days (females)	Rats: 12 days (males) or 14 days (females)
Mice: 13 days (males) or 14 days (females)	Mice: 11 days (males) or 12 days (females)	Mice: 13 days (males) or 15 days (females)
Average Age When Studies Began		
6 weeks	6 weeks	7 weeks
Date of First Exposure		
Rats: 15 September 1986 (males)	Rats: 9 February 1987 (males)	Rats: 5 February 1991 (males)
16 September 1986 (females)	10 February 1987 (females)	7 February 1991 (females)
Mice: 17 September 1986 (males)	Mice: 2 February 1987 (males)	Mice: 2 January 1991 (males)
18 September 1986 (females)	3 February 1987 (females)	4 January 1991 (females)
Duration of Exposure		
14 days	14 weeks	105 weeks
Date of Last Exposure		
Rats: 29 September 1986 (males)	Rats: 11 May 1987 (males)	Rats: 2 February 1993 (males)
30 September 1986 (females)	12 May 1987 (females)	9-10 February 1993 (females)
Mice: 1 October 1986 (males)	Mice: 4 May 1987 (males)	Mice: 30-31 December 1992 (males)
2 October 1986 (females)	5 May 1987 (females)	7 January 1993 (females)
Necropsy Dates		
Rats: 29 September 1986 (males)	Rats: 11 May 1987 (males)	Rats: 2 February 1993 (males)
30 September 1986 (females)	12 May 1987 (females)	9-10 February 1993 (females)
Mice: 1 October 1986 (males)	Mice: 4 May 1987 (males)	Mice: 30-31 December 1992 (males)
2 October 1986 (females)	5 May 1987 (females)	7 January 1993 (females)
Average Age at Necropsy		
8 weeks	19 weeks	111 weeks (males) or 112 weeks (females)
Size of Study Groups		
10 males and 10 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 14-day studies	Same as 14-day studies
Animals per Cage		
Rats: 5	Rats: 5	Rats: 5
Mice: 1	Mice: 1	Mice: 1

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of 1-Chloro-2-propanol

14-Day Studies	14-Week Studies	2-Year Studies
Method of Animal Identification		
Toe clip	Toe clip	Tail tattoo
Diet		
NIH-07 open formula block diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*, changed once per week	Same as 14-day studies	NIH-07 open formula pelleted diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*, changed once per week
Water		
UV treated, deionized water (Menlo Park municipal supply) via glass sipper tube water bottles (Lab Products, Rochelle Park, NJ), available *ad libitum*, changed twice per week	Same as 14-day studies	Deionized water (Worcester municipal supply) via glass sipper tube water bottles (Allentown Cage Co. Inc., Allentown, PA), available *ad libitum*, changed twice per week
Cages		
Polycarbonate cages (Lab Products, Rochelle Park, NJ), changed twice per week	Same as 14-day studies, except changed weekly for mice	Same as 14-day studies, except changed three times per week for male rats, two times per week for female rats, and once per week for mice
Bedding		
Sani-Chips (P.J. Murphy Forest Products Corp., Rochelle Park, NJ), changed twice per week	Same as 14-day studies	Same as 14-day studies, except changed three times per week for male rats, two times per week for female rats, and changed once per week for mice
Cage Filters		
Spun bonded polyester fabric (Snow Filtration, Cincinnati, OH)	Same as 14-day studies, except changed once every two weeks	Same as 14-week studies
Racks		
Stainless-steel (Lab Products, Rochelle Park, NJ)	Same as 14-day studies, except changed once every two weeks	Same as 14-week studies
Animal Room Environment		
Temperature: 22.2°-25.0° C Relative humidity: 41%-60% Room fluorescent light: 12 hours/day Room air changes: 10/hour	Temperature: 18.9°-27.2° C (rats) 18.9°-25.6° C (mice) Relative humidity: 24%-77% (rats) 18%-65% (mice) Room fluorescent light: 12 hours/day Room air changes: 10/hour	Temperature: 18.3°-24.4° C (rats) 20.6°-24.4° C (mice) Relative humidity: 8%-78% (rats) 10%-68% (mice) Room fluorescent light: 12 hours/day Room air changes: 10/hour
Exposure Concentrations		
0, 100, 333, 1,000, 3,300, or 10,000 ppm in drinking water, available *ad libitum*	0, 33, 100, 330, 1,000, or 3,300 ppm in drinking water, available *ad libitum*	Rats: 0, 150, 325, or 650 ppm in drinking water, available *ad libitum* Mice: 0, 250, 500, or 1,000 ppm in drinking water, available *ad libitum*

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of 1-Chloro-2-propanol

14-Day Studies	14-Week Studies	2-Year Studies
Type and Frequency of Observation		
Observed twice daily; animals were weighed initially, weekly, and at the end of the studies; clinical findings were recorded daily. Water consumption was recorded weekly.	Observed twice daily; animals were weighed initially, weekly, and at the end of the studies; clinical findings were recorded weekly. Water consumption was recorded weekly.	Observed twice daily; animals were weighed initially, weekly for 13 weeks, monthly thereafter, and at the end of the studies. Clinical findings were recorded monthly, except for an additional observation at week 6 for male mice. Water consumption was measured approximately monthly.
Method of Sacrifice		
CO_2 asphyxiation	CO_2 asphyxiation	CO_2 asphyxiation
Necropsy		
Necropsy performed on all animals. Organs weighed were brain, heart, right kidney, liver, lung, right testis, and thymus.	Necropsy performed on all animals. Organs weighed were brain, heart, right kidney, liver, lung, right testis, and thymus.	Necropsy performed on all animals.
Clinical Pathology		
None	Blood was collected from the retroorbital sinus of special study rats and core study mice at week 14 for hematology analyses. Blood was collected from the retroorbital sinus of special study rats on days 3, 15, and 45, and at 14 weeks for clinical chemistry. Rats were placed in metabolism cages for 16-hour urine collection at the end of the study. ***Hematology:*** hematocrit; hemoglobin concentration; erythrocyte, reticulocyte, nucleated erythrocyte, and platelet counts; mean cell volume; mean cell hemoglobin; mean cell hemoglobin concentration; and total leukocyte count and differentials ***Clinical chemistry:*** creatinine, albumin, alanine aminotransferase, creatine kinase, sorbitol dehydrogenase, and γ-glutamyltransferase ***Urinalysis:*** glucose, protein, volume, and specific gravity	None

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of 1-Chloro-2-propanol

14-Day Studies	14-Week Studies	2-Year Studies
Histopathology		
Complete histopathology was performed on 0 and 10,000 ppm rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined: adrenal gland, bone (including marrow), brain, clitoral gland, esophagus, gallbladder (mice), heart, 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 (with adjacent skin), nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, stomach (forestomach and glandular), testis (with epididymis and seminal vesicle), thymus, thyroid gland, trachea, urinary bladder, and uterus. In addition, bone marrow in 330 ppm female rats and 1,000 and 3,300 ppm male and female rats; uterus in all female rats; liver in all mice; spleen in 1,000 ppm rats and 3,300 ppm rats and mice; and thymus in 3,300 ppm female rats and female mice were examined.	Complete histopathology was performed on 0 and 3,300 ppm rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined: adrenal gland, bone (including marrow), brain, clitoral gland, esophagus, gallbladder (mice), heart, 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 (with adjacent skin), nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, stomach (forestomach and glandular), testis (with epididymis and seminal vesicle), thymus, thyroid gland, trachea, urinary bladder, and uterus. In addition, the kidney of mice, the liver of male rats and male and female mice, and the pancreas of rats and mice were examined in all remaining exposure groups.	Complete histopathology was performed all rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined: adrenal gland, bone (including marrow), brain, clitoral gland, esophagus, gallbladder (mice), heart, 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 (with adjacent skin), nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, stomach (forestomach and glandular), testis (with epididymis and seminal vesicle), thymus, thyroid gland, trachea, urinary bladder, and uterus.
Sperm Morphology and Vaginal Cytology		
None	At the end of the studies, sperm samples were collected from all male animals in the 0, 33, 330, and 3,300 ppm exposure groups for sperm morphology evaluations. The following parameters were evaluated: epididymal sperm concentration, morphology, and motility. The right cauda epididymis, epididymis, and testis were weighed. Vaginal samples were collected for up to 7 consecutive days prior to the end of the studies from all females exposed to 0, 33, 330, or 3,300 ppm for vaginal cytology evaluations. The parameters evaluated were relative frequency of estrous stages and estrous cycle length.	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 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 as presented in Tables A1, A5, B1, B4, C1, C4, D1, and D5 are given as the number of animals bearing such lesions at a specific anatomic site and the number 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 tests were used in the analysis of lesion incidence, and reported P values are one sided.

Analysis of Continuous Variables

Two approaches were employed to assess the significance of pairwise comparisons between exposed and control groups in the analysis of continuous variables. Organ and body weight data, which have approximately normal distributions, were analyzed with the parametric multiple comparison procedures of Dunnett (1955) and Williams (1971, 1972). Hematology, clinical chemistry, urinalysis, spermatid, and epididymal spermatozoal data, which have typically skewed distributions, were analyzed using the nonparametric multiple comparison methods of Shirley (1977) 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

Although the concurrent control group is always the first and most appropriate control group used for evaluation, historical control data can be helpful in the overall assessment of neoplasm incidence in certain instances. Consequently, neoplasm incidences from the NTP historical control database, which is updated yearly, are included in the NTP reports for neoplasms appearing to show compound-related effects.

QUALITY ASSURANCE METHODS

The 14-week 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 covering completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and a draft of this NTP Technical Report were conducted. 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, so all comments had been resolved or were otherwise addressed during the preparation of this Technical Report.

GENETIC TOXICOLOGY

The genetic toxicity of 1-chloro-2-propanol was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium*, sister chromatid exchanges and chromosomal aberrations in cultured Chinese hamster ovary cells, sex-linked recessive lethal mutations in *Drosophila melanogaster*, and increases in the frequency of micronucleated erythrocytes in peripheral blood of mice. The protocols for these studies and the results are given in Appendix E.

The genetic toxicity studies of 1-chloro-2-propanol are part of a larger effort by the NTP to develop a database that would permit the evaluation of carcinogenicity in experimental animals from the molecular structure and the effects of the chemical in short-term *in vitro* and *in vivo* genetic toxicity tests. These genetic toxicity tests were originally developed to study mechanisms of chemical-induced DNA damage and to predict carcinogenicity in animals, based on the electrophilicity theory of chemical mutagenesis and the somatic mutation theory of cancer (Miller and Miller, 1977; Straus, 1981; Crawford, 1985).

There is a strong correlation between a chemical's potential electrophilicity (structural alert to DNA reactivity), mutagenicity in *Salmonella*, and carcinogenicity in rodents. The combination of electrophilicity and *Salmonella* mutagenicity is highly correlated with the induction of carcinogenicity in rats and mice and/or at multiple tissue sites (Ashby and Tennant, 1991). Other *in vitro* genetic toxicity tests correlate less well with rodent carcinogenicity (Tennant *et al.*, 1987; Zeiger *et al.*, 1990), although these other tests can provide information on the types of DNA and chromosome effects that can be induced by the chemical being investigated. Data from NTP studies show that a positive response in *Salmonella* is the

most predictive *in vitro* test for rodent carcinogenicity (89% of the *Salmonella* mutagens are rodent carcinogens), and that there is no complementarity among the *in vitro* genetic toxicity tests. That is, no battery of tests that included the *Salmonella* test improved the predictivity of the *Salmonella* test alone.

The predictivity for carcinogenicity of a positive response in bone marrow chromosome aberration or micronucleus tests appears to be less than the *Salmonella* test (Shelby *et al.*, 1993; Shelby and Witt, 1995). Positive responses in long-term peripheral blood micronucleus tests have not been formally evaluated for their predictivity for rodent carcinogenicity. But, because of the theoretical and observed associations between induced genetic damage and adverse effects in somatic and germ cells, the determination of *in vivo* genetic effects is important to the overall understanding of the risks associated with exposure to a particular chemical.

RESULTS

RATS

14-DAY STUDY

Two 10,000 ppm female rats died before the end of the study (Table 3). The final mean body weights and body weight gains of 3,300 and 10,000 ppm males and females were significantly less than those of the controls; male and female rats in the 10,000 ppm groups lost weight during the study. Water consumption by the 3,300 and 10,000 ppm males and females was significantly less than that by the controls throughout the study. Drinking water concentrations of 100, 330, 1,000, 3,300, or 10,000 ppm 1-chloro-2-propanol resulted in average daily doses of approximately 15, 45, 140, 260, or 265 mg 1-chloro-2-propanol/kg body weight. Clinical findings observed in the 10,000 ppm males and females included eye exudate, hypoactivity, thinness, and hunched posture.

The absolute and relative thymus weights of 10,000 ppm males and females were significantly less than those of the controls (Table H1). No other biologically significant organ weight changes were observed.

TABLE 3
Survival, Body Weights, and Water Consumption of Rats in the 14-Day Drinking Water Study of 1-Chloro-2-propanol

Concentration (ppm)	Survival[a]	Mean Body Weight[b] (g) Initial	Final	Change	Final Weight Relative to Controls (%)	Water Consumption[c] Week 1	Week 2
Male							
0	10/10	121 ± 2	196 ± 3	74 ± 2		19.9 ± 0.1	22.3 ± 0.1
100	10/10	117 ± 3	193 ± 5	75 ± 2	99	19.4 ± 0.1	21.6 ± 0.7
330	10/10	117 ± 3	198 ± 3	81 ± 2	101	20.1 ± 0.4	23.2 ± 1.6
1,000	10/10	119 ± 3	195 ± 5	76 ± 3	100	20.2 ± 0.0	22.5 ± 0.1
3,300	10/10	118 ± 2	162 ± 4**	44 ± 2**	83	10.8 ± 0.0**	13.4 ± 0.2**
10,000	10/10	123 ± 2	88 ± 2**	–36 ± 3**	45	2.7 ± 0.2**	3.2 ± 0.1**
Female							
0	10/10	105 ± 2	136 ± 2	31 ± 1		18.2 ± 0.9	18.0 ± 2.1
100	10/10	104 ± 2	139 ± 2	35 ± 1	102	17.5 ± 0.3	17.9 ± 0.4
330	10/10	103 ± 2	139 ± 2	36 ± 1	102	17.9 ± 0.8	18.7 ± 1.1
1,000	10/10	105 ± 2	139 ± 3	34 ± 1	102	17.6 ± 0.3	17.8 ± 0.2
3,300	10/10	103 ± 2	123 ± 1**	20 ± 1**	90	8.5 ± 0.1**	9.9 ± 0.2**
10,000	8/10[d]	103 ± 2	67 ± 3**	–36 ± 3**	49	2.0 ± 0.2**	2.2 ± 0.2**

** Significantly different ($P \leq 0.01$) from the control group by Williams' or Dunnett's test
[a] Number of animals surviving at 14 days/number initially in group. Subsequent calculations are based on animals surviving to the end of the study.
[b] Weights and weight changes are given as mean ± standard error.
[c] Water consumption is expressed as grams per animal per day ± standard error.
[d] Day of deaths: 12

The incidences of cytoplasmic alteration and degeneration of the acinar cells of the exocrine pancreas in 3,300 and 10,000 ppm males and females and 1,000 ppm females were significantly increased compared to the controls (Table 4). The incidences of fatty change in 3,300 ppm males and females and 10,000 ppm males were significantly increased compared to the controls. Cytoplasmic alteration was characterized by basophilic cells having reduced amounts of acidophilic cytoplasmic granules (zymogen) and small acini. In some animals, the basophilic acinar cells appeared to be hyperplastic or hypertrophic. Degeneration was defined as the presence of cellular or nuclear debris within acinar cells (autophagic vacuoles and/or apoptosis). The fatty change consisted of mature fat cells that appeared to be within the interstitium.

There were increased incidences of minimal to moderate atrophy of the bone marrow in the 3,300 and 10,000 ppm male and female rats and in 1,000 ppm females compared to the controls (Table 4). Atrophy was characterized by a reduction in the number of hematopoietic cells with a concomitant increase in the amount of adipose tissue within the marrow.

There were increased incidences of minimal to mild diffuse atrophy of the spleen in 10,000 ppm males and females compared to the controls (Table 4). Minimal to mild hematopoiesis of the spleen occurred in males and females in the 3,300 ppm groups.

TABLE 4
Incidence of Selected Nonneoplastic Lesions in Rats in the 14-Day Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm	10,000 ppm
Male						
Pancreas[a]	10	—[c]	—	10	10	10
Acinar Cell, Cytoplasmic Alteration[b]	0			0	10**	9**
Degeneration	0			0	10**	7**
Fatty Change	0			0	6**	4*
Bone Marrow	10	—	—	10	10	10
Atrophy	0			0	10** (1.0)[d]	10** (3.0)
Spleen	10	—	—	10	10	10
Atrophy, Diffuse	0			0	0	10** (1.9)
Hematopoiesis	0			0	7** (1.0)	0
Female						
Pancreas	10	—	—	10	10	10
Acinar Cell, Cytoplasmic Alteration	0			10**	10**	5*
Degeneration	0			5*	10**	6**
Fatty Change	0			0	6**	1
Bone Marrow	10	—	10	10	10	10
Atrophy	0		0	8** (1.3)	10** (1.8)	10** (3.2)
Spleen	10	2	—	10	10	10
Atrophy, Diffuse	0	0		0	0	10** (2.0)
Hematopoiesis	0	0		0	6** (2.2)	0

* 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] Tissue not examined at this exposure concentration
[d] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

14-WEEK STUDY

All rats survived to the end of the study (Table 5). The final mean body weights and body weight gains of 3,300 ppm males and females were significantly less than those of the controls. Water consumption by the 3,300 ppm male and female rats was significantly less than that by the controls throughout the study. Drinking water concentrations of 33, 100, 330, 1,000, or 3,300 ppm 1-chloro-2-propanol resulted in average daily doses of approximately 5, 10, 35, 100, or 220 mg 1-chloro-2-propanol/kg body weight. No clinical findings that could be attributed to 1-chloro-2-propanol exposure were observed.

TABLE 5
Survival, Body Weights, and Water Consumption of Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol

Concentration (ppm)	Survival[a]	Mean Body Weight[b] (g) Initial	Final	Change	Final Weight Relative to Controls (%)	Water Consumption[c] Week 1	Week 13
Male							
0	10/10	116 ± 3	383 ± 6	267 ± 5		19.5 ± 0.6	21.8 ± 0.4
33	10/10	114 ± 3	372 ± 9	257 ± 7	97	19.7 ± 0.7	20.7 ± 0.5
100	10/10	120 ± 4	373 ± 9	254 ± 6	98	19.6 ± 0.5	22.7 ± 1.6
330	10/10	118 ± 3	378 ± 8	260 ± 6	99	19.3 ± 0.1	21.5 ± 1.0
1,000	10/10	115 ± 2	373 ± 5	258 ± 5	97	18.5 ± 0.2	19.7 ± 0.2
3,300	10/10	116 ± 3	312 ± 5**	196 ± 4**	82	8.7 ± 0.1**	14.1 ± 0.0**
Female							
0	10/10	103 ± 2	211 ± 5	108 ± 4		16.2 ± 0.4	17.7 ± 0.8
33	10/10	103 ± 2	209 ± 3	106 ± 3	99	16.7 ± 0.3	16.9 ± 1.7
100	10/10	103 ± 2	212 ± 3	109 ± 2	101	15.8 ± 0.1	17.4 ± 0.3
330	10/10	101 ± 2	205 ± 3	104 ± 2	97	17.1 ± 0.4	18.5 ± 1.2
1,000	10/10	102 ± 2	202 ± 3	100 ± 3*	96	16.3 ± 0.0	16.8 ± 0.8
3,300	10/10	100 ± 2	182 ± 2**	82 ± 1**	86	7.0 ± 0.1**	8.8 ± 0.6**

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Number of animals surviving at 14 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 ± standard error.

The hematology, clinical chemistry, and urinalysis data are listed in Table G1. At study termination, a treatment-related anemia occurred in the exposed female rats; the anemia was evidenced by decreases in hematocrit values, hemoglobin concentrations, and erythrocyte counts. The anemia was of minimal to mild severity and was most pronounced in the 1,000 and 3,300 ppm groups. The male rats were less affected, and hemoglobin concentrations decreased only in the 3,300 ppm group. Slightly lower water consumption by 3,300 ppm males and females suggests that dehydration could have occurred. Dehydration can cause a relative erythrocytosis due to decreased blood volume and hemoconcentration. If significant dehydration occurred in these animals, the severity of the anemia could have been masked. The anemia in female rats was characterized as macrocytic, normochromic, and responsive. Macrocytosis was evidenced by minimal increases in the mean cell volumes in 3,300 ppm females. Normochromatic erythrocytes were evidenced by the absence of change in the mean cell hemoglobin concentrations. Evidence of an erythropoietic response was demonstrated by minimal increases in the reticulocyte counts in the 33, 100, and 3,300 ppm female groups.

An exposure-related decrease in serum alanine aminotransferase activity occurred at all time points for male and female rats in the 1,000 and 3,300 ppm groups; transient decreases occurred in the lower exposure groups on day 3 and/or day 15. The decreased enzyme activity could suggest altered enzyme metabolism (e.g., decreased synthesis or increased catabolism) or an enzyme-inhibitory effect of 1-chloro-2-propanol. A transient decrease in albumin concentration occurred on day 3 for all exposed groups. The decreases, while treatment related, were not exposure related, and the magnitude of the decreases were equal for all exposed groups. Decreased albumin concentrations could suggest altered albumin/protein metabolism by the liver and could be consistent with the decreased alanine aminotransferase activity. A marked decrease in the 16-hour urine volume and concomitant increase in urine specific gravity occurred in 3,300 ppm male and female rats on day 15 and at week 14. These alterations in urine volume and specific gravity would reflect a physiologic response of water conservation and would be consistent with the decreased water intake that occurred.

The cauda epididymis and epididymis weights of 3,300 ppm males were significantly less than those of the controls (Table I1). The percentage of abnormal sperm in 3,300 ppm males and the concentration of epididymal sperm in 330 ppm males were significantly increased compared to the controls. No significant differences from the controls in estrous cycle length or percentage of time spent in estrous cycle stages were observed in female rats (Table I2).

The absolute kidney weights of 100 ppm males and females and 1,000 ppm females and the relative kidney weights of 100 ppm or greater males and females were significantly greater than those of the controls (Table H2). The absolute liver weights of 330 and 1,000 ppm males and 100 and 1,000 ppm females and the relative liver weights of males and females exposed to 100 ppm or greater were significantly greater than those of the controls.

The incidences of acinar cell degeneration and fatty change of the pancreas in 1,000 and 3,300 ppm males and females were significantly increased compared to the controls (Table 6). In the most severely affected animals, much of the normal parenchyma was replaced by large vacuolated cells (adipocytes) (Plates 1 through 3). The adipocytes appeared to be of interstitial origin and were much less common in the 1,000 ppm animals. Within residual acinar cells, the number of zymogen granules was reduced or absent (Plates 4 and 5); cellular or nuclear debris was often observed within or adjacent to these cells (autophagic vacuoles and/or apoptosis; Plate 6) and was diagnosed as degeneration. An increased number of cells in the interstitium was also observed.

In general, pancreatic islets (endocrine pancreas) remained intact; however, hepatocytic metaplasia was observed in a few islets in five females in the 3,300 ppm group. Within the peripheral region of affected islets, there was a variably thick band of large polygonal cells with abundant eosinophilic cytoplasm which resembled hepatocytes (Plate 7).

TABLE 6
Incidence of Selected Nonneoplastic Lesions in Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol

	0 ppm		33 ppm		100 ppm		330 ppm		1,000 ppm		3,300 ppm	
Male												
Pancreas[a]	10		10		10		10		10		9	
Acinar Cell, Degeneration[b]	0		0		0		0		10**	(1.0)[c]	9**	(3.0)
Fatty Change	0		0		0		0		10**	(1.4)	9**	(3.0)
Liver	10		10		10		10		10		10	
Cytoplasmic Vacuolization	0		1	(1.0)	6**	(1.2)	2	(1.0)	7**	(1.0)	10**	(1.4)
Kidney	10		10		10		10		10		10	
Epithelium, Regeneration, Tubular	8	(1.0)	0		0		0		0		10	(1.0)
Female												
Pancreas	10		10		10		10		10		10	
Acinar Cell, Degeneration	0		0		0		0		10**	(1.0)	10**	(3.0)
Fatty Change	0		0		0		1	(1.0)	10**	(1.0)	10**	(3.0)
Pancreatic Islets	10		10		10		10		10		10	
Metaplasia, Focal	0		0		0		0		0		5*	(1.0)
Kidney	10		10		10		10		10		10	
Epithelium, Regeneration, Tubular	1	(1.0)	0		0		1	(1.0)	2	(1.0)	8**	(1.0)

* 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 lesions
[c] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

There were increased incidences of cytoplasmic vacuolization of the liver in 100, 1,000, and 3,300 ppm males compared to the controls. The cytoplasmic vacuolization was primarily observed within hepatocytes in the centrilobular region of the liver. Plate 8 represents one of the more severely affected animals. Vacuoles were variable in size with the largest slightly displacing the nucleus. Eosinophilic staining material was often observed within the vacuoles. Vacuolar change is often a nonspecific change in the liver, and this minimal change is considered of little biologic significance.

There was an increased incidence of regeneration of renal tubule epithelium in the 3,300 ppm female rats compared to the controls (Table 6). Within the renal cortex of the affected kidneys, there were occasional tubules composed of slightly smaller and more basophilic appearing cells which were considered to represent a regenerative response to injury. This change is very similar to that observed in the early stages of the background nephropathy that occurs in the F344/N rat. This was an extremely subtle change, and it is not certain if it represents a slight exacerbation of the background nephropathy or a primary insult to the kidney. The spontaneous nephropathy that occurs in the F344/N rat is most severe in males, and at 14 weeks virtually all males have regenerative tubules while females do not. While a difference was not observed between control and exposed males, detection of a subtle increase in regenerative tubules is very difficult with the background nephropathy.

Exposure Concentration Selection Rationale: Based on chemical-related lesions of the pancreas, 1-chloro-2-propanol exposure concentrations selected for the 2-year drinking water study in rats were 150, 325, and 650 ppm.

2-YEAR STUDY

Survival

Estimates of 2-year survival probabilities for male and female rats are shown in Table 7 and in the Kaplan-Meier survival curves (Figure 1). Survival of all exposed groups was similar to that of the controls.

Body Weights, Water and Compound Consumption, and Clinical Findings

Mean body weights of exposed males and females were generally similar to those of the controls throughout the study (Tables 8 and 9 and Figure 2). Water consumption by all groups of exposed rats was similar to that by the controls (Tables K1 and K2). Drinking water concentrations of 150, 325, or 650 ppm 1-chloro-2-propanol resulted in average daily doses of approximately 15, 30, or 65 mg 1-chloro-2-propanol/kg body weight to males and females during the first several months of the study and 8, 17, or 34 mg/kg for the remainder of the 2-year study. No clinical findings that could be attributed to 1-chloro-2-propanol exposure were observed.

TABLE 7
Survival of Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Male				
Animals initially in study	50	50	50	50
Moribund	12	13	7	10
Natural deaths	18	14	19	17
Animals surviving to study termination	20[d]	23	24	23
Percent probability of survival at end of study[a]	40	46	48	46
Mean survival (days)[b]	659	678	672	680
Survival analysis[c]	P=0.564N	P=0.476N	P=0.507N	P=0.514N
Female				
Animals initially in study	50	50	50	50
Moribund	12	7	7	5
Natural deaths	13	10	13	14
Animals surviving to study termination	25	33	30	31
Percent probability of survival at end of study	50	66	60	62
Mean survival (days)	698	705	700	701
Survival analysis	P=0.513N	P=0.137N	P=0.474N	P=0.334N

[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] Includes one animal that died during the last week of the study

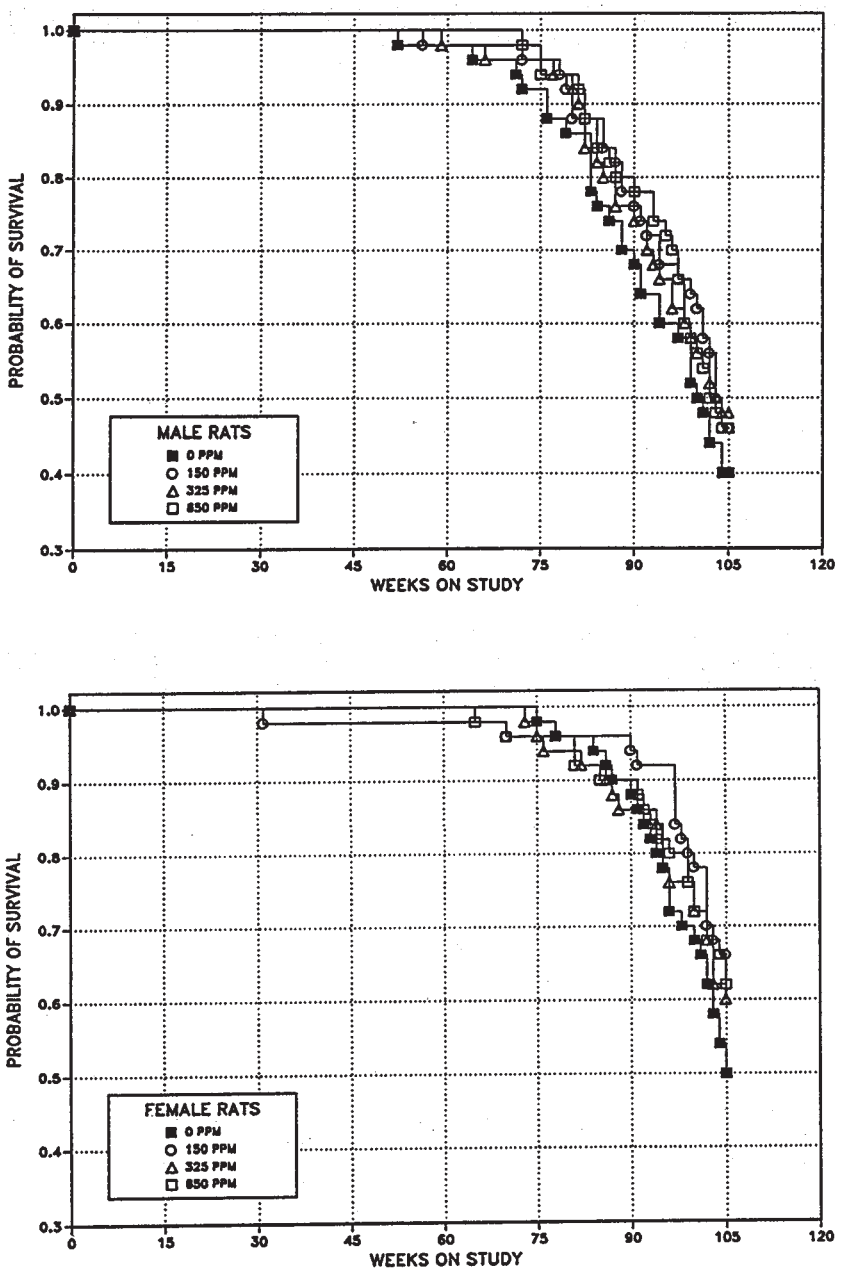


FIGURE 1
Kaplan-Meier Survival Curves for Male and Female Rats Administered 1-Chloro-2-propanol in Drinking Water for 2 Years

TABLE 8
Mean Body Weights and Survival of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

Weeks on Study	0 ppm		150 ppm			325 ppm			650 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	132	50	130	99	50	131	99	50	131	100	50
2	166	50	163	99	50	166	100	50	167	101	50
3	194	50	197	102	50	201	104	50	202	104	50
4	224	50	225	101	50	231	103	50	230	103	50
5	247	50	249	101	50	256	104	50	253	103	50
6	263	50	266	101	50	274	104	50	270	103	50
7	277	50	282	102	50	289	104	50	285	103	50
8	289	50	293	101	50	296	103	50	294	102	50
9	306	50	306	100	50	312	102	50	308	101	50
10	314	50	319	101	50	324	103	50	320	102	50
11	325	50	328	101	50	332	102	50	329	101	50
12	337	50	341	101	50	346	103	50	340	101	50
13	349	50	351	100	50	355	102	50	351	101	50
17	375	50	378	101	50	383	102	50	382	102	50
21	410	50	409	100	50	414	101	50	413	101	50
25	426	50	424	100	50	432	101	50	428	101	50
29	445	50	444	100	50	451	101	50	450	101	50
33	454	50	454	100	50	462	102	50	461	102	50
37	462	50	462	100	50	473	102	50	470	102	50
41	478	50	478	100	50	491	103	50	488	102	50
45	488	50	487	100	50	501	103	50	496	102	50
49	484	50	485	100	50	497	103	50	494	102	50
53	503	49	500	99	50	516	103	50	507	101	50
57	504	49	503	100	49	517	103	50	509	101	50
61	505	49	507	100	49	523	104	49	516	102	50
65	502	48	502	100	49	518	103	49	508	101	50
69	502	48	504	100	49	520	104	48	508	101	50
73	510	46	514	101	48	529	104	48	510	100	49
77	512	44	513	100	48	524	102	48	509	100	47
81	513	43	516	101	44	532	104	46	503	98	47
85	514	38	516	100	44	537	104	41	505	98	42
89	512	35	504	98	39	524	102	38	497	97	40
93	516	32	497	96	36	522	101	35	487	94	39
97	516	29	502	97	34	506	98	31	477	93	35
101	481	25	492	102	31	495	103	28	468	97	28
104	464	20	479	103	23	488	105	24	460	99	23
Mean for weeks											
1-13	263		265	101		270	103		268	102	
14-52	447		447	100		456	102		454	102	
53-104	504		504	100		518	103		497	99	

TABLE 9
Mean Body Weights and Survival of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

Weeks on Study	0 ppm		150 ppm			325 ppm			650 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	111	50	111	100	50	111	100	50	110	99	50
2	128	50	128	100	50	128	100	50	127	99	50
3	144	50	143	99	50	143	100	50	143	100	50
4	152	50	151	100	50	152	100	50	153	101	50
5	160	50	160	100	50	161	100	50	163	102	50
6	169	50	169	100	50	169	100	50	172	101	50
7	174	50	175	100	50	173	99	50	176	101	50
8	182	50	180	99	50	180	99	50	182	100	50
9	188	50	187	99	50	186	99	50	189	101	50
10	191	50	190	99	50	190	99	50	192	100	50
11	193	50	192	99	50	193	100	50	195	101	50
12	198	50	198	100	50	199	100	50	201	101	50
13	201	50	201	100	50	201	100	50	205	102	50
17	216	50	216	100	50	213	99	50	218	101	50
21	224	50	221	99	50	220	98	50	224	100	50
25	230	50	228	99	50	227	99	50	231	100	50
29	240	50	238	99	50	238	99	50	242	101	50
33	246	50	244	99	49	244	99	50	247	100	50
37	254	50	252	99	49	252	99	50	255	101	50
41	266	50	265	100	49	266	100	50	268	101	50
45	269	50	268	99	49	269	100	50	270	100	50
49	281	50	278	99	49	280	100	50	282	100	50
53	292	50	293	100	49	290	99	50	297	102	50
57	296	50	298	101	49	295	100	50	301	102	50
61	305	50	305	100	49	302	99	50	309	101	50
65	305	50	307	101	49	303	99	50	311	102	49
69	315	50	315	100	49	311	99	50	318	101	49
73	321	50	323	101	48	316	99	50	324	101	48
77	329	49	332	101	48	328	100	47	333	101	48
81	326	48	334	102	48	326	100	47	331	102	47
85	333	47	337	101	48	327	98	46	338	101	46
89	339	45	343	101	48	337	99	43	348	103	45
93	338	42	344	102	46	336	100	43	353	105	43
97	345	36	336	97	46	337	98	38	358	104	40
101	345	33	341	99	39	333	96	36	367	107	36
Mean for weeks											
1-13	169		168	99		168	99		170	101	
14-52	247		246	100		245	99		249	101	
53-101	322		324	101		319	99		330	102	

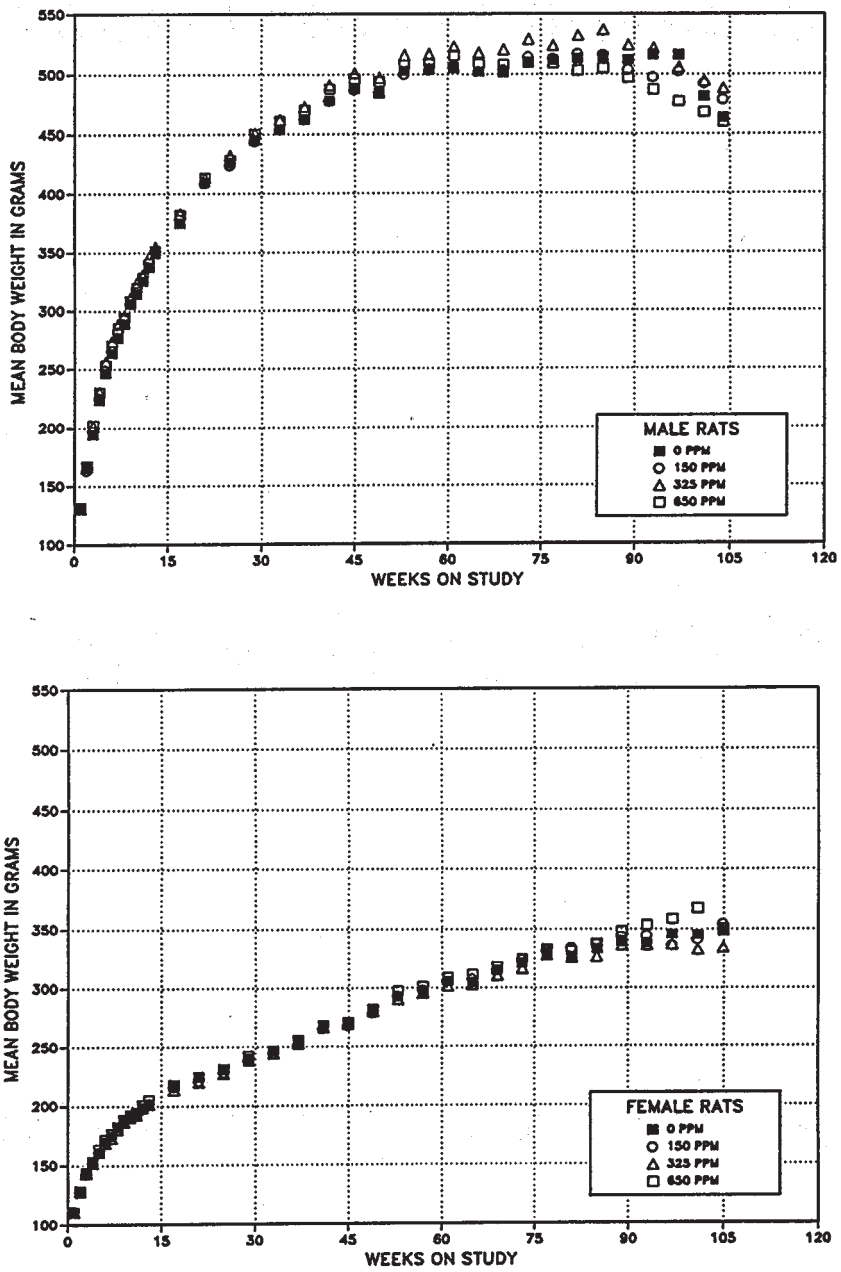


FIGURE 2
Growth Curves for Male and Female Rats Administered 1-Chloro-2-propanol in Drinking Water for 2 Years

Pathology and Statistical Analyses

This section describes the statistically significant or biologically noteworthy changes in the incidences of neoplasms of the 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.

There were no significant increases or decreases in the incidences of neoplastic or nonneoplastic lesions that were attributed to administration of 1-chloro-2-propanol in drinking water for 2 years.

Mammary Gland: The incidence of fibroadenoma was significantly decreased in 150 ppm males compared to the controls (0 ppm, 7/50; 150 ppm, 0/50; 325 ppm, 6/50; 650 ppm, 6/50; Table A3). The incidence of fibroadenoma in control male rats exceeded that observed in historical control groups from drinking water, feed, corn oil gavage, and inhalation studies (Table A4).

MICE

14-DAY STUDY

One male mouse in the 10,000 ppm group died before the end of the study (Table 10). The final mean body weights and body weight gains of 10,000 ppm males and females were significantly less than those of the controls, and the male mice in the 10,000 ppm group lost weight during the study. Water consumption by 3,300 and 10,000 ppm males and females was significantly less than that by the controls throughout the study. Drinking water concentrations of 100, 330, 1,000, 3,300, or 10,000 ppm 1-chloro-2-propanol resulted in average daily doses of approximately 20, 60, 175, 430, or 630 mg 1-chloro-2-propanol/kg body weight to males and 25, 95, 290, 640, or 940 mg/kg to females. No clinical findings that could be attributed to 1-chloro-2-propanol exposure were observed.

The relative liver weights of 1,000, 3,300, and 10,000 ppm males and females were significantly greater than those of the controls (Table H3). The absolute and relative thymus weights of 10,000 ppm males and females were significantly less than those of the controls. The relative kidney weights of 10,000 ppm males and females were significantly greater than those of the controls, probably reflecting decreased water consumption.

The incidences of minimal to mild hepatocellular vacuolization in 1,000, 3,300, and 10,000 ppm male and female mice were significantly increased compared to the controls (Table 11). In general, the vacuolar change involved hepatocytes scattered throughout the liver, but it was sometimes more pronounced in the periportal regions. Affected hepatocytes contained

TABLE 10
Survival, Body Weights, and Water Consumption of Mice in the 14-Day Drinking Water Study of 1-Chloro-2-propanol

Concentration (ppm)	Survival[a]	Mean Body Weight[b] (g) Initial	Final	Change	Final Weight Relative to Controls (%)	Water Consumption[c] Week 1	Week 2
Male							
0	10/10	26.0 ± 0.6	28.1 ± 0.6	2.0 ± 0.2		4.6 ± 0.2	4.8 ± 0.3
100	10/10	25.3 ± 0.5	27.7 ± 0.5	2.5 ± 0.2	99	4.4 ± 0.3	5.2 ± 0.2
330	10/10	24.8 ± 0.7	27.5 ± 0.7	2.7 ± 1.1	98	4.7 ± 0.4	5.0 ± 0.3
1,000	10/10	25.7 ± 0.4	28.7 ± 0.4	3.0 ± 0.2	102	4.7 ± 0.2	4.8 ± 0.2
3,300	10/10	25.0 ± 0.4	28.4 ± 0.5	3.4 ± 0.2	101	3.4 ± 0.2**	3.5 ± 0.2**
10,000	9/10[d]	24.8 ± 0.4	24.3 ± 0.6**	–0.5 ± 0.5**	87	1.3 ± 0.1**[e]	1.8 ± 0.1**[e]
Female							
0	10/10	19.3 ± 0.2	21.6 ± 0.2	2.3 ± 0.2		5.4 ± 0.3	5.7 ± 0.2
100	10/10	19.5 ± 0.4	22.0 ± 0.4	2.5 ± 0.2	102	5.2 ± 0.3	5.5 ± 0.2
330	10/10	19.0 ± 0.3	21.6 ± 0.4	2.6 ± 0.2	100	5.4 ± 0.5	6.2 ± 0.4
1,000	10/10	19.1 ± 0.3	22.0 ± 0.3	2.9 ± 0.4	102	5.8 ± 0.5	6.2 ± 0.6
3,300	10/10	19.8 ± 0.4	22.9 ± 0.3	3.1 ± 0.2	106	3.7 ± 0.2**	3.9 ± 0.2**
10,000	10/10	19.5 ± 0.3	19.8 ± 0.8*	0.3 ± 0.9**	92	1.5 ± 0.2**	1.9 ± 0.1**

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Number of animals surviving at 14 days/number initially in group. Subsequent calculations are based on animals surviving to the end of the study.
[b] Weights and weight changes are given as mean ± standard error.
[c] Water consumption is expressed as grams per animal per day ± standard error.
[d] Day of death: 3
[e] n=9

small, sometimes coalescing vacuoles that often filled the cytoplasm but did not displace the nucleus.

As was observed in the rats, there were increased incidences of minimal to mild cytoplasmic alteration in 3,300 and 10,000 ppm male and female mice and minimal to mild degeneration of the pancreatic acinar cells in 3,300 ppm males and 3,300 and 10,000 ppm females compared to those in the controls (Table 11). The lesions were qualitatively similar to those described in the rats. Fatty change was not observed in the mice, however.

Minimal to mild atrophy of red pulp (hematopoietic cells) was observed in the spleen of four 10,000 ppm males and five 10,000 ppm females (Table 11).

TABLE 11
Incidence of Selected Nonneoplastic Lesions in Mice in the 14-Day Drinking Water Study of 1-Chloro-2-propanol

	0 ppm		100 ppm		330 ppm		1,000 ppm		3,300 ppm		10,000 ppm	
Male												
Liver[a]	10		10		10		10		10		10	
Hepatocyte, Cytoplasmic, Vacuolization[b]	1	(3.0)[c]	3	(1.3)	5	(1.4)	10**	(2.1)	10**	(2.0)	10**	(2.0)
Pancreas	10		10		10		10		10		10	
Acinar Cell, Cytoplasmic Alteration	0		0		0		0		7**		8**	
Degeneration	0		0		0		0		10**		3	
Spleen	10		—[d]		—		—		10		10	
Atrophy	0								0		4*	(1.5)
Female												
Liver	10		10		10		10		10		10	
Hepatocyte, Cytoplasmic, Vacuolization	0		0		3	(2.0)	8**	(1.5)	10**	(1.8)	9**	(1.8)
Pancreas	10		10		10		10		10		10	
Acinar Cell, Cytoplasmic Alteration	0		0		0		0		7**		9**	
Degeneration	0		0		0		0		9**		10**	
Spleen	10		—		—		—		10		10	
Atrophy	0								0		5*	(1.6)

* 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
[d] Tissue not examined at this exposure concentration

14-WEEK STUDY

One 330 ppm male died before the end of the study (Table 12). Final mean body weights and body weight gains of exposed groups were similar to those of the controls. Water consumption by exposed groups was generally similar to that by the controls, except at 13 weeks, when water consumption by the 3,300 ppm females was less than that by the controls. Drinking water concentrations of 33, 100, 330, 1,000, or 3,300 ppm 1-chloro-2-propanol resulted in average daily doses of approximately 5, 15, 50, 170, or 340 mg 1-chloro-2-propanol/kg body weight to males and 7, 20, 70, 260, or 420 mg/kg to females. No clinical findings that could be attributed to 1-chloro-2-propanol exposure were observed.

Hematology data are listed in Table G2. There was some evidence of minimal anemia in 3,300 ppm male mice; this was characterized by decreased erythrocyte count and hemoglobin concentration. The lower water consumption by 3,300 ppm mice suggests that dehydration may have occurred. Dehydration can cause a relative erythrocytosis due to decreased blood volumes and hemoconcentration. If significant dehydration occurred in these animals, the severity of the anemia could have been masked. The erythrocytes of 330, 1,000, and 3,300 ppm male mice were minimally larger, as evidenced by increases in mean cell volume. Increases in mean cell volume usually suggest increased numbers of larger immature erythrocytes (reticulocytes) in the bloodstream. However,

TABLE 12
Survival, Body Weights, and Water Consumption of Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol

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	22.8 ± 0.3	38.4 ± 0.9	15.6 ± 0.7		4.4 ± 0.2	4.1 ± 0.2
33	10/10	23.5 ± 0.4	40.2 ± 1.1	16.8 ± 1.0	105	4.9 ± 0.2	5.0 ± 1.0
100	10/10	23.6 ± 0.6	39.5 ± 1.1	16.0 ± 1.0	103	4.7 ± 0.2[e]	4.6 ± 0.5
330	9/10[d]	23.1 ± 0.3	39.2 ± 1.3	16.1 ± 1.1	102	5.1 ± 0.4[e]	4.4 ± 0.4[e]
1,000	10/10	23.4 ± 0.5	39.0 ± 0.8	15.6 ± 0.5	101	5.1 ± 0.3[e]	4.2 ± 0.2
3,300	10/10	24.2 ± 0.4	39.8 ± 0.7	15.6 ± 0.5	103	3.5 ± 0.2*	3.1 ± 0.2*
Female							
0	10/10	20.0 ± 0.2	34.0 ± 1.0	14.0 ± 0.9		3.8 ± 0.1	6.0 ± 0.6
33	10/10	19.3 ± 0.3	33.8 ± 0.9	14.5 ± 0.8	99	4.0 ± 1.1	5.8 ± 0.4
100	10/10	19.1 ± 0.3	31.5 ± 1.5	12.4 ± 1.4	93	4.1 ± 0.6	6.3 ± 0.7
330	10/10	19.7 ± 0.2	34.8 ± 0.9	15.1 ± 0.8	102	4.3 ± 0.3	5.6 ± 0.6
1,000	10/10	19.9 ± 0.5	33.5 ± 1.2	13.7 ± 0.8	99	3.8 ± 0.3	5.1 ± 0.4
3,300	10/10	19.4 ± 0.2	33.5 ± 0.8	14.1 ± 0.7	99	3.0 ± 0.6[e]	3.4 ± 0.3**

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Number of animals surviving at 14 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[c] Water consumption is expressed as grams per animal per day ± standard error.
[d] Week of death: 7
[e] n=9

the reticulocyte counts were not increased, suggesting that the anemia observed in 3,300 ppm males was too minimal to stimulate a strong bone marrow response. Other hematologic changes were not considered to be toxicologically relevant.

The right epididymis weight of 3,300 ppm males was significantly greater than that of the controls (Table I3). No significant differences from the controls were observed in the length of estrous cycle or the percentage of time spent in estrous cycle stages (Table I4).

The absolute and relative right kidney weights of 3,300 ppm males and females were significantly greater than those of the controls (Table H4). The absolute and relative liver weights of 1,000 ppm males and of all exposed groups of females were significantly greater than those of the controls. The absolute and relative thymus weights of 1,000 ppm females and the absolute thymus weight of 3,300 ppm females were significantly greater than those of the controls.

The incidences of pancreatic acinar cell degeneration and fatty change in 3,300 ppm males and females were significantly increased compared to the controls (Table 13). The degeneration and fatty change were qualitatively similar to that described for the rats, but the lesions were much milder in mice.

The severities of renal tubule cytoplasmic vacuolization were greater in 1,000 and 3,300 ppm males than in the controls (Table 13).

TABLE 13
Incidence of Selected Nonneoplastic Lesions in Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol

	0 ppm		33 ppm		100 ppm		330 ppm		1,000 ppm		3,300 ppm	
Male												
Pancreas[a]	10		10		10		10		10		10	
Acinar Cell, Degeneration[b]	0		0		0		0		2	(1.0)[c]	10**	(1.1)
Fatty Change	0		0		0		0		2	(1.0)	9**	(1.1)
Kidney	10		10		10		10		10		10	
Renal Tubule, Vacuolization, Cytoplasmic	10	(1.1)	10	(1.1)	10	(1.4)	8	(1.1)	10	(1.6)	10	(1.7)
Female												
Pancreas	10		10		10		10		10		10	
Acinar Cell, Degeneration	0		0		0		0		0		9**	(1.0)
Fatty Change	0		0		0		0		0		4*	(1.0)
Liver	10		10		10		10		10		10	
Cytoplasmic Vacuolization	0		7**	(1.0)	10**	(1.5)	7**	(1.1)	9**	(1.4)	10**	(2.0)

* 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 lesions
[c] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

The incidences of cytoplasmic vacuolization of the liver in all groups of exposed females were significantly increased compared to the controls (Table 13). The nature of the vacuolization was similar between groups and was generally characterized by indistinct borders and irregularly shaped clear spaces in the cytoplasm.

Exposure Concentration Selection Rationale: Based on chemical-related lesions of the pancreas in the 3,300 ppm groups, 1-chloro-2-propanol exposure concentrations selected for the 2-year drinking water study in mice were 250, 500, and 1,000 ppm.

2-YEAR STUDY

Survival

Estimates of 2-year survival probabilities for male and female mice are shown in Table 14 and in the Kaplan-Meier survival curves (Figure 3). Survival of all exposed groups was similar to that of the controls.

Body Weights, Water and Compound Consumption, and Clinical Findings

The mean body weights of all groups of exposed males and females were generally similar to those of the controls throughout the study (Figure 4 and Tables 15 and 16). Water consumption by all exposed groups of mice was similar to that by the controls (Tables K3 and K4). Drinking water concentrations of 0, 250, 500, or 1,000 ppm 1-chloro-2-propanol resulted in average daily doses of approximately 45, 75, or 150 mg 1-chloro-2-propanol/kg body weight to males and 60, 105, or 210 mg/kg to females during the first several months of the study and 25, 50, or 100 mg/kg for the remainder of the 2-year study. No clinical findings related to 1-chloro-2-propanol exposure were observed.

TABLE 14
Survival of Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Male				
Animals initially in study	50	50	50	50
Accidental deaths[a]	0	0	5	3
Moribund	8	0	7	4
Natural deaths	2	6	9	4
Animals surviving to study termination	40	44	29	39
Percent probability of survival at end of study[b]	80	88	65	83
Mean survival (days)[c]	689	712	624	686
Survival analysis[d]	P=0.986	P=0.386N	P=0.151	P=0.824N
Female				
Animals initially in study	50	50	50	50
Accidental deaths[a]	3	0	1	2
Moribund	8	7	3	5
Natural deaths	7	11	10	11
Animals surviving to study termination	32	32	36	32
Percent probability of survival at end of study	68	64	74	67
Mean survival (days)	692	700	680	662
Survival analysis	P=0.888	P=0.650	P=0.944N	P=0.812

[a] Censored from survival analyses; some accidental deaths were attributed to hypothermia due to leakage of water bottles and flooding of cages.
[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**.

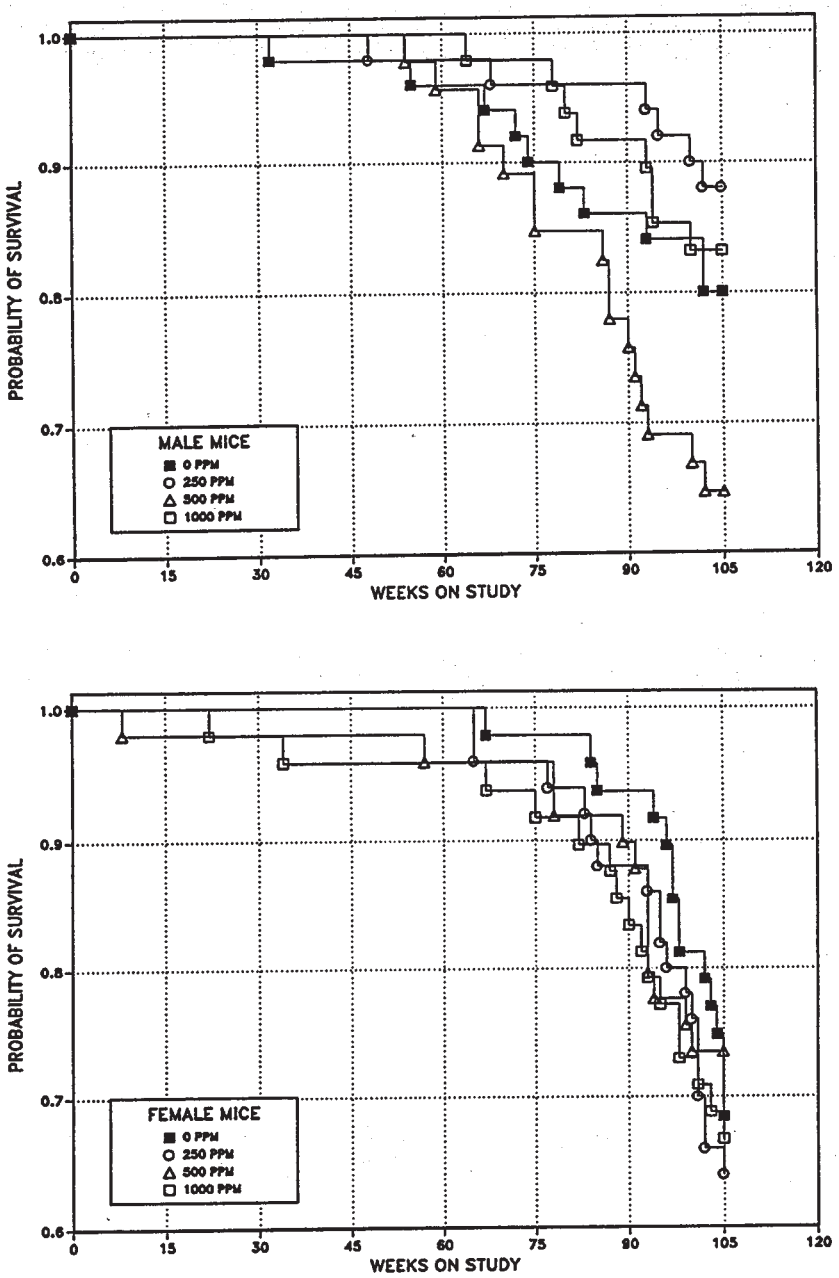
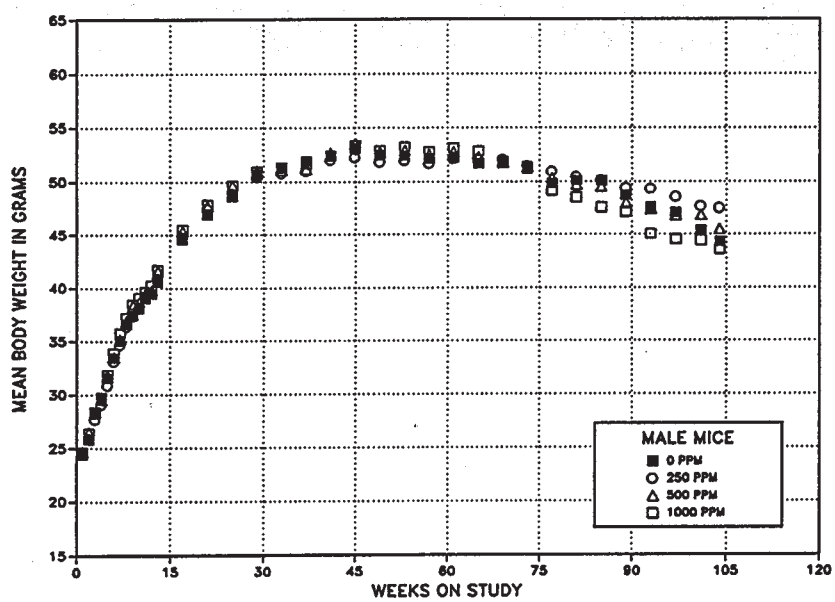


FIGURE 3
Kaplan-Meier Survival Curves for Male and Female Mice Administered 1-Chloro-2-propanol in Drinking Water for 2 Years



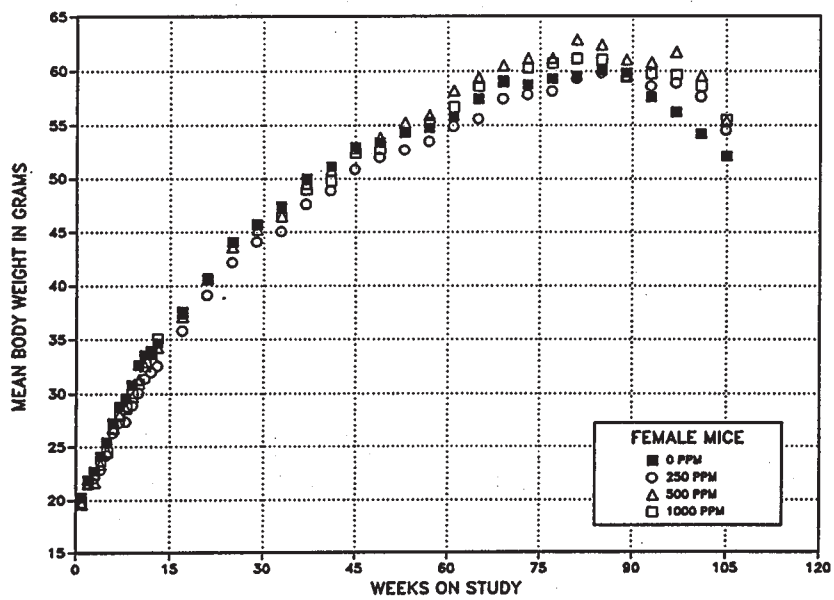


FIGURE 4
Growth Curves for Male and Female Mice Administered 1-Chloro-2-propanol in Drinking Water for 2 Years

TABLE 15
Mean Body Weights and Survival of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

Weeks on Study	0 ppm		250 ppm			500 ppm			1,000 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	24.4	50	24.6	101	50	24.7	101	50	24.6	101	50
2	25.8	50	25.9	100	50	26.5	103	50	26.4	102	50
3	28.2	50	27.7	98	50	28.4	101	50	28.4	101	50
4	29.7	50	29.1	98	50	29.6	100	50	29.8	100	50
5	31.5	50	30.9	98	50	31.7	101	50	31.9	101	50
6	33.4	50	33.1	99	50	33.5	100	50	33.9	102	50
7	35.0	50	34.7	99	50	35.2	101	50	35.7	102	50
8	36.6	50	36.3	99	50	36.9	101	50	37.2	102	50
9	37.4	50	37.4	100	50	38.3	102	50	38.5	103	50
10	38.0	50	38.1	100	50	38.7	102	50	39.1	103	50
11	39.0	50	39.2	101	50	39.5	101	50	39.7	102	50
12	39.5	50	39.6	100	50	39.8	101	50	40.2	102	50
13	40.6	50	40.9	101	50	41.6	103	49	41.7	103	50
17	44.6	50	44.8	100	50	45.3	102	48	45.5	102	50
21	46.9	50	47.5	101	50	47.7	102	48	47.9	102	50
25	48.6	50	48.9	101	50	49.6	102	48	49.7	102	50
29	50.7	50	50.5	100	50	51.0	101	46	50.9	100	50
33	51.3	49	50.8	99	50	51.1	100	46	51.3	100	50
37	51.9	49	51.0	98	50	51.2	99	46	51.6	99	48
41	52.4	49	52.0	99	50	52.7	101	46	52.4	100	48
45	53.1	49	52.2	98	50	53.5	101	46	53.4	101	48
49	52.4	49	51.8	99	49	52.7	101	46	52.9	101	48
53	52.4	49	52.0	99	49	52.9	101	46	53.2	102	48
57	52.1	48	51.7	99	49	52.5	101	45	52.8	101	48
61	52.3	48	52.1	100	49	52.7	101	44	53.1	102	48
65	51.7	48	52.1	101	49	52.3	101	44	52.9	102	47
69	51.8	47	52.1	101	48	51.8	100	42	51.9	100	47
73	51.4	46	51.5	100	48	51.4	100	41	51.2	100	47
77	49.8	45	51.0	102	48	50.3	101	38	49.2	99	47
81	50.1	44	50.4	101	48	49.7	99	38	48.5	97	45
85	50.1	43	50.1	100	48	49.5	99	38	47.6	95	44
89	48.7	43	49.4	101	48	48.0	99	35	47.2	97	44
93	47.6	43	49.3	104	47	47.4	100	31	45.1	95	43
97	47.0	42	48.6	103	46	46.8	100	31	44.6	95	40
101	45.4	42	47.7	105	45	46.9	103	30	44.4	98	39
104	44.3	40	47.5	107	44	45.5	103	29	43.6	98	39
Mean for weeks											
1-13	33.8		33.7	100		34.2	101		34.4	102	
14-52	50.2		49.9	99		50.5	101		50.6	101	
53-104	49.6		50.4	102		49.8	100		49.0	99	

TABLE 16
Mean Body Weights and Survival of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

Weeks on Study	0 ppm		250 ppm			500 ppm			1,000 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	20.3	50	19.6	97	50	19.6	97	50	19.8	98	50
2	21.9	50	21.6	99	50	21.6	99	50	21.5	98	50
3	22.7	50	22.1	97	50	21.7	96	50	22.4	99	50
4	24.1	50	22.8	95	50	23.4	97	50	23.6	98	50
5	25.5	50	24.2	95	50	24.6	97	50	24.5	96	50
6	27.2	50	26.3	97	50	26.9	99	50	26.7	98	50
7	28.8	50	27.3	95	50	28.0	97	50	28.0	97	50
8	29.6	50	27.4	93	50	28.6	97	49	28.9	98	50
9	30.8	50	28.9	94	50	29.7	96	49	30.1	98	50
10	32.6	50	30.1	92	50	31.3	96	49	30.9	95	50
11	33.5	50	31.4	94	50	32.5	97	49	32.9	98	50
12	33.9	49	32.0	94	50	33.6	99	49	33.8	100	49
13	34.6	49	32.6	94	50	34.2	99	49	35.1	101	49
17	37.6	49	35.8	95	50	37.1	99	48	37.4	100	49
21	40.7	49	39.1	96	50	40.7	100	48	40.6	100	49
25	44.0	49	42.2	96	50	43.6	99	48	44.1	100	48
29	45.7	49	44.1	97	50	45.3	99	48	45.7	100	48
33	47.4	49	45.1	95	50	46.5	98	48	46.4	98	48
37	50.0	49	47.6	95	50	49.5	99	48	49.0	98	47
41	51.1	48	48.9	96	50	50.8	99	48	49.8	98	46
45	53.0	48	50.9	96	50	52.8	100	48	52.4	99	46
49	53.3	48	52.0	98	50	53.9	101	48	52.8	99	46
53	54.4	48	52.7	97	50	55.3	102	48	54.4	100	46
57	54.7	48	53.5	98	50	55.9	102	48	55.2	101	46
61	55.8	48	54.9	98	50	58.2	104	47	56.7	102	46
65	57.4	48	55.6	97	50	59.4	104	47	58.6	102	46
69	59.1	47	57.4	97	48	60.5	102	47	59.0	100	45
73	58.7	47	57.8	99	48	61.1	104	47	60.3	103	45
77	59.3	47	58.1	98	48	61.2	103	47	60.7	102	44
81	59.5	47	59.3	100	47	62.9	106	45	61.2	103	44
85	60.1	46	59.8	100	45	62.4	104	45	61.0	102	43
89	59.8	45	59.5	100	44	61.0	102	45	59.5	100	41
93	57.6	45	58.6	102	44	60.8	106	43	59.7	104	39
97	56.2	42	58.9	105	40	61.7	110	38	59.7	106	37
101	54.2	38	57.6	106	38	59.6	110	36	58.6	108	34
Mean for weeks											
1-13	28.1		26.6	95		27.4	98		27.6	98	
14-52	47.0		45.1	96		46.7	99		46.5	99	
53-101	57.4		57.2	100		60.0	105		58.8	102	

Pathology and Statistical Analyses

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

There were no significant increases or decreases in the incidences of neoplasms or nonneoplastic lesions that were attributed to administration of 1-chloro-2-propanol in drinking water for 2 years.

Liver: There were high incidences of hepatocellular adenoma, hepatocellular carcinoma, or hepatoblastoma (combined) in all groups of male and female mice (males: 0 ppm, 40/50; 250 ppm, 39/50; 500 ppm, 37/50; 1,000 ppm, 36/50; females: 41/50, 41/50, 43/50, 42/50; Tables C3 and D3). The incidence of these combined lesions in the female control group (82%) was at the upper limit of the historical control range for drinking water studies (32% to 82%; Table D4).

GENETIC TOXICOLOGY

1-Chloro-2-propanol is genotoxic *in vitro*. It was tested for mutation induction in *Salmonella typhimurium* in three studies at two laboratories, and all test responses were similar (Table E1; Zeiger *et al.*, 1987). In strain TA100, equivocal responses were obtained in the absence of S9; with S9, equivocal or weakly positive mutagenic activity was seen. Clearly positive, reproducible responses were seen across laboratories with strain TA1535, with and without S9. No mutagenic activity was detected with strain TA97, TA98, or TA1537, with or without S9.

1-Chloro-2-propanol induced marked increases in sister chromatid exchanges (Table E2) and chromosomal aberrations (Table E3) in cultured Chinese hamster ovary cells, with and without S9. Cell cycle delay was induced in cultures treated with concentrations of 1,700 µg/mL 1-chloro-2-propanol and greater; to obtain sufficient cells for scoring, incubation time was extended to up to 34 hours in the sister chromatid exchange test. Experimental design normally calls for no more than 33 hours exposure to BrdU, but, because increases in sister chromatid exchange frequencies were also seen at standard harvest times, in the absence of S9, the delayed harvest results were accepted as confirmatory of the results seen in Trial 1. In the sister chromatid exchange test with S9, the only concentration that produced a significant increase in sister chromatid exchanges was the 1,700 µg/mL dose, which employed a culture time of 33.5 hours. However, because the response was so strong, it was accepted that even if BrdU exposure contributed to some extent to the induction of sister chromatid exchanges, much of the increase was due to exposure to 1-chloro-2-propanol. This trial was not repeated because it was apparent from the combined results of the three trials that 1-chloro-2-propanol induced sister chromatid exchanges in cultured Chinese hamster ovary cells. In the cultured Chinese hamster ovary cell chromosomal aberrations test with 1-chloro-2-propanol, fewer than the usual 200 cells per concentration were scored because a marked increase in aberrations as well as in the percentage of cells with aberrations was observed.

The chromosomal effects seen *in vitro* were not apparent in the *in vivo* studies, but induction of gene mutations was observed. Positive results were obtained in the *Drosophila melanogaster* test for induction of sex-linked recessive lethal mutations in germ cells of male flies administered 1-chloro-2-propanol via injection (Table E4; Foureman *et al.*, 1994). However, a subsequent test for induction of reciprocal chromosomal translocations in germ cells of male *D. melanogaster* yielded negative results (Table E5; Foureman *et al.*, 1994). Additional negative results were obtained for chromosomal effects in mice. No induction of micronucleated erythrocytes was observed in peripheral blood of male or female mice administered 1-chloro-2-propanol in drinking water for 14 weeks (Table E6).

CONTINUOUS BREEDING STUDY IN SPRAGUE-DAWLEY RATS

The complete methods and results of the continuous breeding study are presented in Appendix F. Exposure to 1-chloro-2-propanol did not cause significant

reproductive toxicity in rats. All exposed and control pairs except one 300 ppm pair were fertile; all pairs exposed to 1,300 ppm delivered five litters. The average numbers of litters per pair of all exposed groups were similar to that of the controls. The cumulative number of days to litter for the 1,300 ppm group was slightly but significantly greater than that of the controls for litter 5. At delivery of each litter, the mean body weights of dams in the 650 ppm group (except for the second litter) and the 1,300 ppm group were significantly less than those of the controls. Mean body weights of litter 5 dams in the 650 ppm group were significantly less than those of the controls from lactation days 0 to 14, and the mean body weights of dams in the 1,300 ppm group were significantly less than those of the controls throughout lactation.

The survival of the final litters of exposed F_1 pups was similar to that of the controls throughout lactation. Male and female F_1 pup weights were significantly less than those of the controls in the 1,300 ppm group on days 7, 14, and 21 and in the 650 ppm group on days 14 and 21.

During the offspring assessment phase of the continuous breeding study, the mean body weight of dams in the 1,300 ppm group at delivery was significantly less than that of the controls. Exposure to 1,300 ppm did not affect the number of live pups per litter, the sex ratio, or pup or organ weights. The percentage of abnormal sperm was significantly greater in 1,300 ppm male rats than in the controls. There were no significant differences in estrous cycle parameters between control and 1,300 ppm females.

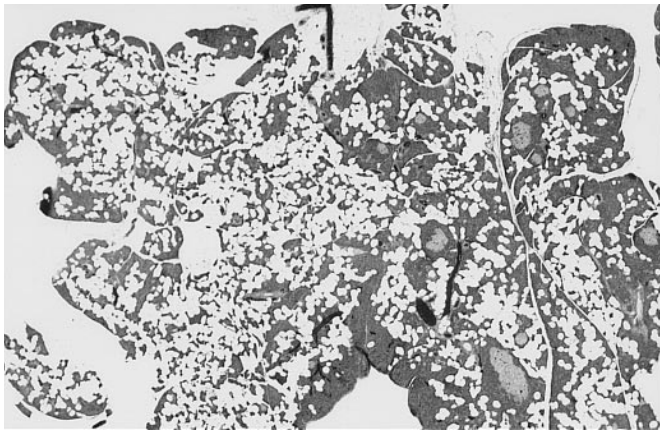


PLATE 1

Pancreas from a male F344 rat exposed to 3,300 ppm 1-chloro-2-propanol in drinking water for 90 days. Note the diffuse vacuolated appearance of the pancreas compared to a normal pancreas in Plate 2. H&E; 13 ×

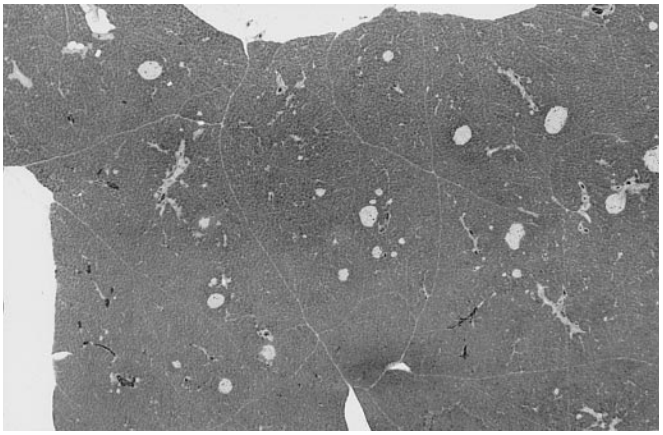


PLATE 2

Pancreas from a control F344 rat at the same magnification as Plate 1. H&E; 13 ×

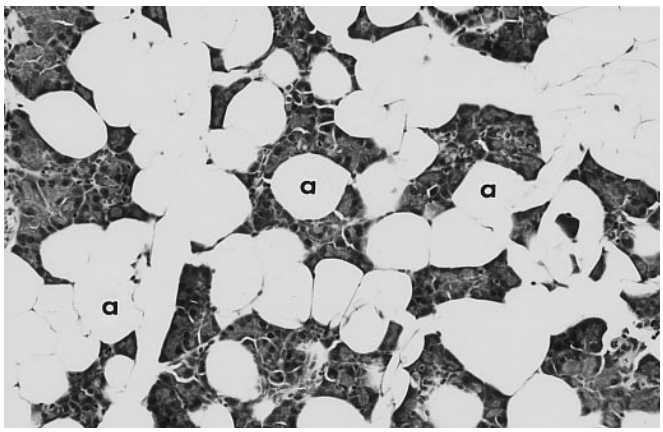


PLATE 3

Pancreas from a male F344 rat exposed to 3,300 ppm 1-chloro-2-propanol in drinking water for 90 days. Higher magnification of Plate 1 showing the large adiposytes (a) and interspersed residual exocrine pancreatic tissue. H&E; 125 ×

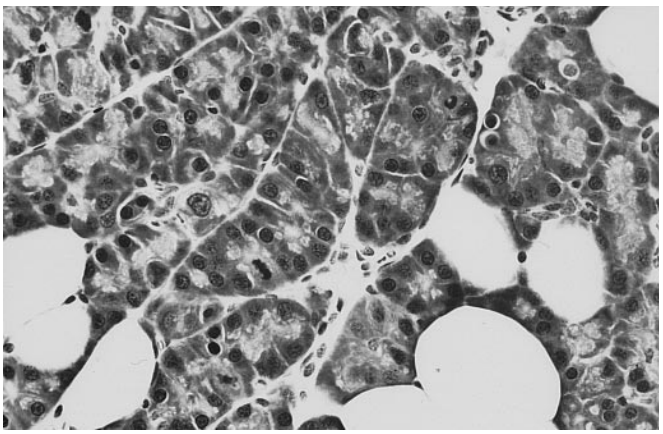


PLATE 4

Pancreas from a male F344 rat exposed to 3,300 ppm 1-chloro-2-propanol in drinking water for 90 days. Zymogen granules are lacking in the apical region of the acinar cells, compared with a normal pancreas in Plate 5. H&E; 250 ×

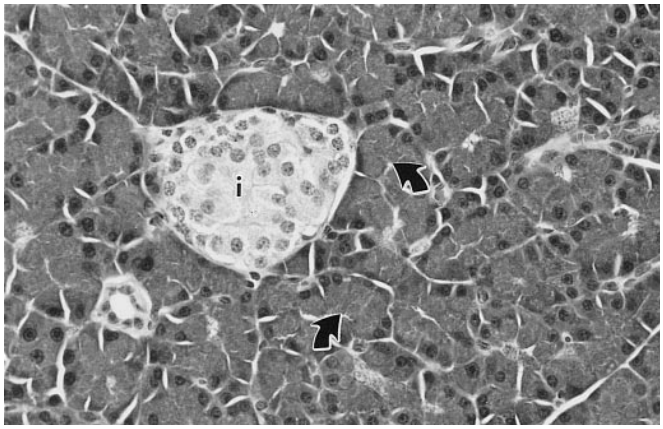


PLATE 5

Pancreas from a control male F344 rat. The pancreas is normal; note the abundant zymogen granules in the apical region of the acinar cells (arrows). The structure in the center is an islet (I). H&E; 250 ×

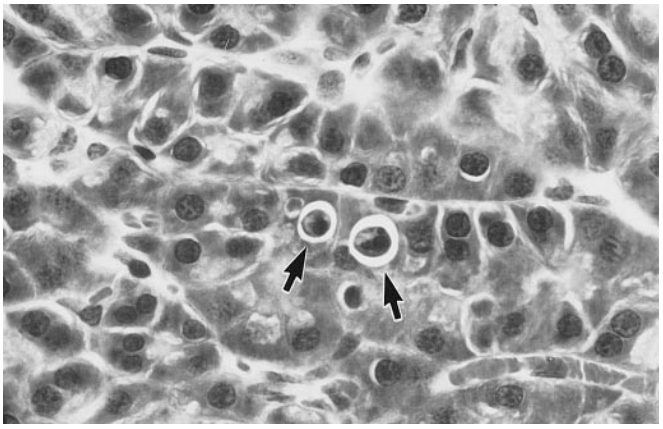


PLATE 6

Pancreas from a male F344 rat exposed to 3,300 ppm 1-chloro-2-propanol in drinking water for 90 days. Note the cellular debris (apoptosis) which appears to be within acinar cells (arrows). H&E; 500 ×

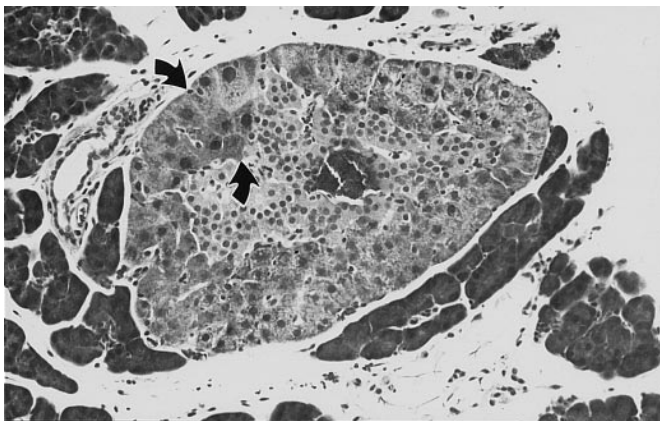


PLATE 7

Pancreas from a female F344 rat exposed to 3,300 ppm 1-chloro-2-propanol in drinking water for 90 days. Note the large polygonal cells (hepatocyte metaplasia) at the border of the pancreatic islet (between arrows); compare to the centrally located smaller, normal islet cells. H&E; 125 ×

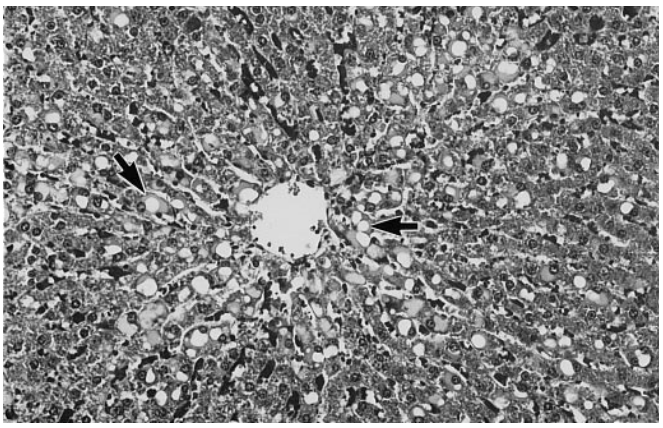


PLATE 8

Liver from a male F344 rat exposed to 3,300 ppm 1-chloro-2-propanol in drinking water for 90 days. Vacuoles (arrows) are present within hepatocytes in the centrilobular region of the liver. H&E; 125 ×

DISCUSSION AND CONCLUSIONS

The NTP conducted toxicology and carcinogenesis studies of technical grade 1-chloro-2-propanol (75% to 76% 1-chloro-2-propanol and 24% to 25% 2-chloro-1-propanol; also known as chlorohydrins). The National Cancer Institute nominated 1-chloro-2-propanol for study because of the potential for human exposure to chlorohydrins that are formed as a by-product of sterilization of various foods fumigated with ethylene oxide or propylene oxide. Such fumigation may be used for sterilizing foodstuffs including spices, cocoa, flour, dried egg powder, desiccated coconut, dried fruits, and dehydrated vegetables (Wesley *et al.*, 1965; Ragelis *et al.*, 1966; Fishbein, 1969).

In the 14-day studies, rats and mice received 1-chloro-2-propanol in drinking water at concentrations of 0, 100, 330, 1,000, 3,300, or 10,000 ppm. Two female rats and one male mouse in the 10,000 ppm groups died before the end of the studies. Minimal to mild lesions of the exocrine pancreas were observed in the 3,300 and 10,000 ppm male and female groups of rats and mice. Atrophy and/or hematopoiesis of the bone marrow and spleen occurred in 3,300 and 10,000 ppm male and female rats. A minimal to mild hepatocellular vacuolization of the liver in 1,000, 3,300, and 10,000 ppm male and female mice and atrophy of the spleen in 10,000 ppm male and female mice were observed.

In the 14-week studies, rats and mice received 0, 33, 100, 330, 1,000 or 3,300 ppm 1-chloro-2-propanol in drinking water. No treatment-related effects on survival occurred. The exocrine pancreatic lesions observed in the 14-day studies were also observed in the 14-week studies; however, the lesions were more severe and occurred in 1,000 and 3,300 ppm male and female rats and in 3,300 ppm male and female mice. In general, pancreatic islets (endocrine pancreas) remained intact; however, metaplasia (hepatocytic) was observed in a few islets in five of ten 3,300 ppm female rats. Within the peripheral region of affected islets, there was a variably thick band of large polygonal cells with abundant eosinophilic cytoplasm which resembled hepatocytes (Plate 7). In other studies, these cells have been shown to have characteristics of hepatocytes, not of exocrine or endocrine pancreatic cells. These "pancreatic hepatocytes" may occur spontaneously and increases have been observed with administration of some chemicals/agents (McDonald and Boorman, 1989). In many instances, increased incidences have been associated with pancreatic atrophy and fibrosis.

Rodent acinar cells are sensitive to the toxic effects of a wide variety of chemicals and also to viruses, nutritional deficit, and trauma (Angiolelli and Rio, 1972; Lansdown, 1976; Longnecker, 1982; Rao *et al.*, 1987). Acute pancreatitis can be caused by direct injury of acinar cells, resulting in necrosis and release of enzymes into the interstitium, which causes injury to adjacent acinar cells. The acinar cells of the pancreas comprise approximately 85% of the pancreas volume. These cells synthesize and store digestive proenzymes packaged into zymogen granules, and this elaborate intercellular compartmentation of enzymes protects the cell from destruction by its own enzymes (deoxyribonuclease, ribonuclease, lipase, amylase, etc.) (Longnecker, 1982). Ingestion of food "activates" the zymogen granules into the duct system, where the enzymes mix with water and bicarbonate ions, and this pancreatic juice is released into the duodenoma.

The exposure concentrations for the 2-year studies were set just below the concentrations that were known to induce exocrine pancreas lesions in the 14-day and 14-week studies. The severity of the exocrine pancreatic lesions progressed when treatment was lengthened from 14 days to 14 weeks, and it was thought that the severities of these lesions would continue to progress during the 2-year studies; therefore, exposure concentrations at which these lesions occurred would not be suitable for the 2-year studies. When enzyme secretion from the pancreas is reduced more than 10% by necrosis, clinical evidence of malabsorption develops (Longnecker, 1982).

In the 2-year rat study, animals received 0, 150, 325, or 650 ppm 1-chloro-2-propanol in drinking water (equivalent to average daily doses of approximately 15, 30, or 65 mg/kg to males and females during the first several months of the study and 8, 17, or 34 mg/kg for the remainder of the 2-year study). In the 2-year mouse study, animals received exposure concentrations of 0, 250, 500 or 1,000 ppm in drinking water (equivalent to average daily doses of approximately 45, 75, or 150 mg/kg to males and 60, 105, or 210 mg/kg to females during the first several months of the study and 25, 50, or 100 mg/kg for the remainder of the study). There were no treatment-related effects on survival or body weights and no treatment-related neoplasms or nonneoplastic lesions.

Inflammatory pancreatic responses occur in humans and may be due to a variety of causes (e.g., alcohol, gall stones, etc.) (Mack *et al.*, 1986; Steinberg and Tenner, 1994; Steer *et al.*, 1995), but this syndrome did not occur with 1-chloro-2-propanol at the time points evaluated, although there was significant loss of exocrine pancreatic tissue and replacement by mature adipocytes. In the 1-chloro-2-propanol studies, the pancreatic changes were suggestive of a mild insult rather than acute pancreatitis in which the released enzymes and necrotic debris incite an acute inflammation and pancreatitis. With chemicals that cause a subtle insult, the only histologic evidence of injury may be autophagic vacuoles and/or apoptotic bodies and little to no inflammatory response. In these studies, acinar cells containing minimal zymogen granules and autophagic vacuoles and/or apoptotic bodies were commonly observed.

In 13-week NTP studies of another chlorohydrin, ethylene chlorohydrin (NTP, 1985b), exocrine pancreatic lesions were also observed in rats and mice. The pancreatic lesions were composed of minimal to mild vacuolar changes within acinar cells and an apparent reduction of zymogen granules. The extensive fatty change and acinar cell degeneration seen in the 1-chloro-2-propanol studies did not occur.

Several studies have been conducted to characterize the putative preneoplastic pancreatic lesions in rodents following exposure to pancreatic carcinogens. With azaserine, a pancreatic carcinogen in rats, a small proportion of acidophilic foci and/or focal acinar cell hyperplasia is thought to progress to adenocarcinoma in lifetime studies (Longnecker *et al.*, 1984; Roebuck *et al.*, 1987; Longnecker and Millar, 1990). The acinar cell is considered to be the cell of origin for pancreatic exocrine tumors in rats. In general, tumors of the exocrine pancreas are more frequent in male rats than in female rats (Longnecker and Millar, 1990). Acidophilic foci (or acinar cell hyperplasia) were not observed in rats or mice in the 14-week studies of 1-chloro-2-propanol, and the lesions observed in the 14-week studies did not occur in the 2-year studies.

The following chemicals studied by the NTP have been found to cause some or clear evidence of causing pancreatic neoplasms [exocrine tumors (acinar cell adenoma/adenocarcinoma)] in the rat, most often in males: nitrofen (NCI, 1978), cinnamyl anthranilate (NCI, 1980), commercial grade 2,4 (80%)- and 2,6 (20%)-toluene diisocyanate (NTP, 1986), chlorendic acid (NTP, 1987a), 2-amino-5-nitrophenol (NTP, 1988a), 2-mercaptobenzothiazole (NTP, 1988b), dichlorvos (NTP, 1989), and 1,2,3-trichloropropane (NTP, 1993). In the NTP historical database there are no chemicals reported to cause pancreatic neoplasms in mice. Other chemicals, particularly N-nitroso compounds, have been reported to cause pancreatic neoplasms in rats (Longnecker *et al.*, 1984). The NTP has found increased incidences of focal acinar hyperplasia and acinar adenoma in male rats administered corn oil by gavage for 2 years as compared to male rats not administered corn oil (Eustis and Boorman, 1985).

With these pancreatic carcinogens studied by the NTP, with corn oil, and with azaserine and other rodent pancreatic carcinogens, increased preneoplastic acinar cell hyperplasia may occur at various time points after treatment. In the studies of pancreatic carcinogens by the NTP, acinar cell hyperplasia was often observed at the end of the 2-year studies. No lesions of the exocrine pancreas similar to those observed at 13 weeks in the current study were seen in NTP studies of chemicals that caused pancreatic neoplasms. In the 1-chloro-2-propanol rat studies, acinar cell hyperplasia occurred in three males in the 650 ppm group, but there was no evidence of a neoplasm response. While there is no established database for nonneoplastic pancreatic lesions, the incidence of pancreatic hyperplasia in untreated male F344/N rats from 17 NTP feed studies was 2.6%, with a range of 0% to 10% (Eustis and Boorman, 1985). This minimal incidence of pancreatic hyperplasia was not considered to be related to chemical administration.

In the United States, carcinoma of the exocrine pancreas ranks fifth among all cancers and is the fourth leading cause of cancer deaths (Benson and Teta, 1993). The etiology of pancreatic carcinoma is not known, although some studies have shown an association between smoking and pancreatic cancer (Mack *et al.*, 1986). It would be of interest to study the progression of pancreatic lesions seen in the 14-day and 14-week studies of 1-chloro-2-propanol. That pancreatic cancer is rising in incidence suggests that environmental factors may play a role in this disease (Longnecker, 1982; Longnecker and Millar, 1990). The incidence of pancreatic cancer is low in the Japanese population, but Japanese who have migrated to the United States have a higher incidence of pancreatic cancer, which supports the hypothesis that environmental factors play a role in the etiology of this cancer (Longnecker, 1982).

In the workplace (at a chlorohydrin plant in South Carolina), where chlorohydrins are one of several chemicals to which exposures are possible, there is evidence for increased mortality from pancreatic cancer (type of pancreatic cancer not specified) and lymphocytic leukemia (Greenberg *et al.*, 1990; Benson and Teta, 1993). Studies of other chlorohydrin production facilities in Louisiana and Texas did not find any association between work in the plant and an increase in pancreatic cancer incidences (Olsen *et al.*, 1997), although the duration of follow-up was 25 years versus 36 years in the studies of the South Carolina workers. In addition, other differences in the plant processes were noted (e.g., closed facility versus open facility at the South Carolina plant). Other epidemiological studies have implicated short-chain hydrocarbons in the occurrence of pancreatic cancer (Benson and Teta, 1993).

1-Chloro-2-propanol (technical grade) was weakly mutagenic in *Salmonella typhimurium* with and without metabolic activation in strains TA100 and TA1535 but not in strain TA97, TA98, or TA1537 (the strains that revert via frameshift mutation) (Carr and Rosenkranz, 1978; Pfeiffer and Dunkelberg, 1980; Zeiger *et al.*, 1987). In addition, 1-chloro-2-propanol was positive in the mouse lymphoma assay and induced significant chromosomal aberrations consisting mainly of chromatid breaks in rat bone marrow cells at doses of 10, 31, or 100 mg/kg per day (Biles and Piper, 1983). In general, these mutagenicity studies used the same technical grade 1-chloro-2-propanol as was used in the 14-day, 14-week, and 2-year studies. Assay systems are available to detect damage to the DNA in pancreatic acinar cells (Curphey *et al.*, 1987), and testing chlorinated hydrocarbons in these assay systems may be warranted.

In the 14-week studies, sperm morphology results showed a greater percentage of abnormal sperm and lower cauda epididymis and epididymis weights in 3,300 ppm male rats than those in the controls. In mice, there was no effect on sperm morphology or concentration, although there was a significantly lower epididymis weight in 3,300 ppm males than in the controls. This effect may have been related in part to body weights lower than those of the controls. However, to more completely examine the potential of 1-chloro-2-propanol to affect fertility, a rat continuous breeding study was conducted according to an NTP study design (Gulati *et al.*, 1991). Morrissey *et al.* (1989) and Chapin *et al.* (1997) have found that the organ weight change that best correlates with reduced fertility is reduced epididymal weight.

In the NTP CD BR outbred Sprague-Dawley albino rat continuous breeding study, 1-chloro-2-propanol did not affect fertility or reproduction when given in the drinking water at exposure concentrations of 300, 650, or 1,300 ppm. The percentage of abnormal sperm was significantly greater in 1,300 ppm F_1 rats than in the controls. Therefore, in these follow-up rat continuous breeding studies, which used a study design sensitive to small changes (8%) in fertility, there were no changes in fertility after exposure to 1-chloro-2-propanol.

CONCLUSIONS

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity** of technical grade 1-chloro-2-propanol in male or female F344/N rats exposed to 150, 325, or 650 ppm. There was *no evidence of carcinogenic activity* of technical grade 1-chloro-2-propanol in male or female $B6C3F_1$ mice exposed to 250, 500, or 1,000 ppm.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 9. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 11.

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APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 1-CHLORO-2-PROPANOL

TABLE A1 Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 68

TABLE A2 Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 72

TABLE A3 Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 88

TABLE A4 Historical Incidence of Mammary Gland Fibroadenoma in Untreated Male F344/N Rats 92

TABLE A5 Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 93

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	150 ppm	325 ppm	650 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	12	13	7	10
Natural deaths	18	14	19	17
Survivors				
Died last week of study	1			
Terminal sacrifice	19	23	24	23
Animals examined microscopically	50	50	50	50
Alimentary System				
Esophagus	(50)	(50)	(50)	(50)
Squamous cell carcinoma	1 (2%)			
Intestine large, colon	(46)	(46)	(48)	(47)
Squamous cell carcinoma, metastatic, skin		1 (2%)		
Intestine large, cecum	(45)	(46)	(45)	(44)
Intestine small, duodenum	(46)	(45)	(46)	(48)
Intestine small, jejunum	(39)	(42)	(41)	(42)
Intestine small, ileum	(39)	(41)	(41)	(43)
Liver	(50)	(50)	(50)	(50)
Hepatocellular carcinoma			1 (2%)	1 (2%)
Hepatocellular adenoma	1 (2%)	3 (6%)	1 (2%)	2 (4%)
Histiocytic sarcoma		1 (2%)		1 (2%)
Mesentery	(12)	(11)	(10)	(14)
Lipoma				1 (7%)
Oral mucosa	(2)			
Squamous cell papilloma	1 (50%)			
Pancreas	(48)	(45)	(46)	(48)
Acinus, adenoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Salivary glands	(50)	(50)	(49)	(50)
Histiocytic sarcoma				1 (2%)
Stomach, forestomach	(50)	(49)	(48)	(49)
Stomach, glandular	(50)	(49)	(48)	(50)
Cardiovascular System				
Blood vessel	(48)	(50)	(50)	(50)
Heart	(50)	(50)	(50)	(50)
Endocrine System				
Adrenal cortex	(50)	(49)	(49)	(50)
Carcinoma		1 (2%)		
Adrenal medulla	(50)	(49)	(49)	(50)
Pheochromocytoma malignant	1 (2%)		1 (2%)	2 (4%)
Pheochromocytoma benign	7 (14%)	13 (27%)	13 (27%)	11 (22%)
Bilateral, pheochromocytoma benign	6 (12%)	1 (2%)	4 (8%)	1 (2%)
Islets, pancreatic	(49)	(45)	(46)	(47)
Adenoma	2 (4%)	1 (2%)	2 (4%)	3 (6%)
Carcinoma				1 (2%)
Pituitary gland	(48)	(49)	(49)	(50)
Pars distalis, adenoma	15 (31%)	20 (41%)	25 (51%)	24 (48%)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Endocrine System (continued)				
Thyroid gland	(50)	(50)	(50)	(50)
C-cell, adenoma	5 (10%)	1 (2%)	6 (12%)	3 (6%)
C-cell, carcinoma		2 (4%)		1 (2%)
Follicular cell, adenoma	1 (2%)			1 (2%)
General Body System				
Peritoneum	(3)			(1)
Genital System				
Epididymis	(50)	(49)	(50)	(50)
Preputial gland	(50)	(50)	(50)	(49)
Adenoma	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Carcinoma	1 (2%)	4 (8%)	4 (8%)	3 (6%)
Bilateral, carcinoma			1 (2%)	
Prostate	(50)	(50)	(50)	(50)
Adenoma	1 (2%)			
Seminal vesicle	(50)	(50)	(50)	(50)
Testes	(50)	(49)	(50)	(50)
Bilateral, interstitial cell, adenoma	36 (72%)	32 (65%)	31 (62%)	34 (68%)
Interstitial cell, adenoma	10 (20%)	11 (22%)	9 (18%)	12 (24%)
Hematopoietic System				
Bone marrow	(47)	(45)	(47)	(49)
Lymph node	(24)	(23)	(23)	(24)
Iliac, squamous cell carcinoma, metastatic, skin		1 (4%)		
Lymph node, mandibular	(50)	(50)	(50)	(50)
Carcinoma, metastatic, Zymbal's gland		1 (2%)		
Histiocytic sarcoma				1 (2%)
Squamous cell carcinoma, metastatic, uncertain primary site	1 (2%)			
Lymph node, mesenteric	(49)	(50)	(50)	(50)
Spleen	(50)	(50)	(50)	(50)
Thymus	(49)	(47)	(48)	(47)
Thymoma benign		1 (2%)		
Integumentary System				
Mammary gland	(50)	(45)	(48)	(47)
Fibroadenoma	7 (14%)		5 (10%)	6 (13%)
Fibroadenoma, multiple			1 (2%)	

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Integumentary System (continued)				
Skin	(50)	(50)	(50)	(50)
Basal cell carcinoma	1 (2%)			
Keratoacanthoma	2 (4%)	3 (6%)	3 (6%)	6 (12%)
Keratoacanthoma, multiple		1 (2%)		
Squamous cell carcinoma, multiple		1 (2%)		
Squamous cell papilloma				1 (2%)
Trichoepithelioma		1 (2%)		
Subcutaneous tissue, fibroma	3 (6%)	8 (16%)	7 (14%)	6 (12%)
Subcutaneous tissue, fibrosarcoma		1 (2%)		1 (2%)
Subcutaneous tissue, histiocytic sarcoma		1 (2%)		
Subcutaneous tissue, lipoma				1 (2%)
Subcutaneous tissue, melanoma malignant		1 (2%)		
Subcutaneous tissue, sarcoma	1 (2%)			
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma				1 (2%)
Vertebra, osteosarcoma	1 (2%)			
Skeletal muscle	(2)			(1)
Histiocytic sarcoma				1 (100%)
Nervous System				
Brain	(50)	(50)	(50)	(50)
Carcinoma, metastatic, Zymbal's gland		1 (2%)		
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma		2 (4%)	1 (2%)	
Alveolar/bronchiolar carcinoma			2 (4%)	1 (2%)
Carcinoma, metastatic, uncertain primary site	1 (2%)			
Hepatocellular carcinoma, metastatic, liver				1 (2%)
Osteosarcoma, metastatic, bone	1 (2%)			
Osteosarcoma, metastatic, uncertain primary site		1 (2%)		
Nose	(50)	(47)	(49)	(50)
Histiocytic sarcoma				1 (2%)
Respiratory epithelium, adenoma		1 (2%)		
Special Senses System				
Harderian gland				(1)
Histiocytic sarcoma				1 (100%)
Zymbal's gland	(1)	(3)	(3)	
Carcinoma	1 (100%)	3 (100%)	3 (100%)	
Urinary System				
Kidney	(50)	(49)	(49)	(50)
Renal tubule, adenoma			1 (2%)	1 (2%)
Renal tubule, carcinoma			1 (2%)	
Urinary bladder	(48)	(50)	(49)	(49)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma		1 (2%)		1 (2%)
Leukemia mononuclear	32 (64%)	33 (66%)	30 (60%)	31 (62%)
Mesothelioma malignant	3 (6%)		1 (2%)	2 (4%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	48	50	50	50
Total primary neoplasms	141	148	156	161
Total animals with benign neoplasms	48	48	48	50
Total benign neoplasms	99	101	112	116
Total animals with malignant neoplasms	39	38	37	37
Total malignant neoplasms	42	47	44	45
Total animals with metastatic neoplasms	3	4		1
Total metastatic neoplasms	3	5		1
Total animals with malignant neoplasms of uncertain primary site	2	1		

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

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	362	445	494	502	529	532	551	578	579	579	580	585	599	611	616	629	635	637	655	658	673	687	693	693	697
Carcass ID Number	007	008	004	032	013	022	019	046	018	042	001	009	033	005	028	011	048	003	034	021	035	015	045	049	017
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																X									
Intestine large, colon	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Intestine large, rectum	+	+	+	+	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	A	A	A	A	+	+	+	+	+	A	+	+	A	A	+	A	+	A
Intestine small, ileum	M	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	A	+	+	A	A	A	A	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Mesentery								+								+					+			+	
Oral mucosa		+								+															
Squamous cell papilloma										X															
Pancreas	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																								X	
Pheochromocytoma benign											X									X					
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																		X							
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Pituitary gland	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma				X									X	X							X		X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma						X																			
Follicular cell, adenoma																								X	
General Body System																									
Peritoneum								+													+				
Tissue NOS																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis			+																						
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									

+: 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 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	703	709	714	726	726	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	023	043	037	002	050	006	010	012	014	016	020	024	025	026	027	029	030	031	036	038	039	040	041	044	047	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Intestine large, colon	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, cecum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, duodenum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Intestine small, ileum	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																							X			1
Mesentery		+			+					+			+						+		+			+	+	12
Oral mucosa																										2
Squamous cell papilloma																										1
Pancreas	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Acinus, adenoma														X												1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Pheochromocytoma benign	X		X									X	X											X		7
Bilateral, pheochromocytoma benign					X	X								X	X	X			X							6
Islets, pancreatic	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma				X																						2
Parathyroid gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma				X	X		X	X			X							X	X	X				X		15
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma						X		X			X										X					5
Follicular cell, adenoma																										1
General Body System																										
Peritoneum																					+					3
Tissue NOS											+															1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Penis																										1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X																								1
Carcinoma									X																	1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma											X															1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	362	445	494	502	529	532	551	578	579	579	580	585	599	611	616	629	635	637	655	658	673	687	693	693	697
Carcass ID Number	007	008	004	032	013	022	019	046	018	042	001	009	033	005	028	011	048	003	034	021	035	015	045	049	017
Genital System (continued)																									
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma							X	X	X	X					X		X	X	X	X	X	X	X		X
Interstitial cell, adenoma		X			X	X					X	X	X			X								X	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Lymph node		+				+		+			+					+		+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, uncertain primary site										X															
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma												X										X			
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Keratoacanthoma																									X
Subcutaneous tissue, fibroma																	X					X			
Subcutaneous tissue, sarcoma																							X		
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Vertebra, osteosarcoma						X																			
Skeletal muscle																					+				
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve			+			+																			
Spinal cord			+			+																			
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site																									
Osteosarcoma, metastatic, bone						X																			
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Zymbal's gland													+												
Carcinoma													X												
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X						X	X		X				X		X	X	X	X		X		X	X
Mesothelioma malignant																					X				

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	703	709	714	726	726	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	023	043	037	002	050	006	010	012	014	016	020	024	025	026	027	029	030	031	036	038	039	040	041	044	047	Total Tissues/ Tumors
Genital System (continued)																										
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X	X	X	X		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	36
Interstitial cell, adenoma					X		X																			10
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node	+	+			+	+				+							+		+		+	+		+	+	24
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, uncertain primary site																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroadenoma						X		X		X		X													X	7
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma																		X								1
Keratoacanthoma																			X							2
Subcutaneous tissue, fibroma													X													3
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Vertebra, osteosarcoma																										1
Skeletal muscle		+																								2
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										2
Spinal cord																										2
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, uncertain primary site														X												1
Osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X	X	X	X	X	X				X	X		X	X	X	X		X	X	X	X	X	X	X	32
Mesothelioma malignant											X										X					3

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	388	502	544	548	555	555	592	593	609	611	613	630	636	643	655	657	675	693	697	706	707	711	716	718	721
Carcass ID Number	053	076	058	096	077	086	056	057	073	055	074	052	079	081	064	093	070	061	060	099	054	098	089	078	062
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+
Squamous cell carcinoma, metastatic, skin			X																						
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	A	A	A	A	A	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	A	A	+	A	+	+	+	+	A	A	A	A	+	+	+	+	A	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma												X													
Histiocytic sarcoma																									
Mesentery			+	+							+		+			+				+		+			
Pancreas	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign									X									X		X		X	X	X	
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X								X							X	X			X		X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																									
C-cell, carcinoma																									
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma				X					X		X		X		X			X	X	X		X		X	X
Interstitial cell, adenoma					X	X	X			X		X		X		X	X				X				

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	723	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	065	091	051	059	063	066	067	068	069	071	072	075	080	082	083	084	085	087	088	090	092	094	095	097	010	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Squamous cell carcinoma, metastatic, skin																										1
Intestine large, rectum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma										X									X							3
Histiocytic sarcoma																					X					1
Mesentery	+		+		+					+																11
Pancreas	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Acinus, adenoma																X										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma									X																	1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign																X		X	X	X	X		X	X		13
Bilateral, pheochromocytoma benign							X																			1
Islets, pancreatic	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenoma			X																							1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma		X	X				X	X		X		X		X			X	X		X		X	X		X	20
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma												X														1
C-cell, carcinoma							X	X																		2
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma													X													1
Carcinoma			X														X		X		X					4
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bilateral, interstitial cell, adenoma	X	X		X	X		X		X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	32
Interstitial cell, adenoma						X								X												11

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	388	502	544	548	555	555	592	593	609	611	613	630	636	643	655	657	675	693	697	706	707	711	716	718	721
Carcass ID Number	053	076	058	096	077	086	056	057	073	055	074	052	079	081	064	093	070	061	060	099	054	098	089	078	062
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	A	+	A	+	+	+	+	+	+	+
Lymph node			+	+	+	+	+	+	+	+		+	+			+		+	+		+	+			
Iliac, squamous cell carcinoma, metastatic, skin			X																						
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, Zymbal's gland															X										
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	I	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																									
Integumentary System																									
Mammary gland	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	M	+	+	+	+	M	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma													X										X		
Keratoacanthoma, multiple																									
Squamous cell carcinoma, multiple			X																						
Trichoepithelioma																									
Subcutaneous tissue, fibroma					X					X									X			X		X	
Subcutaneous tissue, fibrosarcoma																									X
Subcutaneous tissue, histiocytic sarcoma																									
Subcutaneous tissue, melanoma malignant																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, Zymbal's gland														X											
Peripheral nerve																									
Spinal cord																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma	X																								
Osteosarcoma, metastatic, uncertain primary site																									
Nose	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Respiratory epithelium, adenoma																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear		+																							
Eye										+															
Zymbal's gland	+													+	+										
Carcinoma	X													X	X										
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Leukemia mononuclear				X	X	X		X	X		X	X	X		X	X		X	X	X	X	X	X		

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	723	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	065	091	051	059	063	066	067	068	069	071	072	075	080	082	083	084	085	087	088	090	092	094	095	097	010	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymph node	+	+		+				+				+	+	+									+			23
Iliac, squamous cell carcinoma, metastatic, skin																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, Zymbal's gland																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thymoma benign								X																		1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma									X																	3
Keratoacanthoma, multiple																							X			1
Squamous cell carcinoma, multiple																										1
Trichoepithelioma																								X		1
Subcutaneous tissue, fibroma	X									X									X							8
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, histiocytic sarcoma																					X					1
Subcutaneous tissue, melanoma malignant																			X							1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, Zymbal's gland																										1
Peripheral nerve																					+					1
Spinal cord																					+					1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma									X																	2
Osteosarcoma, metastatic, uncertain primary site																					X					1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Respiratory epithelium, adenoma																				X						1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Eye																										1
Zymbal's gland																										3
Carcinoma																										3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																					X					1
Leukemia mononuclear	X	X	X	X	X	X	X	X	X	X				X	X	X	X		X			X	X			33

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	408	457	533	559	564	571	572	573	582	592	603	606	627	639	641	648	653	667	668	686	690	695	710	714	720
Carcass ID Number	138	113	143	102	125	123	116	108	106	144	132	131	101	109	122	146	115	141	127	121	129	105	150	149	139
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Intestine large, rectum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	A
Intestine large, cecum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	A
Intestine small, duodenum	+	+	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Intestine small, jejunum	+	A	+	A	+	A	A	A	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	A
Intestine small, ileum	+	A	+	A	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	A
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																									
Hepatocellular adenoma																									
Mesentery		+												+	+			+				+			
Pancreas	+	+	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign													X				X				X				
Bilateral, pheochromocytoma benign																							X	X	
Islets, pancreatic	+	+	+	A	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Adenoma																		X							
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma				X		X		X			X		X	X			X		X	X			X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma										X										X		X	X		
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma										X			X								X				
Bilateral, carcinoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma			X						X			X		X	X	X		X	X		X	X		X	X
Interstitial cell, adenoma		X			X					X										X					

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 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	729	729	729	729	729	
Carcass ID Number	114	103	104	107	110	111	112	117	118	119	120	124	126	128	130	133	134	135	136	137	140	142	145	147	148	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma																					X					1
Hepatocellular adenoma				X																						1
Mesentery			+			+	+																	+	+	10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Acinus, adenoma																								X		1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant							X																			1
Pheochromocytoma benign					X			X		X					X	X				X		X	X	X	X	13
Bilateral, pheochromocytoma benign	X		X																							4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma																X										2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma	X	X	X					X	X		X	X	X	X	X		X	X		X				X		25
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma								X									X									6
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X																				X				2
Carcinoma							X																			4
Bilateral, carcinoma																									X	1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X			X	X	X	X		X	X	X	X	X			X	X	X	X		X	X	X	X	X	31
Interstitial cell, adenoma		X	X											X	X					X						9

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	408	457	533	559	564	571	572	573	582	592	603	606	627	639	641	648	653	667	668	686	690	695	710	714	720
Carcass ID Number	138	113	143	102	125	123	116	108	106	144	132	131	101	109	122	146	115	141	127	121	129	105	150	149	139
Hematopoietic System																									
Bone marrow	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Lymph node			+					+	+	+		+		+	+	+		+			+		+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+
Fibroadenoma								X																	
Fibroadenoma, multiple																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									X
Subcutaneous tissue, fibroma										X	X								X						
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve			+																						
Spinal cord			+																						
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																				X					
Nose	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Zymbal's gland	+																								
Carcinoma	X																								
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																									
Renal tubule, carcinoma																									
Urinary bladder	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X	X			X		X		X	X	X	X	X	X			X	X	X	X	X	X	X
Mesothelioma malignant																		X							

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 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	729	729	729	729	729	
Carcass ID Number	114	103	104	107	110	111	112	117	118	119	120	124	126	128	130	133	134	135	136	137	140	142	145	147	148	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node	+	+	+					+	+	+			+		+					+			+			23
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibroadenoma				X		X	X				X															5
Fibroadenoma, multiple																									X	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma		X																		X						3
Subcutaneous tissue, fibroma			X	X					X												X					7
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																					X					1
Alveolar/bronchiolar carcinoma																								X		2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Zymbal's gland	+										+															3
Carcinoma	X										X															3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Renal tubule, adenoma												X														1
Renal tubule, carcinoma											X															1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X		X		X	X		X		X	X	X	X		X			X		X			X			30
Mesothelioma malignant																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	502	520	520	564	569	569	582	585	597	605	630	648	648	663	672	676	676	682	683	686	690	697	707	709	714
Carcass ID Number	171	166	190	158	188	193	151	200	198	187	189	155	174	196	183	186	197	172	195	157	159	165	169	184	191
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	A	+	+	+
Intestine large, rectum	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	A	+	+	A	A	A	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+
Intestine small, jejunum	+	+	+	+	A	+	+	A	+	+	+	+	+	A	+	+	+	+	A	+	A	A	+	A	+
Intestine small, ileum	+	+	+	+	A	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	A	A	+	A	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma					X																				
Hepatocellular adenoma																	X								
Histiocytic sarcoma										X															
Mesentery		+					+					+			+	+			+		+	+		+	+
Lipoma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign								X			X								X						
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	A	+	+
Adenoma																									
Carcinoma																									
Parathyroid gland	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X				X	X	X		X			X				X	X								
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																X				X					
C-cell, carcinoma												X													
Follicular cell, adenoma																									
General Body System																									
Peritoneum																			+						
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma								X																	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma					X					X	X		X	X	X			X	X		X	X	X	X	X
Interstitial cell, adenoma	X	X	X	X			X	X				X					X			X					

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	721	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	179	173	152	153	154	156	160	161	162	163	164	167	168	170	175	176	177	178	180	181	182	185	192	194	199	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma																										1
Hepatocellular adenoma																X										2
Histiocytic sarcoma																										1
Mesentery							+	+												+	+					14
Lipoma							X																			1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Acinus, adenoma																							X			1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																					X		X			2
Pheochromocytoma benign	X					X	X					X		X				X	X				X			11
Bilateral, pheochromocytoma benign																						X				1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																	X					X		X		3
Carcinoma																		X								1
Parathyroid gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X			X	X	X	X		X				X		X	X	X	X	X		X	X		X	X	24
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma																					X					3
C-cell, carcinoma																										1
Follicular cell, adenoma									X																	1
General Body System																										
Peritoneum																										1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																X					X					2
Carcinoma					X																	X				3
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma		X	X	X		X		X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	34
Interstitial cell, adenoma	X						X						X													12

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	502	520	520	564	569	569	582	585	597	605	630	648	648	663	672	676	676	682	683	686	690	697	707	709	714
Carcass ID Number	171	166	190	158	188	193	151	200	198	187	189	155	174	196	183	186	197	172	195	157	159	165	169	184	191
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Lymph node			+	+	+			+			+			+	+	+	+	+	+	+	+	+		+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	M	+
Fibroadenoma												X									X				X
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma							X															X			
Squamous cell papilloma																									X
Subcutaneous tissue, fibroma			X																X						
Subcutaneous tissue, fibrosarcoma								X																	
Subcutaneous tissue, lipoma			X																						
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma													X												
Skeletal muscle										+															
Histiocytic sarcoma										X															
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Hepatocellular carcinoma, metastatic, liver					X																				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye										+															
Harderian gland										+															
Histiocytic sarcoma										X															
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Leukemia mononuclear	X	X		X	X			X			X			X	X		X	X	X	X	X	X	X	X	X
Mesothelioma malignant																			X						

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	721	728	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	179	173	152	153	154	156	160	161	162	163	164	167	168	170	175	176	177	178	180	181	182	185	192	194	199	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+				+									+	+	+					+	+			24
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Fibroadenoma												X									X	X				6
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma	X											X											X		X	6
Squamous cell papilloma																										1
Subcutaneous tissue, fibroma	X			X						X									X							6
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, lipoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle																										1
Histiocytic sarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma																					X					1
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye														+												2
Harderian gland																										1
Histiocytic sarcoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenoma										X																1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear	X	X	X	X		X	X		X		X	X				X		X	X	X			X			31
Mesothelioma malignant					X																					2

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	13/50 (26%)	14/49 (29%)	17/49 (35%)	12/50 (24%)
Adjusted rate[b]	32.7%	33.5%	41.4%	28.1%
Terminal rate[c]	8/20 (40%)	8/23 (35%)	11/24 (46%)	8/23 (35%)
First incidence (days)	580	609	627	585
Poly-3 test[d]	P=0.375N	P=0.585	P=0.295	P=0.433N
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rate	14/50 (28%)	14/49 (29%)	18/49 (37%)	13/50 (26%)
Adjusted rate	35.1%	33.5%	43.8%	30.4%
Terminal rate	8/20 (40%)	8/23 (35%)	12/24 (50%)	9/23 (39%)
First incidence (days)	580	609	627	585
Poly-3 test	P=0.413N	P=0.552N	P=0.295	P=0.432N
Liver: Hepatocellular Adenoma				
Overall rate	1/50 (2%)	3/50 (6%)	1/50 (2%)	2/50 (4%)
Adjusted rate	2.6%	7.1%	2.5%	4.8%
Terminal rate	1/20 (5%)	2/23 (9%)	1/24 (4%)	1/23 (4%)
First incidence (days)	729 (T)	630	729 (T)	676
Poly-3 test	P=0.588	P=0.379	P=0.805N	P=0.583
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	1/50 (2%)	3/50 (6%)	2/50 (4%)	3/50 (6%)
Adjusted rate	2.6%	7.1%	4.9%	7.1%
Terminal rate	1/20 (5%)	2/23 (9%)	2/24 (8%)	1/23 (4%)
First incidence (days)	729 (T)	630	729 (T)	569
Poly-3 test	P=0.360	P=0.379	P=0.576	P=0.382
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	0/50 (0%)	2/50 (4%)	3/50 (6%)	1/50 (2%)
Adjusted rate	0.0%	4.7%	7.3%	2.4%
Terminal rate	0/20 (0%)	1/23 (4%)	2/24 (8%)	1/23 (4%)
First incidence (days)	—[e]	388	686	729 (T)
Poly-3 test	P=0.509	P=0.314	P=0.161	P=0.611
Mammary Gland: Fibroadenoma				
Overall rate	7/50 (14%)	0/50 (0%)	6/50 (12%)	6/50 (12%)
Adjusted rate	17.7%	0.0%	14.6%	14.2%
Terminal rate	5/20 (25%)	0/23 (0%)	5/24 (21%)	3/23 (13%)
First incidence (days)	585	—	573	648
Poly-3 test	P=0.394	P=0.007N	P=0.496N	P=0.474N
Pancreatic Islets: Adenoma				
Overall rate	2/49 (4%)	1/45 (2%)	2/46 (4%)	3/47 (6%)
Adjusted rate	5.2%	2.6%	5.2%	7.7%
Terminal rate	0/20 (0%)	1/23 (4%)	1/24 (4%)	3/23 (13%)
First incidence (days)	637	729 (T)	667	729 (T)
Poly-3 test	P=0.333	P=0.557N	P=0.734N	P=0.555
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	2/49 (4%)	1/45 (2%)	2/46 (4%)	4/47 (9%)
Adjusted rate	5.2%	2.6%	5.2%	10.2%
Terminal rate	0/20 (0%)	1/23 (4%)	1/24 (4%)	4/23 (17%)
First incidence (days)	637	729 (T)	667	729 (T)
Poly-3 test	P=0.176	P=0.557N	P=0.734N	P=0.386

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	15/48 (31%)	20/49 (41%)	25/49 (51%)	24/50 (48%)
Adjusted rate	37.4%	46.9%	57.2%	53.2%
Terminal rate	7/20 (35%)	12/23 (52%)	13/24 (54%)	15/23 (65%)
First incidence (days)	502	502	559	502
Poly-3 test	P=0.090	P=0.264	P=0.052	P=0.106
Preputial Gland: Carcinoma				
Overall rate	1/50 (2%)	4/50 (8%)	5/50 (10%)	3/49 (6%)
Adjusted rate	2.6%	9.6%	12.0%	7.2%
Terminal rate	1/20 (5%)	4/23 (17%)	2/24 (8%)	2/23 (9%)
First incidence (days)	729 (T)	729 (T)	592	585
Poly-3 test	P=0.394	P=0.232	P=0.138	P=0.373
Preputial Gland: Adenoma or Carcinoma				
Overall rate	2/50 (4%)	5/50 (10%)	7/50 (14%)	5/49 (10%)
Adjusted rate	5.1%	12.0%	16.8%	12.0%
Terminal rate	1/20 (5%)	5/23 (22%)	4/24 (17%)	4/23 (17%)
First incidence (days)	709	729 (T)	592	585
Poly-3 test	P=0.267	P=0.273	P=0.109	P=0.271
Skin: Keratoacanthoma				
Overall rate	2/50 (4%)	4/50 (8%)	3/50 (6%)	6/50 (12%)
Adjusted rate	5.1%	9.5%	7.4%	14.2%
Terminal rate	1/20 (5%)	2/23 (9%)	2/24 (8%)	3/23 (13%)
First incidence (days)	697	636	720	582
Poly-3 test	P=0.138	P=0.410	P=0.567	P=0.182
Skin: Squamous Cell Papilloma or Keratoacanthoma				
Overall rate	2/50 (4%)	4/50 (8%)	3/50 (6%)	7/50 (14%)
Adjusted rate	5.1%	9.5%	7.4%	16.5%
Terminal rate	1/20 (5%)	2/23 (9%)	2/24 (8%)	3/23 (13%)
First incidence (days)	697	636	720	582
Poly-3 test	P=0.072	P=0.410	P=0.567	P=0.114
Skin: Squamous Cell Papilloma, Keratoacanthoma, or Squamous Cell Carcinoma				
Overall rate	2/50 (4%)	5/50 (10%)	3/50 (6%)	7/50 (14%)
Adjusted rate	5.1%	11.7%	7.4%	16.5%
Terminal rate	1/20 (5%)	2/23 (9%)	2/24 (8%)	3/23 (13%)
First incidence (days)	697	544	720	582
Poly-3 test	P=0.101	P=0.282	P=0.567	P=0.114
Skin: Squamous Cell Papilloma, Keratoacanthoma, Trichoepithelioma, Basal Cell Carcinoma, or Squamous Cell Carcinoma				
Overall rate	3/50 (6%)	6/50 (12%)	3/50 (6%)	7/50 (14%)
Adjusted rate	7.7%	14.1%	7.4%	16.5%
Terminal rate	2/20 (10%)	3/23 (13%)	2/24 (8%)	3/23 (13%)
First incidence (days)	697	544	720	582
Poly-3 test	P=0.216	P=0.314	P=0.683N	P=0.214
Skin (Subcutaneous Tissue): Fibroma				
Overall rate	3/50 (6%)	8/50 (16%)	7/50 (14%)	6/50 (12%)
Adjusted rate	7.6%	18.7%	16.7%	14.1%
Terminal rate	1/20 (5%)	2/23 (9%)	4/24 (17%)	3/23 (13%)
First incidence (days)	635	555	592	520
Poly-3 test	P=0.406	P=0.140	P=0.202	P=0.308

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Skin (Subcutaneous Tissue): Fibroma, Fibrosarcoma, or Sarcoma				
Overall rate	4/50 (8%)	9/50 (18%)	7/50 (14%)	7/50 (14%)
Adjusted rate	10.1%	21.0%	16.7%	16.3%
Terminal rate	1/20 (5%)	2/23 (9%)	4/24 (17%)	3/23 (13%)
First incidence (days)	635	555	592	520
Poly-3 test	P=0.436	P=0.161	P=0.318	P=0.336
Testes: Adenoma				
Overall rate	46/50 (92%)	43/49 (88%)	40/50 (80%)	46/50 (92%)
Adjusted rate	97.2%	91.8%	87.1%	94.2%
Terminal rate	20/20 (100%)	21/23 (91%)	23/24 (96%)	22/23 (96%)
First incidence (days)	445	548	457	502
Poly-3 test	P=0.400N	P=0.221N	P=0.041N	P=0.411N
Thyroid Gland (C-cell): Adenoma				
Overall rate	5/50 (10%)	1/50 (2%)	6/50 (12%)	3/50 (6%)
Adjusted rate	12.7%	2.4%	14.5%	7.1%
Terminal rate	4/20 (20%)	1/23 (4%)	2/24 (8%)	1/23 (4%)
First incidence (days)	532	729 (T)	592	676
Poly-3 test	P=0.488N	P=0.105N	P=0.567	P=0.351N
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rate	5/50 (10%)	3/50 (6%)	6/50 (12%)	4/50 (8%)
Adjusted rate	12.7%	7.2%	14.5%	9.4%
Terminal rate	4/20 (20%)	3/23 (13%)	2/24 (8%)	1/23 (4%)
First incidence (days)	532	729 (T)	592	648
Poly-3 test	P=0.517N	P=0.358N	P=0.567	P=0.486N
Zymbal's Gland: Carcinoma				
Overall rate	1/50 (2%)	3/50 (6%)	3/50 (6%)	0/50 (0%)
Adjusted rate	2.5%	7.0%	7.2%	0.0%
Terminal rate	0/20 (0%)	0/23 (0%)	1/24 (4%)	0/23 (0%)
First incidence (days)	599	388	408	—
Poly-3 test	P=0.264N	P=0.380	P=0.370	P=0.582N
All Organs: Mononuclear Cell Leukemia				
Overall rate	32/50 (64%)	33/50 (66%)	30/50 (60%)	31/50 (62%)
Adjusted rate	73.7%	71.1%	65.4%	66.4%
Terminal rate	15/20 (75%)	15/23 (65%)	12/24 (50%)	12/23 (52%)
First incidence (days)	445	548	533	502
Poly-3 test	P=0.239N	P=0.494N	P=0.265N	P=0.299N
All Organs: Malignant Mesothelioma				
Overall rate	3/50 (6%)	0/50 (0%)	1/50 (2%)	2/50 (4%)
Adjusted rate	7.7%	0.0%	2.4%	4.8%
Terminal rate	2/20 (10%)	0/23 (0%)	0/24 (0%)	1/23 (4%)
First incidence (days)	673	—	667	683
Poly-3 test	P=0.592N	P=0.136N	P=0.333N	P=0.511N
All Organs: Benign Neoplasms				
Overall rate	48/50 (96%)	48/50 (96%)	48/50 (96%)	50/50 (100%)
Adjusted rate	99.1%	98.1%	98.6%	100.0%
Terminal rate	20/20 (100%)	23/23 (100%)	24/24 (100%)	23/23 (100%)
First incidence (days)	445	388	457	502
Poly-3 test	P=0.391	P=0.749N	P=0.903N	P=0.957

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
All Organs: Malignant Neoplasms				
Overall rate	40/50 (80%)	38/50 (76%)	37/50 (74%)	37/50 (74%)
Adjusted rate	87.6%	78.8%	78.1%	77.6%
Terminal rate	17/20 (85%)	16/23 (70%)	16/24 (67%)	15/23 (65%)
First incidence (days)	445	388	408	502
Poly-3 test	P=0.175N	P=0.187N	P=0.162N	P=0.147N
All Organs: Benign or Malignant Neoplasms				
Overall rate	48/50 (96%)	50/50 (100%)	50/50 (100%)	50/50 (100%)
Adjusted rate	99.1%	100.0%	100.0%	100.0%
Terminal rate	20/20 (100%)	23/23 (100%)	24/24 (100%)	23/23 (100%)
First incidence (days)	445	388	408	502
Poly-3 test	P=0.702	P=0.957	P=0.957	P=0.957

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, liver, lung, pancreatic islets, pituitary gland, preputial gland, testis, 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 are the P values 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 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 A4
Historical Incidence of Mammary Gland Fibroadenoma in Untreated Male F344/N Rats[a]

Study	Incidence in Controls
Historical Incidence at TSI Mason Research Institute: Feed Study	
Phenolphthalein	6/50
Overall Historical Incidence: Drinking Water Studies	
Total	13/281 (4.6%)
Standard deviation	2.2%
Range	2%-8%
Overall Historical Incidence: Feed Studies	
Total	58/1,354 (4.3%)
Standard deviation	3.3%
Range	0%-12%
Overall Historical Incidence: Gavage (Corn Oil) Studies	
Total	44/772 (5.7%)
Standard deviation	2.5%
Range	2%-12%
Overall Historical Incidence: Inhalation Studies	
Total	17/905 (1.9%)
Standard deviation	2.0%
Range	0%-6%

[a] Data as of 15 October 1996

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	150 ppm	325 ppm	650 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	12	13	7	10
Natural deaths	18	14	19	17
Survivors				
Died last week of study	1			
Terminal sacrifice	19	23	24	23
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(46)	(46)	(48)	(47)
Hemorrhage			1 (2%)	
Parasite metazoan	1 (2%)	3 (7%)	1 (2%)	2 (4%)
Intestine large, rectum	(45)	(47)	(46)	(47)
Parasite metazoan	3 (7%)	3 (6%)	3 (7%)	2 (4%)
Intestine large, cecum	(45)	(46)	(45)	(44)
Inflammation, chronic active			1 (2%)	
Necrosis				1 (2%)
Parasite metazoan		1 (2%)		
Intestine small, jejunum	(39)	(42)	(41)	(42)
Fibrosis				1 (2%)
Intestine small, ileum	(39)	(41)	(41)	(43)
Parasite metazoan		1 (2%)		
Liver	(50)	(50)	(50)	(50)
Angiectasis	5 (10%)	11 (22%)	7 (14%)	9 (18%)
Basophilic focus	3 (6%)			
Clear cell focus	7 (14%)	8 (16%)	7 (14%)	3 (6%)
Congestion	2 (4%)			
Cyst	1 (2%)			
Deformity	1 (2%)	2 (4%)	1 (2%)	
Degeneration, cystic	12 (24%)	8 (16%)	12 (24%)	12 (24%)
Eosinophilic focus	4 (8%)	10 (20%)	10 (20%)	3 (6%)
Hemorrhage		2 (4%)		
Hepatodiaphragmatic nodule	2 (4%)	3 (6%)	5 (10%)	
Inflammation, chronic active	1 (2%)		1 (2%)	
Mixed cell focus	6 (12%)	6 (12%)	2 (4%)	5 (10%)
Necrosis			1 (2%)	2 (4%)
Vacuolization cytoplasmic	2 (4%)		4 (8%)	1 (2%)
Bile duct, hyperplasia	1 (2%)	2 (4%)	3 (6%)	
Centrilobular, congestion		1 (2%)		
Centrilobular, degeneration	1 (2%)		1 (2%)	
Centrilobular, vacuolization cytoplasmic	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Kupffer cell, pigmentation	1 (2%)			
Vein, dilatation		1 (2%)		
Mesentery	(12)	(11)	(10)	(14)
Accessory spleen				1 (7%)
Inflammation, chronic active		1 (9%)		
Necrosis	1 (8%)			
Pigmentation	1 (8%)			
Fat, necrosis	9 (75%)	10 (91%)	9 (90%)	12 (86%)
Fat, pigmentation			1 (10%)	

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

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Alimentary System (continued)				
Oral mucosa	(2)			
Hyperplasia	1 (50%)			
Pancreas	(48)	(45)	(46)	(48)
Acinus, atrophy	10 (21%)	9 (20%)	13 (28%)	12 (25%)
Acinus, hyperplasia			1 (2%)	3 (6%)
Artery, hyperplasia	2 (4%)			
Salivary glands	(50)	(50)	(49)	(50)
Atrophy		1 (2%)		
Duct, hyperplasia		1 (2%)		
Stomach, forestomach	(50)	(49)	(48)	(49)
Diverticulum			1 (2%)	
Hemorrhage				1 (2%)
Inflammation, chronic active	3 (6%)	2 (4%)	2 (4%)	
Ulcer	10 (20%)	10 (20%)	8 (17%)	13 (27%)
Epithelium, hyperplasia	3 (6%)	4 (8%)	2 (4%)	1 (2%)
Stomach, glandular	(50)	(49)	(48)	(50)
Atrophy			1 (2%)	
Hyperplasia, lymphoid	2 (4%)	1 (2%)		
Inflammation, chronic active			1 (2%)	1 (2%)
Mineralization	1 (2%)	1 (2%)		
Necrosis	17 (34%)	14 (29%)	13 (27%)	17 (34%)
Cardiovascular System				
Blood vessel	(48)	(50)	(50)	(50)
Aorta, inflammation, chronic active		1 (2%)		
Aorta, mineralization	1 (2%)			
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	35 (70%)	41 (82%)	42 (84%)	33 (66%)
Fibrosis				1 (2%)
Mineralization	2 (4%)			1 (2%)
Thrombosis		1 (2%)		
Artery, inflammation, chronic active	1 (2%)			
Atrium, thrombosis	3 (6%)		6 (12%)	4 (8%)
Ventricle, pigmentation			1 (2%)	
Endocrine System				
Adrenal cortex	(50)	(49)	(49)	(50)
Angiectasis			1 (2%)	
Cytoplasmic alteration		2 (4%)	2 (4%)	
Degeneration, cystic			1 (2%)	
Hemorrhage	1 (2%)	1 (2%)		1 (2%)
Hyperplasia			1 (2%)	
Necrosis	1 (2%)	1 (2%)		
Vacuolization cytoplasmic			3 (6%)	
Adrenal medulla	(50)	(49)	(49)	(50)
Angiectasis				1 (2%)
Hemorrhage				1 (2%)
Hyperplasia	10 (20%)	8 (16%)	8 (16%)	4 (8%)
Islets, pancreatic	(49)	(45)	(46)	(47)
Hyperplasia				1 (2%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Endocrine System (continued)				
Parathyroid gland	(48)	(49)	(50)	(47)
Hyperplasia	1 (2%)	2 (4%)	1 (2%)	
Pituitary gland	(48)	(49)	(49)	(50)
Pars distalis, angiectasis	3 (6%)	1 (2%)	3 (6%)	5 (10%)
Pars distalis, cyst	1 (2%)	3 (6%)	2 (4%)	2 (4%)
Pars distalis, hemorrhage		1 (2%)		
Pars distalis, hyperplasia	8 (17%)	5 (10%)	5 (10%)	7 (14%)
Pars intermedia, cyst		1 (2%)		1 (2%)
Pars nervosa, hemorrhage		1 (2%)		
Thyroid gland	(50)	(50)	(50)	(50)
Cyst	1 (2%)			
C-cell, hyperplasia	4 (8%)	6 (12%)	5 (10%)	4 (8%)
Follicular cell, hyperplasia			1 (2%)	
General Body System				
Peritoneum	(3)			(1)
Necrosis	1 (33%)			
Tissue NOS	(1)			
Abdominal, hemorrhage	1 (100%)			
Genital System				
Epididymis	(50)	(49)	(50)	(50)
Inflammation, chronic active			1 (2%)	
Penis	(1)			
Inflammation, chronic active	1 (100%)			
Preputial gland	(50)	(50)	(50)	(49)
Cyst	3 (6%)	1 (2%)	2 (4%)	3 (6%)
Fibrosis				1 (2%)
Inflammation, chronic	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Inflammation, chronic active	5 (10%)	1 (2%)	3 (6%)	5 (10%)
Prostate	(50)	(50)	(50)	(50)
Hyperplasia	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Inflammation, chronic active	4 (8%)	5 (10%)	7 (14%)	5 (10%)
Seminal vesicle	(50)	(50)	(50)	(50)
Hyperplasia			1 (2%)	
Inflammation, chronic active	1 (2%)			
Testes	(50)	(49)	(50)	(50)
Atrophy	8 (16%)	9 (18%)	12 (24%)	8 (16%)
Artery, inflammation, chronic active			2 (4%)	2 (4%)
Interstitial cell, hyperplasia	8 (16%)	11 (22%)	10 (20%)	8 (16%)
Hematopoietic System				
Bone marrow	(47)	(45)	(47)	(49)
Atrophy	4 (9%)		1 (2%)	3 (6%)
Fibrosis			2 (4%)	
Hyperplasia	2 (4%)	4 (9%)	2 (4%)	1 (2%)
Myeloid cell, hyperplasia		1 (2%)		

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Hematopoietic System (continued)				
Lymph node	(24)	(23)	(23)	(24)
Hemorrhage	1 (4%)	1 (4%)		1 (4%)
Iliac, hemorrhage	1 (4%)	1 (4%)		
Iliac, hyperplasia, lymphoid			1 (4%)	
Iliac, hyperplasia, plasma cell		1 (4%)		
Mediastinal, congestion			1 (4%)	
Mediastinal, ectasia			1 (4%)	
Mediastinal, hemorrhage	11 (46%)	11 (48%)	8 (35%)	11 (46%)
Mediastinal, hyperplasia, lymphoid	3 (13%)	2 (9%)		
Mediastinal, hyperplasia, plasma cell		1 (4%)		
Mediastinal, infiltration cellular, histiocyte		1 (4%)	1 (4%)	
Mediastinal, pigmentation	3 (13%)	2 (9%)	1 (4%)	
Pancreatic, ectasia		1 (4%)		
Pancreatic, hemorrhage	1 (4%)	4 (17%)	2 (9%)	5 (21%)
Pancreatic, hyperplasia, lymphoid				1 (4%)
Renal, ectasia		3 (13%)		
Renal, hemorrhage	3 (13%)	3 (13%)	1 (4%)	8 (33%)
Renal, hyperplasia, lymphoid				1 (4%)
Renal, hyperplasia, plasma cell	1 (4%)			
Renal, pigmentation	3 (13%)	4 (17%)	2 (9%)	7 (29%)
Lymph node, mandibular	(50)	(50)	(50)	(50)
Ectasia	1 (2%)	8 (16%)	2 (4%)	3 (6%)
Hemorrhage	3 (6%)	1 (2%)	3 (6%)	2 (4%)
Hyperplasia, lymphoid	5 (10%)	2 (4%)	3 (6%)	2 (4%)
Hyperplasia, plasma cell	2 (4%)	4 (8%)	5 (10%)	2 (4%)
Infiltration cellular, histiocyte		1 (2%)		
Lymph node, mesenteric	(49)	(50)	(50)	(50)
Ectasia	3 (6%)	1 (2%)	2 (4%)	1 (2%)
Hemorrhage	4 (8%)	4 (8%)	4 (8%)	6 (12%)
Hyperplasia, lymphoid	4 (8%)	2 (4%)		2 (4%)
Inflammation, chronic active		1 (2%)		
Spleen	(50)	(50)	(50)	(50)
Angiectasis	2 (4%)			
Atrophy		1 (2%)		
Congestion	3 (6%)		2 (4%)	
Cyst				1 (2%)
Fibrosis	10 (20%)	16 (32%)	19 (38%)	14 (28%)
Hematopoietic cell proliferation	3 (6%)	5 (10%)	2 (4%)	2 (4%)
Necrosis	3 (6%)	1 (2%)	2 (4%)	1 (2%)
Pigmentation	2 (4%)		2 (4%)	2 (4%)
Capsule, fibrosis	2 (4%)	2 (4%)	2 (4%)	
Capsule, pigmentation	1 (2%)			1 (2%)
Thymus	(49)	(47)	(48)	(47)
Atrophy	30 (61%)	19 (40%)	18 (38%)	27 (57%)
Hemorrhage	3 (6%)		3 (6%)	2 (4%)
Epithelial cell, hyperplasia	5 (10%)	3 (6%)	2 (4%)	3 (6%)
Integumentary System				
Mammary gland	(50)	(45)	(48)	(47)
Dilatation	8 (16%)	13 (29%)	9 (19%)	6 (13%)
Hyperplasia	1 (2%)	3 (7%)	5 (10%)	6 (13%)
Inflammation, chronic active				2 (4%)
Pigmentation	1 (2%)			

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Integumentary System (continued)				
Skin	(50)	(50)	(50)	(50)
Cyst epithelial inclusion	1 (2%)		1 (2%)	
Hyperkeratosis	2 (4%)			1 (2%)
Inflammation, chronic active	2 (4%)	1 (2%)	1 (2%)	
Ulcer				2 (4%)
Epidermis, hyperplasia		1 (2%)		
Hair follicle, atrophy				1 (2%)
Subcutaneous tissue, fibrosis				1 (2%)
Subcutaneous tissue, foreign body				1 (2%)
Subcutaneous tissue, inflammation, chronic active				1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hyperostosis	1 (2%)	1 (2%)		1 (2%)
Nervous System				
Brain	(50)	(50)	(50)	(50)
Hemorrhage	1 (2%)	2 (4%)	1 (2%)	4 (8%)
Mineralization	1 (2%)			
Necrosis				1 (2%)
Meninges, angiectasis	1 (2%)			
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Hemorrhage		1 (2%)	1 (2%)	4 (8%)
Inflammation, acute	1 (2%)			1 (2%)
Inflammation, chronic active			3 (6%)	1 (2%)
Alveolar epithelium, hyperplasia	4 (8%)	1 (2%)	6 (12%)	1 (2%)
Alveolus, metaplasia, squamous			1 (2%)	
Nose	(50)	(47)	(49)	(50)
Foreign body		2 (4%)		1 (2%)
Nasopharyngeal duct, inflammation, chronic active	1 (2%)			
Olfactory epithelium, degeneration, hyaline	1 (2%)			2 (4%)
Olfactory epithelium, foreign body	1 (2%)			1 (2%)
Olfactory epithelium, hyperplasia	1 (2%)			
Olfactory epithelium, inflammation, chronic active	10 (20%)	2 (4%)	6 (12%)	5 (10%)
Olfactory epithelium, metaplasia	1 (2%)			
Respiratory epithelium, degeneration, hyaline		2 (4%)	1 (2%)	
Respiratory epithelium, foreign body	3 (6%)			
Respiratory epithelium, hyperplasia	22 (44%)	20 (43%)	16 (33%)	28 (56%)
Respiratory epithelium, inflammation			1 (2%)	
Respiratory epithelium, inflammation, chronic	1 (2%)		1 (2%)	1 (2%)
Respiratory epithelium, inflammation, chronic active	22 (44%)	15 (32%)	22 (45%)	27 (54%)
Respiratory epithelium, metaplasia				1 (2%)
Respiratory epithelium, metaplasia, squamous	2 (4%)			1 (2%)
Respiratory epithelium, thrombosis	4 (8%)			1 (2%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Special Senses System				
Eye		(1)		(2)
Atrophy				2 (100%)
Hemorrhage		1 (100%)		
Lens, cataract		1 (100%)		
Urinary System				
Kidney	(50)	(49)	(49)	(50)
Angiectasis			1 (2%)	
Atrophy				1 (2%)
Cyst	3 (6%)		2 (4%)	3 (6%)
Fibrosis		1 (2%)		
Hemorrhage	1 (2%)			
Hydronephrosis	1 (2%)			
Infiltration cellular, polymorphonuclear		1 (2%)		
Mineralization	2 (4%)			1 (2%)
Necrosis		1 (2%)		
Nephropathy	46 (92%)	46 (94%)	46 (94%)	49 (98%)
Renal tubule, hyperplasia		1 (2%)	1 (2%)	
Renal tubule, pigmentation	4 (8%)	3 (6%)	4 (8%)	3 (6%)
Urinary bladder	(48)	(50)	(49)	(49)
Hemorrhage			1 (2%)	1 (2%)
Inflammation, acute	1 (2%)			
Inflammation, chronic active		1 (2%)		

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 1-CHLORO-2-PROPANOL

TABLE B1 Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 100

TABLE B2 Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 104

TABLE B3 Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 122

TABLE B4 Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 125

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	150 ppm	325 ppm	650 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	12	7	7	5
Natural deaths	13	10	13	14
Survivors				
Terminal sacrifice	25	33	30	31
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, cecum	(47)	(49)	(48)	(48)
Intestine small, jejunum	(44)	(44)	(43)	(46)
Intestine small, ileum	(42)	(45)	(43)	(45)
Liver	(50)	(50)	(50)	(50)
Hepatocellular adenoma			1 (2%)	1 (2%)
Histiocytic sarcoma	1 (2%)		1 (2%)	
Mesentery	(9)	(11)	(12)	(10)
Histiocytic sarcoma	1 (11%)			
Oral mucosa		(1)	(1)	
Squamous cell carcinoma		1 (100%)		
Squamous cell papilloma			1 (100%)	
Pancreas	(47)	(49)	(49)	(48)
Histiocytic sarcoma			1 (2%)	
Acinus, adenoma				1 (2%)
Salivary glands	(50)	(50)	(50)	(50)
Stomach, forestomach	(50)	(50)	(50)	(50)
Stomach, glandular	(50)	(50)	(50)	(50)
Tongue	(2)	(2)		(1)
Squamous cell carcinoma, metastatic, oral mucosa		1 (50%)		
Squamous cell papilloma	2 (100%)	1 (50%)		1 (100%)
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Histiocytic sarcoma			1 (2%)	
Endocrine System				
Adrenal cortex	(49)	(50)	(50)	(50)
Carcinoma	1 (2%)			
Adrenal medulla	(49)	(50)	(50)	(50)
Ganglioneuroma				1 (2%)
Pheochromocytoma malignant	1 (2%)	1 (2%)		1 (2%)
Pheochromocytoma complex	1 (2%)			
Pheochromocytoma benign	2 (4%)	4 (8%)	1 (2%)	4 (8%)
Bilateral, pheochromocytoma benign		1 (2%)		
Islets, pancreatic	(46)	(49)	(48)	(48)
Adenoma	1 (2%)	1 (2%)	1 (2%)	
Carcinoma		1 (2%)		
Pituitary gland	(49)	(50)	(50)	(50)
Pars distalis, adenoma	29 (59%)	30 (60%)	32 (64%)	35 (70%)
Pars distalis, carcinoma	1 (2%)			
Pars distalis, histiocytic sarcoma			1 (2%)	

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Endocrine System (continued)				
Thyroid gland	(50)	(50)	(50)	(50)
Histiocytic sarcoma	1 (2%)			
C-cell, adenoma	2 (4%)	8 (16%)	5 (10%)	3 (6%)
C-cell, carcinoma			1 (2%)	2 (4%)
Follicular cell, adenoma				1 (2%)
General Body System				
Tissue NOS	(1)			
Abdominal, sarcoma	1 (100%)			
Genital System				
Clitoral gland	(49)	(49)	(49)	(49)
Adenoma	1 (2%)		2 (4%)	4 (8%)
Carcinoma	2 (4%)	3 (6%)	2 (4%)	3 (6%)
Histiocytic sarcoma	1 (2%)		1 (2%)	
Bilateral, carcinoma	2 (4%)	1 (2%)		
Ovary	(50)	(50)	(50)	(50)
Cystadenoma			1 (2%)	
Granulosa cell tumor benign			1 (2%)	
Granulosa-theca tumor malignant			1 (2%)	
Histiocytic sarcoma			1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Histiocytic sarcoma			1 (2%)	
Polyp stromal	6 (12%)	6 (12%)	6 (12%)	4 (8%)
Bilateral, polyp stromal	1 (2%)			
Hematopoietic System				
Bone marrow	(47)	(50)	(47)	(49)
Histiocytic sarcoma		1 (2%)		1 (2%)
Lymph node	(11)	(9)	(15)	(7)
Mediastinal, histiocytic sarcoma			1 (7%)	
Pancreatic, histiocytic sarcoma			1 (7%)	
Lymph node, mandibular	(50)	(50)	(50)	(49)
Histiocytic sarcoma			1 (2%)	
Lymph node, mesenteric	(50)	(50)	(49)	(50)
Histiocytic sarcoma			1 (2%)	
Spleen	(50)	(50)	(50)	(49)
Histiocytic sarcoma			1 (2%)	
Thymus	(48)	(49)	(50)	(50)
Histiocytic sarcoma			1 (2%)	
Thymoma benign		1 (2%)		1 (2%)
Integumentary System				
Mammary gland	(50)	(50)	(49)	(50)
Adenoma		1 (2%)		
Carcinoma	1 (2%)	1 (2%)	1 (2%)	
Fibroadenoma	21 (42%)	21 (42%)	26 (53%)	14 (28%)
Fibroadenoma, multiple	8 (16%)	7 (14%)	5 (10%)	9 (18%)
Histiocytic sarcoma			1 (2%)	

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Integumentary System (continued)				
Skin	(50)	(50)	(50)	(50)
Squamous cell papilloma	1 (2%)			
Subcutaneous tissue, fibroma	1 (2%)		1 (2%)	2 (4%)
Subcutaneous tissue, fibrous histiocytoma				1 (2%)
Subcutaneous tissue, histiocytic sarcoma	1 (2%)		1 (2%)	
Subcutaneous tissue, melanoma malignant		1 (2%)	1 (2%)	
Subcutaneous tissue, sarcoma	1 (2%)		1 (2%)	
Subcutaneous tissue, schwannoma malignant		1 (2%)		
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma			1 (2%)	
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma				1 (2%)
Histiocytic sarcoma	1 (2%)		1 (2%)	
Melanoma malignant, metastatic, skin		1 (2%)		
Osteosarcoma, metastatic, bone			1 (2%)	
Pheochromocytoma complex, metastatic, adrenal medulla	1 (2%)			
Nose	(50)	(48)	(49)	(49)
Respiratory epithelium, histiocytic sarcoma			1 (2%)	
Special Senses System				
Zymbal's gland		(1)	(1)	
Carcinoma			1 (100%)	
Urinary System				
Kidney	(46)	(49)	(50)	(50)
Mesenchymal tumor malignant			1 (2%)	
Transitional epithelium, papilloma	1 (2%)			
Urinary bladder	(49)	(50)	(50)	(49)
Histiocytic sarcoma			1 (2%)	
Papilloma				1 (2%)
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Leukemia mononuclear	19 (38%)	19 (38%)	18 (36%)	13 (26%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Neoplasm Summary				
Total animals with primary neoplasms[c]	48	46	49	48
Total primary neoplasms	107	111	112	104
Total animals with benign neoplasms	43	42	48	42
Total benign neoplasms	76	81	83	83
Total animals with malignant neoplasms	26	24	26	18
Total malignant neoplasms	31	30	29	21
Total animals with metastatic neoplasms	1	2	1	
Total metastatic neoplasms	1	2	1	

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	519	541	582	597	609	629	635	641	646	653	659	670	672	672	680	698	701	709	712	719	720	722	727	729	729
Carcass ID Number	250	254	265	237	243	247	249	261	264	245	257	221	226	227	228	252	259	234	219	260	229	256	248	230	244
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	A	+	A	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	A	+	A	+	+	+	A	+	+	+	A	A	A	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	A	+	A	+	+	+	A	+	+	A	A	A	A	+	A	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Mesentery							+		+		+		+	+	+		+								
Histiocytic sarcoma														X											
Pancreas	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Squamous cell papilloma																									
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																	X								
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																	X								
Pheochromocytoma complex						X																			
Pheochromocytoma benign											X								X						
Islets, pancreatic	+	+	+	+	+	A	+	+	+	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+
Adenoma																								X	
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X		X	X			X	X	X					X			X		X	X		X		X
Pars distalis, carcinoma																			X						
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
C-cell, adenoma																									
General Body System																									
Tissue NOS																							+		
Abdominal, sarcoma																							X		
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Adenoma																									
Carcinoma																									
Histiocytic sarcoma														X											
Bilateral, carcinoma																									

+: 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 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	217	218	220	223	224	231	240	241	242	246	253	255	258	262	263	216	222	225	232	233	235	236	238	239	251	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Mesentery																	+					+				9
Histiocytic sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue															+				+							2
Squamous cell papilloma															X				X							2
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma																										1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																										1
Pheochromocytoma complex																										1
Pheochromocytoma benign																										2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma		X	X	X		X		X		X	X			X		X	X	X	X	X	X	X		X	X	29
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
C-cell, adenoma						X												X								2
General Body System																										
Tissue NOS																										1
Abdominal, sarcoma																										1
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma	X																									1
Carcinoma										X								X								2
Histiocytic sarcoma																										1
Bilateral, carcinoma																				X					X	2

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	519	541	582	597	609	629	635	641	646	653	659	670	672	672	680	698	701	709	712	719	720	722	727	729	729
Carcass ID Number	250	254	265	237	243	247	249	261	264	245	257	221	226	227	228	252	259	234	219	260	229	256	248	230	244
Genital System (continued)																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal							X		X								X			X			X		
Bilateral, polyp stromal																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+
Lymph node	+		+				+				+	+			+	+	+								
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									X
Fibroadenoma					X	X		X					X		X			X	X			X		X	
Fibroadenoma, multiple		X								X							X			X					
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, histiocytic sarcoma														X											
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve	+																						+		
Spinal cord	+																						+		
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Pheochromocytoma complex, metastatic, adrenal medulla						X																			
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	A	+	+	+	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+
Transitional epithelium, papilloma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Leukemia mononuclear	X		X				X				X	X	X	X	X	X	X					X		X	

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	217	218	220	223	224	231	240	241	242	246	253	255	258	262	263	216	222	225	232	233	235	236	238	239	251	Total Tissues/ Tumors
Genital System (continued)																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal																							X			6
Bilateral, polyp stromal																X										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node												+							+	+						11
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Fibroadenoma	X	X						X	X		X	X				X		X	X	X	X			X		21
Fibroadenoma, multiple			X										X				X					X				8
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma	X																									1
Subcutaneous tissue, fibroma																		X								1
Subcutaneous tissue, histiocytic sarcoma																										1
Subcutaneous tissue, sarcoma													X													1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										2
Spinal cord																										2
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Pheochromocytoma complex, metastatic, adrenal medulla																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Transitional epithelium, papilloma																								X		1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear		X											X	X			X	X	X		X					19

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	217	484	627	636	676	677	678	688	682	691	699	708	708	712	712	716	728	734	734	734	734	734	734	734	734
Carcass ID Number	293	306	280	299	271	266	297	298	273	291	269	276	281	268	284	296	283	267	270	272	274	275	277	278	279
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	A	+	+	+	+	+	+	A	A	+	+	A	A	+	A	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	A	A	+	+	A	A	+	A	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery			+					+													+				
Oral mucosa												+													
Squamous cell carcinoma												X													
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue												+													
Squamous cell carcinoma, metastatic, oral mucosa												X													
Squamous cell papilloma																									
Tooth																									
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																							X		
Pheochromocytoma benign			X																				X		
Bilateral, pheochromocytoma benign							X																		
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma					X	X	X	X	X	X			X			X	X		X		X			X	X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma							X						X			X					X	X			
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma													X		X										
Bilateral, carcinoma																						X			
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal				X				X													X				
Vagina								+		+															

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	
Carcass ID Number	282	285	286	287	288	289	290	292	294	295	300	301	302	303	304	305	307	308	309	310	311	312	313	314	315	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery	+							+	+	+	+		+				+								+	11
Oral mucosa																										1
Squamous cell carcinoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue																						+				2
Squamous cell carcinoma, metastatic, oral mucosa																										1
Squamous cell papilloma																						X				1
Tooth													+													1
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Pheochromocytoma benign																	X				X					4
Bilateral, pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma								X																		1
Carcinoma					X																					1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X		X	X	X	X	X	X	X		X	X	X		X	X		X	X	X		X		30
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma			X								X										X					8
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma					X																					3
Bilateral, carcinoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal														X						X					X	6
Vagina																										2

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	217	484	627	636	667	677	678	688	682	691	699	708	708	712	712	716	728	734	734	734	734	734	734	734	734
Carcass ID Number	293	306	280	299	271	266	297	298	273	291	269	276	281	268	284	296	283	267	270	272	274	275	277	278	279
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Lymph node			+				+			+	+			+	+						+				
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma			X																						
Fibroadenoma			X	X				X			X				X				X			X		X	
Fibroadenoma, multiple						X						X													
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, melanoma malignant																									
Subcutaneous tissue, schwannoma malignant	X																								
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+																								
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve	+																								
Spinal cord	+																								
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Melanoma malignant, metastatic, skin																									
Nose	+	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																+									
Zymbal's gland																+									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Leukemia mononuclear			X	X	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 1-Chloro-2-propanol: 150 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	
Carcass ID Number	282	285	286	287	288	289	290	292	294	295	300	301	302	303	304	305	307	308	309	310	311	312	313	314	315	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																			X							1
Lymph node																			+				+			9
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymoma benign																					X					1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma								X																		1
Carcinoma																										1
Fibroadenoma	X		X			X	X	X			X		X		X		X	X	X		X				X	21
Fibroadenoma, multiple		X			X					X				X		X										7
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, melanoma malignant																		X								1
Subcutaneous tissue, schwannoma malignant																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Melanoma malignant, metastatic, skin																		X								1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Zymbal's gland																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																			X							1
Leukemia mononuclear	X				X				X					X				X		X			X		X	19

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	506	525	528	571	597	608	613	655	659	661	663	668	694	697	708	714	717	718	721	733	734	734	734	734	734
Carcass ID Number	348	353	334	333	354	322	341	323	358	361	316	331	362	342	360	351	324	320	363	350	317	318	319	321	325
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	A	+	+	+	A	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	A	+	+	+	A	+	+	A	+	+	A	A	+	A	+	+	+	+	+
Intestine small, ileum	+	A	+	+	+	+	A	+	+	+	A	+	+	A	+	+	A	A	+	A	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Histiocytic sarcoma										X															
Mesentery			+					+		+			+	+									+		+
Oral mucosa																									
Squamous cell papilloma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																						X			
Islets, pancreatic	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X	X		X	X	X	X		X				X		X	X	X	X		X	X	X	X		X
Pars distalis, histiocytic sarcoma										X															
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																									
C-cell, carcinoma																									
General Body System																									
None																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	735	735	
Carcass ID Number	326	327	328	329	330	332	335	336	337	338	339	340	343	344	345	346	352	355	356	357	359	364	365	347	349	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																				X						1
Histiocytic sarcoma																										1
Mesentery	+														+	+				+		+				12
Oral mucosa														+												1
Squamous cell papilloma														X												1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma	X																									1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X	X	X	X	X	X				X	X		X		X	X	X	X			X			X		32
Pars distalis, histiocytic sarcoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma				X		X						X							X						X	5
C-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 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	506	525	528	571	597	608	613	655	659	661	663	668	694	697	708	714	717	718	721	733	734	734	734	734	734
Carcass ID Number	348	353	334	333	354	322	341	323	358	361	316	331	362	342	360	351	324	320	363	350	317	318	319	321	325
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Adenoma						X																			
Carcinoma																									
Histiocytic sarcoma										X															
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma														X											
Granulosa cell tumor benign																	X								
Granulosa-theca tumor malignant																									
Histiocytic sarcoma										X															
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Polyp stromal			X								X											X			X
Hematopoietic System																									
Bone marrow	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Lymph node		+	+	+				+	+	+	+	+	+			+			+		+				
Mediastinal, histiocytic sarcoma										X															
Pancreatic, histiocytic sarcoma										X															
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Histiocytic sarcoma										X															
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Integumentary System																									
Mammary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma						X																			
Fibroadenoma						X			X	X		X	X		X		X	X			X				X
Fibroadenoma, multiple																			X			X	X		
Histiocytic sarcoma										X															
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma									X																
Subcutaneous tissue, histiocytic sarcoma										X															
Subcutaneous tissue, melanoma malignant														X											
Subcutaneous tissue, sarcoma													X												
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma		X																							
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	735	735	
Carcass ID Number	326	327	328	329	330	332	335	336	337	338	339	340	443	444	445	446	352	355	356	357	359	364	365	347	349	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma												X														2
Carcinoma											X								X							2
Histiocytic sarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma																										1
Granulosa cell tumor benign																										1
Granulosa-theca tumor malignant																		X								1
Histiocytic sarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Polyp stromal							X															X				6
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node																+	+					+				15
Mediastinal, histiocytic sarcoma																										1
Pancreatic, histiocytic sarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma																										1
Fibroadenoma		X	X		X	X			X	X		X	X		X		X	X	X	X		X	X	X		26
Fibroadenoma, multiple							X	X																		5
Histiocytic sarcoma																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibroma																										1
Subcutaneous tissue, histiocytic sarcoma																										1
Subcutaneous tissue, melanoma malignant																										1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	506	525	528	571	597	608	613	655	659	661	663	668	694	697	708	714	717	718	721	733	734	734	734	734	734
Carcass ID Number	348	353	334	333	354	322	341	323	358	361	316	331	362	342	360	351	324	320	363	350	317	318	319	321	325
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Osteosarcoma, metastatic, bone		X																							
Nose	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory epithelium, histiocytic sarcoma										X															
Pleura																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Zymbal's gland								+																	
Carcinoma								X																	
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenchymal tumor malignant																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma										X															
Leukemia mononuclear			X	X				X	X		X	X	X					X	X		X				

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 325 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	735	735	
Carcass ID Number	326	327	328	329	330	332	335	336	337	338	339	340	443	444	445	446	552	555	556	557	559	564	565	447	449	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Respiratory epithelium, histiocytic sarcoma																										1
Pleura			+																							1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesenchymal tumor malignant																									X	1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear	X					X	X		X			X		X		X			X							18

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	449	489	561	562	592	634	639	649	656	668	691	693	698	700	708	714	722	731	733	734	734	734	734	734	734
Carcass ID Number	394	407	387	375	383	406	380	410	381	396	399	392	371	366	384	414	369	395	372	370	374	376	377	378	379
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	+	A	+	A	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									X
Mesentery					+	+			+					+		+		+			+				+
Pancreas	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma										X															
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Squamous cell papilloma																									
Cardiovascular System																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ganglioneuroma			X																						
Pheochromocytoma malignant																								X	
Pheochromocytoma benign												X													
Islets, pancreatic	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X	X			X	X	X		X		X		X	X	X	X		X	X	X	X	X	X	X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																									
C-cell, carcinoma										X															
Follicular cell, adenoma																	X								
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Adenoma								X																	
Carcinoma												X													
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal																		X							

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	735	735	735	735	735	735	
Carcass ID Number	382	388	390	391	393	397	398	400	401	402	403	404	405	408	409	411	412	413	415	367	368	373	385	386	389	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																										1
Mesentery									+		+															10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Acinus, adenoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue	+																									1
Squamous cell papilloma	X																									1
Cardiovascular System																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Ganglioneuroma																										1
Pheochromocytoma malignant																										1
Pheochromocytoma benign																				X	X				X	4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma		X	X	X	X	X	X	X	X	X	X	X				X	X	X			X			X	X	35
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma												X										X	X			3
C-cell, carcinoma																			X							2
Follicular cell, adenoma																										1
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma			X						X											X						4
Carcinoma						X											X									3
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal	X	X							X																	4

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	449	489	561	562	592	634	639	649	656	668	691	693	698	700	708	714	722	731	733	734	734	734	734	734	734
Carcass ID Number	394	407	387	375	383	406	380	410	381	396	399	392	371	366	384	414	369	395	372	370	374	376	377	378	379
Hematopoietic System																									
Bone marrow	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Lymph node					+				+		+	+	+	+				+							
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma			X									X					X		X	X		X		X	
Fibroadenoma, multiple														X				X					X		
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma															X						X				
Subcutaneous tissue, fibrous histiocytoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																							X		
Nose	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																+									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
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 1-Chloro-2-propanol: 650 ppm

Number of Days on Study	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	734	735	735	735	735	735	735	735
Carcass ID Number	382	388	390	391	393	397	398	400	401	402	403	404	405	408	409	411	412	413	415	367	368	373	385	386	389	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma													X													1
Lymph node																										7
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymoma benign				X																						1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroadenoma		X									X		X	X		X								X	X	14
Fibroadenoma, multiple					X		X	X	X			X					X									9
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibroma																										2
Subcutaneous tissue, fibrous histiocytoma																				X						1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																		+								2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papilloma											X															1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma													X													1
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 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	2/49 (4%)	5/50 (10%)	1/50 (2%)	4/50 (8%)
Adjusted rate[b]	4.6%	10.8%	2.3%	8.9%
Terminal rate[c]	0/25 (0%)	3/33 (9%)	1/30 (3%)	3/31 (10%)
First incidence (days)	659	627	734 (T)	693
Poly-3 test[d]	P=0.451	P=0.256	P=0.524N	P=0.370
Adrenal Medulla: Benign, Complex, or Malignant Pheochromocytoma				
Overall rate	4/49 (8%)	5/50 (10%)	1/50 (2%)	5/50 (10%)
Adjusted rate	9.1%	10.8%	2.3%	11.2%
Terminal rate	0/25 (0%)	3/33 (9%)	1/30 (3%)	4/31 (13%)
First incidence (days)	629	627	734 (T)	693
Poly-3 test	P=0.535	P=0.547	P=0.191N	P=0.528
Clitoral Gland: Adenoma				
Overall rate	1/49 (2%)	0/49 (0%)	2/49 (4%)	4/49 (8%)
Adjusted rate	2.3%	0.0%	4.6%	9.1%
Terminal rate	1/25 (4%)	0/32 (0%)	1/29 (3%)	3/31 (10%)
First incidence (days)	734 (T)	—[e]	608	649
Poly-3 test	P=0.039	P=0.539N	P=0.537	P=0.202
Clitoral Gland: Carcinoma				
Overall rate	4/49 (8%)	4/49 (8%)	2/49 (4%)	3/49 (6%)
Adjusted rate	9.3%	8.9%	4.6%	6.9%
Terminal rate	4/25 (16%)	2/32 (6%)	2/29 (7%)	2/31 (7%)
First incidence (days)	734 (T)	708	734 (T)	693
Poly-3 test	P=0.371N	P=0.634N	P=0.354N	P=0.510N
Clitoral Gland: Adenoma or Carcinoma				
Overall rate	5/49 (10%)	4/49 (8%)	4/49 (8%)	7/49 (14%)
Adjusted rate	11.7%	8.9%	9.2%	15.9%
Terminal rate	5/25 (20%)	2/32 (6%)	3/29 (10%)	5/31 (16%)
First incidence (days)	734 (T)	708	608	649
Poly-3 test	P=0.268	P=0.487N	P=0.507N	P=0.413
Mammary Gland: Fibroadenoma				
Overall rate	29/50 (58%)	28/50 (56%)	31/50 (62%)	23/50 (46%)
Adjusted rate	62.1%	59.3%	67.6%	50.6%
Terminal rate	16/25 (64%)	21/33 (64%)	22/30 (73%)	17/31 (55%)
First incidence (days)	541	627	608	561
Poly-3 test	P=0.175N	P=0.479N	P=0.371	P=0.182N
Mammary Gland: Fibroadenoma, Adenoma, or Carcinoma				
Overall rate	30/50 (60%)	28/50 (56%)	31/50 (62%)	23/50 (46%)
Adjusted rate	64.2%	59.3%	67.6%	50.6%
Terminal rate	16/25 (64%)	21/33 (64%)	22/30 (73%)	17/31 (55%)
First incidence (days)	541	627	608	561
Poly-3 test	P=0.133N	P=0.395N	P=0.456	P=0.130N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	29/49 (59%)	30/50 (60%)	32/50 (64%)	35/50 (70%)
Adjusted rate	62.9%	63.6%	66.5%	73.5%
Terminal rate	17/25 (68%)	21/33 (64%)	19/30 (63%)	23/31 (74%)
First incidence (days)	541	676	506	489
Poly-3 test	P=0.132	P=0.565	P=0.444	P=0.185

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rate	30/49 (61%)	30/50 (60%)	32/50 (64%)	35/50 (70%)
Adjusted rate	65.0%	63.6%	66.5%	73.5%
Terminal rate	17/25 (68%)	21/33 (64%)	19/30 (63%)	23/31 (74%)
First incidence (days)	541	676	506	489
Poly-3 test	P=0.173	P=0.537N	P=0.528	P=0.247
Skin (Subcutaneous Tissue): Fibroma, Fibrous Histiocytoma, or Sarcoma				
Overall rate	2/50 (4%)	0/50 (0%)	2/50 (4%)	3/50 (6%)
Adjusted rate	4.6%	0.0%	4.5%	6.7%
Terminal rate	2/25 (8%)	0/33 (0%)	0/30 (0%)	2/31 (6%)
First incidence (days)	734 (T)	—	659	708
Poly-3 test	P=0.235	P=0.254N	P=0.710N	P=0.533
Thyroid Gland (C-cell): Adenoma				
Overall rate	2/50 (4%)	8/50 (16%)	5/50 (10%)	3/50 (6%)
Adjusted rate	4.6%	17.3%	11.3%	6.7%
Terminal rate	2/25 (8%)	5/33 (15%)	5/30 (17%)	3/31 (10%)
First incidence (days)	734 (T)	678	734 (T)	734 (T)
Poly-3 test	P=0.446N	P=0.058	P=0.235	P=0.532
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rate	2/50 (4%)	8/50 (16%)	6/50 (12%)	5/50 (10%)
Adjusted rate	4.6%	17.3%	13.6%	11.2%
Terminal rate	2/25 (8%)	5/33 (15%)	6/30 (20%)	4/31 (13%)
First incidence (days)	734 (T)	678	734 (T)	668
Poly-3 test	P=0.396	P=0.058	P=0.146	P=0.240
Uterus: Stromal Polyp				
Overall rate	7/50 (14%)	6/50 (12%)	6/50 (12%)	4/50 (8%)
Adjusted rate	15.7%	13.0%	13.3%	9.0%
Terminal rate	2/25 (8%)	4/33 (12%)	4/30 (13%)	3/31 (10%)
First incidence (days)	635	636	528	731
Poly-3 test	P=0.230N	P=0.484N	P=0.507N	P=0.274N
All Organs: Mononuclear Cell Leukemia				
Overall rate	19/50 (38%)	19/50 (38%)	18/50 (36%)	13/50 (26%)
Adjusted rate	40.6%	40.1%	38.5%	27.8%
Terminal rate	7/25 (28%)	11/33 (33%)	9/30 (30%)	4/31 (13%)
First incidence (days)	519	627	528	562
Poly-3 test	P=0.099N	P=0.572N	P=0.510N	P=0.141N
All Organs: Benign Neoplasms				
Overall rate	43/50 (86%)	42/50 (84%)	48/50 (96%)	42/50 (84%)
Adjusted rate	89.1%	87.1%	96.6%	88.2%
Terminal rate	23/25 (92%)	28/33 (85%)	29/30 (97%)	29/31 (94%)
First incidence (days)	541	627	506	489
Poly-3 test	P=0.512	P=0.506N	P=0.131	P=0.584N
All Organs: Malignant Neoplasms				
Overall rate	26/50 (52%)	24/50 (48%)	26/50 (52%)	18/50 (36%)
Adjusted rate	54.9%	49.6%	53.9%	38.5%
Terminal rate	10/25 (40%)	14/33 (42%)	13/30 (43%)	9/31 (29%)
First incidence (days)	519	217	525	562
Poly-3 test	P=0.078N	P=0.378N	P=0.548N	P=0.081N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
All Organs: Benign or Malignant Neoplasms				
Overall rate	48/50 (96%)	46/50 (92%)	49/50 (98%)	48/50 (96%)
Adjusted rate	96.0%	93.3%	98.0%	97.5%
Terminal rate	23/25 (92%)	30/33 (91%)	29/30 (97%)	30/31 (97%)
First incidence (days)	519	217	506	489
Poly-3 test	P=0.306	P=0.443N	P=0.500	P=0.560

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, clitoral gland, pituitary gland, thyroid gland, and uterus; 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 are the P values 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 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 B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	150 ppm	325 ppm	650 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	12	7	7	5
Natural deaths	13	10	13	14
Survivors				
Terminal sacrifice	25	33	30	31
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(47)	(49)	(49)	(48)
Dilatation		1 (2%)		
Inflammation, chronic active			1 (2%)	
Parasite metazoan	3 (6%)	2 (4%)	2 (4%)	1 (2%)
Intestine large, rectum	(49)	(49)	(48)	(49)
Parasite metazoan	6 (12%)	4 (8%)	3 (6%)	7 (14%)
Intestine large, cecum	(47)	(49)	(48)	(48)
Dilatation		1 (2%)		
Hemorrhage		1 (2%)		
Inflammation, chronic active			1 (2%)	
Mineralization	1 (2%)			
Parasite metazoan				1 (2%)
Ulcer			1 (2%)	
Intestine small, jejunum	(44)	(44)	(43)	(46)
Hemorrhage		1 (2%)		
Intestine small, ileum	(42)	(45)	(43)	(45)
Hemorrhage		1 (2%)		
Liver	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)	5 (10%)	3 (6%)	7 (14%)
Basophilic focus	29 (58%)	33 (66%)	27 (54%)	32 (64%)
Clear cell focus	3 (6%)	7 (14%)	7 (14%)	2 (4%)
Congestion		2 (4%)		
Deformity	3 (6%)	6 (12%)	3 (6%)	
Eosinophilic focus	6 (12%)	3 (6%)	7 (14%)	4 (8%)
Fibrosis				1 (2%)
Hemorrhage	2 (4%)			
Hepatodiaphragmatic nodule	2 (4%)	3 (6%)	12 (24%)	4 (8%)
Infiltration cellular, lymphocyte	1 (2%)	1 (2%)	1 (2%)	
Inflammation, granulomatous	12 (24%)	5 (10%)	9 (18%)	11 (22%)
Mixed cell focus	4 (8%)	8 (16%)	5 (10%)	6 (12%)
Necrosis	3 (6%)	2 (4%)	5 (10%)	1 (2%)
Pigmentation, bile	1 (2%)			
Vacuolization cytoplasmic	1 (2%)	2 (4%)	3 (6%)	3 (6%)
Artery, thrombosis	1 (2%)			
Bile duct, hyperplasia	1 (2%)			
Centrilobular, necrosis	1 (2%)			
Kupffer cell, pigmentation		1 (2%)		
Mesentery	(9)	(11)	(12)	(10)
Hemorrhage	1 (11%)			
Fat, necrosis	8 (89%)	10 (91%)	11 (92%)	9 (90%)

[a] Number of animals examined microscopically at the site and the 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 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Alimentary System (continued)				
Pancreas	(47)	(49)	(49)	(48)
Infiltration cellular, mixed cell			1 (2%)	
Inflammation, acute		1 (2%)		
Acinus, atrophy	12 (26%)	4 (8%)	3 (6%)	5 (10%)
Acinus, hyperplasia		1 (2%)	1 (2%)	
Salivary glands	(50)	(50)	(50)	(50)
Atrophy		1 (2%)		
Stomach, forestomach	(50)	(50)	(50)	(50)
Inflammation, chronic active	5 (10%)	1 (2%)		3 (6%)
Ulcer	2 (4%)	2 (4%)	3 (6%)	4 (8%)
Epithelium, hyperplasia	4 (8%)	3 (6%)	3 (6%)	3 (6%)
Stomach, glandular	(50)	(50)	(50)	(50)
Inflammation, chronic active	1 (2%)			
Necrosis	12 (24%)	6 (12%)	7 (14%)	7 (14%)
Ulcer			2 (4%)	
Tooth		(1)		
Developmental malformation		1 (100%)		
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	18 (36%)	21 (42%)	15 (30%)	11 (22%)
Hemorrhage				1 (2%)
Inflammation, chronic active	1 (2%)			
Artery, inflammation, chronic active	1 (2%)			
Atrium, inflammation, chronic active		1 (2%)		
Atrium, thrombosis	4 (8%)	2 (4%)	3 (6%)	3 (6%)
Endocrine System				
Adrenal cortex	(49)	(50)	(50)	(50)
Angiectasis	7 (14%)	8 (16%)	9 (18%)	10 (20%)
Cytoplasmic alteration	5 (10%)	3 (6%)	1 (2%)	4 (8%)
Degeneration, cystic		1 (2%)	1 (2%)	
Hemorrhage	2 (4%)	3 (6%)		
Vacuolization cytoplasmic	4 (8%)	5 (10%)	7 (14%)	8 (16%)
Adrenal medulla	(49)	(50)	(50)	(50)
Hyperplasia	5 (10%)		1 (2%)	2 (4%)
Infiltration cellular, lymphocyte	1 (2%)			
Necrosis		1 (2%)		
Islets, pancreatic	(46)	(49)	(48)	(48)
Hyperplasia		1 (2%)		
Metaplasia	1 (2%)			
Parathyroid gland	(50)	(50)	(50)	(49)
Angiectasis		1 (2%)		
Hyperplasia		1 (2%)		
Pituitary gland	(49)	(50)	(50)	(50)
Necrosis				1 (2%)
Pars distalis, angiectasis	1 (2%)		4 (8%)	1 (2%)
Pars distalis, cyst	13 (27%)	11 (22%)	11 (22%)	13 (26%)
Pars distalis, hemorrhage	2 (4%)	1 (2%)		
Pars distalis, hyperplasia	4 (8%)	6 (12%)	6 (12%)	
Pars distalis, pigmentation				1 (2%)
Pars nervosa, cyst		1 (2%)		

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Endocrine System (continued)				
Thyroid gland	(50)	(50)	(50)	(50)
Infiltration cellular, mixed cell	1 (2%)			
Inflammation, chronic active	1 (2%)			
C-cell, hyperplasia	10 (20%)	11 (22%)	6 (12%)	8 (16%)
Follicle, cyst				1 (2%)
General Body System				
None				
Genital System				
Clitoral gland	(49)	(49)	(49)	(49)
Atrophy				2 (4%)
Cyst	4 (8%)	4 (8%)	4 (8%)	6 (12%)
Hyperplasia	1 (2%)	1 (2%)	1 (2%)	
Inflammation, chronic active	3 (6%)		1 (2%)	
Bilateral, cyst			1 (2%)	
Ovary	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)			
Cyst	6 (12%)	4 (8%)	10 (20%)	8 (16%)
Hyperplasia, histiocytic		1 (2%)		
Inflammation, granulomatous			1 (2%)	
Bilateral, cyst	1 (2%)			
Interstitial cell, hyperplasia				1 (2%)
Uterus	(50)	(50)	(50)	(50)
Abscess			1 (2%)	
Cyst		1 (2%)	2 (4%)	
Fibrosis	1 (2%)			
Hemorrhage	1 (2%)	1 (2%)	1 (2%)	
Hydrometra	4 (8%)		3 (6%)	4 (8%)
Hyperplasia, cystic	1 (2%)		1 (2%)	1 (2%)
Inflammation, chronic active		1 (2%)	3 (6%)	
Bilateral, hydrometra				1 (2%)
Epithelium, hyperplasia		1 (2%)		
Vagina		(2)		
Hemorrhage		1 (50%)		
Infiltration cellular, polymorphonuclear		1 (50%)		
Inflammation, chronic active		1 (50%)		
Pigmentation		1 (50%)		
Hematopoietic System				
Bone marrow	(47)	(50)	(47)	(49)
Atrophy				2 (4%)
Fibrosis				1 (2%)
Hyperplasia	1 (2%)	3 (6%)		1 (2%)
Inflammation, chronic active	1 (2%)			
Myeloid cell, hyperplasia	3 (6%)			

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Hematopoietic System (continued)				
Lymph node	(11)	(9)	(15)	(7)
Hemorrhage	1 (9%)	2 (22%)	1 (7%)	
Hyperplasia, lymphoid			1 (7%)	
Pigmentation			1 (7%)	
Deep cervical, hemorrhage	1 (9%)		1 (7%)	
Deep cervical, hyperplasia, plasma cell			1 (7%)	
Deep cervical, pigmentation			1 (7%)	
Iliac, amyloid deposition		1 (11%)		
Iliac, hemorrhage	2 (18%)	1 (11%)		
Iliac, pigmentation		1 (11%)		
Mediastinal, hemorrhage	4 (36%)	2 (22%)	7 (47%)	1 (14%)
Mediastinal, hyperplasia, lymphoid			1 (7%)	
Mediastinal, hyperplasia, plasma cell			1 (7%)	
Mediastinal, inflammation, acute		1 (11%)		
Mediastinal, pigmentation	2 (18%)		5 (33%)	
Pancreatic, hemorrhage	2 (18%)		2 (13%)	1 (14%)
Pancreatic, hyperplasia, histiocytic	1 (9%)		1 (7%)	
Pancreatic, hyperplasia, lymphoid			1 (7%)	
Renal, hemorrhage	3 (27%)	2 (22%)	4 (27%)	1 (14%)
Renal, hyperplasia, histiocytic	1 (9%)			
Renal, pigmentation	1 (9%)	2 (22%)	1 (7%)	1 (14%)
Lymph node, mandibular	(50)	(50)	(50)	(49)
Amyloid deposition		1 (2%)		
Atrophy	1 (2%)			
Ectasia	1 (2%)		1 (2%)	
Hemorrhage	6 (12%)	4 (8%)	4 (8%)	2 (4%)
Hyperplasia, lymphoid	1 (2%)		2 (4%)	
Hyperplasia, plasma cell	1 (2%)		4 (8%)	1 (2%)
Inflammation, chronic active			1 (2%)	
Pigmentation	1 (2%)	1 (2%)		1 (2%)
Lymph node, mesenteric	(50)	(50)	(49)	(50)
Atrophy	2 (4%)			
Hemorrhage	7 (14%)	3 (6%)	6 (12%)	5 (10%)
Hyperplasia, histiocytic		3 (6%)	4 (8%)	2 (4%)
Hyperplasia, lymphoid		1 (2%)		
Pigmentation		1 (2%)	1 (2%)	
Spleen	(50)	(50)	(50)	(49)
Accessory spleen			1 (2%)	
Atrophy	1 (2%)			
Congestion	1 (2%)			
Fibrosis	3 (6%)	2 (4%)	2 (4%)	1 (2%)
Hematopoietic cell proliferation	7 (14%)	2 (4%)	3 (6%)	1 (2%)
Hyperplasia, histiocytic		1 (2%)		
Necrosis				1 (2%)
Pigmentation	7 (14%)	11 (22%)	8 (16%)	10 (20%)
Capsule, cyst				1 (2%)
Capsule, fibrosis				2 (4%)
Thymus	(48)	(49)	(50)	(50)
Atrophy	16 (33%)	10 (20%)	17 (34%)	14 (28%)
Ectopic parathyroid gland	1 (2%)			
Hemorrhage	1 (2%)	1 (2%)	1 (2%)	3 (6%)
Epithelial cell, hyperplasia	7 (15%)	6 (12%)	9 (18%)	4 (8%)

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Integumentary System				
Mammary gland	(50)	(50)	(49)	(50)
Dilatation	34 (68%)	33 (66%)	25 (51%)	27 (54%)
Hyperplasia	20 (40%)	23 (46%)	14 (29%)	19 (38%)
Inflammation, chronic active	1 (2%)			
Pigmentation		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Exudate		1 (2%)		
Inflammation, chronic active		1 (2%)		1 (2%)
Ulcer	1 (2%)			1 (2%)
Subcutaneous tissue, edema		1 (2%)		
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hyperostosis	6 (12%)	7 (14%)	7 (14%)	4 (8%)
Malformation			1 (2%)	
Femur, callus	1 (2%)			
Femur, hyperostosis	2 (4%)		1 (2%)	
Nervous System				
Brain	(50)	(50)	(50)	(50)
Hemorrhage	2 (4%)	2 (4%)	3 (6%)	2 (4%)
Spinal cord	(2)	(1)		
Hemorrhage	1 (50%)			
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion		1 (2%)		
Hemorrhage	1 (2%)		2 (4%)	2 (4%)
Inflammation, acute			1 (2%)	
Inflammation, chronic active	3 (6%)		1 (2%)	2 (4%)
Alveolus, infiltration cellular, histiocyte	1 (2%)		3 (6%)	2 (4%)
Artery, inflammation, chronic active	1 (2%)	1 (2%)		
Mediastinum, necrosis				1 (2%)
Nose	(50)	(48)	(49)	(49)
Foreign body			1 (2%)	
Olfactory epithelium, atrophy			1 (2%)	
Olfactory epithelium, degeneration, hyaline	2 (4%)	9 (19%)	4 (8%)	3 (6%)
Olfactory epithelium, inflammation, chronic active	2 (4%)	2 (4%)		
Respiratory epithelium, degeneration, hyaline	6 (12%)	3 (6%)	8 (16%)	12 (24%)
Respiratory epithelium, hyperplasia	1 (2%)	10 (21%)	1 (2%)	5 (10%)
Respiratory epithelium, inflammation, chronic active	13 (26%)	9 (19%)	18 (37%)	6 (12%)
Respiratory epithelium, thrombosis		1 (2%)		
Special Senses System				
Ear		(1)		(2)
External ear, hyperplasia				1 (50%)
Zymbal's gland		(1)	(1)	
Hyperplasia		1 (100%)		

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	150 ppm	325 ppm	650 ppm
Urinary System				
Kidney	(46)	(49)	(50)	(50)
Casts			1 (2%)	
Cyst	1 (2%)			2 (4%)
Hydronephrosis		1 (2%)		
Infarct	1 (2%)			
Inflammation, acute			1 (2%)	
Inflammation, chronic active	1 (2%)			1 (2%)
Mineralization	24 (52%)	28 (57%)	26 (52%)	30 (60%)
Nephropathy	23 (50%)	23 (47%)	15 (30%)	20 (40%)
Pelvis, mineralization	1 (2%)			
Renal tubule, degeneration, hyaline	1 (2%)		1 (2%)	
Renal tubule, pigmentation	2 (4%)	2 (4%)	4 (8%)	1 (2%)
Transitional epithelium, hyperplasia	1 (2%)			
Urinary bladder	(49)	(50)	(50)	(49)
Dilatation		1 (2%)		

APPENDIX C
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 1-CHLORO-2-PROPANOL

TABLE C1 Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 132

TABLE C2 Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 136

TABLE C3 Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 154

TABLE C4 Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 157

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	250 ppm	500 ppm	1,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental deaths			5	3
Moribund	8		7	4
Natural deaths	2	6	9	4
Survivors				
Terminal sacrifice	40	44	29	39
Animals examined microscopically	50	50	50	50
Alimentary System				
Gallbladder	(45)	(45)	(42)	(47)
Adenoma		1 (2%)		
Intestine large, rectum	(50)	(50)	(50)	(50)
Fibrous histiocytoma, metastatic, skin	1 (2%)			
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)		
Intestine large, cecum	(49)	(50)	(48)	(47)
Intestine small, duodenum	(49)	(49)	(47)	(47)
Intestine small, jejunum	(49)	(49)	(44)	(47)
Liver	(50)	(50)	(50)	(50)
Fibrous histiocytoma		1 (2%)		
Hemangiosarcoma	2 (4%)		1 (2%)	2 (4%)
Hemangiosarcoma, multiple	1 (2%)		1 (2%)	
Hepatoblastoma	6 (12%)	2 (4%)		6 (12%)
Hepatoblastoma, multiple		1 (2%)		
Hepatocellular carcinoma	12 (24%)	6 (12%)	5 (10%)	7 (14%)
Hepatocellular carcinoma, multiple	1 (2%)		1 (2%)	1 (2%)
Hepatocellular adenoma	7 (14%)	13 (26%)	21 (42%)	11 (22%)
Hepatocellular adenoma, multiple	28 (56%)	22 (44%)	13 (26%)	19 (38%)
Histiocytic sarcoma	2 (4%)	1 (2%)		
Pancreas	(50)	(50)	(50)	(50)
Fibrous histiocytoma				1 (2%)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)		
Salivary glands	(50)	(50)	(50)	(50)
Stomach, forestomach	(49)	(50)	(49)	(50)
Squamous cell papilloma	1 (2%)		1 (2%)	1 (2%)
Stomach, glandular	(49)	(50)	(50)	(49)
Mast cell tumor benign			1 (2%)	
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)		
Hemangiosarcoma			1 (2%)	1 (2%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Adenoma				1 (2%)
Capsule, adenoma		1 (2%)	2 (4%)	1 (2%)
Islets, pancreatic	(50)	(50)	(50)	(50)
Adenoma	1 (2%)			2 (4%)
Pituitary gland	(50)	(49)	(49)	(47)
Pars distalis, adenoma		1 (2%)		
Thyroid gland	(50)	(50)	(50)	(50)
C-cell, carcinoma	1 (2%)			
Follicular cell, adenoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
General Body System				
None				
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Histiocytic sarcoma	1 (2%)			
Prostate	(50)	(50)	(49)	(50)
Hemangiosarcoma	1 (2%)			
Seminal vesicle	(50)	(50)	(50)	(50)
Testes	(50)	(50)	(50)	(50)
Interstitial cell, adenoma			2 (4%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hemangiosarcoma	1 (2%)		1 (2%)	1 (2%)
Lymph node	(4)	(5)	(2)	(3)
Fibrous histiocytoma		1 (20%)		
Iliac, fibrous histiocytoma		1 (20%)		
Mediastinal, fibrous histiocytoma		1 (20%)		
Pancreatic, fibrous histiocytoma		1 (20%)		
Renal, fibrous histiocytoma		1 (20%)		1 (33%)
Lymph node, mandibular	(50)	(50)	(50)	(50)
Carcinoma, metastatic, harderian gland			1 (2%)	
Fibrous histiocytoma		1 (2%)		
Lymph node, mesenteric	(49)	(50)	(50)	(50)
Fibrous histiocytoma		1 (2%)		
Hemangiosarcoma			1 (2%)	
Histiocytic sarcoma	1 (2%)			
Spleen	(50)	(50)	(50)	(50)
Fibrous histiocytoma		1 (2%)		1 (2%)
Hemangiosarcoma		1 (2%)	1 (2%)	1 (2%)
Histiocytic sarcoma	1 (2%)			
Thymus	(37)	(47)	(45)	(41)
Thymoma benign		1 (2%)		
Thymoma malignant				1 (2%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Subcutaneous tissue, fibrous histiocytoma	1 (2%)			
Subcutaneous tissue, hemangioma	1 (2%)			
Subcutaneous tissue, hemangiosarcoma	1 (2%)	1 (2%)		
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma	1 (2%)			
Skeletal muscle		(1)		(1)
Hemangiosarcoma		1 (100%)		
Sarcoma				1 (100%)
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	11 (22%)	5 (10%)	4 (8%)	4 (8%)
Alveolar/bronchiolar adenoma, multiple	1 (2%)	3 (6%)		1 (2%)
Alveolar/bronchiolar carcinoma	4 (8%)	2 (4%)	4 (8%)	4 (8%)
Alveolar/bronchiolar carcinoma, multiple		1 (2%)	1 (2%)	
Carcinoma, metastatic, harderian gland			1 (2%)	
Fibrous histiocytoma		1 (2%)		
Hepatoblastoma, metastatic, liver		1 (2%)		1 (2%)
Hepatocellular carcinoma, metastatic, liver	6 (12%)	2 (4%)	1 (2%)	2 (4%)
Histiocytic sarcoma		1 (2%)		
Nose	(50)	(50)	(50)	(50)
Carcinoma, metastatic, harderian gland	1 (2%)		1 (2%)	
Hemangiosarcoma	1 (2%)			
Special Senses System				
Harderian gland	(1)	(5)	(3)	(1)
Adenoma	1 (100%)	4 (80%)	2 (67%)	1 (100%)
Carcinoma	1 (100%)	1 (20%)	1 (33%)	
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Renal tubule, adenoma				1 (2%)
Urinary bladder	(50)	(50)	(49)	(50)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)		
Hemangioma	1 (2%)			
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma	2 (4%)	1 (2%)		
Lymphoma malignant	1 (2%)	1 (2%)		4 (8%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Neoplasm Summary				
Total animals with primary neoplasms[c]	48	44	40	42
Total primary neoplasms	90	80	65	75
Total animals with benign neoplasms	41	39	36	34
Total benign neoplasms	53	52	47	43
Total animals with malignant neoplasms	32	17	15	24
Total malignant neoplasms	37	28	18	32
Total animals with metastatic neoplasms	8	4	2	3
Total metastatic neoplasms	8	7	4	3
Total animals with malignant neoplasms of uncertain primary site		1		

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	220	380	464	501	518	547	578	646	708	714	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729
Carcass ID Number	003	025	024	034	041	049	023	016	045	044	001	004	005	007	008	009	010	011	012	013	014	017	018	019	020
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																									
Intestine large, cecum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma															X										X
Hemangiosarcoma, multiple				X																					
Hepatoblastoma					X	X																			
Hepatocellular carcinoma								X				X	X								X				
Hepatocellular carcinoma, multiple																									
Hepatocellular adenoma			X		X					X			X								X				
Hepatocellular adenoma, multiple											X			X	X	X	X	X		X		X	X	X	
Histiocytic sarcoma																									
Mesentery		+															+								
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																								X	
Stomach, glandular	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																								+	
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, carcinoma																									
Follicular cell, adenoma																		X							
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma									X																
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

+ : 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 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	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	021	022	027	029	030	031	032	033	035	038	039	040	042	043	046	047	002	006	015	026	028	036	037	048	050	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	45
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, skin																	X									1
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Hemangiosarcoma, multiple																										1
Hepatoblastoma							X	X		X													X			6
Hepatocellular carcinoma		X	X	X		X				X		X									X	X				12
Hepatocellular carcinoma, multiple																									X	1
Hepatocellular adenoma													X	X												7
Hepatocellular adenoma, multiple	X	X		X	X	X	X	X	X	X		X				X	X	X		X	X		X	X	X	28
Histiocytic sarcoma											X								X							2
Mesentery										+				+												4
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth			+						+								+									4
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma							X																			1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, carcinoma													X													1
Follicular cell, adenoma																										1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																			X							1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	220	380	464	501	518	547	578	646	708	714	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729
Carcass ID Number	003	025	024	034	041	049	023	016	045	044	001	004	005	007	008	009	010	011	012	013	014	017	018	019	020
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									X
Lymph node		+																						+	
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	M
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrous histiocytoma																									
Subcutaneous tissue, hemangioma																									
Subcutaneous tissue, hemangiosarcoma																									
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma	X																								
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal cord	+																								
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma	X								X			X		X					X			X			X
Alveolar/bronchiolar adenoma, multiple																				X					
Alveolar/bronchiolar carcinoma																X									
Hepatocellular carcinoma, metastatic, liver								X				X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland																	X								
Hemangiosarcoma									X																
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Ear	+																								
Harderian gland																	+								
Adenoma																	X								
Carcinoma																	X								
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urethra							+																		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Lymphoma malignant																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	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	021	022	027	029	030	031	032	033	035	038	039	040	042	043	046	047	002	006	015	026	028	036	037	048	050	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Lymph node					+																			+		4
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma											X															1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma											X															1
Thymus	+	M	M	+	+	+	M	M	+	M	M	M	+	+	+	M	+	+	M	+	+	+	+	+	+	37
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	2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrous histiocytoma																	X									1
Subcutaneous tissue, hemangioma																								X		1
Subcutaneous tissue, hemangiosarcoma																		X								1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X								X					X			X			11
Alveolar/bronchiolar adenoma, multiple																										1
Alveolar/bronchiolar carcinoma		X											X	X												4
Hepatocellular carcinoma, metastatic, liver			X			X						X													X	6
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Hemangiosarcoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Harderian gland																										1
Adenoma																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urethra																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma						X																				1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma											X								X							2
Lymphoma malignant					X																					1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	335	471	645	665	700	710	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729
Carcass ID Number	074	069	095	057	083	089	054	055	056	058	059	060	062	063	065	066	070	071	072	073	076	077	078	080	082
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	A	+	A	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site																									
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hepatoblastoma													X												
Hepatoblastoma, multiple																							X		
Hepatocellular carcinoma	X	X								X															
Hepatocellular adenoma			X					X					X		X		X				X				X
Hepatocellular adenoma, multiple						X	X		X			X		X					X	X		X	X	X	
Histiocytic sarcoma				X																					
Mesentery					+															+					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth							+																		
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site																									
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																									
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Pars distalis, adenoma																		X							
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																				X					
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	
Carcass ID Number	084	085	087	090	091	092	093	097	098	099	051	052	053	061	064	067	068	075	079	081	086	088	094	096	100	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenoma					X																					1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																		X								1
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																		X								1
Hepatoblastoma				X																						2
Hepatoblastoma, multiple																										1
Hepatocellular carcinoma										X						X			X							6
Hepatocellular adenoma						X	X				X					X						X		X		13
Hepatocellular adenoma, multiple	X	X	X					X	X	X		X		X					X	X	X		X			22
Histiocytic sarcoma																										1
Mesentery																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																		X								1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																				+				+		3
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																		X								1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma	X																									1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																										1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	335	471	645	665	700	710	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729
Carcass ID Number	074	069	095	057	083	089	054	055	056	058	059	060	062	063	065	066	070	071	072	073	076	077	078	080	082
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node													+	+						+					
Fibrous histiocytoma																									
Iliac, fibrous histiocytoma																									
Mediastinal, fibrous histiocytoma																									
Pancreatic, fibrous histiocytoma																									
Renal, fibrous histiocytoma																									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangiosarcoma																									
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign															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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangiosarcoma								X																	
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																									
Hemangiosarcoma																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma							X						X					X							
Alveolar/bronchiolar adenoma, multiple										X									X	X					
Alveolar/bronchiolar carcinoma						X																	X		
Alveolar/bronchiolar carcinoma, multiple																									
Fibrous histiocytoma																									
Hepatoblastoma, metastatic, liver																							X		
Hepatocellular carcinoma, metastatic, liver	X																								
Histiocytic sarcoma				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 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	
Carcass ID Number	084	085	087	090	091	092	093	097	098	099	051	052	053	061	064	067	068	075	079	081	086	088	094	096	100	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node									+									+								5
Fibrous histiocytoma																		X								1
Iliac, fibrous histiocytoma																		X								1
Mediastinal, fibrous histiocytoma																		X								1
Pancreatic, fibrous histiocytoma																		X								1
Renal, fibrous histiocytoma																		X								1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																		X								1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																		X								1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																		X								1
Hemangiosarcoma									X																	1
Thymus	+	+	+	+	+	+	+	+	+	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	47
Thymoma benign																										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	5
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, hemangiosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle											+															1
Hemangiosarcoma											X															1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma					X																	X				5
Alveolar/bronchiolar adenoma, multiple																										3
Alveolar/bronchiolar carcinoma																										2
Alveolar/bronchiolar carcinoma, multiple																			X							1
Fibrous histiocytoma																		X								1
Hepatoblastoma, metastatic, liver																										1
Hepatocellular carcinoma, metastatic, liver																			X							2
Histiocytic sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland									+			+		+			+									5
Adenoma									X			X					X									4
Carcinoma														X												1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	335	471	645	665	700	710	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729
Carcass ID Number	074	069	095	057	083	089	054	055	056	058	059	060	062	063	065	066	070	071	072	073	076	077	078	080	082
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Lymphoma malignant														X											

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	
Carcass ID Number	084	085	087	090	091	092	093	097	098	099	051	052	053	061	064	067	068	075	079	081	086	088	094	096	010	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																		X								1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant																										1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	079	092	180	189	377	408	458	458	484	511	519	519	602	607	608	625	637	638	645	700	714	729	729	729	729
Carcass ID Number	102	143	145	140	137	116	103	122	126	138	131	139	147	105	110	104	141	107	132	150	121	101	106	108	109
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	+	+	+	+	A	+	+	+	+	M	+	+	A	+	A	+	+	M	A	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma													X												
Hemangiosarcoma, multiple																									X
Hepatocellular carcinoma							X				X			X	X										
Hepatocellular carcinoma, multiple																			X						
Hepatocellular adenoma					X					X	X	X		X		X		X		X		X			
Hepatocellular adenoma, multiple								X					X								X		X		X
Mesentery																									+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mast cell tumor benign																									
Tooth																									
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma													X												
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																									
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis									+																
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 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	730	
Carcass ID Number	111	112	113	114	115	117	118	119	120	123	124	125	127	128	129	130	133	134	135	136	142	144	146	148	149	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	42
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Hemangiosarcoma, multiple																										1
Hepatocellular carcinoma		X																								5
Hepatocellular carcinoma, multiple																										1
Hepatocellular adenoma		X		X		X			X	X	X			X		X	X	X				X	X			21
Hepatocellular adenoma, multiple			X		X								X		X				X	X				X	X	13
Mesentery					+		+								+		+								+	6
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell papilloma														X												1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mast cell tumor benign				X																						1
Tooth		+					+				+		+													4
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma												X						X								2
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																	X									1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Penis				+																						2
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell, adenoma									X										X							2

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	079	092	180	189	377	408	458	458	484	511	519	519	602	607	608	625	637	638	645	700	714	729	729	729	729
Carcass ID Number	102	143	145	140	137	116	103	122	126	138	131	139	147	105	110	104	141	107	132	150	121	101	106	108	109
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma													X												
Lymph node																									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland															X										
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																							X		
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma										X															X
Alveolar/bronchiolar carcinoma												X									X				
Alveolar/bronchiolar carcinoma, multiple																	X								
Carcinoma, metastatic, harderian gland															X										
Hepatocellular carcinoma, metastatic, liver														X											
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland															X										
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland															+										
Adenoma																									
Carcinoma															X										
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	730	
Carcass ID Number	111	112	113	114	115	117	118	119	120	123	124	125	127	128	129	130	133	134	135	136	142	144	146	148	149	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Lymph node																+				+						2
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma														X												1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Thymus	M	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
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
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																		X	X							4
Alveolar/bronchiolar carcinoma																X									X	4
Alveolar/bronchiolar carcinoma, multiple																										1
Carcinoma, metastatic, harderian gland																										1
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland								+									+									3
Adenoma								X									X									2
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 ppm

Number of Days on Study	233	246	443	543	556	568	617	645	652	657	700	729	729	729	729	729	729	729	729	729	729	729	729	729	729
Carcass ID Number	152	180	190	163	177	172	183	153	186	191	156	151	154	155	157	158	159	160	161	162	164	165	166	168	171
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	M	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																			X						
Hepatoblastoma						X			X										X		X		X		
Hepatocellular carcinoma							X		X	X	X		X												
Hepatocellular carcinoma, multiple																									
Hepatocellular adenoma							X			X	X			X	X										
Hepatocellular adenoma, multiple					X	X						X				X	X					X			X
Mesentery						+	+			+									+		+	+			+
Oral mucosa																				+					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Stomach, glandular	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth															+							+			
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma															X										
Capsule, adenoma				X																					
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma								X																	
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 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	
Carcass ID Number	173	175	176	178	179	181	182	184	187	188	189	193	194	197	198	199	200	167	169	170	174	185	192	195	196	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma													X													2
Hepatoblastoma					X																					6
Hepatocellular carcinoma											X														X	7
Hepatocellular carcinoma, multiple						X																				1
Hepatocellular adenoma										X	X	X			X	X			X							11
Hepatocellular adenoma, multiple			X			X	X	X	X				X	X			X				X		X	X	X	19
Mesentery										+																8
Oral mucosa																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																					X					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma														X												1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth			+	+					+									+					+			7
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma		X																								1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Capsule, adenoma																										1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																		X								2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																					X					1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 ppm

Number of Days on Study	233	246	443	543	556	568	617	645	652	657	700	729	729	729	729	729	729	729	729	729	729	729	729	729	729
Carcass ID Number	152	180	190	163	177	172	183	153	186	191	156	151	154	155	157	158	159	160	161	162	164	165	166	168	171
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph node														+											
Renal, fibrous histiocytoma																									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangiosarcoma																									
Thymus	+	+	+	+	+	+	M	+	M	+	+	M	M	+	+	+	M	+	+	+	+	+	M	+	+
Thymoma malignant																									
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																									
Sarcoma																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma						X															X	X			
Alveolar/bronchiolar adenoma, multiple																	X								
Alveolar/bronchiolar carcinoma				X									X			X									
Hepatoblastoma, metastatic, liver																					X				
Hepatocellular carcinoma, metastatic, liver									X																
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear								+																	
Harderian gland																+									
Adenoma																X									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant							X							X											

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 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	
Carcass ID Number	173	175	176	178	179	181	182	184	187	188	189	193	194	197	198	199	200	167	169	170	174	185	192	195	196	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																		X								1
Lymph node																			+		+					3
Renal, fibrous histiocytoma																					X					1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																					X					1
Hemangiosarcoma																		X								1
Thymus	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	41
Thymoma malignant	X																									1
Integumentary System																										
Mammary gland	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																				+						1
Sarcoma																				X						1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma														X												4
Alveolar/bronchiolar adenoma, multiple																										1
Alveolar/bronchiolar carcinoma						X																				4
Hepatoblastoma, metastatic, liver																										1
Hepatocellular carcinoma, metastatic, liver						X																				2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Harderian gland																										1
Adenoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenoma															X											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant									X										X							4

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Harderian Gland: Adenoma				
Overall rate[a]	1/50 (2%)	4/50 (8%)	2/50 (4%)	1/50 (2%)
Adjusted rate[b]	2.2%	8.4%	5.3%	2.3%
Terminal rate[c]	1/40 (3%)	4/44 (9%)	2/29 (7%)	1/39 (3%)
First incidence (days)	729 (T)	729 (T)	729 (T)	729 (T)
Poly-3 test[d]	P=0.428N	P=0.211	P=0.494	P=0.786
Harderian Gland: Adenoma or Carcinoma				
Overall rate	1/50 (2%)	5/50 (10%)	3/50 (6%)	1/50 (2%)
Adjusted rate	2.2%	10.5%	7.9%	2.3%
Terminal rate	1/40 (3%)	5/44 (11%)	2/29 (7%)	1/39 (3%)
First incidence (days)	729 (T)	729 (T)	608	729 (T)
Poly-3 test	P=0.393N	P=0.125	P=0.288	P=0.786
Liver: Hemangiosarcoma				
Overall rate	3/50 (6%)	0/50 (0%)	2/50 (4%)	2/50 (4%)
Adjusted rate	6.6%	0.0%	5.3%	4.5%
Terminal rate	2/40 (5%)	0/44 (0%)	1/29 (3%)	2/39 (5%)
First incidence (days)	501	—[e]	602	729 (T)
Poly-3 test	P=0.613	P=0.119N	P=0.620N	P=0.532N
Liver: Hepatocellular Adenoma				
Overall rate	35/50 (70%)	35/50 (70%)	34/50 (68%)	30/50 (60%)
Adjusted rate	76.0%	72.9%	79.6%	65.1%
Terminal rate	32/40 (80%)	33/44 (75%)	23/29 (79%)	25/39 (64%)
First incidence (days)	464	645	377	556
Poly-3 test	P=0.151N	P=0.460N	P=0.451	P=0.176N
Liver: Hepatocellular Carcinoma				
Overall rate	13/50 (26%)	6/50 (12%)	6/50 (12%)	8/50 (16%)
Adjusted rate	29.0%	12.2%	15.0%	17.7%
Terminal rate	12/40 (30%)	4/44 (9%)	1/29 (3%)	4/39 (10%)
First incidence (days)	646	335	458	617
Poly-3 test	P=0.228N	P=0.038N	P=0.109N	P=0.159N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	39/50 (78%)	38/50 (76%)	37/50 (74%)	32/50 (64%)
Adjusted rate	84.2%	76.5%	83.8%	69.0%
Terminal rate	35/40 (88%)	34/44 (77%)	23/29 (79%)	26/39 (67%)
First incidence (days)	464	335	377	556
Poly-3 test	P=0.068N	P=0.247N	P=0.608N	P=0.064N
Liver: Hepatoblastoma				
Overall rate	6/50 (12%)	3/50 (6%)	0/50 (0%)	6/50 (12%)
Adjusted rate	13.1%	6.3%	0.0%	13.3%
Terminal rate	4/40 (10%)	3/44 (7%)	0/29 (0%)	4/39 (10%)
First incidence (days)	518	729 (T)	—	568
Poly-3 test	P=0.483	P=0.231N	P=0.037N	P=0.621
Liver: Hepatocellular Carcinoma or Hepatoblastoma				
Overall rate	18/50 (36%)	9/50 (18%)	6/50 (12%)	13/50 (26%)
Adjusted rate	39.0%	18.3%	15.0%	28.4%
Terminal rate	15/40 (38%)	7/44 (16%)	1/29 (3%)	8/39 (21%)
First incidence (days)	518	335	458	568
Poly-3 test	P=0.280N	P=0.020N	P=0.012N	P=0.199N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma				
Overall rate	40/50 (80%)	39/50 (78%)	37/50 (74%)	36/50 (72%)
Adjusted rate	85.3%	78.6%	83.8%	77.6%
Terminal rate	35/40 (88%)	35/44 (80%)	23/29 (79%)	30/39 (77%)
First incidence (days)	464	335	377	556
Poly-3 test	P=0.271N	P=0.277N	P=0.549N	P=0.245N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	12/50 (24%)	8/50 (16%)	4/50 (8%)	5/50 (10%)
Adjusted rate	26.3%	16.8%	10.5%	11.2%
Terminal rate	10/40 (25%)	8/44 (18%)	3/29 (10%)	4/39 (10%)
First incidence (days)	220	729 (T)	511	568
Poly-3 test	P=0.040N	P=0.199N	P=0.067N	P=0.059N
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	4/50 (8%)	3/50 (6%)	5/50 (10%)	4/50 (8%)
Adjusted rate	9.0%	6.3%	13.0%	8.9%
Terminal rate	4/40 (10%)	2/44 (5%)	2/29 (7%)	3/39 (8%)
First incidence (days)	729 (T)	710	519	543
Poly-3 test	P=0.487	P=0.477N	P=0.438	P=0.656N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	16/50 (32%)	11/50 (22%)	9/50 (18%)	9/50 (18%)
Adjusted rate	35.1%	23.1%	23.0%	19.8%
Terminal rate	14/40 (35%)	10/44 (23%)	5/29 (17%)	7/39 (18%)
First incidence (days)	220	710	511	543
Poly-3 test	P=0.087N	P=0.150N	P=0.177N	P=0.084N
All Organs: Hemangiosarcoma				
Overall rate	5/50 (10%)	3/50 (6%)	4/50 (8%)	4/50 (8%)
Adjusted rate	11.0%	6.3%	10.6%	9.0%
Terminal rate	3/40 (8%)	3/44 (7%)	3/29 (10%)	4/39 (10%)
First incidence (days)	501	729 (T)	602	729 (T)
Poly-3 test	P=0.548N	P=0.340N	P=0.641N	P=0.531N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	7/50 (14%)	3/50 (6%)	4/50 (8%)	4/50 (8%)
Adjusted rate	15.4%	6.3%	10.6%	9.0%
Terminal rate	5/40 (13%)	3/44 (7%)	3/29 (10%)	4/39 (10%)
First incidence (days)	501	729 (T)	602	729 (T)
Poly-3 test	P=0.324N	P=0.144N	P=0.400N	P=0.287N
All Organs: Malignant Lymphoma				
Overall rate	1/50 (2%)	1/50 (2%)	0/50 (0%)	4/50 (8%)
Adjusted rate	2.2%	2.1%	0.0%	9.0%
Terminal rate	1/40 (3%)	1/44 (2%)	0/29 (0%)	3/39 (8%)
First incidence (days)	729 (T)	729 (T)	—	617
Poly-3 test	P=0.057	P=0.765N	P=0.627N	P=0.194
All Organs: Benign Neoplasms				
Overall rate	41/50 (82%)	39/50 (78%)	36/50 (72%)	34/50 (68%)
Adjusted rate	87.1%	81.2%	84.3%	72.3%
Terminal rate	36/40 (90%)	37/44 (84%)	25/29 (86%)	27/39 (69%)
First incidence (days)	220	645	377	543
Poly-3 test	P=0.044N	P=0.307N	P=0.485N	P=0.058N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
All Organs: Malignant Neoplasms				
Overall rate	32/50 (64%)	17/50 (34%)	15/50 (30%)	24/50 (48%)
Adjusted rate	66.9%	34.3%	36.2%	51.7%
Terminal rate	26/40 (65%)	13/44 (30%)	6/29 (21%)	18/39 (46%)
First incidence (days)	220	335	458	543
Poly-3 test	P=0.237N	P < 0.001N	P=0.003N	P=0.098N
All Organs: Benign or Malignant Neoplasms				
Overall rate	48/50 (96%)	44/50 (88%)	40/50 (80%)	42/50 (84%)
Adjusted rate	98.7%	88.2%	89.9%	88.8%
Terminal rate	40/40 (100%)	39/44 (89%)	25/29 (86%)	34/39 (87%)
First incidence (days)	220	335	377	543
Poly-3 test	P=0.106N	P=0.039N	P=0.068N	P=0.048N

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for liver and lung; for other tissues, denominator is number of animals necropsied.
[b] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the control incidence are the P values 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 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 C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	250 ppm	500 ppm	1,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental deaths			5	3
Moribund	8		7	4
Natural deaths	2	6	9	4
Survivors				
Terminal sacrifice	40	44	29	39
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(50)	(50)	(49)	(49)
Serosa, inflammation, chronic		1 (2%)		
Intestine large, cecum	(49)	(50)	(48)	(47)
Serosa, inflammation, chronic		1 (2%)		
Intestine small, jejunum	(49)	(49)	(44)	(47)
Diverticulum	1 (2%)			
Liver	(50)	(50)	(50)	(50)
Angiectasis		1 (2%)		1 (2%)
Clear cell focus	2 (4%)	11 (22%)	6 (12%)	3 (6%)
Eosinophilic focus	27 (54%)	34 (68%)	33 (66%)	29 (58%)
Erythrophagocytosis		1 (2%)		
Inflammation, chronic	2 (4%)	1 (2%)		1 (2%)
Mixed cell focus	2 (4%)	5 (10%)	1 (2%)	3 (6%)
Necrosis	6 (12%)	3 (6%)	1 (2%)	3 (6%)
Vacuolization cytoplasmic			1 (2%)	2 (4%)
Hepatocyte, centrilobular, vacuolization cytoplasmic				1 (2%)
Mesentery	(4)	(2)	(6)	(8)
Fat, necrosis	4 (100%)	2 (100%)	6 (100%)	8 (100%)
Pancreas	(50)	(50)	(50)	(50)
Hemorrhage				1 (2%)
Inflammation, chronic		1 (2%)		
Acinus, atrophy	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Duct, cyst	2 (4%)			
Duct, hemorrhage	1 (2%)			
Duct, inflammation, chronic	1 (2%)			
Salivary glands	(50)	(50)	(50)	(50)
Metaplasia, squamous				1 (2%)
Stomach, forestomach	(49)	(50)	(49)	(50)
Angiectasis	1 (2%)			
Hyperplasia, squamous	4 (8%)	3 (6%)		2 (4%)
Inflammation, chronic	1 (2%)			
Ulcer				1 (2%)
Serosa, inflammation, acute		1 (2%)		
Stomach, glandular	(49)	(50)	(50)	(49)
Cyst		1 (2%)		1 (2%)
Erosion	3 (6%)	1 (2%)	1 (2%)	2 (4%)
Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Inflammation, chronic	1 (2%)			1 (2%)
Metaplasia, squamous	1 (2%)			
Ulcer	1 (2%)			
Glands, hyperplasia		1 (2%)		

[a] Number of animals examined microscopically at the site and the 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 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Alimentary System (continued)				
Tooth	(4)	(3)	(4)	(7)
Degeneration	4 (100%)	3 (100%)	4 (100%)	7 (100%)
Inflammation, chronic active	1 (25%)			
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	6 (12%)	2 (4%)	2 (4%)	2 (4%)
Mineralization	2 (4%)			
Atrium, thrombosis				1 (2%)
Valve, inflammation, acute				1 (2%)
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Hemorrhage				1 (2%)
Hyperplasia			2 (4%)	
Hypertrophy, focal	18 (36%)	25 (50%)	21 (42%)	17 (34%)
Capsule, hyperplasia	39 (78%)	42 (84%)	38 (76%)	38 (76%)
Adrenal medulla	(50)	(50)	(50)	(50)
Hemorrhage		1 (2%)		
Islets, pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	48 (96%)	47 (94%)	45 (90%)	47 (94%)
Pituitary gland	(50)	(49)	(49)	(47)
Pars distalis, cyst	2 (4%)	3 (6%)	2 (4%)	
Pars distalis, hyperplasia	1 (2%)			
Thyroid gland	(50)	(50)	(50)	(50)
Cyst	1 (2%)			3 (6%)
Follicular cell, hyperplasia	6 (12%)	9 (18%)	3 (6%)	5 (10%)
General Body System				
None				
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Granuloma sperm	1 (2%)			
Hemorrhage		1 (2%)		
Inflammation, chronic	1 (2%)	3 (6%)		3 (6%)
Spermatocele		2 (4%)	1 (2%)	
Penis			(2)	
Congestion			1 (50%)	
Preputial gland	(50)	(50)	(50)	(50)
Atrophy		1 (2%)		1 (2%)
Cyst	30 (60%)	33 (66%)	26 (52%)	30 (60%)
Inflammation, acute			1 (2%)	
Inflammation, chronic	1 (2%)	7 (14%)	5 (10%)	5 (10%)
Inflammation, chronic active	6 (12%)	6 (12%)	4 (8%)	7 (14%)
Pigmentation	1 (2%)			
Prostate	(50)	(50)	(49)	(50)
Inflammation, acute			1 (2%)	
Inflammation, chronic	3 (6%)	1 (2%)		3 (6%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Genital System (continued)				
Seminal vesicle	(50)	(50)	(50)	(50)
Atrophy				1 (2%)
Hypertrophy		1 (2%)		1 (2%)
Inflammation, chronic	3 (6%)	9 (18%)	8 (16%)	1 (2%)
Inflammation, chronic active				1 (2%)
Mineralization				1 (2%)
Testes	(50)	(50)	(50)	(50)
Germinal epithelium, degeneration		1 (2%)	1 (2%)	2 (4%)
Interstitial cell, hyperplasia			1 (2%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)			
Hyperplasia, mast cell		1 (2%)		
Myeloid cell, hyperplasia		2 (4%)		
Lymph node	(4)	(5)	(2)	(3)
Infiltration cellular, plasma cell		1 (20%)		
Iliac, infiltration cellular, plasma cell		1 (20%)		
Iliac, infiltration cellular, histiocyte	1 (25%)			
Iliac, pigmentation	3 (75%)	1 (20%)		
Inguinal, hyperplasia, lymphoid		1 (20%)		
Mediastinal, hyperplasia, lymphoid			1 (50%)	
Mediastinal, infiltration cellular, plasma cell		1 (20%)		
Mediastinal, pigmentation	1 (25%)			
Renal, angiectasis		1 (20%)		
Renal, hyperplasia, lymphoid			1 (50%)	
Lymph node, mandibular	(50)	(50)	(50)	(50)
Hyperplasia, lymphoid	2 (4%)	1 (2%)	1 (2%)	
Infiltration cellular, plasma cell		1 (2%)	1 (2%)	1 (2%)
Lymph node, mesenteric	(49)	(50)	(50)	(50)
Angiectasis	7 (14%)	8 (16%)	3 (6%)	5 (10%)
Hemorrhage	1 (2%)			
Hyperplasia, lymphoid	1 (2%)	1 (2%)		
Spleen	(50)	(50)	(50)	(50)
Hematopoietic cell proliferation	9 (18%)	8 (16%)	5 (10%)	6 (12%)
Hyperplasia, lymphoid	1 (2%)	3 (6%)		
Lymphoid follicle, atrophy			2 (4%)	
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Epidermis, cyst	1 (2%)			
Epidermis, necrosis			1 (2%)	
Subcutaneous tissue, edema		1 (2%)		
Subcutaneous tissue, hemorrhage		1 (2%)	1 (2%)	
Subcutaneous tissue, inflammation, acute			1 (2%)	
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Callus		1 (2%)		
Fibrous osteodystrophy				1 (2%)
Hyperostosis		1 (2%)		

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Nervous System				
Brain	(50)	(50)	(50)	(50)
Demyelination				1 (2%)
Hemorrhage			1 (2%)	
Thalamus, mineralization	30 (60%)	25 (50%)	23 (46%)	26 (52%)
Spinal cord	(1)			
Demyelination	1 (100%)			
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Hemorrhage		2 (4%)	1 (2%)	2 (4%)
Infiltration cellular, histiocyte	2 (4%)	2 (4%)	4 (8%)	5 (10%)
Inflammation, chronic				2 (4%)
Leukocytosis		1 (2%)		
Necrosis	1 (2%)			
Alveolar epithelium, hyperplasia	5 (10%)	5 (10%)	2 (4%)	3 (6%)
Nose	(50)	(50)	(50)	(50)
Foreign body	1 (2%)			
Inflammation, acute	4 (8%)			1 (2%)
Glands, amyloid deposition	1 (2%)			
Nasolacrimal duct, inflammation, acute	1 (2%)			
Special Senses System				
None				
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Cyst	11 (22%)	13 (26%)	10 (20%)	15 (30%)
Hemorrhage	1 (2%)			
Hydronephrosis	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Inflammation, acute				1 (2%)
Mineralization			5 (10%)	2 (4%)
Nephropathy, acute	1 (2%)	1 (2%)	6 (12%)	1 (2%)
Nephropathy, chronic	43 (86%)	45 (90%)	38 (76%)	46 (92%)
Arteriole, thrombosis				1 (2%)
Papilla, necrosis			1 (2%)	
Pelvis, calculus microscopic observation only			1 (2%)	
Renal tubule, hyperplasia	4 (8%)			1 (2%)
Transitional epithelium, hyperplasia				1 (2%)
Urethra	(1)			
Inflammation, acute	1 (100%)			
Urinary bladder	(50)	(50)	(49)	(50)
Calculus, gross observation				1 (2%)
Calculus, microscopic observation only	1 (2%)			
Hemorrhage	1 (2%)			
Inflammation, acute	1 (2%)		3 (6%)	1 (2%)
Inflammation, chronic	1 (2%)			

APPENDIX D
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 1-CHLORO-2-PROPANOL

TABLE D1	Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol	163
TABLE D2	Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol	168
TABLE D3	Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol	190
TABLE D4	Historical Incidence of Liver Neoplasms in Untreated Female B6C3F$_1$ Mice	193
TABLE D5	Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol	194

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	250 ppm	500 ppm	1,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental deaths	3		1	2
Moribund	8	7	3	5
Natural deaths	7	11	10	11
Survivors				
Terminal sacrifice	32	32	36	32
Animals examined microscopically	50	50	50	50
Alimentary System				
Esophagus	(50)	(50)	(50)	(50)
Gallbladder	(42)	(44)	(45)	(40)
Carcinoma, metastatic, uncertain primary site		1 (2%)		
Carcinoma, metastatic, urinary bladder			1 (2%)	
Histiocytic sarcoma	1 (2%)			
Intestine large, cecum	(44)	(46)	(48)	(49)
Intestine small, duodenum	(43)	(46)	(46)	(47)
Intestine small, jejunum	(46)	(45)	(47)	(46)
Carcinoma	1 (2%)			
Leiomyosarcoma, metastatic, uncertain primary site			1 (2%)	
Intestine small, ileum	(46)	(44)	(45)	(45)
Liver	(50)	(50)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung				1 (2%)
Carcinoma, metastatic, uncertain primary site		1 (2%)		
Carcinoma, metastatic, urinary bladder			1 (2%)	
Carcinoma, metastatic, intestine small, jejunum	1 (2%)			
Fibrous histiocytoma, metastatic, uncertain primary site			1 (2%)	
Hemangiosarcoma	1 (2%)		1 (2%)	1 (2%)
Hepatoblastoma		1 (2%)	1 (2%)	1 (2%)
Hepatocellular carcinoma	6 (12%)	9 (18%)	7 (14%)	9 (18%)
Hepatocellular carcinoma, multiple			2 (4%)	1 (2%)
Hepatocellular adenoma	12 (24%)	12 (24%)	10 (20%)	10 (20%)
Hepatocellular adenoma, multiple	28 (56%)	27 (54%)	32 (64%)	30 (60%)
Histiocytic sarcoma	2 (4%)	1 (2%)	2 (4%)	
Leiomyosarcoma, metastatic, uncertain primary site			1 (2%)	
Lipoma		1 (2%)		
Mesentery	(20)	(19)	(16)	(12)
Carcinoma, metastatic, uncertain primary site		2 (11%)		
Carcinoma, metastatic, urinary bladder			1 (6%)	
Carcinoma, metastatic, intestine small, jejunum	1 (5%)			
Hemangioma		1 (5%)		
Hemangiosarcoma, metastatic, uterus	1 (5%)			
Histiocytic sarcoma	1 (5%)		1 (6%)	

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Alimentary System (continued)				
Pancreas	(50)	(50)	(50)	(50)
Carcinoma, metastatic, uncertain primary site		2 (4%)		
Carcinoma, metastatic, urinary bladder			1 (2%)	
Fibrous histiocytoma, metastatic, uncertain primary site			1 (2%)	
Histiocytic sarcoma	1 (2%)			
Leiomyosarcoma, metastatic, uncertain primary site			1 (2%)	
Acinus, adenoma		1 (2%)		
Salivary glands	(50)	(50)	(49)	(50)
Stomach, forestomach	(50)	(50)	(50)	(50)
Carcinoma, metastatic, urinary bladder			1 (2%)	
Squamous cell papilloma	1 (2%)	1 (2%)		
Stomach, glandular	(50)	(50)	(48)	(50)
Carcinoma, metastatic, uncertain primary site		1 (2%)		
Carcinoma, metastatic, urinary bladder			1 (2%)	
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung	1 (2%)			1 (2%)
Histiocytic sarcoma		1 (2%)		
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Adenoma		1 (2%)		
Histiocytic sarcoma	1 (2%)			
Adrenal medulla	(50)	(50)	(50)	(50)
Pheochromocytoma malignant	1 (2%)			
Islets, pancreatic	(50)	(50)	(50)	(50)
Adenoma	1 (2%)			
Pituitary gland	(49)	(49)	(47)	(46)
Pars distalis, adenoma	6 (12%)	5 (10%)	3 (6%)	4 (9%)
Pars intermedia, adenoma		1 (2%)	1 (2%)	
Thyroid gland	(50)	(50)	(50)	(50)
Follicular cell, adenoma	1 (2%)	2 (4%)	1 (2%)	
General Body System				
Tissue NOS	(3)	(1)	(2)	
Histiocytic sarcoma	1 (33%)			
Leiomyosarcoma, metastatic, uncertain primary site			1 (50%)	
Pelvic, hemangiosarcoma	1 (33%)			

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Genital System				
Clitoral gland	(50)	(49)	(48)	(49)
Histiocytic sarcoma			1 (2%)	
Ovary	(50)	(49)	(50)	(50)
Carcinoma, metastatic, uncertain primary site		1 (2%)		
Carcinoma, metastatic, urinary bladder			1 (2%)	
Cystadenoma	1 (2%)		1 (2%)	2 (4%)
Granulosa cell tumor benign	1 (2%)			
Granulosa-theca tumor benign				1 (2%)
Hemangioma	1 (2%)	1 (2%)		
Histiocytic sarcoma	1 (2%)	1 (2%)	2 (4%)	
Uterus	(50)	(50)	(50)	(50)
Hemangioma				1 (2%)
Hemangiosarcoma	1 (2%)		1 (2%)	
Histiocytic sarcoma	1 (2%)	1 (2%)	2 (4%)	
Polyp stromal	1 (2%)	2 (4%)	1 (2%)	
Sarcoma stromal	1 (2%)	1 (2%)		1 (2%)
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hemangiosarcoma		1 (2%)		
Histiocytic sarcoma	1 (2%)		1 (2%)	
Lymph node	(8)	(12)	(15)	(9)
Histiocytic sarcoma	1 (13%)			
Deep cervical, histiocytic sarcoma	1 (13%)			
Iliac, hemangiosarcoma		1 (8%)		
Iliac, hemangiosarcoma, metastatic, uterus	1 (13%)			
Iliac, histiocytic sarcoma	2 (25%)	1 (8%)		
Inguinal, histiocytic sarcoma	1 (13%)			
Mediastinal, histiocytic sarcoma	1 (13%)	1 (8%)		
Pancreatic, fibrous histiocytoma, metastatic, uncertain primary site			1 (7%)	
Pancreatic, histiocytic sarcoma	1 (13%)			
Renal, histiocytic sarcoma	1 (13%)		1 (7%)	
Lymph node, mandibular	(50)	(49)	(49)	(50)
Carcinoma, metastatic, harderian gland	1 (2%)			
Carcinoma, metastatic, urinary bladder			1 (2%)	
Histiocytic sarcoma	1 (2%)	1 (2%)		
Lymph node, mesenteric	(49)	(48)	(47)	(49)
Fibrous histiocytoma, metastatic, uncertain primary site			1 (2%)	
Hemangioma			1 (2%)	
Histiocytic sarcoma	2 (4%)	1 (2%)	2 (4%)	
Leiomyosarcoma, metastatic, uncertain primary site			1 (2%)	
Spleen	(49)	(50)	(50)	(50)
Fibrous histiocytoma, metastatic, uncertain primary site			1 (2%)	
Hemangiosarcoma	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Histiocytic sarcoma	1 (2%)			
Thymus	(48)	(48)	(45)	(49)
Carcinoma, metastatic, harderian gland		1 (2%)		

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Subcutaneous tissue, fibrosarcoma		1 (2%)	1 (2%)	1 (2%)
Subcutaneous tissue, fibrosarcoma, multiple	1 (2%)			
Subcutaneous tissue, fibrous histiocytoma		1 (2%)		
Subcutaneous tissue, hemangiosarcoma	1 (2%)	2 (4%)	1 (2%)	
Subcutaneous tissue, sarcoma		1 (2%)		1 (2%)
Musculoskeletal System				
Skeletal muscle		(1)		(2)
Alveolar/bronchiolar carcinoma, metastatic, lung				1 (50%)
Sarcoma, metastatic, skin				1 (50%)
Nervous System				
Brain	(50)	(49)	(50)	(50)
Carcinoma, metastatic, harderian gland	1 (2%)			
Histiocytic sarcoma	1 (2%)			
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	4 (8%)	1 (2%)	4 (8%)	4 (8%)
Alveolar/bronchiolar carcinoma	5 (10%)	1 (2%)	2 (4%)	3 (6%)
Carcinoma, metastatic, harderian gland	2 (4%)	1 (2%)		
Carcinoma, metastatic, uncertain primary site	1 (2%)	1 (2%)		
Carcinoma, metastatic, urinary bladder			1 (2%)	
Hemangiosarcoma, metastatic, uterus	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	2 (4%)	4 (8%)	3 (6%)	1 (2%)
Histiocytic sarcoma	2 (4%)	1 (2%)	2 (4%)	
Nose	(50)	(50)	(50)	(50)
Carcinoma, metastatic, harderian gland	1 (2%)	1 (2%)	1 (2%)	
Histiocytic sarcoma			1 (2%)	
Trachea	(50)	(50)	(50)	(50)
Special Senses System				
Harderian gland	(5)	(3)	(2)	(1)
Adenoma	3 (60%)	1 (33%)	1 (50%)	
Carcinoma	2 (40%)	2 (67%)	1 (50%)	1 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung				1 (2%)
Carcinoma, metastatic, uncertain primary site		1 (2%)		
Histiocytic sarcoma	1 (2%)	1 (2%)	1 (2%)	
Urinary bladder	(48)	(49)	(48)	(49)
Fibrous histiocytoma, metastatic, uncertain primary site			1 (2%)	
Histiocytic sarcoma			1 (2%)	
Transitional epithelium, carcinoma			1 (2%)	

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma	2 (4%)	1 (2%)	2 (4%)	
Lymphoma malignant	10 (20%)	14 (28%)	10 (20%)	11 (22%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	46	49	46	44
Total primary neoplasms	94	95	86	84
Total animals with benign neoplasms	42	43	43	41
Total benign neoplasms	60	57	55	52
Total animals with malignant neoplasms	28	30	25	22
Total malignant neoplasms	34	38	31	32
Total animals with metastatic neoplasms	8	6	6	3
Total metastatic neoplasms	14	17	24	6
Total animals with malignant neoplasms of uncertain primary site	1	2	2	

[a] Number of animals examined microscopically at the site and the number of animals with neoplasms
[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 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	076	264	465	587	593	657	670	673	677	683	683	698	714	721	726	731	732	733	735	735	735	735	735	735	735
Carcass ID Number	262	242	228	251	227	230	246	258	254	221	226	231	255	236	238	237	235	239	216	217	218	219	220	222	223
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	A	+	+	A	+	+	+	A	A	+	A	+	+	A	+	M	A	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Intestine large, colon	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	A	+	A	+	A	+	+	+	+	+	A	A	+	A	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	A	+	A	+	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+
Carcinoma					X																				
Intestine small, ileum	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, intestine small, jejunum					X																				
Hemangiosarcoma																									
Hepatocellular carcinoma															X		X								
Hepatocellular adenoma				X						X	X			X				X					X		
Hepatocellular adenoma, multiple					X	X	X	X				X			X				X	X	X	X		X	X
Histiocytic sarcoma															X	X									
Mesentery					+			+	+	+					+							+		+	
Carcinoma, metastatic, intestine small, jejunum					X																				
Hemangiosarcoma, metastatic, uterus								X																	
Histiocytic sarcoma															X										
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung			X																						
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant									X																
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																		X				X			
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									

+: 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 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	224	225	229	232	233	234	240	241	243	244	245	247	248	249	250	252	253	256	257	259	260	261	263	264	265	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Histiocytic sarcoma																										1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Carcinoma																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, intestine small, jejunum																										1
Hemangiosarcoma																	X									1
Hepatocellular carcinoma						X						X				X					X					6
Hepatocellular adenoma	X																X				X	X	X	X		12
Hepatocellular adenoma, multiple		X	X		X	X	X		X	X	X	X	X		X	X		X	X	X					X	28
Histiocytic sarcoma																										2
Mesentery	+		+			+	+		+	+	+		+		+				+	+		+		+		20
Carcinoma, metastatic, intestine small, jejunum																										1
Hemangiosarcoma, metastatic, uterus																										1
Histiocytic sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma										X																1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																									X	1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma			X						X						X										X	6
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma			X																							1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	076	264	465	587	593	657	670	673	677	683	683	698	714	721	726	731	732	733	735	735	735	735	735	735	735
Carcass ID Number	262	242	228	251	227	230	246	258	254	221	226	231	255	236	238	237	235	239	216	217	218	219	220	222	223
General Body System																									
Tissue NOS										+						+									
Histiocytic sarcoma																X									
Pelvic, hemangiosarcoma																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma																									
Granulosa cell tumor benign																									
Hemangioma									X																
Histiocytic sarcoma																X									
Oviduct				+																					
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma								X																	
Histiocytic sarcoma															X										
Polyp stromal																									
Sarcoma stromal																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Lymph node							+	+		+				+	+	+		+							
Histiocytic sarcoma																X									
Deep cervical, histiocytic sarcoma																X									
Iliac, hemangiosarcoma, metastatic, uterus								X																	
Iliac, histiocytic sarcoma															X	X									
Inguinal, histiocytic sarcoma																X									
Mediastinal, histiocytic sarcoma																X									
Pancreatic, histiocytic sarcoma																X									
Renal, histiocytic sarcoma																X									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland						X																			
Histiocytic sarcoma																X									
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma															X	X									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																						X			
Histiocytic sarcoma																X									
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma, multiple																									
Subcutaneous tissue, hemangiosarcoma																						X			
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	224	225	229	232	233	234	240	241	243	244	245	247	248	249	250	252	253	256	257	259	260	261	263	264	265	Total Tissues/ Tumors
General Body System																										
Tissue NOS	+																									3
Histiocytic sarcoma																										1
Pelvic, hemangiosarcoma	X																									1
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma																									X	1
Granulosa cell tumor benign				X																						1
Hemangioma																										1
Histiocytic sarcoma																										1
Oviduct																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Histiocytic sarcoma																										1
Polyp stromal									X																	1
Sarcoma stromal						X																				1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymph node																			+							8
Histiocytic sarcoma																										1
Deep cervical, histiocytic sarcoma																										1
Iliac, hemangiosarcoma, metastatic, uterus																										1
Iliac, histiocytic sarcoma																										2
Inguinal, histiocytic sarcoma																										1
Mediastinal, histiocytic sarcoma																										1
Pancreatic, histiocytic sarcoma																										1
Renal, histiocytic sarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Histiocytic sarcoma																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										2
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																										1
Histiocytic sarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma, multiple														X												1
Subcutaneous tissue, hemangiosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	076	264	465	587	593	657	670	673	677	683	683	698	714	721	726	731	732	733	735	735	735	735	735	735	735
Carcass ID Number	262	242	228	251	227	230	246	258	254	221	226	231	255	236	238	237	235	239	216	217	218	219	220	222	223
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland						X																			
Histiocytic sarcoma																X									
Peripheral nerve														+											
Spinal cord														+											
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																		X		X			X		
Alveolar/bronchiolar carcinoma			X	X	X										X										
Carcinoma, metastatic, harderian gland						X																		X	
Carcinoma, metastatic, uncertain primary site																									X
Hemangiosarcoma, metastatic, uterus								X																	
Hepatocellular carcinoma, metastatic, liver															X		X								
Histiocytic sarcoma															X	X									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland						X																			
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland				+		+														+				+	
Adenoma				X																X					
Carcinoma						X																		X	
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Urinary bladder	+	+	+	+	+	+	M	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma															X	X									
Lymphoma malignant										X								X		X			X		X

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 0 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	224	225	229	232	233	234	240	241	243	244	245	247	248	249	250	252	253	256	257	259	260	261	263	264	265	Total Tissues/ Tumors
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Histiocytic sarcoma																										1
Peripheral nerve																						+				2
Spinal cord																						+				2
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma						X																				4
Alveolar/bronchiolar carcinoma																							X			5
Carcinoma, metastatic, harderian gland																										2
Carcinoma, metastatic, uncertain primary site																										1
Hemangiosarcoma, metastatic, uterus																										1
Hepatocellular carcinoma, metastatic, liver																										2
Histiocytic sarcoma																										2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland																						+				5
Adenoma																						X				3
Carcinoma																										2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										2
Lymphoma malignant			X															X				X	X	X		10

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	449	449	538	575	582	594	647	662	663	668	691	695	703	704	707	710	712	732	735	735	735	735	735	735	735
Carcass ID Number	284	292	275	307	268	312	302	314	315	286	271	303	306	308	290	297	295	277	266	267	269	270	272	273	274
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	A	A	+	A	+	+	+	A	+	A	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site				X																					
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	A	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	A	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	A	A	+	A	+	A	+	+	+	A	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	A	A	A	A	+	A	+	+	+	A	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site										X															
Hepatoblastoma																									
Hepatocellular carcinoma				X	X	X		X		X				X						X		X			
Hepatocellular adenoma		X				X		X			X					X	X	X					X		X
Hepatocellular adenoma, multiple					X				X			X		X	X					X	X	X		X	
Histiocytic sarcoma								X																	
Lipoma				X																					
Mesentery				+				+	+	+				+							+	+			
Carcinoma, metastatic, uncertain primary site				X						X															
Hemangioma																						X			
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site				X						X															
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site										X															
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																	
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma												X									X				
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
Tissue NOS																									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	276	278	279	280	281	282	283	285	287	288	289	291	293	294	296	298	299	300	301	304	305	309	310	311	313	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Carcinoma, metastatic, uncertain primary site																										1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, uncertain primary site																										1
Hepatoblastoma															X											1
Hepatocellular carcinoma											X															9
Hepatocellular adenoma													X	X		X										12
Hepatocellular adenoma, multiple	X			X	X	X		X	X	X	X				X		X	X	X	X	X	X	X	X	X	27
Histiocytic sarcoma																										1
Lipoma																										1
Mesentery				+				+			+				+		+	+	+	+	+	+		+	+	19
Carcinoma, metastatic, uncertain primary site																										2
Hemangioma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, uncertain primary site																										2
Acinus, adenoma				X																						1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																					X					1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, uncertain primary site																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																								X		1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma			X				X							X												5
Pars intermedia, adenoma										X																1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																						X		X		2
General Body System																										
Tissue NOS												+														1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	449	449	538	575	582	594	647	662	663	668	691	695	703	704	707	710	712	732	735	735	735	735	735	735	735
Carcass ID Number	284	292	275	307	268	312	302	314	315	286	271	303	306	308	290	297	295	277	266	267	269	270	272	273	274
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site										X															
Hemangioma													X												
Histiocytic sarcoma								X																	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																	
Polyp stromal												X													
Sarcoma stromal																							X		
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma											X														
Lymph node	+	+	+					+			+			+	+	+			+						+
Iliac, hemangiosarcoma											X														
Iliac, histiocytic sarcoma								X																	
Mediastinal, histiocytic sarcoma								X																	
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																	
Lymph node, mesenteric	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma											X		X												
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland							X																		
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma																			X						
Subcutaneous tissue, fibrous histiocytoma																									
Subcutaneous tissue, hemangiosarcoma											X		X												
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																						+			
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	276	278	279	280	281	282	283	285	287	288	289	291	293	294	296	298	299	300	301	304	305	309	310	311	313	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, uncertain primary site																										1
Hemangioma																										1
Histiocytic sarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Polyp stromal																							X			2
Sarcoma stromal																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Lymph node				+																			+			12
Iliac, hemangiosarcoma																										1
Iliac, histiocytic sarcoma																										1
Mediastinal, histiocytic sarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, harderian gland																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, fibrous histiocytoma																						X				1
Subcutaneous tissue, hemangiosarcoma																										2
Subcutaneous tissue, sarcoma															X											1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	449	449	538	575	582	594	647	662	663	668	691	695	703	704	707	710	712	732	735	735	735	735	735	735	735
Carcass ID Number	284	292	275	307	268	312	302	314	315	286	271	303	306	308	290	297	295	277	266	267	269	270	272	273	274
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																X									
Carcinoma, metastatic, harderian gland							X																		
Carcinoma, metastatic, uncertain primary site				X																					
Hepatocellular carcinoma, metastatic, liver					X					X										X		X			
Histiocytic sarcoma								X																	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland							X																		
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland							+													+					
Adenoma																				X					
Carcinoma							X																		
Lacrimal gland																			+						
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site				X																					
Histiocytic sarcoma								X																	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																	
Lymphoma malignant	X	X	X						X							X									X

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 250 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	276	278	279	280	281	282	283	285	287	288	289	291	293	294	296	298	299	300	301	304	305	309	310	311	313	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																			X							1
Alveolar/bronchiolar carcinoma																										1
Carcinoma, metastatic, harderian gland																										1
Carcinoma, metastatic, uncertain primary site																										1
Hepatocellular carcinoma, metastatic, liver																										4
Histiocytic sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland																			+							3
Adenoma																										1
Carcinoma																			X							2
Lacrimal gland																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, uncertain primary site																										1
Histiocytic sarcoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant				X					X	X		X				X			X				X		X	14

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	050	113	393	540	544	622	633	645	645	646	649	655	689	697	735	735	735	735	735	735	735	735	735	735	735
Carcass ID Number	345	319	355	328	362	323	316	359	364	360	339	333	354	338	317	318	320	321	322	324	325	326	327	329	330
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	A	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, urinary bladder											X														
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma, metastatic, uncertain primary site								X																	
Intestine small, ileum	+	A	+	+	+	+	A	+	+	+	A	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, urinary bladder											X														
Fibrous histiocytoma, metastatic, uncertain primary site				X																					
Hemangiosarcoma																									
Hepatoblastoma																									
Hepatocellular carcinoma								X		X			X												
Hepatocellular carcinoma, multiple												X													
Hepatocellular adenoma					X	X						X			X			X		X		X			
Hepatocellular adenoma, multiple							X	X					X			X	X		X		X		X	X	X
Histiocytic sarcoma														X						X					
Leiomyosarcoma, metastatic, uncertain primary site								X																	
Mesentery						+	+				+						+			+			+	+	+
Carcinoma, metastatic, urinary bladder											X														
Histiocytic sarcoma																				X					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, urinary bladder											X														
Fibrous histiocytoma, metastatic, uncertain primary site				X																					
Leiomyosarcoma, metastatic, uncertain primary site								X																	
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, urinary bladder											X														
Stomach, glandular	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, urinary bladder											X														
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	+	+	+	+	+	+	+	+	M	+	M	M	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	331	332	334	335	336	337	340	341	342	343	344	346	347	348	349	350	351	352	353	356	357	358	361	363	365	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Carcinoma, metastatic, urinary bladder																										1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Leiomyosarcoma, metastatic, uncertain primary site																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, urinary bladder																										1
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Hemangiosarcoma																							X			1
Hepatoblastoma																						X				1
Hepatocellular carcinoma	X			X									X					X								7
Hepatocellular carcinoma, multiple		X																								2
Hepatocellular adenoma			X														X			X						10
Hepatocellular adenoma, multiple	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X		X	X		X	X	X	X	X	32
Histiocytic sarcoma																										2
Leiomyosarcoma, metastatic, uncertain primary site																										1
Mesentery								+		+	+					+	+	+		+					+	16
Carcinoma, metastatic, urinary bladder																										1
Histiocytic sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, urinary bladder																										1
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Leiomyosarcoma, metastatic, uncertain primary site																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, urinary bladder																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, urinary bladder																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma		X																		X			X			3
Pars intermedia, adenoma															X											1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma				X																						1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	050	113	393	540	543	622	623	645	645	646	649	655	689	697	735	735	735	735	735	735	735	735	735	735	735
Carcass ID Number	345	319	355	328	362	223	116	359	364	360	339	333	354	338	317	318	320	221	222	324	325	326	327	329	330
General Body System																									
Tissue NOS								+	+																
Leiomyosarcoma, metastatic, uncertain primary site								X																	
Genital System																									
Clitoral gland	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, urinary bladder											X														
Cystadenoma																									
Histiocytic sarcoma														X						X					
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma												X													
Histiocytic sarcoma														X						X					
Polyp stromal																									
Vagina				+																					
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Lymph node				+		+		+	+							+				+			+		
Pancreatic, fibrous histiocytoma, metastatic, uncertain primary site				X																					
Renal, histiocytic sarcoma																				X					
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Carcinoma, metastatic, urinary bladder											X														
Lymph node, mesenteric	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site				X																					
Hemangioma																									
Histiocytic sarcoma														X						X					
Leiomyosarcoma, metastatic, uncertain primary site								X																	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site				X																					
Hemangiosarcoma																									
Thymus	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	I	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, hemangiosarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	331	332	334	335	336	337	340	341	342	343	344	346	347	348	349	350	351	352	353	356	357	358	361	363	365	Total Tissues/ Tumors
General Body System																										
Tissue NOS																										2
Leiomyosarcoma, metastatic, uncertain primary site																										1
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, urinary bladder																										1
Cystadenoma																						X				1
Histiocytic sarcoma																										2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Histiocytic sarcoma																										2
Polyp stromal																								X		1
Vagina																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymph node		+			+									+			+	+	+	+		+				15
Pancreatic, fibrous histiocytoma, metastatic, uncertain primary site																										1
Renal, histiocytic sarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, urinary bladder																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	47
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Hemangioma																								X		1
Histiocytic sarcoma																										2
Leiomyosarcoma, metastatic, uncertain primary site																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Hemangiosarcoma																							X			1
Thymus	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	45
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																								X		1
Subcutaneous tissue, hemangiosarcoma												X														1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	050	113	393	540	543	622	633	645	645	646	649	655	689	697	735	735	735	735	735	735	735	735	735	735	735
Carcass ID Number	345	319	355	328	362	323	316	359	364	360	339	333	354	338	317	318	320	321	322	324	325	326	327	329	330
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal cord			+																						
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma									X			X								X					
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, urinary bladder											X														
Hepatocellular carcinoma, metastatic, liver								X				X													
Histiocytic sarcoma														X						X					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland																							X		
Histiocytic sarcoma														X											
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland												+											+		
Adenoma												X													
Carcinoma																							X		
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																				X					
Urinary bladder	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site				X																					
Histiocytic sarcoma														X											
Transitional epithelium, carcinoma											X														
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X						X					
Lymphoma malignant									X															X	

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 500 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	331	332	334	335	336	337	340	341	342	343	344	346	347	348	349	350	351	352	353	356	357	358	361	363	365	Total Tissues/ Tumors
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma													X													4
Alveolar/bronchiolar carcinoma								X					X													2
Carcinoma, metastatic, urinary bladder																										1
Hepatocellular carcinoma, metastatic, liver		X																								3
Histiocytic sarcoma																										2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Histiocytic sarcoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland																										2
Adenoma																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Urinary bladder	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Histiocytic sarcoma																										1
Transitional epithelium, carcinoma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										2
Lymphoma malignant	X				X									X	X				X		X	X	X			10

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 ppm

Number of Days on Study	077	150	238	261	466	523	569	606	616	629	642	646	664	681	681	701	717	734	735	735	735	735	735	735	735
Carcass ID Number	405	391	385	409	399	371	406	394	377	410	379	397	404	374	386	388	414	408	366	367	368	369	370	372	373
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	+	A	A	+	+	+	+	A	M	+	+	A	+	A	A	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	A	A	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	A	+	+	+	+	+	A	A	+	+	A	+	+	A	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung					X																				
Hemangiosarcoma																		X							
Hepatoblastoma																									
Hepatocellular carcinoma					X							X		X					X			X			
Hepatocellular carcinoma, multiple																									
Hepatocellular adenoma					X	X									X								X		
Hepatocellular adenoma, multiple								X	X	X	X	X				X	X	X	X	X	X	X		X	X
Mesentery							+	+										+	+						
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung					X																				
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Pituitary gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									
Genital System																									
Clitoral gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma											X			X											
Granulosa-theca tumor benign																			X						
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma									X																
Sarcoma stromal																									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	375	376	378	380	381	382	383	384	387	389	390	392	393	395	396	398	400	401	402	403	407	411	412	413	415	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	40
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Hemangiosarcoma																										1
Hepatoblastoma															X											1
Hepatocellular carcinoma								X		X					X									X		9
Hepatocellular carcinoma, multiple																						X				1
Hepatocellular adenoma		X				X				X		X	X								X					10
Hepatocellular adenoma, multiple	X		X	X	X		X		X					X	X	X		X	X	X		X	X	X	X	30
Mesentery			+		+			+	+			+				+					+		+			12
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	46
Pars distalis, adenoma				X		X							X					X								4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma																										2
Granulosa-theca tumor benign																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Sarcoma stromal									X																	1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 ppm

Number of Days on Study	077	150	238	261	466	523	569	606	616	629	642	646	664	681	681	701	717	734	735	735	735	735	735	735	735
Carcass ID Number	405	391	385	409	399	371	406	394	377	410	379	397	404	374	386	388	414	408	366	367	368	369	370	372	373
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node			+						+	+		+				+						+			
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma													X					X							
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, sarcoma																							X		
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle					+																		+		
Alveolar/bronchiolar carcinoma, metastatic, lung					X																				
Sarcoma, metastatic, skin																							X		
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma					X													X							
Alveolar/bronchiolar carcinoma					X																		X		
Hepatocellular carcinoma, metastatic, liver																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear		+																							
Eye		+								+															
Harderian gland																									
Carcinoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung					X																				
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant			X						X	X												X			X

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol: 1,000 ppm

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	735	
Carcass ID Number	375	376	378	380	381	382	383	384	387	389	390	392	393	395	396	398	400	401	402	403	407	411	412	413	415	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node			+												+		+									9
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma								X																		1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										2
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Sarcoma, metastatic, skin																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X																				X				4
Alveolar/bronchiolar carcinoma																								X		3
Hepatocellular carcinoma, metastatic, liver																						X				1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Eye																				+						3
Harderian gland																				+						1
Carcinoma																				X						1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant			X						X	X		X			X						X					11

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Harderian Gland: Adenoma				
Overall rate[a]	3/50 (6%)	1/50 (2%)	1/50 (2%)	0/50 (0%)
Adjusted rate[b]	6.7%	2.3%	2.3%	0.0%
Terminal rate[c]	2/32 (6%)	1/32 (3%)	0/36 (0%)	0/32 (0%)
First incidence (days)	587	735 (T)	655	—[e]
Poly-3 test[d]	P=0.089N	P=0.333N	P=0.341N	P=0.156N
Harderian Gland: Adenoma or Carcinoma				
Overall rate	5/50 (10%)	3/50 (6%)	2/50 (4%)	1/50 (2%)
Adjusted rate	11.0%	6.7%	4.6%	2.4%
Terminal rate	3/32 (9%)	2/32 (6%)	1/36 (3%)	1/32 (3%)
First incidence (days)	587	647	655	735 (T)
Poly-3 test	P=0.082N	P=0.380N	P=0.248N	P=0.138N
Liver: Hepatocellular Adenoma				
Overall rate	40/50 (80%)	39/50 (78%)	42/50 (84%)	40/50 (80%)
Adjusted rate	85.2%	82.3%	92.4%	88.7%
Terminal rate	29/32 (91%)	27/32 (84%)	36/36 (100%)	29/32 (91%)
First incidence (days)	587	449	543	466
Poly-3 test	P=0.237	P=0.465N	P=0.211	P=0.430
Liver: Hepatocellular Carcinoma				
Overall rate	6/50 (12%)	9/50 (18%)	9/50 (18%)	10/50 (20%)
Adjusted rate	13.4%	19.4%	20.3%	23.4%
Terminal rate	4/32 (13%)	3/32 (9%)	5/36 (14%)	7/32 (22%)
First incidence (days)	726	575	645	466
Poly-3 test	P=0.168	P=0.326	P=0.294	P=0.186
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	41/50 (82%)	41/50 (82%)	43/50 (86%)	42/50 (84%)
Adjusted rate	87.3%	85.1%	93.9%	92.7%
Terminal rate	29/32 (91%)	27/32 (84%)	36/36 (100%)	30/32 (94%)
First incidence (days)	587	449	543	466
Poly-3 test	P=0.140	P=0.503N	P=0.219	P=0.301
Liver: Hepatocellular Carcinoma or Hepatoblastoma				
Overall rate	6/50 (12%)	10/50 (20%)	10/50 (20%)	10/50 (20%)
Adjusted rate	13.4%	21.5%	22.5%	23.4%
Terminal rate	4/32 (13%)	4/32 (13%)	6/36 (17%)	7/32 (22%)
First incidence (days)	726	575	645	466
Poly-3 test	P=0.186	P=0.239	P=0.210	P=0.186
Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma				
Overall rate	41/50 (82%)	41/50 (82%)	43/50 (86%)	42/50 (84%)
Adjusted rate	87.3%	85.1%	93.9%	92.7%
Terminal rate	29/32 (91%)	27/32 (84%)	36/36 (100%)	30/32 (94%)
First incidence (days)	587	449	543	466
Poly-3 test	P=0.140	P=0.503N	P=0.219	P=0.301
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	4/50 (8%)	1/50 (2%)	4/50 (8%)	4/50 (8%)
Adjusted rate	9.0%	2.3%	9.1%	9.5%
Terminal rate	3/32 (9%)	1/32 (3%)	2/36 (6%)	2/32 (6%)
First incidence (days)	733	735 (T)	645	466
Poly-3 test	P=0.388	P=0.195N	P=0.653	P=0.634

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	5/50 (10%)	1/50 (2%)	2/50 (4%)	3/50 (6%)
Adjusted rate	10.8%	2.2%	4.6%	7.1%
Terminal rate	1/32 (3%)	0/32 (0%)	2/36 (6%)	2/32 (6%)
First incidence (days)	465	710	735 (T)	466
Poly-3 test	P=0.435N	P=0.120N	P=0.259N	P=0.429N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	9/50 (18%)	2/50 (4%)	5/50 (10%)	6/50 (12%)
Adjusted rate	19.4%	4.5%	11.4%	14.2%
Terminal rate	4/32 (13%)	1/32 (3%)	3/36 (8%)	4/32 (13%)
First incidence (days)	465	710	645	466
Poly-3 test	P=0.461N	P=0.032N	P=0.233N	P=0.373N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	6/49 (12%)	5/49 (10%)	3/47 (6%)	4/46 (9%)
Adjusted rate	13.6%	11.4%	7.3%	10.5%
Terminal rate	5/32 (16%)	4/32 (13%)	3/35 (9%)	4/30 (13%)
First incidence (days)	733	695	735 (T)	735 (T)
Poly-3 test	P=0.374N	P=0.519N	P=0.295N	P=0.487N
Skin (Subcutaneous Tissue): Fibrous Histiocytoma, Fibrosarcoma, or Sarcoma				
Overall rate	1/50 (2%)	3/50 (6%)	1/50 (2%)	2/50 (4%)
Adjusted rate	2.2%	6.8%	2.3%	4.8%
Terminal rate	1/32 (3%)	3/32 (9%)	1/36 (3%)	2/32 (6%)
First incidence (days)	735 (T)	735 (T)	735 (T)	735 (T)
Poly-3 test	P=0.513	P=0.326	P=0.784	P=0.513
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rate	2/50 (4%)	3/50 (6%)	1/50 (2%)	1/50 (2%)
Adjusted rate	4.5%	6.7%	2.3%	2.4%
Terminal rate	2/32 (6%)	2/32 (6%)	1/36 (3%)	1/32 (3%)
First incidence (days)	735 (T)	695	735 (T)	735 (T)
Poly-3 test	P=0.322N	P=0.521	P=0.542N	P=0.564N
All Organs: Hemangiosarcoma				
Overall rate	4/50 (8%)	2/50 (4%)	3/50 (6%)	2/50 (4%)
Adjusted rate	8.9%	4.5%	6.9%	4.8%
Terminal rate	3/32 (9%)	0/32 (0%)	2/36 (6%)	0/32 (0%)
First incidence (days)	673	691	655	664
Poly-3 test	P=0.365N	P=0.357N	P=0.536N	P=0.397N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	5/50 (10%)	3/50 (6%)	4/50 (8%)	3/50 (6%)
Adjusted rate	11.1%	6.7%	9.2%	7.1%
Terminal rate	3/32 (9%)	1/32 (3%)	3/36 (8%)	0/32 (0%)
First incidence (days)	673	691	655	616
Poly-3 test	P=0.390N	P=0.377N	P=0.538N	P=0.416N
All Organs: Malignant Lymphoma				
Overall rate	10/50 (20%)	14/50 (28%)	10/50 (20%)	11/50 (22%)
Adjusted rate	22.3%	29.9%	22.9%	25.5%
Terminal rate	8/32 (25%)	9/32 (28%)	9/36 (25%)	8/32 (25%)
First incidence (days)	683	449	645	238
Poly-3 test	P=0.525	P=0.287	P=0.587	P=0.474

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
All Organs: Benign Neoplasms				
Overall rate	42/50 (84%)	43/50 (86%)	43/50 (86%)	41/50 (82%)
Adjusted rate	89.0%	89.5%	93.9%	90.5%
Terminal rate	30/32 (94%)	29/32 (91%)	36/36 (100%)	29/32 (91%)
First incidence (days)	587	449	543	466
Poly-3 test	P=0.428	P=0.612	P=0.314	P=0.553
All Organs: Malignant Neoplasms				
Overall rate	28/50 (56%)	30/50 (60%)	26/50 (52%)	22/50 (44%)
Adjusted rate	59.2%	60.4%	56.8%	49.2%
Terminal rate	17/32 (53%)	16/32 (50%)	18/36 (50%)	14/32 (44%)
First incidence (days)	465	449	540	238
Poly-3 test	P=0.162N	P=0.534	P=0.496N	P=0.231N
All Organs: Benign or Malignant Neoplasms				
Overall rate	46/50 (92%)	49/50 (98%)	47/50 (94%)	44/50 (88%)
Adjusted rate	95.9%	98.0%	99.7%	94.6%
Terminal rate	31/32 (97%)	31/32 (97%)	36/36 (100%)	30/32 (94%)
First incidence (days)	465	449	540	238
Poly-3 test	P=0.431N	P=0.499	P=0.293	P=0.587N

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for liver, lung, pituitary gland, and uterus; 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 are the P values 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 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
Historical Incidence of Liver Neoplasms in Untreated Female B6C3F$_1$ Mice[a]

Study	Incidence in Controls			
	Hepatocellular Adenoma	Hepatocellular Carcinoma	Hepatoblastoma	Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma
Historical Incidence at TSI Mason Research Institute: Drinking Water Study				
Pyridine	37/49	13/49	1/49	41/49
Overall Historical Incidence: Drinking Water Studies				
Total	147/288 (51.0%)	62/288 (21.5%)	1/288 (0.3%)	173/288 (60.1%)
Standard deviation	19.5%	13.6%	0.9%	21.9%
Range	26%-74%	8%-42%	0%-2%	32%-82%

[a] Data as of 15 October 1997

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	250 ppm	500 ppm	1,000 ppm
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental deaths	3		1	2
Moribund	8	7	3	5
Natural deaths	7	11	10	11
Survivors				
Terminal sacrifice	32	32	36	32
Animals examined microscopically	50	50	50	50
Alimentary System				
Gallbladder	(42)	(44)	(45)	(40)
Inflammation, acute	1 (2%)			
Necrosis				1 (3%)
Intestine large, cecum	(44)	(46)	(48)	(49)
Lymphoid tissue, hyperplasia			1 (2%)	
Serosa, inflammation, chronic active			1 (2%)	
Intestine small, jejunum	(46)	(45)	(47)	(46)
Hyperplasia, lymphoid				1 (2%)
Peyer's patch, hyperplasia, lymphoid	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Peyer's patch, inflammation, acute				1 (2%)
Serosa, inflammation, chronic active	1 (2%)			
Intestine small, ileum	(46)	(44)	(45)	(45)
Serosa, inflammation, chronic active			1 (2%)	
Liver	(50)	(50)	(50)	(50)
Amyloid deposition	1 (2%)			
Angiectasis	1 (2%)	1 (2%)		
Clear cell focus	2 (4%)	3 (6%)	2 (4%)	2 (4%)
Cyst		1 (2%)	1 (2%)	
Eosinophilic focus	29 (58%)	24 (48%)	29 (58%)	31 (62%)
Fibrosis		1 (2%)		
Hematopoietic cell proliferation		1 (2%)	2 (4%)	
Infiltration cellular, polymorphonuclear	1 (2%)			
Inflammation, chronic	1 (2%)	1 (2%)		
Inflammation, suppurative			1 (2%)	
Leukocytosis	1 (2%)		1 (2%)	
Mixed cell focus		2 (4%)		1 (2%)
Necrosis	1 (2%)	3 (6%)	1 (2%)	
Bile duct, hyperplasia				1 (2%)
Hepatocyte, vacuolization cytoplasmic	1 (2%)	1 (2%)		
Hepatocyte, portal, vacuolization cytoplasmic				1 (2%)
Hepatocyte, centrilobular, vacuolization cytoplasmic			1 (2%)	
Serosa, inflammation, chronic active	1 (2%)		1 (2%)	
Mesentery	(20)	(19)	(16)	(12)
Inflammation, chronic active			1 (6%)	
Fat, necrosis	19 (95%)	17 (89%)	14 (88%)	11 (92%)
Pancreas	(50)	(50)	(50)	(50)
Acinus, atrophy	1 (2%)	1 (2%)		3 (6%)
Acinus, hyperplasia			1 (2%)	1 (2%)
Duct, cyst		1 (2%)		2 (4%)
Serosa, inflammation, chronic active				1 (2%)

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

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Alimentary System (continued)				
Stomach, forestomach	(50)	(50)	(50)	(50)
Hyperplasia, squamous	3 (6%)	2 (4%)		
Inflammation, chronic			1 (2%)	
Ulcer	1 (2%)	2 (4%)	3 (6%)	
Stomach, glandular	(50)	(50)	(48)	(50)
Erosion	5 (10%)	2 (4%)	2 (4%)	2 (4%)
Mineralization		1 (2%)		
Glands, hyperplasia		1 (2%)		
Serosa, inflammation, chronic active	1 (2%)			
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)			
Cardiomyopathy	5 (10%)	2 (4%)		2 (4%)
Inflammation, acute	1 (2%)			
Inflammation, chronic		1 (2%)	1 (2%)	
Inflammation, chronic active			1 (2%)	1 (2%)
Mineralization	1 (2%)	1 (2%)	2 (4%)	
Atrium, thrombosis	1 (2%)		1 (2%)	
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)	1 (2%)		
Cyst			1 (2%)	
Hyperplasia				1 (2%)
Capsule, hyperplasia	48 (96%)	50 (100%)	49 (98%)	48 (96%)
Adrenal medulla	(50)	(50)	(50)	(50)
Hyperplasia				2 (4%)
Islets, pancreatic	(50)	(50)	(50)	(50)
Hyperplasia	28 (56%)	30 (60%)	30 (60%)	31 (62%)
Hypertrophy				1 (2%)
Pituitary gland	(49)	(49)	(47)	(46)
Hemorrhage	1 (2%)			
Pars distalis, angiectasis	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Pars distalis, cyst		1 (2%)		
Pars distalis, hemorrhage		1 (2%)		
Pars distalis, hyperplasia	5 (10%)	3 (6%)	8 (17%)	10 (22%)
Pars intermedia, hemorrhage	1 (2%)			
Thyroid gland	(50)	(50)	(50)	(50)
C-cell, hyperplasia		1 (2%)		
Follicular cell, hyperplasia	13 (26%)	6 (12%)	15 (30%)	13 (26%)
General Body System				
None				

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Genital System				
Clitoral gland	(50)	(49)	(48)	(49)
Cyst	1 (2%)		1 (2%)	
Pigmentation	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Ovary	(50)	(49)	(50)	(50)
Angiectasis		2 (4%)		2 (4%)
Cyst	11 (22%)	9 (18%)	9 (18%)	11 (22%)
Hemorrhage	1 (2%)	1 (2%)	2 (4%)	
Inflammation, chronic active	1 (2%)		1 (2%)	
Oviduct	(1)			
Cyst	1 (100%)			
Uterus	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)	1 (2%)		3 (6%)
Hemorrhage	1 (2%)		1 (2%)	
Hyperplasia, cystic	41 (82%)	46 (92%)	43 (86%)	44 (88%)
Inflammation, acute	1 (2%)	1 (2%)	1 (2%)	
Inflammation, chronic	1 (2%)			
Vagina			(1)	
Fibrosis			1 (100%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Angiectasis		1 (2%)		
Depletion cellular		2 (4%)		
Myelofibrosis			1 (2%)	
Lymph node	(8)	(12)	(15)	(9)
Iliac, angiectasis			2 (13%)	
Iliac, hemorrhage				1 (11%)
Iliac, hyperplasia, lymphoid	2 (25%)	2 (17%)	2 (13%)	
Iliac, infiltration cellular, plasma cell	1 (13%)	1 (8%)	1 (7%)	
Mediastinal, angiectasis			1 (7%)	
Mediastinal, hemorrhage	1 (13%)			
Mediastinal, inflammation, acute	1 (13%)			
Mediastinal, pigmentation				1 (11%)
Renal, angiectasis		1 (8%)		
Renal, ectasia		1 (8%)		
Renal, hemorrhage			1 (7%)	
Renal, hyperplasia, lymphoid			4 (27%)	
Renal, infiltration cellular, plasma cell			1 (7%)	
Lymph node, mandibular	(50)	(49)	(49)	(50)
Angiectasis		1 (2%)		
Hyperplasia, lymphoid	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Infiltration cellular, plasma cell	1 (2%)		1 (2%)	1 (2%)
Infiltration cellular, histiocyte			1 (2%)	
Lymph node, mesenteric	(49)	(48)	(47)	(49)
Angiectasis	1 (2%)	2 (4%)	3 (6%)	1 (2%)
Ectasia		1 (2%)	1 (2%)	
Fibrosis	1 (2%)			
Hemorrhage			1 (2%)	1 (2%)
Hyperplasia, lymphoid		1 (2%)		1 (2%)
Infiltration cellular, plasma cell			1 (2%)	
Inflammation, acute	1 (2%)			
Inflammation, granulomatous				1 (2%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Hematopoietic System (continued)				
Spleen	(49)	(50)	(50)	(50)
Congestion		1 (2%)		
Hematopoietic cell proliferation	13 (27%)	9 (18%)	16 (32%)	11 (22%)
Hyperplasia, lymphoid		3 (6%)	1 (2%)	
Infiltration cellular, histiocyte				1 (2%)
Metaplasia, osseous	1 (2%)			1 (2%)
Pigmentation	1 (2%)			
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Ulcer	1 (2%)	1 (2%)		1 (2%)
Subcutaneous tissue, inflammation, acute	1 (2%)			1 (2%)
Subcutaneous tissue, inflammation, chronic		1 (2%)		1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Fibrous osteodystrophy	8 (16%)	6 (12%)	5 (10%)	4 (8%)
Hyperplasia			2 (4%)	
Skeletal muscle		(1)		(2)
Inflammation, chronic		1 (100%)		
Nervous System				
Brain	(50)	(49)	(50)	(50)
Demyelination	1 (2%)			1 (2%)
Hemorrhage	1 (2%)			1 (2%)
Thalamus, mineralization	22 (44%)	27 (55%)	22 (44%)	22 (44%)
Peripheral nerve	(2)			
Demyelination	1 (50%)			
Spinal cord	(2)		(1)	
Cyst epithelial inclusion			1 (100%)	
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Hemorrhage	4 (8%)	3 (6%)	6 (12%)	3 (6%)
Infiltration cellular, lymphocyte			1 (2%)	
Infiltration cellular, histiocyte	4 (8%)	2 (4%)	2 (4%)	4 (8%)
Inflammation, acute	1 (2%)			
Inflammation, chronic	1 (2%)			1 (2%)
Thrombosis	1 (2%)		1 (2%)	1 (2%)
Alveolar epithelium, hyperplasia		1 (2%)		1 (2%)
Nose	(50)	(50)	(50)	(50)
Hemorrhage				1 (2%)
Inflammation, acute				1 (2%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	250 ppm	500 ppm	1,000 ppm
Special Senses System				
Ear				(1)
External ear, inflammation, chronic				1 (100%)
Eye				(3)
Atrophy				1 (33%)
Inflammation, acute				1 (33%)
Cornea, inflammation, acute				1 (33%)
Cornea, necrosis				1 (33%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Cyst	1 (2%)		1 (2%)	
Hydronephrosis	1 (2%)		3 (6%)	1 (2%)
Inflammation, acute	1 (2%)			
Inflammation, chronic	1 (2%)		1 (2%)	
Metaplasia, osseous	2 (4%)		1 (2%)	1 (2%)
Mineralization	1 (2%)	1 (2%)		1 (2%)
Nephropathy, acute		1 (2%)		
Nephropathy, chronic	16 (32%)	6 (12%)	9 (18%)	11 (22%)
Pigmentation	1 (2%)			
Renal tubule, accumulation, hyaline droplet	3 (6%)	3 (6%)	1 (2%)	
Renal tubule, dilatation				1 (2%)
Urinary bladder	(48)	(49)	(48)	(49)
Inflammation, acute			1 (2%)	

APPENDIX E
GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST PROTOCOL 200
CHINESE HAMSTER OVARY CELL CYTOGENETICS PROTOCOLS 200
DROSOPHILA MELANOGASTER TEST PROTOCOLS 201
MOUSE PERIPHERAL BLOOD MICRONUCLEUS TEST PROTOCOL 202
RESULTS 203
TABLE E1 Mutagenicity of 1-Chloro-2-propanol in *Salmonella typhimurium* 204
TABLE E2 Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by 1-Chloro-2-propanol 207
TABLE E3 Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by 1-Chloro-2-propanol 208
TABLE E4 Induction of Sex-Linked Recessive Lethal Mutations in *Drosophila melanogaster* by 1-Chloro-2-propanol 209
TABLE E5 Induction of Reciprocal Translocations in *Drosophila melanogaster* by 1-Chloro-2-propanol 209
TABLE E6 Frequency of Micronuclei in Mouse Peripheral Blood Erythrocytes Following Treatment with 1-Chloro-2-propanol in Drinking Water for 14 Weeks 210

GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST PROTOCOL

Testing was performed as reported by Zeiger *et al*. (1987). 1-Chloro-2-propanol was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). It was incubated with the *Salmonella typhimurium* tester strains TA97, TA98, TA100, TA1535, and TA1537 either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver) for 20 minutes at 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 1-chloro-2-propanol. In the absence of toxicity, 10,000 µg/plate was selected as the high dose. All positive trials were repeated under the conditions that elicited the positive response.

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

CHINESE HAMSTER OVARY CELL CYTOGENETICS PROTOCOLS

Testing was performed as reported by Galloway *et al*. (1987). 1-Chloro-2-propanol was sent to the laboratory as a coded aliquot by Radian Corporation. It was tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCEs) and chromosomal aberrations (Abs), both in the presence and absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Each test consisted of concurrent solvent and positive controls and of three doses of 1-chloro-2-propanol; the high dose was limited to 5,000 µg/mL. A single flask per dose was used.

Sister Chromatid Exchange Test: In the SCE test without S9, CHO cells were incubated for 25.5 hours with 1-chloro-2-propanol in supplemental McCoy's 5A medium. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 25.5 hours, the medium containing 1-chloro-2-propanol was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with 1-chloro-2-propanol, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing serum and BrdU and no 1-chloro-2-propanol. Incubation proceeded for an additional 25.5 hours, with Colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9. All slides were scored blind and those from a single test were read by the same person. Up to 50 second-division metaphase cells were scored for frequency of SCEs/cell from each dose level. Because significant chemical-induced cell cycle delay was seen with and without S9 at 1,700 µg/mL and greater, incubation time was lengthened to ensure a sufficient number of scorable (second-division metaphase) cells.

Statistical analyses were conducted on the slopes of the dose-response curves and the individual dose points (Galloway *et al.*, 1987). An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than

0.001. An increase of 20% or greater at any single dose was considered weak evidence of activity; increases at two or more doses resulted in a determination that the trial was positive. A statistically significant trend ($P < 0.005$) in the absence of any responses reaching 20% above background led to a call of equivocal.

Chromosomal Aberrations Test: In the Abs test without S9, cells were incubated in McCoy's 5A medium with 1-chloro-2-propanol for 18.5 hours; Colcemid was added and incubation continued for 2 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the Abs test with S9, cells were treated with 1-chloro-2-propanol and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 18.5 hours in fresh medium, with Colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9. The harvest time for the Abs test was based on the cell cycle information obtained in the SCE test: because cell cycle delay was anticipated, the incubation period was extended from the normal duration of approximately 12 hours.

Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind and those from a single test were read by the same person. Twenty or fifty first-division metaphase cells were scored at each concentration. Normally 200 cells are scored, but due to the high percentage of aberrant cells observed after treatment with 1-chloro-2-propanol, few metaphase cells were scored. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

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

DROSOPHILA MELANOGASTER TEST PROTOCOLS

The assays for induction of sex-linked recessive lethal (SLRL) mutations and chromosomal reciprocal translocations (RTs) were performed with adult flies as described by Foureman *et al.* (1994). 1-Chloro-2-propanol was supplied as a coded aliquot by Radian Corporation.

Sex-Linked Recessive Lethal Mutation Test: 1-Chloro-2-propanol was assayed in the SLRL test by feeding for 3 days to adult Canton-S wild-type males no more than 24 hours old at the beginning of treatment. Because no response was obtained, 1-chloro-2-propanol was retested by injection into adult males.

To administer 1-chloro-2-propanol by injection, a glass Pasteur pipette was drawn out in a flame to a microfine filament, and the tip was broken off to allow delivery of the test solution. Injection was performed either manually, by attaching a rubber bulb to the other end of the pipette and forcing through sufficient solution (0.2 to 0.3 µL) to slightly distend the abdomen of the fly, or by attaching the pipette to a microinjector that automatically delivered a calibrated volume. Flies were anesthetized with ether and immobilized on a strip of tape. Injection into the thorax, under the wing, was performed with the aid of a dissecting microscope.

Toxicity tests were performed to set concentrations of 1-chloro-2-propanol at a level that would induce 30% mortality after 72 hours of feeding or 24 hours after injection, while keeping induced sterility at an acceptable level. Canton-S males were allowed to feed for 72 hours on a solution of 1-chloro-2-propanol in 5% sucrose. In the injection experiments, 24- to 72-hour old Canton-S males were treated with a solution of

1-chloro-2-propanol dissolved in saline and allowed to recover for 24 hours. A concurrent saline control group was also included. Treated males were mated to three *Basc* females for 3 days and were given fresh females at 2-day intervals to produce three matings of 3, 2, and 2 days (in each case, sample sperm from successive matings was treated at successively earlier postmeiotic stages). F_1 heterozygous females were mated with their siblings and then placed in individual vials. F_1 daughters from the same parental male were kept together to identify clusters. (A cluster occurs when a number of mutants from a given male result from a single spontaneous premeiotic mutation event and is identified when the number of mutants from that male exceeds the number predicted by a Poisson distribution.) If a cluster was identified, all data from the male in question were discarded. Presumptive lethal mutations were identified as vials containing fewer than 5% of the expected number of wild-type males after 17 days; these were retested to confirm the response.

SLRL data were analyzed by simultaneous comparison with the concurrent and historical controls (Mason *et al.*, 1992) using a normal approximation to the binomial test (Margolin *et al.*, 1983). A test result was considered positive if the P value was less than or equal to 0.01 and the mutation frequency in the tested group was greater than 0.10% or if the P value was less than or equal to 0.05 and the frequency in the treatment group was greater than 0.15%. A test was considered to be inconclusive if the P value was between 0.05 and 0.01 but the frequency in the treatment group was between 0.10% and 0.15% or if the P value was between 0.10 and 0.05 but the frequency in the treatment group was greater than 0.10%. A test was considered negative if the P value was greater than or equal to 0.10 or if the frequency in the treatment group was less than 0.10%.

Reciprocal Translocation Test: Because the injection route produced a positive result in the SLRL test, 1-chloro-2-propanol was assayed for induction of RTs using the same method of exposure. The treatment regimen was essentially the same as that for the SLRL test, except that Canton-S males were mated *en masse* to marker (*bw;st*) females. The females were transferred to fresh medium every 3 to 4 days for a period of about 3 weeks to produce a total of six broods. The results of the SLRL test were used to determine the germ cell stages most likely to be affected by 1-chloro-2-propanol. F_1 heterozygous males were backcrossed individually to *bw;st* females, and the F_2 progeny were screened for pseudolinkage, which results from the induction of a translocation in a germ cell of the parental male. Flies suspected of carrying RTs were retested to confirm the findings. The translocation data were compared to the concurrent and historical controls, and significance was analyzed according to the conditional binomial response of Kastenbaum and Bowman (1970).

MOUSE PERIPHERAL BLOOD MICRONUCLEUS TEST PROTOCOL

A detailed discussion of this assay is presented in MacGregor *et al.* (1990). At the end of the 14-week toxicity study, peripheral blood samples were obtained from male and female mice. Smears were immediately prepared and fixed in absolute methanol. The methanol-fixed slides were stained with a chromatin-specific fluorescent dye mixture of Hoechst 33258/pyronin Y (MacGregor *et al.*, 1983) and coded. Slides were scanned to determine the frequency of micronuclei in 2,000 polychromatic erythrocytes (PCEs) and 10,000 normochromatic erythrocytes (NCEs) in each of 10 animals per exposure group.

Log transformation of the NCE data, testing for normality by the Shapiro-Wilk test, and testing for heterogeneity of variance by Cochran's test were performed before statistical analyses. The frequency of micronucleated cells among NCEs was determined by analysis of variance with the SAS GLM procedure. The NCE data for each exposure group were compared with the concurrent solvent control by Student's *t*-test. The frequency of micronucleated cells among PCEs was analyzed by the Cochran-Armitage trend test, and individual exposure groups were compared to the concurrent solvent control by Kastenbaum-Bowman's binomial test. The percentage of PCEs among total erythrocytes was determined by an analysis of variance on ranks (classed by sex), and individual exposure groups were compared with the concurrent solvent control with a *t*-test on ranks.

RESULTS

1-Chloro-2-propanol is genotoxic *in vitro*. It was tested for mutation induction in *Salmonella typhimurium* in three studies at two laboratories, and all test responses were similar (Table E1; Zeiger *et al.*, 1987). In strain TA100, equivocal responses were obtained in the absence of S9; with S9, equivocal or weakly positive mutagenic activity was seen. Clearly positive, reproducible responses were seen across studies with strain TA1535, with and without S9. No mutagenic activity was detected with strain TA97, TA98, or TA1537, with or without S9.

1-Chloro-2-propanol induced marked increases in SCEs (Table E2) and Abs (Table E3) in cultured CHO cells, with and without S9. Cell cycle delay was induced in cultures treated with concentrations of 1,700 µg/mL 1-chloro-2-propanol and greater; to obtain sufficient cells for scoring, incubation time was extended to up to 34 hours in the SCE test. Experimental design normally calls for no more than 33 hours of exposure to BrdU, but, because increases in SCE frequencies were also seen at standard harvest times, in the absence of S9, the delayed harvest results were accepted as confirmatory of the results seen in Trial 1. In the SCE test with S9, the only concentration that produced a significant increase in SCEs was the 1,700 µg/mL dose, which employed a culture time of 33.5 hours. However, because the response was so strong, it was accepted that even if BrdU exposure contributed to some extent to the induction of SCEs, much of the increase was due to exposure to 1-chloro-2-propanol. This trial was not repeated because it was apparent from the combined results of the three trials that 1-chloro-2-propanol induced SCEs in cultured CHO cells. In the cultured CHO cell Abs test with 1-chloro-2-propanol, fewer than the usual 200 cells per concentration were scored because a marked increase in aberrations as well as in the percentage of cells with aberrations were observed.

The chromosomal effects seen *in vitro* were not apparent in the *in vivo* studies, but induction of gene mutations was observed. Positive results were obtained in the *Drosophila melanogaster* test for induction of SLRL mutations in germ cells of male flies administered 1-chloro-2-propanol via injection (Table E4; Foureman *et al.*, 1994). However, a subsequent test for induction of reciprocal chromosomal translocations in germ cells of male *D. melanogaster* yielded negative results (Table E5; Foureman *et al.*, 1994). Additional negative results were obtained for chromosomal effects in mice. No increase in the frequency of micronucleated erythrocytes was observed in peripheral blood of male or female mice administered 1-chloro-2-propanol in drinking water for 14 weeks (Table E6).

TABLE E1
Mutagenicity of 1-Chloro-2-propanol in *Salmonella typhimurium*[a]

Strain	Dose (µg/plate)	Revertants/plate[b] S9 Trial 1	S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
Study 1 Performed at SRI International							
TA100	0	119 ± 3.8	120 ± 4.4	129 ± 3.8	128 ± 5.9	133 ± 4.8	136 ± 4.9
	100	120 ± 7.8		144 ± 10.1		131 ± 3.2	
	333	117 ± 4.7	147 ± 7.1	143 ± 11.4	124 ± 3.8	126 ± 5.9	146 ± 7.8
	1,000	116 ± 3.5		142 ± 2.4	129 ± 6.2	136 ± 3.1	138 ± 13.7
	1,666		153 ± 4.3				
	3,333	144 ± 21.7	147 ± 2.8	133 ± 4.4	158 ± 4.7	162 ± 13.0	161 ± 8.7
	6,666		160 ± 6.0		195 ± 11.8		200 ± 5.2
	10,000	188 ± 4.9	172 ± 10.4	151 ± 2.3	201 ± 11.7	197 ± 7.4	227 ± 9.3
Trial summary		Equivocal	Equivocal	Negative	Weakly positive	Equivocal	Weakly positive
Positive control[c]		229 ± 34.4	274 ± 6.4	790 ± 67.8	718 ± 68.9	326 ± 7.6	352 ± 26.3
TA1535	0	14 ± 2.3	19 ± 3.8	9 ± 2.3	10 ± 2.7	8 ± 2.0	9 ± 2.6
	100	21 ± 5.2		12 ± 1.7		11 ± 1.5	
	333	17 ± 2.3	30 ± 3.4	7 ± 2.8	12 ± 1.8	7 ± 0.9	14 ± 2.9
	1,000	18 ± 5.8		16 ± 0.6	21 ± 1.5	16 ± 1.3	22 ± 2.2
	1,666		54 ± 6.0				
	3,333	29 ± 0.9	69 ± 6.3	26 ± 5.5	37 ± 4.4	21 ± 3.2	60 ± 6.2
	6,666		93 ± 5.2		78 ± 2.2		73 ± 8.5
	10,000	58 ± 9.7	122 ± 4.6	41 ± 1.8	108 ± 4.2	47 ± 5.2	112 ± 9.0
Trial summary		Positive	Positive	Positive	Positive	Positive	Positive
Positive control		134 ± 10.7	236 ± 12.4	161 ± 9.0	216 ± 9.7	152 ± 4.3	172 ± 8.7
TA1537	0	5 ± 1.2		7 ± 1.2		4 ± 1.0	
	100	5 ± 0.6		4 ± 0.9		6 ± 0.7	
	333	5 ± 1.5		4 ± 0.9		5 ± 0.9	
	1,000	6 ± 1.3		3 ± 0.9		6 ± 1.7	
	3,333	7 ± 2.6		5 ± 0.6		5 ± 0.3	
	10,000	5 ± 0.7		3 ± 1.2		3 ± 0.3	
Trial summary		Negative		Negative		Negative	
Positive control		143 ± 13.3		253 ± 40.8		160 ± 10.6	
TA98	0	17 ± 2.4		25 ± 3.0		17 ± 1.7	
	100	15 ± 3.5		33 ± 4.8		30 ± 7.1	
	333	16 ± 1.2		24 ± 3.8		30 ± 5.2	
	1,000	13 ± 2.3		26 ± 3.5		31 ± 3.2	
	3,333	20 ± 2.7		19 ± 1.2		22 ± 2.3	
	10,000	14 ± 3.5		20 ± 5.2		25 ± 2.2	
Trial summary		Negative		Negative		Negative	
Positive control		913 ± 42.2		620 ± 90.5		255 ± 12.2	

TABLE E1
Mutagenicity of 1-Chloro-2-propanol in *Salmonella typhimurium*

Strain	Dose (µg/plate)	Revertants/plate					
		S9		+10% hamster S9		+10% rat S9	
		Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
Study 2 Performed at SRI International							
TA100	0	127 ± 7.5		153 ± 3.5		124 ± 14.5	
	100	135 ± 16.5		135 ± 12.4		134 ± 6.7	
	333	131 ± 8.3		136 ± 8.1		123 ± 3.3	
	1,000	127 ± 5.9		144 ± 14.1		132 ± 4.6	
	3,333	130 ± 1.3		161 ± 10.4		148 ± 5.0	
	10,000	149 ± 10.7		159 ± 15.8		177 ± 5.5	
Trial summary		Negative		Negative		Equivocal	
Positive control		444 ± 11.0		875 ± 68.8		719 ± 59.3	
TA1535	0	20 ± 1.5	34 ± 0.7	13 ± 2.4	11 ± 2.2	15 ± 2.2	13 ± 3.2
	100	30 ± 3.3		10 ± 2.1		9 ± 1.2	
	333	37 ± 2.4	29 ± 2.8	11 ± 0.9	11 ± 3.0	10 ± 4.3	11 ± 1.8
	1,000	39 ± 2.7	29 ± 0.3	14 ± 0.9	16 ± 2.6	13 ± 1.0	13 ± 1.0
	3,333	37 ± 0.6	34 ± 2.4	27 ± 2.3	40 ± 6.4	17 ± 1.7	21 ± 2.0
	6,666		49 ± 5.0		53 ± 0.9		42 ± 5.5
	10,000	64 ± 2.5	67 ± 15.0	39 ± 4.7	55 ± 1.2	48 ± 1.7	52 ± 1.5
Trial summary		Weakly positive	Equivocal	Positive	Positive	Equivocal	Positive
Positive control		344 ± 18.5	347 ± 43.9	331 ± 11.7	134 ± 10.1	217 ± 1.3	89 ± 4.0
TA97	0	152 ± 22.8		179 ± 16.9		206 ± 4.4	
	100	151 ± 15.5		186 ± 18.0		199 ± 7.8	
	333	142 ± 14.7		196 ± 4.5		191 ± 12.2	
	1,000	139 ± 5.5		178 ± 17.9		209 ± 5.5	
	3,333	148 ± 10.1		69 ± 24.0		214 ± 15.5	
	10,000	156 ± 4.5		0 ± 0.0[d]		175 ± 20.0	
Trial summary		Negative		Negative		Negative	
Positive control		479 ± 28.3		628 ± 35.9		589 ± 27.5	
TA98	0	24 ± 3.8		32 ± 3.6		41 ± 4.9	
	100	14 ± 1.5		29 ± 1.7		28 ± 4.9	
	333	25 ± 3.8		25 ± 0.9		34 ± 3.4	
	1,000	22 ± 2.3		29 ± 4.9		28 ± 2.5	
	3,333	22 ± 1.0		26 ± 1.5		24 ± 1.2	
	10,000	17 ± 1.2		18 ± 2.0		27 ± 0.6	
Trial summary		Negative		Negative		Negative	
Positive control		746 ± 39.0		577 ± 51.1		424 ± 11.4	

TABLE E1
Mutagenicity of 1-Chloro-2-propanol in *Salmonella typhimurium*

Strain	Dose (µg/plate)	Revertants/plate: S9 Trial 1	S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
Study 3 Performed at Microbiological Associates, Inc.							
TA100	0	89 ± 7.3	115 ± 8.0	85 ± 7.3	112 ± 14.9	93 ± 2.4	93 ± 5.5
	100	100 ± 5.3	97 ± 4.1	90 ± 0.7	94 ± 8.8	94 ± 7.9	101 ± 5.1
	333	102 ± 4.1	113 ± 5.3	104 ± 6.4	127 ± 6.4	101 ± 4.0	104 ± 2.5
	1,000	98 ± 3.2	106 ± 3.3	93 ± 4.3	122 ± 2.6	85 ± 1.9	122 ± 7.7
	3,333	111 ± 3.5	141 ± 8.4	112 ± 4.3	156 ± 6.1	120 ± 6.2	149 ± 13.4
	6,667			128 ± 5.0		151 ± 4.7	176 ± 5.9
	10,000	194 ± 0.7	195 ± 6.4		163 ± 7.6		
Trial summary		Equivocal	Equivocal	Equivocal	Equivocal	Equivocal	Weakly positive
Positive control		343 ± 19.5	329 ± 7.3	721 ± 11.4	363 ± 20.8	452 ± 20.0	466 ± 47.8
TA1535	0	18 ± 0.3	17 ± 2.2	13 ± 2.2	9 ± 1.0	7 ± 1.5	6 ± 0.3
	100	19 ± 1.9	21 ± 3.5	10 ± 1.2	15 ± 4.0	10 ± 1.9	10 ± 2.1
	333	21 ± 2.0	25 ± 3.8	14 ± 3.2	19 ± 0.9	10 ± 0.6	13 ± 1.5
	1,000	29 ± 3.7	25 ± 1.3	22 ± 3.0	23 ± 1.8	22 ± 1.5	21 ± 1.7
	3,333	51 ± 2.9	62 ± 3.5	51 ± 1.2	67 ± 3.5	50 ± 2.2	44 ± 3.5
	6,667			67 ± 3.2	110 ± 2.8	83 ± 3.5	65 ± 2.1
	10,000	92 ± 2.3	125 ± 10.8				
Trial summary		Positive	Positive	Positive	Positive	Positive	Positive
Positive control		199 ± 11.4	171 ± 16.5	79 ± 7.0	69 ± 11.8	116 ± 8.1	124 ± 2.0
TA97	0	102 ± 9.2		135 ± 4.2		102 ± 7.8	
	100	85 ± 12.1		108 ± 8.1		130 ± 7.2	
	333	71 ± 9.8		97 ± 8.5		104 ± 3.5	
	1,000	76 ± 1.0		68 ± 4.2		79 ± 9.2	
	3,333	81 ± 11.3		97 ± 4.1		111 ± 10.0	
	6,667			17 ± 4.3		104 ± 9.3	
	10,000	102 ± 0.6					
Trial summary		Negative		Negative		Negative	
Positive control		276 ± 16.2		783 ± 65.7		848 ± 48.6	
TA98	0	18 ± 2.0		22 ± 4.4		27 ± 3.2	
	100	14 ± 4.3		26 ± 0.6		21 ± 2.2	
	333	19 ± 2.0		28 ± 0.0		21 ± 3.9	
	1,000	18 ± 4.5		17 ± 0.3		21 ± 0.9	
	3,333	20 ± 1.8		17 ± 2.6		20 ± 4.1	
	6,667			14 ± 1.5		27 ± 1.2	
	10,000	16 ± 0.9					
Trial summary		Negative		Negative		Negative	
Positive control		117 ± 0.9		115 ± 5.9		157 ± 10.1	

[a] The detailed protocol and these data are presented in 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 TA1537), and 4-nitro-*o*-phenylenediamine (TA98). The positive control for metabolic activation with all strains was 2-aminoanthracene.
[d] Slight toxicity

TABLE E2
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by 1-Chloro-2-propanol[a]

Compound	Concentration (µg/mL)	Total Cells Scored	No. of Chromo-somes	No. of SCEs	SCEs/ Chromo-some	SCEs/ Cell	Hrs in BrdU	Relative Change of SCEs/ Chromosome[b] (%)
S9								
Trial 1								
Summary: Positive								
Medium[c]		50	1,025	366	0.35	7.3	25.5	
Mitomycin-C[d]	0.001	50	1,035	637	0.61	12.7	25.5	72.36
	0.01	5	104	236	2.26	47.2	25.5	535.51
1-Chloro-2-propanol	167	50	1,051	506	0.48	10.1	25.5	34.83*
	500	25	517	543	1.05	21.7	25.5	194.14*
	1,700	25	527	675	1.28	27.0	33.5	258.71*
					P≤0.000[e]			
Trial 2								
Summary: Positive								
Medium		50	1,052	357	0.33	7.1	26.0	
Mitomycin-C	0.001	50	1,050	599	0.57	12.0	26.0	68.11
	0.01	5	105	223	2.12	44.6	26.0	525.84
1-Chloro-2-propanol	1,700	10	211	309	1.46	30.9	34.0	331.55*
	3,000	5	105	175	1.66	35.0	34.0	391.13*
	4,000	5	106	185	1.74	37.0	34.0	414.30*
					P≤0.000			
+S9								
Summary: Positive								
Medium		50	1,039	398	0.38	8.0	25.5	
Cyclophosphamide[d]	0.4	50	1,046	626	0.59	12.5	25.5	56.23
	2	5	105	218	2.07	43.6	25.5	442.00
1-Chloro-2-propanol	167	50	1,046	373	0.35	7.5	25.5	–6.91
	500	50	1,041	431	0.41	8.6	25.5	8.08
	1,700	50	1,041	664	0.63	13.3	33.5	66.51*
					P≤0.000			

* Positive response (20% increase over solvent control)
[a] Study was performed at Litton Bionetics, Inc. A detailed description of the protocol is presented in Galloway *et al*. (1987). SCE=sister chromatid exchange; BrdU=bromodeoxyuridine
[b] SCEs/chromosome in treated cells versus SCEs/chromosome in solvent control cells
[c] Solvent control
[d] Positive control
[e] Significance of SCEs/chromosome tested by the linear regression trend test versus log of the dose

TABLE E3
Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by 1-Chloro-2-propanol[a]

Compound	Concentration (µg/mL)	Total Cells Scored	Number of Aberrations	Aberrations/ Cell	Cells with Aberrations (%)
S9					
Harvest time: 20.5 hours[b]					
Summary: Positive					
Medium[c]		100	3	0.03	3.0
Mitomycin-C[d]	0.05	50	27	0.54	32.0
	0.08	25	22	0.88	52.0
1-Chloro-2-propanol	3,000	50	5	0.10	10.0
	4,000	50	11	0.22	18.0*
	5,000	50	12	0.24	22.0*
					P≤0.000[e]
+S9					
Harvest time: 20.5 hours[b]					
Summary: Positive					
Medium		200	10	0.05	4.0
Cyclophosphamide[d]	6.25	200	57	0.29	22.0
	12.5	25	18	0.72	40.0
1-Chloro-2-propanol	3,000	20	47	2.35	75.0*
	4,000	20	74	3.70	95.0*
	5,000	20	79	3.95	90.0*
					P≤0.000

* Positive response (P≤0.05) versus the solvent control
[a] Study was performed at Litton Bionetics, Inc. The detailed protocol is presented in Galloway *et al*. (1987).
[b] Due to cell cycle delay, harvest time was extended to maximize the number of first-division metaphase cells available for analysis.
[c] Solvent control
[d] Positive control
[e] Significance of percent cells with aberrations tested by the linear regression trend test versus log of the dose

TABLE E4
Induction of Sex-Linked Recessive Lethal Mutations in *Drosophila melanogaster* by 1-Chloro-2-propanol[a]

Route of Exposure	Dose (ppm)	Incidence of Death (%)	Incidence of Sterility (%)	No. of Lethals/No. of X Chromosomes Tested			Total[b]
				Mating 1	Mating 2	Mating 3	
Feed	200	16	5	0/1,948	1/1,645	1/1,556	2/5,149 (0.04%)
	0			3/3,060	9/2,972	6/2,679	18/8,711 (0.21%)
							P=0.994[c]
Injection	1,000	24	12	3/2,044	3/1,607	3/1,735	9/5,386 (0.17%)
	0			1/2,001	1/1,967	1/1,988	3/5,956 (0.05%)
							P=0.028[c]

[a] Study was performed at the University of Wisconsin, Madison. The detailed protocol and these data are presented in Foureman *et al*. (1994). The mean mutant frequency from 518 negative control experiments is 0.074% (Mason *et al.*, 1992).
[b] Total number of lethal mutations/total number of X chromosomes tested for three mating trials
[c] Significance of total number of lethal mutations/total number of X chromosomes tested by a normal approximation to the binomial test (Margolin *et al.*, 1983).

TABLE E5
Induction of Reciprocal Translocations in *Drosophila melanogaster* by 1-Chloro-2-propanol[a]

Route of Exposure	Dose (ppm)	Translocations/Total F_1 Tested						No. of Tests	Total No. of Translocations	Total Translocations (%)
		1	2	3	4	5	6			
Injection	1,000	0/2,268	1/1,941	0/768	0/308	0/26	0/9	5,312	1	0.00
Concurrent control								77,700	1	0.00
Historical control								116,163	2	0.00
										P=0.126

[a] Study was performed at the University of Wisconsin, Madison. The detailed protocol and these data are presented in Foureman *et al*. (1994). Results were not significant at the 5% level (Kastenbaum and Bowman, 1970).

TABLE E6
Frequency of Micronuclei in Mouse Peripheral Blood Erythrocytes Following Treatment with 1-Chloro-2-propanol in Drinking Water for 14 Weeks[a]

Compound	Dose (ppm)	Number of Mice	Micronucleated Cells/1,000 Cells[b]		PCEs[b] (%)
			PCEs	NCEs	
Male					
Water[c]		10	1.21 ± 0.19	1.34 ± 0.13	2.19 ± 0.11
1-Chloro-2-	33	9	2.08 ± 0.53	1.42 ± 0.12	2.35 ± 0.14
	100	10	1.79 ± 0.26	1.43 ± 0.13	2.07 ± 0.08
	330	9	1.26 ± 0.17	1.11 ± 0.06	2.39 ± 0.16
	1,000	10	1.41 ± 0.16	1.40 ± 0.09	2.17 ± 0.09
	3,000	10	1.81 ± 0.36	1.31 ± 0.08	2.59 ± 0.12
			P=0.290[d]	P=0.635	
Female					
Water		10	2.15 ± 0.38	0.98 ± 0.08	1.99 ± 0.12
1-Chloro-2-	33	10	1.12 ± 0.26	1.20 ± 0.08	2.05 ± 0.11
	100	10	1.64 ± 0.30	1.12 ± 0.07	2.08 ± 0.16
	330	10	1.24 ± 0.26	1.03 ± 0.09	2.11 ± 0.19
	1,000	10	1.58 ± 0.34	1.03 ± 0.07	1.97 ± 0.08
	3,000	10	1.51 ± 0.30	1.09 ± 0.05	2.45 ± 0.09
			P=0.559	P=0.503	

[a] Study was performed at the United States Department of Agriculture. The detailed protocol is presented in MacGregor *et al*. (1990). PCE=polychromatic erythrocyte; NCE=normochromatic erythrocyte.
[b] Mean ± standard error
[c] Vehicle control
[d] Significance of micronucleated cells/1,000 cells tested by the one-tailed trend test, significant at $P \leq 0.025$ (Margolin *et al*., 1990)

APPENDIX F
CONTINUOUS BREEDING STUDY IN SPRAGUE-DAWLEY RATS

INTRODUCTION 212
MATERIALS AND METHODS 212
RESULTS 214
TABLE F1 Fertility, Reproductive Performance, Length of Gestation, and Body Weight Data for F_0 and F_1 Sprague-Dawley Rats in the Continuous Breeding Study of 1-Chloro-2-propanol 215
TABLE F2 Litter and Body Weight Data for F_1 Sprague-Dawley Rat Pups in the Continuous Breeding Study of 1-Chloro-2-propanol 217
TABLE F3 Survival and Body Weight Data for F_1 Sprague-Dawley Rat Pups (Final Litter) in the Continuous Breeding Study of 1-Chloro-2-propanol 218
TABLE F4 Fertility, Reproductive Performance, Length of Gestation, and Body Weight Data for F_1 and F_2 Sprague-Dawley Rats in the Offspring Assessment Phase of the Continuous Breeding Study of 1-Chloro-2-propanol 219
TABLE F5 Organ Weights and Organ-Weight-to-Body-Weight Ratios for F_1 Sprague-Dawley Rats in the Offspring Assessment Phase of the Continuous Breeding Study of 1-Chloro-2-propanol 220
TABLE F6 Sperm Parameters and Estrous Cycle Characterization for F_1 Sprague-Dawley Rats in the Offspring Assessment Phase of the Continuous Breeding Study of 1-Chloro-2-propanol 221

CONTINUOUS BREEDING STUDY IN SPRAGUE-DAWLEY RATS

INTRODUCTION

The potential reproductive toxicity of 1-chloro-2-propanol was evaluated by Research Triangle Institute (Research Triangle Park, NC) in Sprague-Dawley rats because evidence in the literature suggests that exposure to 1-chloro-2-propanol may have reproductive effects (NTP, 1987b) and because data collected at the end of the 14-week NTP study in F344/N rats indicated chemical-related effects in male rats (Appendix I).

Reproductive assessment by the methods presented in Lamb (1985), NTP (1987b), and Heindel *et al.*, (1989) consists of four phases: dose setting, continuous breeding, identification of the affected sex (crossover mating trial), and offspring assessment. A 2-week dose-setting phase is conducted to determine exposure concentrations for the continuous breeding phase. During the continuous breeding phase, the effects of the maximum tolerated exposure concentration estimated in the dose-setting phase and two lower exposure concentrations on fertility and reproduction of first-generation (F_0) animals are determined. If fertility is significantly affected during the continuous breeding phase, crossover mating trials are performed to determine if males or females, or both, are affected. Offspring assessment includes evaluation of reproductive performance of second-generation (F_1) animals from the final litters of the continuous breeding phase. The F_1 animals are raised to sexual maturity while receiving the same exposure concentrations as their parents, are mated, and are allowed to deliver the third generation (F_2) offspring.

Because fertility was not significantly affected during the continuous breeding phase of the 1-chloro-2-propanol study, crossover mating trials were not conducted. The 0 and 1,300 ppm groups of the F_1 generation were assessed for fertility measures in the offspring assessment phase.

MATERIALS AND METHODS

Technical grade 1-chloro-2-propanol was obtained from Eastman Kodak Laboratory Chemicals (Rochester, NY) in one lot (B15), which was also used in the 14-day, 14-week, and 2-year studies conducted at SRI International (Menlo Park, CA) and TSI Mason Laboratories (Worcester, MA). Results of purity and stability analyses of lot B15 are given in Appendix J. Dose formulations of 1-chloro-2-propanol in deionized water were prepared at least every 3 weeks, and analyses by the study laboratory indicated that the dose formulations were within 10% of the target concentration.

Male and female VAF Crl:CD BR outbred Sprague-Dawley albino rats were obtained from Charles River Breeding Laboratories, Inc. (Portage, MI). Upon receipt, serum samples were collected from sentinel male and female rats, and the serum samples were analyzed for antibody titers to rodent viruses. All sera were negative. Rats were quarantined for approximately 2 weeks and were 10 weeks old at the start of the dose-setting phase and the continuous breeding phase. Rats were housed two per cage by sex during quarantine and the dose-setting phase. NIH-07 open formula pelleted diet and deionized water containing the appropriate concentrations of 1-chloro-2-propanol were available *ad libitum* for all phases of the study.

For the 2-week dose-setting phase, groups of eight male and eight female rats received 0, 1,000, 2,000, 4,000, 6,000, or 8,000 ppm 1-chloro-2-propanol in drinking water. Survival, clinical findings, body weights, and water consumption were recorded.

During the continuous breeding phase, rats were housed two per cage by sex for 1 week while being exposed to 0, 300, 650, or 1,300 ppm 1-chloro-2-propanol; rats were then housed in breeding pairs (40 control pairs

and 20 dosed pairs per group) for 112 days during exposure. After the mating period, rats continued to be exposed while housed separately for approximately 21 days to allow delivery of the final litter of pups. Clinical observations, water consumption, pregnancy index, litters per pair, cumulative number of days to litter, dam body weights, live pups per litter, proportion of pups born alive, sex of live pups, and pup body weights were recorded. For the last litter, pup survival and body weights were recorded on lactation days 0, 4, 7, 14, and 21.

To assess the offspring of exposed rats, the final litter of pups born to each F_0 rat in the 0 and 1,300 ppm groups was raised to sexual maturity. After weaning, siblings were housed two per cage by sex and were administered the same exposure concentrations as their parents. At sexual maturity (88 ± 10 days of age), nonsibling male and female rats from within the same exposure group (20 pairs per group) were housed as breeding pairs for 7 days. Female rats were examined for a copulatory plug or sperm, and rats were then housed individually through the delivery of the pups. Clinical observations, water consumption, mating index, pregnancy index, fertility index, dam body weights, length of gestation, live pups per litter, proportion of pups born alive, sex of live pups, and pup body weights were recorded. For the 12 days before necropsy of the F_1 rats, estrous cycle data were collected. At necropsy, epididymal spermatozoal data were collected, and the following organs were weighed: right cauda epididymis, right epididymis, kidneys, liver, right ovary, prostate gland, seminal vesicles, and right testis. Selected organs were fixed in 10% neutral buffered formalin or Bouin's fixative (ovaries only) and embedded in plastic or paraffin. Sections were stained with hematoxylin and eosin (testis only) or PAS and hematoxylin.

For data expressed as proportions (fertility, mating, and pregnancy indices), the Cochran-Armitage test (Armitage, 1971) was used to test for exposure-related trends, and pairwise comparisons were performed with a chi-square test (Conover, 1971). The number of litters and the number of live pups per litter were determined per fertile pair and then exposure group means were determined. The proportion of live pups was defined as the number of pups born alive divided by the total number of pups produced by each pair. The sex ratio was expressed as the number of male pups born alive divided by the total number of live pups born to each fertile pair.

Exposure group means for data with skewed distributions were analyzed by the nonparametric multiple comparisons methods of Shirley (1977) or Dunn (1964). Jonkheere's test (Jonkheere, 1954) or Wilcoxon's test (Conover, 1971) was used to assess the significance of exposure-response trends and to determine whether a trend-sensitive test (Shirley's) was more appropriate for pairwise comparisons than a test that does not assume a monotonic exposure-related trend (Dunn's). Multiple comparisons in the offspring assessment phase were made with Dunn's test or Wilcoxon's test (Conover, 1971).

Analysis of covariance (Neter and Wasserman, 1974), with average litter size as the covariate, was performed to remove the potential effect of number of pups per litter on average pup weight. Analysis of covariance was also used to adjust organ weights for total body weight. Least-square estimates of exposure group means adjusted for litter size were tested for overall equality by an F-test and for pairwise equality by Dunnett's test (Dunnett, 1955) or a *t*-test; these tests were performed on the data from males, females, and males and females (combined) to analyze potential sex differences. Unadjusted body and organ weights were analyzed by the Kruskal-Wallis (Kruskal and Wallis, 1952) and the Mann-Whitney-U test (Mann and Whitney, 1947).

For vaginal cytology data, 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.

RESULTS

All rats survived to the end of the dose setting study. Final mean body weights were less in 8,000 ppm males and females than in the controls; rats in these two groups lost weight during the study. Water consumption decreased with increasing exposure concentration throughout the study. Estimated daily exposure concentrations ranged from 0.9 to 0.16 g 1-chloro-2-propanol/kg body weight. Based on the adverse effects on mean body weights and water consumption, the exposure concentrations selected for the continuous breeding phase were 0, 300, 650, and 1,300 ppm.

During the continuous breeding phase, exposure to 1-chloro-2-propanol did not cause significant reproductive toxicity in rats (Table F1). All exposed and control pairs except one 300 ppm pair were fertile; all pairs exposed to 1,300 ppm delivered five litters. The average numbers of litters per pair of all exposed groups were similar to that of the controls. The cumulative number of days to litter for the 1,300 ppm group was slightly but significantly greater than that of the controls for litter 5. At delivery of each litter, the mean body weights of dams in the 650 ppm group (except for the second litter) and the 1,300 ppm group were significantly less than those of the controls. Mean body weights of litter 5 dams in the 650 ppm exposure group were significantly less than those of the controls from lactation days 0 to 14, and the mean body weights of dams in the 1,300 ppm group were significantly less than those of the controls throughout lactation. Total and adjusted pup weights, sex ratios, and number of live pups per litter were similar to those of the controls for all exposed groups for all litters (Tables F1 and F2).

The survival of the final litters of exposed F_1 pups was similar to that of the controls throughout lactation (Table F3). Male and female F_1 pup weights were significantly less than those of the controls in the 1,300 ppm group on days 7, 14, and 21 and in the 650 ppm group on days 14 and 21 (Table F3).

During the offspring assessment phase of the continuous breeding study, the mean body weight of dams in the 1,300 ppm group at delivery was significantly less than that of the controls (Table F4). Exposure to 1,300 ppm 1-chloro-2-propanol did not affect the number of live pups per litter, the sex ratio, or pup weights (Table F4) or organ weights (Table F5). The percentage of abnormal sperm was significantly greater in 1,300 ppm male rats than in the controls (Table F6). There were no significant differences in estrous cycle parameters between control and 1,300 ppm females.

TABLE F1
Fertility, Reproductive Performance, Length of Gestation, and Body Weight Data for F_0 and F_1 Sprague-Dawley Rats in the Continuous Breeding Study of 1-Chloro-2-propanol[a]

	0 ppm	300 ppm	650 ppm	1,300 ppm
F_0 Adult Data				
Pregnancy index[b]				
Litter 1	40/40 (100%)	18/19 (95%)	20/20 (100%)	20/20 (100%)
Litter 2	40/40 (100%)	18/19 (95%)	20/20 (100%)	20/20 (100%)
Litter 3	39/40 (98%)	18/19 (95%)	20/20 (100%)	20/20 (100%)
Litter 4	38/40 (95%)	17/19 (89%)	20/20 (100%)	20/20 (100%)
Litter 5	34/40 (85%)	17/19 (89%)	19/20 (95%)	20/20 (100%)
Average litters/pair	4.8 ± 0.1	4.9 ± 0.1	5.0 ± 0.1	5.0 ± 0.0
Cumulative days to litter				
Litter 1	27.00 ± 1.92	25.78 ± 0.92	25.80 ± 0.87	26.05 ± 0.91
Litter 2	50.13 ± 2.04	49.94 ± 1.63	48.50 ± 0.90	48.95 ± 0.86
Litter 3	71.10 ± 1.06	73.89 ± 2.92	71.55 ± 0.95	71.65 ± 0.89
Litter 4	94.11 ± 1.06	94.24 ± 0.98	95.60 ± 1.42	94.75 ± 0.91
Litter 5	116.74 ± 1.08	118.24 ± 1.33	118.74 ± 1.24	118.75 ± 1.00*
Dam weight at delivery (g)				
n	40	18	20	20
Litter 1	282 ± 4	277 ± 6	269 ± 5*	253 ± 5**
Litter 2	305 ± 5	303 ± 7	293 ± 6	272 ± 7**
Litter 3	330 ± 6[c]	322 ± 8	311 ± 7*	287 ± 8**
Litter 4	355 ± 7[d]	343 ± 10[e]	331 ± 8*	303 ± 7**
Litter 5	370 ± 7[f]	361 ± 11[e]	342 ± 9*[g]	314 ± 9**
Dam weight during lactation of litter 5 (g)				
n	35	18	20	19
Lactation day 0	372 ± 7	363 ± 10	342 ± 8*	315 ± 9*
Lactation day 4	370 ± 6	362 ± 1	347 ± 7*	311 ± 8*
Lactation day 7	374 ± 5	368 ± 8	351 ± 7*	319 ± 9*
Lactation day 14	379 ± 5	370 ± 8	355 ± 7*	316 ± 9*
Lactation day 21	355 ± 6	349 ± 7	342 ± 7	303 ± 7*

TABLE F1
Fertility, Reproductive Performance, Length of Gestation, and Body Weight Data for F_0 and F_1 Sprague-Dawley Rats in the Continuous Breeding Study of 1-Chloro-2-propanol

	0 ppm	300 ppm	650 ppm	1,300 ppm
F_1 Pup Data (Litters 1 Through 5)				
Number of breeding pairs	40	18	20	20
Live male pups/litter	5.7 ± 0.2	6.3 ± 0.3	5.5 ± 0.2	5.5 ± 0.2
Live female pups/litter	6.4 ± 0.2	6.3 ± 0.3	6.3 ± 0.3	6.1 ± 0.2
Total live pups/litter	12.2 ± 0.2	12.7 ± 0.6	11.8 ± 0.4	11.6 ± 0.3
Average live pups/litter (%)	97 ± 0	98 ± 0	98 ± 0	98 ± 0
Sex ratio[h] (%)	47 ± 0	50 ± 0	47 ± 0	48 ± 0
Male pup weight (g)	6.22 ± 0.06	6.36 ± 0.09	6.23 ± 0.10	6.22 ± 0.09
Female pup weight (g)	5.85 ± 0.05	5.85 ± 0.08	5.96 ± 0.09	5.93 ± 0.10
Total live pup weight[i] (g)	6.01 ± 0.05	6.11 ± 0.09	6.08 ± 0.09	6.07 ± 0.09
Adjusted total pup weight[j] (g)	6.02 ± 0.06	6.13 ± 0.09	6.07 ± 0.08	6.04 ± 0.08

* Significantly different ($P \leq 0.05$) from the control group by Shirley's test
** $P \leq 0.01$
[a] Data for average litters/pair, cumulative days to litter, body weights, live pups/litter, and sex ratio are given as mean ± standard error. Differences from the control group were not significant by the chi-square test (pregnancy index), Shirley's test (average litters/pair), Dunn's test (live pups/litter, sex ratio, and pup weights), or Dunnett's test (adjusted total pup weight).
[b] Pregnant females/cohabiting pairs
[c] n=39
[d] n=38
[e] n=17
[f] n=34
[g] n=19
[h] Live male pups/live pups
[i] Mean of average live pup weight for each fertile pair
[j] Least-squares estimate of the mean of the average pup weight for each fertile pair, adjusted for average litter size

TABLE F2
Litter and Body Weight Data for F_1 Sprague-Dawley Rat Pups in the Continuous Breeding Study of 1-Chloro-2-propanol[a]

	0 ppm	300 ppm	650 ppm	1,300 ppm
Litter 1				
Number of pairs delivering	40	18	20	20
Live pups/litter[b]	14.05 ± 0.35	14.50 ± 0.53	12.85 ± 0.89	12.85 ± 0.50
Total live pup weight[c] (g)	5.72 ± 0.07	5.69 ± 0.10	5.93 ± 0.16	5.87 ± 0.14
Adjusted total live pup weight[d] (g)	5.78 ± 0.07	5.78 ± 0.11	5.82 ± 0.11	5.78 ± 0.11
Litter 2				
Number of pairs delivering	40	18	20	20
Live pups/litter	13.00 ± 0.44	11.03 ± 0.92	11.35 ± 0.75	12.40 ± 0.52
Total live pup weight (g)	5.91 ± 0.11	6.23 ± 0.13	6.28 ± 0.17	6.03 ± 0.15
Adjusted total live pup weight (g)	6.00 ± 0.09	6.16 ± 0.13	6.15 ± 0.13	6.04 ± 0.12
Litter 3				
Number of pairs delivering	39	18	20	20
Live pups/litter	12.31 ± 0.58	12.03 ± 0.80	11.60 ± 0.59	11.45 ± 0.44
Total live pup weight (g)	6.20 ± 0.10	6.10 ± 0.11	6.16 ± 0.11	6.19 ± 0.11
Adjusted total live pup weight (g)	6.22 ± 0.08	6.15 ± 0.12	6.13 ± 0.11	6.14 ± 0.11
Litter 4				
Number of pairs delivering	38	17	20	20
Live pups/litter	10.26 ± 0.53	12.53 ± 0.66	10.70 ± 0.76	11.45 ± 0.63
Total live pup weight (g)	6.44 ± 0.09	6.35 ± 0.14	6.39 ± 0.16	6.29 ± 0.11
Adjusted total live pup weight (g)	6.36 ± 0.08	6.52 ± 0.12	6.37 ± 0.11	6.33 ± 0.11
Litter 5				
Number of pairs delivering	34	17	19	20
Live pups/litter	10.68 ± 0.53	12.18 ± 0.89	12.74 ± 0.62	9.80 ± 0.79
Total live pup weight (g)	6.33 ± 0.11	6.52 ± 0.17	6.13 ± 0.14	6.29 ± 0.15
Adjusted total live pup weight (g)	6.29 ± 0.09	6.61 ± 0.13	6.29 ± 0.12	6.12 ± 0.12
Litters 1 Through 5				
Number of pairs delivering	40	18	20	20
Live pups/litter	12.16 ± 0.21	12.65 ± 0.55	11.80 ± 0.44	11.59 ± 0.31
Total live pup weight (g)	6.01 ± 0.05	6.11 ± 0.09	6.08 ± 0.09	6.07 ± 0.09
Adjusted total live pup weight[e] (g)	6.02 ± 0.06	6.13 ± 0.09	6.07 ± 0.08	6.04 ± 0.08

[a] Data given as mean ± standard error. Differences from the control group were not significant by Shirley's or Dunn's test (live pups/litter), Dunn's test (weights), or Dunnett's test (adjusted weights)
[b] Mean of average number of live pups/litter for each fertile pair
[c] Mean of average live pup weight for each fertile pair
[d] Least-squares estimate of the mean pup weight adjusted for average litter size
[e] Least-squares estimate of the mean of the average pup weight for each fertile pair, adjusted for average litter size

TABLE F3
Survival and Body Weight Data for F_1 Sprague-Dawley Rat Pups (Final Litter) in the Continuous Breeding Study of 1-Chloro-2-propanol[a]

	0 ppm	300 ppm	650 ppm	1,300 ppm
Day 0				
Number of litters	35	18	20	19[b]
Male pup weight (g)	6.51 ± 0.14	6.64 ± 0.15	6.33 ± 0.14	6.37 ± 0.15
Female pup weight (g)	6.16 ± 0.10	6.33 ± 0.17	5.91 ± 0.13	6.22 ± 0.17
Day 4				
Male survival (%)	98 ± 0	98 ± 0	99 ± 0	97 ± 0
Female survival (%)	98 ± 0	100 ± 0	98 ± 0	100 ± 0
Total survival (%)	98 ± 0	99 ± 0	99 ± 0	99 ± 0
Male pup weight (g)	10.61 ± 0.25	10.67 ± 0.47	10.08 ± 0.34	10.04 ± 0.30
Female pup weight (g)	10.15 ± 0.19	10.36 ± 0.51	9.35 ± 0.28	9.61 ± 0.36
Day 7				
Male survival (%)	97 ± 0	96 ± 0	96 ± 0	95 ± 0
Female survival (%)	98 ± 0	100 ± 0	95 ± 0	99 ± 0
Total survival (%)	98 ± 0	98 ± 0	95 ± 0	98 ± 0
Male pup weight (g)	15.62 ± 0.38	15.78 ± 0.75	14.89 ± 0.54	14.06 ± 0.58*
Female pup weight (g)	15.00 ± 0.35	15.10 ± 0.77	13.88 ± 0.45	13.17 ± 0.55*
Day 14				
Male survival (%)	95 ± 0	91 ± 0	92 ± 0	90 ± 0
Female survival (%)	93 ± 0	95 ± 0	92 ± 0	91 ± 0
Total survival (%)	94 ± 0	94 ± 0	91 ± 0	90 ± 0
Male pup weight (g)	30.24 ± 0.72	30.80 ± 1.18	20.04 ± 0.75*	24.52 ± 1.39*
Female pup weight (g)	29.47 ± 0.58[c]	29.67 ± 1.11	26.30 ± 0.58*	24.00 ± 1.21*
Day 21				
Male survival (%)	94 ± 0	91 ± 0	92 ± 0	90 ± 0
Female survival (%)	93 ± 0	94 ± 0	91 ± 0	89 ± 0
Total survival (%)	93 ± 0	93 ± 0	91 ± 0	89 ± 0
Male pup weight (g)	48.90 ± 1.22	49.44 ± 1.88	45.31 ± 1.40*	37.83 ± 2.87*
Female pup weight (g)	46.96 ± 0.92[d]	46.78 ± 1.88	41.82 ± 1.07*	37.52 ± 2.37*

* Significantly different ($P \leq 0.05$) from the control group by Shirley's test
[a] Data are given as mean ± standard error. Differences from the control group for survival were not significant by Shirley's or Dunn's test.
[b] Because no live male pups were born in two litters, n=17 for male pup survival and body weights.
[c] n=34
[d] n=33

TABLE F4
Fertility, Reproductive Performance, Length of Gestation, and Body Weight Data for F_1 and F_2 Sprague-Dawley Rats in the Offspring Assessment Phase of the Continuous Breeding Study of 1-Chloro-2-propanol[a]

	0 ppm	1,300 ppm
F_1 Adult Data		
Mating index[b]	18/20 (90%)	18/20 (90%)
Pregnancy index[c]	17/20 (85%)	18/20 (90%)
Fertility index[d]	17/18 (94%)	18/18 (100%)
Mean dam weight at delivery (g)	317 ± 9	264 ± 4**
Days to litter	22.2 ± 0.1	22.1 ± 0.1
F_2 Pup Data		
Number of litters	17	18
Live male pups/litter	7.1 ± 0.7	7.1 ± 0.6
Live female pups/litter	7.1 ± 0.6	6.7 ± 0.4
Total live pups/litter	14.1 ± 0.8	13.8 ± 0.5
Total live pups/litter (%)	99 ± 0	100 ± 0
Sex ratio[e] (%)	50 ± 0	51 ± 0
Male pup weight (g)	6.18 ± 0.16	6.04 ± 0.12
Female pup weight (g)	5.84 ± 0.16	5.72 ± 0.10
Total live pup weight (g)	6.01 ± 0.15	5.88 ± 0.11
Adjusted total live pup weight[f] (g)	6.03 ± 0.12	5.87 ± 0.11

** Significantly different ($P \leq 0.01$) from the controls by Wilcoxon's test
[a] Data for body weights, days to litter, live pups/litter, and sex ratio are given as mean ± standard error. Differences from the control group were not significant by the chi-square test (mating and fertility indexes), Wilcoxon's test (days to litter, pups/litter, live pups, and weights), or Dunnett's test (adjusted pup weight).
[b] Females with sperm plug/cohabiting pairs
[c] Pregnant females/cohabiting pairs
[d] Pregnant females/females with sperm plug
[e] Live male pups/live pups
[f] Least-squares estimate of the mean pup weight adjusted for average litter size

TABLE F5
Organ Weights and Organ-Weight-to-Body-Weight Ratios for F_1 Sprague-Dawley Rats in the Offspring Assessment Phase of the Continuous Breeding Study of 1-Chloro-2-propanol[a]

	0 ppm	1,300 ppm
n	20	20
Male		
Necropsy body wt	520 ± 8	448 ± 8
R. Cauda Epididymis		
Absolute	224.74 ± 6.64	215.17 ± 6.61
Relative	0.434 ± 0.013	0.481 ± 0.014
R. Epididymis		
Absolute	550.86 ± 10.15	509.08 ± 10.75
Relative	1.06 ± 0.022	1.14 ± 0.022
Kidneys		
Absolute	3.85 ± 0.082	3.54 ± 0.077
Relative	7.40 ± 0.133	7.91 ± 0.070
Liver		
Absolute	22.41 ± 0.593	19.39 ± 0.554
Relative	43.12 ± 1.14	43.20 ± 0.672
Prostate Gland		
Absolute	644.88 ± 33.74	594.45 ± 31.88
Relative	1.25 ± 0.071	1.33 ± 0.073
Seminal Vesicles		
Absolute	2,424.71 ± 78.25	2,224.54 ± 72.94
Relative	4.67 ± 0.152	4.99 ± 0.175
R. Testis		
Absolute	1,741.02 ± 43.95	1,594.86 ± 36.26
Relative	3.35 ± 0.084	3.57 ± 0.066
Female		
Necropsy body wt	316 ± 8	280 ± 4
Kidneys		
Absolute	2.44 ± 0.057	2.33 ± 0.034
Relative	7.76 ± 0.131	8.36 ± 0.137
Liver		
Absolute	12.74 ± 0.416	11.43 ± 0.249
Relative	40.35 ± 0.776	40.81 ± 0.600
R. Ovary		
Absolute	56.26 ± 2.44	47.84 ± 1.79
Relative	0.181 ± 0.008	0.171 ± 0.006

[a] Liver, kidney, and body weights are given in grams; all other organ weights (absolute weights) are in milligrams; organ weights and organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error). Differences from the controls were not significant by Wilcoxon's test.

TABLE F6
Sperm Parameters and Estrous Cycle Characterization for F_1 Sprague-Dawley Rats in the Offspring Assessment Phase of the Continuous Breeding Study of 1-Chloro-2-propanol[a]

	0 ppm	1,300 ppm
Male		
n	19	20
Epididymal spermatozoal measurements		
Motility (%)	85.0 ± 1.4[b]	86.7 ± 1.7
Abnormal (%)	0.78 ± 0.11	2.4 ± 0.53*
Concentration (10^6/g cauda epididymal tissue)	497 ± 25	488 ± 20
Female		
n	20	20
Estrous cycle length (days)	4.20 ± 0.08	4.55 ± 0.18
Estrous stages (% of cycle)		
Diestrus	30.8	38.3
Proestrus	22.1	19.6
Estrus	26.2	24.6
Metestrus	20.4	16.2
Uncertain diagnosis	0.4	1.2

* Significantly different ($P \leq 0.05$) from the control group by Wilcoxon's test
[a] Epididymal spermatozoal measurements and estrous cycle length data are given as mean ± standard error. Differences from the control group are not significant by Dunn's test (motility and concentration) or Wilcoxon's test (estrous cycle length). By multivariate analysis of variance, exposed females do not differ significantly from control females in the relative length of time spent in estrous stages.
[b] n=20

APPENDIX G
HEMATOLOGY, CLINICAL CHEMISTRY, AND URINALYSIS RESULTS

TABLE G1 **Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol** 224
TABLE G2 **Hematology Data for Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol** 228

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm
Male						
n	10	10	10	10	10	10
Hematology						
Hematocrit (%)	45.7 ± 0.6	46.7 ± 0.4	45.2 ± 0.5	47.1 ± 0.7	46.7 ± 0.4	45.8 ± 0.5
Hemoglobin (g/dL)	16.4 ± 0.2	16.7 ± 0.1	16.5 ± 0.1	16.7 ± 0.3	16.4 ± 0.1	15.7 ± 0.1**
Erythrocytes (10^6/µL)	8.71 ± 0.12	8.92 ± 0.08	8.72 ± 0.09	9.05 ± 0.16	8.94 ± 0.07	8.59 ± 0.08
Reticulocytes (10^6/µL)	0.26 ± 0.03	0.22 ± 0.02	0.21 ± 0.02	0.22 ± 0.01	0.22 ± 0.02	0.27 ± 0.02
Nucleated erythrocytes (10^3/µL)	0.01 ± 0.01	0.00 ± 0.00	0.01 ± 0.01	0.02 ± 0.01	0.01 ± 0.01	0.01 ± 0.01
Mean cell volume (fL)	51.4 ± 0.3	51.3 ± 0.2	50.9 ± 0.2	51.4 ± 0.3	51.1 ± 0.3	52.3 ± 0.2
Mean cell hemoglobin (pg)	18.8 ± 0.1	18.6 ± 0.2	18.8 ± 0.3	18.3 ± 0.2	18.1 ± 0.1**	18.0 ± 0.0**
Mean cell hemoglobin concentration (g/dL)	36.0 ± 0.0	36.0 ± 0.1	36.7 ± 0.4	35.3 ± 0.2*	35.1 ± 0.2**	34.2 ± 0.1**
Platelets (10^3/µL)	687.0 ± 22.1	687.4 ± 21.8	708.0 ± 17.0	649.8 ± 15.8	667.4 ± 10.7	615.0 ± 21.1
Mean platelet volume (fL)	7.35 ± 0.03	7.18 ± 0.07	7.32 ± 0.08	7.23 ± 0.07	7.17 ± 0.06	7.36 ± 0.08
Leukocytes (10^3/µL)	10.36 ± 0.36	10.04 ± 0.38	10.24 ± 0.34	9.53 ± 0.42	9.93 ± 0.33	7.72 ± 0.37**
Segmented neutrophils (10^3/µL)	1.16 ± 0.11	1.10 ± 0.17	1.54 ± 0.12	1.04 ± 0.12	1.25 ± 0.19	1.04 ± 0.07
Lymphocytes (10^3/µL)	8.91 ± 0.35	8.47 ± 0.35	8.12 ± 0.31	8.29 ± 0.43	8.15 ± 0.28	6.50 ± 0.36**
Monocytes (10^3/µL)	0.21 ± 0.06	0.43 ± 0.09	0.50 ± 0.16	0.08 ± 0.03	0.42 ± 0.15	0.05 ± 0.02*
Eosinophils (10^3/µL)	0.07 ± 0.02	0.05 ± 0.02	0.07 ± 0.03	0.05 ± 0.02	0.06 ± 0.02	0.07 ± 0.03
Clinical Chemistry						
Creatinine (mg/dL)						
Day 3	0.66 ± 0.03	0.55 ± 0.04	0.45 ± 0.02**	0.47 ± 0.02**	0.51 ± 0.01*	0.53 ± 0.02[b]
Day 15	0.35 ± 0.02	0.47 ± 0.02*	0.50 ± 0.05	0.55 ± 0.02**	0.36 ± 0.02	0.34 ± 0.02
Day 45	0.68 ± 0.03	0.58 ± 0.03	0.58 ± 0.05	0.62 ± 0.03	0.63 ± 0.03	0.67 ± 0.03
Week 14	0.56 ± 0.03	0.58 ± 0.05	0.58 ± 0.06[b]	0.66 ± 0.04	0.60 ± 0.05	0.63 ± 0.03
Albumin (g/dL)						
Day 3	4.5 ± 0.1	4.0 ± 0.1**[b]	4.0 ± 0.1**	3.8 ± 0.0**	4.0 ± 0.1**	4.0 ± 0.1**[b]
Day 15	4.4 ± 0.1[b]	4.7 ± 0.1	4.6 ± 0.1	4.5 ± 0.1[b]	4.3 ± 0.1[b]	4.0 ± 0.1*
Day 45	4.3 ± 0.1	4.3 ± 0.2	4.4 ± 0.2	4.4 ± 0.1	4.3 ± 0.1	4.4 ± 0.1
Week 14	4.9 ± 0.1[b]	4.8 ± 0.1[c]	4.7 ± 0.1[b]	4.7 ± 0.1	4.9 ± 0.1	4.6 ± 0.1
Alanine aminotransferase (IU/L)						
Day 3	33 ± 1	31 ± 1	33 ± 1	30 ± 2	19 ± 1**	16 ± 1**
Day 15	31 ± 1	28 ± 1*	24 ± 1**	22 ± 1**	16 ± 0**	6 ± 1**
Day 45	34 ± 2	35 ± 2	34 ± 1	31 ± 1	20 ± 1**	11 ± 0**
Week 14	30 ± 1	34 ± 1	31 ± 1	33 ± 2	22 ± 1**	12 ± 2**
Creatine kinase (IU/L)						
Day 3	266 ± 41	462 ± 129	334 ± 76	478 ± 124	413 ± 121	444 ± 92
Day 15	619 ± 122	831 ± 244	368 ± 58	588 ± 161	719 ± 119	579 ± 141
Day 45	267 ± 47	305 ± 31	476 ± 88	305 ± 33	245 ± 32	315 ± 54
Week 14	175 ± 36	236 ± 41	220 ± 37	227 ± 54	226 ± 32	154 ± 15
Sorbitol dehydrogenase (IU/L)						
Day 3	14 ± 1[b]	15 ± 1	14 ± 0	14 ± 1	13 ± 1	23 ± 2**
Day 15	20 ± 3[b]	14 ± 0	13 ± 0	14 ± 1	16 ± 1[c]	14 ± 1
Day 45	25 ± 2	22 ± 1	22 ± 1	19 ± 1**	20 ± 1*	18 ± 2**
Week 14	20 ± 2	21 ± 2	19 ± 1	18 ± 1	19 ± 2	19 ± 2

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	33 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm
Male (continued)						
n	10	10	10	10	10	10
Clinical Chemistry (continued)						
γ-Glutamyltransferase (IU/L)						
Day 3	2.3 ± 0.7[b]	1.7 ± 0.2[b]	1.8 ± 0.3[d]	2.3 ± 0.2[e]	2.3 ± 0.4	2.4 ± 0.3[c]
Day 15	—[f]	—	—	—	—	—
Day 45	—	—	—	—	—	—
Week 14	—	—	—	—	—	—
Urinalysis						
Glucose (mg/100 g per 16 hr)						
Day 15	0.599 ± 0.028	0.884 ± 0.021**	0.622 ± 0.055	0.680 ± 0.044	0.695 ± 0.034	0.491 ± 0.044
Week 14	0.441 ± 0.046	0.430 ± 0.029	0.417 ± 0.026	0.424 ± 0.032	0.389 ± 0.022	0.618 ± 0.038*
Protein (mg/100 g per 16 hr)						
Day 15	2.048 ± 0.220	2.391 ± 0.086	1.872 ± 0.234	1.364 ± 0.153*	1.423 ± 0.145*	0.486 ± 0.082**
Week 14	0.985 ± 0.104	1.217 ± 0.096	1.145 ± 0.088	1.199 ± 0.103	1.006 ± 0.131	0.829 ± 0.073
Volume (mL/16 hr)						
Day 15	5.6 ± 0.8	8.0 ± 0.1	6.6 ± 0.8	5.0 ± 0.6	4.5 ± 0.6	0.9 ± 0.1**
Week 14	5.9 ± 0.9	6.8 ± 0.7	6.2 ± 0.6	5.6 ± 0.5	4.7 ± 0.4	2.7 ± 0.3**
Specific gravity						
Day 15	1.030 ± 0.003	1.024 ± 0.002	1.025 ± 0.003	1.033 ± 0.003	1.038 ± 0.004	1.099 ± 0.012**
Week 14	1.039 ± 0.004	1.034 ± 0.004	1.040 ± 0.004	1.039 ± 0.002	1.047 ± 0.004	1.070 ± 0.004**
Female						
n	10	10	10	10	9	10
Hematology						
Hematocrit (%)	47.6 ± 0.4	45.2 ± 0.5**	45.7 ± 0.4**	46.5 ± 0.3**	44.7 ± 0.3**	45.6 ± 0.4**
Hemoglobin (g/dL)	16.9 ± 0.1	16.3 ± 0.1**	16.7 ± 0.1	16.7 ± 0.1	15.9 ± 0.1**	16.0 ± 0.1**
Erythrocytes (10^6/μL)	8.34 ± 0.07	8.14 ± 0.08	8.29 ± 0.06	8.27 ± 0.06	7.83 ± 0.05**	7.61 ± 0.06**
Reticulocytes (10^6/μL)	0.15 ± 0.01	0.20 ± 0.02*	0.20 ± 0.02*	0.19 ± 0.02	0.18 ± 0.02	0.33 ± 0.03**
Nucleated erythrocytes (10^3/μL)	0.01 ± 0.01	0.02 ± 0.01	0.00 ± 0.00	0.00 ± 0.00	0.01 ± 0.01	0.01 ± 0.01
Mean cell volume (fL)	55.8 ± 0.2	54.4 ± 0.3	53.8 ± 0.1	54.9 ± 0.2	56.1 ± 0.4	58.2 ± 0.2*
Mean cell hemoglobin (pg)	20.0 ± 0.0	20.0 ± 0.1	20.0 ± 0.0	20.0 ± 0.0	20.1 ± 0.1	21.0 ± 0.0**
Mean cell hemoglobin concentration (g/dL)	35.6 ± 0.2	36.3 ± 0.3	36.5 ± 0.2	36.1 ± 0.2	35.6 ± 0.2	35.1 ± 0.1
Platelets (10^3/μL)	633.8 ± 20.8	668.6 ± 23.5	674.2 ± 25.5	727.2 ± 16.2**	738.4 ± 14.2**	672.8 ± 15.0
Mean platelet volume (fL)	6.88 ± 0.05	7.19 ± 0.06**	7.15 ± 0.06*	6.89 ± 0.06	7.10 ± 0.05[g]	7.09 ± 0.06
Leukocytes (10^3/μL)	8.41 ± 0.38	8.78 ± 0.48	9.49 ± 0.33	9.16 ± 0.35	9.16 ± 0.50	9.46 ± 0.30
Segmented neutrophils (10^3/μL)	0.98 ± 0.10	1.23 ± 0.14	1.08 ± 0.12	0.93 ± 0.13	0.96 ± 0.15	1.30 ± 0.14
Lymphocytes (10^3/μL)	7.13 ± 0.33	7.36 ± 0.48	7.97 ± 0.25	7.97 ± 0.33	8.08 ± 0.48	7.69 ± 0.37
Monocytes (10^3/μL)	0.27 ± 0.06	0.09 ± 0.02	0.34 ± 0.07	0.21 ± 0.06	0.08 ± 0.02	0.36 ± 0.05
Eosinophils (10^3/μL)	0.04 ± 0.02	0.07 ± 0.02	0.06 ± 0.02	0.02 ± 0.01	0.03 ± 0.02	0.07 ± 0.03

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	33 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm
Female (continued)						
n	10	10	10	10	10	10
Clinical Chemistry						
Creatinine (mg/dL)						
Day 3	0.58 ± 0.03	0.55 ± 0.02	0.58 ± 0.02	0.45 ± 0.03*	0.57 ± 0.03	0.49 ± 0.02
Day 15	0.57 ± 0.03	0.50 ± 0.04	0.56 ± 0.04	0.52 ± 0.03	0.57 ± 0.03	0.64 ± 0.02
Day 45	0.49 ± 0.03	0.36 ± 0.02*	0.49 ± 0.05	0.51 ± 0.02	0.42 ± 0.02	0.55 ± 0.03
Week 14	0.57 ± 0.02	0.62 ± 0.03[b]	0.58 ± 0.06	0.66 ± 0.03	0.59 ± 0.04[b]	0.64 ± 0.04
Albumin (g/dL)						
Day 3	4.7 ± 0.1	4.3 ± 0.1**	4.3 ± 0.0*	4.4 ± 0.1	4.4 ± 0.1*	4.3 ± 0.1**
Day 15	4.8 ± 0.1	4.7 ± 0.1[b]	4.6 ± 0.1	4.3 ± 0.1**[b]	4.6 ± 0.1[b]	5.0 ± 0.1
Day 45	5.2 ± 0.1	4.8 ± 0.1*	4.7 ± 0.1**	4.9 ± 0.1	5.0 ± 0.1	4.9 ± 0.1
Week 14	5.1 ± 0.1[b]	4.5 ± 0.4[b]	5.0 ± 0.1	5.0 ± 0.1	4.8 ± 0.1*[b]	5.2 ± 0.1
Alanine aminotransferase (IU/L)						
Day 3	29 ± 1	28 ± 1	22 ± 1**	22 ± 2**	16 ± 1**	17 ± 1**
Day 15	23 ± 2	26 ± 1	24 ± 1	19 ± 1*	11 ± 1**	7 ± 1**
Day 45	25 ± 1	24 ± 2	22 ± 1*	23 ± 2	16 ± 1**	10 ± 1**
Week 14	28 ± 2	36 ± 3	29 ± 2	24 ± 1	18 ± 1**	9 ± 1**[b]
Creatine kinase (IU/L)						
Day 3	347 ± 75	416 ± 69	670 ± 331	731 ± 272	246 ± 57	251 ± 32
Day 15	306 ± 76	396 ± 113	285 ± 31	318 ± 61	318 ± 78	296 ± 63
Day 45	197 ± 26	200 ± 32	134 ± 14[h]	286 ± 76[h]	263 ± 45[h]	186 ± 34
Week 14	186 ± 40	214 ± 59	160 ± 27	178 ± 17	176 ± 30	278 ± 63
Sorbitol dehydrogenase (IU/L)						
Day 3	12 ± 0	12 ± 1	12 ± 0	11 ± 0	11 ± 0	16 ± 2
Day 15	18 ± 1	19 ± 2	17 ± 1	20 ± 2	17 ± 1	16 ± 1
Day 45	19 ± 1	18 ± 2	21 ± 1	23 ± 2	21 ± 1	21 ± 2
Week 14	18 ± 2	16 ± 1	15 ± 1	17 ± 1	16 ± 1	18 ± 2
γ-Glutamyltransferase (IU/L)						
Day 3	1.8 ± 0.2	3.2 ± 0.4*[b]	1.8 ± 0.3[b]	3.4 ± 0.4*[c]	2.6 ± 0.2[b]	2.7 ± 0.4[b]
Day 15	—	—	—	—	—	—
Day 45	—	—	—	—	—	—
Week 14	—	—	—	—	—	—

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol

	0 ppm	33 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm
Female (continued)						
n						
Day 15	10	10	10	10	10	10
Week 14	10	10	10	10	10	9
Urinalysis						
Glucose (mg/100 g per 16 hr)						
Day 15	0.781 ± 0.072	0.403 ± 0.056**	0.676 ± 0.049	0.724 ± 0.040	0.732 ± 0.030	0.787 ± 0.043
Week 14	0.495 ± 0.022	0.529 ± 0.040	0.405 ± 0.029	0.484 ± 0.036	0.487 ± 0.032	0.418 ± 0.046
Protein (mg/100 g per 16 hr)						
Day 15	6.311 ± 0.614	5.386 ± 0.680	6.520 ± 0.517	5.479 ± 0.468	4.332 ± 0.185	4.805 ± 0.358
Week 14	0.359 ± 0.029	0.418 ± 0.027	0.318 ± 0.029	0.330 ± 0.031	0.299 ± 0.017	0.262 ± 0.041
Volume (mL/16 hr)						
Day 15	8.7 ± 1.2	10.9 ± 1.7	9.5 ± 1.0	7.7 ± 0.8	8.5 ± 0.8	3.3 ± 0.3**
Week 14	6.7 ± 1.1	5.2 ± 0.7	3.8 ± 1.0*	7.3 ± 1.4	4.5 ± 0.9	1.8 ± 0.4**
Specific gravity						
Day 15	1.021 ± 0.002	1.016 ± 0.002	1.019 ± 0.002	1.022 ± 0.003	1.019 ± 0.001	1.040 ± 0.003**
Week 14	1.031 ± 0.004	1.031 ± 0.004	1.043 ± 0.006	1.027 ± 0.005	1.036 ± 0.004	1.072 ± 0.007**

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error. Statistical tests were performed on unrounded data.
[b] n=9
[c] n=8
[d] n=6
[e] n=7
[f] Data for γ-glutamyltransferase were below 1 IU/L; therefore, no mean or standard error was calculated.
[g] n=10
[h] n=5

TABLE G2
Hematology Data for Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm
Male						
n	10	10	10	9	10	9
Hematocrit (%)	52.9 ± 0.9	53.0 ± 0.8	52.5 ± 0.7	54.5 ± 0.8	52.4 ± 0.4	49.4 ± 1.3
Hemoglobin (g/dL)	17.6 ± 0.3	17.6 ± 0.3	17.5 ± 0.1	17.7 ± 0.3	17.1 ± 0.1*	15.9 ± 0.4**
Erythrocytes (10^6/µL)	10.46 ± 0.16	10.49 ± 0.19	10.31 ± 0.16	10.53 ± 0.17	10.17 ± 0.07	9.49 ± 0.24**
Reticulocytes (10^6/µL)	0.23 ± 0.02	0.26 ± 0.02	0.19 ± 0.02	0.22 ± 0.03	0.24 ± 0.03	0.25 ± 0.03
Nucleated erythrocytes (10^3/µL)	0.00 ± 0.00	0.00 ± 0.00	0.01 ± 0.01	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Mean cell volume (fL)	49.3 ± 0.2	49.5 ± 0.4	49.9 ± 0.2	50.7 ± 0.3**	50.2 ± 0.1**	50.9 ± 0.3**
Mean cell hemoglobin (pg)	17.0 ± 0.0	16.8 ± 0.1	17.2 ± 0.2	16.8 ± 0.1	17.0 ± 0.0	16.9 ± 0.1
Mean cell hemoglobin concentration (g/dL)	33.5 ± 0.2	32.9 ± 0.2	33.4 ± 0.3	32.4 ± 0.2**	32.6 ± 0.2**	32.2 ± 0.2**
Platelets (10^3/µL)	1,058.2 ± 18.4[b]	1,005.6 ± 22.8	1,059.2 ± 23.0	1,033.6 ± 28.7	1,053.8 ± 15.6	917.0 ± 22.2**
Mean platelet volume (fL)	5.66 ± 0.05	5.75 ± 0.02	5.73 ± 0.04	5.58 ± 0.03	5.72 ± 0.04	5.66 ± 0.06
Leukocytes (10^3/µL)	5.19 ± 0.28	4.84 ± 0.33	5.18 ± 0.34	3.09 ± 0.28**	4.52 ± 0.28	4.56 ± 0.26
Segmented neutrophils (10^3/µL)	0.64 ± 0.07	0.49 ± 0.03	0.63 ± 0.12	0.32 ± 0.04**	0.43 ± 0.03	0.47 ± 0.04
Lymphocytes (10^3/µL)	4.49 ± 0.24	4.13 ± 0.32	4.41 ± 0.25	2.67 ± 0.24**	3.99 ± 0.25	3.96 ± 0.24
Monocytes (10^3/µL)	0.02 ± 0.01	0.16 ± 0.06*	0.05 ± 0.01	0.09 ± 0.03	0.04 ± 0.01	0.04 ± 0.01
Eosinophils (10^3/µL)	0.03 ± 0.01	0.02 ± 0.01	0.05 ± 0.02	0.01 ± 0.00	0.03 ± 0.02	0.05 ± 0.02
Female						
n	10	10	10	9	10	10
Hematocrit (%)	51.4 ± 1.3	55.0 ± 0.9	54.9 ± 0.6	54.8 ± 0.7	53.9 ± 1.1	56.0 ± 1.7
Hemoglobin (g/dL)	18.6 ± 0.3	18.2 ± 0.2	17.8 ± 0.2	18.4 ± 0.2	17.3 ± 0.3*	18.0 ± 0.5
Erythrocytes (10^6/µL)	9.62 ± 0.30	10.28 ± 0.14	10.16 ± 0.15	10.36 ± 0.15	9.97 ± 0.20	10.52 ± 0.29*
Reticulocytes (10^6/µL)	0.20 ± 0.01	0.18 ± 0.02	0.17 ± 0.01	0.19 ± 0.02	0.18 ± 0.01	0.24 ± 0.01
Nucleated erythrocytes (10^3/µL)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Mean cell volume (fL)	51.8 ± 0.3	52.3 ± 0.3	52.8 ± 0.4	51.8 ± 0.4	53.0 ± 0.3	52.2 ± 0.2
Mean cell hemoglobin (pg)	19.5 ± 0.4	17.7 ± 0.2**	17.3 ± 0.2**	17.7 ± 0.2**	17.4 ± 0.2**	17.1 ± 0.1**
Mean cell hemoglobin concentration (g/dL)	36.4 ± 0.6	32.9 ± 0.2**	32.5 ± 0.3**	33.8 ± 0.3**	32.2 ± 0.2**	32.2 ± 0.2**
Platelets (10^3/µL)	893.1 ± 32.2[b]	942.4 ± 36.4	912.2 ± 31.5	882.8 ± 17.1[c]	915.8 ± 34.5	804.2 ± 73.8
Mean platelet volume (fL)	5.54 ± 0.04	5.79 ± 0.03**	5.77 ± 0.05*	5.70 ± 0.06[c]	5.58 ± 0.04	5.85 ± 0.05**
Leukocytes (10^3/µL)	5.18 ± 0.20	6.14 ± 0.33	5.22 ± 0.29	5.24 ± 0.51	5.86 ± 0.28	3.62 ± 0.26
Segmented neutrophils (10^3/µL)	0.58 ± 0.06	0.62 ± 0.06	0.63 ± 0.07	0.51 ± 0.09	0.46 ± 0.05	0.24 ± 0.05**
Lymphocytes (10^3/µL)	4.32 ± 0.17	5.18 ± 0.32	4.30 ± 0.24	4.50 ± 0.46	5.04 ± 0.28	3.18 ± 0.25
Monocytes (10^3/µL)	0.21 ± 0.05	0.29 ± 0.10	0.25 ± 0.08	0.18 ± 0.05	0.32 ± 0.10	0.14 ± 0.04
Eosinophils (10^3/µL)	0.04 ± 0.01	0.02 ± 0.01	0.02 ± 0.02	0.05 ± 0.03	0.02 ± 0.01	0.03 ± 0.01

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

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

TABLE H1 Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 14-Day Drinking Water Study of 1-Chloro-2-propanol 230
TABLE H2 Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol 231
TABLE H3 Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 14-Day Drinking Water Study of 1-Chloro-2-propanol 232
TABLE H4 Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol 233

TABLE H1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 14-Day Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm	10,000 ppm
Male						
n	10	10	10	10	10	10
Necropsy body wt	196 ± 3	193 ± 5	198 ± 3	195 ± 5	162 ± 4**	88 ± 2**
Brain						
Absolute	1.899 ± 0.011	1.875 ± 0.012	1.848 ± 0.027	1.888 ± 0.014	1.804 ± 0.020**	1.740 ± 0.012**
Relative	9.73 ± 0.11	9.78 ± 0.23	9.35 ± 0.13	9.72 ± 0.25	11.16 ± 0.23**	19.99 ± 0.48**
Heart						
Absolute	0.805 ± 0.033	0.787 ± 0.015	0.810 ± 0.012	0.822 ± 0.027	0.636 ± 0.014**	0.417 ± 0.013**
Relative	4.11 ± 0.13	4.10 ± 0.09	4.10 ± 0.07	4.21 ± 0.09	3.93 ± 0.08	4.77 ± 0.12**
R. Kidney						
Absolute	1.044 ± 0.020	1.031 ± 0.020	1.074 ± 0.038	1.041 ± 0.025	0.967 ± 0.014*	0.686 ± 0.016**
Relative	5.34 ± 0.08	5.37 ± 0.13	5.42 ± 0.14	5.34 ± 0.10	5.98 ± 0.09**	7.85 ± 0.14**
Liver						
Absolute	10.796 ± 0.288	11.039 ± 0.307	11.440 ± 0.262	11.638 ± 0.387	9.613 ± 0.187**	4.562 ± 0.176**
Relative	55.21 ± 1.16	57.36 ± 1.22	57.76 ± 0.66	59.46 ± 0.82*	59.35 ± 0.76*	52.02 ± 0.94
Lung						
Absolute	1.232 ± 0.035	1.217 ± 0.035	1.200 ± 0.030	1.177 ± 0.035	0.955 ± 0.020**	0.709 ± 0.017**
Relative	6.30 ± 0.16	6.34 ± 0.20	6.07 ± 0.14	6.03 ± 0.15	5.90 ± 0.11	8.15 ± 0.27**
R. Testis						
Absolute	1.181 ± 0.021	1.135 ± 0.024	1.163 ± 0.020	1.143 ± 0.025	1.110 ± 0.028	0.898 ± 0.036**
Relative	6.04 ± 0.10	5.90 ± 0.10	5.88 ± 0.10	5.87 ± 0.13	6.85 ± 0.14**	10.24 ± 0.22**
Thymus						
Absolute	0.517 ± 0.012	0.540 ± 0.019	0.557 ± 0.019	0.553 ± 0.013	0.455 ± 0.018**	0.136 ± 0.013**
Relative	2.64 ± 0.05	2.81 ± 0.12	2.82 ± 0.09	2.84 ± 0.09	2.81 ± 0.11	1.54 ± 0.12**
Female						
n	10	10	10	10	10	8
Necropsy body wt	136 ± 2	139 ± 2	139 ± 2	139 ± 3	123 ± 1**	67 ± 3**
Brain						
Absolute	1.781 ± 0.022	1.829 ± 0.013	1.797 ± 0.017	1.793 ± 0.015	1.753 ± 0.016	1.625 ± 0.022**
Relative	13.09 ± 0.22	13.18 ± 0.29	12.98 ± 0.17	12.96 ± 0.25	14.28 ± 0.14*	24.39 ± 0.90**
Heart						
Absolute	0.605 ± 0.014	0.596 ± 0.015	0.612 ± 0.011	0.616 ± 0.013	0.559 ± 0.009*	0.356 ± 0.016**
Relative	4.44 ± 0.07	4.28 ± 0.10	4.42 ± 0.09	4.44 ± 0.06	4.55 ± 0.06	5.31 ± 0.16**
R. Kidney						
Absolute	0.733 ± 0.017	0.739 ± 0.017	0.753 ± 0.019	0.789 ± 0.022	0.774 ± 0.017	0.556 ± 0.019**
Relative	5.38 ± 0.09	5.31 ± 0.12	5.43 ± 0.09	5.69 ± 0.10	6.30 ± 0.10**	8.30 ± 0.21**
Liver						
Absolute	6.775 ± 0.123	7.025 ± 0.098	7.430 ± 0.148*	7.656 ± 0.173**	6.789 ± 0.104	3.471 ± 0.246**
Relative	49.73 ± 0.71	50.50 ± 0.55	53.58 ± 0.52**	55.20 ± 0.73**	55.27 ± 0.57**	51.19 ± 2.07**
Lung						
Absolute	0.995 ± 0.015	0.988 ± 0.016	0.969 ± 0.026	0.997 ± 0.021	0.839 ± 0.011**	0.641 ± 0.018**
Relative	7.31 ± 0.15	7.11 ± 0.13	6.98 ± 0.11	7.20 ± 0.13	6.83 ± 0.06	9.58 ± 0.25**
Thymus						
Absolute	0.420 ± 0.015	0.413 ± 0.013	0.465 ± 0.014	0.435 ± 0.015	0.421 ± 0.014	0.093 ± 0.026**
Relative	3.08 ± 0.10	2.97 ± 0.09	3.36 ± 0.08	3.13 ± 0.08	3.42 ± 0.10	1.32 ± 0.35**

* 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 H2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm
n	10	10	10	10	10	10
Male						
Necropsy body wt	379 ± 6	377 ± 9	377 ± 9	385 ± 8	383 ± 6	322 ± 5**
Brain						
Absolute	1.985 ± 0.023	2.004 ± 0.027	2.036 ± 0.019	1.999 ± 0.024	1.986 ± 0.016	1.937 ± 0.015
Relative	5.24 ± 0.05	5.34 ± 0.09	5.42 ± 0.11	5.20 ± 0.08	5.20 ± 0.09	6.02 ± 0.08**
Heart						
Absolute	1.148 ± 0.029	1.112 ± 0.032	1.167 ± 0.038	1.147 ± 0.028	1.124 ± 0.017	1.034 ± 0.032*
Relative	3.03 ± 0.04	2.95 ± 0.03	3.09 ± 0.06	2.98 ± 0.04	2.94 ± 0.05	3.20 ± 0.07
R. Kidney						
Absolute	1.268 ± 0.029	1.238 ± 0.041	1.448 ± 0.049**	1.316 ± 0.035	1.393 ± 0.035	1.258 ± 0.022
Relative	3.35 ± 0.05	3.28 ± 0.04	3.84 ± 0.09**	3.42 ± 0.06**	3.64 ± 0.05**	3.90 ± 0.06**
Liver						
Absolute	14.030 ± 0.355	14.181 ± 0.404	15.281 ± 0.696	16.100 ± 0.468*	16.374 ± 0.292**	14.103 ± 0.444
Relative	37.01 ± 0.65	37.64 ± 0.37	40.53 ± 1.51**	41.76 ± 0.54**	42.79 ± 0.56**	43.73 ± 1.16**
Lung						
Absolute	1.648 ± 0.048	1.656 ± 0.065	1.524 ± 0.031	1.724 ± 0.030	1.542 ± 0.056	1.422 ± 0.041**
Relative	4.35 ± 0.12	4.40 ± 0.13	4.05 ± 0.07	4.49 ± 0.10	4.03 ± 0.13	4.41 ± 0.12
R. Testis						
Absolute	1.514 ± 0.028	1.489 ± 0.033	1.561 ± 0.034	1.547 ± 0.031	1.505 ± 0.024	1.487 ± 0.025
Relative	4.00 ± 0.03	3.96 ± 0.06	4.14 ± 0.05	4.02 ± 0.05	3.93 ± 0.03	4.61 ± 0.05**
Thymus						
Absolute	0.290 ± 0.009	0.314 ± 0.013	0.283 ± 0.008	0.304 ± 0.009	0.312 ± 0.010	0.285 ± 0.011
Relative	0.77 ± 0.02	0.83 ± 0.03	0.75 ± 0.02	0.79 ± 0.03	0.82 ± 0.03	0.88 ± 0.03*
Female						
Necropsy body wt	212 ± 7	207 ± 4	218 ± 4	209 ± 3	207 ± 3	185 ± 3**
Brain						
Absolute	1.816 ± 0.016	1.819 ± 0.015	1.835 ± 0.010	1.834 ± 0.013	1.816 ± 0.013	1.770 ± 0.025
Relative	8.66 ± 0.33	8.83 ± 0.10	8.43 ± 0.14	8.81 ± 0.14	8.80 ± 0.12	9.60 ± 0.11**
Heart						
Absolute	0.730 ± 0.016	0.714 ± 0.011	0.764 ± 0.017	0.729 ± 0.015	0.709 ± 0.012	0.644 ± 0.011**
Relative	3.49 ± 0.18	3.46 ± 0.05	3.51 ± 0.07	3.50 ± 0.04	3.43 ± 0.06	3.49 ± 0.03
R. Kidney						
Absolute	0.720 ± 0.019	0.743 ± 0.018	0.821 ± 0.014**	0.758 ± 0.023	0.797 ± 0.010*	0.762 ± 0.019
Relative	3.40 ± 0.05	3.60 ± 0.08*	3.77 ± 0.04**	3.63 ± 0.09**	3.86 ± 0.05**	4.13 ± 0.08**
Liver						
Absolute	7.273 ± 0.221	7.286 ± 0.204	7.963 ± 0.170*	7.785 ± 0.154	8.077 ± 0.168*	6.777 ± 0.150
Relative	34.37 ± 0.59	35.27 ± 0.68	36.52 ± 0.56*	37.40 ± 0.83**	39.06 ± 0.51**	36.72 ± 0.63**
Lung						
Absolute	1.155 ± 0.052	1.210 ± 0.044	1.110 ± 0.019	1.211 ± 0.037	1.048 ± 0.023*	0.960 ± 0.013**
Relative	5.45 ± 0.18	5.86 ± 0.20	5.09 ± 0.06	5.82 ± 0.18	5.07 ± 0.09	5.21 ± 0.06
Thymus						
Absolute	0.261 ± 0.011	0.237 ± 0.009	0.261 ± 0.006	0.254 ± 0.010	0.238 ± 0.007	0.227 ± 0.008*
Relative	1.24 ± 0.06	1.15 ± 0.04	1.20 ± 0.02	1.22 ± 0.04	1.16 ± 0.04	1.23 ± 0.03

* 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 H3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 14-Day Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm	10,000 ppm
Male						
n	10	10	10	10	10	9
Necropsy body wt	28.1 ± 0.6	27.7 ± 0.5	27.5 ± 0.7	28.7 ± 0.4	28.4 ± 0.5	24.3 ± 0.6**
Brain						
Absolute	0.525 ± 0.009	0.515 ± 0.010	0.509 ± 0.009	0.534 ± 0.009	0.502 ± 0.008	0.510 ± 0.009
Relative	18.75 ± 0.34	18.61 ± 0.42	18.60 ± 0.54	18.65 ± 0.43	17.73 ± 0.34	21.10 ± 0.71**
Heart						
Absolute	0.167 ± 0.005	0.150 ± 0.005	0.154 ± 0.008	0.159 ± 0.006	0.156 ± 0.009	0.141 ± 0.009
Relative	5.97 ± 0.20	5.41 ± 0.14	5.58 ± 0.21	5.55 ± 0.22	5.49 ± 0.29	5.82 ± 0.37
R. Kidney						
Absolute	0.325 ± 0.010	0.319 ± 0.012	0.321 ± 0.012	0.356 ± 0.010	0.337 ± 0.012	0.336 ± 0.017
Relative	11.59 ± 0.30	11.48 ± 0.28	11.66 ± 0.29	12.41 ± 0.28	11.85 ± 0.26	13.76 ± 0.44**
Liver						
Absolute	1.697 ± 0.042	1.723 ± 0.038	1.749 ± 0.071	1.966 ± 0.051*	2.041 ± 0.045*	1.671 ± 0.081
Relative	60.52 ± 1.09	62.11 ± 0.69	63.42 ± 1.61	68.44 ± 0.98**	71.98 ± 1.33**	68.46 ± 1.91**
Lung						
Absolute	0.217 ± 0.007	0.221 ± 0.008	0.223 ± 0.006	0.220 ± 0.004	0.219 ± 0.006	0.214 ± 0.013
Relative	7.77 ± 0.31	7.99 ± 0.32	8.14 ± 0.28	7.68 ± 0.16	7.72 ± 0.16	8.81 ± 0.46
R. Testis						
Absolute	0.120 ± 0.003	0.116 ± 0.002	0.118 ± 0.002	0.116 ± 0.002	0.115 ± 0.004	0.113 ± 0.003
Relative	4.27 ± 0.06	4.19 ± 0.07	4.30 ± 0.10	4.06 ± 0.08	4.05 ± 0.11	4.64 ± 0.09*
Thymus						
Absolute	0.065 ± 0.004	0.070 ± 0.004	0.062 ± 0.004	0.070 ± 0.003	0.065 ± 0.004	0.031 ± 0.002**
Relative	2.32 ± 0.13	2.53 ± 0.14	2.24 ± 0.13	2.43 ± 0.13	2.28 ± 0.14	1.26 ± 0.09**
Female						
n	10	10	10	10	10	10
Necropsy body wt	21.6 ± 0.2	22.0 ± 0.4	21.6 ± 0.4	22.0 ± 0.3	22.9 ± 0.3	19.8 ± 0.8*
Brain						
Absolute	0.507 ± 0.006	0.518 ± 0.008	0.510 ± 0.006	0.508 ± 0.008	0.516 ± 0.005	0.519 ± 0.016
Relative	23.55 ± 0.44	23.53 ± 0.21	23.64 ± 0.41	23.13 ± 0.43	22.59 ± 0.33	27.09 ± 2.39
Heart						
Absolute	0.132 ± 0.009	0.129 ± 0.005	0.132 ± 0.004	0.134 ± 0.005	0.139 ± 0.005	0.130 ± 0.006
Relative	6.12 ± 0.38	5.85 ± 0.15	6.10 ± 0.16	6.09 ± 0.19	6.08 ± 0.18	6.68 ± 0.46
R. Kidney						
Absolute	0.214 ± 0.005	0.212 ± 0.004	0.214 ± 0.005	0.209 ± 0.004	0.229 ± 0.005	0.224 ± 0.007
Relative	9.93 ± 0.21	9.64 ± 0.16	9.90 ± 0.21	9.50 ± 0.11	10.01 ± 0.17	11.48 ± 0.50**
Liver						
Absolute	1.412 ± 0.017	1.390 ± 0.022	1.486 ± 0.031	1.551 ± 0.030*	1.704 ± 0.032*	1.427 ± 0.084
Relative	65.51 ± 0.61	63.13 ± 0.56	68.79 ± 1.26	70.59 ± 1.27**	74.50 ± 0.98**	71.69 ± 2.05**
Lung						
Absolute	0.204 ± 0.008	0.217 ± 0.007	0.213 ± 0.006	0.206 ± 0.007	0.205 ± 0.007	0.203 ± 0.007
Relative	9.45 ± 0.30	9.86 ± 0.28	9.87 ± 0.32	9.39 ± 0.37	8.95 ± 0.25	10.43 ± 0.52
Thymus						
Absolute	0.094 ± 0.003	0.096 ± 0.003	0.096 ± 0.002	0.095 ± 0.007	0.099 ± 0.003	0.066 ± 0.009**
Relative	4.37 ± 0.16	4.37 ± 0.10	4.44 ± 0.12	4.31 ± 0.29	4.31 ± 0.12	3.20 ± 0.40**

* 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 H4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	100 ppm	330 ppm	1,000 ppm	3,300 ppm
Male						
n	10	10	10	9	10	10
Necropsy body wt	39.2 ± 1.0	41.0 ± 1.2	40.3 ± 1.1	40.3 ± 1.3	40.0 ± 0.8	40.2 ± 0.8
Brain						
Absolute	0.460 ± 0.007	0.472 ± 0.005	0.477 ± 0.007	0.477 ± 0.014	0.460 ± 0.005	0.456 ± 0.005
Relative	11.80 ± 0.27	11.62 ± 0.38	11.90 ± 0.33	11.86 ± 0.25	11.54 ± 0.30	11.38 ± 0.24
Heart						
Absolute	0.202 ± 0.009	0.189 ± 0.011	0.202 ± 0.009	0.187 ± 0.007	0.212 ± 0.006	0.214 ± 0.011
Relative	5.18 ± 0.22	4.64 ± 0.29	5.04 ± 0.26	4.66 ± 0.18	5.30 ± 0.13	5.32 ± 0.24
R. Kidney						
Absolute	0.316 ± 0.010	0.334 ± 0.018	0.357 ± 0.013	0.321 ± 0.012	0.352 ± 0.011	0.389 ± 0.008**
Relative	8.08 ± 0.21	8.22 ± 0.49	8.87 ± 0.29	7.99 ± 0.27	8.80 ± 0.27	9.69 ± 0.20**
Liver						
Absolute	1.812 ± 0.063	1.762 ± 0.096	1.999 ± 0.094	1.624 ± 0.082	2.094 ± 0.048*	1.915 ± 0.019
Relative	46.29 ± 1.07	42.84 ± 1.46	49.69 ± 2.22	40.36 ± 1.63*	52.30 ± 0.52*	47.74 ± 0.75
Lung						
Absolute	0.293 ± 0.013	0.339 ± 0.015	0.325 ± 0.021	0.319 ± 0.022	0.315 ± 0.012	0.323 ± 0.012
Relative	7.47 ± 0.25	8.37 ± 0.52	8.04 ± 0.39	7.91 ± 0.44	7.87 ± 0.24	8.04 ± 0.26
R. Testis						
Absolute	0.121 ± 0.003	0.120 ± 0.002	0.136 ± 0.004	0.121 ± 0.003	0.137 ± 0.004**	0.127 ± 0.001**
Relative	3.10 ± 0.11	2.95 ± 0.10	3.38 ± 0.11	3.01 ± 0.08	3.44 ± 0.11	3.18 ± 0.06
Thymus						
Absolute	0.039 ± 0.003	0.043 ± 0.003	0.048 ± 0.005	0.040 ± 0.002	0.047 ± 0.004	0.041 ± 0.003
Relative	1.00 ± 0.06	1.06 ± 0.07	1.21 ± 0.14	0.99 ± 0.03	1.16 ± 0.08	1.02 ± 0.08
Female						
n	10	10	10	10	10	10
Necropsy body wt	33.2 ± 0.9	32.6 ± 0.9	32.6 ± 1.6	33.5 ± 0.9	34.7 ± 1.2	33.3 ± 0.9
Brain						
Absolute	0.482 ± 0.004	0.481 ± 0.007	0.483 ± 0.005	0.477 ± 0.006	0.484 ± 0.008	0.469 ± 0.004
Relative	14.62 ± 0.47	14.87 ± 0.45	15.09 ± 0.66	14.31 ± 0.42	14.13 ± 0.60	14.17 ± 0.35
Heart						
Absolute	0.157 ± 0.004[b]	0.166 ± 0.006	0.168 ± 0.008	0.170 ± 0.010	0.166 ± 0.005	0.177 ± 0.006
Relative	4.76 ± 0.14[b]	5.14 ± 0.24	5.28 ± 0.39	5.08 ± 0.28	4.83 ± 0.19	5.32 ± 0.15
R. Kidney						
Absolute	0.210 ± 0.005	0.216 ± 0.006	0.218 ± 0.007	0.212 ± 0.006	0.225 ± 0.008	0.246 ± 0.008**
Relative	6.37 ± 0.26	6.65 ± 0.17	6.77 ± 0.24	6.35 ± 0.21	6.51 ± 0.17	7.39 ± 0.18**
Liver						
Absolute	1.430 ± 0.025	1.597 ± 0.054*	1.725 ± 0.054*	1.478 ± 0.030*	1.698 ± 0.056**	1.783 ± 0.049**
Relative	43.23 ± 0.87	49.10 ± 1.20**	53.44 ± 1.52**	44.21 ± 0.90**	49.11 ± 1.01**	53.65 ± 1.21**
Lung						
Absolute	0.312 ± 0.013	0.325 ± 0.018	0.352 ± 0.015	0.313 ± 0.010	0.325 ± 0.015	0.340 ± 0.011
Relative	9.45 ± 0.45	9.99 ± 0.48	10.94 ± 0.56	9.35 ± 0.23	9.44 ± 0.44	10.22 ± 0.22
Thymus						
Absolute	0.046 ± 0.002	0.051 ± 0.003	0.055 ± 0.003	0.050 ± 0.003	0.060 ± 0.003**	0.056 ± 0.003**
Relative	1.39 ± 0.08	1.58 ± 0.09	1.70 ± 0.10*	1.50 ± 0.10	1.74 ± 0.06*	1.68 ± 0.06

* 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).
[b] n=9

APPENDIX I
REPRODUCTIVE TISSUE EVALUATIONS AND ESTROUS CYCLE CHARACTERIZATION

TABLE I1 Summary of Reproductive Tissue Evaluations for Male Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol 236

TABLE I2 Summary of Estrous Cycle Characterization for Female Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol 236

TABLE I3 Summary of Reproductive Tissue Evaluations for Male Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol 237

TABLE I4 Summary of Estrous Cycle Characterization for Female Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol 237

TABLE I1
Summary of Reproductive Tissue Evaluations for Male Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	330 ppm	3,300 ppm
n	10	10	10	10
Weights (g)				
Necropsy body wt	379 ± 6	376 ± 9	385 ± 8	322 ± 5**
R. cauda epididymis	0.1490 ± 0.0051	0.1370 ± 0.0061	0.1371 ± 0.0051	0.1152 ± 0.0046**
R. epididymis	0.4650 ± 0.0091	0.4501 ± 0.0197	0.4720 ± 0.0092	0.4188 ± 0.0077*
R. testis	1.5141 ± 0.0284	1.4878 ± 0.0336	1.5465 ± 0.0311	1.4871 ± 0.0252
Epididymal spermatozoal measurements				
Motility (%)	67.20 ± 2.00	64.20 ± 2.59	64.20 ± 3.82	67.00 ± 3.28
Abnormal (%)	0.78 ± 0.17	0.90 ± 0.11	0.86 ± 0.11	1.50 ± 0.16**
Concentration (10^6/g cauda epididymal tissue)	742 ± 45	812 ± 46	887 ± 32*	725 ± 41

* Significantly different ($P \leq 0.05$) from the control group by Dunnett's test (right epididymis weight) or by Dunn's test (concentration)
** Significantly different ($P \leq 0.01$) from the control group by Williams' test (body and tissue weights) or by Shirley's test (abnormal sperm)
[a] Data are presented as mean ± standard error.

TABLE I2
Summary of Estrous Cycle Characterization for Female Rats in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	330 ppm	3,300 ppm
n	10	10	10	10
Necropsy body wt (g)	212 ± 7	206 ± 4	208 ± 3	185 ± 3**
Estrous cycle length (days)	4.89 ± 0.2[b]	4.78 ± 0.15[b]	5.22 ± 0.22[b]	4.40 ± 0.22
Estrous stages (% of cycle)				
Diestrus	34.3	24.3	31.4	30.0
Proestrus	15.7	14.3	11.4	21.4
Estrus	31.4	40.0	37.1	30.0
Metestrus	18.6	20.0	20.0	18.6
Uncertain diagnoses	0.0	1.4	0.0	0.0

** Significantly different ($P \leq 0.01$) from the control group by Williams' test
[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.
[b] Estrous cycle was longer than 12 days or unclear in 1 of 10 animals.

TABLE I3
Summary of Reproductive Tissue Evaluations for Male Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	330 ppm	3,300 ppm
n	10	10	9	10
Weights (g)				
Necropsy body wt	39.0 ± 1.0	41.0 ± 1.2	40.3 ± 1.3	40.2 ± 0.8
R. cauda epididymis	0.0113 ± 0.0012	0.0108 ± 0.0005	0.0111 ± 0.0006	0.0123 ± 0.0010
R. epididymis	0.0530 ± 0.0021	0.0493 ± 0.0012	0.0484 ± 0.0009	0.0586 ± 0.0014*
R. testis	0.1205 ± 0.0028	0.1198 ± 0.0022	0.1203 ± 0.0027	0.1273 ± 0.0011
Epididymal spermatozoal measurements				
Motility (%)	74.22 ± 4.31[b]	76.60 ± 4.58	70.22 ± 4.47	71.00 ± 4.14
Abnormal (%)	1.40 ± 0.26[b]	1.82 ± 0.23	1.64 ± 0.16	1.66 ± 0.16
Concentration (10^6/g cauda epididymal tissue)	1,237 ± 208[b]	1,504 ± 134	1,285 ± 87	1,140 ± 126

* 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 (body weight) or Dunn's test (epididymal spermatozoal measurements).
[b] n=9

TABLE I4
Summary of Estrous Cycle Characterization for Female Mice in the 14-Week Drinking Water Study of 1-Chloro-2-propanol[a]

	0 ppm	33 ppm	330 ppm	3,300 ppm
n	10	10	10	10
Necropsy body wt (g)	33.2 ± 0.9	32.6 ± 0.9	33.5 ± 0.9	33.3 ± 0.9
Estrous cycle length (days)	4.25 ± 0.16[b]	4.13 ± 0.13[b]	4.33 ± 0.17[c]	4.60 ± 0.16
Estrous stages (% of cycle)				
Diestrus	24.3	31.4	25.7	14.3
Proestrus	18.6	22.9	18.6	25.7
Estrus	30.0	32.9	34.3	37.1
Metestrus	27.1	12.9	21.4	22.9

[a] Weights and estrous cycle lengths are presented as mean ± standard error. Differences from the control group are not significant by Dunnett's test (body weight) or Dunn's test (estrous cycle length). By multivariate analysis of variance, exposed females do not differ significantly from the control females in the relative length of time spent in the estrous stages.
[b] Estrous cycle was longer than 12 days or unclear in 2 of 10 animals.
[c] Estrous cycle was longer than 12 days or unclear in 1 of 10 animals.

APPENDIX J
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

PROCUREMENT AND CHARACTERIZATION OF 1-CHLORO-2-PROPANOL 240
PREPARATION AND ANALYSIS OF DOSE FORMULATIONS 241
FIGURE J1 Infrared Absorption Spectrum of 1-Chloro-2-propanol 242
FIGURE J2 Nuclear Magnetic Resonance Spectrum of 1-Chloro-2-propanol 243
TABLE J1 Preparation and Storage of Dose Formulations in the Drinking Water Studies of 1-Chloro-2-propanol 244
TABLE J2 Results of Analyses of Dose Formulations Administered to Rats and Mice in the 14-Day Drinking Water Studies of 1-Chloro-2-propanol 245
TABLE J3 Results of Analyses of Dose Formulations Administered to Rats and Mice in the 14-Week Drinking Water Studies of 1-Chloro-2-propanol 246
TABLE J4 Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of 1-Chloro-2-propanol 247
TABLE J5 Results of Referee Analyses of Dose Formulations Administered to Rats and Mice in the 14-Week Drinking Water Studies of 1-Chloro-2-propanol 250

CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

PROCUREMENT AND CHARACTERIZATION OF 1-CHLORO-2-PROPANOL

Technical grade 1-chloro-2-propanol (approximately 75% 1-chloro-2-propanol and 25% 2-chloro-1-propanol) was obtained from Eastman Kodak Laboratory Chemicals (Rochester, NY) in one lot (B15), which was used during the 14-day, 14-week, and 2-year studies. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO). Reports on analyses performed in support of the 1-chloro-2-propanol studies are on file at the National Institute of Environmental Health Sciences.

The major component of the test chemical, a clear, colorless liquid, was identified as 1-chloro-2-propanol by infrared, ultraviolet/visible, and nuclear magnetic resonance (NMR) spectroscopy. The infrared and ultraviolet/visible spectra were consistent with those expected for 1-chloro-2-propanol; the NMR spectrum was consistent with a mixture of isomers (1-chloro-2-propanol and 2-chloro-1-propanol). The NMR and infrared spectra were also consistent with a literature reference (*Sadtler Standard Spectra*). The infrared and nuclear magnetic spectra are presented in Figures J1 and J2. The boiling point and density of lot B15 were consistent with a literature reference (*Merck Index*, 1989).

The purity of lot B15 was determined by elemental analyses, Karl Fischer water analysis, free acid titration, and gas chromatography. For free acid titration, samples were dissolved in methanol and titrated with 0.01N sodium hydroxide to a potentiometric endpoint; free acid was detected with a combination pH/mV electrode filled with aqueous 4M potassium chloride. Gas chromatography was performed using a flame ionization detector with a nitrogen carrier gas at a flow rate of 70 mL/minute. Two systems were used:

A) 10% SP-1000 on 80/100 Supelcoport glass column, with an oven temperature program of 50° C for 5 minutes, then 50° to 250° C at 10° C per minute, and

B) 20% SP-2100/0.1% Carbowax 1500 on 100/120 Supelcoport glass column, with an oven temperature program of 30° C for 5 minutes, then 30° to 175° C at 10° C per minute.

Elemental analyses for carbon, chlorine, and hydrogen were in agreement with the theoretical values for 1-chloro-2-propanol. Karl Fischer water analysis indicated 0.62% ± 0.02% water. Free acid titration indicated a hydrochloric acid content of 1,149 ± 2 ppm, equivalent to 0.0315 ± 0.0001 mEq of acid per gram of sample. Gas chromatography using system A indicated two major peaks and two impurities with a combined area of 0.47% relative to the total major peak area. Gas chromatography using system B indicated two major peaks and three impurities with a combined area of 0.67% relative to the total major peak area. No additional impurities with areas of 0.1% or greater relative to the major peak were detected using either system. The second major peak represents 2-chloro-1-propanol, a positional isomer of 1-chloro-2-propanol. The concentrations of 1-chloro-2-propanol and 2-chloro-1-propanol were estimated to be approximately 75% to 76% and 24% to 25%, respectively.

Stability studies of the bulk chemical were performed by the analytical chemistry laboratory. Gas chromatography was performed using system A as described above with an oven temperature program of 100° C for 5 minutes, then 100° to 110° C at 30° C per minute with a 2-minute hold at 110° C. Heptyl alcohol was added as an internal standard. These studies indicated that 1-chloro-2-propanol was stable as a bulk chemical for 2 weeks when stored protected from light at temperatures up to 60° C. To ensure stability, the bulk chemical was stored at 5.5° C (14-day and 14-week studies) or 1° to 8° C (2-year studies) protected from light in sealed glass containers. Stability was monitored during the 14-week studies using gas

chromatography and free acid titration and during the 14-day and 2-year studies using gas chromatography. No degradation of the bulk chemical was detected.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared twice during the 14-day studies, every 2 weeks in the 14-week studies, and as needed in the 2-year studies by mixing 1-chloro-2-propanol with ultraviolet light-treated, deionized water for the 14-day and 14-week studies and with deionized water for the 2-year studies (Table J1). Formulations were stored in amber glass jars at room temperature.

Stability studies of the 100 ppm dose formulation were performed at the analytical chemistry laboratory using gas chromatography with flame ionization detection with system A with a flow rate of 55 mL/minute and an isothermal column oven temperature of 105° C. The isothermal column oven temperature was changed to 87° C and the nitrogen flow rate was changed to 30 mL/minute for the analyses conducted during the 2-year studies. The internal standard was 1-heptanol for the 14-day and 14-week studies. The stability of the dose formulation was confirmed for 3 weeks when stored at room temperature protected from light and for 72 hours when stored in drinking water bottles at room temperature exposed to light.

Periodic analyses of the dose formulations of 1-chloro-2-propanol were conducted at the study laboratory using gas chromatography with the same system used for the stability studies. During the 14-day studies, formulations were analyzed once per week (Table J2). For the 14-week studies, formulations were analyzed at the beginning, midpoint, and end of the studies (Table J3). During the 2-year studies, formulations were analyzed approximately every 8 weeks (Table J4). Of the dose formulations analyzed and used during the 14-day studies, 95% (19/20) were within 10% of the target concentration, with no value greater than 10% of the target concentration. A 1,000 ppm dose prepared on 10 September 1986 was −39% of the target and was remixed; the reformulated dose was found to be within the acceptable range. All five of the animal room samples analyzed were within 10% of the target concentration. All 25 of the dose formulations analyzed and used during the 14-week studies were within 10% of the target concentration with no value greater than 106% of the target concentration, and all 15 of the animal room samples analyzed were within 10% of the target concentration. All 104 of the dose formulations analyzed and used during the 2-year studies were within 10% of the target concentration with no value greater than 104% of the target concentration, and 33/34 of the animal room samples analyzed were within 10% of the target concentration. The high concentration determined for the 250 ppm animal room sample was attributed to technical error; the sample was contaminated with the 650 ppm rat dose formulation. Results of periodic referee analyses performed by the analytical chemistry laboratory agreed with the results obtained by the study laboratory for the 14-week studies (Table J5).

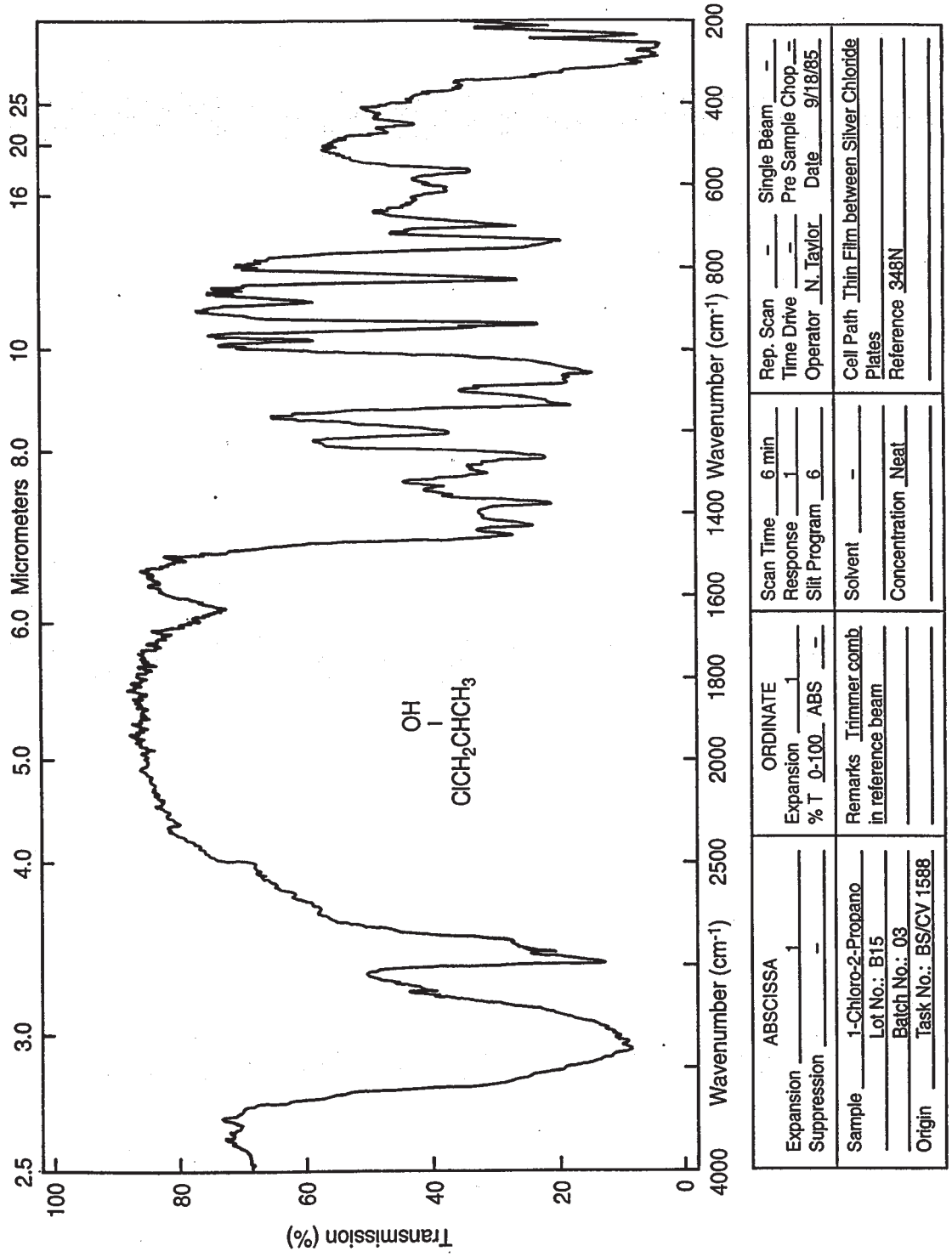

FIGURE J1
Infrared Absorption Spectrum of 1-Chloro-2-propanol

Assignments (δ ppm)	Multiplicity	Integration Observed	Integration Theoretical
(a) 1.28	d, $J_{a\text{-}g}$=5.9 Hz	2.9	3.0
(b) 1.51	d, $J_{b\text{-}h}$=6.3 Hz		
(c) 2.17*	s	1.5	1.0
(d) 3.43-3.49	d of d, $J_{d\text{-}e}$=11.0 Hz $J_{d\text{-}g}$=7.0 Hz		2.0
(e) 3.58-3.66	m	2.1	
(f) 3.73-3.78	d of d, $J_{e\text{-}f}$=12.2 Hz $J_{f\text{-}h}$=3.7 Hz		
(g) 3.96-4.06	m	1.0	1.0
(h) 4.13-4.19	m		

*Exchangeable proton not included in total

1-chloro-2-propanol 2 -chloro-1-propanol

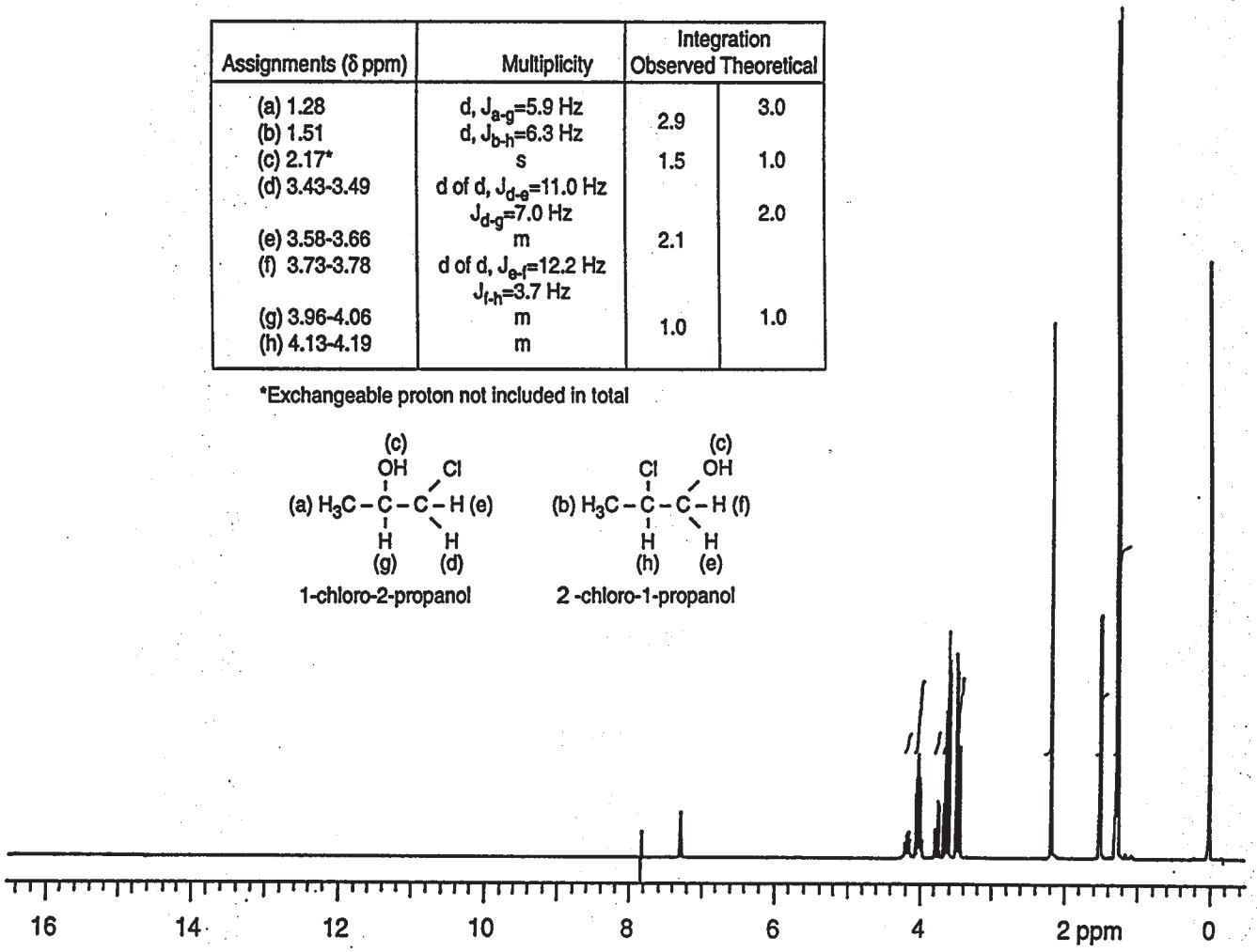

FIGURE J2
Nuclear Magnetic Resonance Spectrum of 1-Chloro-2-propanol

TABLE J1
Preparation and Storage of Dose Formulations in the Drinking Water Studies of 1-Chloro-2-propanol

14-Day Studies	14-Week Studies	2-Year Studies
Preparation A mixture of ultraviolet light-treated deionized water and 1-chloro-2-propanol was prepared. Doses were prepared weekly.	A mixture of ultraviolet light-treated deionized water and 1-chloro-2-propanol was prepared. Doses were prepared every 2 weeks.	A mixture of deionized water and 1-chloro-2-propanol was prepared. Doses were prepared as needed.
Chemical Lot Number B15	B15	B15
Maximum Storage Time Approximately 15 days	3 weeks	3 weeks
Storage Conditions Stored in amber glass bottles, protected from light, at room temperature	Same as 14-day studies	Same as 14-day studies
Study Laboratory SRI International (Menlo Park, CA)	SRI International (Menlo Park, CA)	TSI Mason Laboratories (Worcester, MA)
Referee Laboratory None	Midwest Research Institute (Kansas City, MO)	None

TABLE J2
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 14-Day Drinking Water Studies of 1-Chloro-2-propanol

Date Prepared	Target Concentration (ppm)	Determined Concentration[a] (ppm)	Difference from Target (%)
10 September 1986	100	105	+5
	100	96	−4
	330	335	+2
	330	334	+1
	1,000	614	−39
	1,000	993	−1
	3,300	3,213	−3
	3,300	3,206	−3
	10,000	9,727	−3
	10,000	9,252	−7
16 September 1986	1,000	1,062[b]	+6
23 September 1986[c]	100	98	−2
	330	316	−4
	1,000	974	−3
	3,300	3,120	−5
	10,000	9,460	−5
17 September 1986	100	103	+3
	100	106	+6
	330	339	+3
	330	342	+4
	1,000	998	0
	1,000	970	−3
	3,300	3,325	+1
	3,300	3,309	0
	10,000	9,814	−2
	10,000	10,181	+2

[a] Results of duplicate analyses
[b] Results of remix
[c] Animal room samples (taken from first batch of dose formulations prepared and from 16 September 1986 remix)

TABLE J3
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 14-Week Drinking Water Studies of 1-Chloro-2-propanol

Date Prepared	Target Concentration (ppm)	Determined Concentration[a] (ppm)	Difference from Target (%)
28 January 1987	33	32	−3
	100	95	−5
	330	323	−2
	1,000	982	−2
	3,300	3,246	−2
17 February 1987[b]	33	33	0
	100	101	+1
	330	343	+4
	1,000	1,007	+1
	3,300	3,315	0
12 March 1987	33	33	0
	33	35	+6
	100	98	−2
	100	98	−2
	330	323	−2
	330	325	−2
	1,000	998	0
	1,000	1,017	+2
	3,300	3,200	−3
	3,300	3,230	−2
1 April 1987[b]	33	30	−9
	100	94	−6
	330	315	−5
	1,000	978	−2
	3,300	3,395	+3
23 April 1987	33	32	−3
	33	33	0
	100	99	−1
	100	98	−2
	330	323	−2
	330	323	−2
	1,000	1,008	+1
	1,000	998	0
	3,300	3,375	+2
	3,300	3,275	−1
12 May 1987[b]	33	30	−9
	100	96	−4
	330	321	−3
	1,000	964	−4
	3,300	3,320	+1

[a] Results of duplicate analyses
[b] Animal room samples (taken from first batch of dose formulations prepared)

TABLE J4
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of 1-Chloro-2-propanol

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration[a] (ppm)	Difference from Target (%)
Rats				
23 January 1991	23 January 1991	150	147	−2
		325	319	−2
		650	631	−3
	7 February 1991[b]	150	144	−4
		325	322	−1
		650	644	−1
27 March 1991	28 March 1991	150	146	−3
		150	146	−3
		325	316	−3
		325	317	−2
		650	638	−2
		650	631	−3
22 May 1991	23 May 1991	150	147	−2
		150	148	−1
		325	320	−2
		650	640	−2
17 July 1991	17 July 1991	150	151	+1
		325	324	0
		650	644	−1
	31 July 1991[b]	150	146	−3
		325	314	−3
		650	630	−3
11 September 1991	12–13 September 1991	150	150	0
		325	321	−1
		650	647	0
6 November 1991	7 November 1991	150	147	−2
		325	314	−3
		650	617	−5
31 December 1991	2 January 1992	150	147	−2
		325	316	−3
		650	632	−3
	15 January 1992[b]	150	147	−2
		325	318	−2
		650	643	−1
26 February 1992	27 February 1992	150	147	−2
		150	149	−1
		325	319	−2
		325	323	−1
		650	638	−2
		650	640	−2

TABLE J4
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of 1-Chloro-2-propanol

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	Difference from Target (%)
Rats (continued)				
22 April 1992	23 April 1992	150	147	−2
		325	316	−3
		650	628	−3
17 June 1992	18 June 1992	150	150	0
		325	314	−3
		650	628	−3
12 August 1992	13 August 1992	150	150	0
		325	327	+1
		650	649	0
	9 September 1992[b]	150	147	−2
		325	320	−2
		650	642	−1
13 October 1992	14 October 1992	150	148	−1
		325	319	−2
		650	637	−2
2 December 1992	3 December 1992	150	148	−1
		150	148	−1
		325	322	−1
		325	325	0
		650	639	−2
		650	640	−2
14 January 1993	14 January 1993	150	147	−2
		325	323	−1
		650	644	−1
	3 February 1993[b]	150	149	−1
		325	323	−1
		650	643	−1
Mice				
19 December 1990	19 December 1990	250	246	−2
		500	492	−2
		1,000	984	−2
	9 January 1991[b]	250	244	−2
		500	477	−5
		1,000	969	−3
6 February 1991	7 February 1991	250	243	−3
		500	490	−2
		1,000	1,002	0
27 March 1991	28 March 1991	250	247	−1
		500	491	−2
		1,000	990	−1

TABLE J4
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of 1-Chloro-2-propanol

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	Difference from Target (%)
Mice (continued)				
22 May 1991	23 May 1991	250	248	−1
		500	487	−3
		1,000	990	−1
		1,000	991	−1
	5 June 1991[b]	250	240	−4
		500	490	−2
		1,000	982	−2
		1,000	989	−1
17 July 1991	17 July 1991	250	261	+4
		500	499	0
		1,000	991	−1
11 September 1991	12–13 September 1991	250	250	0
		500	496	−1
		1,000	999	0
6 November 1991	7 November 1991	250	246	−2
		500	486	−3
		1,000	983	−2
	22 November 1991[b]	250	247	−1
		500	492	−2
		1,000	975	−2
31 December 1991	2 January 1992	250	244	−2
		500	482	−4
		1,000	992	−1
26 February 1992	27 February 1992	250	252	+1
		500	489	−2
		1,000	983	−2
22 April 1992	23 April 1992	250	243	−3
		250	244	−2
		500	481	−4
		500	484	−3
		1,000	969	−3
		1,000	980	−2
	14 May 1992[b]	250	250	0
		250	420	+68
		500	487	−3
		500	495	−1
		1,000	993	−1
		1,000	1,005	+1

TABLE J4
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of 1-Chloro-2-propanol

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	Difference from Target (%)
Mice (continued)				
17 June 1992	18 June 1992	250	246	−2
		250	240	−4
		500	481	−4
		500	482	−4
		1,000	971	−3
		1,000	969	−3
12 August 1992	13 August 1992	250	251	0
		500	497	−1
		1,000	998	0
13 October 1992	14 October 1992	250	246	−2
		500	497	−1
		1,000	989	−1
	2 November 1992[b]	250	242	−3
		500	491	−2
		1,000	1,004	0
2 December 1992	3 December 1992	250	251	0
		250	248	−1
		500	492	−2
		500	496	−1
		1,000	982	−2
		1,000	989	−1

[a] Results of duplicate analyses
[b] Animal room samples

TABLE J5
Results of Referee Analyses of Dose Formulations Administered to Rats and Mice in the 14-Week Drinking Water Studies of 1-Chloro-2-propanol

Date Prepared	Target Concentration (ppm)	Determined Concentration (ppm)	
		Study Laboratory[a]	Referee Laboratory[b]
28 January 1987	1,000	982	992 ± 8
23 April 1987	100	99	96.4 ± 1.9

[a] Results of duplicate analyses
[b] Results of triplicate analyses

APPENDIX K
WATER AND COMPOUND CONSUMPTION IN THE 2-YEAR DRINKING WATER STUDIES OF 1-CHLORO-2-PROPANOL

TABLE K1 Water and Compound Consumption by Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 252

TABLE K2 Water and Compound Consumption by Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 253

TABLE K3 Water and Compound Consumption by Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 254

TABLE K4 Water and Compound Consumption by Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol 255

TABLE K1
Water and Compound Consumption by Male Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm		150 ppm			325 ppm			650 ppm		
Week	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)
1	18.3	132	18.2	130	21	18.1	131	45	18.8	131	93
2	23.4	166	23.3	163	21	24.2	166	47	23.6	167	92
4	19.2	224	20.2	225	13	21.9	231	31	21.0	230	59
5	18.0	247	18.3	249	11	19.0	256	24	19.7	253	51
8	24.0	289	23.2	293	12	22.5	296	25	22.7	294	50
9	22.1	306	22.6	306	11	21.7	312	23	21.7	308	46
12	18.0	337	18.1	341	8	19.7	346	19	19.8	340	38
13	22.1	349	21.3	351	9	22.8	355	21	24.6	351	46
17	22.1	375	21.2	378	8	22.8	383	19	21.3	382	36
21	21.0	410	20.4	409	7	20.0	414	16	20.4	413	32
25	21.1	426	19.8	424	7	21.8	432	16	22.5	428	34
29	19.8	445	20.7	444	7	22.1	451	16	22.7	450	33
33	22.1	454	21.2	454	7	23.6	462	17	22.7	461	32
37	20.8	462	20.2	462	7	21.3	473	15	22.2	470	31
41	23.6	478	22.5	478	7	23.3	491	15	22.9	488	31
45	24.4	488	24.8	487	8	23.9	501	15	27.2	496	36
49	25.4	484	22.8	485	7	25.9	497	17	27.4	494	36
53	24.4	503	23.4	500	7	22.9	516	14	24.9	507	32
57	21.8	504	20.3	503	6	22.2	517	14	23.0	509	29
61	21.7	505	20.2	507	6	21.1	523	13	22.2	516	28
65	22.9	502	22.2	502	7	24.1	518	15	23.8	508	30
69	22.6	502	21.4	504	6	24.4	520	15	23.6	508	30
73	20.9	510	20.6	514	6	25.5	529	16	24.4	510	31
77	23.6	512	25.3	513	7	25.9	524	16	28.8	509	37
81	20.0	513	20.3	516	6	21.7	532	13	21.0	503	27
85	24.2	514	25.9	516	8	26.0	537	16	26.3	505	34
89	22.5	512	21.4	504	6	28.5	524	18	25.3	497	33
93	23.4	516	23.1	497	7	25.5	522	16	27.9	487	37
97	28.7	516	26.1	502	8	29.1	506	19	31.3	477	43
101	28.2	481	24.1	492	7	30.8	495	20	30.9	468	43
104	26.0	464	26.1	479	8	30.3	488	20	26.9	460	38
Mean for weeks											
1-13	20.6	256	20.6	257	13	21.2	262	29	21.5	260	59
14-52	22.3	447	21.5	447	7	22.8	456	16	23.3	454	33
53-104	23.6	504	22.9	504	7	25.6	518	16	25.7	498	34

[a] Grams of water consumed per animal per day
[b] Milligrams of 1-chloro-2-propanol consumed per kilogram body weight per day

TABLE K2
Water and Compound Consumption by Female Rats in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm		150 ppm			325 ppm			650 ppm		
Week	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)
1	16.3	111	16.0	111	22	15.7	111	46	16.1	110	95
2	17.8	128	16.9	128	20	18.9	128	48	17.8	127	91
4	13.4	152	14.1	151	14	14.5	152	31	14.5	153	61
8	14.5	182	14.8	180	12	15.5	180	28	15.0	182	54
12	12.0	198	13.7	198	10	13.3	199	22	13.1	201	42
17	14.2	216	15.9	216	11	15.5	213	24	14.7	218	44
21	12.5	224	13.9	221	9	15.2	220	22	14.6	224	42
25	13.2	230	13.6	228	9	13.7	227	20	13.6	231	38
29	12.8	240	14.5	238	9	14.2	238	19	14.5	242	39
33	13.1	246	13.9	244	9	14.3	244	19	14.5	247	38
37	13.5	254	14.1	252	8	14.0	252	18	14.4	255	37
41	14.2	266	15.9	265	9	16.6	266	20	16.6	268	40
45	12.9	269	13.9	268	8	13.7	269	16	13.7	270	33
49	13.7	281	14.9	278	8	14.9	280	17	14.8	282	34
53	13.3	292	13.9	293	7	14.5	290	16	14.2	297	31
57	13.7	296	14.4	298	7	15.1	295	17	14.6	301	31
61	13.0	305	14.3	305	7	14.9	302	16	15.0	309	31
65	14.1	305	14.9	307	7	15.6	303	17	15.9	311	33
69	15.7	315	16.2	315	8	17.0	311	18	17.1	318	35
73	15.3	321	16.7	323	8	16.7	316	17	16.7	324	33
77	15.7	329	16.9	332	8	17.2	328	17	17.3	333	34
81	15.9	326	16.6	334	7	16.6	326	17	16.5	331	32
85	17.3	333	17.7	337	8	17.5	327	17	17.7	338	34
89	16.4	339	17.3	343	8	18.5	337	18	18.0	348	34
93	16.5	338	18.1	344	8	18.7	336	18	17.9	353	33
97	18.0	345	19.9	336	9	20.5	337	20	20.7	358	38
101	16.5	345	18.1	341	8	19.4	333	19	18.5	367	33
105	18.9	348	18.8	354	8	20.8	334	20	20.3	350	38
Mean for weeks											
1-13	14.8	154	15.1	153	16	15.6	154	35	15.3	155	69
14-52	13.3	247	14.5	246	9	14.7	246	20	14.6	249	38
53-105	15.7	324	16.7	326	8	17.4	320	18	17.2	331	34

[a] Grams of water consumed per animal per day
[b] Milligrams of 1-chloro-2-propanol consumed per kilogram body weight per day

TABLE K3
Water and Compound Consumption by Male Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm		250 ppm			500 ppm			1,000 ppm		
Week	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)
2	6.8	25.8	7.2	25.9	70	5.7	26.5	107	5.8	26.4	221
5	5.1	31.5	5.4	30.9	44	4.9	31.7	77	4.6	31.9	145
8	4.5	36.6	5.3	36.3	36	4.4	36.9	59	4.5	37.2	121
12	4.2	39.5	4.4	39.6	28	4.1	39.8	52	4.4	40.2	108
17	4.6	44.6	4.2	44.8	24	4.3	45.3	47	4.2	45.5	93
21	4.4	46.9	4.3	47.5	23	4.4	47.7	46	4.3	47.9	90
25	5.0	48.6	4.5	48.9	23	4.6	49.6	46	4.3	49.7	87
29	4.9	50.7	4.7	50.5	24	4.7	51.0	46	4.6	50.9	91
33	4.6	51.3	4.8	50.8	24	4.7	51.1	46	4.7	51.3	92
37	4.5	51.9	4.5	51.0	22	4.5	51.2	44	4.6	51.6	89
41	4.4	52.4	4.6	52.0	22	4.7	52.7	45	4.6	52.4	87
45	5.1	53.1	5.0	52.2	24	4.8	53.5	45	4.7	53.4	89
49	5.2	52.4	5.0	51.8	24	4.9	52.7	46	4.9	52.9	93
53	5.8	52.4	5.7	52.0	27	5.7	52.9	54	5.3	53.2	99
57	5.6	52.1	5.3	51.7	26	5.3	52.5	51	5.3	52.8	100
61	5.7	52.3	5.0	52.1	24	5.6	52.7	53	5.2	53.1	98
65	5.6	51.7	5.0	52.1	24	5.3	52.3	50	5.1	52.9	97
69	5.2	51.8	4.9	52.1	24	5.1	51.8	50	5.0	51.9	97
73	5.4	51.4	5.1	51.5	25	5.6	51.4	55	5.1	51.2	100
77	5.7	49.8	5.3	51.0	26	5.8	50.3	58	5.4	49.2	110
81	5.4	50.1	5.0	50.4	25	5.2	49.7	52	5.0	48.5	103
85	5.8	50.1	5.2	50.1	26	5.8	49.5	59	6.3	47.6	133
89	6.1	48.7	5.6	49.4	28	5.3	48.0	55	5.8	47.2	123
93	5.9	47.6	5.1	49.3	26	5.4	47.4	57	5.6	45.1	125
97	6.2	47.0	5.2	48.6	27	5.2	46.8	55	5.4	44.6	120
104	6.6	44.3	5.4	47.5	28	5.2	45.5	57	5.6	43.6	129
Mean for weeks											
1-13	5.2	33.3	5.6	33.2	44	4.8	33.7	74	4.8	33.9	149
14-52	4.7	50.2	4.6	50.0	23	4.6	50.6	46	4.6	50.6	90
53-104	5.8	49.9	5.2	50.6	26	5.4	50.1	54	5.4	49.3	110

[a] Grams of water consumed per animal per day
[b] Milligrams of 1-chloro-2-propanol consumed per kilogram body weight per day

TABLE K4
Water and Compound Consumption by Female Mice in the 2-Year Drinking Water Study of 1-Chloro-2-propanol

	0 ppm		250 ppm			500 ppm			1,000 ppm		
Week	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg)
2	4.9	21.9	6.3	21.6	73	5.2	21.6	121	5.4	21.5	250
5	4.9	25.5	5.8	24.2	60	5.4	24.6	110	5.8	24.5	236
7	5.0	28.8	6.4	27.3	58	6.5	28.0	117	6.2	28.0	222
8	5.2	29.6	6.0	27.4	55	5.6	28.6	98	5.4	28.9	186
12	5.2	33.9	5.4	32.0	43	5.2	33.6	77	5.3	33.8	157
17	5.2	37.6	5.0	35.8	35	4.8	37.1	65	5.0	37.4	132
21	4.6	40.7	5.1	39.1	33	4.6	40.7	56	4.5	40.6	111
25	4.8	44.0	5.0	42.2	29	4.9	43.6	56	4.9	44.1	111
29	4.5	45.7	4.9	44.1	28	4.8	45.3	53	4.0	45.7	88
33	4.5	47.4	4.9	45.1	27	4.7	46.5	51	4.5	46.4	97
37	4.1	50.0	4.3	47.6	23	4.2	49.5	43	4.3	49.0	88
41	4.5	51.1	4.4	48.9	23	4.4	50.8	43	4.4	49.8	89
45	4.6	53.0	4.5	50.9	22	4.5	52.8	42	5.1	52.4	97
49	4.7	53.3	4.7	52.0	22	4.6	53.9	42	4.4	52.8	84
53	4.7	54.4	4.7	52.7	22	4.8	55.3	43	4.6	54.4	85
57	5.0	54.7	4.8	53.5	23	4.9	55.9	44	4.9	55.2	89
61	4.6	55.8	5.0	54.9	23	4.9	58.2	42	4.8	56.7	85
65	4.8	57.4	4.9	55.6	22	5.1	59.4	43	4.9	58.6	83
69	4.8	59.1	4.9	57.4	21	4.9	60.5	40	4.6	59.0	78
73	5.3	58.7	5.4	57.8	23	5.2	61.1	43	5.0	60.3	84
77	5.6	59.3	5.5	58.1	23	5.7	61.2	47	5.6	60.7	92
81	4.9	59.5	5.3	59.3	22	5.0	62.9	40	4.7	61.2	78
85	5.2	60.1	5.4	59.8	23	5.1	62.4	41	4.8	61.0	78
89	5.7	59.8	5.2	59.5	22	5.4	61.0	45	5.2	59.5	87
93	5.7	57.6	5.3	58.6	23	5.7	60.8	47	5.5	59.7	92
97	5.8	56.2	5.3	58.9	23	5.3	61.7	43	5.5	59.7	92
101	5.8	54.2	5.9	57.6	26	5.7	59.6	48	5.6	58.6	96
105	5.9	52.1	5.8	54.5	26	6.3	55.4	57	6.2	55.5	111
Mean for weeks											
1-13	5.0	27.9	6.0	26.5	58	5.6	27.3	104	5.6	27.3	210
14-52	4.6	47.0	4.8	45.1	27	4.6	46.7	50	4.6	46.5	100
53-105	5.3	57.1	5.2	57.0	23	5.3	59.7	44	5.1	58.6	88

[a] Grams of water consumed per animal per day
[b] Milligrams of 1-chloro-2-propanol consumed per kilogram body weight per day

APPENDIX L
INGREDIENTS, NUTRIENT COMPOSITION, AND CONTAMINANT LEVELS IN NIH-07 RAT AND MOUSE RATION

TABLE L1 Ingredients of NIH-07 Rat and Mouse Ration 258
TABLE L2 Vitamins and Minerals in NIH-07 Rat and Mouse Ration 258
TABLE L3 Nutrient Composition of NIH-07 Rat and Mouse Ration 259
TABLE L4 Contaminant Levels in NIH-07 Rat and Mouse Ration 260

TABLE L1
Ingredients of NIH-07 Rat and Mouse Ration[a]

Ingredients[b]	Percent by Weight
Ground #2 yellow shelled corn	24.50
Ground hard winter wheat	23.00
Soybean meal (49% protein)	12.00
Fish meal (60% protein)	10.00
Wheat middlings	10.00
Dried skim milk	5.00
Alfalfa meal (dehydrated, 17% protein)	4.00
Corn gluten meal (60% protein)	3.00
Soy oil	2.50
Dried brewer's yeast	2.00
Dry molasses	1.50
Dicalcium phosphate	1.25
Ground limestone	0.50
Salt	0.50
Premixes (vitamin and mineral)	0.25

[a] NCI, 1976; NIH, 1978
[b] Ingredients were ground to pass through a U.S. Standard Screen No. 16 before being mixed.

TABLE L2
Vitamins and Minerals in NIH-07 Rat and Mouse Ration[a]

	Amount	Source
Vitamins		
A	5,500,000 IU	Stabilized vitamin A palmitate or acetate
D_3	4,600,000 IU	D-activated animal sterol
K_3	2.8 g	Menadione
d-α-Tocopheryl acetate	20,000 IU	
Choline	560.0 g	Choline chloride
Folic acid	2.2 g	
Niacin	30.0 g	
d-Pantothenic acid	18.0 g	*d*-Calcium pantothenate
Riboflavin	3.4 g	
Thiamine	10.0 g	Thiamine mononitrate
B_{12}	4,000 µg	
Pyridoxine	1.7 g	Pyridoxine hydrochloride
Biotin	140.0 mg	*d*-Biotin
Minerals		
Iron	120.0 g	Iron sulfate
Manganese	60.0 g	Manganous oxide
Zinc	16.0 g	Zinc oxide
Copper	4.0 g	Copper sulfate
Iodine	1.4 g	Calcium iodate
Cobalt	0.4 g	Cobalt carbonate

[a] Per ton (2,000 lb) of finished product

TABLE L3
Nutrient Composition of NIH-07 Rat and Mouse Ration

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	23.44 ± 0.51	22.2) 24.3	25
Crude fat (% by weight)	5.32 ± 0.19	5.00) 5.90	25
Crude fiber (% by weight)	3.34 ± 0.32	2.60) 4.30	25
Ash (% by weight)	6.45 ± 0.18	6.12) 6.81	25
Amino Acids (% of total diet)			
Arginine	1.273 ± 0.083	1.100) 1.390	12
Cystine	0.307 ± 0.068	0.181) 0.400	12
Glycine	1.152 ± 0.051	1.060) 1.220	12
Histidine	0.581 ± 0.029	0.531) 0.630	12
Isoleucine	0.913 ± 0.034	0.867) 0.965	12
Leucine	1.969 ± 0.053	1.850) 2.040	12
Lysine	1.269 ± 0.050	1.200) 1.370	12
Methionine	0.436 ± 0.104	0.306) 0.699	12
Phenylalanine	0.999 ± 0.114	0.665) 1.110	12
Threonine	0.899 ± 0.059	0.824) 0.985	12
Tryptophan	0.216 ± 0.146	0.107) 0.671	12
Tyrosine	0.690 ± 0.091	0.564) 0.794	12
Valine	1.079 ± 0.057	0.962) 1.170	12
Essential Fatty Acids (% of total diet)			
Linoleic	2.389 ± 0.223	1.830) 2.570	11
Linolenic	0.273 ± 0.034	0.210) 0.320	11
Vitamins			
Vitamin A (IU/kg)	6,584 ± 1,215	5,280) 11,450	25
Vitamin D (IU/kg)	4,450 ± 1,382	3,000) 6,300	4
α-Tocopherol (ppm)	35.24 ± 8.58	22.5) 48.9	12
Thiamine (ppm)	17.28 ± 2.03	14.0) 22.0	25
Riboflavin (ppm)	7.78 ± 0.899	6.10) 9.00	12
Niacin (ppm)	98.73 ± 23.21	65.0) 150.0	12
Pantothenic acid (ppm)	32.94 ± 8.92	23.0) 59.2	12
Pyridoxine (ppm)	9.28 ± 2.49	5.60) 14.0	12
Folic acid (ppm)	2.56 ± 0.70	1.80) 3.70	12
Biotin (ppm)	0.265 ± 0.046	0.190) 0.354	12
Vitamin B_{12} (ppb)	41.6 ± 18.6	10.6) 65.0	12
Choline (ppm)	2,995 ± 382	2,300) 3,430	11
Minerals			
Calcium (%)	1.17 ± 0.06	1.09) 1.31	25
Phosphorus (%)	0.92 ± 0.05	0.760) 1.00	25
Potassium (%)	0.886 ± 0.059	0.772) 0.971	10
Chloride (%)	0.531 ± 0.082	0.380) 0.635	10
Sodium (%)	0.316 ± 0.031	0.258) 0.370	12
Magnesium (%)	0.165 ± 0.010	0.148) 0.180	12
Sulfur (%)	0.266 ± 0.060	0.208) 0.420	11
Iron (ppm)	348.0 ± 83.7	255.0) 523.0	12
Manganese (ppm)	93.27 ± 5.62	81.7) 102.0	12
Zinc (ppm)	59.42 ± 9.73	46.1) 81.6	12
Copper (ppm)	11.63 ± 2.46	8.09) 15.4	12
Iodine (ppm)	3.49 ± 1.14	1.52) 5.83	11
Chromium (ppm)	1.57 ± 0.53	0.60) 2.09	12
Cobalt (ppm)	0.81 ± 0.27	0.49) 1.23	8

TABLE L4
Contaminant Levels in NIH-07 Rat and Mouse Ration[a]

	Mean ± Standard Deviation[b]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.47 ± 0.18	0.10) 0.70	25
Cadmium (ppm)	0.14 ± 0.07	0.04) 0.20	25
Lead (ppm)	0.36 ± 0.24	0.10) 1.00	25
Mercury (ppm)[c]	0.02	0.02) 0.03	25
Selenium (ppm)	0.33 ± 0.11	0.05) 0.40	25
Aflatoxins (ppb)	< 5.0		25
Nitrate nitrogen (ppm)[d]	7.92 ± 4.09	2.90) 17.0	25
Nitrite nitrogen (ppm)[d]	0.14 ± 0.06	0.10) 0.30	25
BHA (ppm)[e]	1.76 ± 1.92	1.00) 10.0	25
BHT (ppm)[e]	1.60 ± 1.58	1.0) 8.00	25
Aerobic plate count (CFU/g)	97,244 ± 161,922	6,500) 710,000	25
Coliform (MPN/g)	3 ± 0.3	3) 4	25
Escherichia coli (MPN/g)	< 3		25
Salmonella (MPN/g)	Negative		25
Total nitrosoamines (ppb)[f]	7.52 ± 1.84	4.7) 11.4	25
N-Nitrosodimethylamine (ppb)[f]	5.46 ± 1.24	2.9) 8.2	25
N-Nitrosopyrrolidine (ppb)[f]	2.06 ± 1.08	1.0) 4.3	25
Pesticides (ppm)			
α-BHC	< 0.01		25
β-BHC	< 0.02		25
γ-BHC	< 0.01		25
δ-BHC	< 0.01		25
Heptachlor	< 0.01		25
Aldrin	< 0.01		25
Heptachlor epoxide	< 0.01		25
DDE	< 0.01		25
DDD	< 0.01		25
DDT	< 0.01		25
HCB	< 0.01		25
Mirex	< 0.01		25
Methoxychlor	< 0.05		25
Dieldrin	< 0.01		25
Endrin	< 0.01		25
Telodrin	< 0.01		25
Chlordane	< 0.05		25
Toxaphene	< 0.10		25
Estimated PCBs	< 0.20		25
Ronnel	< 0.01		25
Ethion	< 0.02		25
Trithion	< 0.05		25
Diazinon	< 0.10		25
Methyl parathion	< 0.02		25
Ethyl parathion	< 0.02		25
Malathion	0.25 ± 0.24	0.05) 0.97	25
Endosulfan I	< 0.01		25
Endosulfan II	< 0.01		25
Endosulfan sulfate	< 0.03		25

[a] 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] All values except for lots milled November and December 1991 were less than the detection limit. The detection limit is given as the mean.
[d] Sources of contamination: alfalfa, grains, and fish meal
[e] Sources of contamination: soy oil and fish meal
[f] All values were corrected for percent recovery.

APPENDIX M
SENTINEL ANIMAL PROGRAM

METHODS 262
TABLE M1 Murine Virus Antibody Determinations for Rats and Mice in the 14-Week and 2-Year Studies of 1-Chloro-2-propanol 264

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 14-week 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	
14-Week 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	22 months
Mycoplasma pulmonis	22 months
PVM	6, 10, 12, 18, and 22 months, study termination
RCV/SDA	6, 10, 12, 18, and 22 months, study termination
Sendai	6, 10, 12, 18, and 22 months, study termination
Hemagglutination Inhibition	
H-1	6, 10, 12, 18, and 22 months, study termination
KRV	6, 10, 12, 18, and 22 months, study termination

Method and Test	Time of Analysis
MICE	
14-Week Study	
ELISA	
Ectromelia virus	Study termination
GDVII (mouse encephalomyelitis virus)	Study termination
LCM (lymphocytic choriomeningitis virus)	Study termination
MVM (minute virus of mice)	Study termination
PVM	Study termination
Reovirus 3	Study termination
Sendai	Study termination
Hemagglutination Inhibition	
Polyoma virus	Study termination
2-Year Study	
ELISA	
Ectromelia virus	6, 12, and 18 months, study termination
EDIM (epizootic diarrhea of infant mice)	12 and 18 months, study termination
GDVII	6, 12, and 18 months, study termination
LCM	6, 12, and 18 months, study termination
Mouse adenoma virus-FL	6, 12, and 18 months, study termination
MHV (mouse hepatitis virus)	6, 12, and 18 months, study termination
PVM	6, 12, and 18 months, study termination
Reovirus 3	6, 12, and 18 months, study termination
Sendai	6, 12, and 18 months, study termination
Immunofluorescence Assay	
Ectromelia virus	6 and 12 months
EDIM	6, 12, and 18 months
LCM	6 months
Reovirus 3	12 months
Hemagglutination Inhibition	
K (papovavirus)	6, 12, and 18 months, study termination
MVM	6, 12, and 18 months, study termination
Polyoma virus	6, 12, and 18 months, study termination

Results of serology tests are presented in Table M1.

TABLE M1
Murine Virus Antibody Determinations for Rats and Mice in the 14-Week and 2-Year Studies of 1-Chloro-2-propanol

Interval	Incidence of Antibody in Sentinel Animals	Positive Serologic Reaction for
14-Week Studies		
Rats		
Study termination	0/10	None positive
Mice		
Study termination	0/10	None positive
2-Year Studies		
Rats		
6 Months	0/10	None positive
10 Months	0/10	None positive
12 Months	0/10	None positive
18 Months	0/11	None positive
22 Months	1/1[a]	*M. arthritidis*
Study termination	0/16	None positive
Mice		
6 Months	0/10	None positive
12 Months	1/10[b]	Reovirus 3
18 Months	0/8	None positive
Study termination	0/10	None positive

[a] One rat with clinical symptoms that could be due to an infectious disease was evaluated for murine virus antibody titers. The serum sample from this rat had a low antibody titer for *M. arthritidis*. A larger set of samples (16) evaluated at study termination was negative for the panel of viruses included in the sentinel animal program including *M. arthritidis*. Evaluation of samples positive for *M. arthritidis* in various studies by immunoblot and Western blot procedures indicated that positive titers may be due to cross reaction with antibodies of nonpathogenic *Mycoplasma* or other agents. Only one sample was positive in this study, and there were no clinical findings or histopathologic changes of *M. arthritidis* infection in the animal with the positive titer. Accordingly, the *M. arthritidis*-positive titer was considered a false positive.

[b] Only one sample was positive for Reovirus 3 at 12 months with a low antibody titer. Samples from the same colony at 18 months and 2 years were negative. Sporadic low-titer positive reactions have been associated with false positives for Reovirus 3. Accordingly, the Reovirus 3 positive titer was considered a false positive.