NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 392

TOXICOLOGY AND CARCINOGENESIS STUDIES OF CHLORINATED WATER

(CAS NOS. 7782-50-5 and 7681-52-9)

AND CHLORAMINATED WATER

(CAS NO. 10599-90-3)

(DEIONIZED AND CHARCOAL-FILTERED)

IN F344/N RATS AND B6C3F$_1$ MICE

(DRINKING WATER STUDIES)

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. Selection *per se* is not an indicator of a chemical's carcinogenic potential.

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NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

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CONTENTS

ABSTRACT

Cl_2	NaOCl	NH_2Cl
Chlorine	**Sodium Hypochlorite**	**Chloramine**
CAS No.: 7782-50-5 Molecular Weight: 70.9 gas	CAS No.: 7681-52-9 Molecular Weight: 74.4 solid	CAS No.: 10599-90-3 Molecular Weight: 51.48 colorless liquid

Chlorine and chloramine are used as disinfectants in water supplies to prevent the spread of waterborne diseases. The U.S. Environmental Protection Agency and the U.S. Congress, through the Safe Drinking Water Acts and Amendments, initiated studies to determine the most effective way to disinfect water supplies and, at the same time, minimize any potential long-term health effects associated with direct chemical exposure or indirect chemical exposure through the formation of by-products. As part of this evaluation, 2-year studies of chlorinated or chloraminated deionized charcoal-filtered drinking water were conducted in F344/N rats and B6C3F$_1$ mice to determine the potential toxicity and carcinogenicity associated with prolonged exposure and eliminate possible confounding effects of byproducts of chlorination.

Chlorinated Water Studies

Water containing 0, 70, 140, or 275 ppm chlorine (based on available atomic chlorine) was provided to groups of 70 F344/N rats or B6C3F$_1$ mice of each sex for up to 2 years. Groups of 10 rats or mice of each sex were predesignated for evaluation at 14 or 15 weeks and 66 weeks.

Survival at 2 years of rats and mice receiving chlorinated water was similar to that of the controls. Mean body weights of dosed male rats, high-dose female rats, and dosed mice were slightly lower than those of their respective control groups. There was a dose-related decrease in water consumption by rats and mice. Water consumption by high-dose rats during the second year of the studies was 21% lower than controls for males and 23% lower than controls for females; water consumption by high-dose mice was 31% lower than controls for males and 26% lower than controls for females.

The incidence of mononuclear cell leukemia in mid-dose, but not high-dose, female rats was significantly higher than that in controls (control, 8/50; low-dose, 7/50; mid-dose, 19/51; high-dose, 16/50). The proportion of female rats that died of leukemia before the end of the study and the mean time for observation of animals dying with leukemia were similar among all dose groups and controls. Although the marginal increase in leukemia incidence in the mid- and high-dose female rats suggested a possible association with the administration of chlorinated water, the incidence of leukemia was not clearly dose related. There was no indication of reduced latency of leukemia, and the incidence of leukemia in concurrent controls was less than the mean for historical controls; furthermore, there was no supporting evidence of an effect in male rats. Thus, the marginal increase in leukemia incidence in female rats was considered equivocal evidence of carcinogenic activity. There were no neoplasms or nonneoplastic lesions in male rats or in male or female mice that were clearly associated with the consumption of chlorinated water.

Chloraminated Water Studies

Water containing 50, 100, or 200 ppm chloramine was provided to groups of 70 F344/N rats or B6C3F$_1$ mice of each sex for up to 2 years. The same control groups were used for the chlorinated water and chloraminated water studies. Groups of 9 or 10 rats or mice of each sex were evaluated at 14 or 15 weeks and 66 weeks.

Survival at 2 years of rats and mice receiving chloraminated water was similar to that of the controls. Mean body weights of high-dose rats and dosed mice were lower than those of their respective control groups. There was a dose-related decrease in water consumption by rats and mice. Water consumption during the second year of the studies by high-dose rats was 34% lower than controls for males and 31% lower than controls for females; water consumption by high-dose mice was 42% lower than controls for males and 40% lower than controls for females.

Mononuclear cell leukemia occurred with a marginally increased incidence in the mid- and high-dose female rats receiving chloraminated water (control, 8/50; low dose, 11/50; mid dose, 15/50; and high dose, 16/50). As in female rats receiving chlorinated water, the proportion of female rats that died of leukemia before the end of the study and the mean time for observation of animals dying with leukemia were similar among all dose groups and controls. The marginal increase in leukemia incidence in females receiving chloraminated water was considered equivocal evidence of carcinogenic activity for the same reasons given for female rats receiving chlorinated water. There were no neoplasms or nonneoplastic lesions in male rats or in male or female mice that were clearly associated with the consumption of chloraminated water.

Conclusions

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity** of chlorinated water in male F344/N rats receiving 70, 140, or 275 ppm. There was *equivocal evidence of carcinogenic activity* of chlorinated water in female F344/N rats based on an increase in the incidence of mononuclear cell leukemia. There was *no evidence of carcinogenic activity* of chlorinated water in male or female $B6C3F_1$ mice receiving 70, 140, or 275 ppm.

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity* of chloraminated water in male F344/N rats receiving 50, 100, or 200 ppm. There was *equivocal evidence of carcinogenic activity* of chloraminated water in female F344/N rats based on an increase in the incidence of mononuclear cell leukemia. There was *no evidence of carcinogenic activity* of chloraminated water in male or female $B6C3F_1$ mice receiving 50, 100, or 200 ppm.

* Explanation of Levels of Evidence of Carcinogenic Activity is on page 8. A summary of peer review comments and the public discussion on this Technical Report appears on page 10.

Summary of the 2-Year Carcinogenesis Studies of Chlorinated Water

Variable	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Doses	0, 70, 140, or 275 ppm in buffered water	0, 70, 140, or 275 ppm in buffered water	0, 70, 140, or 275 ppm in buffered water	0, 70, 140, or 275 ppm in buffered water
2-Year survival rates	14/51, 6/51, 16/50, 17/51	31/50, 31/50, 28/51, 35/50	34/50, 28/50, 35/50, 32/51	33/50, 31/51, 28/50, 35/50
Body weights	Slightly lower than controls	High-dose slightly lower than controls	Slightly lower than controls	Slightly lower than controls
Water consumption	Mid- and high-dose less than controls	Dosed less than controls	Dosed less than controls	Dosed less than controls
Nonneoplastic effects	None	None	None	None
Neoplastic effects	None	Mononuclear cell leukemia (8/50, 7/50, 19/51, 16/50)	None	None
Level of evidence of carcinogenic activity	No evidence	Equivocal evidence	No evidence	No evidence

Summary of the 2-Year Carcinogenesis Studies of Chloraminated Water

Variable	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Doses	0, 50, 100, or 200 ppm in buffered water	0, 50, 100, or 200 ppm in buffered water	0, 50, 100, or 200 ppm in buffered water	0, 50, 100, or 200 ppm in buffered water
2-Year survival rates	14/51; 22/50; 14/51; 16/50	31/50; 28/50; 29/50; 24/50	34/50; 23/50; 34/50; 37/51	33/50; 32/50; 35/50; 42/50
Body weights	High-dose lower than controls	High-dose lower than controls	Dosed lower than controls	Dosed lower than controls
Water consumption	Dosed less than controls	Dosed less than controls	Dosed less than controls	Dosed less than controls
Nonneoplastic effects	None	None	None	None
Neoplastic effects	None	Mononuclear cell leukemia (8/50, 11/50, 15/50, 16/50)	None	None
Level of evidence of carcinogenic activity	No evidence	Equivocal evidence	No evidence	No evidence

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 because of major flaws cannot be evaluated **inadequate study**. These categories of interpretative conclusions were first adopted in June 1983 and then revised in March 1986 for use in the Technical Reports 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 quintet is selected to describe the findings. These categories refer to the strength of the experimental evidence and not to either 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 describes 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. This 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:

- The 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 incidences 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);
- The presence or absence of dose relationships;
- The statistical significance of the observed tumor increase;
- The 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.

PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the NTP draft Technical Report on chlorinated and chloraminated water on November 19, 1990 are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, panel members have five major responsibilities in reviewing 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 PEER REVIEW COMMENTS

On November 19, 1990, the draft Technical Report on the toxicology and carcinogenesis studies of chlorinated and chloraminated water received public review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Committee and associated Panel of Experts. The review 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 chlorinated and chloraminated water by discussing the uses of chlorine and chloramine, experimental design, survival and water consumption in rats and mice, and results. The proposed conclusions were that there was *no evidence of carcinogenic activity* of chlorinated water for male F344/N rats or male or female B6C3F$_1$ mice and *equivocal evidence of carcinogenic activity* of chlorinated water for female F344/N rats. There was *no evidence of carcinogenic activity* of chloraminated water for male F344/N rats or male or female B6C3F$_1$ mice and *equivocal evidence of carcinogenic activity* of chloraminated water for female F344/N rats.

Dr. Longnecker, the first principal reviewer, agreed with the conclusions but asked for more discussion of the rationale for *equivocal evidence* in female rats. He asked why there was such low survival in dosed and control male rats and what impact this low survival might have had on the validity of the studies. Dr. S. Eustis, NIEHS, commented that higher incidences of leukemias, pituitary gland tumors, and kidney disease contributed to lower survival in male rats in these studies as well as in other more recent studies.

Dr. Goodman, the second principal reviewer, agreed with the conclusions in male rats and male and female mice, but did not agree with the conclusions in female rats, which he recommended be changed to *no evidence of carcinogenic activity*. He cited the high and variable incidence of leukemias in historical controls, noting that the incidences of leukemias in treated groups in these studies were within the range of historical controls, the relatively low incidence in concurrent controls, and the lack of a dose-response relationship. He further noted that the statistical significance ($P<0.05$) was marginal for such commonly occurring neoplasms. Dr. Dunnick responded by saying that emphasis is given primarily to concurrent control values.

Dr. Ashby, the third principal reviewer, agreed with the conclusions. He commented that because the water used had been treated with activated carbon and deionized prior to chlorination, a more descriptive title than "chlorinated drinking water" might be appropriate. Dr. Dunnick said text would be added to the Abstract and elsewhere to point out that the studies were intended to determine the toxicity and carcinogenicity of chlorinated or chloraminated water without the confounding effects of byproducts. Dr. Ashby expressed concern about the survival of male rats and its effect on the adequacy of the studies. Dr. J. Haseman, NIEHS, said that, in the judgment of the NTP, survival of male rats was sufficient to permit an evaluation of carcinogenicity.

There was some debate over whether discussion of the effects of trihalomethanes should be included, as the water purification processes would have removed any of these chemicals present. Dr. Silbergeld questioned the relevance to human exposure. There was also considerable discussion about the variability and increasing incidence of mononuclear cell leukemias in rats and how this affected the interpretation of the findings in dosed female rats.

Dr. Longnecker moved that the draft Technical Report on the studies of chlorinated and chloraminated water be accepted with the revisions discussed, including a modification of the report title and of the description of what was tested, and with the conclusions as written for male rats and male and female mice, *no evidence of carcinogenic activity*, and for female rats, *equivocal evidence of carcinogenic activity*. Dr. Ashby seconded the motion. Dr. Zeise offered an amendment that the studies of chlorinated water in male rats be considered an *inadequate study of carcinogenic activity* due to poor survival and inadequate dosing. Dr. Silbergeld seconded the motion, which was defeated by ten votes to two (Drs. Silbergeld, Zeise). Dr. Goodman offered an amendment that the conclusions in female rats be changed to *no evidence of carcinogenic activity*. Dr. Carlson seconded the motion, which

was defeated by nine votes to three (Drs. Carlson, Gold, Goodman). The original motion by Dr. Longnecker was then accepted by eight votes to three (Drs. Carlson, Gold, Goodman), with one abstention (Dr. Silbergeld).

INTRODUCTION

Cl_2	NaOCl	NH_2Cl
Chlorine	**Sodium Hypochlorite**	**Chloramine**
CAS No.: 7782-50-5 Molecular Weight: 70.9 gas	CAS No.: 7681-52-9 Molecular Weight: 74.4 solid	CAS No.: 10599-90-3 Molecular Weight: 51.48 colorless liquid

Chlorine was first introduced into an urban water supply in the United States in 1908 as a method for reducing the bacterial count (NRC, 1977). Chlorination is still the predominant method of water disinfection practiced in the United States (NRC, 1987). Once in the drinking water supplies, chlorine may react with organic material to produce various organic byproducts, including trihalomethanes. A recent survey of 35 water treatment facilities showed that common disinfection byproducts found in US drinking water include trihalomethanes, haloacetic acid, haloketones, and haloacetonitriles (Krasner *et al.*, 1989). The amount of these compounds in the water supplies varied with the source of water, season, and other factors specific to the particular water treatment facilities.

The National Cancer Institute and the National Institute of Environmental Health Sciences (NCI, 1976b; NTP, 1985a, 1987, 1989b) have reported tumors in rodents caused by the trihalomethanes - chloroform, chlorodibromomethane, bromodichloromethane, and bromoform. Mink *et al.* (1983) showed that after oral administration of sodium hypochlorite to rats, trihalomethanes were found in the plasma, indicating that chlorine can also form byproducts *in vivo* as well as *in vitro*.

Because of the concern over the carcinogenic potential of the trihalomethanes, the U.S. Environmental Protection Agency (USEPA) is considering alternative ways to disinfect water supplies, including the use of chloramine. The Safe Drinking Water Act of 1974 required a reexamination of national drinking water standards and initiated studies on the adverse health effects of drinking water contaminants (NRC, 1977; USEPA, 1977; Cotruvo, 1984; McGuire and Meadow, 1988; USEPA, 1988). Several groups have studied the long-term effects of consuming chlorinated surface water versus non-chlorinated ground water. The composition of the chlorinated water was variable, and the risk from a specific chemical such as chlorine or a chlorinated byproduct could not be identified. The USEPA requested that the NTP conduct 2-year rodent studies of chlorine and chloramine to evaluate the carcinogenic potential of these water disinfectants.

Chlorine effectively inactivates bacteria in 20 minutes at concentrations of 0.03 to 0.06 mg/L at a pH range of 7.0 to 8.5 and a temperature range of 4° to 22° C (Brodtmann and Russo, 1979; NRC, 1980; USEPA, 1989). One hundred percent inactivation of bacteria is achieved at a chloramine concentration of 0.6 mg/L at pH 7 or at a concentration of 1.2 mg/L at pH 8.5 with an exposure period of 60 minutes and a temperature of 20 °C. Typical residue levels in treated water are up to 1.5 mg/L (1.5 ppm) for chlorine and up to 4.0 mg/L (4 ppm) for chloramine (USEPA, 1988).

CHEMISTRY OF CHLORINE AND CHLORAMINE

Chlorination of water occurs through the addition of chlorine gas (Cl_2) or hypochlorite salts, such as NaOCl. The reaction of chlorine gas and water is as follows:

$$Cl_2 + H_2O \rightleftharpoons HOCl + H^+ + Cl^-$$
$$HOCl \rightleftharpoons H^+ + OCl^-$$

The total concentrations of hypochlorous acid (HOCl) and hypochlorite ions (OCl^-) are expressed as available atomic chlorine (free chlorine) and are used to express chlorine concentration in this report (Jolley and Carpenter, 1983).

Inorganic chloramines are formed when water containing ammonia is chlorinated. Monochloramine (NH_2Cl) is the primary chloramine formed when the pH of ammonia-containing water is greater than 8, and the molar ratio of hypochlorite to ammonia is less than 1 (Figure 1) (Jolley and Carpenter, 1983; Morris and Isaac, 1983). The reaction involved in this process is:

$$NH_3 + HOCl \rightleftharpoons NH_2Cl + H_2O$$

Dichloramine and trichloramine may be formed at lower pH (Morris and Isaac, 1983). In the studies reported here, pH was kept at 9 to minimize the formation of these other chloramines.

Chloramine (also called monochloramine) is a colorless, pungent liquid. Monochloramine differs from the commercial products chloramine B, chloramine T, and dichloramine T, which are organic compounds synthesized through the chlorination of benzene sulfonamide or *para*-toluene sulfonamide (USEPA, 1989).

In water, both chlorine and monochloramine can substitute a chlorine atom for a hydrogen atom in organic compounds to form halomethanes. Monochloramine is less reactive than chlorine in the formation of trihalomethanes (Stevens *et al.*, 1978; USEPA, 1989). Rickabaugh and Kinman (1978) found that chloramination resulted in the formation of 90% fewer trihalomethanes than did chlorination using hypochlorous acid.

Studies on the chemistry of chlorine and chloramine have shown that hypochlorous acid may react with amino acids (Pereira *et al.*, 1973), cytosine (Patton *et al.*, 1972) and other pyrimidine and purine bases (Hoyano *et al.*, 1973), and nucleic acids (Oliveri *et al.*, 1980) to produce chlorinated derivatives. Chlorine and chloramine also serve as oxidizing agents (*Kirk-Othmer*, 1964).

Production, Use, and Exposure

Chlorine production in the United States is reported to be 10,753,109 short tons. Besides its use as a water disinfectant, chlorine is also used in the pulp and paper industry for bleaching and in the production of plastic and resins for the manufacture of upholstery fabrics, floor coverings, food packaging, films, bottles, utensils, hose and tubing, and electrical insulation. Chlorine is an intermediate for the production of automotive fluids, such as ethylene glycol antifreeze and ethylene chloride. Chlorine is used in textile and household bleaches, refrigerants, pharmaceuticals, cosmetics, and metal extractions. It is estimated that 26,000 persons employed in the chloralkali manufacturing industry may potentially be exposed to chlorine (NIOSH, 1990). While the exposure to chlorine in the industrial setting is primarily by inhalation or dermal absorption, the general population may be exposed through consumption of treated water.

Used as a war gas in World War I, chlorine caused death or respiratory toxicity in those exposed (WHO, 1982; NIOSH, 1990). Because of this respiratory toxicity, as well as the skin and eye irritation associated with exposure to this chemical, the recommended time-weighted average exposure for chlorine is 0.5 ppm (1 mg/m^2) (ACGIH, 1989).

Chloramine is used as a water disinfectant and also as a reagent in a variety of organic syntheses (Drago, 1957; *Kirk-Othmer*, 1964; Kovacic *et al.*, 1970). Exposure to chloramine occurs primarily through exposure to treated water supplies. Chloramine is formed *in situ* from hypochlorous acid and ammonia as previously described.

Metabolism of Chlorine and Chloramine

Abdel-Rahman *et al.* (1983, 1984a, 1985) studied the kinetics of absorption of hypochlorous acid (HOCl) and monochloramine after oral administration of $HO^{36}Cl$ or $NH_2{}^{36}Cl$ to Sprague-Dawley rats. Peak plasma levels of chlorine (as atomic chlorine) occurred 2 hours after HOCl administration and 8 hours after NH_2Cl administration. The absorption half-life was 2 hours for $HO^{36}Cl$ and 2.5 hours for $NH_2{}^{36}Cl$, and the plasma elimination half-life was 39 to 44 hours. In metabolism studies both hypochlorous acid and monochloramine were converted and eliminated in the chloride form, and excretion was primarily via urine. The ^{36}Cl was distributed throughout the major organ systems, with plasma and blood containing the highest concentrations.

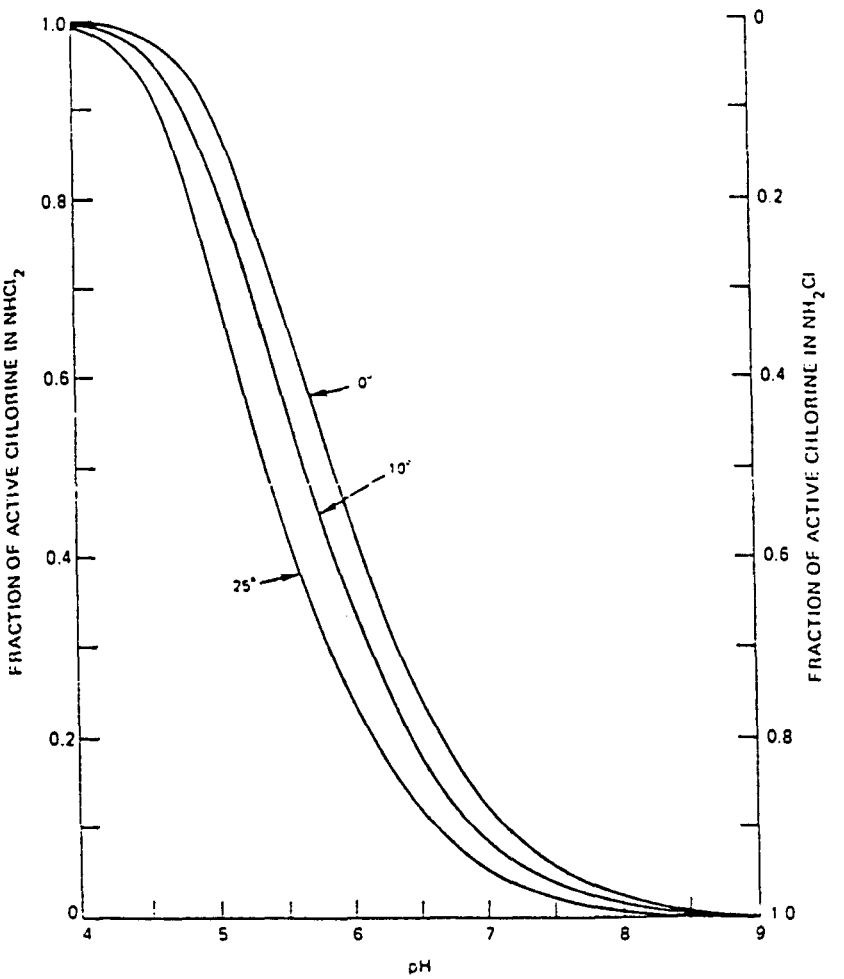

FIGURE 1
Proportions of Mono- and Dichloramine (NH_2Cl and $NHCl_2$) in Water Chlorination with Equimolar Concentrations of Chlorine and Ammonia. (NRC, 1980)

HUMAN EXPOSURE TO CHLORINE AND CHLORAMINE IN WATER

Humans may be exposed to chlorine and chloramine through the consumption of drinking water and foods and through other means, including showering, bathing, and swimming in water containing disinfectants (NRC, 1987). Several groups of scientists are studying the long-term effects of consuming chlorinated surface water versus non-chlorinated ground water (control groups). Because the chlorinated water contains a variety of chlorinated byproducts and the composition of chlorinated water is variable, the risk associated with exposure to a specific chemical such as chlorine is difficult to identify.

Some epidemiologic studies have indicated an association between consumption of chlorinated drinking water and an increased risk of cancer, particularly of the urinary bladder (Craun, 1985; Cantor *et al.*, 1987; NRC, 1987; Zierler *et al.*, 1988). In September 1989 the EPA sponsored an *ad hoc* review of the current epidemiologic studies of chlorine in the United states (Stober *et al.*, 1990). The EPA *ad hoc* review group recommended some reanalysis of the data and follow-up studies to further explore the long-term effects of consumption of chlorinated drinking water.

TOXICITY

General Effects

Daniel *et al.* (1990) reported on the toxicity of chlorine, chloramine, and chlorine dioxide in 13-week drinking water studies. Male and female Sprague-Dawley rats received 25, 100, 175, or 200 mg/L chlorine, or 25, 50, 100, or 200 mg/L chloramine or chlorine dioxide; controls received pH-buffered water. There were no treatment-related effects on survival for any of these three water disinfectants. Water consumption was significantly decreased in treated groups.

In the chlorine-treated groups, final body weights and histopathological lesions were similar to those seen in controls, but water consumption by the high-dose groups was 36% to 38% of the control values. In rats that received the high dose of chloramine, final body weight was 45% to 50% of the control value, and water consumption, about 35% of the control value. Results for the chlorine dioxide-treated rats were similar to those for the chloramine-treated rats. Chlorine dioxide treatment was also associated with histopathologic lesions in the nasal cavity that were characterized by goblet-cell hyperplasia and subacute inflammation.

When male Sprague-Dawley rats were given chloramine in drinking water at concentrations of 0, 1, 10, or 100 mg/L for up to 4 months, blood glutathione content, red blood cell count, and hematocrit were decreased in the exposed groups (Abdel-Rahman *et al.*, 1984b). Red blood cell counts, white blood cell counts, hematocrit or hemoglobin concentrations, mean cell hemoglobin, mean cell volume, mean cell hemoglobin concentration or methemoglobin concentration, and reticulocyte count were measured in male A/J mice treated for 30 days with monochloramine in drinking water at doses ranging from 2.5 to 200 ppm. With the exception of a slight increase in hematocrit, the blood parameters measured showed no changes that could be attributed to the administration of monochloramine (Moore and Calabrese, 1980).

Immunotoxicologic Effects

Sprague-Dawley rats were evaluated from weaning to 12 weeks of age for immunotoxicity after having received 5, 15, or 30 ppm chlorine or 9, 19, or 38 ppm chloramine in drinking water (Exon *et al.*, 1987). Parameters measured included spleen and thymus weights, antibody production, delayed-type hypersensitivity reactions, natural killer cell cytotoxicity, oxidative metabolic response and phagocytosis by macrophages, and production of cytokines (interleukins and prostaglandins). Significant reductions in spleen weight, delayed-type hypersensitivity reactions, and oxidative metabolism by macrophages were observed in rats exposed to 30 ppm chlorine. Reduced spleen weights and decreased antibody synthesis and prostaglandin production were seen in rats receiving 38 ppm chloramine. Other investigations have shown impaired macrophage function in mice receiving chlorinated drinking water at dose levels of 25 to 30 ppm (Fidler, 1977).

Reproductive Effects

In a teratology study, female Sprague-Dawley rats were administered chlorine, as HOCl, or monochloramine in drinking water at concentrations of 0, 1, 10, or 100 mg/L for 2.5 months prior to conception and throughout gestation. Rats were killed on day 20 of gestation, and the fetuses were examined for soft tissue and skeletal abnormalities. No increase in fetal resorptions was found in any treatment

group. Chlorine (HOCl) exposure *in utero* produced some soft-tissue defects, such as improper orientation of the heart and adrenal agenesis, in the offspring of dams receiving 100 mg/L. Chlorine exposure was also associated with a slightly increased incidence of skeletal variants, such as incompletely ossified or missing sternebrae or rudimentary ribs. Chloramine did not produce any significant changes in rat fetuses at any dose level (Abdel-Rahman *et al.*, 1982).

In another study assessing the teratogenic and reproductive toxicity of chlorine and chloramine, male Long-Evans rats were administered doses of 0, 1, 2, or 5 mg of chlorine per kg body weight or doses of 0, 2.5, 5, or 10 mg chloramine/kg by gavage for 56 days prior to breeding and throughout the 10-day breeding cycle. Female rats received the same concentrations by gavage for 14 days prior to breeding and throughout breeding, gestation, and lactation, until the pups were weaned on day 21. No alterations in sperm count, sperm motility, or sperm morphology were observed. There were no dose-related effects on fertility, fetal viability, litter size, day of eye opening, or day of vaginal patency (Carlton *et al.*, 1986). Other teratology studies examining the effects of chlorinated drinking water on fetal development in mice found no evidence for a teratologic effect (Chernoff *et al.*, 1979; Kavlock *et al.*, 1979; Staples *et al.*, 1979).

Carcinogenic Potential

The potential carcinogenicity of chlorinated drinking water has been examined using several different approaches, including long-term studies of organic extracts of chlorinated water (Truhaut *et al.*, 1979; Kool *et al.*, 1985; Van Duuren *et al.*, 1986), long-term studies of byproducts of chlorination such as the trihalomethanes (NCI, 1976b; Jorgenson *et al.*, 1985; NTP, 1985a, 1987; 1989b), and long-term studies of chlorinated tap water or tap water treated with sodium hypochlorite (Druckrey, 1968; Hasegawa *et al.*, 1986; Kurokawa *et al.*, 1986).

Truhaut *et al.* (1979) described studies examining the effects of organic micropollutants (extracted by chloroform at neutral pH) from a water source in France. In these life-time studies, groups of 50 mice and rats of each sex received micropollutants in their diet. Total numbers of malignant tumors were increased in animals receiving the organic extracts. Van Duuren *et al.* (1986) administered an extract of chlorinated humic acids to mice for 24 months and found no treatment-related carcinogenic effects. In a study conducted in the Netherlands, Wistar rats were administered organic extracts of tap water for 106 weeks, and there was no evidence of treatment-related carcinogenicity. The dose levels used in these studies correspond to 4 to 68 times the expected human exposure, based on a 70 kg man consuming 2 L of water per day (Kool *et al.*, 1985).

Trihalomethanes are common byproducts found in chlorinated drinking water. The NCI and NTP have conducted 2-year rodent toxicity and carcinogenicity studies on four trihalomethanes: chloroform, bromodichloromethane, chlorodibromomethane, and bromoform. Administered by oral gavage, each of these trihalomethanes gave a positive carcinogenic response in one or more of the following organs: kidney, liver, and colon/rectum (NCI, 1976b; NTP, 1985a, 1987, 1989b). In the chloroform study (NCI, 1976b), treatment-related kidney tumors were seen in male Osborne-Mendel rats and liver tumors were seen in male and female B6C3F$_1$ mice. In a drinking water study, chloroform administered at similar doses to those used in the NCI study also resulted in treatment-related kidney tumors in male Osborne-Mendel rats, but no treatment-related liver tumors were seen in female B6C3F$_1$ mice (Jorgenson *et al.*, 1985). In follow-up studies designed to evaluate liver toxicity in male and female B6C3F$_1$ mice (Bull *et al.*, 1986), chloroform was administered by oral gavage in either corn oil or a 2% Emulphor suspension for 13 weeks. Liver toxicity was observed only in mice receiving chloroform in the corn oil vehicle.

Several long-term studies have examined the effects of administering chlorine or a hypochlorite salt to rodents. In a lifetime study, Druckrey (1968) administered tap water containing 100 mg/L chlorine to seven generations of rats for a maximum of 2 years. Survival and tumor incidence were similar in control and treated groups. However, the number of animals in each group was small, and the study was not designed to determine carcinogenicity. Several studies in which sodium hypochlorite was administered to the skin of mice were judged to be inadequate for carcinogenic evaluation of chlorine or chloramine (Daniel *et al.*, 1990).

In studies by Kurokawa *et al.* (1986) and Hasegawa *et al.* (1986), sodium hypochlorite was administered to male and female mice and male rats at levels up to 0.1% (1,000 mg/L) and to female rats at levels up to 0.02% (200 mg/L) for 103 to 104 weeks. No

treatment-related increases in tumor incidence were found.

Chloramine, chloroform, and other disinfectant byproducts were tested in a rat liver foci assay using γ-glutamyltranspeptidase (GGT)-positive foci as indicators of carcinogenicity. Neither chloramine nor chloroform induced GGT-positive foci, and the authors concluded that these compounds alone have no significant potential to initiate carcinogenesis (Herren-Freund and Pereira, 1986).

Exposure of fish to chlorinated water supplies has been associated with papillomas of the oral cavity. Grizzle *et al.* (1984) noted that the incidence of oral cavity papillomas in fish decreased when the level of residual chlorine in the water was reduced; however, the authors did not identify the component in the water associated with this response.

Genetic Toxicity

Chloramine was weakly mutagenic when assayed in *Bacillus subtilis* for the reversion of trpC colonies to Trp^+ (Shih and Lederberg, 1976). Sodium hypochlorite was reported to induce DNA damage in polymerase-deficient *Escherichia coli* (Rosenkranz, 1973) and gene mutations in *Salmonella typhimurium* (Wlodkowski and Rosenkranz, 1975). However, Thomas *et al.* (1987) reported that monochloramine did not increase the numbers of revertant colonies over untreated control levels in assays using a modified preincubation protocol (1 hour preincubation followed by reduction of the unreacted oxidizing agents prior to plating) and a variety of *S. typhimurium* tester strains (TA97, TA100, TA102). Mickey and Holden (1971) reported that chlorine (supplied as sodium hypochlorite with a minimum of 5% available chlorine) induced chromosomal aberrations (breaks and rearrangements) and endomitotic figures in human lymphocytes, Chinese hamster ovary cells, and muntjac cell cultures. Positive results were reported for sodium hypochlorite in a chromosome aberration test with Chinese hamster fibroblasts (Ishidate *et al.*, 1984).

In vivo, significant increases in micronucleated erythrocytes were reported in newt larvae reared in purified, reconstituted water treated with sodium hypochlorite or monochloramine (Gauthier *et al.*, 1989). Likewise, sodium hypochlorite (6.6% available chlorine), administered as a single intraperitoneal injection of 312.5 to 2,500 mg/kg, did not induce a significant increase in the frequency of micronucleated polychromatic erythrocytes in the bone marrow of male ddY mice sampled 24 hours after treatment (Hayashi *et al.*, 1988). Additional *in vivo* studies have investigated the ability of chlorine or chloramine to induce chromosome aberrations or micronuclei in CD-1 mice or sperm-head abnormalities in $B6C3F_1$ mice. In these studies, the chemicals were administered by gavage, using either an acute (single dose) or subchronic (5 successive dosings at 24-hour intervals) protocol (Meier *et al.*, 1985). Neither compound induced micronuclei or aberrations, but chlorine (administered at pH 8.5, where the hypochlorite form predominates) did produce a significant, dose-related increase in sperm-head abnormalities in samples collected 3 weeks after administration of the final subchronic dose; no increases were noted 1 or 5 weeks after final dosing.

Rationale for Study

Toxicity and carcinogenicity studies of chlorinated and chloraminated water were conducted in rodents to determine the long-term effects of using chlorine or chloramine as water disinfectants. The water used in these studies was deionized and charcoal-filtered prior to treatment to eliminate possible confounding effects of chlorination byproducts.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF CHLORINE

Two 18.1 kg cylinders of chlorine gas from the same lot (lot no. A081584) and a third cylinder from a different lot (lot no. 12152-5) were obtained from Air Products (Lenexa, KS). Identity and purity analyses were conducted at the analytical chemistry laboratory (Midwest Research Institute, Kansas City, MO). The chemical was identified as chlorine by infrared spectroscopy and physical appearance (Appendix K, Figure K1). Gas chromatography indicated that the known possible impurities, hexachloroethane and hexachlorobenzene, were not present at concentrations greater than 0.01%.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The chlorine and chloramine dose formulations were prepared from a stock solution of buffered sodium hypochlorite. The stock solution was prepared by bubbling chlorine gas into charcoal-filtered, deionized water, determining the concentration of available atomic chlorine in the solution, and adding an equivalent weight of sodium hydroxide. The solution was then buffered to approximately pH 9 with sodium bicarbonate and sodium carbonate monohydrate.

Chlorine dose formulations as sodium hypochlorite solutions were prepared by mixing the appropriate volume of stock solution with sodium chloride and bicarbonate-carbonate buffer solution, then diluting with charcoal-filtered, deionized water. Concentrations were expressed in ppm of available atomic chlorine. Chloramine dose formulations were prepared in the same manner, but dilute ammonium hydroxide solution was added to generate monochloramine. Concentrations of chloramine were expressed in ppm. All solutions were approximately 0.022 M carbonate and 0.035 M sodium at pH 9, the pH of the most concentrated chloramine solutions. Further details of dose formulation preparation are given in Table K1.

Stability studies indicated that the buffered hypochlorite stock solution was approximately 96% of its original concentration after storage for 7 days at 5° C. Chlorinated water formulations at levels of 70 to 275 ppm retained 95% of their original concentrations after storage for 1 day and 90% after 2 days. Chloraminated water formulations at levels of 50 to 200 ppm retained 96% of the original concentration after 1 day and 92% after 2 days. Based on these findings, the buffered hypochlorite stock solution used in these studies was stored at 5° C for no longer than 7 days, and the dose formulations were stored at room temperature for no longer than 48 hours.

Periodic analyses of the dose formulations for available atomic chlorine, monochloramine, dichloramine, and trihalomethane content were conducted as described in Appendix K. During the 2-year studies, dose formulations were within 10% of the target concentrations of monochloramine or chlorine more than 99% of the time (Tables K2 and K3).

2-YEAR STUDIES

Study Design

Groups of 70 F344/N rats and 70 B6C3F$_1$ mice of each sex were administered 70, 140, or 275 ppm available atomic chlorine, or 50, 100, or 200 ppm chloramine in buffered, charcoal-filtered, deionized drinking water for 103 to 104 weeks. Control animals received buffered deionized water only. Ten rats per dose group were predesignated for interim evaluation (necropsy, organ weights, histopathology, and hematology) during week 14. Similarly, 10 mice per dose group were predesignated for evaluation at 15 weeks. Another 10 rats and 10 mice per dose group were predesignated for evaluation at 66 weeks.

The doses for the 2-year studies of chlorine and chloramine were based on data from unpublished studies of chloramine conducted at the Gulf South Research Institute (GSRI), New Iberia, Louisiana. In the 13-week studies chloramine was administered to F344/N rats and B6C3F$_1$ mice at doses of 0, 25, 50, 100, 200, or 400 ppm. Decreased body weights were seen in the higher dose groups. No histopathologic lesions were clearly associated with

chemical administration in either rats or mice. In 2-year studies at GSRI, male and female F344/N rats and $B6C3F_1$ mice received chloramine in drinking water at doses of 0, 50, 100, or 200 ppm. During these 2-year studies, water consumption in the high-dose group was decreased, and at week 70 water consumption in the treated groups was approximately 20% to 48% less than that in the control groups. For this reason, 200 ppm was considered the maximum dose of chloramine that the animals would drink.

The studies reported here were conducted at the Southern Research Institute, Birmingham, AL. At the request of EPA, these studies evaluated both chlorine and chloramine. Two of the chlorine and chloramine dose levels used in these studies were equimolar in concentration of available atomic chlorine. The doses used in the 2-year studies of chlorine (molecular weight of available atomic chlorine, 35 g) were 70, 140, and 275 ppm (2, 4, and 8 mmolar). The doses used in the 2-year studies of chloramine (molecular weight of available atomic chlorine, 51.5 g) were 0, 50, 100, and 200 ppm (0, 1, 2, and 4 mmolar). Chlorine and chloramine were administered in charcoal-filtered, deionized water. Data from EPA have shown that the rate-limiting factor in administering these chemicals in drinking water is their palatability (Daniel *et al.*, 1990). Drinking water for the controls was buffered, charcoal-filtered, deionized water adjusted to the same pH as the dosed preparations.

Source and Specification of Animals

The male and female F344/N rats and $B6C3F_1$ mice used in these studies were obtained from the Frederick Cancer Research Facility (Frederick, MD). Because of the large number of animals needed and because of restrictions on animal availability, each study was conducted with two groups of animals, separated by an interval of 2 weeks (Table 1). The animals used in each study were housed in separate rooms. Rats and mice were shipped to the study laboratory at 4 weeks of age and were quarantined for 12 to 15 days. During this time, animals were examined daily. To assess the health status of the animals, five rats and five mice of each sex per room were killed for gross examination of abdominal and thoracic viscera and determination of pathogen burden. Pathogens evaluated included ectoparasites (mites, fleas, lice), intestinal parasites, bacteria, and viruses. A special health exam was performed on additional rats and mice prior to the initiation of dosing. The rats and mice were placed on study at 5 to 6 weeks of age. The health of the animals was monitored during the course of the studies according to the protocols of the NTP Sentinel Animal Program (Appendix O).

Animal Maintenance

Rats were housed five per cage; mice were housed individually. Feed and dosed water were available *ad libitum*. Further details of animal maintenance are given in Table 1.

Clinical Examinations and Pathology

All animals were observed twice daily for morbidity and mortality. Clinical findings and body weights were recorded once per week for the first 13 weeks of the studies and once per month thereafter. Mean body weights were calculated for each group.

Animals predesignated for the 14-week (rats) or 15-week (mice) and 66-week interim evaluations were killed, and the blood was collected for hematologic analysis. Parameters measured are listed in Table 1. Blood collected from the rats at the interim evaluations was also used to screen for pathogens. All predesignated animals, including those found dead prior to the interim evaluations, were necropsied. All animals in the control, high-dose chlorine, and high-dose chloramine groups were examined histopathologically. Tissues and groups examined are listed in Table 1. Organ weights were obtained for the liver, right kidney, brain, and thymus of all predesignated animals surviving until the interim evaluations.

During the 2-year studies, animals found moribund and those surviving to the end of the studies were killed. All animals, including those found dead, were necropsied. During necropsy all organs and tissues were examined for grossly visible lesions. Tissues were preserved in 10% neutral buffered formalin and routinely processed for microscopic examination (embedded in paraffin, sectioned at 4 to 5 μm, and stained with hematoxylin and eosin). A complete histopathologic evaluation inclusive of gross lesions was performed on all animals. Tissues examined microscopically are listed in Table 1.

Upon completion of the microscopic evaluation by the laboratory pathologist, the slides, paraffin blocks,

and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit. The slides, individual animal data records, and pathology tables were sent to an independent pathology quality assessment laboratory. The individual animal records and pathology tables were compared for accuracy, slide and tissue counts were verified, and histotechnique was evaluated. All tumor diagnoses, kidneys of all rats, of all male mice, and of all female mice given chloramine and all tissues from a random selection of 10% of all rats and 10% of all mice from control, mid- and high-dose groups were reevaluated microscopically by quality assessment pathologists.

The quality assessment reports and slides were submitted to the NTP Pathology Working Group (PWG) chair, who reviewed selected tissues microscopically, including tissues for which there was a disagreement in diagnosis between the laboratory and quality assessment pathologists. Representative examples of potentially chemical-related nonneoplastic lesions and neoplasms, including examples of differences in diagnosis between the study pathologist and the reviewing pathologist, were selected by the chairs for review by the PWGs. For rats, the PWG examined all differences of opinion regarding the presence of mononuclear cell leukemia, particularly the very early or uncertain cases of leukemia, all renal tubule neoplasms, all pancreatic islet-cell neoplasms, and miscellaneous other neoplasms. For mice, the PWG examined all renal tubule cell neoplasms, uterine neoplasms, harderian gland neoplasms, and miscellaneous lesions. The PWGs consisted of the quality assessment pathologists and other pathologists experienced in rodent toxicologic pathology. The groups examined the tissues without knowledge of dose groups or previously rendered diagnoses. When the consensus opinion of the PWG differed from that of the laboratory pathologist, the diagnosis was changed to reflect the opinion of the PWG. Thus, the final diagnoses represent a consensus of contractor pathologists and the PWG. Details of these review procedures have been described by Maronpot and Boorman (1982) and Boorman *et al.* (1985). For subsequent analysis of pathology data, the diagnosed lesions for each tissue type were evaluated separately or combined according to the guidelines of McConnell *et al.* (1986).

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 were censored from the survival analyses at the time they were found dead of other than natural causes or were found to be missing; animals dying from natural causes were not censored. Statistical analyses for a possible dose-related effect on survival used Cox's method (1972) 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 incidence of neoplasms or nonneoplastic lesions is given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators include only those animals for which the site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions had multiple potential sites of occurrence (e.g., lymphomas), the denominators consist of the number of animals that were necropsied.

Analysis of Tumor Incidence

The majority of tumors in these studies were considered to be incidental to the cause of death or not rapidly lethal. Thus, the primary statistical method used was a logistic regression analysis, which assumed that the diagnosed tumors were discovered as the result of death from an unrelated cause and therefore did not affect the risk of death. In this approach, tumor prevalence was modeled as a logistic function of chemical exposure and time. Both linear and quadratic terms in time were incorporated initially, and the quadratic term was eliminated if it did not significantly enhance the fit of the model. The dosed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and

Haseman (1986). When tumors are incidental, this comparison of the time-specific tumor prevalences also provides a comparison of the time-specific tumor incidences (McKnight and Crowley, 1984).

In addition to logistic regression, alternative methods of statistical analysis were used, and the results of these tests are summarized in the appendixes. These methods include the life table test (Cox, 1972; Tarone, 1975), appropriate for rapidly lethal tumors, and the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart et al., 1979), procedures based on the overall proportion of tumor-bearing animals.

Tests of significance included pairwise comparisons of each dosed group with controls and a test for an overall dose-response trend. Continuity-corrected tests were used in the analysis of tumor incidence. Reported P values are one sided. The procedures described above also were used to evaluate selected nonneoplastic lesions. (For further discussion of these statistical methods, see Haseman, 1984.)

Historical Control Data

Although the concurrent control group is the first and most appropriate control group used for evaluation, there are certain instances in which historical control data can be helpful in the overall assessment of tumor incidence. Consequently, control tumor incidences from the NTP historical control database (Haseman *et al.*, 1984, 1985) are included in NTP reports for tumors appearing to show compound-related effects.

Analysis of Continuous Variables

The nonparametric multiple comparison procedures of Dunn (1964) or Shirley (1977) were used to assess the significance of pairwise comparisons between dosed and control groups in the analysis of organ weight and hematology data. Jonckheere's test (Jonckheere, 1954) was used to evaluate the significance of dose-response trends and to determine whether Dunn's or Shirley's test was more appropriate for pairwise comparisons.

QUALITY ASSURANCE METHODS

The 2-year studies were conducted in compliance with the Food and Drug Administration Good Laboratory Practice Regulations (CFR, 21, Part 58). In addition, as study records were submitted to the NTP Archives, they 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 preliminary review draft of this NTP Technical Report were conducted. Audit procedures and findings are presented in the reports, which are on file at the NIEHS. The audit findings were reviewed and assessed by NTP staff so that all discrepancies had been resolved or were otherwise addressed during the preparation of this Technical Report.

TABLE 1
Experimental Design and Materials and Methods in the 2-Year Studies of Chlorinated and Chloraminated Water

Study Laboratory
Southern Research Institute, Birmingham, AL

Strain and Species
Rats: F344/N
Mice: $B6C3F_1$

Animal Source
Frederick Cancer Research Facility, Frederick, MD

Date of Birth
Rats[a] (Group 1): 18 December 1984
Rats (Group 2): 1 January 1985
Mice[a] (Group 1): 16 October 1984
Mice (Group 2): 30 October 1984

Time Held Before Study
Rats (Both Groups): 12 days
Mice (Group 1): 15 days
Mice (Group 2): 12 days

Average Age When Placed on Study
Rats (Both Groups): 5 weeks
Mice (Group 1): 6 weeks
Mice (Group 2): 5 weeks

Date of First Dose
Rats (Group 1): 28 January 1985
Rats (Group 2): 11 February 1985
Mice (Group 1): 29 November 1984
Mice (Group 2): 10 December 1984

Duration of Dosing
Rats: 14 weeks, 66 weeks, and 103 weeks
Mice: 15 weeks, 66 weeks, and 104 weeks

Date of Last Dose
Rats (Group 1): 30 April-2 May 1985, 29 April-1 May 1986, and 19 January 1987
Rats (Group 2): 14-16 May 1985, 13-15 May 1986, and 2 February 1987
Mice (Group 1): 5-7 March 1985, 26-28 February 1986, and 23 November 1986
Mice (Group 2): 19-21 March 1985, 10-12 March 1986, and 7 December 1986

Necropsy Dates
Rats (Group 1): 30 April-2 May 1985, 29 April-2 May 1986, and 26-29 January 1987
Rats (Group 2): 14-16 May 1985, 13-15 May 1986, and 9-12 February 1987
Mice (Group 1): 5-7 March 1985, 26-28 February 1986, and 1-5 December 1986
Mice (Group 2): 19-21 March 1985, 10-12 March 1986, and 12-17 December 1986

Average Age at Necropsy
Rats (Both Groups): 19 weeks, 71 weeks, and 110 weeks
Mice (Both Groups): 20 weeks, 71 weeks, and 111 weeks (Group 1); 110 weeks (Group 2)

[a] Due to the large number of animals involved and restrictions on animal availability, the study was conducted in two parts. The treatment procedure was the same for both groups, but dosing was initiated on different days. Therefore, milestone dates and ages differ.

TABLE 1
Experimental Design and Materials and Methods in the 2-Year Studies of Chlorinated and Chloraminated Water (continued)

Size of Study Groups
50 males and 50 females of each species
Interim Evaluations: 10 males and 10 females of each species

Method of Animal Distribution
Animals were grouped by weight intervals and assigned to cages. Cages were then assigned to treatment groups by a random number table.

Animals per Cage
Rats: 5
Mice: 1

Method of Animal Identification
Toe clip

Feed
NIH-07 Rat and Mouse Ration (Zeigler Bros., Inc., Gardners, PA), available *ad libitum*

Maximum Storage Time for Feed
120 days after milling

Feeders
Stainless steel (Lab Products, Inc., Garfield, NJ), changed weekly

Water
City water, buffered, charcoal-filtered, and deionized through a conditioning unit (Continental Water Systems, Birmingham, AL), water and bottles changed each mix day.
Rats: 16-ounce glass water bottles (Lab Products, Inc., Garfield, NJ)
Mice: 2-ounce glass water bottles (Sargent-Welch, Birmingham, AL)

Cages
Polycarbonate (Lab Products, Inc., Garfield, NJ), changed twice weekly (rats) or weekly (mice)

Bedding
BetaChips (Northeastern Products Corporation, Warrensburg, NY), changed twice weekly (rats) or weekly (mice)

Cage Filters
Reemay spun-bonded polyester (Andico, Birmingham, AL), changed once every two weeks

Racks
Stainless steel (Lab Products, Inc., Rochelle Park, NJ, and Maywood, NJ), changed once every two weeks

Animal Room Environment
Rats -
Temperature (Room 17): Week 1-14, 67°-79° F; Week 15-66, 64°-79° F; and Week 67-103, 65°-82° F
Temperature (Room 19): Week 1-14, 67°-74° F; Week 15-66, 66°-77° F; and Week 67-103; 61°-77° F
Relative Humidity (Room 17): Week 1-14, 21%-62%; Week 15-66, 21%-66%; and Week 67-103, 21%-74%
Relative Humidity (Room 19): Week 1-14, 42%-58%; Week 15-66, 20%-67%; and Week 67-103, 20%-87%
Light (both rooms): fluorescent, 12 hours/day
Room air changes (both rooms): minimum of 10 changes/hour

TABLE 1
Experimental Design and Materials and Methods in the 2-Year Studies of Chlorinated and Chloraminated Water (continued)

Animal Room Environment (continued)
Mice -
Temperature (Room 16): Week 1-15, 68°-78° F; Week 16-66, 65°-82° F; and Week 67-104, 59°-82° F
Temperature (Room 18): Week 1-15, 64°-78° F; Week 16-66, 64°-83° F; and Week 67-104, 60°-83° F
Relative Humidity (Room 16): Week 1-15, 33%-68%; Week 16-66, 33%-68%; and Week 67-104, 22%-73%
Relative Humidity (Room 18): Week 1-15, 21%-62%; Week 16-66, 21%-72%; and Week 67-104, 21%-72%
Light (both rooms): fluorescent, 12 hours/day
Room air changes (both rooms): minimum of 10 changes/hour

Doses
Chloramine: 0, 50, 100, or 200 ppm. Chlorine: 0, 70, 140, or 275 ppm. Administered in buffered, charcoal-filtered, deionized water.

Storage Conditions for Dosing Solutions
Polypropylene bottles at room temperature

Maximum Storage Time for Dosing Solutions
48 hours

Type and Frequency of Observation
14-Week (Rats)/15-Week (Mice) Interim Evaluations: Observed twice daily. Clinical signs and body weights recorded weekly and at time animals killed. Water consumption measured weekly. Feed consumption measured daily per cage 1 week per month.

66-Week Interim Evaluations and 2-Year Studies (Both Species): Observed twice daily. Clinical signs, body weights, and water consumption recorded weekly through week 13, then monthly, and at necropsy. Feed consumption measured daily per cage 1 week per month.

Hematology
Blood was collected at the 14-week/15-week and 66-week interim evaluations. The following parameters were evaluated: platelet, erythrocyte, reticulocyte, and leukocyte counts, hematocrit, hemoglobin, mean cell hemoglobin, mean cell hemoglobin concentration, mean cell volume, leukocyte differential, and erythrocyte fragility.

Necropsy and Histopathologic Examinations
Necropsy performed on all animals. Brain, right kidney, liver, and thymus weights were obtained for all predesignated animals surviving until Week 14 (rats) or 15 (mice), until Week 66 (both species), or until Week 103 (rats) or Week 103-104 (mice).

Complete histopathology performed on all early deaths and on control, high-dose chlorine, and high-dose chloramine animals. The following tissues were evaluated: adrenal gland, bone (femur, including marrow), brain (frontal cortex and basal ganglia, parietal cortex, and thalamus, cerebellum, and pons), esophagus, gallbladder (mice), gross lesions, heart, intestines (duodenum, jejunum, ileum, cecum, colon, rectum), kidney, liver, lung, lymph nodes (mandibular, mesenteric), mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial or clitoral glands (rats), prostate gland, salivary gland, skin, spleen, stomach (forestomach, glandular), testis, epididymis, seminal vesicle, thymus, thyroid gland, trachea, urinary bladder, and uterus.

RESULTS

CHLORINATED WATER IN RATS

Water, Compound, and Feed Consumption

Administration of chlorinated water resulted in a dose-related decrease in water consumption by both sexes that was evident in the first week and continued throughout the studies (Tables L1 and L2). Within dose groups, estimated ingestion of chlorine by males was lower than that by females the first year, but higher than that by females the second year. Feed consumption by dosed rats was similar to controls, with males consuming more feed than females (Tables N1 and N2).

Body Weights, Organ Weights, Hematology, and Clinical Findings

Mean body weights of rats receiving chlorinated water were within 10% of those of controls throughout the studies (Figure 2, Tables 2 and 3). Mean body weights, organ weights, and organ-weight-to-body-weight ratios for male and female rats evaluated at 14 or 66 weeks are shown in Tables I1-I4. Mean body weights at necropsy were similar among dosed and control groups at both the 14-week and 66-week interim evaluations, and there were no biologically significant differences in organ weights or organ-weight-to-body-weight ratios between dosed and control groups. The results of analyses performed on blood samples collected at the interim evaluations are presented in Tables J1 and J2. There were no alterations in hematologic parameters attributable to the consumption of chlorinated water for 14 or 66 weeks. There were no clinical findings attributable to the consumption of chlorinated water.

Survival

Estimates of the probability of survival of male and female rats receiving chlorinated water at the doses used in these studies and for controls are shown in the Kaplan-Meier curves in Figure 3. The numbers of rats dying early, killed moribund, or surviving to the end of the studies are given in Table 4. Three males and one female rat predesignated for the 66-week interim evaluations died or were killed moribund before the 66-week interim evaluations. The clinical and pathology data from these animals were therefore included with the core group of 2-year animals. The survival of rats receiving chlorinated water was not significantly different from that of controls.

Pathology and Statistical Analysis of Results

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one dose group, and historical control incidences for the neoplasms mentioned in this section are presented in Appendixes A and B for male and female rats given chlorinated water. No gross or microscopic lesions attributable to chlorinated water consumption were seen in the 14- or 66-week interim evaluations.

Mononuclear cell leukemia: The incidence of mononuclear cell leukemia in mid-dose, but not high-dose, female rats receiving chlorinated water was significantly greater than for controls ($P=0.014$) by the life table test (Table 5). Because leukemia is a rapidly progressing disease, the life table test is generally considered the most appropriate statistical test for analysis. The incidence of leukemia in mid-dose female rats (37%) also exceeded the incidence in untreated historical controls for feed and drinking water studies (170/680 (25%) with a range of 14%-36%; Table B4a). The proportion of animals with leukemia that died before the end of the studies and the mean time to leukemia observation for animals dying with leukemia were similar among all dosed and control groups (for control: proportion, 50%, and time to observation, 601 days; low-dose: 70% and 624 days; mid-dose: 53% and 604 days; high-dose: 44% and 653 days).

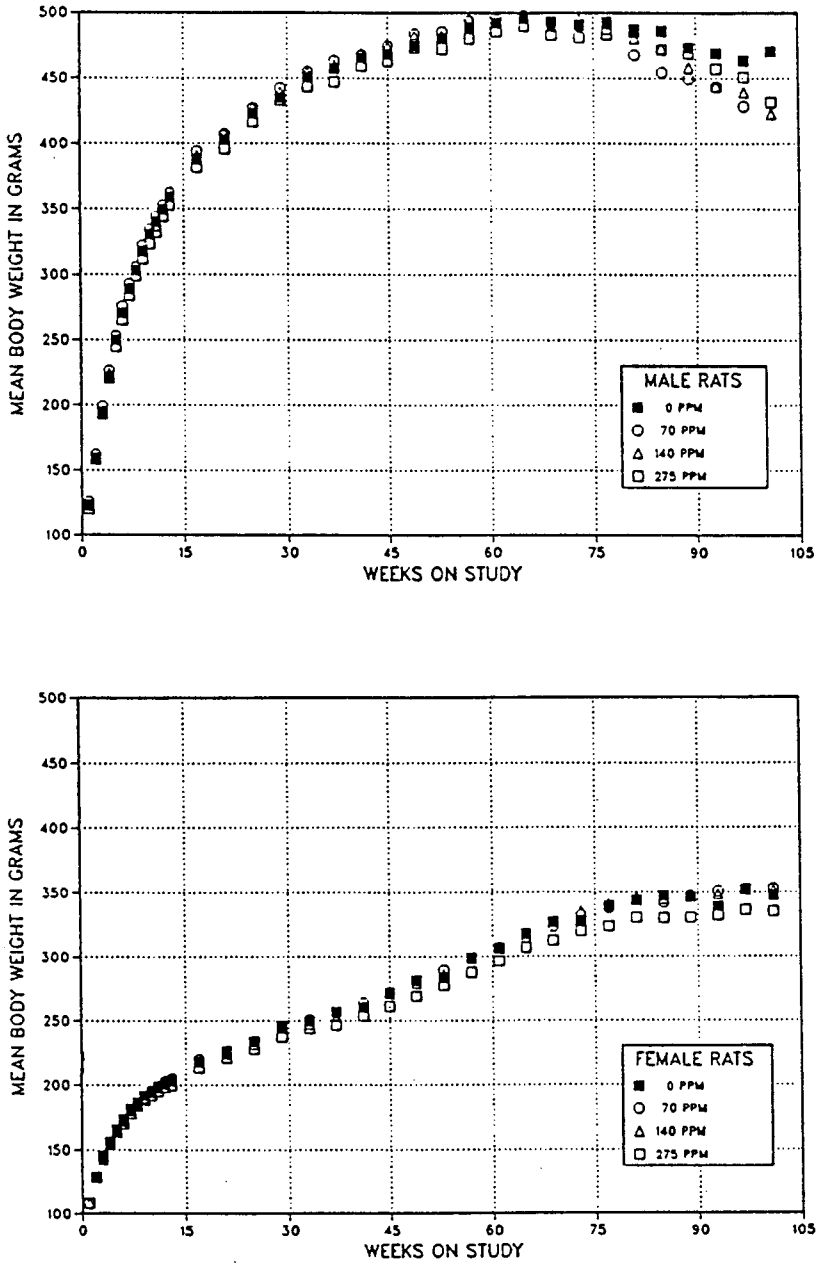

FIGURE 2
Growth Curves for Male and Female Rats Administered Chlorinated Water for 2 Years

TABLE 2
Mean Body Weights and Survival of Male Rats in the 2-Year Study of Chlorinated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	70 ppm Av. Wt. (g)	70 ppm Wt. (% of controls)	70 ppm No. of Survivors	140 ppm Av. Wt. (g)	140 ppm Wt. (% of controls)	140 ppm No. of Survivors	275 ppm Av. Wt. (g)	275 ppm Wt. (% of controls)	275 ppm No. of Survivors
1	121	70[a]	123	101	70[a]	121	100	70[a]	119	98	70[a]
2	159	70	162	102	70	159	100	70	158	99	70
3	195	70	199	102	70	194	100	70	193	99	70
4	222	70	227	102	70	225	101	70	220	99	70
5	250	70	253	101	70	251	100	70	245	98	70
6	270	70	276	102	70	270	100	70	266	98	70
7	289	70	293	102	70	290	101	70	284	98	70
8	303	70	306	101	70	303	100	70	299	99	70
9	318	70	323	102	69	318	100	70	312	98	70
10	331	70	335	101	69	330	100	70	324	98	70
11	340	70	344	101	69	337	99	70	332	98	70
12	349	70	353	101	69	350	100	70	344	99	70
13	359	70	362	101	69	360	100	70	353	98	70
17[b]	388	60	394	102	59	391	101	60	382	99	60
21	403	60	407	101	59	408	101	60	396	98	60
25	423	60	427	101	59	428	101	60	417	99	60
29	435	60	442	102	59	440	101	60	433	100	60
33	450	60	455	101	59	455	101	60	443	98	60
37	457	60	463	101	59	460	101	60	447	98	60
41	465	60	468	101	59	469	101	60	459	99	60
45	468	60	475	101	58	474	101	60	463	99	60
49	475	59	484	102	58	482	102	60	474	100	60
53	480	58	485	101	58	483	101	59	472	98	60
57	489	58	494	101	57	495	101	58	480	98	60
61	492	58	495	101	57	495	101	58	486	99	58
65	496	57	498	101	56	498	101	58	490	99	58
69[b]	493	46	492	100	47	490	99	47	483	98	49
73	491	46	489	100	44	495	101	46	481	98	48
77	493	44	488	99	41	493	100	44	484	98	45
81	487	41	468	96	39	481	99	43	485	100	43
85	486	38	455	94	37	473	97	42	472	97	43
89	473	33	450	95	31	459	97	38	469	99	39
93	469	29	443	95	25	444	95	32	457	97	33
97	463	26	429	93	20	439	95	26	451	97	26
101	471	19	425	90	13	423	90	22	432	92	20
Terminal sacrifice		14			6			16			17
Mean for weeks											
1-13	270		274	101		270	100		267	99	
17-49	440		446	101		445	101		435	99	
53-101	483		470	97		474	98		472	98	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.

TABLE 3
Mean Body Weights and Survival of Female Rats in the 2-Year Study of Chlorinated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	70 ppm Av. Wt. (g)	70 ppm Wt. (% of controls)	70 ppm No. of Survivors	140 ppm Av. Wt. (g)	140 ppm Wt. (% of controls)	140 ppm No. of Survivors	275 ppm Av. Wt. (g)	275 ppm Wt. (% of controls)	275 ppm No. of Survivors
1	105	70[a]	103	98	70[a]	104	99	70[a]	104	99	70[a]
2	128	70	129	101	70	129	100	70	129	101	70
3	145	70	144	99	70	142	98	70	144	99	70
4	156	70	155	99	70	155	99	70	154	99	70
5	165	70	164	99	70	164	99	70	163	99	70
6	173	70	172	99	70	171	99	70	170	98	70
7	181	70	180	100	70	180	99	70	178	98	70
8	186	70	186	100	70	184	99	70	183	98	70
9	192	70	190	99	70	189	98	70	188	98	70
10	195	70	196	100	70	194	99	70	192	98	70
11	198	70	199	100	70	198	100	70	195	98	70
12	202	70	203	101	70	200	99	70	198	98	70
13	204	70	205	101	70	203	100	70	200	98	70
17[b]	218	60	220	101	60	218	100	60	214	98	60
21	226	60	227	100	60	224	99	60	221	98	60
25	234	60	234	100	60	232	99	60	228	98	60
29	246	60	245	100	60	244	99	60	238	97	60
33	250	60	251	101	60	247	99	60	244	98	60
37	257	60	256	100	60	253	99	60	247	96	60
41	260	60	264	102	60	261	101	60	254	98	60
45	271	60	272	100	60	271	100	60	261	96	60
49	281	60	281	100	60	279	99	59	269	96	60
53	283	60	289	102	60	286	101	59	278	98	60
57	299	60	298	100	59	298	100	59	288	96	59
61	306	60	307	100	59	308	101	57	297	97	59
65	318	60	315	99	58	317	100	56	307	97	58
69[b]	327	49	323	99	48	328	100	47	312	96	49
73	327	49	332	102	47	336	103	47	320	98	49
77	339	47	338	100	45	342	101	47	324	95	48
81	344	47	344	100	44	347	101	45	330	96	47
85	347	45	342	99	44	345	99	44	330	95	47
89	346	45	348	101	41	348	101	41	330	96	44
93	339	43	351	103	39	349	103	40	332	98	43
97	352	35	353	100	37	352	100	37	337	96	40
101	348	34	353	102	37	352	101	32	335	97	39
Terminal sacrifice		31			31			28			35
Mean for weeks											
1-13	172		171	99		170	99		169	98	
17-49	249		250	100		248	100		242	97	
53-101	329		330	100		331	101		317	96	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.

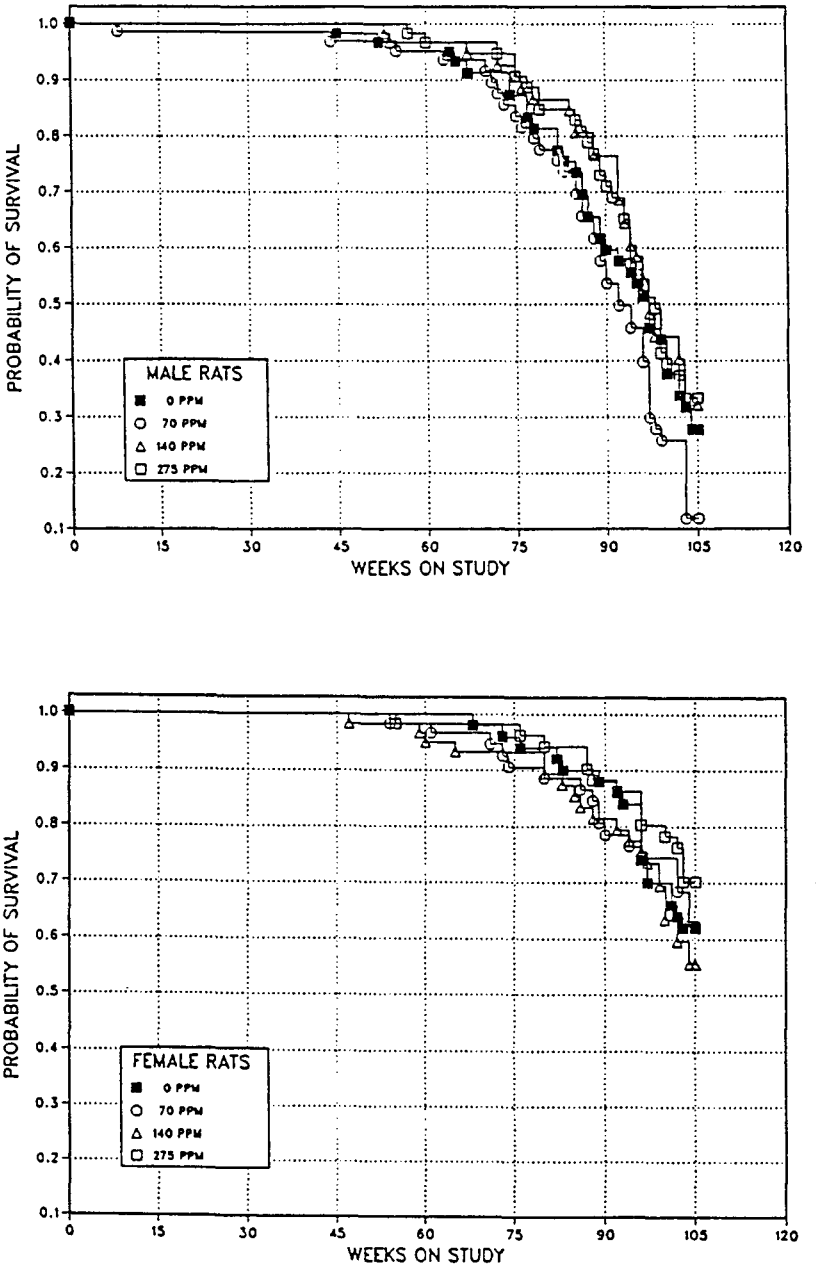

FIGURE 3
Kaplan-Meier Survival Curves for Male and Female Rats Administered Chlorinated Water for 2 Years

TABLE 4
Survival of Rats in the 2-Year Studies of Chlorinated Water

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
Animals initially in study	70	70	70	70
14-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	9	9	10	9
Natural deaths	34	40	30	27
Moribund	3	5	4	7
Animals surviving to end of study	14	6	16	17
Percent survival at end of study[b]	28	12	32	33
Mean survival (days)[c]	637	614	656	656
Survival analysis[d]	P=0.151N	P=0.119	P=0.533N	P=0.543N
Female				
Animals initially in study	70	70	70	70
14-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	10	10	9	10
Natural deaths	16	18	19	14
Moribund	3	1	4	1
Animals surviving to end of study	31	31	28	35
Percent survival at end of study[b]	62	62	55	70
Mean survival (days)[c]	694	683	676	700
Survival analysis[d]	P=0.474N	P=0.920	P=0.570	P=0.495N

[a] Censored from survival analyses
[b] Kaplan-Meier determinations
[c] Mean of all deaths (uncensored, censored, terminal sacrifice)
[d] The entry under the "0 ppm" column is the trend test (Tarone, 1975) result. Subsequent entries are the results of pairwise tests (Cox, 1972). A negative trend or lower mortality is indicated by N.

TABLE 5
Incidence of Mononuclear Cell Leukemia in Female Rats in the 2-Year Study of Chlorinated Water[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Overall rates[b]	8/50 (16%)	7/50 (14%)	19/51 (37%)	16/50 (32%)
Adjusted rates[c]	20.8%	17.5%	48.1%	37.4%
Terminal rates[d]	4/31 (13%)	2/31 (6%)	9/28 (32%)	9/35 (26%)
First incidence (days)	472	514	329	554
Life table tests[e]	P=0.037	P=0.513N	P=0.014	P=0.102

[a] Historical incidence for 2-year studies of all leukemias for untreated control groups in NTP studies is: 124/500 (25% ± 6.1%), range 14%-36% (feed studies); 46/180 (26% ± 8.5%), range 16%-33% (drinking water studies).
[b] Number of tumor-bearing animals/number of animals necropsied
[c] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. A lower incidence in a dose group is indicated by N.

Kidney: Renal tubule cell adenomas occurred in two high-dose male rats and a tubule cell carcinoma occurred in a low-dose male; no tubule cell neoplasms were seen in controls (Table A1). Renal tubule neoplasms are relatively uncommon; the incidence of renal tubule neoplasms in historical controls is only 8/499 (2%) with a range of 0%-6% for feed studies and 0/180 for drinking water studies (Table A4a). Focal tubule cell hyperplasia occurred in 3/51 control, 3/50 low-dose, 1/50 mid-dose, and 1/51 high-dose males (Table A5). Because the number of tubule cell neoplasms in dosed male rats was low, and the incidence of focal hyperplasia was slightly decreased in mid- and high-dose males, these renal neoplasms were not considered related to the consumption of chlorinated water.

Pancreas: Islet cell adenomas of the pancreas occurred in 2/51 mid-dose and 3/50 high-dose female rats, and an islet cell carcinoma occurred in one mid-dose female; no islet cell neoplasms were seen in the controls (Table B1). Although the trend test was marginally significant (P=0.044), the pairwise comparisons were not (Table B3). Moreover, the incidence of pancreatic islet neoplasms in historical controls for drinking water studies is 4/180 (2%) with a range of 0%-4% (Table B4b). Therefore, the islet cell neoplasms of the pancreas were not considered related to the consumption of chlorinated water.

Oral cavity: Squamous cell papilloma or carcinoma arising from the oral mucosa occurred in three high-dose male rats, but did not occur in controls. Papillomas occurred in the palate of one male and the tongue of another; the squamous cell carcinoma occurred in the gingiva (Table A1). The incidence of these neoplasms in historical controls is 0/181 (0%) for drinking water studies and 4/500 (1%), with a range of 0%-4%, for feed studies (Table A4b). Because of the low incidence of these neoplasms and lack of supporting evidence of hyperplasia, they are not considered to be related to the consumption of chlorinated water.

Spleen: Nodular lesions consisting of lymphocytes with scattered focal aggregates of histiocytes occurred in the spleen with a slightly increased incidence in dosed female rats (control, 3/50; low-dose, 6/50; mid-dose, 5/51; high-dose, 8/50). One lesion was seen in the spleen of a low-dose male rat, and similar lesions occurred in the liver of one control female and two low-dose females. These lesions were diagnosed as histiocytic lymphoid hyperplasia, but are similar in cellular composition to a granuloma. Since they are composed of well-differentiated lymphocytes and histiocytes, they may represent a chronic inflammatory or immunological response. In the liver, the incidence of commonly occurring small granulomas composed of histiocytes with only a few lymphocytes was not increased in dosed female rats (Table B5). Because of the marginal increase in incidence, lack of dose response, and small numbers, histiocytic lymphoid hyperplasia of the spleen was not considered related to the consumption of chlorinated water.

CHLORAMINATED WATER IN RATS

Water, Compound, and Feed Consumption

Administration of chloraminated water resulted in a dose-related decrease in water consumption by both sexes that was evident in the first week and continued throughout the studies (Tables L3 and L4). Within dose groups, estimated ingestion of chloramine by males was lower than that by females during the first year, but higher than that by females during the second year except for the high-dose group. Feed consumption by dosed rats was similar to controls, with males consuming more feed than females (Tables N3 and N4).

Body Weights, Organ Weights, Hematology, and Clinical Findings

Mean body weights of rats receiving chloraminated water were within 10% of those of controls until week 97 for high-dose females and week 101 for high-dose males Tables 6 and 7, Figure 4). However, the mean body weights of high-dose rats were consistently 5% to 10% lower than those of the other dosed groups throughout the studies. At the 14-week interim evaluation, the mean body weight at necropsy of high-dose males was 9% lower than that of controls, which was statistically significant ($P \leq 0.01$) (Table I5); mean body weights of low- and mid-dose males and dosed females were similar to those of controls. At the 66-week interim evaluation the mean body weights of high-dose rats were 94% of controls for males and 92% of controls for females, which were statistically significant ($P \leq 0.05$) (Table I7). There were no biologically significant differences in organ weights or organ-weight-to-body-weight ratios between dosed and control groups. Slight decreases in liver and kidney weights in high-dose male rats and increases in brain- and kidney-weight-to-body-weight ratios in high-dose rats were related to the lower body weights in these groups (Table I8). There were no alterations in hematologic parameters attributable to the consumption of chloraminated water for 14 or 66 weeks (Tables J3 and J4). There were no clinical findings attributable to the consumption of chloraminated water.

Survival

Estimates of the probability of survival of male and female rats receiving chloraminated water at the doses used in these studies and for controls are shown in the Kaplan-Meier curves in Figure 5. The numbers of rats dying early, killed in a moribund, or surviving to the end of the studies are given in Table 8. With the exception of the low-dose male group, in which survival was greater than that of controls, the survival of rats receiving chloraminated water was not significantly different from that of controls. Two males died or were killed while moribund before the 66-week interim evaluation (Table 8). The clinical and pathology data from these animals were therefore included with the core group of 2-year animals.

TABLE 6
Mean Body Weights and Survival of Male Rats in the 2-Year Study of Chloraminated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	50 ppm Av. Wt. (g)	50 ppm Wt. (% of controls)	50 ppm No. of Survivors	100 ppm Av. Wt. (g)	100 ppm Wt. (% of controls)	100 ppm No. of Survivors	200 ppm Av. Wt. (g)	200 ppm Wt. (% of controls)	200 ppm No. of Survivors
1	121	70[a]	119	98	70[a]	120	99	70[a]	117	96	70[a]
2	159	70	159	100	70	156	98	70	145	91	70
3	195	70	194	100	70	191	98	70	177	91	70
4	222	70	223	101	70	218	98	70	204	92	70
5	250	70	249	100	70	244	98	70	229	92	70
6	270	70	267	99	70	265	98	70	249	92	70
7	289	70	289	100	70	284	98	70	266	92	70
8	303	70	302	100	70	297	98	70	282	93	70
9	318	70	316	99	70	312	98	70	295	93	70
10	331	70	328	99	70	324	98	70	306	92	70
11	340	70	338	99	70	335	98	70	317	93	70
12	349	70	349	100	70	344	99	70	326	93	70
13	359	70	357	100	70	353	98	70	333	93	70
17[b]	388	60	388	100	60	381	98	60	363	94	60
21	403	60	405	101	60	395	98	60	379	94	60
25	423	60	424	100	60	419	99	60	397	94	60
29	435	60	438	101	60	431	99	60	413	95	60
33	450	60	453	101	60	447	99	60	425	94	60
37	457	60	456	100	60	454	99	60	431	94	60
41	465	60	468	101	60	462	99	60	442	95	60
45	468	60	475	101	60	467	100	60	444	95	60
49	475	59	480	101	60	475	100	60	451	95	60
53	480	58	484	101	60	480	100	60	455	95	60
57	489	58	489	100	60	491	100	60	467	95	60
61	492	58	491	100	60	491	100	60	470	96	60
65	496	57	497	100	60	499	101	58	474	96	60
69[b]	493	46	494	100	49	494	100	49	466	95	50
73	491	46	503	103	49	498	102	49	466	95	49
77	493	44	491	100	49	489	99	46	467	95	47
81	487	41	485	100	49	480	98	44	460	94	46
85	486	38	480	99	47	478	98	41	452	93	44
89	473	33	466	98	43	465	98	34	438	93	41
93	469	29	455	97	39	457	98	30	435	93	35
97	463	26	449	97	31	448	97	26	429	93	26
101	471	19	442	94	24	431	92	18	415	88	21
Terminal sacrifice		14			22			14			16
Mean for weeks											
1-13	270		268	99		265	98		250	93	
17-49	440		443	101		437	99		416	95	
53-101	483		479	99		477	99		453	94	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.

TABLE 7
Mean Body Weights and Survival of Female Rats in the 2-Year Study of Chloraminated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	50 ppm Av. Wt. (g)	50 ppm Wt. (% of controls)	50 ppm No. of Survivors	100 ppm Av. Wt. (g)	100 ppm Wt. (% of controls)	100 ppm No. of Survivors	200 ppm Av. Wt. (g)	200 ppm Wt. (% of controls)	200 ppm No. of Survivors
1	105	70[a]	103	98	70[a]	102	98	70[a]	99	95	70[a]
2	128	70	128	100	70	126	98	70	121	95	70
3	145	70	144	99	70	141	97	70	136	94	70
4	156	70	153	98	70	153	98	70	148	95	70
5	165	70	163	98	70	162	98	70	157	95	70
6	173	70	170	98	70	170	98	70	164	95	70
7	181	70	179	99	70	179	99	70	172	95	70
8	186	70	184	99	70	185	99	70	176	95	70
9	192	70	189	99	70	189	99	70	181	95	70
10	195	70	195	100	70	194	99	70	186	95	70
11	198	70	198	100	70	197	99	70	191	96	70
12	202	70	202	100	70	199	99	70	193	96	70
13	204	70	204	100	70	202	99	70	196	96	70
17[b]	218	60	219	100	60	216	99	60	206	95	60
21	226	60	227	100	60	223	99	60	214	95	60
25	234	60	235	101	60	232	99	60	222	95	60
29	246	60	245	100	60	243	99	60	228	93	60
33	250	60	250	100	60	246	98	59	234	94	60
37	257	60	256	100	60	252	98	59	236	92	60
41	260	60	263	101	60	257	99	59	244	94	60
45	271	60	270	100	59	266	98	59	250	92	60
49	281	60	279	99	59	274	97	59	256	91	60
53	283	60	288	102	58	281	99	59	267	94	60
57	299	60	298	100	58	294	98	59	275	92	60
61	306	60	308	101	58	301	98	59	283	92	60
65	318	60	318	100	58	309	97	59	293	92	60
69[b]	327	49	331	101	47	320	98	47	295	90	49
73	327	49	339	104	47	327	100	47	303	93	49
77	339	47	342	101	47	336	99	46	309	91	46
81	344	47	349	102	46	340	99	45	313	91	46
85	347	45	349	101	44	339	98	43	316	91	42
89	346	45	347	100	44	344	99	41	311	90	41
93	339	43	348	103	40	340	100	39	311	92	39
97	352	35	359	102	37	340	97	37	307	87	37
101	348	34	363	105	34	346	100	32	307	88	29
Terminal sacrifice		31			28			29			24
Mean for weeks											
1-13	172		170	99		169	98		163	95	
17-49	249		249	100		245	98		232	93	
53-101	329		334	102		324	98		299	91	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.

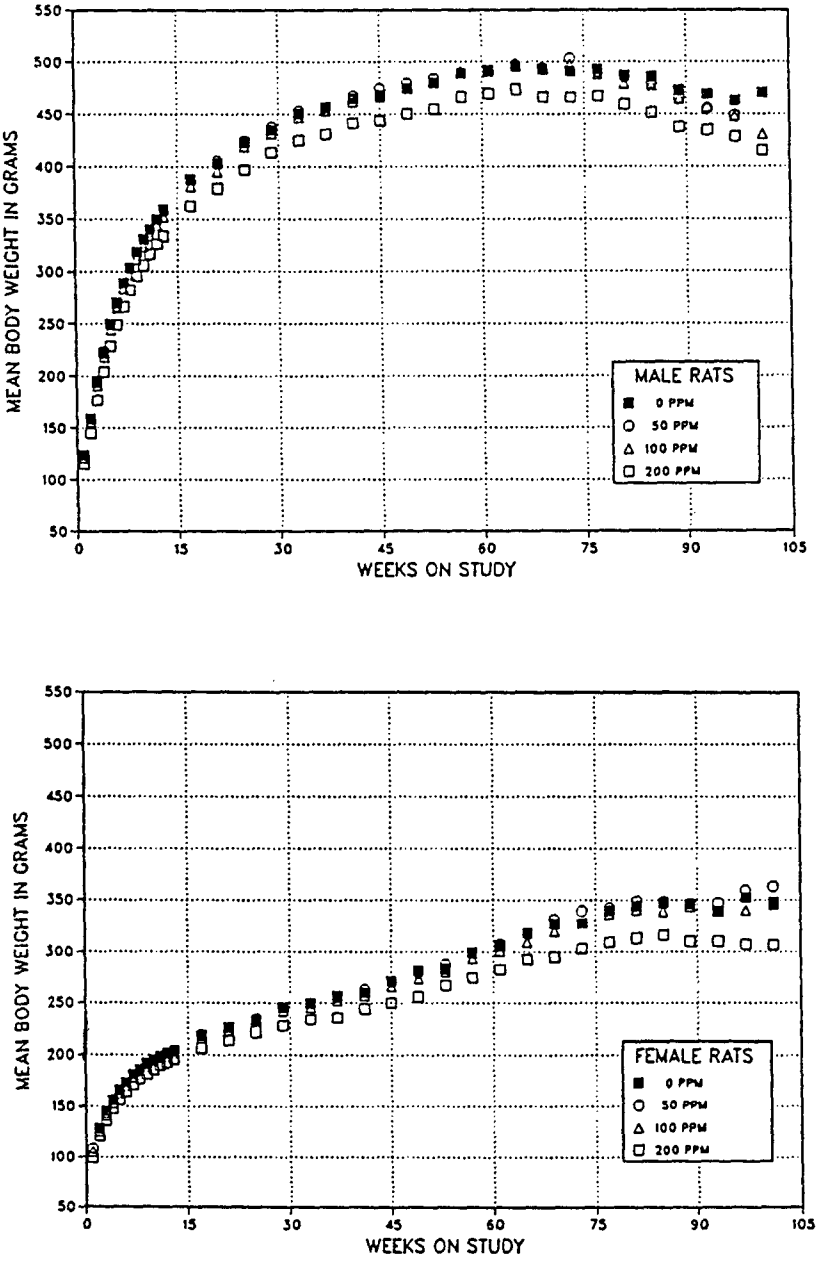

FIGURE 4
Growth Curves for Male and Female Rats Administered Chloraminated Water for 2 Years

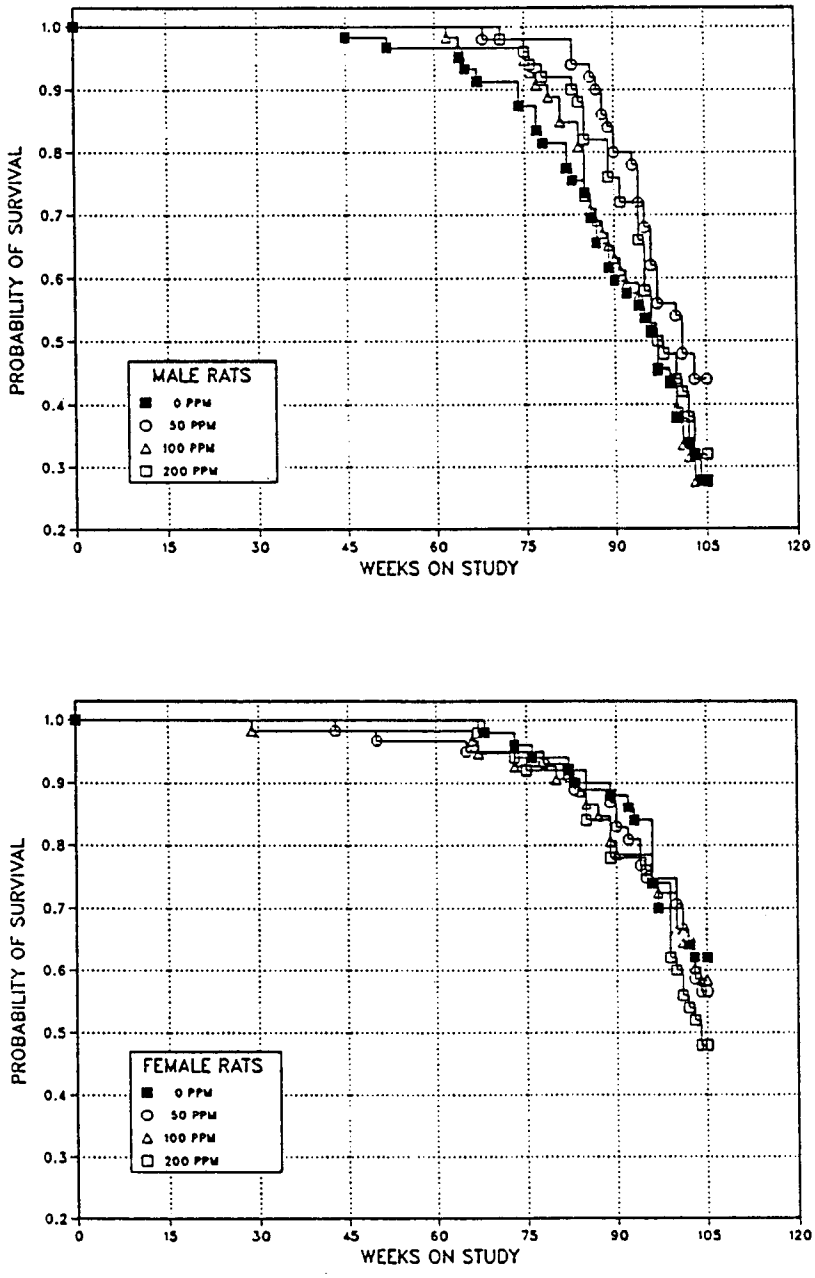

FIGURE 5
Kaplan-Meier Survival Curves for Male and Female Rats Administered Chloraminated Water for 2 Years

TABLE 8
Survival of Rats in the 2-Year Studies of Chloraminated Water

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
Animals initially in study	70	70	70	70
14-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	9	10	9	10
Natural deaths	3	1	3	1
Moribund	34	27	34	33
Animals surviving to end of study	14	22	14	16
Percent survival at end of study[b]	28	44	28	32
Mean survival (days)[c]	637	683	651	669
Survival analysis[d]	P=0.870N	P=0.049N	P=0.984N	P=0.433N
Female				
Animals initially in study	70	70	70	70
14-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	10	10	10	10
Natural deaths	3	5	1	3
Moribund	16	17	20	23
Animals surviving to end of study	31	28	29	24
Percent survival at end of study[b]	62	56	58	48
Mean survival (days)[c]	694	682	679	683
Survival analysis[d]	P=0.232	P=0.683	P=0.792	P=0.272

[a] Censored from survival analyses
[b] Kaplan-Meier determinations
[b] Mean of all deaths (uncensored, censored, terminal sacrifice)
[c] The entry under the "0 ppm" column is the trend test (Tarone, 1975) result. Subsequent entries are the results of pairwise tests (Cox, 1972). A negative trend or lower mortality is indicated by N.

Pathology and Statistical Analysis of Results

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one dose group, and historical control incidences for the neoplasms mentioned in this section are presented in Appendixes C and D for male and female rats given chloraminated water. No gross or microscopic lesions attributable to chloraminated water consumption were seen in the 14- or 66-week interim evaluations.

Mononuclear cell leukemia: The incidence of mononuclear cell leukemia in dosed female rats was marginally greater than that in controls, and the incidence in the mid-dose and high-dose groups was in the upper range of that for historical controls (Table 9). The incidence of all leukemias in

untreated historical controls is 170/680 (25%) with a range of 14%-36% (Table D4a). The proportion of animals with leukemia that died before the end of the studies and the mean time to leukemia observation for animals dying with leukemia were generally similar among all dosed and control groups (for control: proportion, 50%, and time to observation, 601 days; low-dose: 64% and 663 days; mid-dose: 47% and 621 days; high-dose: 75% and 666 days).

Spleen: The incidence of splenic histiocytic lymphoid hyperplasia was also marginally increased in high-dose females (control, 3/50; low-dose, 4/50; mid-dose, 2/50; high-dose, 6/50) (Table D5). This lesion was similar in structure to the splenic histiocytic lymphoid hyperplasia seen in the chlorinated water studies. Because of the marginal increase in incidence and lack of dose response, this lesion was not considered related to the consumption of chloraminated water.

TABLE 9
Incidence of Mononuclear Cell Leukemia in Female Rats in the 2-Year Study of Chloraminated Water

	0 ppm	50 ppm	100 ppm	200 ppm
All Organs: Mononuclear Cell Leukemia[a]				
Overall rates[b]	8/50 (16%)	11/50 (22%)	15/50 (30%)	16/50 (32%)
Adjusted rates[c]	20.8%	29.0%	39.3%	41.4%
Terminal rates[d]	4/31 (13%)	4/28 (14%)	8/29 (28%)	4/24 (17%)
First incidence (days)	472	540	465	592
Life table tests[e]	P=0.021	P=0.280	P=0.077	P=0.036

[a] Historical incidence for 2-year studies of all leukemias for untreated control groups in NTP studies is: 124/500 (25% ± 6.1%), range 14%-36% (feed studies); 46/180 (26% ± 8.5%), range 16%-33% (drinking water studies).
[b] Number of tumor-bearing animals/number of animals necropsied
[c] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death.

CHLORINATED WATER IN MICE

Water, Compound, and Feed Consumption

Administration of chlorinated water resulted in a dose-related decrease in water consumption by both sexes that was evident in the first week and continued throughout the studies (Tables L5 and L6). Within dose groups, estimated ingestion of chlorine by males was lower than that by females the first year, but higher than that by females the second year. Mean feed consumption by dosed male mice was slightly higher than the controls for weeks 1-52 (Tables N5 and N6). During the same period, mean feed consumption for female mice was slightly lower than the controls. The mean feed consumption for weeks 53 to 101 was similar for both sexes and all treatment groups.

Body Weights, Organ Weights, Hematology, and Clinical Findings

Mean body weights of mice receiving chlorinated water were within 10% of those of controls throughout the studies. Body weights of high-dose mice were 5% to 8% lower after week 49 in males and 5% to 7% lower after week 45 in females. Mean body weights, organ weights, and organ-weight-to-body-weight ratios for male and female mice evaluated at 15 or 66 weeks are shown in Tables I9-I12. Mean body weights at necropsy were similar among dosed and control groups at the 15-week evaluation. At 66 weeks, however, the body weight of the high-dose males was significantly lower than that of controls (Table I11). There were no biologically significant differences in organ weights or organ-weight-to-body-weight ratios between dosed and control groups. Decreases in brain weights at 15 weeks (Table I9) and liver weights at 66 weeks (Table I11) in high-dose males were related to the lower body weights in these groups. The results of analyses performed on blood samples collected at the interim evaluations are presented in Tables J5 and J6. There were no alterations in hematologic parameters attributable to the consumption of chlorinated water for 15 or 66 weeks (Tables 10 and 11, Figure 6). There were no clinical findings attributable to the consumption of chlorinated water.

Survival

Estimates of the probability of survival of male and female mice receiving chlorinated water at the doses used in these studies and for controls are shown in the Kaplan-Meier curves in Figure 7. The numbers of mice dying early, killed while moribund, or surviving to the end of the studies are given in Table 12. One male and one female predesignated for the 66-week interim evaluations died or were killed while moribund before the 66-week interim evaluations. The clinical and pathology data from these animals were therefore included with the core group of 2-year study animals for evaluation. The survival rates of mice receiving chlorinated water were not significantly different from those of controls.

Pathology and Statistical Analysis of Results

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one dose group, and historical control incidences for the neoplasms mentioned in this section are presented in Appendixes E and F for male and female mice given chlorinated water. No gross or microscopic lesions attributable to chlorinated water consumption were seen in the 15- or 66-week interim evaluations.

TABLE 10
Mean Body Weights and Survival of Male Mice in the 2-Year Study of Chlorinated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	70 ppm Av. Wt. (g)	70 ppm Wt. (% of controls)	70 ppm No. of Survivors	140 ppm Av. Wt. (g)	140 ppm Wt. (% of controls)	140 ppm No. of Survivors	275 ppm Av. Wt. (g)	275 ppm Wt. (% of controls)	275 ppm No. of Survivors
1	22.4	70[a]	22.2	99	70[a]	22.3	100	70[a]	21.7	97	70[a]
2	24.4	70	24.3	100	70	24.5	100	70	23.8	98	70
3	25.5	70	25.5	100	70	25.8	101	70	25.1	98	70
4	26.6	70	26.9	101	70	26.8	101	70	25.9	97	69
5	27.8	70	27.7	100	70	28.1	101	70	27.0	97	69
6	29.3	70	29.2	100	70	29.4	100	70	28.3	97	69
7	30.5	70	30.3	99	70	30.3	99	70	29.4	96	69
8	31.5	70	31.2	99	70	31.3	99	70	30.0	95	69
9	31.9	70	32.2	101	70	32.0	100	70	31.0	97	69
10	33.0	70	33.6	102	70	33.3	101	70	32.0	97	69
11	34.2	70	34.6	101	70	34.4	101	70	33.0	97	69
12	35.1	70	35.3	101	70	35.1	100	70	33.6	96	69
13	36.4	70	36.5	100	70	36.4	100	70	34.8	96	69
17[b]	39.4	60	39.9	101	60	39.5	100	60	38.0	96	59
21	42.4	60	42.4	100	60	42.4	100	60	40.9	97	59
25	45.0	60	44.8	100	60	44.8	100	60	43.6	97	59
29	46.1	60	45.8	99	60	45.9	100	60	44.5	97	59
33	46.2	60	45.8	99	60	45.8	99	60	44.5	96	59
37	46.7	60	45.9	98	60	45.8	98	60	45.0	96	59
41	46.9	60	46.5	99	60	46.2	99	60	45.3	97	59
45	48.1	60	47.6	99	60	47.2	98	60	46.0	96	59
49	48.4	60	47.6	98	60	47.5	98	60	46.1	95	59
53	49.0	60	48.0	98	60	47.8	98	60	46.4	95	58
57	49.9	60	48.6	97	60	48.2	97	60	47.6	95	57
61	49.8	60	48.2	97	60	48.0	96	60	46.7	94	57
65	50.2	60	48.4	96	60	48.3	96	60	47.3	94	57
69[b]	50.9	50	48.7	96	50	48.2	95	50	47.4	93	47
73	50.4	50	48.1	95	49	47.3	94	50	47.4	94	46
77	50.3	50	49.0	97	48	47.5	94	50	47.4	94	46
81	50.9	46	49.4	97	46	48.2	95	45	47.5	93	45
85	50.6	45	48.6	96	45	48.4	96	44	47.4	94	43
89	50.2	45	48.0	96	44	48.3	96	44	46.8	93	43
93	49.6	44	48.7	98	41	47.8	96	43	46.5	94	43
97	48.8	41	47.4	97	38	47.5	97	42	45.2	93	43
101	48.8	38	47.0	96	34	47.0	96	38	44.9	92	35
Terminal sacrifice		34			28			35			32
Mean for weeks											
1-13	29.9		30.0	100		30.0	100		28.9	97	
17-49	45.5		45.1	99		45.0	99		43.8	96	
53-101	50.0		48.3	97		47.9	96		46.8	94	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.

TABLE 11
Mean Body Weights and Survival of Female Mice in the 2-Year Study of Chlorinated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	70 ppm Av. Wt. (g)	70 ppm Wt. (% of controls)	70 ppm No. of Survivors	140 ppm Av. Wt. (g)	140 ppm Wt. (% of controls)	140 ppm No. of Survivors	275 ppm Av. Wt. (g)	275 ppm Wt. (% of controls)	275 ppm No. of Survivors
1	18.1	70[a]	18.1	100	70[a]	17.9	99	70[a]	18.0	99	70[a]
2	19.9	70	19.7	99	70	19.5	98	70	19.5	98	70
3	20.6	69	20.8	101	70	20.5	100	70	20.5	100	70
4	22.0	69	22.0	100	70	21.6	98	70	21.7	99	70
5	23.1	69	22.9	99	70	22.8	99	70	22.6	98	70
6	23.7	69	24.0	101	70	23.4	99	70	23.1	98	70
7	24.4	69	24.7	101	70	24.1	99	70	23.9	98	70
8	25.5	69	25.5	100	70	25.0	98	70	24.7	97	70
9	26.3	69	26.3	100	70	25.6	97	70	25.1	95	70
10	27.4	69	27.6	101	70	26.5	97	70	26.2	96	70
11	28.2	69	28.6	101	70	27.7	98	70	27.1	96	70
12	28.9	69	29.2	101	70	28.3	98	70	27.8	96	70
13	30.0	69	30.2	101	70	29.2	97	70	28.7	96	70
17[b]	33.3	59	33.4	100	60	33.2	100	60	32.4	97	60
21	36.7	59	37.1	101	60	36.6	100	60	35.5	97	60
25	39.5	59	39.5	100	60	39.2	99	60	38.2	97	60
29	41.6	59	41.1	99	60	41.1	99	60	39.7	95	60
33	41.5	59	42.0	101	59	41.5	100	60	40.5	98	60
37	43.0	59	42.8	100	59	42.5	99	60	41.5	97	60
41	44.2	59	44.3	100	59	43.5	98	59	42.4	96	60
45	46.4	59	46.0	99	59	45.2	97	58	43.9	95	60
49	47.2	59	47.1	100	59	46.2	98	58	44.9	95	60
52	47.0	59[c]	48.0	102	58[c]	47.7	102	57[c]	45.0	96	60[c]
53	51.0	59[c]	50.0	98	58[c]	48.4	95	57[c]	48.2	95	60[c]
57	50.6	59	50.7	100	58	49.8	98	57	48.1	95	60
61	50.7	59	51.0	101	58	50.1	99	57	48.3	95	60
65	51.8	59	52.3	101	58	50.3	97	57	49.4	95	60
69[b]	53.9	48	52.6	98	49	51.6	96	46	51.2	95	49
73	53.7	48	52.1	97	48	51.3	96	46	50.8	95	47
77	55.5	46	53.2	96	47	52.6	95	45	52.3	94	46
81	55.2	45	53.3	97	46	52.4	95	42	52.2	95	45
85	56.9	42	53.3	94	45	52.9	93	40	53.0	93	45
89	56.3	42	53.7	95	43	53.3	95	40	53.2	95	44
93	55.7	42	53.4	96	40	52.6	94	40	52.5	94	43
97	55.8	40	51.8	93	39	52.6	94	38	51.7	93	41
101	54.7	34	49.6	91	37	50.5	92	37	50.8	93	37
Terminal sacrifice		33			31			28			35
Mean for weeks											
1-13	24.5		24.6	100		24.0	98		23.8	97	
17-49	41.5		41.5	100		41.0	99		39.9	96	
57-101	54.2		52.3	96		51.7	95		51.1	94	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.
[c] The number of animals weighed for this week is fewer than the number of animals surviving.

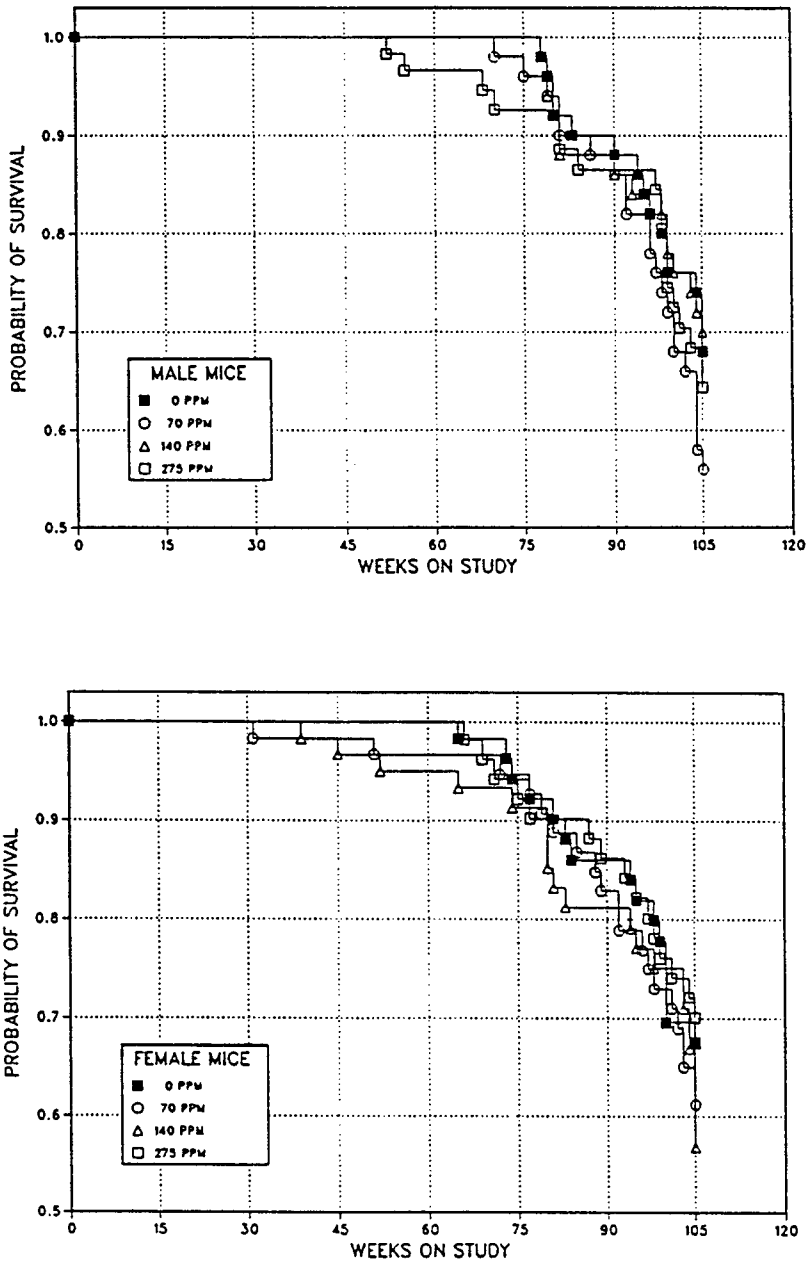

FIGURE 7
Kaplan-Meier Survival Curves for Male and Female Mice Administered Chlorinated Water for 2 Years

TABLE 12
Survival of Mice in the 2-Year Studies of Chlorinated Water

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
Animals initially in study	70	70	70	70
15-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	10	10	10	9
Natural deaths	4	6	2	8
Moribund	12	16	13	10
Accidental deaths[a]	0	0	0	1
Animals surviving to end of study	34	28[b]	35	32
Percent survival at end of study[c]	68	56	70	64
Mean survival (days)[d]	706	697	704	678
Survival analysis[e]	P=0.952	P=0.290	P=1.000N	P=0.799
Female				
Animals initially in study	70	70	70	70
15-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	10	9	10	10
Natural deaths	3	6	3	3
Moribund	13	14	19	12
Accidental deaths[a]	1	0	0	0
Animals surviving to end of study	33	31	28[b]	35
Percent survival at end of study[c]	67	61	56	70
Mean survival (days)[d]	683	684	676	698
Survival analysis[e]	P=0.767N	P=0.635	P=0.364	P=0.938N

[a] Censored from survival analyses
[b] One of these animals was found dead on the last day of the study.
[c] Kaplan-Meier determinations
[d] Mean of all deaths (uncensored, censored, terminal sacrifice)
[e] The entry under the "0 ppm" column is the trend test (Tarone, 1975) result. Subsequent entries are the results of pairwise tests (Cox, 1972). A negative trend or lower mortality is indicated by N.

Kidney: A renal tubule cell adenoma occurred in one high-dose male mouse and a tubule cell carcinoma occurred in a second high-dose male (Table 13). The carcinoma was observed grossly at necropsy, but the adenoma was not. Focal tubule hyperplasia was seen in one low-dose and two high-dose male mice. Renal tubule neoplasms are uncommon in male mice: none have occurred in 129 historical controls in drinking water studies, and in feed studies, the incidence in historical controls is 1/563 (0.2%) (Table E4). Because renal tubule neoplasms are rare in untreated controls, additional step sections (4 to 6 sections/mouse) were prepared of residual formalin-fixed kidney from all male mice and were examined microscopically. Hyperplasia was observed in additional animals from each group, including controls, and a carcinoma was found in one low-dose male (Table 13).

Renal tubule cell proliferative lesions exhibit a morphological continuum from focal hyperplasia to carcinoma. Focal hyperplasia was characterized as slightly enlarged tubules filled by two or more layers of well-differentiated epithelial cells. These lesions were distinct from the regenerative tubules and are lined by a single layer of small, basophilic cells that are associated with chronic nephropathy, which is commonly observed in aged mice. The adenoma was a discrete, expansile mass of epithelial cells arranged in solid nests and tubule-like structures. The carcinomas exhibited greater heterogeneity of growth pattern, cellular pleomorphism, and necrosis.

There were no other kidney lesions that occurred with a greater incidence in exposed male or female mice than in the controls. The histopathology quality assessment review and a second blind

TABLE 13
Incidence of Lesions of the Kidney in Male Mice in the 2-Year Study of Chlorinated Water

	0 ppm	70 ppm	140 ppm	275 ppm
Original Sections[a]				
Renal tubule, hyperplasia, focal	0/50 (0%)	1/50 (2%)	0/50 (0%)	2/51 (4%)
Renal tubule, adenoma[b]	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/51 (2%)
Renal tubule, carcinoma	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/51 (2%)
Renal tubule, adenoma or carcinoma	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/51 (4%)
Adjusted rates[c]	0.0%	0.0%	0.0%	6.3%
Terminal rates[d]	0/34 (0%)	0/28 (0%)	0/35 (0%)	2/32 (6%)
First incidence (days)	-[e]	-	-	733 (T)
Logistic regression tests[f]	P=0.060	-	-	P=0.225
Step Sections				
Renal tubule, hyperplasia, focal	2/50 (4%)	1/50 (2%)	2/50 (4%)	1/51 (2%)
Renal tubule, adenoma	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/51 (0%)
Renal tubule, carcinoma	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/51 (0%)
Original and Step Sections Combined				
Renal tubule, hyperplasia, focal	2/50 (4%)	2/50 (4%)	2/50 (4%)	3/51 (6%)
Renal tubule, adenoma	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/51 (2%)
Renal tubule, carcinoma	0/50 (0%)	1/50 (2%)	0/50 (0%)	1/51 (2%)
Renal tubule, adenoma or carcinoma	0/50 (0%)	1/50 (2%)	0/50 (0%)	2/51 (4%)
Adjusted rates	0.0%	3.6%	0.0%	6.3%
Terminal rates	0/34 (0%)	1/28 (4%)	0/35 (0%)	2/32 (6%)
First incidence (days)	-	733 (T)	-	733 (T)
Logistic regression tests	P=0.158	P=0.461	-	P=0.225

(T) Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined microscopically for this tumor type
[b] Historical incidence for 2-year NTP studies with untreated control groups is: 1/563 (0.2% ± 0.6%), range 0%-2% (feed studies); 0/129 (drinking water studies).
[c] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Not applicable; no tumors in animal group
[f] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The logistic regression tests regard these lesions as nonfatal.

evaluation of the kidney sections did not identify any difference in the incidence or severity of renal tubule atrophy, dilatation, regeneration, focal mineralization, or protein casts. These changes were considered characteristic of the spontaneous nephropathy commonly seen in aging mice.

Uterus: Endometrial stromal polyps of the uterus were seen in 1/50 mid-dose and 3/50 high-dose female mice in the 2-year study and in 1/10 high-dose females at the 66-week interim evaluation (Table 14). Although polyps occurred with a significant (P=0.008) positive trend, the incidence in the high-dose groups was not significantly greater by the pairwise comparison test. Moreover, the incidence in the high-dose group, 4/70 (6%), is within the range of untreated historical controls for feed and drinking water studies (0%-6%), and the only malignant neoplasm (sarcoma) occurred in a control female.

TABLE 14
Incidence of Lesions of the Uterus in Female Mice at the 66-Week Interim Evaluation and in the 2-Year Study of Chlorinated Water

	0 ppm	70 ppm	140 ppm	275 ppm
Stromal Polyp[a]				
66-Week Interim Evaluation[b]				
Overall rates[c]	0/10 (0%)	0/9 (0%)	0/10 (0%)	1/10 (10%)
2-Year Study				
Overall rates	0/50 (0%)	0/51 (0%)	1/50 (2%)	3/50 (6%)
Adjusted rates[d]	0.0%	0.0%	2.4%	7.3%
Terminal rates[e]	0/33 (0%)	0/31 (0%)	0/28 (0%)	1/35 (3%)
First incidence (days)	–[f]	–	561	606
Logistic regression tests[g]	P=0.016	–	P=0.491	P=0.112
Combined				
Overall rates	0/70 (0%)	0/60 (0%)	1/61 (2%)	4/70 (6%)
First incidence (days)	–	–	561	457 (I)
Logistic regression tests	P=0.008	–	P=0.459	P=0.065
Sarcoma				
2-Year Study				
Overall rates	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)

(I) Interim evaluation
[a] Historical incidence for 2-year NTP studies with untreated control groups is: 14/570 (2% ± 1.9%), range 0%-6% (feed studies); 2/130 (2% ± 2.1%), range 0%-3% (drinking water studies).
[b] Number of animals examined at site
[c] Number of tumor-bearing animals/number of animals necropsied
[d] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[e] Observed incidence at terminal kill
[f] No tumors in dosed group or control group; statistical test not performed.
[g] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The logistic regression tests regard these lesions as nonfatal.

CHLORAMINATED WATER IN MICE

Water, Compound, and Feed Consumption

Administration of chloraminated water resulted in a dose-related decrease in water consumption by both sexes that was evident in the first week and continued throughout the studies (Tables L7 and L8). Within dose groups, estimated ingestion of chloramine by males was lower than that by females the first year, but higher than that by females the second year, except for the high-dose group. Feed consumption by dosed male mice was similar to controls throughout the studies. In females, mean feed consumption was similar in all treatment groups except the high-dose group, in which feed consumption was slightly lower than in the other groups (Tables N7 and N8).

Body Weights, Organ Weights, Hematology, and Clinical Findings

There was a dose-related decrease in mean body weights of dosed male and female mice throughout most of the studies (Tables 15 and 16, Figure 8). Mean body weights of high-dose males were 10% to 22% lower than those of controls after week 37, and body weights of high-dose female mice were 10% to 35% lower than controls after week 8. Mean body weights of high-dose male and female mice were 91% and 84% of the control values at 15 weeks (Table I13). At the 66-week evaluation, the body weights of high-dose female mice were similar to controls, but the body weights of mid- and high-dose male mice were lower than controls (Table I15). Although there were some statistically significant differences in organ weights and organ-weight-to-body-weight ratios between dosed and control groups, the differences were not biologically significant. Decreases in liver weights and increases in brain- or kidney-weight-to-body-weight ratios observed in high-dose mice at 15 or 66 weeks were related to the lower body weights in these groups. There were no alterations in hematologic parameters attributable to the consumption of chloraminated water at either the 15-week or 66-week interim evaluation. There were no clinical findings attributable to the consumption of chloraminated water (Tables J7 and J8).

Survival

Estimates of the probability of survival of male and female mice receiving chloraminated water at the doses used in these studies and for controls are shown in the Kaplan-Meier curves in Figure 9. The numbers of mice dying early, killed moribund, or surviving to the end of the studies are given in Table 17. The survival rates of mice receiving chloraminated water were not significantly different from those of controls. One male in the high-dose group died before the 66-week interim evaluation. The clinical and pathology data from this animal was therefore included with the core group of 2-year study animals for evaluation.

Pathology and Statistical Analysis of Results

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one dose group, and historical control incidences for the neoplasms mentioned in this section are presented in Appendixes G and H for male and female mice given chloraminated water. A harderian gland adenoma was observed in one high-dose female mouse at the 66-week interim evaluation.

TABLE 15
Mean Body Weights and Survival of Male Mice in the 2-Year Study of Chloraminated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	50 ppm Av. Wt. (g)	50 ppm Wt. (% of controls)	50 ppm No. of Survivors	100 ppm Av. Wt. (g)	100 ppm Wt. (% of controls)	100 ppm No. of Survivors	200 ppm Av. Wt. (g)	200 ppm Wt. (% of controls)	200 ppm No. of Survivors
1	22.4	70[a]	22.0	98	70[a]	21.6	96	70[a]	21.6	96	70[a]
2	24.4	70	24.3	100	70	23.9	98	70	23.3	96	70
3	25.5	70	25.7	101	70	25.1	98	70	24.6	97	70
4	26.6	70	27.0	102	70	26.1	98	70	25.5	96	70
5	27.8	70	27.9	100	70	27.5	99	70	26.6	96	70
6	29.3	70	29.4	100	70	28.8	98	70	27.9	95	70
7	30.5	70	29.9	98	70	29.8	98	70	28.4	93	70
8	31.5	70	31.5	100	70	30.7	98	70	28.9	92	70
9	31.9	70	32.2	101	70	31.5	99	70	29.9	94	70
10	33.0	70	33.5	102	70	32.5	99	70	30.8	93	70
11	34.2	70	34.2	100	70	33.3	97	70	31.6	92	70
12	35.1	70	35.1	100	70	34.0	97	70	32.2	92	70
13	36.4	70	36.0	99	70	35.2	97	70	33.2	91	70
17[b]	39.4	60	39.4	100	60	38.3	97	60	35.5	90	60
21	42.4	60	41.9	99	60	40.9	97	60	39.1	92	60
25	45.0	60	44.6	99	60	43.4	96	60	41.3	92	60
29	46.1	60	45.8	99	60	44.2	96	60	42.5	92	60
33	46.2	60	45.7	99	60	43.9	95	60	42.1	91	60
37	46.7	60	45.8	98	60	44.3	95	60	42.0	90	60
41	46.9	60	46.1	98	60	44.8	96	60	42.3	90	60
45	48.1	60	47.3	98	60	45.6	95	60	42.7	89	60
49	48.4	60	47.5	98	60	45.9	95	60	42.9	89	60
53	49.0	60	48.0	98	60	46.5	95	60	43.5	89	59
57	49.9	60	48.5	97	60	47.0	94	60	44.1	88	59
61	49.8	60	48.2	97	60	47.0	94	60	43.7	88	59
65	50.2	60	48.5	97	60	47.4	94	60	44.5	89	57
69[b]	50.9	50	48.8	96	50	48.0	94	50	44.8	88	48
73	50.4	50	48.2	96	49	47.2	94	50	44.1	88	48
77	50.3	50	48.3	96	49	47.9	95	50	44.3	88	48
81	50.9	46	48.6	96	46	47.6	94	50	44.1	87	48
85	50.6	45	48.3	96	45	48.2	95	47	43.8	87	46
89	50.2	45	48.0	96	45	47.4	94	46	42.7	85	46
93	49.6	44	46.6	94	43	46.3	93	45	42.4	86	44
97	48.8	41	45.2	93	42	46.0	94	43	39.4	81	43
101	48.8	38	45.3	93	32	45.6	93	38	38.1	78	42
Terminal sacrifice		34			23			34			37
Mean for weeks											
1-13	29.9		29.9	100		29.2	98		28.0	94	
17-49	45.5		44.9	99		43.5	96		41.2	91	
53-101	50.0		47.7	95		47.1	94		43.0	86	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.

TABLE 16
Mean Body Weights and Survival of Female Mice in the 2-Year Study of Chloraminated Water

Study Week	0 ppm Av. Wt. (g)	0 ppm No. of Survivors	50 ppm Av. Wt. (g)	50 ppm Wt. (% of controls)	50 ppm No. of Survivors	100 ppm Av. Wt. (g)	100 ppm Wt. (% of controls)	100 ppm No. of Survivors	200 ppm Av. Wt. (g)	200 ppm Wt. (% of controls)	200 ppm No. of Survivors
1	18.1	70[a]	17.9	99	70[a]	17.8	98	70[a]	17.7	98	70[a]
2	19.9	70	19.7	99	70	19.6	99	70	18.8	95	70
3	20.6	69	20.6	100	70	20.4	99	70	19.5	95	70
4	22.0	69	21.8	99	70	21.6	98	70	20.6	94	70
5	23.1	69	22.9	99	70	22.7	98	70	21.5	93	70
6	23.7	69	23.4	99	70	22.9	97	70	22.0	93	70
7	24.4	69	23.9	98	70	23.8	98	70	22.5	92	70
8	25.5	69	24.7	97	70	24.6	97	70	22.9	90	70
9	26.3	69	25.5	97	70	25.3	96	70	23.4	89	70
10	27.4	69	26.5	97	70	26.2	96	70	24.1	88	69
11	28.2	69	27.3	97	70	27.2	97	70	24.5	87	69
12	28.9	69	27.9	97	70	27.7	96	70	24.7	86	69
13	30.0	69	28.9	96	70	28.7	96	70	25.6	85	69
17[b]	33.3	59	32.3	97	60	31.9	96	60	27.8	84	59
21	36.7	59	35.1	96	60	35.4	97	60[c]	31.0	85	59
25	39.5	59	37.6	95	60	38.2	97	60	33.4	85	59
29	41.6	59	39.4	95	60	39.7	95	60	35.0	84	59
33	41.5	59	40.1	97	60	40.0	96	60	35.1	85	59
37	43.0	59	40.6	94	60	40.3	94	60	35.3	82	59
41	44.2	59	42.0	95	60	41.2	93	60	35.3	80	59
45	46.4	59	43.8	94	60	42.4	91	60	36.3	78	59
49	47.2	59	44.4	94	60	43.4	92	60	37.0	78	59
52	47.0	30[c]	45.5	97	30[c]	41.7	89	30[c]	36.0	77	29[c]
53	51.0	29[c]	46.6	91	30[c]	47.4	93	30[c]	40.3	79	30[c]
57	50.6	59	47.2	93	60	46.0	91	59	38.9	77	59
61	50.7	59	47.8	94	59	46.2	91	59	38.7	76	59
65	51.8	59	48.7	94	59	46.6	90	59	39.3	76	59
69[b]	53.9	48	49.7	92	49	47.1	87	49	39.3	73	49
73	53.7	48	49.5	92	49	46.6	87	49	38.6	72	49
77	55.5	46	50.3	91	49	47.6	86	47	39.5	71	49
81	55.2	45	50.5	92	48	48.5	88	47	39.5	72	49
85	56.9	42	51.4	90	45	48.9	86	47	39.9	70	48
89	56.3	42	51.4	91	44	49.0	87	47	39.2	70	48
93	55.7	42	51.5	93	41	48.5	87	46	38.1	68	47
97	55.8	40	50.9	91	39	47.2	85	44	36.7	66	45
101	54.7	34	48.2	88	37	44.5	81	41	35.3	65	43
Terminal sacrifice		33			32			35			42
Mean for weeks											
1-13	24.5		23.9	98		23.7	97		22.1	90	
17-49	41.5		39.5	95		39.2	94		34.0	82	
57-101	54.2		49.8	92		47.2	87		38.6	71	

[a] Includes interim evaluation animals.
[b] Interim evaluation occurred.
[c] The number of animals weighed for this week is fewer than the number of animals surviving.

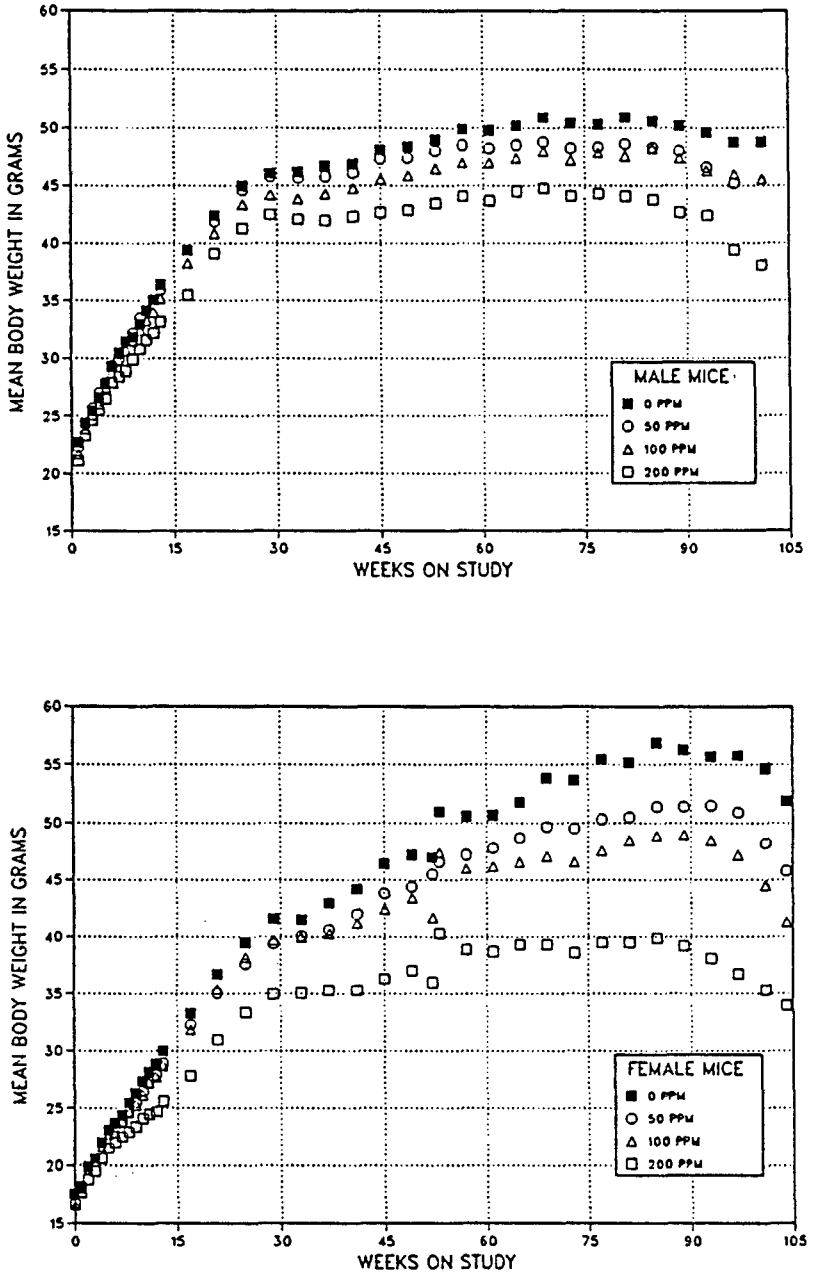

FIGURE 8
Growth Curves for Male and Female Mice Administered Chloraminated Water for 2 Years

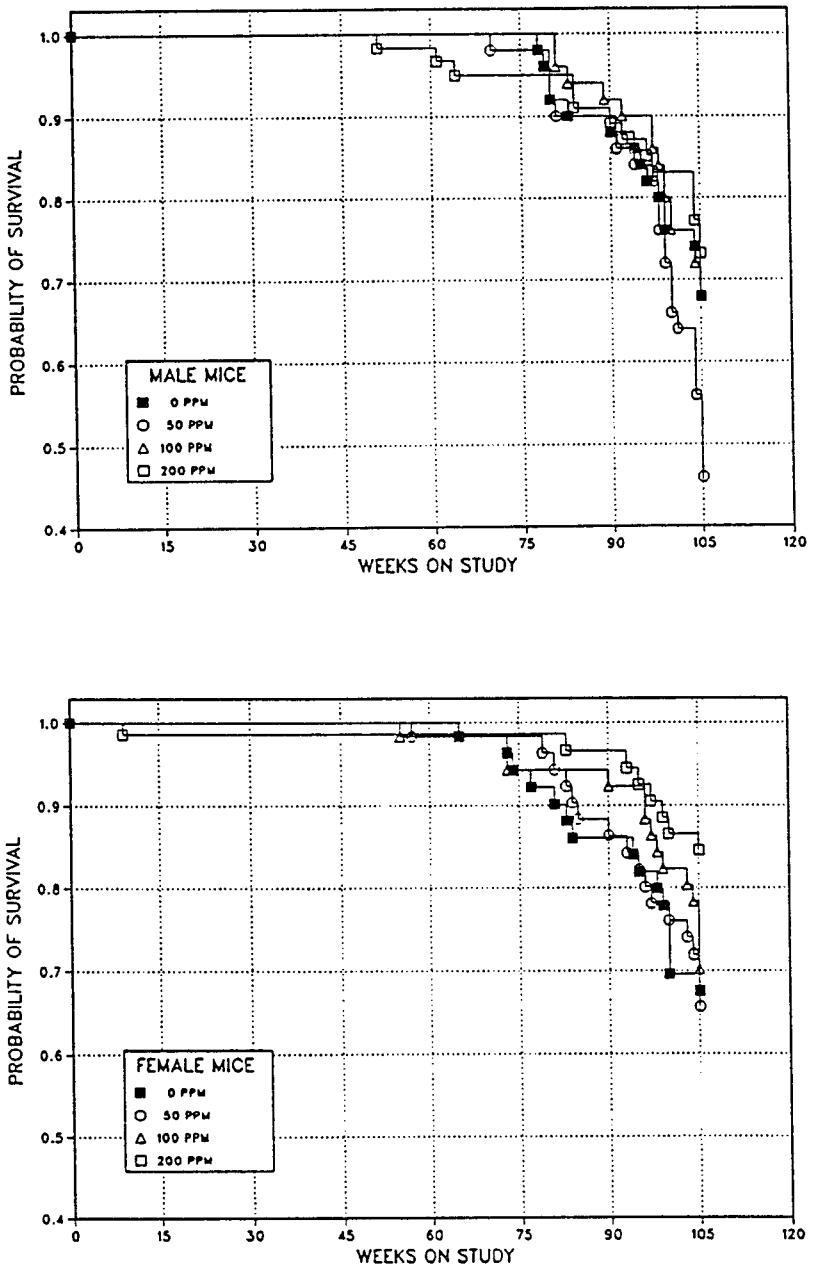

FIGURE 9
Kaplan-Meier Survival Curves for Male and Female Mice Administered Chloraminated Water for 2 Years

TABLE 17
Survival of Mice in the 2-Year Studies of Chloraminated Water

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
Animals initially in study	70	70	70	70
15-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	10	10	10	9
Natural deaths	4	3	3	4
Moribund	12	24	13	10
Animals surviving to end of study	34	23	34	37
Percent survival at end of study[b]	68	46	68	73
Mean survival (days)[c]	706	700	712	701
Survival analysis[d]	P=0.237N	P=0.071	P=1.000N	P=0.770N
Female				
Animals initially in study	70	70	70	70
15-week interim evaluation[a]	10	10	10	10
66-week interim evaluation[a]	10	10	10	10
Natural deaths	3	3	6	3
Moribund	13	14	9	5
Accidental deaths[a]	1	1	0	0
Animals surviving to end of study	33	32	35	42
Percent survival at end of study[b]	67	66	70	84
Mean survival (days)[c]	683	699	709	711
Survival analysis[d]	P=0.042N	P=0.932	P=0.815N	P=0.080N

[a] Censored from survival analyses
[b] Kaplan-Meier determinations (survival rates adjusted for interim evaluation and accidental deaths)
[c] Mean of all deaths (uncensored, censored, terminal sacrifice)
[d] The entry under the "0 ppm" column is the trend test (Tarone, 1975) result. Subsequent entries are the results of pairwise tests (Cox, 1972). A negative trend or lower mortality is indicated by N.

Kidney: Renal tubule cell adenomas occurred in two high-dose male mice, but none were seen in controls (Table 18). Both adenomas were observed by gross examination at necropsy. Focal tubule hyperplasia was seen in one low-dose, two mid-dose, and one high-dose male. Only one renal tubule neoplasm has occurred in feed studies in 563 (0.2%) historical controls (Table G4). Because of the rarity of these lesions in untreated controls, additional step sections of residual formalin-fixed kidney from all male mice were prepared and examined microscopically. Hyperplasia was observed in two control males and one additional mid-dose male, and an adenoma was found in one low-dose male (Table 18).

There were no other kidney lesions that occurred with a greater incidence in exposed male or female mice than in the controls. The histopathology quality assessment review and a second blind evaluation of the kidney sections did not identify any difference in the incidence or severity of renal tubule atrophy, dilatation, regeneration, focal mineralization, or protein casts between treated and control groups. These changes were considered characteristic of the spontaneous nephropathy commonly seen in aging mice.

TABLE 18
Incidence of Lesions of the Kidney in Male Mice in the 2-Year Study of Chloraminated Water

	0 ppm	50 ppm	100 ppm	200 ppm
Original Sections[a]				
Renal tubule, hyperplasia, focal	0/50 (0%)	1/50 (2%)	2/50 (4%)	1/51 (2%)
Renal tubule, adenoma[b]	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/51 (4%)
Adjusted rates[c]	0.0%	0.0%	0.0%	5.4%
Terminal rates[d]	0/34 (0%)	0/23 (0%)	0/34 (0%)	2/37 (5%)
First incidence (days)	-[e]	-	-	733 (T)
Logistic regression tests[f]	P=0.082	-	-	P=0.257
Step Sections				
Renal tubule, hyperplasia, focal	2/50 (4%)	0/50 (0%)	1/50 (2%)	0/51 (0%)
Renal tubule, adenoma	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/51 (0%)
Original and Step Sections Combined				
Renal tubule, hyperplasia, focal	2/50 (4%)	1/50 (2%)	3/50 (6%)	1/51 (2%)
Renal tubule, adenoma	0/50 (0%)	1/50 (2%)	0/50 (0%)	2/51 (4%)
Adjusted rates	0.0%	4.3%	0.0%	5.4%
Terminal rates	0/34 (0%)	1/23 (4%)	0/34 (0%)	2/37 (5%)
First incidence (days)	-	733 (T)	-	733 (T)
Logistic regression tests	P=0.195	P=0.422	-	P=0.257

(T)Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined microscopically for this tumor type
[b] Historical incidence for 2-year NTP studies with untreated control groups is: 1/563 (0.2% ± 0.6%), range 0%-2% (feed studies); 0/129 (drinking water studies).
[c] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Not applicable; no tumors in animal group
[f] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The logistic regression tests regard these lesions as nonfatal.

DISCUSSION AND CONCLUSIONS

Chlorine was first used as a disinfectant in drinking water in the early 1900's, and since then chlorination has become one of the most effective ways to eliminate the spread of waterborne diseases, particularly those caused by pathogenic bacteria such as *Salmonella typhosa* (typhoid fever). The U.S. Congress and the U.S. Environmental Protection Agency (USEPA), through the Safe Drinking Water Act of 1974 and Amendments, mandated studies to determine the most effective way to disinfect water supplies and at the same time minimize potential long-term health effects associated with either the chemicals used in water treatment or with chemical byproducts resulting from water treatment (NRC, 1977; USEPA, 1988).

Untreated water can contain a large number of compounds that react with chlorine, including inorganic reducing agents; ammonia, amines and amino acids; humic substances (complex polymers of natural origin); and other forms of organic nitrogen. The principal result of the reaction of chlorine with these compounds is the formation of halogenated byproducts, particularly trihalomethanes, halogenated acetic acids, halogenated acetonitriles, chlorinated ketones, halogenated hydrocarbons, and others. Bromide can also be present in untreated water and react with compounds in the water to form brominated byproducts. Several of the trihalomethanes, including bromodichloromethane, tribromomethane (bromoform), chlorodibromomethane, and chloroform, have demonstrated carcinogenic activity in rats, mice, or both, when given by oral gavage at relatively high doses (NCI, 1976b; NTP, 1985a, 1987, 1989c).

While chlorine is currently the most widely used disinfectant in the United States, chloramination is a promising alternative to chlorination and is used in 10% to 20% of the water treatment plants. In the chloramination process, inorganic chloramines are formed when water containing ammonia is chlorinated. Although these chloramines are somewhat less effective in disinfecting water than chlorine, they are less likely to react with organic matter to form byproducts, especially the trihalomethanes and the chlorophenols.

The USEPA (Stober, 1990) and the International Agency for Research on Cancer (Daniel *et al.*, 1990) recently reviewed epidemiologic studies examining the relationship between cancer and the consumption of chlorinated drinking water. In particular, studies by Cantor *et. al.* (1987) and Zierler *et. al.* (1988) showed an association between cancer of the urinary bladder and long-term exposure to chlorinated drinking water, especially chlorinated surface water. Although these epidemiologic studies demonstrated some risk associated with the consumption of chlorinated water, they did not identify the causal factor or factors. Thus, it is unknown if the risk was associated with residual available atomic chlorine, chlorinated byproducts, or other contaminants.

At the request of the USEPA, the National Toxicology Program conducted 2-year studies of chlorinated and chloraminated water in F344/N rats and B6C3F$_1$ mice. The intent of these studies was to determine the potential chronic toxicity or carcinogenic activity of chlorinated or chloraminated water without the possible confounding effects of byproducts from chlorination. Thus, the water for all treatment groups was charcoal filtered and deionized to remove organic substances and other contaminants. The levels of trihalomethanes in samples from water bottles in the animal rooms were measured during the course of the studies and varied from <1 to 415 ppb for chlorinated water, from <1 to 8 ppb for chloraminated water, and from <1 to 8 ppb for untreated control water. Water bottles were kept in the animal room for two days. As the animals drank, small amounts of organic matter were possibly introduced into the water and, in the case of chlorinated water, allowed low levels of trihalomethanes to form. Nevertheless, the levels of trihalomethanes found in the water bottles are well below the levels found to produce tumors in rodents in previous NCI/NTP 2-year studies and are not believed to compromise the interpretation of the current drinking water studies.

In these 2-year studies, concentrations of 70, 140, or 275 ppm available atomic chlorine and 50, 100, or 200 ppm chloramine were administered. Common control groups were used for comparison with rats and mice receiving chlorinated or chloraminated water. Water for all groups was deionized, charcoal filtered, then buffered and adjusted to pH 9 to ensure that hypochlorite (chlorinated water) and monochloramine (chloraminated water) were the predominant products.

Palatability was the principal factor limiting the concentrations of available atomic chlorine or chloramine in these studies. There was a dose-related decrease in water consumption by animals receiving chlorinated or chloraminated water (Tables L1-L8). Decreased water consumption was evident during the first week and continued throughout the studies. Toward the end of the studies, the effect on water consumption was generally less than during the first weeks. The animals showed no physiological alterations due to decreased water consumption, and there was no clinical or hematological evidence of dehydration (Tables J1-J9). The concentrations used in these studies therefore represent the maximum doses that could be practically delivered to the animals in drinking water.

Because body weight and water consumption changed as the rats and mice aged, the amount of available atomic chlorine or chloramine ingested during the NTP 2-year studies varied. For both chemicals, the mean daily dose (mg available atomic chlorine or chloramine/kg body weight) was higher during the first 13 weeks than during the second year of the studies. In the chlorinated water studies, high-dose rats received a mean daily dose of approximately 20 mg/kg for the first 13 weeks, which decreased to 13-14 mg/kg during the second year; for high-dose mice, the mean daily dose decreased from 35-44 mg/kg to 20-23 mg/kg. In the chloraminated water studies, the mean daily dose decreased from 12 mg/kg to 9 mg/kg for high-dose rats, and from 20-24 mg/kg to 15-16 mg/kg for high-dose mice. In contrast, the average daily dose of chlorine or chloramine estimated for a 60-kg man drinking 2 L of chlorinated water (1,000 μg chlorine/L) or chloraminated water (2,000 μg chloramine/L) per day is 33 or 66 μg/kg.

The maximum solubility of sodium hypochlorite in water is 62.5 mg/mL (expressed as available atomic chlorine), and that of chloramine in water is 1.4 mg/mL. Assuming a maximum oral gavage volume of 5 mL/kg for rats and 10 mL/kg for mice, the maximum single gavage dose of hypochlorite would be 312.5 mg/kg for rats and 625 mg/kg for mice; for chloramine, these doses would be 7 mg/kg for rats and 14 mg/kg for mice. Although a higher dose of hypochlorite could have been administered by gavage than was received by rats and mice in these drinking water studies, the dose of chloramine administered by gavage would have been less.

Survival of rats and mice in these 2-year studies was similar among treated groups and their respective controls. Survival of all groups of male rats was less than 50% at the end of the studies, following a trend previously reported for all NTP studies (Rao *et al.*, 1990). In an analysis of control groups from 144 2-year carcinogenicity studies from 1971 to 1981, Rao *et al.* reported a statistically significant decreasing trend over time for survival of male rats. The decreased survival was associated with increased maximum mean body weight attained during the course of these studies. Factors considered to contribute to the decreasing survival included age-related degenerative change associated with the increased body weight, the prevalence of mononuclear cell leukemia which also increased over time, and the change in criteria for euthanasia of moribund animals. In the current studies, mononuclear cell leukemia, pituitary neoplasms, and nephropathy were considered the principal diseases contributing to the mortality of male rats. Although survival at 2 years was low in all groups of male rats, survival at week 93 was greater than or equal to 50% (Tables 2 and 6, Figures 3 and 5). Thus, the studies of chlorinated or chloraminated water in male rats were considered adequate for the assessment of carcinogenic activity.

There were no treatment-related lesions in rats or mice at either the 14- or 15-week or at the 66-week interim evaluations. Other investigators also reported no treatment-related lesions in drinking water studies of chlorine, chloramine, or sodium hypochlorite. In a 13-week drinking water study of chlorine at doses of up to 250 ppm and chloramine at doses up to 200 ppm, Daniel *et al.* (1990) reported that there was no evidence of dose-related histopathological lesions in male or female Sprague-Dawley rats. Decreased body weight and decreased water consumption were seen in the high-dose chloramine groups. In the high-dose chlorine groups, the primary effect was a decrease in water

consumption without an accompanying decrease in body weight. Hasegawa *et al.* (1986) also reported no treatment-related neoplastic effects in male or female F344 rats given sodium hypochlorite in drinking water at concentrations up to 1,000 ppm in males and 2,000 ppm in females for 112 weeks.

There were no neoplasms or nonneoplastic lesions in the rats or mice in these 2-year studies that were clearly attributable to the consumption of chlorinated or chloraminated water. However, the incidence of mononuclear cell leukemia was marginally greater than that of controls in the mid- and high-dose groups of female rats consuming chlorinated or chloraminated water. Mononuclear cell leukemia appears sporadically in control rats before 19 months of age and the cumulative incidence increases sharply after 20 months (Stromberg and Vogtsberger, 1983). The neoplastic mononuclear cells have Fc receptors, natural killer cell activity, and the surface antigens thy 1.1, M1/70, OX-8, and Asialo GM_1. These cells seem to be morphologically, biochemically, and functionally similar to a population of cells in humans called large granular lymphocytes. Mononuclear cell leukemia of rats is generally thought to originate in the spleen, since splenomegaly, which is due to the diffuse accumulation of neoplastic cells in the red pulp, is found in virtually all rats dying with leukemia. Moreover, the incidence of leukemia was shown to be reduced from 24% to 2% by splenectomizing rats at one to two months of age (Moloney and King, 1973). Once the disease is clinically apparent, the duration of illness averages about 5 weeks, and death seems to be most closely related to the onset of hemolytic anemia, which is thought to be immune-mediated.

Several factors must be weighed to determine if there is an association between the consumption of either chlorinated or chloraminated water and the occurrence of mononuclear cell leukemia in female rats. Although the increase in leukemia incidence in mid- and high-dose female rats was slight, the incidence of leukemia was significantly greater than controls in mid-dose rats receiving chlorinated water ($P=0.014$) (Table 5) and in high-dose rats receiving chloramine ($P=0.036$) (Table 9). The trend test was also marginally significant for both groups, but there was no clear dose response, as the incidences of leukemia in the mid- and high-dose groups were similar.

The first observation of mononuclear cell leukemia in female rats receiving chlorinated water occurred in the mid-dose group on day 329. In female rats receiving chloraminated water, the first observation also occurred in the mid-dose group, but on day 465. Nevertheless, the mean time to observation for leukemia among early deaths was similar among control and dosed groups (controls, 601 days; chlorinated water: low-dose, 624 days; mid-dose, 604 days; high-dose, 653 days; chloraminated water: low-dose, 663; mid-dose, 621; high-dose, 666). Therefore, there is no evidence of a reduced latency in the occurrence of leukemia in female rats consuming chlorinated or chloraminated water.

Although the incidence of leukemia was increased in female rats consuming either chlorinated or chloraminated water, this apparent consistency of response may be misleading since these groups shared a common control group. Moreover, the incidence of leukemia in the shared female control group (16%) was less than that in the untreated historical controls (25%). The marginal increase may be spurious and due not to the consumption of chlorinated or chloraminated water, but to the slightly lower than expected control incidence. Unlike untreated historical controls, the concurrent controls in these studies received buffered (pH 9), deionized water, forcing greater reliance on within-study comparisons. Untreated control rats from other NTP studies conducted at this and other laboratories generally received tap water from municipal water supplies that may have contained very small amounts of trihalomethanes or other organic compounds. However, none of the trihalomethanes previously studied by the NTP were shown to affect the incidence of mononuclear cell leukemia.

In summary, the overall evidence is only weakly supportive of an association between the occurrence of mononuclear cell leukemia in female rats and the consumption of either chlorinated or chloraminated water. The factors not supporting this association include: (1) the increase in leukemia in dosed female rats was slight and not clearly dose related, (2) there was no decrease in tumor latency, and (3) the incidence in concurrent controls was less than in historical controls. Nevertheless, because of the marginal statistical significance, the increased incidence of leukemia was considered equivocal evidence of carcinogenic activity.

In a survey of the previous NCI/NTP technical reports, ten chemicals have shown equivocal to clear evidence of leukemia in female rats: 3,3′-dimethoxybenzidine-4,4′-diisocyanate (NCI, 1978), butyl benzyl phthalate (NTP, 1982), diallylphthalate (NTP, 1985b), dimethyl morpholinophosphoramidate (NTP 1986a), tetrachloroethylene (NTP, 1986b), hydroquinone (NTP, 1989c), 3,3′-dimethylbenzidine dihydrochloride (NTP, 1991a), glycidol (NTP, 1990b), Mirex (NTP, 1990a), and tris(2-chloroethyl) phosphate, (NTP, 1991b). There is no single structure or group that is common to all of these chemicals.

In the NTP 2-year studies of mice, there were no increases in the incidence of neoplasms or nonneoplastic lesions that could be clearly attributed to the consumption of chlorinated or chloraminated water. In the original evaluation of kidneys from dosed mice, renal tubule cell neoplasms were observed in two high-dose males receiving chlorinated water (a carcinoma in one and an adenoma in the other) and in two high-dose males receiving chloraminated water (both adenomas); no renal neoplasms were observed in control male mice. Focal tubule cell hyperplasia also occurred in dosed mice, but not in controls. Although renal neoplasms are uncommon in mice, it was uncertain if the small number occurring in dosed male mice was caused by the consumption of treated water.

The standard protocol for the examination of the kidneys requires the microscopic examination of any masses observed grossly at necropsy plus a single section from each kidney. With routine single sections, the number of tubule cell neoplasms observed is often so low that statistical analyses are not helpful in the evaluation, as in the current studies of chlorinated or chloraminated water. Moreover, preneoplastic lesions and small adenomas are usually not observed macroscopically at necropsy. Thus, multiple sections might be expected to increase the number of preneoplastic lesions or neoplasms observed and allow for a more rigorous statistical evaluation.

The NTP (1989a) and other investigators (Kurokawa *et al.*, 1986) have found that multiple sectioning of the kidney may allow a more precise evaluation of potential chemical-induced renal tubule neoplasms than that possible with single sectioning. For this reason, the residual halves of the formalin-fixed kidneys from male mice in these studies were step sectioned to provide an additional 4 to 6 tissue sections for microscopic examination. During this subsequent histopathologic examination, an additional tubule cell carcinoma was found in a low-dose male receiving chlorinated water and an adenoma was found in a low-dose male receiving chloraminated water. Focal hyperplasia was found in two controls and one or two males from several of the dosed groups.

Although step sections of kidneys of male rats have been evaluated in several other NTP studies, this is the first in which step sections of the kidneys of mice have been evaluated. Step sections proved to be most helpful in the evaluation of the toxicology and carcinogenesis studies of nitrofurantoin in rats (NTP, 1989a), in which the number of renal tubule cell neoplasms observed was increased from 0/50 to 3/50 in control males and 3/50 to 20/50 in high-dose males. Nearly all the additional neoplasms seen in the step sections were small (microscopic) adenomas believed to be the probable precursor of renal tubule carcinoma. In contrast to the nitrofurantoin studies, the step sections of kidneys of male mice consuming chlorinated or chloraminated water did not provide supportive evidence of a chemical effect. Since no additional renal neoplasms were found in the mid- or high-dose groups and since focal hyperplasia, a potential preneoplastic lesion, was found at similar incidences in the control and dosed groups, the small number of renal tubule cell neoplasms in male mice were not considered related to the consumption of treated water.

CONCLUSIONS

Chlorinated Water

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity*[*] of chlorinated water in male F344/N rats receiving 70, 140, or 275 ppm. There was *equivocal evidence of carcinogenic activity* of chlorinated water in female F344/N rats based on an increase in the incidence of mononuclear cell leukemia. There was *no evidence of carcinogenic activity* of chlorinated water in male or female $B6C3F_1$ mice receiving 70, 140, or 275 ppm.

Chloraminated Water

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity* of chloraminated water in male F344/N rats receiving 50, 100, or 200 ppm. There was *equivocal evidence of carcinogenic activity* of chloraminated water in female F344/N rats based on an increase in the incidence of mononuclear cell leukemia. There was *no evidence of carcinogenic activity* of chloraminated water in male or female $B6C3F_1$ mice receiving 50, 100, or 200 ppm.

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[*] Explanation of Levels of Evidence of Carcinogenic Activity is on page 8. A summary of peer review comments and the public discussion on this Technical Report appears on page 10.

REFERENCES

Abdel-Rahman, M.S. (1985). Pharmacokinetics of chlorine obtained from chlorine dioxide, chlorine, chloramine, and chloride. In *Water Chlorination: Environmental Impact and Health Effects* (R.L. Jolley, R.J. Bull, W.P. Davis, S. Katz, M.H. Roberts, Jr., and V.A. Jacobs, Eds.), Vol. 5, pp. 281-293. Lewis Publishers, Inc., Chelsea, MI.

Abdel-Rahman, M.S., Berardi, M.R., and Bull, R.J. (1982). Effect of chlorine and monochloramine in drinking water on the developing rat fetus. *J. Appl. Toxicol.* **2**, 156-159.

Abdel-Rahman, M.S., Waldron, D.M., and Bull, R.J. (1983). A comparative kinetics study of monochloramine and hypochlorous acid in rat. *J. Appl. Toxicol.* **3**, 175-179.

Abdel-Rahman, M.S., Suh, D.H., and Bull, R.J. (1984a). Pharmacodynamics and toxicity of chlorine in drinking water in the rat. *J. Appl. Toxicol.* **4**, 82-86

Abdel-Rahman, M.S., Suh, D.H., and Bull, R.J. (1984b). Toxicity of monochloramine in rat: An alternative drinking water disinfectant. *J. Toxicol. Environ. Health* **13**, 825-834.

American Conference of Governmental Industrial Hygienists (ACGIH) (1989). Threshold limit values and biological exposure indices for 1988-1989. Cincinnati, OH.

Armitage, P. (1971). *Statistical Methods in Medical Research*, pp. 362-365. John and Wiley and Sons, New York.

Boorman, G.A., Montgomery, C.A., Jr., Eustis, S.L., Wolfe, M.J., McConnell, E.E., and Hardisty, J.F. (1985). Quality assurance in pathology for rodent carcinogenicity studies. In *Handbook of Carcinogen Testing* (H.A. Milman and E.K. Weisburger, Eds.), pp. 345-357. Noyes Publications, Park Ridge, NJ.

Brodtmann, N.V., Jr., and Russo, P.J. (1979). The use of chloramine for reduction of trihalomethanes and disinfection of drinking water. *J. Amer. Water Works Assoc.* **71**, 40-42.

Bull, R.J., Brown, J.M., Meierhenry, E.A., Jorgenson, T.A., Robinson, M., and Stober, J.A. (1986). Enhancement of the hepatotoxicity of chloroform in B6C3F1 mice by corn oil: Implications for chloroform carcinogenesis. *Environ. Health Perspect.* **69**, 49-58.

Cantor, K.P., Hoover, R., Hartge, P., Mason, T.J., Silverman, D.T., and Levin, L.I. (1985). Drinking water source and risk of bladder cancer: A case-control study. In *Water Chlorination: Chemistry, Environmental Impact and Health Effects* (R.L. Jolley, R.J. Bull, W.P. Davis, S. Katz, M.H. Roberts, Jr., and V.A. Jacobs, Eds.), Vol. 5, pp. 145-151. Lewis Publishers, Inc., Chelsea, MI.

Cantor, K.P., Hoover, R., Hartge, P., Mason, T.J., Silverman, D.T., Altman, R., Austin, D.F., Child, M.A., Key, C.R., Marrett, L.D., Myers, M.H., Narayana, A.S., Levin, L.I., Sullivan, J.W., Swanson, G.M., Thomas, D.B., and West, D.W. (1987). Bladder cancer, drinking water source, and tap water consumption: A case-control study. *JNCI* **79**, 1269-1279.

Carlton, B.D., Barlett, P., Basaran, A., Colling, K., Osis, I., and Smith, M.K. (1986). Reproductive effects of alternative disinfectants. *Environ. Health Perspect.* **69**, 237-241.

Chernoff, N., Rogers, E., Carver, B., Kavlock, R., and Gray, E. (1979). The fetotoxic potential of municipal drinking water in the mouse. *Teratology* **19**, 165-170.

Code of Federal Regulations (CFR), **21**, part 58.

Cotruvo, J.A. (1984). The role of government in maintaining drinking water quality. In *Drinking Water and Human Health* (J.A. Bell and T.C. Doege, Eds.), pp. 12-21. American Medical Association, Chicago, IL.

Cox, D.R. (1972). Regression models and life tables. *J. R. Stat. Soc.* **B34**, 187-220.

Craun, G.F. (1985). Epidemiologic studies of organic micropollutants in drinking water. *Sci. Total Environ.* **47**, 461-472.

Daniel, F.B., Condie, L.W., Robinson, M., Stober, J.A., York, R.G., Olson, G.R., and Wang, S. (1990). Comparative 90-day subchronic toxicity studies of three disinfectants. *J. Amer. Water Works Assoc.* **82**, 61-69.

Dinse, G.E., and Haseman, J.K. (1986). Logistic regression analysis of incidental-tumor data from animal carcinogenicity experiments. *Fundam. Appl. Toxicol.* **6**, 44-52.

Dinse, G.E., and Lagakos, S.W. (1983). Regression analysis of tumor prevalence data. *Appl. Statist.* **32**, 236-248.

Drago, R.S. (1957). Chloramine. *J. Chem. Educ.* **34**, 541-545.

Druckrey, H. (1968). Chloriertes Trinkwasser, Toxizitäts-Prüfungen an Ratten über sieben Generationen. *Food Cosmet. Toxicol.* **6**, 147-154.

Dunn, O.J. (1964). Multiple comparisons using rank sums. *Technometrics* **6**, 241-252.

Exon, J.H., Koller, L.D., O'Reilly, C.A., and Bercz, J.P. (1987). Immunotoxicologic evaluation of chlorine-based drinking water disinfectants, sodium hypochlorite and monochloramine. *Toxicology* **44**, 257-269.

Fidler, I.J. (1977). Depression of macrophages in mice drinking hyperchlorinated water. *Nature* **270**, 735-736.

Gart, J.J., Chu, K.C., and Tarone, R.E. (1979). Statistical issues in interpretation of chronic bioassay tests for carcinogenicity. *J. Natl. Cancer. Inst.* **62**, 957-974.

Gauthier, L., Levi, Y., and Jaylet, A. (1989). Evaluation of the clastogenicity of water treated with sodium hypochlorite or monochloramine using a micronucleus test in newt larvae (*Pleurodeles waltl*). *Mutagenesis* **4**, 170-173.

Grizzle, J.M., Melius, P., and Strength, D.R. (1984). Papillomas on fish exposed to chlorinated wastewater effluent. *JNCI* **73**, 1133-1142.

Hasegawa, R., Takahashi, M., Kokubo, T., Furukawa, F., Toyoda, K., Sato, H., Kurokawa, Y., and Hayashi, Y. (1986). Carcinogenity study of sodium hypochlorite in F344 rats. *Food Chem. Toxicol.* **24**, 1295-1302.

Haseman, J.K. (1984). Statistical issues in the design, analysis and interpretation of animal carcinogenicity studies. *Environ. Health Perspect.* **58**, 385-392.

Haseman, J.K., Huff, J., and Boorman, G.A. (1984). Use of historical control data in carcinogenicity studies in rodents. *Toxicol. Pathol.* **12**, 126-135.

Haseman, J.K., Huff, J.E., Rao, G.N., Arnold, J.E., Boorman, G.A., and McConnell, E.E. (1985). Neoplasms observed in untreated and corn oil gavage control groups of F344/N rats and (C57BL/6N × C3H/HeN)F_1 (B6C3F_1) mice. *JNCI* **75**, 975-984.

Hayashi, M., Kishi, M., Sofuni, T., and Ishidate, M., Jr. (1988). Micronucleus tests in mice on 39 food additives and eight miscellaneous chemicals. *Food Chem. Toxicol.* **26**, 487-500.

Herren-Freund, S.L., and Pereira, M.A. (1986). Carcinogenicity of by-products of disinfection in mouse and rat liver. *Environ. Health Perspect.* **69**, 59-65.

Hoyano, Y., Bacon, V., Summons, R.E., Pereira, W.E., Halpern, B., and Duffield, A.M. (1973). Chlorination studies. IV. The reaction of aqueous hypochlorous acid with pyrimidine and purine bases. *Biochem. Biophys. Res. Commun.* **53**, 1195-1199.

Ishidate, M. Jr., Sofuni, T., Yoshikawa, K., Hayashi, M., Nohmi, T., Sawada, M., and Matsuoka, A. (1984). Primary mutagenicity screening of food additives currently used in Japan. *Food Chem. Toxicol.* **22**, 623-636.

Jolley, R.L., and Carpenter, J.H. (1983). A review of the chemistry and environmental fate of reactive oxidant species in chlorinated water. In *Water Chlorination: Environmental Impact and Health Effects* (R.L. Jolley, W.A. Brungs, J.A. Cotruvo, R.B. Cumming, J.S. Mattice, and V.A. Jacobs, Eds.), Vol. 4, pp. 3-47. Ann Arbor Science, Ann Arbor, MI.

Jonckheere, A. (1954). A distribution-free k-sample test against ordered alternatives. *Biometrika* **41**, 133-145.

Jorgenson, T.A., Meierhenry, E.F., Rushbrook, C.J., Bull, R.J., and Robinson, M. (1985). Carcinogenicity of chloroform in drinking water to male Osborne-Mendel rats and female B6C3F1 mice. *Fundam. Appl. Toxicol.* **5**, 760-769.

Kaplan, E.L., and Meier, P. (1958). Nonparametric estimation of incomplete observations. *J. Am. Stat. Assoc.* **53**, 457-481.

Kavlock, R., Chernoff, N., Carver, B., and Kopfler, F. (1979). Teratology studies in mice exposed to municipal drinking-water concentrates during organogenesis. *Food Cosmet. Toxicol.* **17**, 343-347.

Kirk-Othmer Encyclopedia of Chemical Technology (1964). 2nd ed., Vol. 4, pp. 913-925. Wiley Interscience Publishers, New York.

Kool, H.J., Kuper, F., van Haeringen, H., and Koeman, J.H. (1985). A carcinogenicity study with mutagenic organic concentrates of drinking-water in the Netherlands. *Food Chem. Toxicol.* **23**, 79-85.

Kovacic, P., Lowery, M.K., and Field, K.W. (1970). Chemistry of N-bromamines and N-chloramines. *Chem. Rev.* **70**, 639-665.

Krasner, S.W., McGuire, M.J., Jacangelo, J.G., Patania, N.L., Reagan, K.M., and Aieta, E.M. (1989) The occurrence of disinfection by-products in US drinking water. *J. Am. Water Works Assoc.* **81**, 41-53.

Kurokawa, Y., Takayama, S., Konishi, Y., Hiasa, Y., Asahina, S., Takahashi, M., Maekawa, A., and Hayashi, Y. (1986). Long-term *in vivo* carcinogenicity tests of potassium bromate, sodium hypochlorite, and sodium chlorite conducted in Japan. *Environ. Health Perspect.* **69**, 221-235.

Maronpot, R.R., and Boorman, G.A. (1982). Interpretation of rodent hepatocellular proliferative alterations and hepatocellular tumors in chemical safety assessment. *Toxicol. Pathol.* **10**, 71-80.

McConnell, E.E., Solleveld, H.A., Swenberg, J.A., and Boorman, G.A. (1986). Guidelines for combining neoplasms for evaluation of rodent carcinogenesis studies. *JNCI* **76**, 283-289.

McGuire, M.J., and Meadow, R.G. (1988). AWWARF trihalomethane survey. *J. Amer. Water Works Assoc.*, **80**, 61-68.

McKnight, B., and Crowley, J. (1984). Tests for differences in tumor incidence based on animal carcinogenesis experiments. *J. Am. Stat. Assoc.* **79**, 639-648.

Meier, J.R., Bull, R.J., Stober, J.A., and Cimino, M.C. (1985). Evaluation of chemicals used for drinking water disinfection for production of chromosomal damage and sperm-head abnormalities in mice. *Environ. Mutagen.* **7**, 201-211.

Mickey, G.H., and Holden, H. Jr. (1971). Chromosomal effects of chlorine on mammalian cells *in vitro*. *Newsl. Environ. Mutagen. Soc.* **4**, 39-41.

Mink, F.L., Coleman, W.E., Munch, J.W., Kaylor, W.H., and Ringhand, H.P. (1983). *In vivo* formation of halogenated reaction products following peroral sodium hypochlorite. *Bull. Environ. Contam. Toxicol.* **30**, 394-399.

Moloney, W.C., and King, V. (1973). Reduction of leukemia incidence following splenectomy in the rat. *Cancer Res.* **33**, 573-574.

Moore, G.S., and Calabrese, E.J. (1980). The health effects of chloramines in potable water supplies: A literature review. *J. Environ. Pathol. Toxicol.* **4**, 257-263.

Morris, J.C., and Isaac, R.A. (1983). A critical review of kinetic and thermodynamic constants for the aqueous chlorine-ammonia system. In *Water Chlorination: Environmental Impact and Health Effects* (R.L. Jolley, W.A. Brungs, J.A. Cotruvo, R.B. Cumming, J.S. Mattice, and V.A. Jacobs, Eds.), Vol. 4, pp. 49-62. Ann Arbor Science, Ann Arbor, MI.

National Cancer Institute (NCI) (1976a). Guidelines for Carcinogen Bioassay in Small Rodents. Technical Report Series No. 1. NIH Publication No. 76-801. National Institutes of Health, Bethesda, MD.

National Cancer Institute (NCI) (1976b). Report on Carcinogenesis Bioassay of Chloroform. U.S. Department of Commerce, National Technical Information Service. PB-264 018.

National Cancer Institute (NCI) (1979). Bioassay of 3,3'-Dimethoxybenzidine-4,4'-diisocyanate for Possible Carcinogenicity (CAS No. 91-93-0). Technical Report Series No. 128. NIH Publication No. 78-1383. National Institutes of Health, Bethesda, MD.

National Institute for Occupational Safety and Health (NIOSH) (1990). National Occupational Exposure Survey (NOES) (1981-1983), unpublished provisional data as of July 1, 1990.

National Institutes of Health (NIH) (1978). Open Formula Rat and Mouse Ration (NIH-07). NIH Publication No. 11-1335. National Institutes of Health, Bethesda, MD.

National Research Council (NRC) (1977). *Drinking Water and Health*, Vol. 1. National Academy Press, Washington, DC.

National Research Council (NRC) (1980). *Drinking Water and Health*, Vol. 2. National Academy Press, Washington, DC.

National Research Council (NRC) (1987). Disinfectants and disinfectant by-products. In *Drinking Water and Health*, Vol. 7. National Academy Press, Washington, DC.

National Toxicology Program (NTP) (1982). Carcinogenesis Bioassay of Butyl Benzyl Phthalate (CAS No. 85-68-7) in F344/N Rats and B6C3F$_1$ Mice (Feed Study). NTP TR No. 213. NIH Publication No. 82-1769. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1985a). Toxicology and Carcinogenesis Studies of Chlorodibromomethane (CAS No. 124-48-1) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP TR No. 282. NIH Publication No. 85-2538. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1985b). Toxicology and Carcinogenesis Studies of Diallylphthalate (CAS No. 131-17-9) in F344/N Rats (Gavage Studies). NTP TR No. 284. NIH Publication No. 85-2540. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1986a). Toxicology and Carcinogenesis Studies of Dimethyl Morpholinophosphoramidate (CAS No. 597-25-1) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP TR No. 298. NIH Publication No. 86-2554. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1986b). Toxicology and Carcinogenesis Studies of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) in F344/N Rats and B6C3F$_1$ Mice (Inhalation Studies). NTP TR No. 311. NIH Publication No. 86-2567. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1987). Toxicology and Carcinogenesis Studies of Bromodichloromethane (CAS No. 75-27-4) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP TR No. 321. NIH Publication No. 88-2537. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1989a). Toxicology and Carcinogenesis Studies of Nitrofurantoin (CAS No. 67-20-9) in F344/N Rats and B6C3F$_1$ Mice (Feed Studies). NTP TR No. 341. NIH Publication No. 88-2537. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1989b). Toxicology and Carcinogenesis Studies of Tribromomethane (Bromoform) (CAS No. 75-25-2) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP TR No. 350. NIH Publication No. 89-2805. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1989c). Toxicology and Carcinogenesis Studies of Hydroquinone (CAS No. 123-31-9) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP TR No. 366. NIH Publication No. 89-2821. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1990a). Toxicology and Carcinogenesis Studies of Mirex (CAS No. 2385-85-5) in F344/N Rats (Feed Studies). NTP TR No. 313. NIH Publication No. 90-2569. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1990b). Toxicology and Carcinogenesis Studies of Glycidol (CAS No. 556-52-5) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP TR No. 374. NIH Publication No. 90-2829. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1991a). Toxicology and Carcinogenesis Studies of 3,3′-Dimethylbenzidine Dihydrochloride (CAS No. 20325-40-0) in F344/N Rats (Water Studies). NTP TR No. 390. NIH Publication No. 90-2845. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

National Toxicology Program (NTP) (1991b). Toxicology and Carcinogenesis Studies of Tris(2-chloroethyl) Phosphate (CAS No. 115-96-8) in F344/N Rats and B6C3F$_1$ Mice (Gavage Studies). NTP TR No. 391. NIH Publication No. 90-2846. National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Olivieri, V.P., Dennis, W.H., Snead, M.C., Richfiels, D.T., and Krusé, C.W. (1980). Reaction of chlorine and chloramines with nucleic acids under disinfection conditions. In *Water Chlorination: Environmental Impact and Health Effects* (R.L. Jolley, W.A. Brungs, J.A. Cotruvo, R.B. Cumming, J.S. Mattice, and V.A. Jacobs, Eds.), Vol. 3, pp. 651-663. Ann Arbor Science, Ann Arbor, MI.

Patton, W., Bacon, V., Duffield, A.M., Halpern, B., Hoyano, Y., Pereira, W., and Lederberg, J. (1972). Chlorination studies. I. The reaction of aqueous hypochlorous acid with cytosine. *Biochem. Biophys. Res. Comm.* **48**, 880-884.

Pereira, W.E., Hoyano, Y., Summons, R.E., Bacon, V.A., and Duffield, A.M. (1973). Chlorination studies II. The reaction of aqueous hypochlorous acid with α-amino acids and dipeptides. *Biochim. Biophys. Acta* **313**, 170-180.

Rao, G.N., Haseman, J.K., Grumbein, S., Crawford, D., and Eustis, S.L. (1990). Growth, body weight, survival, and tumor trends in F344/N rats during an eleven year period. *Toxicol. Pathol.* **18**, 61-70.

Rickabaugh, J., and Kinman, R.N. (1978). Trihalomethane formation from iodine and chlorine disinfection of Ohio River water. In *Water Chlorination: Environmental Impact and Health Effects* (R.L. Jolley, H. Gorchev, and D.H. Hamilton, Jr., Eds.), Vol. 2, pp. 583-591. Ann Arbor Science, Ann Arbor, MI.

Rosenkranz, H.S. (1973). Sodium hypochlorite and sodium perborate: preferential inhibitors of DNA polymerase-deficient bacteria. *Mutat. Res.* **21**, 171-174.

Sadtler Standard Spectra. (1978). Sadtler Research Laboratories, Philadelphia, PA.

Shih, K.L., and Lederberg, J. (1976). Chloramine mutagenesis in *Bacillus subtilis. Science* **192**, 1141-1143.

Shirley, E. (1977). A non-parametric equivalent of Williams' test for contrasting increasing dose levels of a treatment. *Biometrics* **33**, 386-389.

Staples, R.E., Worthy, W.C., and Marks, T.A. (1979) Influence of drinking water—tap versus purified—on embryo and fetal development in mice. *Teratology* **19**, 237-244.

Stevens, A.A., Slocum, C.J., Seeger, D.R., and Robeck, G.G. (1978). Chlorination of organics in drinking water. In *Water Chlorination: Environmental Impact and Health Effects* (R.L. Jolley, Ed.), Vol. 1, pp. 77-104. Ann Arbor Science, Ann Arbor, MI.

Stober, J. (1990). An evaluation of the role of epidemiology in assessing current and future disinfection technologies for drinking water. In *Summary of the 1989 Conference of the International Society for Environmental Epidemiology* (R.R. Neutra and B. Ostro, Eds.). Brookhaven, NY.

Stromberg, P.C., and Vogtsberger, L.M. (1983). Pathology of the mononuclear cell leukemia of Fischer rats. I. Morphological studies. *Vet. Pathol.* **20**, 698-708.

Tarone, R.E. (1975). Tests for trend in life table analysis. *Biometrika* **62**, 679-682.

Thomas, E.L., Jefferson, M.M., Bennett, J.J., and Learn, D.B. (1987). Mutagenic activity of chloramines. *Mutat. Res.* **188**, 35-43.

Truhaut, R., Gak, J.C., and Graillot, Cl. (1979). Recherches sur les risques pouvant resulter de la pollution chimique des eaux d'alimentation-I. Etude de la toxicite a long terme chez le rat et la souris des micropolluants organiques chloroformo-extractibles a partir d'eaux livrees a la consommation humaine. *Water Research* **13**, 689-697.

U.S. Environmental Protection Agency (USEPA) (1977). National Interim Primary Drinking Water Regulations. EPA-570/9-76-003. Office of Water Supply, U.S. EPA, Washington, DC.

U.S. Environmental Protection Agency (USEPA) (1988). *Comparative Health Effects Assessment of Drinking Water Treatment Technologies.* EPA 570/988-009. U.S. EPA, Washington, DC.

Van Duuren, B.L., Melchionne, S., Seidman, I., and Pereira, M.A. (1986). Chronic bioassays of chlorinated humic acids in B6C3F1 mice. *Environ. Health Prospect.* **69**, 109-117.

Wlodkowski, T.J., and Rosenkranz, H.S. (1975). Mutagenecity of sodium hypochlorite for Salmonella typhimurium. *Mutat. Res.* **31**, 39-42.

World Health Organization (WHO) (1982). Environmental Health Criteria 21, Chlorine and Hydrogen Chloride. World Health Organization **21**, 3-96.

Zierler, S., Feingold, L., Danley, R.A., and Craun, G. (1988). Bladder cancer in Massachusetts related to chlorinated and chloraminated drinking water: A case-control study. *Arch. Environ. Health* **43**, 195-200.

APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR CHLORINATED WATER STUDY

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	9	9	10	9
Early deaths				
Natural death	3	5	4	7
Moribund	34	40	30	27
Survivors				
Terminal sacrifice	14	6	16	17
Animals examined microscopically	51	51	50	51
Alimentary System				
Intestine large, cecum	(51)	(51)	(50)	(51)
Liposarcoma			1 (2%)	
Intestine large, colon	(51)	(51)	(50)	(51)
Intestine large, rectum	(51)	(51)	(49)	(49)
Adenocarcinoma	1 (2%)			
Intestine small, duodenum	(51)	(50)	(50)	(51)
Intestine small, ileum	(51)	(50)	(50)	(51)
Intestine small, jejunum	(51)	(50)	(50)	(51)
Adenocarcinoma	1 (2%)			
Liver	(51)	(51)	(50)	(51)
Cholangioma			1 (2%)	
Hepatocellular carcinoma				1 (2%)
Hepatocellular adenoma	2 (4%)	1 (2%)	3 (6%)	2 (4%)
Hepatocellular adenoma, multiple		1 (2%)		
Hepatocellular adenoma, two, multiple			1 (2%)	
Histiocytic sarcoma		1 (2%)	1 (2%)	
Mesentery	(31)	(25)	(16)	(20)
Osteosarcoma, metastatic, bone	1 (3%)			
Sarcoma				1 (5%)
Pancreas	(51)	(51)	(50)	(51)
Acinar cell, adenoma	4 (8%)	4 (8%)		1 (2%)
Acinar cell, adenoma, multiple			1 (2%)	
Pharynx				(1)
Palate, papilloma squamous				1 (100%)
Salivary glands	(51)	(51)	(50)	(51)
Stomach, forestomach	(51)	(51)	(50)	(51)
Papilloma squamous			2 (4%)	
Stomach, glandular	(51)	(51)	(50)	(51)
Tongue		(1)		(1)
Papilloma squamous				1 (100%)
Tooth	(2)			(1)
Gingiva, squamous cell carcinoma				1 (100%)
Cardiovascular System				
Heart	(51)	(51)	(50)	(51)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Endocrine System				
Adrenal gland, cortex	(51)	(51)	(49)	(51)
Histiocytic sarcoma		1 (2%)		
Osteosarcoma, metastatic, bone	1 (2%)			
Adrenal gland, medulla	(51)	(51)	(49)	(51)
Pheochromocytoma malignant	2 (4%)	1 (2%)	1 (2%)	3 (6%)
Pheochromocytoma complex			1 (2%)	
Pheochromocytoma benign	11 (22%)	13 (25%)	11 (22%)	13 (25%)
Bilateral, pheochromocytoma malignant		2 (4%)		
Bilateral, pheochromocytoma benign	12 (24%)	10 (20%)	10 (20%)	7 (14%)
Islets, pancreatic	(51)	(51)	(50)	(51)
Adenoma	5 (10%)	7 (14%)	2 (4%)	6 (12%)
Adenoma, multiple				1 (2%)
Carcinoma	2 (4%)			
Pituitary gland	(50)	(50)	(49)	(51)
Adenoma				1 (2%)
Pars distalis, adenoma	20 (40%)	20 (40%)	20 (41%)	20 (39%)
Thyroid gland	(51)	(50)	(50)	(51)
Bilateral, C-cell, adenoma		1 (2%)		
C-cell, adenoma	6 (12%)	6 (12%)	4 (8%)	4 (8%)
C-cell, carcinoma	1 (2%)		2 (4%)	1 (2%)
General Body System				
Tissue NOS		(2)	(1)	
Carcinoma, metastatic, lung			1 (100%)	
Genital System				
Preputial gland	(50)	(51)	(47)	(51)
Adenoma	3 (6%)	2 (4%)	1 (2%)	3 (6%)
Carcinoma	1 (2%)	3 (6%)	2 (4%)	2 (4%)
Prostate	(51)	(51)	(50)	(51)
Seminal vesicle	(51)	(51)	(50)	(51)
Testes	(51)	(51)	(50)	(51)
Osteosarcoma, metastatic, bone	1 (2%)			
Bilateral, interstitial cell, adenoma	26 (51%)	26 (51%)	30 (60%)	30 (59%)
Interstitial cell, adenoma	7 (14%)	15 (29%)	12 (24%)	8 (16%)
Hematopoietic System				
Bone marrow	(51)	(51)	(50)	(51)
Histiocytic sarcoma		1 (2%)	1 (2%)	
Lymph node	(51)	(51)	(50)	(51)
Deep cervical, carcinoma, metastatic, thyroid gland			1 (2%)	
Mediastinal, carcinoma, metastatic, lung			1 (2%)	
Mediastinal, carcinoma, metastatic, thyroid gland			1 (2%)	
Pancreatic, histiocytic sarcoma		1 (2%)		

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Hematopoietic System (continued)				
Lymph node, mandibular	(51)	(51)	(49)	(51)
Lymph node, mesenteric	(51)	(50)	(49)	(51)
Spleen	(51)	(51)	(50)	(51)
Histiocytic sarcoma		1 (2%)	1 (2%)	
Osteosarcoma, metastatic, bone	1 (2%)			
Thymus	(46)	(44)	(42)	(49)
Thymoma malignant		1 (2%)		
Integumentary System				
Mammary gland	(48)	(50)	(49)	(49)
Adenoma	1 (2%)			
Fibroadenoma	2 (4%)			3 (6%)
Skin	(51)	(51)	(50)	(51)
Basal cell carcinoma		1 (2%)	2 (4%)	1 (2%)
Keratoacanthoma	3 (6%)	3 (6%)	3 (6%)	3 (6%)
Keratoacanthoma, two, multiple			1 (2%)	
Papilloma squamous	1 (2%)	2 (4%)	2 (4%)	2 (4%)
Squamous cell carcinoma	1 (2%)		1 (2%)	2 (4%)
Trichoepithelioma		1 (2%)		
Subcutaneous tissue, fibroma		3 (6%)	1 (2%)	3 (6%)
Subcutaneous tissue, fibrosarcoma	1 (2%)			
Subcutaneous tissue, hemangioma				1 (2%)
Subcutaneous tissue, lipoma	1 (2%)			1 (2%)
Subcutaneous tissue, sarcoma				1 (2%)
Musculoskeletal System				
Bone	(51)	(51)	(50)	(51)
Osteosarcoma	1 (2%)			
Skeletal muscle		(1)	(3)	
Carcinoma, metastatic, lung			1 (33%)	
Histiocytic sarcoma			1 (33%)	
Nervous System				
Brain	(51)	(51)	(50)	(50)
Glioma benign				1 (2%)
Glioma malignant	1 (2%)	1 (2%)		
Meningioma NOS				1 (2%)
Spinal cord				(1)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Respiratory System				
Lung	(51)	(51)	(50)	(51)
Alveolar/bronchiolar adenoma	1 (2%)		4 (8%)	2 (4%)
Alveolar/bronchiolar carcinoma			1 (2%)	
Carcinoma			1 (2%)	
Histiocytic sarcoma		1 (2%)		
Osteosarcoma, metastatic, bone	1 (2%)			
Thymoma malignant, metastatic, thymus		1 (2%)		
Mediastinum, alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Mediastinum, carcinoma, metastatic, lung			1 (2%)	
Mediastinum, osteosarcoma, metastatic, bone	1 (2%)			
Nose	(51)	(51)	(49)	(51)
Special Senses System				
Ear	(1)		(2)	(1)
Schwannoma NOS				1 (100%)
Pinna, papilloma squamous			2 (100%)	
Eye	(5)	(3)	(3)	
Lids, schwannoma NOS			1 (33%)	
Zymbal's gland	(1)		(3)	(3)
Adenoma			1 (33%)	1 (33%)
Carcinoma	1 (100%)		2 (67%)	1 (33%)
Mixed tumor malignant				1 (33%)
Urinary System				
Kidney	(51)	(50)	(50)	(51)
Carcinoma, metastatic, lung			1 (2%)	
Osteosarcoma, metastatic, bone	1 (2%)			
Pelvis, transitional epithelium, carcinoma		1 (2%)		
Renal tubule, adenoma				2 (4%)
Renal tubule, carcinoma		1 (2%)		
Urinary bladder	(51)	(51)	(50)	(51)
Systemic Lesions				
Multiple organs[a]	(51)	(51)	(50)	(51)
Histiocytic sarcoma		1 (2%)	1 (2%)	
Leukemia mononuclear	25 (49%)	25 (49%)	27 (54%)	29 (57%)
Mesothelioma malignant	1 (2%)	2 (4%)		

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Tumor Summary				
Total animals with primary neoplasms[b]	50	50	50	51
Total primary neoplasms	144	154	155	163
Total animals with benign neoplasms	47	48	48	49
Total benign neoplasms	105	115	112	117
Total animals with malignant neoplasms	31	37	35	38
Total malignant neoplasms	39	39	42	44
Total animals with secondary neoplasms[c]	1	1	3	
Total secondary neoplasms	7	1	8	
Total animals with neoplasms uncertain-benign or malignant			1	2
Total uncertain neoplasms			1	2

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

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

Number of Days on Study	3 1 5	3 6 1	4 4 6	4 5 1	4 6 5	5 1 3	5 1 6	5 3 7	5 3 9	5 4 1	5 6 9	5 7 0	5 7 8	5 9 1	5 9 8	5 9 8	6 0 5	6 0 6	6 1 8	6 1 8	6 2 6	6 3 8	6 5 2	6 5 9	6 6 7	6 7 4
Carcass ID Number	1 1 0 1	0 0 1 1	0 0 5 1	0 0 7 1	1 1 3 1	0 0 4 1	1 1 2 1	1 1 1 1	0 0 3 1	1 0 3 2	1 0 9 1	1 0 9 2	0 0 2 1	0 0 4 2	1 1 0 2	1 1 0 3	0 0 2 2	0 0 1 2	1 1 1 2	1 1 2 2	0 0 2 3	1 1 1 3	0 1 4 3	1 1 2 3	0 0 5 2	0 0 5 3
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																										
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																								X		
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																										
Mesentery	+	+			+		+		+	+			+	+		+	+				+		+	+		+
Osteosarcoma, metastatic, bone													X													
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																										
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth						+														+						
Cardiovascular System																										
Blood vessel																					+					+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																										
Pheochromocytoma benign														X									X		
Bilateral, pheochromocytoma benign										X								X							X	X
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X									
Carcinoma																										
Parathyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma				X					X	X	X	X			X			X	X	X		X		X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma										X	X		X													
C-cell, carcinoma																X										

+: 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 Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	6 7 4	6 7 5	6 8 7	6 9 4	6 9 5	6 9 7	7 1 0	7 1 0	7 1 5	7 2 6	7 2 6	7 2 9	7 2 9	7 2 9	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 0 5 4	0 0 3 2	1 1 2 4	1 0 9 3	1 1 3 5	1 1 2 5	0 0 1 3	0 0 3 3	0 0 3 4	1 0 9 4	1 1 1 4	0 0 2 4	0 0 2 5	0 0 3 5	0 0 1 4	0 0 1 5	0 0 4 4	0 0 4 5	0 0 5 5	0 1 9 5	1 1 0 4	1 1 0 5	1 1 1 5	1 1 3 3	1 1 3 4	**Total Tissues/ Tumors**
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenocarcinoma																							X		1
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenocarcinoma																									1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular adenoma			X															X							2
Mesentery	+	+	+	+	+	+	+	+	+			+		+		+	+	+		+	+			+	31
Osteosarcoma, metastatic, bone																									1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Acinar cell, adenoma								X					X								X			X	4
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tooth																									2
Cardiovascular System																									
Blood vessel															+			+					+		5
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																									1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma malignant		X		X																					2
Pheochromocytoma benign						X	X	X	X	X				X			X					X			X	11
Bilateral, pheochromocytoma benign	X										X	X				X		X			X		X	X		12
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma	X		X														X				X				5
Carcinoma		X									X														2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma		X	X				X			X	X				X		X				X				20
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
C-cell, adenoma							X		X															X	6
C-cell, carcinoma																									1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	3 1 5	3 6 1	4 4 6	4 5 1	4 6 5	5 1 3	5 1 6	5 3 7	5 3 9	5 4 1	5 6 9	5 7 0	5 7 8	5 9 1	5 9 8	5 9 8	6 0 5	6 0 6	6 1 8	6 1 8	6 2 6	6 3 8	6 5 2	6 5 9	6 6 7	6 7 4
Carcass ID Number	1 1 0 1	0 0 1 1	0 0 5 1	0 0 7 1	1 1 3 1	0 1 4 1	1 1 2 1	1 1 1 1	0 1 3 1	1 1 3 2	1 0 9 1	1 0 9 2	0 0 2 1	0 1 4 2	1 1 0 2	1 1 0 2	0 0 2 3	0 0 1 2	1 1 1 2	1 1 2 2	0 1 1 3	1 0 4 3	0 1 2 3	1 0 5 2	0 0 5 3	0 0 5 3
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Adenoma					X																					
Carcinoma								X																		
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Bilateral, interstitial cell, adenoma								X					X			X	X	X				X			X
Interstitial cell, adenoma			X							X				X							X				
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Thymus	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma										X																
Fibroadenoma																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																										
Papilloma squamous																										
Squamous cell carcinoma																										X
Subcutaneous tissue, fibrosarcoma					X																					
Subcutaneous tissue, lipoma																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	6 7 4	6 7 5	6 8 7	6 9 4	6 9 5	6 9 7	7 1 0	7 1 0	7 1 5	7 2 6	7 2 6	7 2 9	7 2 9	7 2 9	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 0 5 4	0 0 3 2	1 1 2 4	1 0 9 3	1 1 3 5	1 1 2 5	0 0 1 3	0 0 3 3	0 0 3 4	1 0 9 4	1 1 1 4	0 0 2 4	0 0 2 4	0 0 3 5	0 0 1 4	0 0 1 5	0 0 4 4	0 0 4 5	0 0 5 5	0 1 9 5	1 1 0 4	1 1 0 5	1 1 1 5	1 1 3 3	1 1 3 4	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma									X										X							3
Carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																										1
Bilateral, interstitial cell, adenoma	X	X		X	X	X		X	X	X		X	X		X	X		X	X	X		X	X	X	X	26
Interstitial cell, adenoma							X							X							X					7
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																										1
Thymus	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Integumentary System																										
Mammary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	48
Adenoma																										1
Fibroadenoma															X							X				2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Keratoacanthoma			X			X																X				3
Papilloma squamous																X										1
Squamous cell carcinoma																										1
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, lipoma											X															1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	3 1 5	3 6 1	4 4 6	4 5 1	4 6 5	5 1 3	5 1 6	5 3 7	5 3 9	5 4 1	5 6 9	5 7 0	5 7 8	5 9 1	5 9 8	5 9 8	6 0 5	6 0 6	6 1 8	6 1 8	6 2 6	6 3 8	6 5 2	6 5 9	6 6 7	6 7 4
Carcass ID Number	1 1 0 1	0 0 1 1	0 0 5 1	0 0 7 1	1 1 3 1	0 1 4 1	1 1 2 1	1 1 1 1	0 1 3 1	1 1 3 2	1 0 9 1	1 0 9 2	0 0 2 1	0 0 4 2	1 1 0 2	1 1 0 2	0 0 2 3	0 0 1 2	1 1 1 2	1 1 2 2	0 1 2 3	1 0 1 3	0 1 4 3	1 0 2 3	0 0 5 2	0 0 5 3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma													X													
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																										X
Osteosarcoma, metastatic, bone													X													
Mediastinum, osteosarcoma, metastatic, bone													X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Ear																										
Eye															+				+	+						
Zymbal's gland						+																				
Carcinoma						X																				
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Urethra																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X	X						X		X	X			X		X	X		X							
Mesothelioma malignant																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	6 7 4	6 7 5	6 8 7	6 9 4	6 9 5	6 9 7	7 1 0	7 1 0	7 1 5	7 2 6	7 2 6	7 2 9	7 2 9	7 2 9	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 0 5 4	0 0 3 2	1 1 2 4	1 0 9 3	1 1 3 5	1 1 2 5	0 0 1 3	0 0 3 3	0 0 3 4	1 0 9 4	1 1 1 4	0 0 2 4	0 0 2 5	0 0 3 5	0 0 1 4	0 0 1 5	0 0 4 4	0 0 4 5	0 0 4 5	0 0 5 5	1 0 9 5	1 1 0 4	1 1 0 5	1 1 1 5	1 1 3 3	1 1 3 4	**Total Tissues/ Tumors**
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Glioma malignant	X																									1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Alveolar/bronchiolar adenoma																										1
Osteosarcoma, metastatic, bone																										1
Mediastinum, osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																										
Ear																	+									1
Eye																			+		+					5
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																										1
Urethra			+																							1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Leukemia mononuclear	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X									25
Mesothelioma malignant								X																		1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 70 ppm

Number of Days on Study	0 5 4	3 0 6	3 8 5	4 3 5	4 9 0	4 9 3	5 0 3	5 0 6	5 2 3	5 2 7	5 4 0	5 4 7	5 6 9	5 8 1	5 9 0	5 9 1	5 9 6	5 9 7	6 1 4	6 1 4	6 1 8	6 1 9	6 2 5	6 2 6	6 3 8	6 3 9
Carcass ID Number	1 5 3 1	1 5 7 1	1 5 1 1	1 5 4 1	1 5 3 2	0 4 4 1	0 4 7 1	1 5 1 2	1 5 2 1	1 5 5 1	0 4 3 1	0 4 7 2	0 4 4 2	0 4 7 3	0 4 4 1	0 4 5 2	0 4 3 3	0 4 4 3	1 5 3 3	0 4 7 4	1 5 1 3	0 4 7 5	1 5 3 4	0 4 5 2	0 4 5 3	1 5 3 5	1 5 5 2
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																					X					
Hepatocellular adenoma, multiple																										
Histiocytic sarcoma				X																						
Mesentery				+		+		+	+	+	+	+	+		+				+			+		+	+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																										
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																										
Cardiovascular System																										
Blood vessel										+					+											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																						
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																										
Pheochromocytoma benign									X			X							X			X	X	X	X	
Bilateral, pheochromocytoma malignant																										
Bilateral, pheochromocytoma benign															X											
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma													X						X	X	X					
Parathyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X				X						X		X		X			X		X				X
Thyroid gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, C-cell, adenoma																				X						
C-cell, adenoma																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	6 5 3	6 5 4	6 6 8	6 6 8	6 6 8	6 7 5	6 7 5	6 7 5	6 7 6	6 7 6	6 8 0	6 9 0	7 1 6	7 1 8	7 1 9	7 1 9	7 1 9	7 2 0	7 2 1	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	
Carcass ID Number	1 5 4 2	1 5 1 4	0 4 3 3	1 5 4 3	1 5 5 3	0 4 4 4	0 4 6 1	0 4 6 2	1 5 2 2	1 5 2 3	0 4 5 4	0 4 6 3	0 4 5 5	1 5 1 5	1 5 4 4	1 5 5 4	1 5 5 4	0 4 6 4	1 5 2 4	0 4 3 4	0 4 4 5	0 4 4 5	0 4 6 5	1 5 2 5	1 5 4 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular adenoma																										1
Hepatocellular adenoma, multiple								X																		1
Histiocytic sarcoma																										1
Mesentery	+				+				+	+	+		+	+	+		+		+	+			+			25
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Acinar cell, adenoma					X													X				X			X	4
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tongue														+												1
Cardiovascular System																										
Blood vessel														+												3
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma malignant																X										1
Pheochromocytoma benign			X	X					X							X					X			X		13
Bilateral, pheochromocytoma malignant										X												X				2
Bilateral, pheochromocytoma benign	X	X			X									X	X		X	X					X		X	10
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma																X	X							X		7
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma				X	X	X	X			X		X				X	X	X					X	X	X	20
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, C-cell, adenoma																										1
C-cell, adenoma				X	X	X													X		X	X				6

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	0 5 4	3 0 6	3 8 5	4 3 5	4 9 0	4 9 3	5 0 3	5 0 6	5 2 3	5 2 7	5 4 0	5 4 7	5 6 9	5 8 1	5 9 0	5 9 1	5 9 6	5 9 7	6 1 4	6 1 4	6 1 8	6 1 9	6 2 5	6 2 6	6 3 8	6 3 9
Carcass ID Number	1 5 3 1	1 5 7 1	1 5 1 1	1 5 4 1	1 5 3 2	0 4 4 1	0 4 7 1	1 5 1 2	1 5 2 1	1 5 5 1	0 4 3 1	0 4 7 2	0 4 4 2	0 4 7 3	0 4 5 1	0 4 3 2	0 5 3 3	0 4 4 3	1 5 3 3	0 4 7 4	1 5 1 3	0 4 7 5	1 5 3 4	0 4 5 2	0 4 5 3	1 5 3 5	1 5 5 2
General Body System																										
Tissue NOS										+									+							
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																			X						X	
Carcinoma																										X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma									X					X					X			X		X		X
Interstitial cell, adenoma				X	X			X		X	X					X		X		X	X		X		X	
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																						
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic, histiocytic sarcoma				X																						
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																						
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+
Thymoma malignant																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																										
Keratoacanthoma																			X					X		
Papilloma squamous				X															X							
Trichoepithelioma										X																
Subcutaneous tissue, fibroma																			X							

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	6 5 3	6 5 4	6 6 8	6 6 8	6 6 8	6 7 5	6 7 5	6 7 5	6 7 6	6 7 6	6 8 0	6 9 0	7 1 6	7 1 8	7 1 9	7 1 9	7 1 9	7 2 0	7 2 1	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	
Carcass ID Number	1 5 4 2	1 5 1 4	0 4 3 3	1 5 4 3	1 5 5 3	0 4 4 4	0 4 6 1	0 4 6 2	1 5 2 2	1 5 2 3	0 4 5 4	0 4 6 3	0 4 5 5	1 5 1 5	1 5 4 4	1 5 5 4	1 5 5 5	0 4 6 4	1 5 2 4	0 4 3 4	0 4 3 5	0 4 4 5	0 4 6 5	1 5 2 5	1 5 4 5	**Total Tissues/ Tumors**
General Body System																									
Tissue NOS																									2
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma																									2
Carcinoma				X								X													3
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Bilateral, interstitial cell, adenoma	X	X	X	X		X	X	X	X	X	X	X			X		X	X	X	X	X	X	X			26
Interstitial cell, adenoma													X	X		X								X		15
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																									1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pancreatic, histiocytic sarcoma																									1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																									1
Thymus	M	+	+	+	+	M	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	M	+	44
Thymoma malignant																			X							1
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Basal cell carcinoma																						X			1
Keratoacanthoma																X									3
Papilloma squamous																									2
Trichoepithelioma																									1
Subcutaneous tissue, fibroma								X									X								3

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	0 5 4	3 0 6	3 8 5	4 3 5	4 9 0	4 9 3	5 0 3	5 0 6	5 2 3	5 2 7	5 4 0	5 4 7	5 6 9	5 8 1	5 9 0	5 9 1	5 9 6	5 9 7	6 1 4	6 1 4	6 1 8	6 1 9	6 2 5	6 2 6	6 3 8	6 3 9
Carcass ID Number	1 5 3 1	1 5 7 1	1 5 1 1	1 5 4 1	1 5 3 2	0 4 4 1	0 4 7 1	1 5 1 2	1 5 2 1	1 5 5 1	0 4 3 1	0 4 7 2	0 4 4 2	0 4 7 3	0 4 5 1	0 4 3 2	0 4 4 3	0 5 3 3	1 5 4 3	0 4 7 4	1 5 1 3	0 4 7 5	1 5 4 4	0 4 3 2	0 4 5 3	1 5 3 5	1 5 5 2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																			+							
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant		X																								
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																						
Thymoma malignant, metastatic, thymus																										
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Eye																										
Urinary System																										
Kidney	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pelvis, transitional epithelium, carcinoma					X																					
Renal tubule, carcinoma																										
Urethra										+																
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																						
Leukemia mononuclear						X	X	X	X		X	X	X	X		X					X	X		X	X	
Mesothelioma malignant										X									X							

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	6 5 3	6 5 4	6 6 8	6 6 8	6 6 8	6 7 5	6 7 5	6 7 5	6 7 6	6 7 6	6 8 0	6 9 0	7 1 6	7 1 8	7 1 9	7 1 9	7 1 9	7 2 0	7 2 1	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	
Carcass ID Number	1 5 4 2	1 5 1 4	0 4 3 3	1 5 4 3	1 5 5 3	0 4 4 4	0 4 6 1	0 4 6 2	1 5 2 2	1 5 2 3	0 4 5 4	0 4 6 3	0 4 5 5	1 5 1 5	1 5 4 4	1 5 5 4	1 5 5 5	1 5 5 5	0 4 6 4	1 5 2 4	0 4 3 4	0 4 3 5	0 4 4 5	0 4 6 5	1 5 2 5	1 5 4 5	**Total Tissues/ Tumors**
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Skeletal muscle																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Glioma malignant																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																										1
Thymoma malignant, metastatic, thymus																			X							1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																										
Eye			+	+												+		I								3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pelvis, transitional epithelium, carcinoma																										1
Renal tubule, carcinoma		X																								1
Urethra																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																										1
Leukemia mononuclear	X	X	X			X	X	X	X				X				X			X			X	X		25
Mesothelioma malignant																										2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 140 ppm

Number of Days on Study	3 6 5	3 7 2	4 6 6	4 9 8	5 2 4	5 2 9	5 4 0	5 8 3	5 9 0	5 9 1	6 1 4	6 1 4	6 3 8	6 3 9	6 3 9	6 4 1	6 4 5	6 4 5	6 5 3	6 5 6	6 6 0	6 6 8	6 6 9	6 7 3	6 7 5
Carcass ID Number	1 4 4 1	1 4 4 2	0 4 0 1	0 3 8 1	1 4 7 1	0 3 9 1	1 4 6 1	1 4 4 3	0 3 7 1	0 3 8 2	1 4 4 4	1 4 4 1	1 4 8 2	1 4 8 5	1 4 4 5	1 4 5 5	0 3 7 2	0 3 6 1	0 4 0 2	1 4 6 2	0 3 8 3	1 4 5 1	0 3 7 3	1 4 6 3	0 4 3 4	0 4 0 3
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liposarcoma																										
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangioma																										
Hepatocellular adenoma																										
Hepatocellular adenoma, two, multiple																						X				
Histiocytic sarcoma								X																		
Mesentery	+	+		+			+			+			+				+			+	+	+	+	+		
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma, multiple																										
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous											X															
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																										
Blood vessel											+										+					
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant							X																			
Pheochromocytoma complex																										
Pheochromocytoma benign														X				X		X			X		X	
Bilateral, pheochromocytoma benign											X				X						X					
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma											X															
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pars distalis, adenoma							X	X			X	X	X		X	X	X	X			X	X	X	X		
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																							X		X	
C-cell, carcinoma																	X									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	6 7 6	6 8 0	6 8 4	7 1 1	7 1 1	7 1 8	7 1 8	7 1 9	7 1 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	
Carcass ID Number	1 4 7 2	0 3 6 2	1 4 7 3	0 3 6 3	0 3 7 4	1 4 5 2	1 4 6 4	1 4 7 4	1 4 7 5	1 3 9 2	0 3 2 3	1 4 5 4	1 4 5 5	1 4 6 5	0 3 6 4	0 3 6 5	0 3 7 5	0 3 8 5	1 4 8 3	1 4 8 4	1 4 8 5	1 4 0 4	0 4 0 5	0 4 9 3	0 4 9 4	0 3 9 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liposarcoma	X																									1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cholangioma																X										1
Hepatocellular adenoma		X										X				X										3
Hepatocellular adenoma, two, multiple																										1
Histiocytic sarcoma																										1
Mesentery		+				+					+	+														16
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell, adenoma, multiple																							X			1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous																								X		2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel							+												+					+		5
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																										1
Pheochromocytoma complex						X																				1
Pheochromocytoma benign							X			X						X	X		X		X					11
Bilateral, pheochromocytoma benign	X		X					X	X						X			X							X	10	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma								X																		2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma			X	X	X	X								X		X								X		20
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma		X												X												4
C-cell, carcinoma				X																						2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	3 6 5	3 7 2	4 6 6	4 9 8	5 2 4	5 2 9	5 4 0	5 8 3	5 9 0	5 9 1	6 1 4	6 1 4	6 3 8	6 3 9	6 3 9	6 4 1	6 4 5	6 4 5	6 5 3	6 5 6	6 6 0	6 6 8	6 6 9	6 7 3	6 7 5
Carcass ID Number	1 4 4 1	1 4 4 2	0 4 0 1	0 3 8 1	1 4 7 1	0 3 9 1	1 4 6 1	1 4 4 3	0 3 7 1	0 3 8 2	1 4 4 4	1 4 8 1	1 4 8 2	1 4 4 5	1 4 5 5	1 4 5 2	0 3 7 1	0 3 6 2	0 4 0 2	1 4 6 2	0 3 8 3	1 4 5 1	0 3 7 3	1 4 6 3	0 3 8 4	0 4 0 3
General Body System																									
Tissue NOS	+																								
Carcinoma, metastatic, lung	X																								
Genital System																									
Coagulating gland											+														
Ductus deferens																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis																		+							
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Adenoma																									
Carcinoma														X	X										
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma					X			X	X		X			X	X				X	X			X		X
Interstitial cell, adenoma			X	X		X				X							X	X				X		X	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																	
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Deep cervical, carcinoma, metastatic, thyroid gland																									
Mediastinal, carcinoma, metastatic, lung	X																								
Mediastinal, carcinoma, metastatic, thyroid gland																									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																	
Thymus	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma													X												
Keratoacanthoma												X										X			
Keratoacanthoma, two, multiple																									
Papilloma squamous																									
Squamous cell carcinoma																									
Subcutaneous tissue, fibroma																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	6 7 6	6 8 0	6 8 4	7 1 1	7 1 1	7 1 8	7 1 8	7 1 9	7 1 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	
Carcass ID Number	1 4 7 2	0 3 6 2	1 4 7 3	0 3 6 3	0 3 7 4	1 4 5 2	1 4 6 4	1 4 7 4	1 4 7 5	1 3 9 2	0 4 5 3	1 4 5 4	1 4 4 5	1 4 6 5	0 3 6 4	0 3 6 5	0 3 7 5	0 3 8 5	1 4 8 3	1 4 8 4	1 4 8 5	1 4 0 4	0 4 0 5	0 4 9 3	0 3 9 4	0 3 9 5	**Total Tissues/ Tumors**
General Body System																										
Tissue NOS																										1
Carcinoma, metastatic, lung																										1
Genital System																										
Coagulating gland																										1
Ductus deferens							+																			1
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Penis																										1
Preputial gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	47
Adenoma	X																									1
Carcinoma																										2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X	X			X		X	X	X	X	X	X	X	X		X		X	X	X	X	X	X	X	X	30
Interstitial cell, adenoma			X	X											X		X									12
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Deep cervical, carcinoma, metastatic, thyroid gland				X																						1
Mediastinal, carcinoma, metastatic, lung																										1
Mediastinal, carcinoma, metastatic, thyroid gland				X																						1
Lymph node, mandibular	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Thymus	M	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	42
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma						X																				2
Keratoacanthoma	X																									3
Keratoacanthoma, two, multiple			X																							1
Papilloma squamous							X										X									2
Squamous cell carcinoma				X																						1
Subcutaneous tissue, fibroma			X																							1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	3 6 5	3 7 2	4 6 6	4 9 8	5 2 4	5 2 9	5 4 0	5 8 3	5 9 0	5 9 1	6 1 4	6 1 4	6 3 8	6 3 9	6 3 9	6 4 1	6 4 5	6 4 5	6 5 3	6 5 6	6 6 0	6 6 8	6 6 9	6 7 3	6 7 5
Carcass ID Number	1 4 4 1	1 4 4 2	0 4 0 1	0 3 8 1	1 4 7 1	0 3 9 1	1 4 6 1	1 4 4 3	0 3 7 1	0 3 8 2	1 4 4 4	1 4 4 1	1 4 8 2	1 4 4 5	1 4 5 5	1 4 5 2	0 3 7 1	0 3 6 2	0 4 0 2	1 4 6 2	0 3 8 3	1 4 5 1	0 3 7 3	1 4 6 3	0 3 4 4	0 4 0 3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+							+																		
Carcinoma, metastatic, lung	X																									
Histiocytic sarcoma								X																		
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																										
Alveolar/bronchiolar carcinoma																				X						
Carcinoma	X																									
Mediastinum, alveolar/-bronchiolar carcinoma, metastatic, lung																				X						
Mediastinum, carcinoma, metastatic, lung	X																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Ear											+															
Pinna, papilloma squamous											X															
Eye																	+								+	
Lids, schwannoma NOS																									X	
Zymbal's gland												+									+					
Adenoma																										
Carcinoma												X									X					
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, lung	X																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	6 7 6	6 8 0	6 8 4	7 1 1	7 1 1	7 1 8	7 1 8	7 1 9	7 1 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	
Carcass ID Number	1 4 7 2	0 3 6 2	1 4 7 3	0 3 6 3	0 3 7 4	1 4 5 2	1 4 6 4	1 4 7 4	1 4 7 5	0 3 9 2	1 4 5 3	1 4 5 4	1 4 6 5	0 3 6 4	0 3 6 5	0 3 7 5	0 3 8 5	1 4 8 3	1 4 8 4	1 4 8 5	0 4 0 4	0 4 0 5	0 4 9 3	0 3 9 4	0 3 9 5	**Total Tissues/ Tumors**
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle							+																		3
Carcinoma, metastatic, lung																									1
Histiocytic sarcoma																									1
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma	X										X						X							X	4
Alveolar/bronchiolar carcinoma																									1
Carcinoma																									1
Mediastinum, alveolar/-bronchiolar carcinoma, metastatic, lung																									1
Mediastinum, carcinoma, metastatic, lung																									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																									
Ear														+											2
Pinna, papilloma squamous														X											2
Eye										+															3
Lids, schwannoma NOS																									1
Zymbal's gland		+																							3
Adenoma		X																							1
Carcinoma																									2
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, lung																									1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																									1
Leukemia mononuclear		X	X			X		X	X		X	X		X		X	X						X		27

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 275 ppm

Number of Days on Study	3 9 6	4 1 5	5 0 1	5 2 0	5 2 2	5 3 3	5 4 7	5 5 0	5 9 1	6 0 0	6 0 5	6 1 4	6 1 8	6 2 2	6 2 4	6 3 5	6 4 5	6 4 5	6 5 2	6 5 2	6 5 3	6 5 4	6 6 1	6 6 8	6 6 9	6 8 5
Carcass ID Number	0 3 0 1	1 4 3 1	1 4 0 1	1 3 8 1	1 3 9 1	1 3 9 2	1 4 0 2	1 4 1 1	0 3 3 1	1 3 7 4	0 3 2 1	0 2 9 1	0 3 0 2	0 3 1 1	0 4 1 3	1 2 0 4	0 3 9 2	0 4 1 2	1 2 9 2	0 3 0 3	1 3 3 1	1 3 3 2	0 3 3 2	0 3 0 4	1 4 0 4	1 3 0 3
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																										
Hepatocellular adenoma																										
Mesentery	+	+		+		+				+	+	+				+			+			+	+	+	+	
Sarcoma						X																				
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																										
Pharynx																	+									
Palate, papilloma squamous																	X									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																										
Papilloma squamous																										
Tooth									+																	
Gingiva, squamous cell carcinoma									X																	
Cardiovascular System																										
Blood vessel																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																			X							
Pheochromocytoma benign					X								X	X					X		X			X		
Bilateral, pheochromocytoma benign							X																			
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																		X			X			X		
Adenoma, multiple																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	6 8 7	6 9 0	6 9 0	6 9 0	6 9 7	7 0 8	7 1 9	7 2 1	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	1 3 7 2	0 2 9 3	0 3 0 5	0 3 2 2	1 4 1 5	1 4 1 3	1 4 0 5	1 3 9 3	1 3 7 3	1 3 7 5	1 3 8 4	1 3 8 5	1 3 9 4	1 3 9 5	1 4 1 4	1 4 2 5	0 9 1 3	0 3 3 4	0 3 3 4	0 3 3 5	0 3 3 5	0 3 3 3	0 3 3 4	0 3 3 5	0 3 3 3	0 3 3 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular carcinoma														X												1
Hepatocellular adenoma							X												X							2
Mesentery		+	+									+	+				+		+	+						20
Sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Acinar cell, adenoma									X																	1
Pharynx																										1
Palate, papilloma squamous																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tongue																			+							1
Papilloma squamous																			X							1
Tooth																										1
Gingiva, squamous cell carcinoma																										1
Cardiovascular System																										
Blood vessel											+								+							2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma malignant								X						X												3
Pheochromocytoma benign	X					X				X			X			X					X	X				13
Bilateral, pheochromocytoma benign							X				X	X			X								X		X	7
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma	X			X							X															6
Adenoma, multiple								X																		1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	3 9 6	4 1 5	5 0 1	5 2 0	5 2 2	5 3 3	5 4 7	5 5 0	5 9 1	6 0 0	6 0 5	6 1 4	6 1 8	6 2 2	6 2 4	6 3 5	6 4 5	6 4 5	6 5 2	6 5 2	6 5 3	6 5 4	6 6 1	6 6 8	6 6 9	6 8 5
Carcass ID Number	0 3 0 1	1 4 3 1	1 4 0 1	1 3 8 1	1 3 9 1	1 3 9 2	1 4 0 2	1 4 1 1	0 3 3 1	1 3 7 4	0 3 2 1	0 2 9 1	0 3 0 2	0 3 3 1	1 4 0 3	0 2 9 4	0 3 1 2	0 4 1 2	1 2 9 2	0 3 0 3	0 3 7 1	1 3 8 2	1 3 3 2	0 3 0 4	0 3 0 4	1 4 4 3	1 3 8 3
Endocrine System (continued)																										
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma						X																				
Pars distalis, adenoma									X				X	X			X	X			X				X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma							X														X					
C-cell, carcinoma																										
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma				X																						
Carcinoma										X																
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					X							
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma													X													
Keratoacanthoma				X																						X
Papilloma squamous																										
Squamous cell carcinoma																										
Subcutaneous tissue, fibroma		X																				X				
Subcutaneous tissue, hemangioma				X																						
Subcutaneous tissue, lipoma																						X				
Subcutaneous tissue, sarcoma							X																			

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	6 8 7	6 9 0	6 9 0	6 9 0	6 9 7	7 0 8	7 1 9	7 2 1	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	1 3 7 2	0 2 9 3	0 3 0 5	0 3 2 2	1 4 1 5	1 4 1 3	1 4 0 5	1 3 9 3	1 3 7 3	1 3 7 5	1 3 8 4	1 3 8 5	1 3 9 4	1 3 9 5	1 4 1 4	0 2 9 5	0 3 1 3	0 3 1 4	0 3 1 5	0 3 2 3	0 3 2 4	0 3 2 5	0 3 3 3	0 3 3 4	0 3 3 5	**Total Tissues/ Tumors**
Endocrine System (continued)																										
Parathyroid gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma																										1
Pars distalis, adenoma	X	X		X			X	X	X		X	X	X								X	X		X	X	20
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
C-cell, adenoma														X										X		4
C-cell, carcinoma															X											1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma															X				X							3
Carcinoma				X																						2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Bilateral, interstitial cell, adenoma	X		X	X	X	X			X	X	X	X		X	X	X	X	X	X	X	X		X	X		30
Interstitial cell, adenoma		X					X																		X	8
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibroadenoma							X					X								X						3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Basal cell carcinoma																										1
Keratoacanthoma						X																				3
Papilloma squamous									X																X	2
Squamous cell carcinoma													X						X							2
Subcutaneous tissue, fibroma						X																				3
Subcutaneous tissue, hemangioma																										1
Subcutaneous tissue, lipoma																										1
Subcutaneous tissue, sarcoma																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	3	4	5	5	5	5	5	5	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	9	1	0	2	2	3	4	5	9	0	0	1	1	2	2	3	4	4	5	5	5	5	6	6	8
	6	5	1	0	2	3	7	0	1	0	5	4	8	2	4	5	5	5	2	2	3	4	1	8	9	5
Carcass ID Number	0	1	1	1	1	1	1	1	0	1	0	0	0	0	1	0	0	1	0	0	1	1	0	0	1	1
	3	4	4	3	3	3	4	4	3	3	3	2	3	3	4	2	3	4	2	3	3	3	3	3	4	3
	0	3	0	8	9	9	0	1	3	7	2	9	0	1	0	9	1	1	9	0	7	8	3	0	0	8
	1	1	1	1	1	2	2	1	1	4	1	1	2	1	3	4	2	2	2	3	1	2	2	4	4	3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma benign																										
Meningioma NOS																	X									
Spinal cord														+												
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma				X																						
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Ear																										
Schwannoma NOS																										
Zymbal's gland					+			+				+														
Adenoma								X																		
Carcinoma					X																					
Mixed tumor malignant												X														
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	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 Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	6 8 7	6 9 0	6 9 0	6 9 0	6 9 7	7 0 8	7 1 9	7 2 1	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2		
Carcass ID Number	1 3 7 2	0 2 9 3	0 3 0 5	0 3 2 2	1 4 1 5	1 4 1 3	1 4 0 5	1 3 9 3	1 3 7 3	1 3 7 5	1 3 8 4	1 3 8 5	1 3 9 4	1 3 9 5	1 4 1 4	0 2 9 5	0 3 1 3	0 3 1 4	0 3 1 5	0 3 2 3	0 3 2 4	0 3 2 5	0 3 3 3	0 3 3 4	0 3 3 5	**Total Tissues/ Tumors**
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Nervous System																										
Brain	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glioma benign												X														1
Meningioma NOS																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Alveolar/bronchiolar adenoma									X																	2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																										
Ear																			+							1
Schwannoma NOS																			X							1
Zymbal's gland																										3
Adenoma																										1
Carcinoma																										1
Mixed tumor malignant																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Renal tubule, adenoma											X											X				2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Leukemia mononuclear	X	X	X		X	X	X	X	X	X	X								X	X		X			X	29

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

	0 ppm	70 ppm	140 ppm	275 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rates[a]	23/51 (45%)	23/51 (45%)	21/49 (43%)	20/51 (39%)
Adjusted rates[b]	84.2%	88.6%	69.9%	70.8%
Terminal rates[c]	10/14 (71%)	4/6 (67%)	8/16 (50%)	10/17 (59%)
First incidence (days)	541	523	614	522
Life table tests[d]	P=0.052N	P=0.076	P=0.268N	P=0.186N
Logistic regression tests[d]	P=0.102N	P=0.380	P=0.276N	P=0.196N
Cochran-Armitage test[d]	P=0.282N			
Fisher exact test[d]		P=0.579N	P=0.490N	P=0.344N
Adrenal Medulla: Malignant Pheochromocytoma				
Overall rates	2/51 (4%)	3/51 (6%)	1/49 (2%)	3/51 (6%)
Adjusted rates	8.5%	28.7%	2.3%	13.8%
Terminal rates	0/14 (0%)	1/6 (17%)	0/16 (0%)	1/17 (6%)
First incidence (days)	675	676	540	652
Life table tests	P=0.579N	P=0.309	P=0.485N	P=0.542
Logistic regression tests	P=0.531	P=0.400	P=0.522N	P=0.540
Cochran-Armitage test	P=0.476			
Fisher exact test		P=0.500	P=0.515N	P=0.500
Adrenal Medulla: Pheochromocytoma (Benign, Complex, Malignant)				
Overall rates	25/51 (49%)	25/51 (49%)	23/49 (47%)	22/51 (43%)
Adjusted rates	85.5%	94.7%	72.1%	76.4%
Terminal rates	10/14 (71%)	5/6 (83%)	8/16 (50%)	11/17 (65%)
First incidence (days)	541	523	540	522
Life table tests	P=0.049N	P=0.063	P=0.270N	P=0.188N
Logistic regression tests	P=0.090N	P=0.361	P=0.279N	P=0.177N
Cochran-Armitage test	P=0.284N			
Fisher exact test		P=0.578N	P=0.497N	P=0.346N
Liver: Hepatocellular Adenoma				
Overall rates	2/51 (4%)	2/51 (4%)	4/50 (8%)	2/51 (4%)
Adjusted rates	11.2%	8.1%	19.0%	10.8%
Terminal rates	1/14 (7%)	0/6 (0%)	2/16 (13%)	1/17 (6%)
First incidence (days)	687	618	668	719
Life table tests	P=0.484N	P=0.548	P=0.378	P=0.634N
Logistic regression tests	P=0.556N	P=0.654	P=0.378	P=0.664N
Cochran-Armitage test	P=0.537			
Fisher exact test		P=0.691N	P=0.329	P=0.691N
Liver: Hepatocellular Adenoma or Hepatocellular Carcinoma				
Overall rates	2/51 (4%)	2/51 (4%)	4/50 (8%)	3/51 (6%)
Adjusted rates	11.2%	8.1%	19.0%	16.4%
Terminal rates	1/14 (7%)	0/6 (0%)	2/16 (13%)	2/17 (12%)
First incidence (days)	687	618	668	719
Life table tests	P=0.513	P=0.548	P=0.378	P=0.576
Logistic regression tests	P=0.436	P=0.654	P=0.378	P=0.543
Cochran-Armitage test	P=0.352			
Fisher exact test		P=0.691N	P=0.329	P=0.500

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	1/51 (2%)	0/51 (0%)	4/50 (8%)	2/51 (4%)
Adjusted rates	3.8%	0.0%	22.0%	7.8%
Terminal rates	0/14 (0%)	0/6 (0%)	3/16 (19%)	1/17 (6%)
First incidence (days)	674	–[e]	676	520
Life table tests	P=0.346	P=0.552N	P=0.211	P=0.532
Logistic regression tests	P=0.273	P=0.522N	P=0.206	P=0.496
Cochran-Armitage test	P=0.231			
Fisher exact test		P=0.500N	P=0.175	P=0.500
Lung: Alveolar/bronchiolar Adenoma or Alveolar/bronchiolar Carcinoma				
Overall rates	1/51 (2%)	0/51 (0%)	6/50 (12%)	2/51 (4%)
Adjusted rates	3.8%	0.0%	26.0%	7.8%
Terminal rates	0/14 (0%)	0/6 (0%)	3/16 (19%)	1/17 (6%)
First incidence (days)	674	–	365	520
Life table tests	P=0.325	P=0.552N	P=0.078	P=0.532
Logistic regression tests	P=0.222	P=0.522N	P=0.056	P=0.496
Cochran-Armitage test	P=0.219			
Fisher exact test		P=0.500N	P=0.053	P=0.500
Mammary Gland: Fibroadenoma				
Overall rates	2/51 (4%)	0/51 (0%)	0/50 (0%)	3/51 (6%)
Adjusted rates	14.3%	0.0%	0.0%	16.4%
Terminal rates	2/14 (14%)	0/6 (0%)	0/16 (0%)	2/17 (12%)
First incidence (days)	729 (T)	–	–	719
Life table tests	P=0.381	P=0.437N	P=0.207N	P=0.588
Logistic regression tests	P=0.336	P=0.437N	P=0.207N	P=0.548
Cochran-Armitage test	P=0.250			
Fisher exact test		P=0.248N	P=0.252N	P=0.500
Mammary Gland: Adenoma or Fibroadenoma				
Overall rates	3/51 (6%)	0/51 (0%)	0/50 (0%)	3/51 (6%)
Adjusted rates	16.3%	0.0%	0.0%	16.4%
Terminal rates	2/14 (14%)	0/6 (0%)	0/16 (0%)	2/17 (12%)
First incidence (days)	541	–	–	719
Life table tests	P=0.583	P=0.233N	P=0.105N	P=0.583N
Logistic regression tests	P=0.510	P=0.134N	P=0.116N	P=0.623N
Cochran-Armitage test	P=0.451			
Fisher exact test		P=0.121N	P=0.125N	P=0.661N
Oral Cavity (Tongue, Pharynx, Tooth): Squamous Papilloma or Squamous Cell Carcinoma				
Overall rates	0/51 (0%)	0/51 (0%)	0/50 (0%)	3/51 (6%)
Adjusted rates	0.0%	0.0%	0.0%	10.7%
Terminal rates	0/14 (0%)	0/6 (0%)	0/16 (0%)	1/17 (6%)
First incidence (days)	–	–	–	591
Life table tests	P=0.023	–	–	P=0.156
Logistic regression tests	P=0.013	–	–	P=0.123
Cochran-Armitage test	P=0.012			
Fisher exact test		–	–	P=0.121

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Pancreas: Adenoma				
Overall rates	4/51 (8%)	4/51 (8%)	1/50 (2%)	1/51 (2%)
Adjusted rates	25.6%	44.2%	6.3%	5.9%
Terminal rates	3/14 (21%)	2/6 (33%)	1/16 (6%)	1/17 (6%)
First incidence (days)	710	668	729 (T)	729 (T)
Life table tests	P=0.033N	P=0.262	P=0.137N	P=0.132N
Logistic regression tests	P=0.043N	P=0.418	P=0.142N	P=0.144N
Cochran-Armitage test	P=0.076N			
Fisher exact test		P=0.642N	P=0.187N	P=0.181N
Pancreatic Islets: Adenoma				
Overall rates	5/51 (10%)	7/51 (14%)	2/50 (4%)	7/51 (14%)
Adjusted rates	23.4%	39.6%	7.9%	25.9%
Terminal rates	2/14 (14%)	1/6 (17%)	0/16 (0%)	1/17 (6%)
First incidence (days)	605	569	614	645
Life table tests	P=0.504N	P=0.181	P=0.187N	P=0.469
Logistic regression tests	P=0.493	P=0.319	P=0.195N	P=0.431
Cochran-Armitage test	P=0.425			
Fisher exact test		P=0.380	P=0.226N	P=0.380
Pancreatic Islets: Adenoma or Carcinoma				
Overall rates	7/51 (14%)	7/51 (14%)	2/50 (4%)	7/51 (14%)
Adjusted rates	31.2%	39.6%	7.9%	25.9%
Terminal rates	2/14 (14%)	1/6 (17%)	0/16 (0%)	1/17 (6%)
First incidence (days)	605	569	614	645
Life table tests	P=0.305N	P=0.330	P=0.071N	P=0.521N
Logistic regression tests	P=0.402N	P=0.537	P=0.066N	P=0.553N
Cochran-Armitage test	P=0.479N			
Fisher exact test		P=0.613N	P=0.085N	P=0.613N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	20/50 (40%)	20/50 (40%)	20/49 (41%)	20/51 (39%)
Adjusted rates	58.7%	79.6%	54.3%	66.1%
Terminal rates	3/13 (23%)	3/6 (50%)	3/16 (19%)	8/17 (47%)
First incidence (days)	451	385	540	591
Life table tests	P=0.208N	P=0.221	P=0.402N	P=0.373N
Logistic regression tests	P=0.409N	P=0.536	P=0.569	P=0.476N
Cochran-Armitage test	P=0.508N			
Fisher exact test		P=0.581N	P=0.548	P=0.549N
Pituitary Gland (Pars Distalis or Unspecified Site): Adenoma				
Overall rates	20/50 (40%)	20/50 (40%)	20/49 (41%)	21/51 (41%)
Adjusted rates	58.7%	79.6%	54.3%	66.8%
Terminal rates	3/13 (23%)	3/6 (50%)	3/16 (19%)	8/17 (47%)
First incidence (days)	451	385	540	533
Life table tests	P=0.261N	P=0.221	P=0.402N	P=0.437N
Logistic regression tests	P=0.503N	P=0.536	P=0.569	P=0.568N
Cochran-Armitage test	P=0.482			
Fisher exact test		P=0.581N	P=0.548	P=0.533

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Preputial Gland: Adenoma				
Overall rates	3/50 (6%)	2/51 (4%)	1/47 (2%)	3/51 (6%)
Adjusted rates	14.5%	6.6%	4.0%	13.6%
Terminal rates	1/14 (7%)	0/6 (0%)	0/15 (0%)	2/17 (12%)
First incidence (days)	465	614	676	520
Life table tests	P=0.488N	P=0.605N	P=0.279N	P=0.597N
Logistic regression tests	P=0.582	P=0.497N	P=0.326N	P=0.654N
Cochran-Armitage test	P=0.574			
Fisher exact test		P=0.491N	P=0.332N	P=0.652N
Preputial Gland: Carcinoma				
Overall rates	1/50 (2%)	3/51 (6%)	2/47 (4%)	2/51 (4%)
Adjusted rates	2.3%	14.6%	5.4%	6.4%
Terminal rates	0/14 (0%)	0/6 (0%)	0/15 (0%)	0/17 (0%)
First incidence (days)	537	639	639	600
Life table tests	P=0.580	P=0.245	P=0.556	P=0.534
Logistic regression tests	P=0.497	P=0.306	P=0.455	P=0.474
Cochran-Armitage test	P=0.499			
Fisher exact test		P=0.316	P=0.477	P=0.508
Preputial Gland: Adenoma or Carcinoma				
Overall rates	4/50 (8%)	5/51 (10%)	3/47 (6%)	5/51 (10%)
Adjusted rates	16.4%	20.3%	9.2%	19.2%
Terminal rates	1/14 (7%)	0/6 (0%)	0/15 (0%)	2/17 (12%)
First incidence (days)	465	614	639	520
Life table tests	P=0.499N	P=0.373	P=0.438N	P=0.574
Logistic regression tests	P=0.492	P=0.504	P=0.549N	P=0.495
Cochran-Armitage test	P=0.488			
Fisher exact test		P=0.513	P=0.535N	P=0.513
Skin: Keratoacanthoma				
Overall rates	3/51 (6%)	3/51 (6%)	4/50 (8%)	3/51 (6%)
Adjusted rates	15.6%	15.0%	13.6%	10.6%
Terminal rates	1/14 (7%)	0/6 (0%)	0/16 (0%)	0/17 (0%)
First incidence (days)	687	614	614	520
Life table tests	P=0.469N	P=0.485	P=0.543	P=0.614N
Logistic regression tests	P=0.561N	P=0.607	P=0.527	P=0.640N
Cochran-Armitage test	P=0.553			
Fisher exact test		P=0.661N	P=0.489	P=0.661N
Skin: Squamous Papilloma or Squamous Cell Carcinoma				
Overall rates	2/51 (4%)	2/51 (4%)	3/50 (6%)	4/51 (8%)
Adjusted rates	10.7%	5.1%	15.0%	23.5%
Terminal rates	1/14 (7%)	0/6 (0%)	1/16 (6%)	4/17 (24%)
First incidence (days)	674	435	711	729 (T)
Life table tests	P=0.357	P=0.593	P=0.567	P=0.411
Logistic regression tests	P=0.266	P=0.688N	P=0.546	P=0.376
Cochran-Armitage test	P=0.215			
Fisher exact test		P=0.691N	P=0.491	P=0.339

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Skin: Keratoacanthoma, Squamous Papilloma, Trichoepithelioma, Basal Cell Carcinoma or Squamous Cell Carcinoma				
Overall rates	5/51 (10%)	6/51 (12%)	9/50 (18%)	8/51 (16%)
Adjusted rates	25.1%	32.3%	32.2%	33.4%
Terminal rates	2/14 (14%)	1/6 (17%)	1/16 (6%)	4/17 (24%)
First incidence (days)	674	435	614	520
Life table tests	P=0.406	P=0.259	P=0.284	P=0.371
Logistic regression tests	P=0.256	P=0.465	P=0.232	P=0.328
Cochran-Armitage test	P=0.201			
Fisher exact test		P=0.500	P=0.183	P=0.277
Skin (Subcutaneous Tissue): Fibroma				
Overall rates	0/51 (0%)	3/51 (6%)	1/50 (2%)	3/51 (6%)
Adjusted rates	0.0%	16.3%	4.3%	10.0%
Terminal rates	0/14 (0%)	0/6 (0%)	0/16 (0%)	0/17 (0%)
First incidence (days)	-	614	684	415
Life table tests	P=0.223	P=0.093	P=0.500	P=0.133
Logistic regression tests	P=0.161	P=0.103	P=0.512	P=0.093
Cochran-Armitage test	P=0.164			
Fisher exact test		P=0.121	P=0.495	P=0.121
Skin (Subcutaneous Tissue): Fibroma or Fibrosarcoma				
Overall rates	1/51 (2%)	3/51 (6%)	1/50 (2%)	3/51 (6%)
Adjusted rates	2.1%	16.3%	4.3%	10.0%
Terminal rates	0/14 (0%)	0/6 (0%)	0/16 (0%)	0/17 (0%)
First incidence (days)	465	614	684	415
Life table tests	P=0.384	P=0.261	P=0.758N	P=0.325
Logistic regression tests	P=0.284	P=0.308	P=0.729	P=0.217
Cochran-Armitage test	P=0.312			
Fisher exact test		P=0.309	P=0.748	P=0.309
Skin (Subcutaneous Tissue): Fibroma, Fibrosarcoma, or Sarcoma				
Overall rates	1/51 (2%)	3/51 (6%)	1/50 (2%)	4/51 (8%)
Adjusted rates	2.1%	16.3%	4.3%	12.0%
Terminal rates	0/14 (0%)	0/6 (0%)	0/16 (0%)	0/17 (0%)
First incidence (days)	465	614	684	415
Life table tests	P=0.224	P=0.261	P=0.758N	P=0.202
Logistic regression tests	P=0.135	P=0.308	P=0.729	P=0.105
Cochran-Armitage test	P=0.164			
Fisher exact test		P=0.309	P=0.748	P=0.181
Testes: Adenoma				
Overall rates	33/51 (65%)	41/51 (80%)	42/50 (84%)	38/51 (75%)
Adjusted rates	96.7%	100.0%	100.0%	92.1%
Terminal rates	13/14 (93%)	6/6 (100%)	16/16 (100%)	14/17 (82%)
First incidence (days)	446	435	466	415
Life table tests	P=0.185N	P=0.003	P=0.291	P=0.533
Logistic regression tests	P=0.450	P=0.013	P=0.043	P=0.308
Cochran-Armitage test	P=0.223			
Fisher exact test		P=0.060	P=0.023	P=0.195

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Thyroid Gland (C-cell): Adenoma				
Overall rates	6/51 (12%)	7/50 (14%)	4/50 (8%)	4/51 (8%)
Adjusted rates	23.2%	51.9%	16.7%	16.5%
Terminal rates	1/14 (7%)	2/6 (33%)	1/16 (6%)	2/17 (12%)
First incidence (days)	541	614	669	547
Life table tests	P=0.134N	P=0.264	P=0.320N	P=0.310N
Logistic regression tests	P=0.186N	P=0.436	P=0.364N	P=0.364N
Cochran-Armitage test	P=0.227N			
Fisher exact test		P=0.485	P=0.383N	P=0.370N
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rates	7/51 (14%)	7/50 (14%)	6/50 (12%)	5/51 (10%)
Adjusted rates	25.2%	51.9%	22.8%	22.1%
Terminal rates	1/14 (7%)	2/6 (33%)	1/16 (6%)	3/17 (18%)
First incidence (days)	541	614	645	547
Life table tests	P=0.167N	P=0.365	P=0.421N	P=0.307N
Logistic regression tests	P=0.239N	P=0.558	P=0.497N	P=0.370N
Cochran-Armitage test	P=0.291N			
Fisher exact test		P=0.597	P=0.515N	P=0.380N
Upper Digestive Tract: Squamous Papilloma or Squamous Cell Carcinoma				
Overall rates	0/51 (0%)	0/51 (0%)	2/50 (4%)	3/51 (6%)
Adjusted rates	0.0%	0.0%	8.6%	10.7%
Terminal rates	0/14 (0%)	0/6 (0%)	1/16 (6%)	1/17 (6%)
First incidence (days)	-	-	614	591
Life table tests	P=0.055	-	P=0.276	P=0.156
Logistic regression tests	P=0.031	-	P=0.244	P=0.123
Cochran-Armitage test	P=0.027			
Fisher exact test		-	P=0.243	P=0.121
Zymbal's Gland: Adenoma or Carcinoma				
Overall rates	1/51 (2%)	0/51 (0%)	3/50 (6%)	2/51 (4%)
Adjusted rates	2.2%	0.0%	9.7%	4.4%
Terminal rates	0/14 (0%)	0/6 (0%)	0/16 (0%)	0/17 (0%)
First incidence (days)	513	-	614	522
Life table tests	P=0.287	P=0.513N	P=0.339	P=0.521
Logistic regression tests	P=0.191	P=0.450N	P=0.276	P=0.376
Cochran-Armitage test	P=0.238			
Fisher exact test		P=0.500N	P=0.301	P=0.500
All Organs: Mononuclear Leukemia				
Overall rates	25/51 (49%)	25/51 (49%)	27/50 (54%)	29/51 (57%)
Adjusted rates	73.1%	79.4%	68.8%	72.5%
Terminal rates	6/14 (43%)	3/6 (50%)	6/16 (38%)	7/17 (41%)
First incidence (days)	315	493	372	396
Life table tests	P=0.426N	P=0.168	P=0.530N	P=0.492
Logistic regression tests	P=0.207	P=0.543	P=0.369	P=0.280
Cochran-Armitage test	P=0.206			
Fisher exact test		P=0.578N	P=0.382	P=0.276

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
All Organs: Benign Tumors				
Overall rates	47/51 (92%)	48/51 (94%)	48/50 (96%)	49/51 (96%)
Adjusted rates	100.0%	100.0%	100.0%	100.0%
Terminal rates	14/14 (100%)	6/6 (100%)	16/16 (100%)	17/17 (100%)
First incidence (days)	446	385	466	415
Life table tests	P=0.110N	P=0.041	P=0.344N	P=0.358N
Logistic regression tests	P=0.598	P=0.309	P=0.507	P=0.623
Cochran-Armitage test	P=0.247			
Fisher exact test		P=0.500	P=0.348	P=0.339
All Organs: Malignant Tumors				
Overall rates	31/51 (61%)	37/51 (73%)	35/50 (70%)	38/51 (75%)
Adjusted rates	79.7%	92.5%	75.5%	83.7%
Terminal rates	7/14 (50%)	4/6 (67%)	6/16 (38%)	10/17 (59%)
First incidence (days)	315	306	365	396
Life table tests	P=0.411N	P=0.030	P=0.507	P=0.384
Logistic regression tests	P=0.088	P=0.141	P=0.170	P=0.090
Cochran-Armitage test	P=0.119			
Fisher exact test		P=0.147	P=0.223	P=0.102
All Organs: Benign and Malignant Tumors				
Overall rates	50/51 (98%)	50/51 (98%)	50/50 (100%)	51/51 (100%)
Adjusted rates	100.0%	100.0%	100.0%	100.0%
Terminal rates	14/14 (100%)	6/6 (100%)	16/16 (100%)	17/17 (100%)
First incidence (days)	315	306	365	396
Life table tests	P=0.096N	P=0.057	P=0.306N	P=0.313N
Logistic regression tests	P=0.370	P=0.563	P=0.555	P=0.583
Cochran-Armitage test	P=0.232			
Fisher exact test		P=0.752N	P=0.505	P=0.500

(T)Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no tumors in animal group

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

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma, Carcinoma, or Adenocarcinoma
Historical Incidence at Southern Research Institute			
Feed			
Nitrofurantoin	0/50 (0%)	0/50 (0%)	0/50 (0%)
Rhodamine 6G	0/50 (0%)	0/50 (0%)	0/50 (0%)
Roxarsone	1/50 (2%)	1/50 (2%)	2/50 (4%)
Total	1/150 (1%)	1/150 (1%)	2/150 (1%)
Standard deviation	1.2%	1.2%	2.3%
Range	0%-2%	0%-2%	0%-4%
Water			
Chloramine	0/51 (0%)	0/51 (0%)	0/51 (0%)
Overall Historical Incidence			
Feed			
Total	4/499 (1%)	2/499 (0.4%)	8/499 (2%)
Standard deviation	1.9%	0.8%	2.3%
Range	0%-6%	0%-2%	0%-6%
Water			
Total	0/180 (0%)	0/180 (0%)	0/180 (0%)

[a] Data as of 15 September 1990

TABLE A4b
Historical Incidence of Neoplasms of the Oral Cavity in Untreated Male F344/N Rats[a]

Study	Incidence in Controls		
	Papilloma or Squamous Cell Papilloma	Squamous Cell Carcinoma	Papilloma, Squamous Cell Papilloma or Carcinoma
Historical Incidence at Southern Research Institute			
Feed			
Nitrofurantoin	0/50 (0%)	0/50 (0%)	0/50 (0%)
Rhodamine 6G	0/50 (0%)	0/50 (0%)	0/50 (0%)
Roxarsone	2/50 (4%)	0/50 (0%)	2/50 (4%)
Total	2/150 (1%)	0/150 (0%)	2/150 (1%)
Standard deviation	2.3%		2.3%
Range	0%-4%		0%-4%
Water			
Chloramine	0/51 (0%)	0/51 (0%)	0/51 (0%)
Overall Historical Incidence			
Feed			
Total	4/500 (1%)	0/500 (0%)	4/500 (1%)
Standard deviation	1.7%		1.7%
Range	0%-4%		0%-4%
Water			
Total	0/181 (0%)	0/181 (0%)	0/181 (0%)

[a] Data as of 15 September 1990; includes tongue, pharynx (palate), tooth (gingiva), and lip.

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	9	9	10	9
Early deaths				
Natural death	3	5	4	7
Moribund	34	40	30	27
Survivors				
Terminal sacrifice	14	6	16	17
Animals examined microscopically	51	51	50	51
Alimentary System				
Esophagus	(51)	(51)	(50)	(51)
Inflammation, chronic			1 (2%)	
Intestine large, cecum	(51)	(51)	(50)	(51)
Edema	1 (2%)	1 (2%)		
Hemorrhage	1 (2%)			
Inflammation, chronic	1 (2%)		1 (2%)	
Intestine large, colon	(51)	(51)	(50)	(51)
Mineralization			1 (2%)	
Parasite metazoan	1 (2%)	3 (6%)	3 (6%)	5 (10%)
Muscularis, degeneration			1 (2%)	
Intestine large, rectum	(51)	(51)	(49)	(49)
Mineralization			1 (2%)	
Parasite metazoan	5 (10%)	7 (14%)	7 (14%)	8 (16%)
Muscularis, degeneration			1 (2%)	
Intestine small, duodenum	(51)	(50)	(50)	(51)
Mineralization			1 (2%)	
Muscularis, degeneration			1 (2%)	
Intestine small, jejunum	(51)	(50)	(50)	(51)
Metaplasia, osseous	1 (2%)			
Liver	(51)	(51)	(50)	(51)
Angiectasis	8 (16%)	4 (8%)	5 (10%)	8 (16%)
Atrophy, focal	1 (2%)			
Basophilic focus	1 (2%)			
Congestion	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Degeneration, cystic	10 (20%)	11 (22%)	9 (18%)	7 (14%)
Fatty change	14 (27%)	16 (31%)	13 (26%)	8 (16%)
Fibrosis, focal		1 (2%)		
Focal cellular change	11 (22%)	6 (12%)	19 (38%)	17 (33%)
Hematopoietic cell proliferation		1 (2%)		
Hemorrhage	3 (6%)	1 (2%)		
Hepatodiaphragmatic nodule	5 (10%)	5 (10%)	4 (8%)	3 (6%)
Hyperplasia		1 (2%)		
Hyperplasia, multifocal	15 (29%)	13 (25%)	20 (40%)	18 (35%)
Hypertrophy, focal		1 (2%)		
Infiltration cellular, mixed cell	7 (14%)	10 (20%)	11 (22%)	8 (16%)
Inflammation, focal	18 (35%)	20 (39%)	23 (46%)	21 (41%)
Mineralization	1 (2%)			

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Alimentary System				
Liver (continued)				
Necrosis, focal	2 (4%)	1 (2%)	1 (2%)	3 (6%)
Thrombus		1 (2%)		
Bile duct, cyst				1 (2%)
Bile duct, hyperplasia	48 (94%)	49 (96%)	50 (100%)	49 (96%)
Biliary tract, fibrosis	42 (82%)	43 (84%)	45 (90%)	43 (84%)
Centrilobular, atrophy	14 (27%)	19 (37%)	20 (40%)	12 (24%)
Centrilobular, necrosis		2 (4%)	1 (2%)	
Mesentery	(31)	(25)	(16)	(20)
Angiectasis				1 (5%)
Fibrosis				1 (5%)
Hemorrhage	1 (3%)	1 (4%)	1 (6%)	3 (15%)
Inflammation, chronic	7 (23%)	8 (32%)	4 (25%)	4 (20%)
Fat, necrosis	11 (35%)	8 (32%)	6 (38%)	6 (30%)
Pancreas	(51)	(51)	(50)	(51)
Atrophy, focal	13 (25%)	16 (31%)	17 (34%)	11 (22%)
Cytoplasmic alteration	1 (2%)			1 (2%)
Edema		1 (2%)	1 (2%)	
Acinar cell, hyperplasia	3 (6%)			
Duct, dilatation				2 (4%)
Salivary glands	(51)	(51)	(50)	(51)
Inflammation, chronic		1 (2%)		
Stomach, forestomach	(51)	(51)	(50)	(51)
Edema		1 (2%)	1 (2%)	
Inflammation, chronic	7 (14%)	11 (22%)	5 (10%)	3 (6%)
Mineralization		1 (2%)	1 (2%)	
Perforation		2 (4%)		
Ulcer	6 (12%)	11 (22%)	3 (6%)	3 (6%)
Mucosa, hyperplasia, papillary	6 (12%)	14 (27%)	6 (12%)	5 (10%)
Muscularis, degeneration			1 (2%)	
Stomach, glandular	(51)	(51)	(50)	(51)
Edema		1 (2%)	1 (2%)	
Erosion	3 (6%)	1 (2%)		2 (4%)
Infiltration cellular, lymphocytic		1 (2%)		
Inflammation, chronic	8 (16%)	3 (6%)	4 (8%)	3 (6%)
Mineralization	1 (2%)	4 (8%)	1 (2%)	2 (4%)
Pigmentation, focal	2 (4%)			1 (2%)
Ulcer	1 (2%)			
Mucosa, degeneration		3 (6%)		
Mucosa, hyperplasia	1 (2%)	5 (10%)		
Muscularis, degeneration			1 (2%)	
Tongue		(1)		(1)
Epithelium, developmental malformation		1 (100%)		
Tooth	(2)			(1)
Epithelium alveolus, cyst	1 (50%)			

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Cardiovascular System				
Blood vessel	(5)	(3)	(5)	(2)
Aorta, degeneration			1 (20%)	
Aorta, mineralization	1 (20%)	2 (67%)	1 (20%)	
Mesenteric artery, degeneration			1 (20%)	
Mesenteric artery, inflammation, chronic	4 (80%)	3 (100%)	4 (80%)	2 (100%)
Mesenteric artery, mineralization	1 (20%)		1 (20%)	
Thoracic, inflammation, chronic				1 (50%)
Heart	(51)	(51)	(50)	(51)
Degeneration			1 (2%)	
Mineralization		1 (2%)	1 (2%)	
Thrombus		3 (6%)	1 (2%)	
Endocrine System				
Adrenal gland, cortex	(51)	(51)	(49)	(51)
Accessory adrenal cortical nodule				2 (4%)
Atrophy		1 (2%)		
Cyst	1 (2%)			
Focal cellular change	13 (25%)	7 (14%)	14 (29%)	9 (18%)
Hemorrhage	1 (2%)			
Necrosis	1 (2%)			
Vacuolization cytoplasmic		1 (2%)		
Adrenal gland, medulla	(51)	(51)	(49)	(51)
Angiectasis		1 (2%)		
Atrophy		1 (2%)		
Hemorrhage	1 (2%)			
Hyperplasia	10 (20%)	15 (29%)	13 (27%)	9 (18%)
Necrosis	1 (2%)			
Parathyroid gland	(50)	(49)	(50)	(50)
Hyperplasia	4 (8%)	7 (14%)	5 (10%)	2 (4%)
Pituitary gland	(50)	(50)	(49)	(51)
Angiectasis	17 (34%)	15 (30%)	15 (31%)	20 (39%)
Cyst	2 (4%)	3 (6%)	3 (6%)	1 (2%)
Hemorrhage		2 (4%)	2 (4%)	
Hyperplasia, tubular		1 (2%)	1 (2%)	
Necrosis			1 (2%)	
Pigmentation	1 (2%)			
Pars distalis, focal cellular change	1 (2%)	1 (2%)		
Pars distalis, hyperplasia, focal	8 (16%)	8 (16%)	6 (12%)	8 (16%)
Thyroid gland	(51)	(50)	(50)	(51)
Degeneration, cystic	6 (12%)	8 (16%)	9 (18%)	9 (18%)
Pigmentation	1 (2%)			
Ultimobranchial cyst	1 (2%)			1 (2%)
C-cell, hyperplasia	5 (10%)	1 (2%)	3 (6%)	5 (10%)
Follicle, cyst	1 (2%)	2 (4%)	2 (4%)	3 (6%)
Follicular cell, hyperplasia	1 (2%)	2 (4%)	2 (4%)	4 (8%)
General Body System				
None				

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Genital System				
Ductus deferens			(1)	
Degeneration			1 (100%)	
Mineralization			1 (100%)	
Epididymis	(51)	(51)	(50)	(51)
Hemorrhage		1 (2%)		
Inflammation, chronic		1 (2%)		
Necrosis, focal		1 (2%)		
Spermatocele				1 (2%)
Penis			(1)	
Inflammation, chronic			1 (100%)	
Preputial gland	(50)	(51)	(47)	(51)
Degeneration, cystic	3 (6%)		3 (6%)	4 (8%)
Ectopic tissue				1 (2%)
Fibrosis	1 (2%)			
Hyperplasia		1 (2%)		1 (2%)
Inflammation, suppurative	20 (40%)	17 (33%)	28 (60%)	22 (43%)
Prostate	(51)	(51)	(50)	(51)
Edema				1 (2%)
Hyperplasia, focal		1 (2%)	3 (6%)	2 (4%)
Inflammation, suppurative	28 (55%)	36 (71%)	36 (72%)	38 (75%)
Seminal vesicle	(51)	(51)	(50)	(51)
Degeneration			1 (2%)	
Dilatation			1 (2%)	
Inflammation, chronic	1 (2%)		1 (2%)	
Mineralization			1 (2%)	
Testes	(51)	(51)	(50)	(51)
Fibrosis	1 (2%)			
Hemorrhage		1 (2%)		
Hyperplasia				1 (2%)
Mineralization		1 (2%)		
Artery, inflammation, chronic		4 (8%)	1 (2%)	
Germinal epithelium, degeneration	15 (29%)	7 (14%)	8 (16%)	10 (20%)
Interstitial cell, hyperplasia	13 (25%)	7 (14%)	7 (14%)	16 (31%)
Hematopoietic System				
Bone marrow	(51)	(51)	(50)	(51)
Angiectasis				1 (2%)
Hypercellularity		4 (8%)		
Hyperplasia		1 (2%)		
Myelofibrosis	4 (8%)	5 (10%)	3 (6%)	3 (6%)
Lymph node	(51)	(51)	(50)	(51)
Deep cervical, hyperplasia				1 (2%)
Inguinal, hyperplasia		1 (2%)		
Mediastinal, angiectasis	6 (12%)	6 (12%)	1 (2%)	6 (12%)
Mediastinal, hyperplasia	1 (2%)			
Mediastinal, hyperplasia, lymphoid		1 (2%)		
Pancreatic, angiectasis				1 (2%)
Pancreatic, hyperplasia	2 (4%)	1 (2%)		
Renal, angiectasis	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Renal, hyperplasia				1 (2%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Hematopoietic System (continued)				
Lymph node, mandibular	(51)	(51)	(49)	(51)
Angiectasis	3 (6%)	3 (6%)	2 (4%)	2 (4%)
Hyperplasia	4 (8%)	7 (14%)	2 (4%)	6 (12%)
Hyperplasia, lymphoid		2 (4%)	1 (2%)	
Lymph node, mesenteric	(51)	(50)	(49)	(51)
Angiectasis	1 (2%)	1 (2%)	2 (4%)	3 (6%)
Cyst	1 (2%)			
Hyperplasia		2 (4%)		
Hyperplasia, lymphoid		1 (2%)		
Spleen	(51)	(51)	(50)	(51)
Depletion			1 (2%)	
Fibrosis	6 (12%)	8 (16%)	5 (10%)	9 (18%)
Hematopoietic cell proliferation	3 (6%)	7 (14%)	4 (8%)	5 (10%)
Hyperplasia, histiocyte, lymphoid		1 (2%)		
Necrosis, focal	2 (4%)	1 (2%)	1 (2%)	
Pigmentation		1 (2%)		
Artery, degeneration			1 (2%)	
Artery, mineralization			1 (2%)	
Capsule, inflammation, chronic		1 (2%)		
Thymus	(46)	(44)	(42)	(49)
Angiectasis	1 (2%)			
Cyst				1 (2%)
Hyperplasia, lymphoid		2 (5%)		
Integumentary System				
Mammary gland	(48)	(50)	(49)	(49)
Dilatation	16 (33%)	13 (26%)	12 (24%)	17 (35%)
Hemorrhage	1 (2%)	1 (2%)		
Hyperplasia	1 (2%)		2 (4%)	1 (2%)
Skin	(51)	(51)	(50)	(51)
Abscess	1 (2%)			
Cyst epithelial inclusion	1 (2%)	1 (2%)	1 (2%)	
Fibrosis			1 (2%)	
Hyperkeratosis			1 (2%)	2 (4%)
Hyperplasia, squamous			1 (2%)	
Inflammation, chronic	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Artery, subcutaneous tissue, inflammation, chronic				1 (2%)
Epidermis, hyperplasia		1 (2%)	1 (2%)	
Sebaceous gland, hyperplasia		1 (2%)		1 (2%)
Subcutaneous tissue, abscess			1 (2%)	1 (2%)
Subcutaneous tissue, cyst			1 (2%)	
Subcutaneous tissue, fibrosis		2 (4%)		
Subcutaneous tissue, hemorrhage		1 (2%)		
Subcutaneous tissue, inflammation, chronic			1 (2%)	
Subcutaneous tissue, fat, necrosis			1 (2%)	

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Musculoskeletal System				
Bone	(51)	(51)	(50)	(51)
Atrophy			1 (2%)	
Developmental malformation		1 (2%)		
Fracture healed		1 (2%)		
Hyperostosis		2 (4%)	1 (2%)	3 (6%)
Cartilage, hyperplasia		1 (2%)		
Skeletal muscle		(1)	(3)	
Degeneration			1 (33%)	
Diaphragm, mineralization			1 (33%)	
Nervous System				
Brain	(51)	(51)	(50)	(50)
Compression	11 (22%)	8 (16%)	6 (12%)	10 (20%)
Hemorrhage	5 (10%)	2 (4%)	2 (4%)	3 (6%)
Spinal cord				(1)
Hemorrhage				1 (100%)
Respiratory System				
Lung	(51)	(51)	(50)	(51)
Congestion	1 (2%)	1 (2%)	3 (6%)	
Fibrosis, focal	1 (2%)			
Hemorrhage	7 (14%)	1 (2%)	2 (4%)	2 (4%)
Hyperplasia, macrophage	3 (6%)	2 (4%)	1 (2%)	1 (2%)
Infiltration cellular, mixed cell	3 (6%)	3 (6%)	1 (2%)	2 (4%)
Inflammation, acute	1 (2%)			
Inflammation, chronic				1 (2%)
Inflammation, granulomatous		2 (4%)		
Necrosis, focal	1 (2%)			
Alveolar epithelium, degeneration			1 (2%)	
Alveolar epithelium, hyperplasia	4 (8%)	7 (14%)	3 (6%)	7 (14%)
Artery, mineralization			1 (2%)	
Bronchus, degeneration			1 (2%)	
Bronchus, mineralization			1 (2%)	
Mediastinum, angiectasis		1 (2%)		
Mediastinum, hemorrhage	1 (2%)			
Mediastinum, inflammation, chronic	1 (2%)		1 (2%)	
Pleura, inflammation, chronic	1 (2%)			
Nose	(51)	(51)	(49)	(51)
Exudate		1 (2%)		
Fungus	5 (10%)	16 (31%)	7 (14%)	10 (20%)
Hemorrhage		1 (2%)		
Hyperplasia, squamous		1 (2%)		
Inflammation, suppurative	16 (31%)	19 (37%)	9 (18%)	15 (29%)
Mucosa, hyperplasia, squamous	1 (2%)			
Trachea	(51)	(51)	(50)	(51)
Degeneration			1 (2%)	
Mineralization			1 (2%)	
Glands, cyst	1 (2%)			

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Special Senses System				
Ear	(1)		(2)	(1)
Pinna, hyperplasia, squamous	1 (100%)			
Eye	(5)	(3)	(3)	
Atrophy	1 (20%)	1 (33%)		
Cataract	1 (20%)	2 (67%)	1 (33%)	
Anterior chamber, inflammation, acute		1 (33%)		
Cornea, inflammation, acute		1 (33%)		
Retina, degeneration	1 (20%)	1 (33%)	1 (33%)	
Retrobulbar, inflammation, chronic	1 (20%)			
Urinary System				
Kidney	(51)	(50)	(50)	(51)
Cyst	4 (8%)	8 (16%)	3 (6%)	3 (6%)
Hydronephrosis		1 (2%)		
Nephropathy	50 (98%)	49 (98%)	49 (98%)	50 (98%)
Pelvis, dilatation	2 (4%)			
Pelvis, transitional epithelium, hyperplasia	1 (2%)			
Renal tubule, hyperplasia	3 (6%)	3 (6%)	1 (2%)	1 (2%)
Urethra	(1)	(1)		
Bulbourethral gland, dilatation	1 (100%)	1 (100%)		
Urinary bladder	(51)	(51)	(50)	(51)
Angiectasis				1 (2%)
Hemorrhage			2 (4%)	2 (4%)
Inflammation, chronic	1 (2%)	1 (2%)	1 (2%)	
Necrosis			1 (2%)	
Transitional epithelium, hyperplasia	1 (2%)		1 (2%)	

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR CHLORINATED WATER STUDY

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	9	10
Early deaths				
Natural death	3	1	4	1
Moribund	16	18	19	14
Survivors				
Terminal sacrifice	31	31	28	35
Animals examined microscopically	50	50	51	50
Alimentary System				
Intestine large, cecum	(50)	(50)	(51)	(50)
Intestine large, colon	(50)	(50)	(51)	(50)
Intestine large, rectum	(50)	(50)	(50)	(50)
Intestine small, duodenum	(50)	(50)	(50)	(50)
Intestine small, ileum	(50)	(50)	(51)	(50)
Intestine small, jejunum	(50)	(50)	(51)	(50)
Adenoma				1 (2%)
Liver	(50)	(50)	(51)	(50)
Hepatocellular adenoma	1 (2%)	1 (2%)	2 (4%)	
Histiocytic sarcoma		1 (2%)		
Mesentery	(10)	(6)	(9)	(10)
Pancreas	(50)	(50)	(51)	(50)
Acinar cell, adenoma				1 (2%)
Pharynx		(1)		
Palate, papilloma squamous		1 (100%)		
Salivary glands	(49)	(50)	(51)	(50)
Stomach, forestomach	(50)	(50)	(51)	(50)
Papilloma squamous			1 (2%)	
Stomach, glandular	(50)	(50)	(51)	(50)
Carcinoid tumor NOS		1 (2%)		
Tongue	(1)			
Papilloma squamous	1 (100%)			
Tooth	(1)			(1)
Odontoma				1 (100%)
Cardiovascular System				
Heart	(50)	(50)	(51)	(50)
Osteosarcoma, metastatic, skin			1 (2%)	
Endocrine System				
Adrenal gland, cortex	(50)	(49)	(51)	(50)
Adenoma		1 (2%)		3 (6%)
Adrenal gland, medulla	(50)	(49)	(51)	(50)
Pheochromocytoma benign	6 (12%)	4 (8%)	3 (6%)	3 (6%)
Bilateral, pheochromocytoma benign	1 (2%)		1 (2%)	

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm		70 ppm		140 ppm		275 ppm	
Endocrine System (continued)								
Islets, pancreatic	(50)		(50)		(51)		(50)	
Adenoma					2	(4%)	3	(6%)
Carcinoma					1	(2%)		
Pituitary gland	(50)		(49)		(50)		(50)	
Craniopharyngioma			1	(2%)				
Pars distalis, adenoma	33	(66%)	28	(57%)	26	(52%)	25	(50%)
Thyroid gland	(50)		(48)		(51)		(50)	
C-cell, adenoma	4	(8%)			7	(14%)	1	(2%)
C-cell, carcinoma	1	(2%)	3	(6%)				
Follicular cell, adenoma	3	(6%)	1	(2%)			1	(2%)
Follicular cell, carcinoma					1	(2%)		
General Body System								
Tissue NOS	(1)							
Oral, squamous cell carcinoma	1	(100%)						
Genital System								
Clitoral gland	(48)		(50)		(50)		(50)	
Adenoma	5	(10%)	4	(8%)	4	(8%)	8	(16%)
Carcinoma	1	(2%)					1	(2%)
Bilateral, adenoma					1	(2%)		
Ovary	(50)		(50)		(51)		(50)	
Granulosa-theca tumor malignant					1	(2%)		
Histiocytic sarcoma			1	(2%)				
Uterus	(50)		(50)		(51)		(50)	
Adenocarcinoma							1	(2%)
Adenoma							1	(2%)
Granular cell tumor NOS			2	(4%)				
Polyp stromal, multiple			1	(2%)				
Endometrium, deciduoma NOS			1	(2%)				
Endometrium, polyp stromal	10	(20%)	8	(16%)	8	(16%)	13	(26%)
Endometrium, polyp stromal, multiple					1	(2%)		
Vagina	(8)		(14)		(13)		(11)	
Papilloma squamous							1	(9%)
Sarcoma	1	(13%)	1	(7%)				
Hematopoietic System								
Bone marrow	(50)		(50)		(51)		(50)	
Lymph node	(50)		(50)		(51)		(50)	
Mediastinal, carcinoma, metastatic, thyroid gland			1	(2%)				
Mediastinal, histiocytic sarcoma			1	(2%)				
Pancreatic, histiocytic sarcoma			1	(2%)				
Lymph node, mandibular	(48)		(50)		(51)		(49)	
Carcinoma, metastatic, thyroid gland			1	(2%)				
Lymph node, mesenteric	(49)		(49)		(49)		(49)	
Histiocytic sarcoma			1	(2%)				

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Hematopoietic System (continued)				
Spleen	(50)	(50)	(51)	(50)
Histiocytic sarcoma		1 (2%)		
Schwannoma NOS		1 (2%)		
Thymus	(49)	(47)	(50)	(50)
Thymoma benign				1 (2%)
Integumentary System				
Mammary gland	(50)	(50)	(51)	(50)
Adenocarcinoma	2 (4%)			
Adenoma	1 (2%)		1 (2%)	1 (2%)
Adenoma, multiple			1 (2%)	
Fibroadenoma	11 (22%)	11 (22%)	18 (35%)	13 (26%)
Fibroadenoma, multiple	5 (10%)	3 (6%)	3 (6%)	3 (6%)
Skin	(50)	(50)	(51)	(50)
Basal cell carcinoma			1 (2%)	
Keratoacanthoma		1 (2%)	2 (4%)	
Squamous cell carcinoma	1 (2%)			
Subcutaneous tissue, fibroma	2 (4%)		1 (2%)	
Subcutaneous tissue, fibrosarcoma	1 (2%)			1 (2%)
Subcutaneous tissue, histiocytic sarcoma		1 (2%)		
Subcutaneous tissue, osteosarcoma			1 (2%)	
Musculoskeletal System				
Skeletal muscle		(1)		
Histiocytic sarcoma		1 (100%)		
Nervous System				
Brain	(48)	(50)	(51)	(50)
Astrocytoma NOS			1 (2%)	
Glioma malignant				1 (2%)
Glioma NOS			1 (2%)	
Spinal cord			(1)	
Respiratory System				
Lung	(50)	(50)	(51)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	2 (4%)		
Alveolar/bronchiolar carcinoma		1 (2%)		
Carcinoma, metastatic, thyroid gland		1 (2%)		
Histiocytic sarcoma		1 (2%)		
Osteosarcoma, greater than five, metastatic, multiple, skin			1 (2%)	
Nose	(50)	(50)	(51)	(50)
Glands, carcinoma	1 (2%)			
Trachea	(50)	(49)	(51)	(50)
Carcinoma, metastatic, thyroid gland		1 (2%)		

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Special Senses System				
Ear	(1)	(2)	(1)	
Pinna, schwannoma NOS	1 (100%)	2 (100%)		
Zymbal's gland	(1)			
Adenoma	1 (100%)			
Urinary System				
Kidney	(50)	(50)	(51)	(50)
Renal tubule, adenoma			1 (2%)	
Urinary bladder	(50)	(50)	(50)	(50)
Systemic Lesions				
Multiple organs[a]	(50)	(50)	(51)	(50)
Histiocytic sarcoma		1 (2%)		
Leukemia mononuclear	8 (16%)	7 (14%)	19 (37%)	16 (32%)
Lymphoma malignant lymphocytic	1 (2%)			
Tumor Summary				
Total animals with primary neoplasms[b]	48	46	46	43
Total primary neoplasms	104	87	109	100
Total animals with benign neoplasms	45	40	41	39
Total benign neoplasms	85	67	83	80
Total animals with malignant neoplasms	16	12	22	20
Total malignant neoplasms	18	13	24	20
Total animals with secondary neoplasms[c]		1	1	
Total secondary neoplasms		4	2	
Total animals with neoplasms uncertain-benign or malignant	1	6	2	
Total uncertain neoplasms	1	7	2	

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

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

Number of Days on Study	4 7 2	5 0 8	5 3 1	5 6 9	5 7 8	6 2 0	6 3 9	6 5 0	6 6 6	6 6 6	6 6 7	6 6 8	6 6 8	6 7 3	6 7 5	7 0 2	7 0 3	7 1 2	7 2 1	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	1 5 9 1	0 5 0 1	0 5 2 1	1 5 8 1	1 5 9 2	0 5 1 1	1 5 9 5	1 5 8 2	1 6 1 1	1 6 2 1	1 5 9 3	0 5 1 2	0 5 2 2	0 5 3 1	0 5 3 2	1 5 8 3	0 5 1 3	0 5 2	1 6 0 1	0 5 3 3	0 5 5 3	0 5 5 4	0 5 5 5	0 5 4 5	0 5 5 1	0 5 5 5
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Mesentery	+	+	+	+		+													+						
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Papilloma squamous																									
Tooth							+																		
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																			X						X
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X	X		X	X		X			X	X	X	X			X	X	X	X	X	X		X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma						X	X																		
C-cell, carcinoma																									
Follicular cell, adenoma											X						X								

+: 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 Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 2 3	0 5 2 4	0 5 2 5	0 5 3 4	0 5 3 5	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	1 5 8 4	1 5 8 5	1 5 9 4	1 6 0 2	1 6 0 3	1 6 0 4	1 6 0 5	1 6 1 2	1 6 1 3	1 6 1 4	1 6 1 5	1 6 2 2	1 6 2 3	1 6 2 4	1 6 2 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma										X																1
Mesentery			+				+												+					+		10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue													+													1
Papilloma squamous													X													1
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign							X										X					X			X	6
Bilateral, pheochromocytoma benign					X																					1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
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	33
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma															X										X	4
C-cell, carcinoma																					X					1
Follicular cell, adenoma											X															3

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	4 7 2	5 0 8	5 3 1	5 6 9	5 7 8	6 2 0	6 3 9	6 5 0	6 6 6	6 6 6	6 6 7	6 6 8	6 6 8	6 7 3	6 7 5	7 0 2	7 0 3	7 1 2	7 2 1	7 3 0	7 3 1	7 3 3	7 3 1	7 3 1	7 3 1
Carcass ID Number	1 5 9 1	0 5 0 1	0 5 2 1	1 5 8 1	1 5 9 2	0 5 1 1	1 5 9 5	1 5 8 2	1 6 1 1	1 6 2 1	1 5 9 3	0 5 1 2	0 5 2 2	0 5 3 1	0 5 3 2	0 5 3 3	1 5 8 3	0 5 1 3	0 5 0 2	1 6 0 1	0 5 3 3	0 5 0 4	0 5 0 5	0 5 1 4	0 5 1 5
General Body System																									
Tissue NOS																									+
Oral, squamous cell carcinoma																									X
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
Adenoma																				X				X	
Carcinoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal		X			X	X	X								X		X								
Vagina	+													+					+				+		
Sarcoma														X											
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Adenoma																									
Fibroadenoma					X					X	X											X			
Fibroadenoma, multiple																	X		X		X				
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																X									
Subcutaneous tissue, fibroma										X										X					
Subcutaneous tissue, fibrosarcoma												X													
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glands, carcinoma								X																	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 2 3	0 5 2 4	0 5 2 5	0 5 3 4	0 5 3 5	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	0 5 8 4	1 5 8 5	1 5 9 4	1 5 9 5	1 6 0 2	1 6 0 3	1 6 0 4	1 6 0 5	1 6 1 2	1 6 1 3	1 6 1 4	1 6 1 5	1 6 2 2	1 6 2 3	1 6 2 4	1 6 2 5	**Total Tissues/ Tumors**
General Body System																										
Tissue NOS																										1
Oral, squamous cell carcinoma																										1
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma	X																X			X						5
Carcinoma																							X			1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrium, polyp stromal							X		X				X										X			10
Vagina			+										+	+		+										8
Sarcoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma		X																				X				2
Adenoma																		X								1
Fibroadenoma	X					X					X				X	X			X					X		11
Fibroadenoma, multiple										X											X					5
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Subcutaneous tissue, fibroma																										2
Subcutaneous tissue, fibrosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	48
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma								X																		1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glands, carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

Table B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	472	508	531	569	578	620	639	650	666	666	667	668	668	673	675	702	703	712	721	730	731	731	731	731	731
Carcass ID Number	1591	0501	0521	1581	1592	0511	1595	1582	1611	1621	1593	0512	0522	0531	0532	1583	0513	0502	1601	0533	0503	0504	0505	0514	0515
Special Senses System																									
Ear																									+
Pinna, schwannoma NOS																									X
Eye															+								+		
Zymbal's gland																		+							
Adenoma																		X							
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X				X			X								X					X				
Lymphoma malignant lymphocytic																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 2 3	0 5 2 4	0 5 2 5	0 5 2 4	0 5 3 5	0 5 3 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	0 5 5 4	1 5 8 4	1 5 8 5	1 5 9 4	1 6 0 2	1 6 0 3	1 6 0 4	1 6 0 5	1 6 1 2	1 6 1 3	1 6 1 4	1 6 1 5	1 6 2 2	1 6 2 3	1 6 2 4	1 6 2 5	**Total Tissues/ Tumors**
Special Senses System																										
Ear																										1
Pinna, schwannoma NOS																										1
Eye					+																					3
Zymbal's gland																										1
Adenoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																X		X		X						8
Lymphoma malignant lymphocytic												X														1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 70 ppm

Number of Days on Study	3 7 6	4 2 4	4 9 4	5 0 8	5 1 4	5 6 0	5 9 6	6 1 4	6 1 9	6 2 1	6 2 7	6 5 2	6 6 7	7 0 8	7 1 0	7 1 0	7 2 2	7 2 2	7 2 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 9 3 1	2 0 2 1	0 9 4 1	0 9 3 2	0 9 2 1	2 0 1 1	2 0 0 1	2 0 4 1	2 0 3 1	2 0 4 2	0 9 4 2	0 9 3 3	2 0 0 2	2 0 0 3	0 9 2 2	0 9 6 1	0 9 2 3	0 9 6 2	2 0 1 2	2 0 0 4	2 0 0 5	2 0 1 3	2 0 1 4	2 0 1 5	2 0 2 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma														X											
Histiocytic sarcoma																			X						
Mesentery		+						+		+															
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pharynx																+									
Palate, papilloma squamous																X									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
carcinoid tumor NOS																									
Cardiovascular System																									
Blood vessel		+									+														
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Adenoma																				X					
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Craniopharyngioma																									
Pars distalis, adenoma			X	X					X		X	X	X	X	X	X	X	X		X	X			X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, carcinoma																							X		
Follicular cell, adenoma																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	731	731	731	731	731	731	731	731	
Carcass ID Number	20023	20024	20025	20032	20033	20034	20035	20043	20044	20045	20924	20925	20951	20963	20964	20965	20934	20935	20943	20944	20945	20952	20953	20954	20955	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																										1
Histiocytic sarcoma																										1
Mesentery						+							+										+			6
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pharynx																										1
Palate, papilloma squamous																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
carcinoid tumor NOS		X																								1
Cardiovascular System																										
Blood vessel					+	+			+																	5
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign	X													X	X		X									4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	M	+	45
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Craniopharyngioma					X																					1
Pars distalis, adenoma		X				X		X	X	X	X		X	X		X	X	X	X		X		X			28
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	48
C-cell, carcinoma				X		X																				3
Follicular cell, adenoma			X																							1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	3 7 6	4 2 4	4 9 4	5 0 8	5 1 4	5 6 0	5 9 6	6 1 4	6 1 9	6 2 1	6 2 7	6 5 2	6 6 7	7 0 8	7 1 0	7 1 0	7 2 2	7 2 2	7 2 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 9 3 1	2 0 2 1	0 9 4 1	0 9 3 2	0 9 2 1	2 0 1 1	2 0 0 1	2 0 4 1	2 0 3 1	2 0 4 2	0 9 4 2	0 9 3 3	2 9 0 2	2 0 0 3	0 9 2 2	0 9 6 1	0 9 2 3	0 9 6 2	2 0 1 2	2 0 0 4	2 0 0 5	2 0 1 3	2 0 1 4	2 0 1 5	2 0 2 2
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma				X																					
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																			X						
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granular cell tumor NOS																							X		
Polyp stromal, multiple																	X								
Endometrium, deciduoma NOS					X																				
Endometrium, polyp stromal																		X					X	X	
Vagina	+		+				+	+				+						+	+				+		
Sarcoma																			X						
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, carcinoma, metastatic, thyroid gland																									
Mediastinal, histiocytic sarcoma																			X						
Pancreatic, histiocytic sarcoma																			X						
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland																									
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Histiocytic sarcoma																			X						
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																			X						
Schwannoma NOS													X												
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma	X					X														X			X		
Fibroadenoma, multiple													X												
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Subcutaneous tissue, histiocytic sarcoma																			X						

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	2 0 2 3	2 0 2 4	2 0 2 5	2 0 3 2	2 0 3 3	2 0 3 4	2 0 3 5	2 0 3 3	2 0 4 4	2 0 4 5	2 0 2 4	0 0 2 5	0 0 5 1	0 0 6 3	0 0 6 4	0 0 6 5	0 0 3 4	0 0 5 5	0 0 3 3	0 0 4 4	0 0 4 5	0 0 5 2	0 0 3 3	0 0 4 5	0 0 5 5	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma															X	X		X								4
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granular cell tumor NOS						X																				2
Polyp stromal, multiple																										1
Endometrium, deciduoma NOS																										1
Endometrium, polyp stromal				X		X						X			X										X	8
Vagina						+			+				+									+		+	+	14
Sarcoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, carcinoma, metastatic, thyroid gland						X																				1
Mediastinal, histiocytic sarcoma																										1
Pancreatic, histiocytic sarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, thyroid gland						X																				1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Schwannoma NOS																										1
Thymus	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	47
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroadenoma	X								X				X	X			X					X			X	11
Fibroadenoma, multiple																X			X							3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma															X											1
Subcutaneous tissue, histiocytic sarcoma																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	3 7 6	4 2 4	4 9 4	5 0 8	5 1 4	5 6 0	5 9 6	6 1 4	6 1 9	6 2 1	6 2 7	6 5 2	6 6 7	7 0 8	7 1 0	7 1 0	7 2 2	7 2 2	7 2 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 9 3 1	2 0 2 1	0 9 4 1	0 9 3 2	0 9 2 1	2 0 1 1	2 0 0 1	2 0 4 1	2 0 3 1	2 0 4 2	0 9 4 2	0 9 3 3	2 0 0 2	2 0 0 3	0 9 2 2	0 9 6 1	0 9 2 3	0 9 6 2	2 0 1 2	2 0 0 4	2 0 0 5	2 0 1 3	2 0 1 4	2 0 1 5	2 0 2 2
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																			+						
Histiocytic sarcoma																			X						
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma											X														X
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, thyroid gland																									
Histiocytic sarcoma																			X						
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland																									
Special Senses System																									
Ear							+						+												
Pinna, schwannoma NOS							X						X												
Eye															+										
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																			X						
Leukemia mononuclear					X			X		X		X					X							X	

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	2 0 2 3	2 0 2 4	2 0 2 5	2 0 3 2	2 0 3 3	2 0 3 4	2 0 3 5	2 0 4 3	2 0 4 4	2 0 4 5	2 0 4 4	0 9 2 4	0 9 2 5	0 9 5 1	0 9 6 3	0 9 6 4	0 9 6 5	0 9 3 4	0 9 3 5	0 9 4 3	0 9 4 4	0 9 4 5	0 9 5 2	0 9 5 3	0 9 5 4	0 9 5 5	**Total Tissues/ Tumors**
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																											1
Histiocytic sarcoma																											1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																											2
Alveolar/bronchiolar carcinoma														X													1
Carcinoma, metastatic, thyroid gland						X																					1
Histiocytic sarcoma																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, thyroid gland						X																					1
Special Senses System																											
Ear																											2
Pinna, schwannoma NOS																											2
Eye		+	+				+	+																			5
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																											1
Leukemia mononuclear																				X							7

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 140 ppm

Number of Days on Study	3 2 9	4 1 1	4 1 8	4 5 1	5 5 4	5 5 9	5 7 5	5 9 3	5 9 6	6 1 4	6 3 9	6 5 3	6 6 7	6 7 5	6 8 7	6 9 0	6 9 4	6 9 8	6 9 9	7 1 1	7 1 1	7 2 4	7 2 4	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 8 7 1	1 9 7 2	1 9 9 1	0 8 5 1	0 8 6 1	1 9 7 1	0 8 7 2	0 8 8 1	0 8 9 1	0 0 8 2	0 1 8 2	1 1 9 1	1 9 3 1	1 9 5 1	0 8 9 2	1 9 7 3	0 8 8 3	1 9 3 2	1 9 3 3	1 9 3 4	0 8 5 2	1 9 5 2	1 9 5 3	1 9 7 4	1 9 5 4	1 9 5 5	1 9 7 5
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																	X								X	
Mesentery			+	+					+		+				+											
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																										
Blood vessel																		+								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, skin										X																
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																								X		
Bilateral, pheochromocytoma benign																										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Carcinoma																										
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma					X	X								X		X	X			X	X	X	X	X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma										X					X						X					
Follicular cell, carcinoma																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 8 6 3	0 8 6 4	0 8 6 5	0 8 6 8 4	0 8 6 8 5	1 9 3 5	1 9 4 1	1 9 4 2	1 9 4 3	1 9 4 4	1 9 4 5	1 9 6 1	1 9 6 2	1 9 6 3	1 9 6 4	1 9 6 5	1 9 8 3	0 8 5 3	0 8 5 4	0 8 5 5	0 8 7 3	0 8 7 4	0 8 7 5	0 8 9 3	0 8 9 4	0 8 9 5	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular adenoma																											2
Mesentery		+	+																		+						9
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Papilloma squamous																				X							1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Cardiovascular System																											
Blood vessel																											1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, skin																											1
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma benign													X										X				3
Bilateral, pheochromocytoma benign								X																			1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma														X							X						2
Carcinoma																										X	1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma				X	X	X	X	X	X	X	X	X	X	X				X			X		X		X		26
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
C-cell, adenoma													X	X								X		X			7
Follicular cell, carcinoma	X																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	3 2 9	4 1 1	4 1 8	4 5 1	5 5 4	5 5 9	5 7 5	5 9 3	5 9 6	6 1 4	6 3 9	6 5 3	6 6 7	6 7 5	6 8 7	6 9 0	6 9 4	6 9 8	6 9 9	7 1 1	7 1 1	7 2 4	7 2 4	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 8 7 1	1 9 7 2	1 9 9 1	0 8 5 1	0 8 6 1	1 9 7 1	0 8 7 2	0 8 8 1	0 8 9 1	0 8 8 2	0 8 6 2	1 9 3 1	1 9 5 1	1 0 9 2	1 9 7 3	0 8 8 3	1 9 3 2	1 9 3 3	1 9 3 4	0 8 5 2	1 9 5 2	1 9 5 3	1 9 7 4	1 9 5 4	1 9 4 5	1 9 7 5
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Bilateral, adenoma																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa-theca tumor malignant																										
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal									X															X	X	
Endometrium, polyp stromal, multiple																										
Vagina						+				+	+				+			+			+	+	+			+
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									X	
Adenoma, multiple																				X						
Fibroadenoma					X		X				X					X	X	X		X		X		X		
Fibroadenoma, multiple																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																			X							
Keratoacanthoma																					X					
Subcutaneous tissue, fibroma													X													
Subcutaneous tissue, osteosarcoma										X																
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma NOS																			X							
Glioma NOS								X																		
Spinal cord	+																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 8 6 3	0 8 6 4	0 8 6 5	0 8 8 4	0 8 8 5	1 9 3 5	1 9 4 1	1 9 4 2	1 9 4 3	1 9 4 4	1 9 4 5	1 9 6 1	1 9 6 2	1 9 6 3	1 9 6 4	1 9 6 5	1 9 8 3	0 8 5 4	0 8 5 5	0 8 7 3	0 8 7 4	0 8 7 5	0 8 9 3	0 8 9 4	0 8 9 5	**Total Tissues/ Tumors**
General Body System																											
None																											
Genital System																											
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+		50
Adenoma				X	X					X													X				4
Bilateral, adenoma																								X			1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Granulosa-theca tumor malignant	X																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Endometrium, polyp stromal		X							X								X		X					X			8
Endometrium, polyp stromal, multiple					X																						1
Vagina	+	+	+									+															13
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Lymph node, mesenteric	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+		50
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Adenoma																											1
Adenoma, multiple																											1
Fibroadenoma			X					X	X		X	X		X		X				X					X		18
Fibroadenoma, multiple		X																	X		X						3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Basal cell carcinoma																											1
Keratoacanthoma			X																								2
Subcutaneous tissue, fibroma																											1
Subcutaneous tissue, osteosarcoma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Astrocytoma NOS																											1
Glioma NOS																											1
Spinal cord																											1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	3 2 9	4 1 1	4 1 8	4 5 1	5 5 4	5 5 9	5 7 5	5 9 3	5 9 6	6 1 4	6 3 9	6 5 3	6 6 7	6 7 5	6 8 7	6 9 0	6 9 4	6 9 8	6 9 9	7 1 1	7 1 1	7 2 4	7 2 4	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 8 7 1	1 9 7 2	1 9 9 1	0 8 5 1	0 8 6 1	1 9 7 1	0 8 7 2	0 8 8 1	0 8 9 1	0 8 8 2	0 8 6 2	1 9 3 1	1 9 5 1	0 8 9 2	1 9 7 3	0 8 8 3	1 9 3 2	1 9 3 3	1 9 3 4	0 8 5 2	1 9 5 2	1 9 5 3	1 9 7 4	1 9 5 4	1 9 5 5	1 9 7 5
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, greater than five, metastatic, multiple, skin										X																,
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Ear																				+						
Eye														+				+								
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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 Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 8 6 3	0 8 6 4	0 8 6 5	0 8 8 4	0 8 8 5	1 9 3 5	1 9 4 1	1 9 4 2	1 9 4 3	1 9 4 4	1 9 4 5	1 9 6 1	1 9 6 2	1 9 6 3	1 9 6 4	1 9 6 5	1 9 6 3	0 8 5 4	0 8 5 5	0 8 5 5	0 8 7 3	0 8 7 4	0 8 7 5	0 8 9 3	0 8 9 4	0 8 9 5	**Total Tissues/ Tumors**
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, greater than five, metastatic, multiple, skin																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																											
Ear																											1
Eye																											2
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Renal tubule, adenoma													X														1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Leukemia mononuclear			X			X			X		X	X	X			X									X		19

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 275 ppm

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	0 8 1 5	0 8 2 4	0 8 2 5	0 8 2 2	0 8 0 3	0 8 0 4	0 8 0 5	1 8 6 4	1 8 6 5	1 8 7 1	1 8 7 2	1 8 7 3	1 8 7 4	1 8 7 5	1 8 8 1	1 8 8 2	1 8 8 3	1 8 8 4	1 8 8 5	1 8 9 4	1 8 9 5	1 9 0 2	1 9 0 3	1 9 0 4	1 9 0 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma								X																		1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery													+			+			+							10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell, adenoma						X																				1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										1
Odontoma																										1
Cardiovascular System																										
Blood vessel																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X			X	X																					3
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																										3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X																					X				3
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		25
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma												X														1
Follicular cell, adenoma																										1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	3 8 3	5 3 0	5 5 4	6 0 5	6 0 9	6 1 4	6 3 8	6 6 6	6 6 8	6 6 9	6 9 8	7 1 0	7 1 8	7 1 8	7 1 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 7 8 1	0 8 2 1	0 8 1 1	0 8 2 2	1 9 0 1	1 8 9 1	1 8 6 1	1 8 6 2	0 8 2 3	1 8 6 3	1 8 9 2	0 7 8 2	0 8 0 1	0 8 1 2	1 8 9 3	0 7 8 3	0 7 8 4	0 7 8 5	0 7 9 1	0 7 9 2	0 7 9 3	0 7 9 4	0 7 9 5	0 8 1 3	0 8 1 4
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma									X							X							X		
Carcinoma										X															
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Oviduct						+																			
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																			X						
Adenoma																					X				
Endometrium, polyp stromal		X			X			X			X								X				X	X	
Vagina			+		+		+					+										+			
Papilloma squamous																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Fibroadenoma	X						X	X	X							X			X		X				
Fibroadenoma, multiple												X		X								X			
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma		X																							
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye			M																						
Harderian gland	+																								
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X		X	X	X						X	X	X		X								

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	0 8 1 5	0 8 2 4	0 8 2 5	0 8 2 0	0 8 0 3	0 8 0 4	0 8 0 5	1 8 6 4	1 8 6 5	1 8 7 1	1 8 7 2	1 8 7 3	1 8 7 4	1 8 7 5	1 8 8 1	1 8 8 2	1 8 8 3	1 8 8 4	1 8 8 5	1 8 9 4	1 9 9 5	1 9 0 2	1 9 0 3	1 9 0 4	1 9 0 5	**Total Tissues/ Tumors**
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma												X	X						X				X	X		8
Carcinoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Oviduct																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																										1
Adenoma																										1
Endometrium, polyp stromal		X			X				X		X												X	X		13
Vagina											+				+		+	+			+		+			11
Papilloma squamous															X											1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymoma benign	X																									1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																							X			1
Fibroadenoma										X				X	X	X						X	X			13
Fibroadenoma, multiple																										3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glioma malignant																						X				1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye						+							+													2
Harderian gland																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear					X						X		X	X		X			X				X	X		16

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

	0 ppm	70 ppm	140 ppm	275 ppm
Adrenal Cortex: Adenoma				
Overall rates[a]	0/50 (0%)	1/49 (2%)	0/51 (0%)	3/50 (6%)
Adjusted rates[b]	0.0%	3.3%	0.0%	8.6%
Terminal rates[c]	0/31 (0%)	1/30 (3%)	0/28 (0%)	3/35 (9%)
First incidence (days)	–[e]	729 (T)	–	729 (T)
Life table tests[d]	P=0.060	P=0.493	–	P=0.143
Logistic regression tests[d]	P=0.060	P=0.493	–	P=0.143
Cochran-Armitage test[d]	P=0.045			
Fisher exact test[d]		P=0.495	–	P=0.121
Adrenal Medulla: Benign Pheochromocytoma				
Overall rates	7/50 (14%)	4/49 (8%)	4/51 (8%)	3/50 (6%)
Adjusted rates	21.9%	13.3%	14.3%	7.2%
Terminal rates	6/31 (19%)	4/30 (13%)	4/28 (14%)	1/35 (3%)
First incidence (days)	721	729 (T)	729 (T)	609
Life table tests	P=0.105N	P=0.272N	P=0.317N	P=0.125N
Logistic regression tests	P=0.113N	P=0.245N	P=0.291N	P=0.146N
Cochran-Armitage test	P=0.134N			
Fisher exact test		P=0.274N	P=0.251N	P=0.159N
Clitoral Gland: Adenoma				
Overall rates	5/48 (10%)	4/50 (8%)	5/50 (10%)	8/50 (16%)
Adjusted rates	16.1%	11.6%	18.5%	21.9%
Terminal rates	5/31 (16%)	3/31 (10%)	5/27 (19%)	7/35 (20%)
First incidence (days)	729 (T)	508	729 (T)	668
Life table tests	P=0.219	P=0.503N	P=0.543	P=0.356
Logistic regression tests	P=0.204	P=0.488N	P=0.543	P=0.357
Cochran-Armitage test	P=0.176			
Fisher exact test		P=0.474N	P=0.603N	P=0.304
Clitoral Gland: Adenoma or Carcinoma				
Overall rates	6/48 (13%)	4/50 (8%)	5/50 (10%)	9/50 (18%)
Adjusted rates	19.4%	11.6%	18.5%	23.8%
Terminal rates	6/31 (19%)	3/31 (10%)	5/27 (19%)	7/35 (20%)
First incidence (days)	729 (T)	508	729 (T)	668
Life table tests	P=0.214	P=0.371N	P=0.600N	P=0.377
Logistic regression tests	P=0.195	P=0.358N	P=0.600N	P=0.364
Cochran-Armitage test	P=0.168			
Fisher exact test		P=0.344N	P=0.471N	P=0.318
Lung: Alveolar/bronchiolar Adenoma or Alveolar/bronchiolar Carcinoma				
Overall rates	1/49 (2%)	3/50 (6%)	0/51 (0%)	0/50 (0%)
Adjusted rates	3.3%	8.8%	0.0%	0.0%
Terminal rates	1/30 (3%)	2/31 (6%)	0/28 (0%)	0/35 (0%)
First incidence (days)	729 (T)	627	–	–
Life table tests	P=0.139N	P=0.307	P=0.514N	P=0.469N
Logistic regression tests	P=0.145N	P=0.306	P=0.514N	P=0.469N
Cochran-Armitage test	P=0.147N			
Fisher exact test		P=0.316	P=0.490N	P=0.495N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Mammary Gland: Fibroadenoma				
Overall rates	16/50 (32%)	14/50 (28%)	21/51 (41%)	16/50 (32%)
Adjusted rates	43.5%	39.8%	57.1%	38.1%
Terminal rates	11/31 (35%)	11/31 (35%)	13/28 (46%)	10/35 (29%)
First incidence (days)	578	376	554	383
Life table tests	P=0.502N	P=0.422N	P=0.150	P=0.449N
Logistic regression tests	P=0.450	P=0.435N	P=0.170	P=0.576N
Cochran-Armitage test	P=0.428			
Fisher exact test		P=0.414N	P=0.227	P=0.585N
Mammary Gland: Adenoma or Fibroadenoma				
Overall rates	17/50 (34%)	14/50 (28%)	22/51 (43%)	16/50 (32%)
Adjusted rates	46.3%	39.8%	59.9%	38.1%
Terminal rates	12/31 (39%)	11/31 (35%)	14/28 (50%)	10/35 (29%)
First incidence (days)	578	376	554	383
Life table tests	P=0.443N	P=0.343N	P=0.147	P=0.368N
Logistic regression tests	P=0.513	P=0.354N	P=0.168	P=0.489N
Cochran-Armitage test	P=0.488			
Fisher exact test		P=0.333N	P=0.230	P=0.500N
Mammary Gland: Adenoma, Fibroadenoma, or Adenocarcinoma				
Overall rates	19/50 (38%)	14/50 (28%)	22/51 (43%)	16/50 (32%)
Adjusted rates	52.0%	39.8%	59.9%	38.1%
Terminal rates	14/31 (45%)	11/31 (35%)	14/28 (50%)	10/35 (29%)
First incidence (days)	578	376	554	383
Life table tests	P=0.316N	P=0.207N	P=0.246	P=0.228N
Logistic regression tests	P=0.422N	P=0.216N	P=0.290	P=0.322N
Cochran-Armitage test	P=0.449N			
Fisher exact test		P=0.198N	P=0.373	P=0.338N
Pancreatic Islets: Adenoma				
Overall rates	0/50 (0%)	0/50 (0%)	2/51 (4%)	3/50 (6%)
Adjusted rates	0.0%	0.0%	7.1%	8.2%
Terminal rates	0/31 (0%)	0/31 (0%)	2/28 (7%)	2/35 (6%)
First incidence (days)	-	-	729 (T)	718
Life table tests	P=0.039	-	P=0.216	P=0.148
Logistic regression tests	P=0.036	-	P=0.216	P=0.138
Cochran-Armitage test	P=0.027			
Fisher exact test		-	P=0.252	P=0.121
Pancreatic Islets: Adenoma or Carcinoma				
Overall rates	0/50 (0%)	0/50 (0%)	3/51 (6%)	3/50 (6%)
Adjusted rates	0.0%	0.0%	10.7%	8.2%
Terminal rates	0/31 (0%)	0/31 (0%)	3/28 (11%)	2/35 (6%)
First incidence (days)	-	-	729 (T)	718
Life table tests	P=0.048	-	P=0.103	P=0.148
Logistic regression tests	P=0.044	-	P=0.103	P=0.138
Cochran-Armitage test	P=0.033			
Fisher exact test		-	P=0.125	P=0.121

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	33/50 (66%)	28/49 (57%)	26/50 (52%)	25/50 (50%)
Adjusted rates	78.1%	66.2%	68.0%	59.3%
Terminal rates	22/31 (71%)	17/31 (55%)	16/28 (57%)	18/35 (51%)
First incidence (days)	531	494	554	638
Life table tests	P=0.044N	P=0.263N	P=0.260N	P=0.042N
Logistic regression tests	P=0.044N	P=0.286N	P=0.159N	P=0.056N
Cochran-Armitage test	P=0.067N			
Fisher exact test		P=0.242N	P=0.111N	P=0.078N
Skin: Keratoacanthoma, Basal Cell Carcinoma, or Squamous Cell Carcinoma				
Overall rates	1/50 (2%)	1/50 (2%)	3/51 (6%)	0/50 (0%)
Adjusted rates	2.9%	3.2%	9.4%	0.0%
Terminal rates	0/31 (0%)	1/31 (3%)	1/28 (4%)	0/35 (0%)
First incidence (days)	702	729 (T)	699	-
Life table tests	P=0.383N	P=0.754N	P=0.284	P=0.478N
Logistic regression tests	P=0.398N	P=0.759	P=0.293	P=0.498N
Cochran-Armitage test	P=0.413N			
Fisher exact test		P=0.753N	P=0.316	P=0.500N
Skin (Subcutaneous Tissue): Fibroma or Fibrosarcoma				
Overall rates	3/50 (6%)	0/50 (0%)	1/51 (2%)	1/50 (2%)
Adjusted rates	8.0%	0.0%	2.6%	2.0%
Terminal rates	1/31 (3%)	0/31 (0%)	0/28 (0%)	0/35 (0%)
First incidence (days)	666	-	667	530
Life table tests	P=0.276N	P=0.133N	P=0.329N	P=0.288N
Logistic regression tests	P=0.293N	P=0.120N	P=0.294N	P=0.308N
Cochran-Armitage test	P=0.290N			
Fisher exact test		P=0.121N	P=0.301N	P=0.309N
Thyroid Gland (C-cell): Adenoma				
Overall rates	4/50 (8%)	0/48 (0%)	7/51 (14%)	1/50 (2%)
Adjusted rates	10.6%	0.0%	21.1%	2.9%
Terminal rates	2/31 (6%)	0/29 (0%)	4/28 (14%)	1/35 (3%)
First incidence (days)	620	-	614	729 (T)
Life table tests	P=0.306N	P=0.078N	P=0.228	P=0.165N
Logistic regression tests	P=0.334N	P=0.064N	P=0.258	P=0.182N
Cochran-Armitage test	P=0.341N			
Fisher exact test		P=0.064N	P=0.274	P=0.181N
Thyroid Gland (C-cell): Carcinoma				
Overall rates	1/50 (2%)	3/48 (6%)	0/51 (0%)	0/50 (0%)
Adjusted rates	3.2%	10.3%	0.0%	0.0%
Terminal rates	1/31 (3%)	3/29 (10%)	0/28 (0%)	0/35 (0%)
First incidence (days)	729 (T)	729 (T)	-	-
Life table tests	P=0.136N	P=0.280	P=0.520N	P=0.476N
Logistic regression tests	P=0.136N	P=0.280	P=0.520N	P=0.476N
Cochran-Armitage test	P=0.149N			
Fisher exact test		P=0.293	P=0.495N	P=0.500N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rates	5/50 (10%)	3/48 (6%)	7/51 (14%)	1/50 (2%)
Adjusted rates	13.7%	10.3%	21.1%	2.9%
Terminal rates	3/31 (10%)	3/29 (10%)	4/28 (14%)	1/35 (3%)
First incidence (days)	620	729 (T)	614	729 (T)
Life table tests	P=0.120N	P=0.400N	P=0.332	P=0.091N
Logistic regression tests	P=0.134N	P=0.393N	P=0.370	P=0.103N
Cochran-Armitage test	P=0.143N			
Fisher exact test		P=0.381N	P=0.394	P=0.102N
Thyroid Gland (Follicular Cell): Adenoma				
Overall rates	3/50 (6%)	1/48 (2%)	0/51 (0%)	1/50 (2%)
Adjusted rates	8.4%	3.4%	0.0%	2.4%
Terminal rates	1/31 (3%)	1/29 (3%)	0/28 (0%)	0/35 (0%)
First incidence (days)	667	729 (T)	-	669
Life table tests	P=0.177N	P=0.317N	P=0.135N	P=0.273N
Logistic regression tests	P=0.188N	P=0.330N	P=0.123N	P=0.307N
Cochran-Armitage test	P=0.191N			
Fisher exact test		P=0.324N	P=0.118N	P=0.309N
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rates	3/50 (6%)	1/48 (2%)	1/51 (2%)	1/50 (2%)
Adjusted rates	8.4%	3.4%	3.6%	2.4%
Terminal rates	1/31 (3%)	1/29 (3%)	1/28 (4%)	0/35 (0%)
First incidence (days)	667	729 (T)	729 (T)	669
Life table tests	P=0.214N	P=0.317N	P=0.334N	P=0.273N
Logistic regression tests	P=0.227N	P=0.330N	P=0.315N	P=0.307N
Cochran-Armitage test	P=0.233N			
Fisher exact test		P=0.324N	P=0.301N	P=0.309N
Uterus: Stromal Polyp				
Overall rates	10/50 (20%)	9/50 (18%)	9/51 (18%)	13/50 (26%)
Adjusted rates	24.7%	27.1%	30.2%	32.2%
Terminal rates	4/31 (13%)	7/31 (23%)	8/28 (29%)	9/35 (26%)
First incidence (days)	508	722	596	530
Life table tests	P=0.328	P=0.500N	P=0.574N	P=0.412
Logistic regression tests	P=0.247	P=0.509N	P=0.488N	P=0.297
Cochran-Armitage test	P=0.233			
Fisher exact test		P=0.500N	P=0.481N	P=0.318
All Organs: Mononuclear Leukemia				
Overall rates	8/50 (16%)	7/50 (14%)	19/51 (37%)	16/50 (32%)
Adjusted rates	20.8%	17.5%	48.1%	37.4%
Terminal rates	4/31 (13%)	2/31 (6%)	9/28 (32%)	9/35 (26%)
First incidence (days)	472	514	329	554
Life table tests	P=0.037	P=0.513N	P=0.014	P=0.102
Logistic regression tests	P=0.009	P=0.445N	P=0.020	P=0.045
Cochran-Armitage test	P=0.011			
Fisher exact test		P=0.500N	P=0.014	P=0.050

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
All Organs: Benign Tumors				
Overall rates	45/50 (90%)	40/50 (80%)	41/51 (80%)	39/50 (78%)
Adjusted rates	95.7%	90.7%	91.1%	84.6%
Terminal rates	29/31 (94%)	27/31 (87%)	24/28 (86%)	28/35 (80%)
First incidence (days)	508	376	554	383
Life table tests	P=0.068N	P=0.261N	P=0.513N	P=0.058N
Logistic regression tests	P=0.073N	P=0.172N	P=0.265N	P=0.078N
Cochran-Armitage test	P=0.106N			
Fisher exact test		P=0.131N	P=0.141N	P=0.086N
All Organs: Malignant Tumors				
Overall rates	16/50 (32%)	12/50 (24%)	22/51 (43%)	20/50 (40%)
Adjusted rates	40.6%	31.1%	54.6%	44.8%
Terminal rates	9/31 (29%)	6/31 (19%)	11/28 (39%)	11/35 (31%)
First incidence (days)	472	514	329	530
Life table tests	P=0.218	P=0.279N	P=0.131	P=0.408
Logistic regression tests	P=0.098	P=0.248N	P=0.194	P=0.249
Cochran-Armitage test	P=0.105			
Fisher exact test		P=0.252N	P=0.171	P=0.266
All Organs: Benign and Malignant Tumors				
Overall rates	48/50 (96%)	46/50 (92%)	46/51 (90%)	43/50 (86%)
Adjusted rates	96.0%	93.9%	93.8%	87.7%
Terminal rates	29/31 (94%)	28/31 (90%)	25/28 (89%)	29/35 (83%)
First incidence (days)	472	376	329	383
Life table tests	P=0.085N	P=0.461N	P=0.476	P=0.090N
Logistic regression tests	P=0.054N	P=0.346N	P=0.237N	P=0.091N
Cochran-Armitage test	P=0.056N			
Fisher exact test		P=0.339N	P=0.226N	P=0.080N

(T)Terminal sacrifice

[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.

[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality

[c] Observed incidence at terminal kill

[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.

[e] Not applicable; no tumors in animal group

TABLE B4a
Historical Incidence of Leukemias in Untreated Female F344/N Rats[a]

Study	Incidence in Controls
Historical Incidence at Southern Research Institute	
Feed	
Nitrofurantoin	13/50 (26%)
Rhodamine 6G	11/50 (22%)
Roxarsone	14/50 (28%)
Total	38/150 (25%)
Standard deviation	3.1%
Range	22%-28%
Water	
Chloramine	8/50 (16%)
Overall Historical Incidence	
Feed	
Total	124/500 (25%)
Standard deviation	6.1%
Range	14%-36%
Water	
Total	46/180 (26%)
Standard deviation	8.5%
Range	16%-33%

[a] Data as of 15 September 1990; includes data for lymphocytic, monocytic, mononuclear cell, and undifferentiated leukemias.

TABLE B4b
Historical Incidence of Pancreatic Islet Neoplasms in Untreated Female F344/N Rats[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Southern Research Institute			
Feed			
Nitrofurantoin	0/50 (0%)	1/50 (2%)	1/50 (2%)
Rhodamine 6G	2/48 (4%)	1/48 (2%)	3/48 (6%)
Roxarsone	1/50 (2%)	0/50 (0%)	1/50 (2%)
Total	3/148 (2%)	2/148 (1%)	5/148 (3%)
Standard deviation	2.0%	1.2%	2.3%
Range	0%-4%	0%-2%	2%-6%
Water			
Chloramine	0/50 (0%)	0/50 (0%)	0/50 (0%)
Overall Historical Incidence			
Feed			
Total	7/492 (1%)	3/492 (1%)	10/492 (2%)
Standard deviation	1.4%	1.0%	1.6%
Range	0%-4%	0%-2%	0%-6%
Water			
Total	4/180 (2%)	0/180 (0%)	4/180 (2%)
Standard deviation	2.0%		2.0%
Range	0%-4%		0%-4%

[a] Data as of 15 September 1990

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	9	10
Early deaths				
Natural death	3	1	4	1
Moribund	16	18	19	14
Survivors				
Terminal sacrifice	31	31	28	35
Animals examined microscopically	50	50	51	50
Alimentary System				
Intestine large, cecum	(50)	(50)	(51)	(50)
Parasite metazoan		1 (2%)		1 (2%)
Intestine large, colon	(50)	(50)	(51)	(50)
Cyst		1 (2%)		
Parasite metazoan	1 (2%)		2 (4%)	3 (6%)
Intestine large, rectum	(50)	(50)	(50)	(50)
Parasite metazoan	4 (8%)	5 (10%)	4 (8%)	1 (2%)
Intestine small, ileum	(50)	(50)	(51)	(50)
Fibrosis		1 (2%)		
Ulcer		1 (2%)		
Liver	(50)	(50)	(51)	(50)
Angiectasis	3 (6%)	2 (4%)	3 (6%)	1 (2%)
Atrophy, focal				1 (2%)
Basophilic focus	1 (2%)			
Congestion	3 (6%)	1 (2%)	2 (4%)	
Fatty change	10 (20%)	19 (38%)	11 (22%)	9 (18%)
Fibrosis, focal	1 (2%)			
Focal cellular change	36 (72%)	38 (76%)	36 (71%)	35 (70%)
Granuloma	39 (78%)	39 (78%)	36 (71%)	31 (62%)
Hematopoietic cell proliferation	6 (12%)	2 (4%)	1 (2%)	1 (2%)
Hemorrhage	1 (2%)			
Hepatodiaphragmatic nodule	10 (20%)	9 (18%)	7 (14%)	12 (24%)
Hyperplasia, histiocyte, lymphoid	1 (2%)	2 (4%)		
Hyperplasia, multifocal	7 (14%)	8 (16%)	9 (18%)	14 (28%)
Infiltration cellular, mixed cell	4 (8%)	8 (16%)	6 (12%)	6 (12%)
Inflammation, focal				1 (2%)
Necrosis, focal	1 (2%)	2 (4%)	5 (10%)	
Thrombus			1 (2%)	
Bile duct, hyperplasia	34 (68%)	42 (84%)	37 (73%)	41 (82%)
Biliary tract, fibrosis	28 (56%)	31 (62%)	29 (57%)	32 (64%)
Centrilobular, atrophy	4 (8%)	5 (10%)	9 (18%)	12 (24%)
Centrilobular, necrosis		1 (2%)	1 (2%)	
Mesentery	(10)	(6)	(9)	(10)
Accessory spleen	1 (10%)			
Angiectasis			1 (11%)	
Hemorrhage				1 (10%)
Infiltration cellular, lymphocytic	1 (10%)			
Inflammation, chronic	5 (50%)	2 (33%)	1 (11%)	2 (20%)
Fat, necrosis	2 (20%)	2 (33%)	3 (33%)	

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Alimentary System (continued)				
Pancreas	(50)	(50)	(51)	(50)
Atrophy, focal	6 (12%)	7 (14%)	8 (16%)	9 (18%)
Cytoplasmic alteration	1 (2%)			
Inflammation, chronic			1 (2%)	
Acinar cell, hyperplasia			1 (2%)	
Salivary glands	(49)	(50)	(51)	(50)
Atrophy				1 (2%)
Focal cellular change	1 (2%)			1 (2%)
Inflammation, chronic	1 (2%)			
Stomach, forestomach	(50)	(50)	(51)	(50)
Diverticulum			1 (2%)	
Edema		1 (2%)		
Erosion	1 (2%)			
Inflammation, chronic	7 (14%)	3 (6%)	3 (6%)	1 (2%)
Perforation	2 (4%)			
Ulcer	6 (12%)	3 (6%)	1 (2%)	1 (2%)
Mucosa, hyperplasia, papillary	9 (18%)	4 (8%)	3 (6%)	2 (4%)
Stomach, glandular	(50)	(50)	(51)	(50)
Edema			1 (2%)	
Erosion	1 (2%)	1 (2%)		
Inflammation, chronic	2 (4%)	1 (2%)	2 (4%)	1 (2%)
Necrosis		1 (2%)		
Ulcer		1 (2%)		
Mucosa, cyst				1 (2%)
Tooth	(1)			(1)
Dysplasia	1 (100%)			
Inflammation, suppurative	1 (100%)			
Cardiovascular System				
Blood vessel		(5)	(1)	(1)
Mesenteric artery, aneurysm			1 (100%)	
Mesenteric artery, inflammation, chronic		3 (60%)	1 (100%)	1 (100%)
Mesenteric artery, thrombus		1 (20%)	1 (100%)	
Thoracic, inflammation, chronic		1 (20%)		
Heart	(50)	(50)	(51)	(50)
Dilatation				1 (2%)
Inflammation, chronic		1 (2%)		
Thrombus				1 (2%)
Artery, inflammation, chronic	1 (2%)			
Pericardium, edema				1 (2%)
Endocrine System				
Adrenal gland, cortex	(50)	(49)	(51)	(50)
Accessory adrenal cortical nodule	1 (2%)			1 (2%)
Angiectasis			3 (6%)	1 (2%)
Congestion	1 (2%)			2 (4%)
Focal cellular change	16 (32%)	16 (33%)	18 (35%)	14 (28%)
Metaplasia, osseous		1 (2%)		
Vacuolization cytoplasmic	1 (2%)	3 (6%)		

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Endocrine System (continued)				
Adrenal gland, medulla	(50)	(49)	(51)	(50)
Angiectasis				1 (2%)
Hematopoietic cell proliferation				1 (2%)
Hyperplasia	5 (10%)	3 (6%)	8 (16%)	2 (4%)
Islets, pancreatic	(50)	(50)	(51)	(50)
Hyperplasia				1 (2%)
Pituitary gland	(50)	(49)	(50)	(50)
Angiectasis	38 (76%)	42 (86%)	36 (72%)	40 (80%)
Atrophy				1 (2%)
Cyst	3 (6%)	2 (4%)	1 (2%)	6 (12%)
Pars distalis, hyperplasia, focal	6 (12%)	9 (18%)	9 (18%)	9 (18%)
Thyroid gland	(50)	(48)	(51)	(50)
Degeneration, cystic	3 (6%)			2 (4%)
Fibrosis		1 (2%)		
Ultimobranchial cyst	1 (2%)	1 (2%)		
C-cell, hyperplasia	7 (14%)	9 (19%)	11 (22%)	12 (24%)
Follicle, cyst	1 (2%)	1 (2%)	1 (2%)	
Follicular cell, hyperplasia	2 (4%)	1 (2%)	1 (2%)	1 (2%)
General Body System				
None				
Genital System				
Clitoral gland	(48)	(50)	(50)	(50)
Degeneration, cystic	1 (2%)	1 (2%)		1 (2%)
Fibrosis			1 (2%)	
Hyperplasia	3 (6%)	2 (4%)	3 (6%)	7 (14%)
Inflammation, suppurative	11 (23%)	5 (10%)	5 (10%)	6 (12%)
Ovary	(50)	(50)	(51)	(50)
Corpus luteum, proliferation	1 (2%)			
Corpus luteum, thecal cell, hyperplasia	1 (2%)			
Follicle, cyst	2 (4%)	4 (8%)	2 (4%)	6 (12%)
Periovarian tissue, cyst		1 (2%)	2 (4%)	1 (2%)
Oviduct				(1)
Dilatation				1 (100%)
Uterus	(50)	(50)	(51)	(50)
Angiectasis			1 (2%)	
Cyst				1 (2%)
Hemorrhage	2 (4%)	1 (2%)		2 (4%)
Hydrometra	2 (4%)	4 (8%)	3 (6%)	2 (4%)
Inflammation, suppurative		1 (2%)		
Intussusception				1 (2%)
Prolapse		1 (2%)		
Endometrium, hyperplasia, cystic	26 (52%)	33 (66%)	37 (73%)	27 (54%)
Vagina	(8)	(14)	(13)	(11)
Cyst	6 (75%)	9 (64%)	7 (54%)	7 (64%)
Exudate, mucous			1 (8%)	1 (9%)
Inflammation, suppurative	2 (25%)	10 (71%)	5 (38%)	2 (18%)
Mucosa, hyperplasia		1 (7%)		

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Hematopoietic System				
Bone marrow	(50)	(50)	(51)	(50)
Hypercellularity	4 (8%)	4 (8%)	7 (14%)	5 (10%)
Myelofibrosis	1 (2%)		1 (2%)	1 (2%)
Lymph node	(50)	(50)	(51)	(50)
Inguinal, hyperplasia		1 (2%)		
Inguinal, inflammation, suppurative				1 (2%)
Mediastinal, angiectasis	3 (6%)	3 (6%)	7 (14%)	5 (10%)
Mediastinal, hyperplasia				1 (2%)
Mediastinal, hyperplasia, histiocyte			1 (2%)	1 (2%)
Mediastinal, hyperplasia, lymphoid		1 (2%)		1 (2%)
Pancreatic, angiectasis	1 (2%)		1 (2%)	
Pancreatic, hyperplasia				1 (2%)
Pancreatic, hyperplasia, lymphoid			1 (2%)	1 (2%)
Renal, angiectasis			1 (2%)	1 (2%)
Lymph node, mandibular	(48)	(50)	(51)	(49)
Angiectasis	3 (6%)	2 (4%)	2 (4%)	
Hyperplasia	5 (10%)	1 (2%)	1 (2%)	1 (2%)
Hyperplasia, lymphoid	1 (2%)			
Inflammation, suppurative				1 (2%)
Lymph node, mesenteric	(49)	(49)	(49)	(49)
Angiectasis	2 (4%)	1 (2%)	2 (4%)	3 (6%)
Hyperplasia, histiocyte				1 (2%)
Hyperplasia, lymphoid				1 (2%)
Spleen	(50)	(50)	(51)	(50)
Amyloid deposition		1 (2%)		
Congestion			1 (2%)	
Fibrosis			4 (8%)	4 (8%)
Hematopoietic cell proliferation	12 (24%)	9 (18%)	5 (10%)	5 (10%)
Hemorrhage			1 (2%)	1 (2%)
Hyperplasia, histiocyte, lymphoid	2 (4%)	6 (12%)	5 (10%)	8 (16%)
Necrosis, focal				1 (2%)
Capsule, hyperplasia, histiocyte, lymphoid	1 (2%)			
Capsule, inflammation, chronic			1 (2%)	
Thymus	(49)	(47)	(50)	(50)
Cyst		1 (2%)	4 (8%)	1 (2%)
Hyperplasia, lymphoid		1 (2%)		1 (2%)
Inflammation, suppurative				1 (2%)
Integumentary System				
Mammary gland	(50)	(50)	(51)	(50)
Dilatation	40 (80%)	43 (86%)	40 (78%)	42 (84%)
Fibrosis		1 (2%)		
Hyperplasia	3 (6%)	5 (10%)	1 (2%)	7 (14%)
Skin	(50)	(50)	(51)	(50)
Abscess	1 (2%)			
Erosion			1 (2%)	
Hyperplasia, squamous			1 (2%)	
Inflammation, chronic	3 (6%)		2 (4%)	2 (4%)
Ulcer	2 (4%)			
Sebaceous gland, hyperplasia		1 (2%)		

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Musculoskeletal System				
Bone	(50)	(50)	(51)	(50)
Hyperostosis	9 (18%)	10 (20%)	13 (25%)	4 (8%)
Nervous System				
Brain	(48)	(50)	(51)	(50)
Compression	11 (23%)	12 (24%)	7 (14%)	8 (16%)
Hemorrhage		1 (2%)	4 (8%)	
Hydrocephalus		1 (2%)		
Mineralization, focal		1 (2%)		
Necrosis			1 (2%)	
Spinal cord			(1)	
Hemorrhage			1 (100%)	
Respiratory System				
Lung	(50)	(50)	(51)	(50)
Congestion			2 (4%)	
Foreign body	1 (2%)	1 (2%)		
Hemorrhage	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Hyperplasia, macrophage	3 (6%)		1 (2%)	1 (2%)
Infiltration cellular, mixed cell	3 (6%)			
Inflammation, chronic, focal			1 (2%)	1 (2%)
Inflammation, pyogranulomatous	1 (2%)	1 (2%)	1 (2%)	
Alveolar epithelium, hyperplasia	2 (4%)	3 (6%)	2 (4%)	2 (4%)
Nose	(50)	(50)	(51)	(50)
Foreign body	1 (2%)	1 (2%)		
Fungus	3 (6%)	3 (6%)	3 (6%)	2 (4%)
Hemorrhage			2 (4%)	
Inflammation, suppurative	3 (6%)	7 (14%)	4 (8%)	2 (4%)
Special Senses System				
Ear	(1)	(2)	(1)	
Pinna, hemorrhage			1 (100%)	
Pinna, inflammation, chronic			1 (100%)	
Eye	(3)	(5)	(2)	(2)
Atrophy		1 (20%)		
Cataract	3 (100%)	4 (80%)	1 (50%)	1 (50%)
Cornea, inflammation, chronic				1 (50%)
Retina, degeneration	2 (67%)	4 (80%)	2 (100%)	1 (50%)
Harderian gland				(1)
Hyperplasia, lymphoid				1 (100%)

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Urinary System				
Kidney	(50)	(50)	(51)	(50)
Atrophy				1 (2%)
Congestion			1 (2%)	
Fibrosis		1 (2%)	3 (6%)	
Inflammation, suppurative		1 (2%)	1 (2%)	1 (2%)
Mineralization	2 (4%)	2 (4%)	2 (4%)	1 (2%)
Nephropathy	46 (92%)	45 (90%)	47 (92%)	49 (98%)
Pigmentation			2 (4%)	
Pelvis, transitional epithelium, hyperplasia				1 (2%)
Renal tubule, degeneration, hyaline			1 (2%)	
Renal tubule, vacuolization cytoplasmic	1 (2%)			
Urinary bladder	(50)	(50)	(50)	(50)
Transitional epithelium, hyperplasia		1 (2%)		1 (2%)

APPENDIX C
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR CHLORAMINATED WATER STUDY

TABLE C1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	9	10	9	10
Early deaths				
Natural death	3	1	3	1
Moribund	34	27	34	33
Survivors				
Terminal sacrifice	14	22	14	16
Animals examined microscopically	51	50	51	50
Alimentary System				
Esophagus	(51)	(50)	(51)	(50)
Carcinoma, metastatic, thyroid gland			1 (2%)	
Intestine large, cecum	(51)	(50)	(50)	(50)
Intestine large, colon	(51)	(50)	(51)	(49)
Intestine large, rectum	(51)	(50)	(50)	(49)
Adenocarcinoma	1 (2%)			
Intestine small, ileum	(51)	(50)	(51)	(49)
Intestine small, jejunum	(51)	(50)	(51)	(49)
Adenocarcinoma	1 (2%)			
Liver	(51)	(50)	(51)	(50)
Hepatocellular adenoma	2 (4%)	4 (8%)	2 (4%)	
Mesentery	(31)	(15)	(15)	(24)
Osteosarcoma, metastatic, bone	1 (3%)			
Pancreas	(51)	(50)	(51)	(50)
Acinar cell, adenoma	4 (8%)	5 (10%)	1 (2%)	2 (4%)
Acinar cell, adenoma, multiple		1 (2%)		
Pharynx			(1)	
Palate, papilloma squamous			1 (100%)	
Salivary glands	(51)	(50)	(51)	(50)
Stomach, forestomach	(51)	(50)	(51)	(49)
Papilloma squamous			1 (2%)	
Stomach, glandular	(51)	(50)	(51)	(49)
Tongue			(1)	
Papilloma squamous			1 (100%)	
Cardiovascular System				
Heart	(51)	(50)	(51)	(50)
Schwannoma malignant				1 (2%)
Endocrine System				
Adrenal gland, cortex	(51)	(50)	(51)	(50)
Adenoma			1 (2%)	
Osteosarcoma, metastatic, bone	1 (2%)			
Adrenal gland, medulla	(51)	(50)	(51)	(50)
Pheochromocytoma malignant	2 (4%)			
Pheochromocytoma benign	11 (22%)	16 (32%)	17 (33%)	14 (28%)
Bilateral, pheochromocytoma benign	12 (24%)	19 (38%)	10 (20%)	8 (16%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Endocrine System (continued)				
Islets, pancreatic	(51)	(50)	(51)	(50)
Adenoma	5 (10%)	5 (10%)	5 (10%)	10 (20%)
Carcinoma	2 (4%)		1 (2%)	1 (2%)
Pituitary gland	(50)	(50)	(51)	(50)
Pars distalis, adenoma	20 (40%)	29 (58%)	22 (43%)	19 (38%)
Thyroid gland	(51)	(50)	(51)	(50)
C-cell, adenoma	6 (12%)	2 (4%)	3 (6%)	3 (6%)
C-cell, carcinoma	1 (2%)	2 (4%)	1 (2%)	
General Body System				
None				
Genital System				
Epididymis	(51)	(50)	(51)	(50)
Preputial gland	(50)	(50)	(51)	(50)
Adenoma	3 (6%)	2 (4%)	4 (8%)	1 (2%)
Carcinoma	1 (2%)	2 (4%)	3 (6%)	1 (2%)
Sarcoma, metastatic				1 (2%)
Bilateral, carcinoma			1 (2%)	
Prostate	(51)	(50)	(51)	(50)
Sarcoma, metastatic				1 (2%)
Seminal vesicle	(51)	(50)	(51)	(50)
Testes	(51)	(50)	(51)	(50)
Osteosarcoma, metastatic, bone	1 (2%)			
Bilateral, interstitial cell, adenoma	26 (51%)	30 (60%)	30 (59%)	32 (64%)
Interstitial cell, adenoma	7 (14%)	14 (28%)	8 (16%)	11 (22%)
Hematopoietic System				
Bone marrow	(51)	(50)	(51)	(50)
Lymph node	(51)	(50)	(51)	(50)
Lymph node, mandibular	(51)	(50)	(51)	(49)
Lymph node, mesenteric	(51)	(49)	(51)	(50)
Spleen	(51)	(50)	(51)	(50)
Histiocytic sarcoma			1 (2%)	1 (2%)
Osteosarcoma, metastatic, bone	1 (2%)			
Sarcoma		1 (2%)		
Thymus	(46)	(46)	(48)	(49)
Integumentary System				
Mammary gland	(48)	(48)	(49)	(49)
Adenocarcinoma			1 (2%)	
Adenoma	1 (2%)			
Fibroadenoma	2 (4%)	1 (2%)	1 (2%)	2 (4%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Integumentary System (continued)				
Skin	(51)	(50)	(51)	(50)
Basal cell adenoma			1 (2%)	
Keratoacanthoma	3 (6%)	3 (6%)	2 (4%)	2 (4%)
Papilloma squamous	1 (2%)	3 (6%)	1 (2%)	1 (2%)
Squamous cell carcinoma	1 (2%)			
Trichoepithelioma		1 (2%)		1 (2%)
Subcutaneous tissue, fibroma		4 (8%)	2 (4%)	5 (10%)
Subcutaneous tissue, fibrosarcoma	1 (2%)			
Subcutaneous tissue, fibrous histiocytoma				1 (2%)
Subcutaneous tissue, lipoma	1 (2%)			
Subcutaneous tissue, lymphangiosarcoma			1 (2%)	
Musculoskeletal System				
Bone	(51)	(50)	(51)	(50)
Osteosarcoma	1 (2%)			
Skeletal muscle			(1)	(1)
Hindlimb, sarcoma, metastatic				1 (100%)
Nervous System				
Brain	(51)	(50)	(51)	(50)
Glioma malignant	1 (2%)			
Respiratory System				
Larynx			(1)	
Carcinoma, metastatic, thyroid gland			1 (100%)	
Lung	(51)	(50)	(51)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	4 (8%)		2 (4%)
Alveolar/bronchiolar carcinoma		1 (2%)		2 (4%)
Carcinoma, metastatic, thyroid gland			1 (2%)	
Osteosarcoma, metastatic, bone	1 (2%)			
Mediastinum, osteosarcoma, metastatic, bone	1 (2%)			
Nose	(51)	(50)	(51)	(50)
Trachea	(51)	(50)	(51)	(50)
Carcinoma, metastatic, thyroid gland			1 (2%)	
Special Senses System				
Ear	(1)	(2)		
Pinna, papilloma squamous		1 (50%)		
Zymbal's gland	(1)			(1)
Carcinoma	1 (100%)			1 (100%)
Urinary System				
Kidney	(51)	(50)	(51)	(50)
Osteosarcoma, metastatic, bone	1 (2%)			
Renal tubule, adenoma			1 (2%)	
Urinary bladder	(51)	(50)	(51)	(50)
Sarcoma, metastatic				1 (2%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Systemic Lesions				
Multiple organs[a]	(51)	(50)	(51)	(50)
Histiocytic sarcoma			1 (2%)	1 (2%)
Leukemia mononuclear	25 (49%)	26 (52%)	29 (57%)	30 (60%)
Mesothelioma malignant	1 (2%)		2 (4%)	1 (2%)
Tumor Summary				
Total animals with primary neoplasms[b]	50	50	51	50
Total primary neoplasms	144	176	154	152
Total animals with benign neoplasms	47	50	50	49
Total benign neoplasms	105	144	114	113
Total animals with malignant neoplasms	31	28	37	36
Total malignant neoplasms	39	32	40	39
Total animals with secondary neoplasms[c]	1		1	1
Total secondary neoplasms	7		4	4

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 0 ppm

Number of Days on Study	3 1 5	3 6 1	4 4 6	4 5 1	4 6 5	5 1 3	5 1 6	5 3 7	5 3 9	5 4 1	5 6 9	5 7 0	5 7 8	5 9 1	5 9 8	5 9 8	6 0 5	6 0 6	6 1 8	6 1 8	6 2 6	6 3 8	6 5 2	6 5 9	6 6 7	6 7 4
Carcass ID Number	1 1 0 1	0 0 1 1	0 0 5 1	0 0 7 1	1 1 3 1	0 1 4 1	1 0 2 1	1 1 1 1	0 1 3 1	1 3 3 2	1 0 9 1	1 0 9 2	1 0 2 1	0 0 4 2	1 1 0 2	1 1 0 2	0 0 2 2	0 0 1 2	1 1 1 2	1 1 2 2	0 1 2 3	1 0 1 3	0 4 3 3	1 2 3 3	0 5 2 3	0 0 5 3
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																										
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																								X		
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																										
Mesentery	+	+			+		+		+	+			+	+			+	+			+		+	+		+
Osteosarcoma, metastatic, bone													X													
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																										
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth						+														+						
Cardiovascular System																										
Blood vessel																					+					+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																										
Pheochromocytoma benign														X									X		
Bilateral, pheochromocytoma benign										X								X							X	X
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X									
Carcinoma																										

+: 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 Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	6 7 4	6 7 5	6 8 7	6 9 4	6 9 5	6 9 7	7 1 0	7 1 0	7 1 5	7 2 6	7 2 6	7 2 9	7 2 9	7 3 9	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 0 5 4	0 0 3 2	1 0 2 4	1 0 9 3	1 1 3 5	1 1 2 5	0 0 1 3	0 0 3 3	0 0 3 4	1 0 9 4	1 1 1 4	0 0 2 4	0 0 2 5	0 0 3 5	0 0 1 4	0 0 1 5	0 0 4 4	0 0 4 5	0 0 4 5	0 0 5 5	1 1 9 5	1 1 0 4	1 1 0 5	1 1 1 5	1 1 3 3	1 1 3 4	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenocarcinoma																								X		1
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenocarcinoma																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular adenoma			X															X								2
Mesentery	+	+	+	+	+	+	+	+	+			+		+		+	+	+		+	+				+	31
Osteosarcoma, metastatic, bone																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Acinar cell, adenoma								X					X									X			X		4
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tooth																										2
Cardiovascular System																										
Blood vessel															+			+					+			5
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma malignant		X		X																						2
Pheochromocytoma benign						X	X	X	X	X				X			X						X			X	11
Bilateral, pheochromocytoma benign	X										X	X				X		X			X			X	X		12
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma	X		X														X				X					5
Carcinoma		X									X															2

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	3 1 5	3 6 1	4 4 6	4 5 1	4 6 5	5 1 3	5 1 6	5 3 7	5 3 9	5 4 1	5 6 9	5 7 0	5 7 8	5 9 1	5 9 8	5 9 8	6 0 5	6 0 6	6 1 8	6 1 8	6 2 6	6 3 8	6 5 2	6 5 9	6 6 7	6 7 4
Carcass ID Number	1 1 0 1 1	0 0 1 1 1	0 0 5 1 1	0 0 7 1 1	1 1 3 1 1	0 0 4 1 1	1 1 2 1 1	1 1 1 1 1	0 0 3 1 1	1 1 3 2 1	1 0 9 1 1	1 0 9 2 1	0 0 2 1 1	0 0 4 1 2	1 1 0 2 2	1 1 0 3 2	0 0 2 2 2	0 0 1 2 2	1 1 1 2 2	1 1 2 2 2	0 1 2 2 3	1 0 1 4 3	0 1 4 2 3	1 0 1 5 3	0 0 1 2 2	0 0 0 5 3
Endocrine System (continued)																										
Parathyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma				X					X	X	X	X			X			X	X	X		X		X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma										X	X		X													
C-cell, carcinoma																X										
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Adenoma					X																					
Carcinoma								X																		
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Bilateral, interstitial cell, adenoma								X					X			X	X	X				X			X
Interstitial cell, adenoma			X							X				X							X					
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Thymus	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma										X																
Fibroadenoma																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																										
Papilloma squamous																										
Squamous cell carcinoma																										X
Subcutaneous tissue, fibrosarcoma					X																					
Subcutaneous tissue, lipoma																										

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	6 7 4	6 7 5	6 8 7	6 9 4	6 9 5	6 9 7	7 1 0	7 1 0	7 1 5	7 2 6	7 2 6	7 2 9	7 2 9	7 2 9	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 0 5 4	0 0 3 2	1 1 2 4	1 0 9 3	1 1 3 5	1 1 2 5	0 0 1 3	0 0 3 3	0 0 3 4	1 0 9 4	1 1 1 4	0 0 2 4	0 0 2 5	0 0 3 5	0 0 1 4	0 0 1 5	0 0 4 4	0 0 4 5	0 0 5 5	0 1 9 5	1 1 0 4	1 1 0 5	1 1 1 5	1 1 3 3	1 1 3 4	**Total Tissues/ Tumors**
Endocrine System (continued)																										
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma		X	X				X			X	X				X		X				X					20
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
C-cell, adenoma							X		X															X		6
C-cell, carcinoma																										1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma									X										X							3
Carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																										1
Bilateral, interstitial cell, adenoma	X	X		X	X	X		X	X	X		X	X		X	X		X	X	X		X	X	X	X	26
Interstitial cell, adenoma							X							X							X					7
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																										1
Thymus	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Integumentary System																										
Mammary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	48
Adenoma																										1
Fibroadenoma															X							X				2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Keratoacanthoma			X			X																X				3
Papilloma squamous																X										1
Squamous cell carcinoma																										1
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, lipoma											X															1

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	3 1 5	3 6 1	4 4 6	4 5 1	4 6 5	5 1 3	5 1 6	5 3 7	5 3 9	5 4 1	5 6 9	5 7 0	5 7 8	5 9 1	5 9 8	5 9 8	6 0 5	6 0 6	6 1 8	6 1 8	6 2 6	6 3 8	6 5 2	6 5 9	6 6 7	6 7 4
Carcass ID Number	1 0 1 1	0 0 1 1	0 0 5 1	0 0 7 1	1 1 3 1	0 1 4 1	1 1 2 1	1 1 1 1	0 1 3 1	1 0 3 2	1 0 9 1	1 0 9 2	0 0 2 1	0 1 4 2	1 1 0 2	1 1 0 3	0 0 2 2	0 0 1 2	1 1 1 2	1 1 2 2	0 1 2 3	1 0 1 3	0 1 4 3	1 0 2 3	0 1 5 2	0 0 5 3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma													X													
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																										X
Osteosarcoma, metastatic, bone													X													
Mediastinum, osteosarcoma, metastatic, bone													X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Ear																										
Eye														+					+	+						
Zymbal's gland						+																				
Carcinoma						X																				
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone													X													
Urethra																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X	X						X		X	X			X		X	X		X							
Mesothelioma malignant																										

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	6 7 4	6 7 5	6 8 7	6 9 4	6 9 5	6 9 7	7 1 0	7 1 0	7 1 5	7 2 6	7 2 6	7 2 9	7 2 9	7 2 9	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 0 5 4	0 0 3 2	1 1 2 4	1 0 9 3	1 1 3 5	1 1 2 5	0 0 1 3	0 0 3 3	0 0 3 4	1 0 9 4	1 1 1 4	0 0 2 4	0 0 2 5	0 0 3 5	0 0 1 4	0 0 1 5	0 0 4 4	0 0 4 5	0 0 5 5	0 0 5 5	1 0 9 5	1 1 0 4	1 1 0 5	1 1 1 5	1 1 3 3	1 1 3 4	**Total Tissues/ Tumors**
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Glioma malignant	X																									1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Alveolar/bronchiolar adenoma																										1
Osteosarcoma, metastatic, bone																										1
Mediastinum, osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																										
Ear																	+									1
Eye																			+		+					5
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Osteosarcoma, metastatic, bone																										1
Urethra			+																							1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Leukemia mononuclear	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X										25
Mesothelioma malignant								X																		1

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 50 ppm

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

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 0 1	7 1 5	7 1 8	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	
Carcass ID Number	1 3 1 1	1 3 0 4	1 3 4 3	0 2 4 4	0 2 5 4	0 2 2 3	0 2 2 4	0 2 2 5	0 2 4 5	0 2 5 5	0 2 6 4	0 2 6 5	1 3 0 5	1 3 4 4	1 3 4 5	0 2 3 5	1 3 1 2	1 3 1 3	1 3 1 4	1 3 1 5	1 2 3 3	1 2 2 4	1 3 2 5	1 3 4 4	1 3 3 5	**Total Tissues/ Tumors**
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma				X		X				X															4
Mesentery			+		+						+						+								15
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell, adenoma								X						X									X	X	5
Acinar cell, adenoma, multiple																						X			1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																									
Blood vessel					+				+							+							+		4
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign	X				X				X			X				X				X					16
Bilateral, pheochromocytoma benign		X	X	X			X				X				X		X	X	X		X	X	X	X	19
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X																	X				X		5
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma		X	X	X				X				X	X	X		X			X	X		X		X	X	29
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma																									2
C-cell, carcinoma			X													X									2
General Body System																									
None																									

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	4 7 3	5 7 9	5 8 1	6 0 1	6 0 5	6 1 3	6 1 4	6 1 8	6 2 5	6 2 7	6 4 5	6 5 3	6 5 4	6 5 4	6 6 1	6 6 2	6 6 7	6 6 8	6 6 8	6 7 5	6 7 6	6 7 6	6 9 5	7 0 1	7 0 1
Carcass ID Number	0 2 6 1	1 3 0 1	0 2 6 2	0 2 5 1	1 3 0 2	0 2 4 1	0 2 3 1	1 3 3 1	0 2 4 2	0 2 2 1	0 2 5 2	1 3 4 1	1 3 2 1	1 3 3 2	0 2 5 3	0 2 3 2	1 3 4 2	0 2 3 3	0 2 4 3	0 2 2 2	1 3 2 2	1 3 3 3	0 2 3 4	0 2 6 3	1 3 0 3
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma															X										
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				X		X				X	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma																									
Thymus	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																X							X		
Papilloma squamous														X											
Trichoepithelioma																				X					
Subcutaneous tissue, fibroma																	X								
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma								X							X										
Alveolar/bronchiolar carcinoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear									+																
Pinna, papilloma squamous																									
Eye																					+				
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X	X	X		X		X		X	X	X	X	X				X	X	X	X	X		

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 0 1	7 1 5	7 1 8	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	
Carcass ID Number	1 3 1 1	1 3 0 4	1 3 4 3	0 2 4 4	0 2 5 4	0 2 2 3	0 2 2 4	0 2 2 5	0 2 4 5	0 2 5 5	0 2 6 4	0 2 6 5	0 3 0 5	1 3 3 4	1 3 4 4	1 3 4 5	0 2 3 5	1 3 1 2	1 3 3 3	1 3 3 4	1 3 3 5	1 3 3 3	1 3 3 4	1 3 3 5	1 3 3 5	1 3 3 5	**Total Tissues/ Tumors**
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma														X						X						2
Carcinoma																			X							2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X	X	X	X	X	X			X	X	X	X		X	X				X		X	X		X	X	X	30
Interstitial cell, adenoma							X	X					X			X	X			X			X			14
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma											X															1
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibroadenoma																				X						1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma									X																	3
Papilloma squamous												X													X	3
Trichoepithelioma																										1
Subcutaneous tissue, fibroma	X			X																					X	4
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma				X							X															4
Alveolar/bronchiolar carcinoma											X															1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear					+																					2
Pinna, papilloma squamous					X																					1
Eye										+		+														3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear			X	X		X		X			X		X	X	X							X	X		X	26

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 100 ppm

Number of Days on Study	4 2 9	4 4 7	5 1 9	5 3 0	5 3 3	5 4 9	5 6 2	5 6 6	5 8 3	5 8 6	5 9 0	5 9 0	5 9 1	5 9 1	5 9 6	6 0 5	6 1 4	6 1 8	6 2 5	6 3 1	6 3 9	6 5 6	6 6 6	6 6 8	6 6 9	6 7 4
Carcass ID Number	1 2 9 1	1 2 3 1	1 2 4 1	0 1 7 1	1 2 7 1	1 2 3 3	0 1 6 1	1 2 7 2	1 2 5 1	1 2 3 2	0 1 7 2	0 1 9 2	0 1 7 3	0 1 9 2	0 1 7 4	0 1 8 1	0 1 5 1	0 1 7 3	0 2 8 2	0 1 5 2	0 2 6 1	1 0 8 3	0 1 6 2	1 2 5 3	0 1 6 3	1 2 6 2
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland																		X								
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																			X							
Mesentery				+	+	+		+		+			+									+		+		
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell, adenoma																										
Pharynx		+																								
Palate, papilloma squamous		X																								
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue													+													
Papilloma squamous													X													
Cardiovascular System																										
Blood vessel																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma														X												
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign					X					X	X	X				X			X	X				X	X	X
Bilateral, pheochromocytoma benign																									X	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X																				X	
Carcinoma							X																			

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	6 7 5	6 7 5	6 9 0	6 9 6	6 9 8	7 0 1	7 0 2	7 0 3	7 1 0	7 1 9	7 1 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	0 1 6 3	0 1 7 5	0 1 8 4	1 2 5 2	1 2 7 4	1 2 4 2	1 2 4 3	0 1 6 4	1 2 6 4	1 2 3 4	1 2 6 5	0 1 5 4	0 1 5 5	0 1 6 5	0 1 8 5	0 1 9 3	0 1 9 4	0 1 9 5	1 2 3 5	1 2 4 4	1 2 4 5	1 2 5 3	1 2 5 4	1 2 5 5	1 2 7 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Carcinoma, metastatic, thyroid gland																										1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular adenoma														X												2
Mesentery					+	+			+		+		+	+						+						15
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Acinar cell, adenoma																									X	1
Pharynx																										1
Palate, papilloma squamous																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Papilloma squamous							X																			1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tongue																										1
Papilloma squamous																										1
Cardiovascular System																										
Blood vessel				+																	+					2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma benign	X		X				X			X							X					X	X		17
Bilateral, pheochromocytoma benign		X				X		X	X					X	X			X	X						X	10
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma										X												X			X	5
Carcinoma																										1

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	4 2 9	4 4 7	5 1 9	5 3 0	5 3 3	5 4 9	5 6 2	5 6 6	5 8 3	5 8 6	5 9 0	5 9 0	5 9 1	5 9 1	5 9 6	6 0 5	6 1 4	6 1 8	6 2 5	6 3 1	6 3 9	6 5 6	6 6 6	6 6 8	6 6 9	6 7 4
Carcass ID Number	1 2 9 1	1 2 3 1	1 2 4 1	0 1 7 1	1 2 7 1	1 2 3 3	0 1 6 1	1 2 7 2	1 2 5 1	1 2 3 2	0 1 7 2	0 1 9 1	0 1 7 3	0 1 9 2	0 1 7 4	0 1 8 1	0 1 5 1	0 1 7 3	0 2 8 2	0 1 5 2	1 2 6 1	0 1 8 3	1 2 6 2	0 1 5 3	1 2 6 3	0 1 6 2
Endocrine System (continued)																										
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+
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									
C-cell, carcinoma																		X								
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Carcinoma			X							X					X											
Bilateral, carcinoma													X													
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						
Hematopoietic System																										
Blood	+																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																		
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Adenocarcinoma																										
Fibroadenoma																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell adenoma																										
Keratoacanthoma									X																	
Papilloma squamous																										
Subcutaneous tissue, fibroma																										
Subcutaneous tissue, lymphangiosarcoma																	X									

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	6 7 5	6 7 5	6 9 0	6 9 6	6 9 8	7 0 1	7 0 2	7 0 3	7 1 0	7 1 9	7 1 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	0 1 6 3	0 1 7 5	0 1 8 4	1 2 5 2	1 2 7 4	1 2 4 2	1 2 4 3	0 1 6 4	1 2 6 4	1 2 2 4	1 2 2 5	0 1 5 4	0 1 5 5	0 1 1 5	0 1 1 5	0 1 1 5	0 1 1 3	0 1 1 4	0 1 1 5	1 2 2 5	1 2 2 3	1 2 4 4	1 2 4 5	1 2 5 3	1 2 5 4	1 2 5 5	**Total Tissues/ Tumors**
Endocrine System (continued)																										
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pars distalis, adenoma								X			X			X			X	X	X	X	X				X		22
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
C-cell, adenoma																										3
C-cell, carcinoma																										1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma			X				X										X				X					4
Carcinoma																										3
Bilateral, carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Bilateral, interstitial cell, adenoma	X	X	X		X		X		X			X			X	X	X	X	X	X	X	X	X	X	X	30
Interstitial cell, adenoma				X		X				X			X	X												8
Hematopoietic System																										
Blood																										1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																										1
Thymus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma								X																		1
Fibroadenoma																								X		1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Basal cell adenoma																		X								1
Keratoacanthoma							X																			2
Papilloma squamous					X																					1
Subcutaneous tissue, fibroma			X										X													2
Subcutaneous tissue, lymphangiosarcoma																										1

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	4 2 9	4 4 7	5 1 9	5 3 0	5 3 3	5 4 9	5 6 2	5 6 6	5 8 3	5 8 6	5 9 0	5 9 0	5 9 1	5 9 1	5 9 6	6 0 5	6 1 4	6 1 8	6 2 5	6 3 1	6 3 9	6 5 6	6 6 6	6 6 8	6 6 9	6 7 4
Carcass ID Number	1 2 9 1	1 2 3 1	1 2 4 1	0 1 7 1	1 2 7 1	1 2 3 3	0 1 6 1	1 2 7 2	1 2 5 1	1 2 3 2	0 1 7 2	0 1 9 1	0 1 7 3	0 1 9 2	0 1 7 4	0 1 8 1	0 1 5 1	0 1 7 3	0 2 8 2	0 1 5 2	1 2 6 1	0 1 8 3	1 2 6 2	0 1 5 3	1 2 6 3	0 1 6 2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																										
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Larynx																		+								
Carcinoma, metastatic, thyroid gland																		X								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland																		X								
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland																		X								
Special Senses System																										
Eye																										
Harderian gland																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X																		
Leukemia mononuclear	X				X	X					X	X		X		X			X	X					X	X
Mesothelioma malignant																										

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	6 7 5	6 7 5	6 9 0	6 9 6	6 9 8	7 0 1	7 0 2	7 0 3	7 1 0	7 1 9	7 1 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	0 1 6 3	0 1 7 5	0 1 8 4	1 2 5 2	1 2 7 4	1 2 4 2	1 2 4 3	0 1 6 4	1 2 6 4	1 2 3 4	1 2 6 5	0 1 5 4	0 1 5 5	0 1 6 5	0 1 8 5	0 1 9 3	0 1 9 4	0 1 9 5	1 2 3 5	1 2 4 4	1 2 4 5	1 2 5 3	1 2 5 4	1 2 5 5	1 2 7 5	**Total Tissues/ Tumors**
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Skeletal muscle						+																				1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Respiratory System																										
Larynx																										1
Carcinoma, metastatic, thyroid gland																										1
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Carcinoma, metastatic, thyroid gland																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Carcinoma, metastatic, thyroid gland																										1
Special Senses System																										
Eye								+																		1
Harderian gland								+																		1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Renal tubule, adenoma																	X									1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																										1
Leukemia mononuclear	X		X		X	X		X	X		X		X	X	X	X	X	X		X	X	X		X	X	29
Mesothelioma malignant						X														X						2

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 200 ppm

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

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	6 8 0	6 9 7	6 9 8	7 0 1	7 1 2	7 1 2	7 1 8	7 1 8	7 1 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 1 2 2	1 1 8 1	1 1 6 4	1 1 8 2	0 0 8 3	0 0 8 4	1 1 6 5	1 1 8 3	1 1 9 4	0 0 8 5	0 0 9 4	0 1 0 5	1 1 9 5	1 2 0 5	0 1 1 3	0 1 1 4	0 1 1 5	0 1 1 3	0 1 2 4	0 1 2 5	1 1 2 3	1 1 7 4	1 1 7 5	1 1 8 4	1 1 8 5	**Total Tissues/ Tumors**
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery	+	+					+	+		+	+		+		+			+		+					24
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell, adenoma																			X				X		2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Tooth																									1
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma malignant																									1
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign						X	X								X	X	X	X	X				X	X	14
Bilateral, pheochromocytoma benign		X						X					X								X				8
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X	X		X															X		X		X	X	10
Carcinoma									X																1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma				X	X		X		X				X					X			X		X	X	19
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma																			X						3

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	4 9 5	5 2 4	5 3 0	5 4 3	5 7 7	5 8 7	5 9 1	5 9 1	5 9 1	6 1 9	6 2 0	6 2 2	6 3 2	6 3 6	6 5 4	6 5 6	6 6 6	6 6 1	6 6 1	6 6 1	6 6 4	6 6 6	6 6 7	6 6 8	6 7 5
Carcass ID Number	1 2 0 1	1 1 7 1	0 0 9 1	1 1 9 1	0 1 1 1	1 1 6 1	0 0 9 2	0 1 0 1	0 1 0 2	1 1 9 2	1 1 6 2	1 2 0 2	1 2 0 3	0 2 9 3	1 0 8 4	0 0 8 1	0 1 0 3	0 0 9 5	0 1 1 4	0 1 1 2	1 1 6 3	1 1 9 3	1 1 7 2	0 1 8 2	0 1 2 1
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma				X																					
Carcinoma																									
Sarcoma, metastatic										X															
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic										X															
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma			X	X	X	X				X			X			X	X	X	X		X	X	X		X
Interstitial cell, adenoma		X					X	X	X						X					X					
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma													X												
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																	X								
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Papilloma squamous																									
Trichoepithelioma																									
Subcutaneous tissue, fibroma															X		X					X			
Subcutaneous tissue, fibrous histiocytoma										X															
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle										+															
Hindlimb, sarcoma, metastatic										X															

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	6 8 0	6 9 7	6 9 8	7 0 1	7 1 2	7 1 2	7 1 8	7 1 8	7 1 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 1 2 2	1 1 8 1	1 1 6 4	1 1 8 2	0 0 8 3	0 0 8 4	1 1 6 5	1 1 8 3	1 1 9 4	0 0 8 5	0 0 9 4	0 1 0 5	1 1 9 5	1 2 0 5	0 1 1 3	0 1 1 4	0 1 1 5	0 1 2 3	0 2 2 4	0 2 2 5	1 7 3	1 7 4	1 7 5	1 8 4	1 8 5	**Total Tissues/ Tumors**
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																									1
Carcinoma																X									1
Sarcoma, metastatic																									1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic																									1
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	32
Interstitial cell, adenoma		X			X					X						X		X							11
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																									1
Thymus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibroadenoma										X															2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma								X									X								2
Papilloma squamous						X																			1
Trichoepithelioma																X									1
Subcutaneous tissue, fibroma			X														X								5
Subcutaneous tissue, fibrous histiocytoma																									1
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																									1
Hindlimb, sarcoma, metastatic																									1

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	4 9 5	5 2 4	5 3 0	5 4 3	5 7 7	5 8 7	5 9 1	5 9 1	5 9 1	6 1 9	6 2 0	6 2 2	6 3 2	6 3 6	6 5 4	6 5 6	6 6 6	6 6 1	6 6 1	6 6 4	6 6 6	6 6 7	6 6 8	6 7 5
Carcass ID Number	1 2 0 1	1 1 7 1	0 0 9 1	1 1 9 1	0 1 1 1	1 1 6 1	0 0 9 2	0 1 0 1	0 1 0 2	0 1 9 2	1 1 6 2	1 2 0 2	1 2 0 3	1 0 9 3	0 2 0 4	1 0 8 1	0 0 9 3	0 1 0 5	0 1 9 4	0 1 0 2	1 1 1 3	1 1 6 3	1 1 9 3	0 0 7 2	0 1 8 2	0 2 1
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma					X																				X
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye		+						+																	
Zymbal's gland							+																		
Carcinoma							X																		
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic										X															
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma													X												
Leukemia mononuclear	X	X	X					X	X		X	X	X				X	X	X		X	X		X	X
Mesothelioma malignant						X																			

TABLE C2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	6 8 0	6 9 7	6 9 8	7 0 1	7 1 2	7 1 2	7 1 8	7 1 8	7 1 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 1 2 2	1 1 8 1	1 1 6 4	1 1 8 2	0 0 8 3	0 0 8 4	1 1 6 5	1 1 8 3	1 1 9 4	0 0 8 5	0 0 9 4	0 1 0 5	1 1 9 5	1 2 0 5	1 1 1 3	0 1 1 4	0 1 1 5	0 1 2 3	0 2 2 4	0 2 2 5	1 7 3	1 7 7 4	1 7 7 5	1 8 4	1 8 5	**Total Tissues/ Tumors**
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X									X										2
Alveolar/bronchiolar carcinoma																										2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye																										2
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear	X	X				X	X	X			X	X	X		X		X	X				X	X	X	X	30
Mesothelioma malignant																										1

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rates[a]	23/51 (45%)	35/50 (70%)	27/51 (53%)	22/50 (44%)
Adjusted rates[b]	84.2%	84.8%	79.8%	72.6%
Terminal rates[c]	10/14 (71%)	16/22 (73%)	8/14 (57%)	9/16 (56%)
First incidence (days)	541	605	533	543
Life table tests[d]	P=0.231N	P=0.446	P=0.325	P=0.300N
Logistic regression tests[d]	P=0.098N	P=0.111	P=0.343	P=0.275N
Cochran-Armitage test[d]	P=0.210N			
Fisher exact test[d]		P=0.010	P=0.276	P=0.536N
Adrenal Medulla: Pheochromocytoma (Benign or Malignant)				
Overall rates	25/51 (49%)	35/50 (70%)	27/51 (53%)	22/50 (44%)
Adjusted rates	85.5%	84.8%	79.8%	72.6%
Terminal rates	10/14 (71%)	16/22 (73%)	8/14 (57%)	9/16 (56%)
First incidence (days)	541	605	533	543
Life table tests	P=0.160N	P=0.537N	P=0.451	P=0.194N
Logistic regression tests	P=0.048N	P=0.235	P=0.522	P=0.142N
Cochran-Armitage test	P=0.127N			
Fisher exact test		P=0.026	P=0.422	P=0.380N
Liver: Hepatocellular Adenoma				
Overall rates	2/51 (4%)	4/50 (8%)	2/51 (4%)	0/50 (0%)
Adjusted rates	11.2%	15.9%	10.0%	0.0%
Terminal rates	1/14 (7%)	3/22 (14%)	1/14 (7%)	0/16 (0%)
First incidence (days)	687	653	625	-[e]
Life table tests	P=0.107N	P=0.526	P=0.688N	P=0.221N
Logistic regression tests	P=0.100N	P=0.457	P=0.684N	P=0.209N
Cochran-Armitage test	P=0.114N			
Fisher exact test		P=0.329	P=0.691N	P=0.252N
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	1/51 (2%)	4/50 (8%)	0/51 (0%)	2/50 (4%)
Adjusted rates	3.8%	13.7%	0.0%	11.2%
Terminal rates	0/14 (0%)	2/22 (9%)	0/14 (0%)	1/16 (6%)
First incidence (days)	674	618	-	718
Life table tests	P=0.573N	P=0.293	P=0.500N	P=0.535
Logistic regression tests	P=0.560N	P=0.212	P=0.493N	P=0.544
Cochran-Armitage test	P=0.583N			
Fisher exact test		P=0.175	P=0.500N	P=0.492
Lung: Alveolar/bronchiolar Adenoma or Alveolar/bronchiolar Carcinoma				
Overall rates	1/51 (2%)	4/50 (8%)	0/51 (0%)	4/50 (8%)
Adjusted rates	3.8%	13.7%	0.0%	16.5%
Terminal rates	0/14 (0%)	2/22 (9%)	0/14 (0%)	1/16 (6%)
First incidence (days)	674	618	-	577
Life table tests	P=0.234	P=0.293	P=0.500N	P=0.220
Logistic regression tests	P=0.237	P=0.212	P=0.493N	P=0.197
Cochran-Armitage test	P=0.222			
Fisher exact test		P=0.175	P=0.500N	P=0.175

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Mammary Gland: Adenoma or Fibroadenoma				
Overall rates	3/51 (6%)	1/50 (2%)	1/51 (2%)	2/50 (4%)
Adjusted rates	16.3%	4.5%	7.1%	8.9%
Terminal rates	2/14 (14%)	1/22 (5%)	1/14 (7%)	1/16 (6%)
First incidence (days)	541	729 (T)	729 (T)	656
Life table tests	P=0.473N	P=0.182N	P=0.295N	P=0.433N
Logistic regression tests	P=0.456N	P=0.260N	P=0.291N	P=0.467N
Cochran-Armitage test	P=0.479N			
Fisher exact test		P=0.316N	P=0.309N	P=0.509N
Mammary Gland: Adenoma, Fibroadenoma or Adenocarcinoma				
Overall rates	3/51 (6%)	1/50 (2%)	2/51 (4%)	2/50 (4%)
Adjusted rates	16.3%	4.5%	12.3%	8.9%
Terminal rates	2/14 (14%)	1/22 (5%)	1/14 (7%)	1/16 (6%)
First incidence (days)	541	729 (T)	703	656
Life table tests	P=0.499N	P=0.182N	P=0.497N	P=0.433N
Logistic regression tests	P=0.481N	P=0.260N	P=0.483N	P=0.467N
Cochran-Armitage test	P=0.506N			
Fisher exact test		P=0.316N	P=0.500N	P=0.509N
Pancreas: Adenoma				
Overall rates	4/51 (8%)	6/50 (12%)	1/51 (2%)	2/50 (4%)
Adjusted rates	25.6%	27.3%	7.1%	12.5%
Terminal rates	3/14 (21%)	6/22 (27%)	1/14 (7%)	2/16 (13%)
First incidence (days)	710	729 (T)	729 (T)	729 (T)
Life table tests	P=0.126N	P=0.626N	P=0.181N	P=0.274N
Logistic regression tests	P=0.129N	P=0.586	P=0.181N	P=0.286N
Cochran-Armitage test	P=0.136N			
Fisher exact test		P=0.358	P=0.181N	P=0.348N
Pancreatic Islets: Adenoma				
Overall rates	5/51 (10%)	5/50 (10%)	5/51 (10%)	10/50 (20%)
Adjusted rates	23.4%	18.5%	24.3%	40.3%
Terminal rates	2/14 (14%)	2/22 (9%)	2/14 (14%)	4/16 (25%)
First incidence (days)	605	662	533	636
Life table tests	P=0.070	P=0.412N	P=0.619N	P=0.201
Logistic regression tests	P=0.079	P=0.504N	P=0.608N	P=0.183
Cochran-Armitage test	P=0.066			
Fisher exact test		P=0.617	P=0.630N	P=0.123
Pancreatic Islets: Adenoma or Carcinoma				
Overall rates	7/51 (14%)	5/50 (10%)	6/51 (12%)	11/50 (22%)
Adjusted rates	31.2%	18.5%	25.9%	43.8%
Terminal rates	2/14 (14%)	2/22 (9%)	2/14 (14%)	4/16 (25%)
First incidence (days)	605	662	533	636
Life table tests	P=0.107	P=0.189N	P=0.493N	P=0.309
Logistic regression tests	P=0.120	P=0.245N	P=0.472N	P=0.301
Cochran-Armitage test	P=0.099			
Fisher exact test		P=0.394N	P=0.500N	P=0.205

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	20/50 (40%)	29/50 (58%)	22/51 (43%)	19/50 (38%)
Adjusted rates	58.7%	70.2%	69.0%	58.1%
Terminal rates	3/13 (23%)	11/22 (50%)	7/14 (50%)	5/16 (31%)
First incidence (days)	451	473	447	577
Life table tests	P=0.237N	P=0.502	P=0.493	P=0.321N
Logistic regression tests	P=0.235N	P=0.050	P=0.450	P=0.473N
Cochran-Armitage test	P=0.232N			
Fisher exact test		P=0.055	P=0.453	P=0.500N
Preputial Gland: Adenoma				
Overall rates	3/50 (6%)	2/50 (4%)	4/51 (8%)	1/50 (2%)
Adjusted rates	14.5%	9.1%	22.3%	2.1%
Terminal rates	1/14 (7%)	2/22 (9%)	2/14 (14%)	0/16 (0%)
First incidence (days)	465	729 (T)	690	543
Life table tests	P=0.294N	P=0.344N	P=0.502	P=0.270N
Logistic regression tests	P=0.274N	P=0.462N	P=0.528	P=0.372N
Cochran-Armitage test	P=0.290N			
Fisher exact test		P=0.500N	P=0.511	P=0.309N
Preputial Gland: Carcinoma				
Overall rates	1/50 (2%)	2/50 (4%)	4/51 (8%)	1/50 (2%)
Adjusted rates	2.3%	7.2%	9.3%	6.3%
Terminal rates	0/14 (0%)	1/22 (5%)	0/14 (0%)	1/16 (6%)
First incidence (days)	537	661	519	729 (T)
Life table tests	P=0.578N	P=0.597	P=0.202	P=0.738N
Logistic regression tests	P=0.522	P=0.458	P=0.112	P=0.748
Cochran-Armitage test	P=0.596N			
Fisher exact test		P=0.500	P=0.187	P=0.753N
Preputial Gland: Adenoma or Carcinoma				
Overall rates	4/50 (8%)	4/50 (8%)	8/51 (16%)	2/50 (4%)
Adjusted rates	16.4%	16.0%	29.6%	8.2%
Terminal rates	1/14 (7%)	3/22 (14%)	2/14 (14%)	1/16 (6%)
First incidence (days)	465	661	519	543
Life table tests	P=0.332N	P=0.458N	P=0.203	P=0.293N
Logistic regression tests	P=0.355N	P=0.644N	P=0.175	P=0.410N
Cochran-Armitage test	P=0.336N			
Fisher exact test		P=0.643N	P=0.188	P=0.339N
Skin: Keratoacanthoma				
Overall rates	3/51 (6%)	3/50 (6%)	2/51 (4%)	2/50 (4%)
Adjusted rates	15.6%	10.6%	7.5%	11.2%
Terminal rates	1/14 (7%)	1/22 (5%)	0/14 (0%)	1/16 (6%)
First incidence (days)	687	662	583	718
Life table tests	P=0.366N	P=0.506N	P=0.485N	P=0.441N
Logistic regression tests	P=0.349N	P=0.562N	P=0.483N	P=0.443N
Cochran-Armitage test	P=0.377N			
Fisher exact test		P=0.652	P=0.500N	P=0.509N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Skin: Squamous Papilloma				
Overall rates	1/51 (2%)	3/50 (6%)	1/51 (2%)	1/50 (2%)
Adjusted rates	7.1%	11.5%	4.8%	4.8%
Terminal rates	1/14 (7%)	2/22 (9%)	0/14 (0%)	0/16 (0%)
First incidence (days)	729 (T)	654	698	712
Life table tests	P=0.433N	P=0.462	P=0.749N	P=0.722N
Logistic regression tests	P=0.431N	P=0.399	P=0.764N	P=0.740N
Cochran-Armitage test	P=0.449N			
Fisher exact test		P=0.301	P=0.752N	P=0.748
Skin: Squamous Papilloma or Squamous Cell Carcinoma				
Overall rates	2/51 (4%)	3/50 (6%)	1/51 (2%)	1/50 (2%)
Adjusted rates	10.7%	11.5%	4.8%	4.8%
Terminal rates	1/14 (7%)	2/22 (9%)	0/14 (0%)	0/16 (0%)
First incidence (days)	674	654	698	712
Life table tests	P=0.273N	P=0.663	P=0.488N	P=0.460N
Logistic regression tests	P=0.263N	P=0.604	P=0.490N	P=0.456N
Cochran-Armitage test	P=0.283N			
Fisher exact test		P=0.491	P=0.500N	P=0.508N
Skin: Basal Cell Adenoma, Keratoacanthoma, Trichoepithelioma, or Squamous Cell Carcinoma				
Overall rates	5/51 (10%)	7/50 (14%)	4/51 (8%)	4/50 (8%)
Adjusted rates	25.1%	23.8%	18.2%	21.1%
Terminal rates	2/14 (14%)	3/22 (14%)	1/14 (7%)	2/16 (13%)
First incidence (days)	674	654	583	712
Life table tests	P=0.314N	P=0.618	P=0.482N	P=0.423N
Logistic regression tests	P=0.284N	P=0.532	P=0.478N	P=0.420N
Cochran-Armitage test	P=0.325N			
Fisher exact test		P=0.366	P=0.500N	P=0.513N
Skin (Subcutaneous Tissue): Fibroma				
Overall rates	0/51 (0%)	4/50 (8%)	2/51 (4%)	5/50 (10%)
Adjusted rates	0.0%	15.0%	11.2%	18.5%
Terminal rates	0/14 (0%)	2/22 (9%)	1/14 (7%)	1/16 (6%)
First incidence (days)	-	667	690	656
Life table tests	P=0.054	P=0.123	P=0.245	P=0.053
Logistic regression tests	P=0.056	P=0.095	P=0.239	P=0.040
Cochran-Armitage test	P=0.050			
Fisher exact test		P=0.056	P=0.248	P=0.027
Skin (Subcutaneous Tissue): Fibroma or Fibrosarcoma				
Overall rates	1/51 (2%)	4/50 (8%)	2/51 (4%)	5/50 (10%)
Adjusted rates	2.1%	15.0%	11.2%	18.5%
Terminal rates	0/14 (0%)	2/22 (9%)	1/14 (7%)	1/16 (6%)
First incidence (days)	465	667	690	656
Life table tests	P=0.118	P=0.286	P=0.510	P=0.146
Logistic regression tests	P=0.120	P=0.161	P=0.488	P=0.087
Cochran-Armitage test	P=0.110			
Fisher exact test		P=0.175	P=0.500	P=0.098

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Testes: Adenoma				
Overall rates	33/51 (65%)	44/50 (88%)	38/51 (75%)	43/50 (86%)
Adjusted rates	96.7%	100.0%	100.0%	97.6%
Terminal rates	13/14 (93%)	22/22 (100%)	14/14 (100%)	15/16 (94%)
First incidence (days)	446	579	533	524
Life table tests	P=0.175	P=0.420N	P=0.302	P=0.295
Logistic regression tests	P=0.098	P=0.125	P=0.296	P=0.059
Cochran-Armitage test	P=0.035			
Fisher exact test		P=0.005	P=0.195	P=0.012
Thyroid Gland (C-cell): Adenoma				
Overall rates	6/51 (12%)	2/50 (4%)	3/51 (6%)	3/50 (6%)
Adjusted rates	23.2%	5.2%	7.5%	10.6%
Terminal rates	1/14 (7%)	0/22 (0%)	0/14 (0%)	1/16 (6%)
First incidence (days)	541	627	586	530
Life table tests	P=0.238N	P=0.073N	P=0.237N	P=0.193N
Logistic regression tests	P=0.320N	P=0.170N	P=0.260N	P=0.284N
Cochran-Armitage test	P=0.262N			
Fisher exact test		P=0.141N	P=0.244N	P=0.254N
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rates	7/51 (14%)	4/50 (8%)	4/51 (8%)	3/50 (6%)
Adjusted rates	25.2%	13.5%	10.2%	10.6%
Terminal rates	1/14 (7%)	1/22 (5%)	0/14 (0%)	1/16 (6%)
First incidence (days)	541	627	586	530
Life table tests	P=0.130N	P=0.136N	P=0.258N	P=0.124N
Logistic regression tests	P=0.175N	P=0.293N	P=0.286N	P=0.200N
Cochran-Armitage test	P=0.144N			
Fisher exact test		P=0.274N	P=0.263N	P=0.167N
All Organs: Mononuclear Leukemia				
Overall rates	25/51 (49%)	26/50 (52%)	29/51 (57%)	30/50 (60%)
Adjusted rates	73.1%	65.5%	89.1%	80.8%
Terminal rates	6/14 (43%)	10/22 (45%)	11/14 (79%)	10/16 (63%)
First incidence (days)	315	581	429	495
Life table tests	P=0.244	P=0.186N	P=0.337	P=0.463
Logistic regression tests	P=0.164	P=0.503	P=0.318	P=0.213
Cochran-Armitage test	P=0.139			
Fisher exact test		P=0.460	P=0.276	P=0.182
All Organs: Benign Tumors				
Overall rates	47/51 (92%)	50/50 (100%)	50/51 (98%)	49/50 (98%)
Adjusted rates	100.0%	100.0%	100.0%	100.0%
Terminal rates	14/14 (100%)	22/22 (100%)	14/14 (100%)	16/16(100%)
First incidence (days)	446	473	447	524
Life table tests	P=0.504	P=0.066N	P=0.455	P=0.334N
Logistic regression tests	P=0.544N	P=0.543	P=0.522	P=0.667N
Cochran-Armitage test	P=0.166			
Fisher exact test		P=0.061	P=0.181	P=0.187

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
All Organs: Malignant Tumors				
Overall rates	31/51 (61%)	28/50 (56%)	37/51 (73%)	36/50 (72%)
Adjusted rates	79.7%	71.3%	91.1%	86.3%
Terminal rates	7/14 (50%)	12/22 (55%)	11/14 (79%)	11/16 (69%)
First incidence (days)	315	581	429	495
Life table tests	P=0.204	P=0.057N	P=0.278	P=0.507
Logistic regression tests	P=0.060	P=0.392N	P=0.146	P=0.148
Cochran-Armitage test	P=0.067			
Fisher exact test		P=0.388N	P=0.147	P=0.163
All Organs: Benign and Malignant Tumors				
Overall rates	50/51 (98%)	50/50 (100%)	51/51 (100%)	50/50 (100%)
Adjusted rates	100.0%	100.0%	100.0%	100.0%
Terminal rates	14/14 (100%)	22/22 (100%)	14/14 (100%)	16/16 (100%)
First incidence (days)	315	473	429	495
Life table tests	P=0.477N	P=0.032N	P=0.541N	P=0.253N
Logistic regression tests	P=0.432	P=0.736	P=0.603	P=0.694
Cochran-Armitage test	P=0.307			
Fisher exact test		P=0.505	P=0.500	P=0.505

(T)Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no tumors in animal group

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	9	10	9	10
Early deaths				
Natural death	3	1	3	1
Moribund	34	27	34	33
Survivors				
Terminal sacrifice	14	22	14	16
Animals examined microscopically	51	50	51	50
Alimentary System				
Intestine large, cecum	(51)	(50)	(50)	(50)
Edema	1 (2%)			
Hemorrhage	1 (2%)			
Inflammation, chronic	1 (2%)			
Parasite metazoan		1 (2%)	1 (2%)	
Intestine large, colon	(51)	(50)	(51)	(49)
Parasite metazoan	1 (2%)	3 (6%)	2 (4%)	1 (2%)
Intestine large, rectum	(51)	(50)	(50)	(49)
Parasite metazoan	5 (10%)	4 (8%)	1 (2%)	3 (6%)
Intestine small, ileum	(51)	(50)	(51)	(49)
Cyst				1 (2%)
Intestine small, jejunum	(51)	(50)	(51)	(49)
Metaplasia, osseous	1 (2%)			
Liver	(51)	(50)	(51)	(50)
Angiectasis	8 (16%)	3 (6%)	6 (12%)	2 (4%)
Atrophy, focal	1 (2%)			
Basophilic focus	1 (2%)			1 (2%)
Congestion	1 (2%)	2 (4%)	1 (2%)	
Degeneration, cystic	10 (20%)	14 (28%)	10 (20%)	5 (10%)
Eosinophilic focus			1 (2%)	2 (4%)
Fatty change	14 (27%)	21 (42%)	17 (33%)	14 (28%)
Focal cellular change	11 (22%)	12 (24%)	13 (25%)	13 (26%)
Hemorrhage	3 (6%)		1 (2%)	
Hepatodiaphragmatic nodule	5 (10%)	4 (8%)	3 (6%)	4 (8%)
Hyperplasia		2 (4%)		
Hyperplasia, multifocal	15 (29%)	19 (38%)	22 (43%)	12 (24%)
Infiltration cellular, mixed cell	7 (14%)	4 (8%)	10 (20%)	12 (24%)
Inflammation, focal	18 (35%)	24 (48%)	20 (39%)	18 (36%)
Mineralization	1 (2%)			
Mixed cell focus		2 (4%)		1 (2%)
Necrosis, focal	2 (4%)	2 (4%)	3 (6%)	1 (2%)
Thrombus		1 (2%)	2 (4%)	2 (4%)
Bile duct, dilatation			1 (2%)	
Bile duct, hyperplasia	48 (94%)	50 (100%)	49 (96%)	49 (98%)
Biliary tract, fibrosis	42 (82%)	48 (96%)	47 (92%)	44 (88%)
Centrilobular, atrophy	14 (27%)	15 (30%)	15 (29%)	13 (26%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Alimentary System (continued)				
Mesentery	(31)	(15)	(15)	(24)
Hemorrhage	1 (3%)	1 (7%)	1 (7%)	
Inflammation, chronic	7 (23%)	4 (27%)	3 (20%)	3 (13%)
Fat, necrosis	11 (35%)	3 (20%)	6 (40%)	12 (50%)
Pancreas	(51)	(50)	(51)	(50)
Accessory spleen				2 (4%)
Atrophy, diffuse				1 (2%)
Atrophy, focal	13 (25%)	18 (36%)	14 (27%)	16 (32%)
Cytoplasmic alteration	1 (2%)	1 (2%)	1 (2%)	
Edema				1 (2%)
Inflammation, chronic			1 (2%)	
Acinar cell, hyperplasia	3 (6%)	1 (2%)		
Duct, dilatation		3 (6%)		1 (2%)
Salivary glands	(51)	(50)	(51)	(50)
Infiltration cellular, lipocyte		1 (2%)		
Stomach, forestomach	(51)	(50)	(51)	(49)
Hyperplasia, squamous		1 (2%)	1 (2%)	
Inflammation, chronic	7 (14%)	7 (14%)	4 (8%)	5 (10%)
Mineralization		1 (2%)	1 (2%)	
Perforation		1 (2%)	1 (2%)	
Ulcer	6 (12%)	4 (8%)	2 (4%)	1 (2%)
Mucosa, hyperplasia, papillary	6 (12%)	6 (12%)	7 (14%)	6 (12%)
Stomach, glandular	(51)	(50)	(51)	(49)
Edema			1 (2%)	1 (2%)
Erosion	3 (6%)	2 (4%)	2 (4%)	
Inflammation, chronic	8 (16%)	2 (4%)	3 (6%)	2 (4%)
Mineralization	1 (2%)	3 (6%)	1 (2%)	
Pigmentation, focal	2 (4%)			
Ulcer	1 (2%)		1 (2%)	
Epithelium, degeneration, hyaline		1 (2%)		
Mucosa, cyst				1 (2%)
Mucosa, hyperplasia	1 (2%)			
Tooth	(2)			(1)
Epithelium alveolus, cyst	1 (50%)			
Cardiovascular System				
Blood vessel	(5)	(4)	(2)	
Aorta, mineralization	1 (20%)			
Mesenteric artery, hypertrophy		1 (25%)		
Mesenteric artery, inflammation, chronic	4 (80%)	4 (100%)	2 (100%)	
Mesenteric artery, mineralization	1 (20%)	1 (25%)		
Heart	(51)	(50)	(51)	(50)
Mineralization			1 (2%)	
Thrombus		1 (2%)		

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm		50 ppm		100 ppm		200 ppm	
Endocrine System								
Adrenal gland, cortex	(51)		(50)		(51)		(50)	
Angiectasis							1	(2%)
Cyst	1	(2%)						
Focal cellular change	13	(25%)	22	(44%)	11	(22%)	10	(20%)
Hematopoietic cell proliferation					1	(2%)		
Hemorrhage	1	(2%)						
Mineralization					2	(4%)		
Necrosis	1	(2%)	1	(2%)	1	(2%)		
Vacuolization cytoplasmic			2	(4%)	2	(4%)		
Adrenal gland, medulla	(51)		(50)		(51)		(50)	
Cyst							1	(2%)
Hemorrhage	1	(2%)						
Hyperplasia	10	(20%)	12	(24%)	9	(18%)	11	(22%)
Necrosis	1	(2%)						
Islets, pancreatic	(51)		(50)		(51)		(50)	
Hyperplasia					1	(2%)		
Parathyroid gland	(50)		(48)		(49)		(50)	
Hyperplasia	4	(8%)	4	(8%)	1	(2%)		
Pituitary gland	(50)		(50)		(51)		(50)	
Angiectasis	17	(34%)	23	(46%)	18	(35%)	21	(42%)
Atrophy					1	(2%)		
Cyst	2	(4%)	4	(8%)	3	(6%)	1	(2%)
Hemorrhage			3	(6%)				
Pigmentation	1	(2%)						
Pars distalis, focal cellular change	1	(2%)						
Pars distalis, hyperplasia							1	(2%)
Pars distalis, hyperplasia, focal	8	(16%)	4	(8%)	7	(14%)	7	(14%)
Pars nervosa, focal cellular change							1	(2%)
Thyroid gland	(51)		(50)		(51)		(50)	
Degeneration, cystic	6	(12%)	8	(16%)	4	(8%)	7	(14%)
Pigmentation	1	(2%)						
Ultimobranchial cyst	1	(2%)						
C-cell, hyperplasia	5	(10%)	4	(8%)	2	(4%)	5	(10%)
Follicle, cyst	1	(2%)			2	(4%)		
Follicular cell, hyperplasia	1	(2%)	2	(4%)	2	(4%)		
General Body System								
None								
Genital System								
Epididymis	(51)		(50)		(51)		(50)	
Edema							1	(2%)
Inflammation, chronic			1	(2%)	1	(2%)		
Preputial gland	(50)		(50)		(51)		(50)	
Degeneration, cystic	3	(6%)	1	(2%)				
Fibrosis	1	(2%)						
Hyperplasia			2	(4%)	1	(2%)	1	(2%)
Inflammation, suppurative	20	(40%)	23	(46%)	22	(43%)	23	(46%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Genital System				
Prostate	(51)	(50)	(51)	(50)
Degeneration, cystic		1 (2%)		
Edema			1 (2%)	
Hyperplasia, focal		5 (10%)		1 (2%)
Inflammation, suppurative	28 (55%)	42 (84%)	31 (61%)	35 (70%)
Seminal vesicle	(51)	(50)	(51)	(50)
Dilatation				2 (4%)
Inflammation, chronic	1 (2%)		1 (2%)	
Testes	(51)	(50)	(51)	(50)
Fibrosis	1 (2%)			
Hyperplasia		1 (2%)		
Artery, inflammation, chronic		1 (2%)	1 (2%)	
Germinal epithelium, degeneration	15 (29%)	14 (28%)	14 (27%)	11 (22%)
Interstitial cell, hyperplasia	13 (25%)	9 (18%)	11 (22%)	9 (18%)
Hematopoietic System				
Bone marrow	(51)	(50)	(51)	(50)
Hypercellularity			2 (4%)	
Myelofibrosis	4 (8%)	2 (4%)	3 (6%)	1 (2%)
Lymph node	(51)	(50)	(51)	(50)
Bronchial, hyperplasia			1 (2%)	
Iliac, hyperplasia			1 (2%)	
Inguinal, hyperplasia		1 (2%)	1 (2%)	
Mediastinal, angiectasis	6 (12%)	3 (6%)	1 (2%)	1 (2%)
Mediastinal, hyperplasia	1 (2%)	2 (4%)	1 (2%)	
Mediastinal, hyperplasia, lymphoid			1 (2%)	
Pancreatic, angiectasis		1 (2%)		
Pancreatic, hyperplasia	2 (4%)			
Pancreatic, hyperplasia, histiocyte				1 (2%)
Renal, angiectasis	1 (2%)	1 (2%)		
Renal, hyperplasia			1 (2%)	
Lymph node, mandibular	(51)	(50)	(51)	(49)
Angiectasis	3 (6%)	1 (2%)	2 (4%)	
Cyst			1 (2%)	
Hemorrhage		1 (2%)		
Hyperplasia	4 (8%)	4 (8%)	9 (18%)	3 (6%)
Hyperplasia, lymphoid		1 (2%)		
Lymph node, mesenteric	(51)	(49)	(51)	(50)
Angiectasis	1 (2%)	1 (2%)		1 (2%)
Cyst	1 (2%)			
Hyperplasia			1 (2%)	
Hyperplasia, histiocyte				1 (2%)
Spleen	(51)	(50)	(51)	(50)
Angiectasis		1 (2%)	3 (6%)	
Fibrosis	6 (12%)	12 (24%)	7 (14%)	7 (14%)
Hematopoietic cell proliferation	3 (6%)	5 (10%)	10 (20%)	6 (12%)
Hyperplasia, histiocyte			1 (2%)	
Necrosis, focal	2 (4%)	1 (2%)	2 (4%)	1 (2%)
Trabecula, hyperplasia		1 (2%)		

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Hematopoietic System (continued)				
Thymus	(46)	(46)	(48)	(49)
Angiectasis	1 (2%)			
Cyst		1 (2%)	2 (4%)	2 (4%)
Ectopic parathyroid gland			1 (2%)	
Hyperplasia, lymphoid		1 (2%)	1 (2%)	
Integumentary System				
Mammary gland	(48)	(48)	(49)	(49)
Dilatation	16 (33%)	22 (46%)	12 (24%)	14 (29%)
Hemorrhage	1 (2%)			
Hyperplasia	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Inflammation, chronic				1 (2%)
Metaplasia, cartilagenous			1 (2%)	
Skin	(51)	(50)	(51)	(50)
Abscess	1 (2%)			
Cyst epithelial inclusion	1 (2%)	1 (2%)		
Hyperkeratosis			1 (2%)	
Inflammation, chronic	1 (2%)		1 (2%)	1 (2%)
Subcutaneous tissue, fat, necrosis			1 (2%)	
Musculoskeletal System				
Bone	(51)	(50)	(51)	(50)
Hyperostosis		1 (2%)		1 (2%)
Nervous System				
Brain	(51)	(50)	(51)	(50)
Atrophy				1 (2%)
Compression	11 (22%)	12 (24%)	4 (8%)	9 (18%)
Hemorrhage	5 (10%)			2 (4%)
Hydrocephalus				1 (2%)
Respiratory System				
Lung	(51)	(50)	(51)	(50)
Congestion	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Fibrosis, focal	1 (2%)			
Foreign body				1 (2%)
Hemorrhage	7 (14%)	1 (2%)	2 (4%)	3 (6%)
Hyperplasia, macrophage	3 (6%)			
Infiltration cellular, mixed cell	3 (6%)			1 (2%)
Inflammation, acute	1 (2%)			
Inflammation, suppurative				1 (2%)
Necrosis, focal	1 (2%)			
Alveolar epithelium, hyperplasia	4 (8%)	2 (4%)	1 (2%)	3 (6%)
Mediastinum, hemorrhage	1 (2%)			
Mediastinum, inflammation, chronic	1 (2%)			
Pleura, inflammation, chronic	1 (2%)			

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm		50 ppm		100 ppm		200 ppm	
Respiratory System (continued)								
Nose	(51)		(50)		(51)		(50)	
Fungus	5	(10%)	11	(22%)	9	(18%)	8	(16%)
Inflammation, suppurative	16	(31%)	13	(26%)	13	(25%)	11	(22%)
Mucosa, hyperplasia, squamous	1	(2%)						
Trachea	(51)		(50)		(51)		(50)	
Glands, cyst	1	(2%)						
Special Senses System								
Ear	(1)		(2)					
Pinna, hyperplasia, squamous	1	(100%)						
Eye	(5)		(3)		(1)		(2)	
Atrophy	1	(20%)						
Cataract	1	(20%)	2	(67%)			2	(100%)
Retina, degeneration	1	(20%)	3	(100%)	1	(100%)	2	(100%)
Retrobulbar, inflammation, chronic	1	(20%)						
Sclera, metaplasia, osseous					1	(100%)		
Harderian gland					(1)			
Acinus, dilatation					1	(100%)		
Urinary System								
Kidney	(51)		(50)		(51)		(50)	
Cyst	4	(8%)	5	(10%)	1	(2%)	2	(4%)
Necrosis, focal			1	(2%)				
Nephropathy	50	(98%)	50	(100%)	51	(100%)	50	(100%)
Pigmentation					1	(2%)	1	(2%)
Pelvis, dilatation	2	(4%)						
Pelvis, transitional epithelium, hyperplasia	1	(2%)						
Renal tubule, hyperplasia	3	(6%)	3	(6%)	2	(4%)	1	(2%)
Urethra	(1)							
Bulbourethral gland, dilatation	1	(100%)						
Urinary bladder	(51)		(50)		(51)		(50)	
Edema							1	(2%)
Hemorrhage							1	(2%)
Inflammation, chronic	1	(2%)			1	(2%)		
Muscularis, hyperplasia					1	(2%)		
Transitional epithelium, hyperplasia	1	(2%)						

APPENDIX D
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR CHLORAMINATED WATER STUDY

TABLE D1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	10
Early deaths				
Natural death	3	5	1	3
Moribund	16	17	20	23
Survivors				
Terminal sacrifice	31	28	29	24
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, cecum	(50)	(50)	(50)	(50)
Intestine large, colon	(50)	(50)	(50)	(50)
Intestine large, rectum	(50)	(50)	(50)	(50)
Intestine small, duodenum	(50)	(50)	(49)	(50)
Intestine small, ileum	(50)	(49)	(49)	(50)
Intestine small, jejunum	(50)	(50)	(49)	(50)
Liver	(50)	(50)	(50)	(50)
Hepatocellular adenoma	1 (2%)	3 (6%)	1 (2%)	3 (6%)
Mesentery	(10)	(11)	(5)	(9)
Pancreas	(50)	(50)	(49)	(50)
Salivary glands	(49)	(50)	(50)	(50)
Stomach, forestomach	(50)	(50)	(50)	(49)
Stomach, glandular	(50)	(50)	(50)	(50)
Tongue	(1)	(1)	(1)	
Papilloma squamous	1 (100%)		1 (100%)	
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Adenoma		1 (2%)	1 (2%)	1 (2%)
Carcinoma			1 (2%)	
Adrenal gland, medulla	(50)	(49)	(50)	(50)
Pheochromocytoma benign	6 (12%)	2 (4%)	5 (10%)	5 (10%)
Bilateral, pheochromocytoma benign	1 (2%)		1 (2%)	
Islets, pancreatic	(50)	(50)	(49)	(50)
Adenoma		4 (8%)	1 (2%)	
Carcinoma		1 (2%)		
Pituitary gland	(50)	(49)	(50)	(50)
Pars distalis, adenoma	33 (66%)	29 (59%)	18 (36%)	31 (62%)
Thyroid gland	(50)	(50)	(50)	(50)
C-cell, adenoma	4 (8%)	4 (8%)	4 (8%)	3 (6%)
C-cell, carcinoma	1 (2%)	2 (4%)	2 (4%)	
Follicular cell, adenoma	3 (6%)	1 (2%)	2 (4%)	1 (2%)
Follicular cell, carcinoma		1 (2%)		

TABLE D1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
General Body System				
Tissue NOS	(1)	(2)		
Oral, squamous cell carcinoma	1 (100%)			
Genital System				
Clitoral gland	(48)	(50)	(50)	(49)
Adenoma	5 (10%)	8 (16%)	7 (14%)	2 (4%)
Carcinoma	1 (2%)	1 (2%)		1 (2%)
Ovary	(50)	(50)	(50)	(50)
Granulosa cell tumor NOS			1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Adenoma			1 (2%)	1 (2%)
Histiocytic sarcoma			1 (2%)	
Endometrium, deciduoma NOS			1 (2%)	
Endometrium, polyp stromal	10 (20%)	9 (18%)	12 (24%)	11 (22%)
Endometrium, sarcoma stromal		1 (2%)	3 (6%)	1 (2%)
Vagina	(8)	(7)	(11)	(12)
Sarcoma	1 (13%)		1 (9%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Lymph node	(50)	(50)	(50)	(50)
Lymph node, mandibular	(48)	(49)	(49)	(49)
Carcinoma, metastatic, thyroid gland			1 (2%)	
Lymph node, mesenteric	(49)	(50)	(50)	(50)
Spleen	(50)	(50)	(50)	(50)
Hemangiosarcoma				1 (2%)
Thymus	(49)	(47)	(49)	(49)
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Adenocarcinoma	2 (4%)	1 (2%)	1 (2%)	
Adenoma	1 (2%)			1 (2%)
Fibroadenoma	11 (22%)	15 (30%)	13 (26%)	13 (26%)
Fibroadenoma, multiple	5 (10%)	5 (10%)	6 (12%)	2 (4%)
Skin	(50)	(50)	(50)	(50)
Papilloma squamous		1 (2%)		
Squamous cell carcinoma	1 (2%)			
Subcutaneous tissue, fibroma	2 (4%)		1 (2%)	
Subcutaneous tissue, fibrosarcoma	1 (2%)			1 (2%)
Subcutaneous tissue, lipoma				1 (2%)
Subcutaneous tissue, sarcoma				1 (2%)
Musculoskeletal System				
None				

TABLE D1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Nervous System				
Brain	(48)	(50)	(49)	(50)
Glioma malignant			1 (2%)	
Glioma NOS				1 (2%)
Oligodendroglioma NOS		1 (2%)		
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	1 (2%)	2 (4%)	3 (6%)
Carcinoma, greater than five, metastatic, multiple, thyroid gland			2 (4%)	
Nose	(50)	(50)	(50)	(50)
Glands, carcinoma	1 (2%)			
Special Senses System				
Ear	(1)	(1)	(1)	
Pinna, schwannoma NOS	1 (100%)	1 (100%)	1 (100%)	
Eye	(3)	(1)	(5)	(6)
Lids, schwannoma NOS			1 (20%)	
Zymbal's gland	(1)			
Adenoma	1 (100%)			
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Lipoma				1 (2%)
Urinary bladder	(50)	(50)	(50)	(50)
Systemic Lesions				
Multiple organs[a]	(50)	(50)	(50)	(50)
Histiocytic sarcoma			1 (2%)	
Leukemia mononuclear	8 (16%)	11 (22%)	15 (30%)	16 (32%)
Lymphoma malignant lymphocytic	1 (2%)			
Tumor Summary				
Total animals with primary neoplasms[b]	48	45	44	47
Total primary neoplasms	104	103	105	101
Total animals with benign neoplasms	45	42	37	44
Total benign neoplasms	85	83	76	79
Total animals with malignant neoplasms	16	15	22	19
Total malignant neoplasms	18	18	25	21
Total animals with secondary neoplasms			2	
Total secondary neoplasms[c]			3	
Total animals with neoplasms uncertain-benign or malignant	1	2	4	1
Total uncertain neoplasms	1	2	4	1

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 0 ppm

Number of Days on Study	4 7 2	5 0 8	5 3 1	5 6 9	5 7 8	6 2 0	6 3 9	6 5 0	6 6 6	6 6 6	6 6 7	6 6 8	6 6 8	6 7 3	6 7 5	7 0 2	7 0 3	7 1 2	7 2 1	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	1 5 9 1	0 5 0 1	0 5 2 1	1 5 8 1	1 5 9 2	0 5 1 1	1 5 1 5	1 5 8 2	1 6 1 1	1 6 2 1	1 5 9 3	0 5 1 2	0 5 2 2	0 5 3 1	0 5 3 2	1 5 8 3	0 5 1 3	0 5 2 2	1 6 0 1	0 5 3 3	0 5 3 3	0 5 4 4	0 5 5 5	0 5 4 4	0 5 1 5
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Mesentery	+	+	+	+		+													+						
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Papilloma squamous																									
Tooth							+																		
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																			X						X
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X	X		X	X		X			X	X	X	X			X	X	X	X	X	X		X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma						X	X																		
C-cell, carcinoma																									
Follicular cell, adenoma											X						X								

+: 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 Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 2 3	0 5 2 4	0 5 2 5	0 5 3 4	0 5 3 5	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	1 5 8 4	1 5 8 5	1 5 9 4	1 6 0 2	1 6 0 3	1 6 0 4	1 6 0 5	1 6 1 2	1 6 1 3	1 6 1 4	1 6 1 5	1 6 2 2	1 6 2 3	1 6 2 4	1 6 2 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma										X																1
Mesentery			+				+												+					+		10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue													+													1
Papilloma squamous													X													1
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign							X										X				X			X		6
Bilateral, pheochromocytoma benign					X																					1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
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	33
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma															X										X	4
C-cell, carcinoma																					X					1
Follicular cell, adenoma											X															3

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	4 7 2	5 0 8	5 3 1	5 6 9	5 7 8	6 2 0	6 3 9	6 5 0	6 6 6	6 6 7	6 6 8	6 6 8	6 6 3	6 7 5	7 0 2	7 0 3	7 1 2	7 2 1	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	1 5 9 1	0 5 0 1	0 5 2 1	1 5 8 1	1 5 9 2	0 5 1 1	1 5 9 5	1 5 8 2	1 6 1 1	1 6 2 1	1 5 9 3	0 5 1 2	0 5 2 2	0 5 3 1	0 5 3 2	1 5 8 3	0 5 1 3	0 5 0 2	1 6 0 1	0 5 3 3	0 5 3 3	0 5 0 4	0 5 0 5	0 5 1 4	0 5 1 5
General Body System																								
Tissue NOS																								+
Oral, squamous cell carcinoma																								X
Genital System																								
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
Adenoma																				X				X	
Carcinoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal		X			X	X	X								X		X								
Vagina	+													+					+				+		
Sarcoma														X											
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Adenoma																									
Fibroadenoma					X					X	X											X			
Fibroadenoma, multiple																X		X		X					
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma															X										
Subcutaneous tissue, fibroma										X									X						
Subcutaneous tissue, fibrosarcoma												X													
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 2 3	0 5 2 4	0 5 2 5	0 5 3 4	0 5 3 5	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	1 5 8 4	1 5 8 5	1 5 9 4	1 6 0 2	1 6 0 3	1 6 0 4	1 6 0 5	1 6 1 2	1 6 1 3	1 6 1 4	1 6 1 5	1 6 2 2	1 6 2 3	1 6 2 4	1 6 2 5	**Total Tissues/ Tumors**
General Body System																										
Tissue NOS																										1
Oral, squamous cell carcinoma																										1
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma	X															X			X							5
Carcinoma																						X				1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrium, polyp stromal							X		X				X									X				10
Vagina			+										+	+		+										8
Sarcoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma		X																			X					2
Adenoma																	X									1
Fibroadenoma	X					X					X			X	X			X					X			11
Fibroadenoma, multiple										X										X						5
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Subcutaneous tissue, fibroma																										2
Subcutaneous tissue, fibrosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	4 7 2	5 0 8	5 3 1	5 6 9	5 7 8	6 2 0	6 3 9	6 5 0	6 6 6	6 6 6	6 6 7	6 6 8	6 6 8	6 7 3	6 7 5	7 7 0	7 0 2	7 1 3	7 2 2	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	1 5 9 1	0 5 0 1	0 5 2 1	1 5 8 1	1 5 9 2	0 5 1 1	1 5 9 5	1 5 8 2	1 6 1 1	1 6 2 1	1 5 9 3	0 5 1 2	0 5 2 2	0 5 3 1	0 5 3 2	1 5 8 3	0 5 1 3	0 5 3 3	0 5 2 2	1 6 0 1	0 5 3 3	0 5 3 3	0 5 0 4	0 5 0 5	0 5 1 4	0 5 1 5
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glands, carcinoma								X																	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									+
Pinna, schwannoma NOS																									X
Eye															+								+		
Zymbal's gland																		+							
Adenoma																		X							
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X				X			X										X				X			
Lymphoma malignant lymphocytic																									

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 2 3	0 5 2 4	0 5 2 5	0 5 3 4	0 5 3 5	0 5 4 1	0 5 4 2	0 5 4 3	0 5 4 4	0 5 4 5	0 5 5 4	1 5 8 4	1 5 8 5	1 5 9 4	1 6 0 2	1 6 0 3	1 6 0 4	1 6 0 5	1 6 1 2	1 6 1 3	1 6 1 4	1 6 1 5	1 6 2 2	1 6 2 3	1 6 2 4	1 6 2 5	**Total Tissues/ Tumors**
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	48
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma								X																			1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glands, carcinoma																											1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																											
Ear																											1
Pinna, schwannoma NOS																											1
Eye					+																						3
Zymbal's gland																											1
Adenoma																											1
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear															X		X		X								8
Lymphoma malignant lymphocytic												X															1

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 50 ppm

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

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	1 7 9 5	1 8 3 4	1 8 0 3	1 8 0 4	1 8 0 5	1 8 1 4	1 8 1 5	1 8 2 2	1 8 2 3	1 8 2 4	1 8 2 5	1 8 3 5	0 7 1 3	0 7 1 4	0 7 1 5	0 7 2 3	0 7 2 4	0 7 2 5	0 7 3 3	0 7 3 4	0 7 3 5	0 7 5 2	0 7 5 3	0 7 5 4	0 7 5 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma		X															X							X	3
Mesentery					+		+						+					+								11
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue																										1
Cardiovascular System																										
Blood vessel																				+						1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																				X						1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign																		X								2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma									X												X					4
Carcinoma							X																			1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Pituitary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma			X			X	X					X		X		X	X	X	X	X	X	X			X	29
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma			X	X	X					X																4
C-cell, carcinoma								X														X				2
Follicular cell, adenoma																		X								1
Follicular cell, carcinoma																X										1
General Body System																										
Tissue NOS													+													2

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	2 9 9	3 4 8	4 5 2	5 4 0	5 7 0	5 7 6	6 2 2	6 2 6	6 2 6	6 4 1	6 5 2	6 5 6	6 6 2	6 9 5	6 9 8	7 0 2	7 0 3	7 1 4	7 1 9	7 1 9	7 1 9	7 2 6	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 7 4 1	0 7 5 1	1 8 1 1	1 8 3 1	1 7 9 1	1 7 9 2	1 8 0 1	0 7 2 1	0 7 3 1	0 7 2 2	0 7 1 1	1 8 2 1	1 8 3 2	0 7 3 2	1 7 9 3	1 8 0 2	0 7 1 2	1 8 1 2	0 7 4 2	1 7 9 2	1 8 1 3	1 8 3 3	0 7 4 3	0 7 4 4	0 7 4 5
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma				X										X					X			X	X		
Carcinoma			X																						
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal								X			X							X						X
Endometrium, sarcoma stromal																							X		
Vagina					+		+	+		+															
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Fibroadenoma								X	X					X			X			X	X				
Fibroadenoma, multiple												X										X	X		
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																							X		
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Oligodendroglioma NOS	X																								
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear															+										
Pinna, schwannoma NOS															X										
Eye											+														
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X					X		X			X	X			X	X					X	

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	1 7 9 5	1 8 3 4	1 8 0 3	1 8 0 4	1 8 0 5	1 8 1 4	1 8 1 5	1 8 2 2	1 8 2 3	1 8 2 4	1 8 2 5	1 8 3 5	1 8 3 5	0 7 1 3	0 7 1 4	0 7 1 5	0 7 2 3	0 7 2 4	0 7 2 5	0 7 3 3	0 7 3 4	0 7 3 5	0 7 5 2	0 7 5 3	0 7 5 4	0 7 5 5	**Total Tissues/ Tumors**
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma														X							X				X	8
Carcinoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrium, polyp stromal	X		X						X			X	X													9
Endometrium, sarcoma stromal																										1
Vagina				+						+											+					7
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	47
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																									X	1
Fibroadenoma				X					X			X	X			X	X	X			X	X				15
Fibroadenoma, multiple											X									X						5
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Oligodendroglioma NOS																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma														X												1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Pinna, schwannoma NOS																										1
Eye																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear								X	X																X	11

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 100 ppm

Number of Days on Study	2 0 0	4 5 6	4 6 5	5 0 9	5 6 0	5 8 4	5 9 0	6 0 5	6 1 9	6 2 0	6 2 8	6 6 7	6 6 8	6 6 6	6 9 7	6 9 8	6 9 8	7 0 4	7 1 9	7 1 9	7 2 6	7 3 0	7 3 0	7 3 0	7 3 1
Carcass ID Number	1 7 4 1	1 7 6 1	1 7 5 1	0 6 8 1	1 7 2 1	0 6 6 1	0 6 4 1	0 6 7 1	1 7 4 2	0 6 4 2	1 7 6 2	1 7 5 2	0 6 6 2	0 6 8 2	1 7 6 3	1 7 3 1	1 7 5 3	1 7 3 2	0 6 5 1	1 7 2 2	1 7 2 3	0 6 8 3	0 6 8 4	0 6 8 5	0 6 7 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Mesentery						+									+			+	+	+					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Papilloma squamous																									
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X								
Carcinoma																									
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign												X	X						X						
Bilateral, pheochromocytoma benign						X																			
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma							X	X	X		X	X			X	X		X			X			X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																								X	
C-cell, carcinoma																									
Follicular cell, adenoma					X			X																	

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 6 7 3	0 6 7 4	0 6 7 5	0 6 4 3	0 6 4 4	0 6 4 5	0 6 5 2	0 6 5 3	0 6 5 4	0 6 5 5	0 6 6 3	0 6 6 4	0 6 6 5	0 6 7 4	1 7 2 5	1 7 2 5	1 7 3 3	1 7 3 4	1 7 3 5	1 7 4 3	1 7 4 4	1 7 4 5	1 7 5 4	1 7 5 5	1 7 6 4	1 7 6 5	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma											X															1
Mesentery																										5
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue														+												1
Papilloma squamous														X												1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Carcinoma				X																						1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign											X								X							5
Bilateral, pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	49
Adenoma										X																1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X												X	X	X		X				X	X			X	18
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma					X						X											X				4
C-cell, carcinoma			X						X																	2
Follicular cell, adenoma																										2

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	2	4	4	5	5	5	5	6	6	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7
	0	5	6	0	6	8	9	0	1	2	2	6	6	7	9	9	9	0	1	1	2	3	3	3	3
	0	6	5	9	0	4	0	5	9	0	8	7	8	6	7	8	8	4	9	9	6	0	0	0	1
Carcass ID Number	1	1	1	0	1	0	0	0	1	0	1	1	0	0	1	1	1	1	0	1	1	0	0	0	0
	7	7	7	6	7	6	6	6	7	6	7	7	6	6	7	7	7	7	6	7	7	6	6	6	6
	4	6	5	8	2	6	4	7	4	4	6	5	6	8	6	3	5	3	5	2	2	8	8	8	7
	1	1	1	1	1	1	1	1	2	2	2	2	2	2	3	1	3	2	1	2	3	3	4	5	2
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma												X													
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Histiocytic sarcoma																						X			
Endometrium, deciduoma NOS																							X		
Endometrium, polyp stromal								X							X		X	X			X	X			
Endometrium, sarcoma stromal										X			X												
Vagina					+			+							+					+				+	
Sarcoma								X																	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland																									
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Fibroadenoma						X										X	X							X	
Fibroadenoma, multiple											X									X		X			
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																									

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 6 7 3	0 6 7 4	0 6 7 5	0 6 6 3	0 6 4 4	0 6 4 5	0 6 5 2	0 6 5 3	0 6 5 4	0 6 5 5	0 6 6 3	0 6 6 4	0 6 6 5	0 6 6 6	1 7 2 4	1 7 2 5	1 7 3 3	1 7 3 4	1 7 3 5	1 7 4 3	1 7 4 4	1 7 4 5	1 7 5 4	1 7 5 5	1 7 6 4	1 7 6 5	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma											X	X				X	X	X					X			7
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granulosa cell tumor NOS												X														1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma				X																						1
Histiocytic sarcoma																										1
Endometrium, deciduoma NOS																										1
Endometrium, polyp stromal	X				X													X		X	X	X				12
Endometrium, sarcoma stromal																								X		3
Vagina				+						+						+				+	+			+		11
Sarcoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, thyroid gland									X																	1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																								X		1
Fibroadenoma			X		X	X					X		X				X		X		X		X			13
Fibroadenoma, multiple	X																	X				X				6
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibroma																		X								1

Table D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	200	456	465	509	560	584	590	605	619	620	628	667	678	676	697	698	698	704	719	719	726	730	730	730	731
Carcass ID Number	1741	1761	1751	0681	1721	0661	0641	0671	1742	0642	1762	1752	0662	0682	1763	1731	1753	1732	0651	1722	1723	0683	0684	0685	0672
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Glioma malignant							X																		
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma									X																
Carcinoma, greater than five, metastatic, multiple, thyroid gland																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Pinna, schwannoma NOS																									
Eye															+				+						
Lids, schwannoma NOS																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																						X			
Leukemia mononuclear			X		X	X						X		X	X		X					X			

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 6 7 3	0 6 7 4	0 6 7 5	0 6 4 3	0 6 4 4	0 6 4 5	0 6 5 2	0 6 5 3	0 6 5 4	0 6 5 5	0 6 6 3	0 6 6 4	0 6 6 5	0 6 6 6	1 7 2 4	1 7 2 5	1 7 3 3	1 7 3 4	1 7 3 5	1 7 4 3	1 7 4 4	1 7 4 5	1 7 5 4	1 7 5 5	1 7 6 4	1 7 6 5	**Total Tissues/ Tumors**
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Glioma malignant																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma													X													2
Carcinoma, greater than five, metastatic, multiple, thyroid gland			X						X																	2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																			+							1
Pinna, schwannoma NOS																			X							1
Eye																+							+		+	5
Lids, schwannoma NOS																									X	1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear			X				X								X		X			X				X	X	15

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 200 ppm

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

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	725	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	16744	05733	05744	05755	05784	05885	05893	05994	05995	06003	06004	06005	06014	06115	06552	06553	06554	06555	06564	06565	06575	06583	06684	06855	06995	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma		X		X																					X	3
Mesentery																								+		9
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign					X										X											5
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
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		31
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma												X														3
Follicular cell, adenoma																										1
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	4 6 5	5 0 8	5 0 8	5 1 9	5 8 9	5 8 9	5 9 1	5 9 2	6 1 8	6 2 0	6 2 1	6 6 2	6 6 9	6 6 7	6 8 7	6 8 7	6 8 7	6 9 0	6 9 0	6 9 0	7 0 3	7 0 4	7 1 2	7 1 9	7 2 2
Carcass ID Number	1 6 9 1	0 5 9 1	1 6 7 1	0 5 7 1	1 6 6 2	1 6 8 1	0 5 8 1	0 6 0 1	1 6 7 2	0 5 8 2	1 6 6 1	1 6 9 2	1 6 5 1	0 5 9 2	0 6 0 2	1 6 9 3	1 6 9 4	0 6 1 1	0 6 1 2	1 6 7 3	0 6 3 3	1 6 8 2	0 5 7 2	1 6 6 3	0 5 8 3
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Adenoma			X				X																		
Carcinoma																				X					
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Endometrium, polyp stromal							X	X				X					X			X					
Endometrium, sarcoma stromal																									
Vagina							+	+	+	+		+				+	+							+	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Thymus	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+
Adenoma																									
Fibroadenoma	X				X						X				X					X			X		X
Fibroadenoma, multiple																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma													X												
Subcutaneous tissue, lipoma																									
Subcutaneous tissue, sarcoma																				X					
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma NOS															X										
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma						X																		X	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye													+		+								+		
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lipoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear								X	X	X	X	X	X			X		X			X	X	X	X	

TABLE D2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	
	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	
	5	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	
	6	5	5	5	5	5	5	5	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	**Total**
Carcass ID Number	7	7	7	7	8	8	9	9	9	0	0	0	1	1	5	5	5	5	6	6	7	8	8	8	9	**Tissues/**
	4	3	4	5	4	5	3	4	5	3	4	5	4	5	2	3	4	5	4	5	5	3	4	5	5	**Tumors**
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																										2
Carcinoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																		X								1
Endometrium, polyp stromal			X	X												X	X				X				X	11
Endometrium, sarcoma stromal			X																							1
Vagina			+	+							+													+		12
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																								X		1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Fibroadenoma	X				X		X				X									X				X		13
Fibroadenoma, multiple			X																		X					2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, lipoma												X														1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glioma NOS																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																X										3
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye									+			+	+													6
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lipoma								X																		1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X		X												X			X							16

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rates[a]	7/50 (14%)	2/49 (4%)	6/50 (12%)	5/50 (10%)
Adjusted rates[b]	21.9%	7.4%	16.3%	16.8%
Terminal rates[c]	6/31 (19%)	2/27 (7%)	2/29 (7%)	2/24 (8%)
First incidence (days)	721	729 (T)	584	687
Life table tests[d]	P=0.517	P=0.114N	P=0.537N	P=0.526N
Logistic regression tests[d]	P=0.531N	P=0.092N	P=0.526N	P=0.451N
Cochran-Armitage test[d]	P=0.495N			
Fisher exact test[d]		P=0.085N	P=0.500N	P=0.380N
Clitoral Gland: Adenoma				
Overall rates	5/48 (10%)	8/50 (16%)	7/50 (14%)	2/49 (4%)
Adjusted rates	16.1%	23.7%	22.7%	4.3%
Terminal rates	5/31 (16%)	4/28 (14%)	6/29 (21%)	0/24 (0%)
First incidence (days)	729 (T)	540	667	508
Life table tests	P=0.208N	P=0.236	P=0.332	P=0.299N
Logistic regression tests	P=0.129N	P=0.282	P=0.374	P=0.197N
Cochran-Armitage test	P=0.120N			
Fisher exact test		P=0.304	P=0.409	P=0.209N
Clitoral Gland: Adenoma or Carcinoma				
Overall rates	6/48 (13%)	9/50 (18%)	7/50 (14%)	3/49 (6%)
Adjusted rates	19.4%	25.2%	22.7%	7.5%
Terminal rates	6/31 (19%)	4/28 (14%)	6/29 (21%)	0/24 (0%)
First incidence (days)	729 (T)	452	667	508
Life table tests	P=0.220N	P=0.245	P=0.450	P=0.344N
Logistic regression tests	P=0.129N	P=0.308	P=0.498	P=0.229N
Cochran-Armitage test	P=0.125N			
Fisher exact test		P=0.318	P=0.532	P=0.233N
Liver: Hepatocellular Adenoma				
Overall rates	1/50 (2%)	3/50 (6%)	1/50 (2%)	3/50 (6%)
Adjusted rates	3.2%	10.7%	3.4%	12.5%
Terminal rates	1/31 (3%)	3/28 (11%)	1/29 (3%)	3/24 (13%)
First incidence (days)	729 (T)	729 (T)	729 (T)	729 (T)
Life table tests	P=0.223	P=0.268	P=0.747	P=0.217
Logistic regression tests	P=0.223	P=0.268	P=0.747	P=0.217
Cochran-Armitage test	P=0.313			
Fisher exact test		P=0.309	P=0.753N	P=0.309
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	1/49 (2%)	1/50 (2%)	2/50 (4%)	3/50 (6%)
Adjusted rates	3.3%	3.6%	5.7%	9.7%
Terminal rates	1/30 (3%)	1/28 (4%)	1/29 (3%)	1/24 (4%)
First incidence (days)	729 (T)	729 (T)	619	589
Life table tests	P=0.128	P=0.747	P=0.484	P=0.257
Logistic regression tests	P=0.166	P=0.747	P=0.503	P=0.309
Cochran-Armitage test	P=0.168			
Fisher exact test		P=0.747N	P=0.508	P=0.316

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Mammary Gland: Fibroadenoma				
Overall rates[e]	16/50 (32%)	20/50 (40%)	19/50 (38%)	15/50 (30%)
Adjusted rates	43.5%	54.6%	55.0%	44.5%
Terminal rates	11/31 (35%)	12/28 (43%)	14/29 (48%)	7/24 (29%)
First incidence (days)	578	626	584	465
Life table tests	P=0.442	P=0.199	P=0.274	P=0.430
Logistic regression tests	P=0.418N	P=0.229	P=0.284	P=0.536N
Cochran-Armitage test	P=0.363N			
Fisher exact test		P=0.266	P=0.338	P=0.500N
Mammary Gland: Adenoma or Fibroadenoma				
Overall rates	17/50 (34%)	20/50 (40%)	19/50 (38%)	16/50 (32%)
Adjusted rates	46.3%	54.6%	55.0%	46.2%
Terminal rates	12/31 (39%)	12/28 (43%)	14/29 (48%)	7/24 (29%)
First incidence (days)	578	626	584	465
Life table tests	P=0.418	P=0.254	P=0.343	P=0.420
Logistic regression tests	P=0.440N	P=0.298	P=0.359	P=0.540N
Cochran-Armitage test	P=0.383N			
Fisher exact test		P=0.339	P=0.418	P=0.500N
Mammary Gland: Adenoma, Fibroadenoma, or Adenocarcinoma				
Overall rates	19/50 (38%)	21/50 (42%)	19/50 (38%)	16/50 (32%)
Adjusted rates	52.0%	57.5%	55.0%	46.2%
Terminal rates	14/31 (45%)	13/28 (46%)	14/29 (48%)	7/24 (29%)
First incidence (days)	578	626	584	465
Life table tests	P=0.512N	P=0.310	P=0.493	P=0.554
Logistic regression tests	P=0.287N	P=0.373	P=0.523	P=0.381N
Cochran-Armitage test	P=0.237N			
Fisher exact test		P=0.419	P=0.582N	P=0.338N
Pancreatic Islets: Adenoma				
Overall rates	0/50 (0%)	4/50 (8%)	1/49 (2%)	0/50 (0%)
Adjusted rates	0.0%	12.2%	3.6%	0.0%
Terminal rates	0/31 (0%)	2/28 (7%)	1/28 (4%)	0/24 (0%)
First incidence (days)	-[e]	662	729 (T)	-
Life table tests	P=0.348N	P=0.057	P=0.480	-
Logistic regression tests	P=0.312N	P=0.060	P=0.480	-
Cochran-Armitage test	P=0.297N			
Fisher exact test		P=0.059	P=0.495	-
Pancreatic Islets: Adenoma or Carcinoma				
Overall rates	0/50 (0%)	5/50 (10%)	1/49 (2%)	0/50 (0%)
Adjusted rates	0.0%	15.6%	3.6%	0.0%
Terminal rates	0/31 (0%)	3/28 (11%)	1/28 (4%)	0/24 (0%)
First incidence (days)	-	662	729 (T)	-
Life table tests	P=0.296N	P=0.029	P=0.480	-
Logistic regression tests	P=0.261N	P=0.031	P=0.480	-
Cochran-Armitage test	P=0.243N			
Fisher exact test		P=0.028	P=0.495	-

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	33/50 (66%)	29/49 (59%)	18/50 (36%)	31/50 (62%)
Adjusted rates	78.1%	69.5%	46.0%	78.4%
Terminal rates	22/31 (71%)	15/27 (56%)	9/29 (31%)	16/24 (67%)
First incidence (days)	531	540	590	465
Life table tests	P=0.393	P=0.489N	P=0.017N	P=0.331
Logistic regression tests	P=0.359N	P=0.365N	P=0.003N	P=0.469N
Cochran-Armitage test	P=0.326N			
Fisher exact test		P=0.311N	P=0.002N	P=0.418N
Skin (Subcutaneous Tissue): Fibroma or Fibrosarcoma				
Overall rates	3/50 (6%)	0/50 (0%)	1/50 (2%)	1/50 (2%)
Adjusted rates	8.0%	0.0%	3.4%	2.6%
Terminal rates	1/31 (3%)	0/28 (0%)	1/29 (3%)	0/24 (0%)
First incidence (days)	666	-	729 (T)	662
Life table tests	P=0.332N	P=0.141N	P=0.329N	P=0.349N
Logistic regression tests	P=0.299N	P=0.120N	P=0.313N	P=0.298N
Cochran-Armitage test	P=0.296N			
Fisher exact test		P=0.121N	P=0.309N	P=0.309N
Skin (Subcutaneous Tissue): Fibroma, Fibrosarcoma, or Sarcoma				
Overall rates	3/50 (6%)	0/50 (0%)	1/50 (2%)	2/50 (4%)
Adjusted rates	8.0%	0.0%	3.4%	5.7%
Terminal rates	1/31 (3%)	0/28 (0%)	1/29 (3%)	0/24 (0%)
First incidence (days)	666	-	729 (T)	662
Life table tests	P=0.599N	P=0.141N	P=0.329N	P=0.551N
Logistic regression tests	P=0.559N	P=0.120N	P=0.313N	P=0.495N
Cochran-Armitage test	P=0.556N			
Fisher exact test		P=0.121N	P=0.309N	P=0.500N
Thyroid Gland (C-cell): Adenoma				
Overall rates	4/50 (8%)	4/50 (8%)	4/50 (8%)	3/50 (6%)
Adjusted rates	10.6%	14.3%	13.8%	8.6%
Terminal rates	2/31 (6%)	4/28 (14%)	4/29 (14%)	1/24 (4%)
First incidence (days)	620	729 (T)	729 (T)	589
Life table tests	P=0.521N	P=0.594	P=0.600	P=0.580N
Logistic regression tests	P=0.424N	P=0.631	P=0.628	P=0.471N
Cochran-Armitage test	P=0.410N			
Fisher exact test		P=0.643N	P=0.643N	P=0.500N
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rates	5/50 (10%)	6/50 (12%)	6/50 (12%)	3/50 (6%)
Adjusted rates	13.7%	21.4%	20.7%	8.6%
Terminal rates	3/31 (10%)	6/28 (21%)	6/29 (21%)	1/24 (4%)
First incidence (days)	620	729 (T)	729 (T)	589
Life table tests	P=0.382N	P=0.436	P=0.448	P=0.450N
Logistic regression tests	P=0.285N	P=0.482	P=0.475	P=0.336N
Cochran-Armitage test	P=0.262N			
Fisher exact test		P=0.500	P=0.500	P=0.357N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Thyroid Gland (Follicular Cell): Adenoma				
Overall rates	3/50 (6%)	1/50 (2%)	2/50 (4%)	1/50 (2%)
Adjusted rates	8.4%	3.6%	4.4%	2.7%
Terminal rates	1/31 (3%)	1/28 (4%)	0/29 (0%)	0/24 (0%)
First incidence (days)	667	729 (T)	560	687
Life table tests	P=0.313N	P=0.333N	P=0.517N	P=0.342N
Logistic regression tests	P=0.273N	P=0.313N	P=0.458N	P=0.312N
Cochran-Armitage test	P=0.279N			
Fisher exact test		P=0.309N	P=0.500N	P=0.309N
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rates	3/50 (6%)	2/50 (4%)	2/50 (4%)	1/50 (2%)
Adjusted rates	8.4%	7.1%	4.4%	2.7%
Terminal rates	1/31 (3%)	2/28 (7%)	0/29 (0%)	0/24 (0%)
First incidence (days)	667	729 (T)	560	687
Life table tests	P=0.271N	P=0.535N	P=0.517N	P=0.342N
Logistic regression tests	P=0.229N	P=0.512N	P=0.458N	P=0.312N
Cochran-Armitage test	P=0.232N			
Fisher exact test		P=0.500N	P=0.500N	P=0.309N
Uterus: Stromal Polyp				
Overall rates	10/50 (20%)	9/50 (18%)	12/50 (24%)	11/50 (22%)
Adjusted rates	24.7%	27.4%	34.4%	34.3%
Terminal rates	4/31 (13%)	6/28 (21%)	7/29 (24%)	6/24 (25%)
First incidence (days)	508	626	605	591
Life table tests	P=0.240	P=0.558N	P=0.366	P=0.363
Logistic regression tests	P=0.370	P=0.494N	P=0.397	P=0.526
Cochran-Armitage test	P=0.385			
Fisher exact test		P=0.500N	P=0.405	P=0.500
Uterus: Stromal Sarcoma				
Overall rates	0/50 (0%)	1/50 (2%)	3/50 (6%)	1/50 (2%)
Adjusted rates	0.0%	3.6%	8.3%	4.2%
Terminal rates	0/31 (0%)	1/28 (4%)	1/29 (3%)	1/24 (4%)
First incidence (days)	-	729 (T)	620	729 (T)
Life table tests	P=0.301	P=0.480	P=0.113	P=0.449
Logistic regression tests	P=0.346	P=0.480	P=0.124	P=0.449
Cochran-Armitage test	P=0.351			
Fisher exact test		P=0.500	P=0.121	P=0.500
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rates	10/50 (20%)	10/50 (20%)	15/50 (30%)	11/50 (22%)
Adjusted rates	24.7%	30.7%	40.5%	34.3%
Terminal rates	4/31 (13%)	7/28 (25%)	8/29 (28%)	6/24 (25%)
First incidence (days)	508	626	605	591
Life table tests	P=0.239	P=0.532	P=0.166	P=0.363
Logistic regression tests	P=0.374	P=0.597N	P=0.175	P=0.526
Cochran-Armitage test	P=0.388			
Fisher exact test		P=0.598N	P=0.178	P=0.500

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
All Organs: Mononuclear Leukemia				
Overall rates	8/50 (16%)	11/50 (22%)	15/50 (30%)	16/50 (32%)
Adjusted rates	20.8%	29.0%	39.3%	41.4%
Terminal rates	4/31 (13%)	4/28 (14%)	8/29 (28%)	4/24 (17%)
First incidence (days)	472	540	465	592
Life table tests	P=0.021	P=0.280	P=0.077	P=0.036
Logistic regression tests	P=0.035	P=0.322	P=0.087	P=0.058
Cochran-Armitage test	P=0.034			
Fisher exact test		P=0.306	P=0.077	P=0.050
All Organs: Benign Tumors				
Overall rates	45/50 (90%)	42/50 (84%)	37/50 (74%)	44/50 (88%)
Adjusted rates	95.7%	91.3%	84.0%	93.5%
Terminal rates	29/31 (94%)	24/28 (86%)	22/29 (76%)	21/24 (88%)
First incidence (days)	508	540	560	465
Life table tests	P=0.184	P=0.551	P=0.220N	P=0.203
Logistic regression tests	P=0.500N	P=0.400N	P=0.054N	P=0.540N
Cochran-Armitage test	P=0.448N			
Fisher exact test		P=0.277N	P=0.033N	P=0.500N
All Organs: Malignant Tumors				
Overall rates	16/50 (32%)	15/50 (30%)	22/50 (44%)	19/50 (38%)
Adjusted rates	40.6%	39.2%	52.8%	48.9%
Terminal rates	9/31 (29%)	7/28 (25%)	11/29 (38%)	6/24 (25%)
First incidence (days)	472	452	465	592
Life table tests	P=0.117	P=0.571N	P=0.146	P=0.201
Logistic regression tests	P=0.216	P=0.491N	P=0.162	P=0.339
Cochran-Armitage test	P=0.213			
Fisher exact test		P=0.500N	P=0.151	P=0.338
All Organs: Benign and Malignant Tumors				
Overall rates	48/50 (96%)	45/50 (90%)	44/50 (88%)	47/50 (94%)
Adjusted rates	96.0%	93.7%	93.6%	95.9%
Terminal rates	29/31 (94%)	25/28 (89%)	26/29 (90%)	22/24 (92%)
First incidence (days)	472	299	465	465
Life table tests	P=0.154	P=0.540	P=0.468N	P=0.198
Logistic regression tests	P=0.525N	P=0.249N	P=0.209N	P=0.504N
Cochran-Armitage test	P=0.500N			
Fisher exact test		P=0.218N	P=0.134N	P=0.500N

(T)Terminal sacrifice

[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.

[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality

[c] Observed incidence at terminal kill

[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.

[e] Not applicable; no tumors in animal group

TABLE D4a
Historical Incidence of Leukemias in Untreated Female F344/N Rats[a]

Study	Incidence in Controls
Historical Incidence at Southern Research Institute	
Feed	
Nitrofurantoin	13/50 (26%)
Rhodamine 6G	11/50 (22%)
Roxarsone	14/50 (28%)
Total	38/150 (25%)
Standard deviation	3.1%
Range	22%-28%
Water	
Chloramine	8/50 (16%)
Overall Historical Incidence	
Feed	
Total	124/500 (25%)
Standard deviation	6.1%
Range	14%-36%
Water	
Total	46/180 (26%)
Standard deviation	8.5%
Range	16%-33%

[a] Data as of 15 September 1990; includes data for lymphocytic, monocytic, mononuclear cell, and undifferentiated leukemias.

TABLE D4b
Historical Incidence of Pancreatic Islet Neoplasms in Untreated Female F344/N Rats[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Southern Research Institute			
Feed			
Nitrofurantoin	0/50 (0%)	1/50 (2%)	1/50 (2%)
Rhodamine 6G	2/48 (4%)	1/48 (2%)	3/48 (6%)
Roxarsone	1/50 (2%)	0/50 (0%)	1/50 (2%)
Total	3/148 (2%)	2/148 (1%)	5/148 (3%)
Standard deviation	2.0%	1.2%	2.3%
Range	0%-4%	0%-2%	2%-6%
Water			
Chloramine	0/50 (0%)	0/50 (0%)	0/50 (0%)
Overall Historical Incidence			
Feed			
Total	7/492 (1%)	3/492 (1%)	10/492 (2%)
Standard deviation	1.4%	1.0%	1.6%
Range	0%-4%	0%-2%	0%-6%
Water			
Total	4/180 (2%)	0/180 (0%)	4/180 (2%)
Standard deviation	2.0%		2.0%
Range	0%-4%		0%-4%

[a] Data as of 15 September 1990

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
14-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	10
Early deaths				
Natural death	3	5	1	3
Moribund	16	17	20	23
Survivors				
Terminal sacrifice	31	28	29	24
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(50)	(50)	(50)	(50)
Inflammation, chronic		1 (2%)		
Necrosis		1 (2%)		
Parasite metazoan	1 (2%)	2 (4%)	3 (6%)	
Perforation		1 (2%)		
Intestine large, rectum	(50)	(50)	(50)	(50)
Parasite metazoan	4 (8%)	4 (8%)	3 (6%)	4 (8%)
Liver	(50)	(50)	(50)	(50)
Angiectasis	3 (6%)	2 (4%)	3 (6%)	2 (4%)
Basophilic focus	1 (2%)			
Congestion	3 (6%)	1 (2%)		1 (2%)
Cyst			1 (2%)	
Fatty change	10 (20%)	17 (34%)	13 (26%)	11 (22%)
Fibrosis, focal	1 (2%)			
Focal cellular change	36 (72%)	35 (70%)	32 (64%)	30 (60%)
Granuloma	39 (78%)	38 (76%)	36 (72%)	36 (72%)
Hematopoietic cell proliferation	6 (12%)	2 (4%)	3 (6%)	2 (4%)
Hemorrhage	1 (2%)			
Hepatodiaphragmatic nodule	10 (20%)	5 (10%)	6 (12%)	7 (14%)
Hyperplasia, histiocyte, lymphoid	1 (2%)	1 (2%)		2 (4%)
Hyperplasia, multifocal	7 (14%)	6 (12%)	8 (16%)	15 (30%)
Infiltration cellular, mixed cell	4 (8%)	11 (22%)	3 (6%)	9 (18%)
Inflammation, focal				1 (2%)
Necrosis, focal	1 (2%)	3 (6%)	1 (2%)	3 (6%)
Bile duct, hyperplasia	34 (68%)	32 (64%)	35 (70%)	35 (70%)
Biliary tract, fibrosis	28 (56%)	27 (54%)	26 (52%)	24 (48%)
Centrilobular, atrophy	4 (8%)	7 (14%)	4 (8%)	9 (18%)
Centrilobular, necrosis			1 (2%)	2 (4%)
Serosa, fibrosis		1 (2%)		
Mesentery	(10)	(11)	(5)	(9)
Accessory spleen	1 (10%)	1 (9%)		
Infiltration cellular, lymphocytic	1 (10%)			
Inflammation, chronic	5 (50%)	6 (55%)	3 (60%)	1 (11%)
Fat, necrosis	2 (20%)	2 (18%)	1 (20%)	3 (33%)
Pancreas	(50)	(50)	(49)	(50)
Atrophy, focal	6 (12%)	6 (12%)	7 (14%)	4 (8%)
Cytoplasmic alteration	1 (2%)	1 (2%)		
Edema			1 (2%)	
Duct, dilatation				1 (2%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Alimentary System (continued)				
Salivary glands	(49)	(50)	(50)	(50)
Focal cellular change	1 (2%)			
Inflammation, chronic	1 (2%)			
Mineralization				1 (2%)
Stomach, forestomach	(50)	(50)	(50)	(49)
Cyst			1 (2%)	
Edema			1 (2%)	
Erosion	1 (2%)			
Hyperplasia, basal cell		1 (2%)		
Inflammation, chronic	7 (14%)	3 (6%)	5 (10%)	5 (10%)
Perforation	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Ulcer	6 (12%)	2 (4%)	3 (6%)	4 (8%)
Mucosa, hyperplasia, papillary	9 (18%)	2 (4%)	5 (10%)	6 (12%)
Stomach, glandular	(50)	(50)	(50)	(50)
Edema			1 (2%)	
Erosion	1 (2%)		1 (2%)	
Inflammation, chronic	2 (4%)	1 (2%)	2 (4%)	1 (2%)
Mucosa, hyperplasia			1 (2%)	
Tongue	(1)	(1)	(1)	
Hyperplasia, squamous		1 (100%)		
Tooth	(1)			
Dysplasia	1 (100%)			
Inflammation, suppurative	1 (100%)			
Cardiovascular System				
Blood vessel		(1)		
Mesenteric artery, inflammation, chronic		1 (100%)		
Heart	(50)	(50)	(50)	(50)
Thrombus			2 (4%)	
Artery, inflammation, chronic	1 (2%)	1 (2%)		
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule	1 (2%)			
Angiectasis		2 (4%)	1 (2%)	
Congestion	1 (2%)	2 (4%)	1 (2%)	
Degeneration			1 (2%)	
Fibrosis			1 (2%)	
Focal cellular change	16 (32%)	14 (28%)	14 (28%)	16 (32%)
Hyperplasia				2 (4%)
Necrosis		1 (2%)		
Vacuolization cytoplasmic	1 (2%)	3 (6%)	2 (4%)	1 (2%)
Adrenal gland, medulla	(50)	(49)	(50)	(50)
Developmental malformation		1 (2%)		
Hyperplasia	5 (10%)	6 (12%)	6 (12%)	9 (18%)
Infiltration cellular, lymphocytic				1 (2%)
Parathyroid gland	(49)	(47)	(50)	(50)
Hyperplasia				1 (2%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Endocrine System (continued)				
Pituitary gland	(50)	(49)	(50)	(50)
Angiectasis	38 (76%)	40 (82%)	36 (72%)	40 (80%)
Cyst	3 (6%)	1 (2%)	4 (8%)	3 (6%)
Hemorrhage		1 (2%)		1 (2%)
Pars distalis, hyperplasia, focal	6 (12%)	6 (12%)	9 (18%)	2 (4%)
Thyroid gland	(50)	(50)	(50)	(50)
Degeneration, cystic	3 (6%)			
Ultimobranchial cyst	1 (2%)			
C-cell, hyperplasia	7 (14%)	8 (16%)	11 (22%)	4 (8%)
Follicle, cyst	1 (2%)			
Follicular cell, hyperplasia	2 (4%)			
General Body System				
Tissue NOS	(1)	(2)		
Abdominal, hemorrhage		1 (50%)		
Genital System				
Clitoral gland	(48)	(50)	(50)	(49)
Degeneration, cystic	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Hyperplasia	3 (6%)	4 (8%)	6 (12%)	3 (6%)
Inflammation, suppurative	11 (23%)	8 (16%)	9 (18%)	5 (10%)
Ovary	(50)	(50)	(50)	(50)
Angiectasis				1 (2%)
Corpus luteum, proliferation	1 (2%)			1 (2%)
Corpus luteum, thecal cell, hyperplasia	1 (2%)	1 (2%)		1 (2%)
Follicle, cyst	2 (4%)		1 (2%)	2 (4%)
Periovarian tissue, cyst		1 (2%)	1 (2%)	2 (4%)
Uterus	(50)	(50)	(50)	(50)
Cyst				1 (2%)
Decidual reaction			1 (2%)	
Hemorrhage	2 (4%)			
Hydrometra	2 (4%)	1 (2%)	5 (10%)	5 (10%)
Inflammation, suppurative			2 (4%)	2 (4%)
Cervix, lamina propria, hyperplasia				1 (2%)
Endometrium, hyperplasia, cystic	26 (52%)	32 (64%)	38 (76%)	18 (36%)
Horn, atrophy				1 (2%)
Vagina	(8)	(7)	(11)	(12)
Cyst	6 (75%)	6 (86%)	10 (91%)	7 (58%)
Inflammation, suppurative	2 (25%)	4 (57%)	8 (73%)	2 (17%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hypercellularity	4 (8%)	7 (14%)	5 (10%)	5 (10%)
Myelofibrosis	1 (2%)	1 (2%)		
Lymph node	(50)	(50)	(50)	(50)
Inguinal, angiectasis				1 (2%)
Inguinal, hyperplasia			3 (6%)	2 (4%)
Inguinal, inflammation, suppurative				1 (2%)
Mediastinal, angiectasis	3 (6%)	3 (6%)	7 (14%)	7 (14%)
Mediastinal, hyperplasia			1 (2%)	
Pancreatic, angiectasis	1 (2%)		3 (6%)	1 (2%)
Pancreatic, hyperplasia, histiocyte		1 (2%)		
Renal, angiectasis				2 (4%)
Lymph node, mandibular	(48)	(49)	(49)	(49)
Angiectasis	3 (6%)	1 (2%)	3 (6%)	2 (4%)
Hyperplasia	5 (10%)	1 (2%)	3 (6%)	1 (2%)
Hyperplasia, lymphoid	1 (2%)			
Lymph node, mesenteric	(49)	(50)	(50)	(50)
Angiectasis	2 (4%)	1 (2%)	3 (6%)	3 (6%)
Hyperplasia		1 (2%)		
Hyperplasia, lymphoid		1 (2%)		
Spleen	(50)	(50)	(50)	(50)
Depletion		1 (2%)	2 (4%)	
Developmental malformation			1 (2%)	
Fibrosis		1 (2%)	1 (2%)	1 (2%)
Hematopoietic cell proliferation	12 (24%)	8 (16%)	7 (14%)	9 (18%)
Hyperplasia, histiocyte, lymphoid	2 (4%)	4 (8%)	2 (4%)	6 (12%)
Necrosis, focal			1 (2%)	
Capsule, hyperplasia, histiocyte, lymphoid	1 (2%)			
Thymus	(49)	(47)	(49)	(49)
Cyst		3 (6%)	2 (4%)	
Epithelial cell, hyperplasia			1 (2%)	
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Dilatation	40 (80%)	43 (86%)	40 (80%)	38 (76%)
Fibrosis			1 (2%)	
Hyperplasia	3 (6%)	3 (6%)	5 (10%)	7 (14%)
Inflammation, suppurative		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Abscess	1 (2%)			
Erosion			1 (2%)	
Exudate			1 (2%)	
Hemorrhage			1 (2%)	
Hyperkeratosis		1 (2%)		
Inflammation, chronic	3 (6%)	1 (2%)	2 (4%)	1 (2%)
Ulcer	2 (4%)		1 (2%)	1 (2%)
Epidermis, hyperplasia		1 (2%)		
Sebaceous gland, cyst			1 (2%)	
Subcutaneous tissue, foreign body			1 (2%)	

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hyperostosis	9 (18%)	6 (12%)	11 (22%)	9 (18%)
Nervous System				
Brain	(48)	(50)	(49)	(50)
Compression	11 (23%)	16 (32%)	5 (10%)	7 (14%)
Hemorrhage		2 (4%)		3 (6%)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion		3 (6%)	1 (2%)	1 (2%)
Foreign body	1 (2%)			
Hemorrhage	1 (2%)	3 (6%)	1 (2%)	2 (4%)
Hyperplasia, macrophage	3 (6%)	1 (2%)	2 (4%)	3 (6%)
Infiltration cellular, mixed cell	3 (6%)			4 (8%)
Inflammation, acute		1 (2%)		
Inflammation, pyogranulomatous	1 (2%)			
Alveolar epithelium, hyperplasia	2 (4%)		4 (8%)	4 (8%)
Nose	(50)	(50)	(50)	(50)
Foreign body	1 (2%)			
Fungus	3 (6%)	7 (14%)	3 (6%)	3 (6%)
Inflammation, suppurative	3 (6%)	8 (16%)	3 (6%)	4 (8%)
Special Senses System				
Eye	(3)	(1)	(5)	(6)
Atrophy				2 (33%)
Cataract	3 (100%)		4 (80%)	4 (67%)
Hemorrhage			1 (20%)	
Cornea, inflammation, acute		1 (100%)		
Retina, degeneration	2 (67%)		3 (60%)	6 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Atrophy			1 (2%)	1 (2%)
Cyst				3 (6%)
Fibrosis		1 (2%)		
Hydronephrosis				1 (2%)
Inflammation, suppurative		1 (2%)	1 (2%)	1 (2%)
Mineralization	2 (4%)	2 (4%)	2 (4%)	
Nephropathy	46 (92%)	48 (96%)	50 (100%)	49 (98%)
Pigmentation		1 (2%)	1 (2%)	
Pelvis, transitional epithelium, hyperplasia			1 (2%)	1 (2%)
Renal tubule, vacuolization cytoplasmic	1 (2%)			
Urinary bladder	(50)	(50)	(50)	(50)
Hemorrhage			1 (2%)	
Inflammation, chronic			1 (2%)	
Transitional epithelium, hyperplasia		1 (2%)	1 (2%)	

APPENDIX E
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR CHLORINATED WATER STUDY

TABLE E1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	9
Early deaths				
Natural death	4	6	2	8
Moribund	12	16	13	10
Accidental death	0	0	0	1
Survivors				
Terminal sacrifice	34	27	35	32
Died last week of study	0	1	0	0
Animals examined microscopically	50	50	50	51
Alimentary System				
Intestine small, ileum	(48)	(48)	(49)	(49)
Carcinoma	1 (2%)			1 (2%)
Intestine small, jejunum	(49)	(50)	(50)	(49)
Carcinoma		1 (2%)		2 (4%)
Liver	(50)	(50)	(50)	(51)
Carcinoma, metastatic, islets, pancreatic		1 (2%)		
Hemangiosarcoma	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Hemangiosarcoma, metastatic		1 (2%)		
Hepatoblastoma	1 (2%)	2 (4%)		
Hepatocellular carcinoma	9 (18%)	10 (20%)	11 (22%)	10 (20%)
Hepatocellular carcinoma, two, multiple	2 (4%)	3 (6%)	1 (2%)	2 (4%)
Hepatocellular carcinoma, three, multiple	1 (2%)			2 (4%)
Hepatocellular adenoma	8 (16%)	15 (30%)	10 (20%)	15 (29%)
Hepatocellular adenoma, two, multiple	10 (20%)	10 (20%)	11 (22%)	5 (10%)
Hepatocellular adenoma, three, multiple	9 (18%)	2 (4%)	4 (8%)	4 (8%)
Hepatocellular adenoma, four, multiple	2 (4%)	1 (2%)	2 (4%)	
Hepatocellular adenoma, five, multiple		1 (2%)		1 (2%)
Hepatocellular adenoma, greater than five, multiple	1 (2%)			
Histiocytic sarcoma		1 (2%)		
Sarcoma	1 (2%)			
Mesentery	(7)	(3)	(2)	(3)
Fibrosarcoma, metastatic, skeletal muscle	1 (14%)			
Hemangiosarcoma			1 (50%)	
Hepatoblastoma, metastatic, liver	1 (14%)			
Pancreas	(50)	(50)	(50)	(51)
Salivary glands	(50)	(50)	(50)	(51)
Sarcoma	1 (2%)			
Stomach, forestomach	(50)	(50)	(50)	(50)
Hepatoblastoma, metastatic, liver	1 (2%)			
Papilloma squamous	1 (2%)	1 (2%)	1 (2%)	
Squamous cell carcinoma				1 (2%)
Stomach, glandular	(50)	(50)	(50)	(50)

TABLE E1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Cardiovascular System				
Blood vessel				(1)
Hemangioma				1 (100%)
Heart	(50)	(50)	(50)	(51)
Sarcoma	1 (2%)			
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(51)
Adenoma			1 (2%)	1 (2%)
Hepatoblastoma, metastatic, liver	1 (2%)			
Capsule, adenoma	5 (10%)	4 (8%)	1 (2%)	5 (10%)
Adrenal gland, medulla	(49)	(50)	(50)	(51)
Neuroblastoma benign		1 (2%)		
Pheochromocytoma malignant				1 (2%)
Pheochromocytoma benign	1 (2%)	1 (2%)		
Islets, pancreatic	(50)	(50)	(50)	(51)
Adenoma		1 (2%)		1 (2%)
Carcinoma		1 (2%)		
Thyroid gland	(50)	(50)	(50)	(51)
C-cell, carcinoma			1 (2%)	
Follicular cell, adenoma	1 (2%)	1 (2%)	2 (4%)	
General Body System				
Tissue NOS				(1)
Genital System				
Epididymis	(50)	(50)	(50)	(51)
Preputial gland	(4)	(11)	(20)	(7)
Squamous cell carcinoma				1 (14%)
Prostate	(50)	(49)	(50)	(51)
Testes	(50)	(50)	(50)	(51)
Interstitial cell, adenoma	1 (2%)			
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(51)
Carcinoma, metastatic, thyroid gland			1 (2%)	
Hemangiosarcoma	1 (2%)			
Histiocytic sarcoma		1 (2%)		
Lymph node	(50)	(50)	(50)	(51)
Inguinal, renal, popliteal, sarcoma	1 (2%)			
Mediastinal, hepatoblastoma, metastatic, liver	1 (2%)			
Mediastinal, hepatocellular carcinoma, metastatic, liver	1 (2%)	1 (2%)		
Mediastinal, squamous cell carcinoma, metastatic, preputial gland				1 (2%)
Lymph node, mandibular	(49)	(48)	(48)	(48)
Carcinoma, metastatic, harderian gland		1 (2%)		

TABLE E1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chlorinated Drinking Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Hematopoietic System (continued)				
Lymph node, mesenteric	(46)	(48)	(50)	(50)
Hemangiosarcoma		1 (2%)		
Histiocytic sarcoma		1 (2%)		
Spleen	(50)	(50)	(50)	(51)
Hemangioma	1 (2%)		1 (2%)	1 (2%)
Hemangiosarcoma	3 (6%)	2 (4%)	1 (2%)	
Hepatoblastoma, metastatic, liver	1 (2%)			
Histiocytic sarcoma		1 (2%)		
Thymus	(47)	(43)	(46)	(49)
Hemangioma	1 (2%)			
Integumentary System				
Skin	(50)	(49)	(50)	(51)
Subcutaneous tissue, fibrosarcoma		1 (2%)		
Subcutaneous tissue, hemangiosarcoma			1 (2%)	
Subcutaneous tissue, melanoma malignant		1 (2%)		
Subcutaneous tissue, sarcoma			1 (2%)	
Musculoskeletal System				
Skeletal muscle	(3)			(1)
Fibrosarcoma	1 (33%)			
Hepatoblastoma, metastatic, liver	1 (33%)			
Sarcoma	1 (33%)			
Squamous cell carcinoma, metastatic, preputial gland				1 (100%)
Nervous System				
Brain	(50)	(50)	(50)	(51)
Respiratory System				
Lung	(50)	(50)	(50)	(51)
Alveolar/bronchiolar adenoma	14 (28%)	8 (16%)	14 (28%)	13 (25%)
Alveolar/bronchiolar adenoma, two, multiple	1 (2%)	2 (4%)	1 (2%)	
Alveolar/bronchiolar carcinoma	8 (16%)	2 (4%)	5 (10%)	7 (14%)
Alveolar/bronchiolar carcinoma, three, multiple			1 (2%)	1 (2%)
Carcinoma, metastatic, harderian gland		1 (2%)		1 (2%)
Fibrosarcoma, metastatic, skeletal muscle	1 (2%)			
Hepatoblastoma, metastatic, liver	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	3 (6%)	2 (4%)	1 (2%)	1 (2%)
Sarcoma	1 (2%)			
Squamous cell carcinoma, metastatic, preputial gland				1 (2%)
Mediastinum, hemangioma	1 (2%)			
Nose	(50)	(50)	(50)	(51)
Carcinoma, metastatic, harderian gland		1 (2%)		

TABLE E1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Special Senses System				
Harderian gland	(3)	(5)	(4)	(1)
Adenoma	3 (100%)	3 (60%)	4 (100%)	
Carcinoma		1 (20%)		1 (100%)
Urinary System				
Kidney	(50)	(50)	(50)	(51)
Hepatoblastoma, metastatic, liver	1 (2%)			
Hepatocellular carcinoma, metastatic, liver		1 (2%)		
Sarcoma	1 (2%)			
Renal tubule, adenoma				1 (2%)
Renal tubule, carcinoma				1 (2%)
Urinary bladder	(50)	(50)	(50)	(51)
Systemic Lesions				
Multiple organs[a]	(50)	(50)	(50)	(51)
Histiocytic sarcoma		1 (2%)		
Lymphoma malignant mixed		3 (6%)	2 (4%)	4 (8%)
Lymphoma malignant undifferentiated cell			1 (2%)	
Tumor Summary				
Total animals with primary neoplasms[b]	42	45	44	47
Total primary neoplasms	95	82	80	83
Total animals with benign neoplasms	39	35	37	34
Total benign neoplasms	60	51	52	48
Total animals with malignant neoplasms	22	26	20	29
Total malignant neoplasms	35	31	28	35
Total animals with secondary neoplasms[c]	4	5	2	3
Total secondary neoplasms	14	9	2	5

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 0 ppm

Number of Days on Study	5 4 1	5 5 1	5 5 8	5 5 9	5 7 9	6 2 5	6 5 7	6 6 1	6 7 1	6 8 1	6 9 1	6 9 1	7 2 7	7 3 0	7 3 0	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	0 0 3 1	0 2 0 1	0 0 7 1	0 2 3 1	5 3 3 1	0 3 9 1	5 0 0 1	5 4 1 1	5 2 6 1	5 3 2 1	0 2 8 1	5 1 3 1	0 2 3 1	5 1 9 1	0 4 2 1	5 4 3 1	5 3 5 1	0 0 1 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	5 2 7 1	5 2 9 1	5 3 0 1	5 3 1 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Intestine small, jejunum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Hepatoblastoma											X														
Hepatocellular carcinoma	X	X			X		X			X						X			X						
Hepatocellular carcinoma, two, multiple			X																						
Hepatocellular carcinoma, three, multiple														X											
Hepatocellular adenoma					X											X							X		
Hepatocellular adenoma, two, multiple			X								X		X						X						X
Hepatocellular adenoma, three, multiple									X	X					X			X	X			X			
Hepatocellular adenoma, four, multiple																									
Hepatocellular adenoma, greater than five, multiple																									
Sarcoma							X																		
Mesentery	+									+	+											+			
Fibrosarcoma, metastatic, skeletal muscle	X																								
Hepatoblastoma, metastatic, liver											X														
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatoblastoma, metastatic, liver											X														
Papilloma squamous											X														
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth					+	+		+	+	+		+						+	+	+					

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

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 1 1	0 2 1 1	0 2 8 1	0 1 0 1	0 1 1 1	0 1 2 1	0 1 4 1	0 1 5 1	0 1 6 1	0 1 7 1	0 1 8 1	0 2 4 1	0 2 5 1	0 5 4 1	5 3 6 1	5 3 7 1	5 3 8 1	5 4 4 1	5 4 5 1	5 3 9 1	5 4 1 1	5 2 1 1	5 2 2 1	5 4 1 1	5 2 5 1	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	44
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma		X																									1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																			X								1
Hepatoblastoma																											1
Hepatocellular carcinoma													X		X												9
Hepatocellular carcinoma, two, multiple						X																					2
Hepatocellular carcinoma, three, multiple																											1
Hepatocellular adenoma		X							X			X										X	X				8
Hepatocellular adenoma, two, multiple					X		X			X	X					X											10
Hepatocellular adenoma, three, multiple				X		X													X								9
Hepatocellular adenoma, four, multiple													X											X			2
Hepatocellular adenoma, greater than five, multiple																		X									1
Sarcoma																											1
Mesentery						+				+															+		7
Fibrosarcoma, metastatic, skeletal muscle																											1
Hepatoblastoma, metastatic, liver																											1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																											1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatoblastoma, metastatic, liver																											1
Papilloma squamous																											1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth	+	+		+		+				+			+				+								+		17

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	5 4 1	5 5 1	5 5 8	5 5 9	5 7 9	6 2 5	6 5 7	6 6 1	6 7 1	6 8 1	6 9 1	6 9 1	7 2 7	7 3 0	7 3 0	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	0 0 3 1	0 2 0 1	0 0 7 1	0 2 3 1	5 3 3 1	0 0 9 1	5 4 0 1	5 2 6 1	5 3 2 1	5 2 8 1	0 1 3 1	5 2 3 1	0 1 9 1	5 4 2 1	5 4 3 1	5 3 5 1	0 0 1 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	5 2 7 1	5 2 9 1	5 3 0 1	5 3 1 1
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatoblastoma, metastatic, liver											X														
Capsule, adenoma										X															
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma											X														
General Body System																									
None																									
Genital System																									
Coagulating gland								+					+		+			+	+						
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland																						+		+	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma									X																
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Inguinal, renal, popliteal, sarcoma							X																		
Mediastinal, hepatoblastoma, metastatic, liver											X														
Mediastinal, hepatocellular carcinoma, metastatic, liver	X																								
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma														X											
Hemangiosarcoma																									
Hepatoblastoma, metastatic, liver											X														
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 1 1	0 2 2 1	0 0 8 1	0 1 0 1	0 1 1 1	0 1 2 1	0 1 4 1	0 1 5 1	0 1 6 1	0 1 7 1	0 1 8 1	0 2 4 1	0 2 5 1	0 3 4 1	5 3 6 1	5 3 7 1	5 3 8 1	5 4 4 1	5 4 5 1	5 4 3 9 1	5 4 1 1	5 2 1 1	5 2 2 1	5 2 4 1	5 2 5 1	**Total Tissues/ Tumors**
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																											1
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatoblastoma, metastatic, liver																											1
Capsule, adenoma							X	X							X							X					5
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign																						X					1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	48
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																											1
General Body System																											
None																											
Genital System																											
Coagulating gland					+		+										+										8
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland								+									I					+					4
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell, adenoma																											1
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																						X					1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Inguinal, renal, popliteal, sarcoma																											1
Mediastinal, hepatoblastoma, metastatic, liver																											1
Mediastinal, hepatocellular carcinoma, metastatic, liver																											1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+		49
Lymph node, mesenteric	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Hemangioma																											1
Hemangiosarcoma																		X	X			X					3
Hepatoblastoma, metastatic, liver																											1
Thymus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+		47
Hemangioma		X																									1

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	5 4 1	5 5 1	5 5 8	5 5 9	5 7 9	6 2 5	6 5 7	6 6 1	6 7 1	6 8 1	6 9 1	6 9 1	7 2 7	7 3 0	7 3 0	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	0 0 3 1	0 2 0 1	0 0 7 1	0 2 3 1	5 3 3 1	0 3 9 1	5 4 0 1	5 2 6 1	5 3 2 1	5 2 8 1	0 1 3 1	5 2 3 1	0 1 9 1	5 4 2 1	5 4 3 1	5 3 5 1	0 0 1 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	5 2 7 1	5 2 9 1	5 3 0 1	5 3 1 1
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+						+				+														
Fibrosarcoma	X																								
Hepatoblastoma, metastatic, liver											X														
Sarcoma							X																		
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma	X	X	X			X								X		X	X								X
Alveolar/bronchiolar adenoma, two, multiple																									
Alveolar/bronchiolar carcinoma				X						X			X				X								
Fibrosarcoma, metastatic, skeletal muscle	X																								
Hepatoblastoma, metastatic, liver											X														
Hepatocellular carcinoma, metastatic, liver	X	X	X																						
Sarcoma							X																		
Mediastinum, hemangioma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatoblastoma, metastatic, liver											X														
Sarcoma							X																		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 1 1	0 2 2 1	0 2 8 1	0 1 0 1	0 1 1 1	0 1 1 1	0 1 2 1	0 1 4 1	0 1 5 1	0 1 6 1	0 1 7 1	0 1 8 1	0 2 4 1	0 2 5 1	0 5 4 1	5 3 6 1	5 3 7 1	5 3 8 1	5 4 4 1	5 4 5 1	5 3 9 1	5 4 1 1	5 2 1 1	5 2 2 1	5 2 4 1	5 2 5 1	**Total Tissues/ Tumors**
Integumentary System																											
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																											3
Fibrosarcoma																											1
Hepatoblastoma, metastatic, liver																											1
Sarcoma																											1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma										X	X		X	X								X			X		14
Alveolar/bronchiolar adenoma, two, multiple																							X				1
Alveolar/bronchiolar carcinoma								X					X		X						X						8
Fibrosarcoma, metastatic, skeletal muscle																											1
Hepatoblastoma, metastatic, liver																											1
Hepatocellular carcinoma, metastatic, liver																											3
Sarcoma																											1
Mediastinum, hemangioma								X																			1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																											
Harderian gland						+										+						+					3
Adenoma						X										X						X					3
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatoblastoma, metastatic, liver																											1
Sarcoma																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 70 ppm

Number of Days on Study	4 9 0	5 2 2	5 4 8	5 6 2	5 6 2	6 0 1	6 2 6	6 3 8	6 4 0	6 6 6	6 6 8	6 7 7	6 8 2	6 8 8	6 9 8	6 9 9	7 1 4	7 2 3	7 2 7	7 2 7	7 2 7	7 3 0	7 3 3	7 3 3	7 3 3
Carcass ID Number	2 3 0 1	2 3 1 1	2 1 7 1	7 3 7 1	7 4 0 1	2 1 6 1	2 1 8 1	7 3 1 1	7 3 4 1	7 4 4 1	2 2 0 1	2 2 8 1	7 3 2 1	7 3 9 1	2 1 1 1	2 2 7 1	2 3 3 1	7 3 8 1	2 1 4 1	2 2 4 1	2 3 2 1	7 4 7 1	2 2 9 1	2 3 4 1	2 3 5 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																						X			
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, islets, pancreatic																					X				
Hemangiosarcoma								X														X			
Hemangiosarcoma, metastatic																									
Hepatoblastoma															X										
Hepatocellular carcinoma	X		X	X			X				X		X							X	X				
Hepatocellular carcinoma, two, multiple												X													X
Hepatocellular adenoma					X			X							X	X	X								
Hepatocellular adenoma, two, multiple														X				X		X				X	
Hepatocellular adenoma, three, multiple													X												
Hepatocellular adenoma, four, multiple																			X						
Hepatocellular adenoma, five, multiple																									
Histiocytic sarcoma																									
Mesentery		+																						+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth										+						+					+		+	+	
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	7 4 3 1	7 4 5 1	7 4 6 1	7 4 8 1	7 5 3 1	7 2 3 1	7 2 2 1	7 2 5 1	7 2 6 1	7 1 2 1	7 1 3 1	7 1 5 1	7 1 9 1	7 2 1 1	7 2 2 1	7 2 3 1	7 3 3 1	7 3 5 1	7 3 6 1	7 4 1 1	7 4 2 1	7 4 9 1	7 5 0 1	7 5 1 1	7 5 2 1	7 5 4 1	7 5 5 1	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																											1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, islets, pancreatic																											1
Hemangiosarcoma																											2
Hemangiosarcoma, metastatic																								X			1
Hepatoblastoma																				X							2
Hepatocellular carcinoma			X						X																		10
Hepatocellular carcinoma, two, multiple																				X							3
Hepatocellular adenoma	X				X						X	X		X						X		X	X	X		X	15
Hepatocellular adenoma, two, multiple		X	X							X			X						X						X		10
Hepatocellular adenoma, three, multiple									X																		2
Hepatocellular adenoma, four, multiple																											1
Hepatocellular adenoma, five, multiple																		X									1
Histiocytic sarcoma					X																						1
Mesentery		+																									3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous																									X		1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth		+	M																						+		7
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	4 9 0	5 2 2	5 4 8	5 6 2	5 6 2	6 0 1	6 2 6	6 3 8	6 4 0	6 6 6	6 6 8	6 7 7	6 8 2	6 8 8	6 9 8	6 9 9	7 1 4	7 2 3	7 2 7	7 2 7	7 2 7	7 3 0	7 3 3	7 3 3	7 3 3
Carcass ID Number	2 3 0 1	2 3 1 1	2 1 7 1	7 3 7 1	7 4 0 1	2 1 6 1	2 1 8 1	7 3 1 1	7 3 4 1	7 4 4 1	2 2 0 1	2 2 8 1	7 3 2 1	7 3 9 1	2 1 1 1	2 2 7 1	2 3 3 1	7 3 8 1	2 1 4 1	2 2 4 1	2 3 2 1	7 4 7 1	2 2 9 1	2 3 4 1	2 3 5 1
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma													X								X				
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neuroblastoma benign																	X								
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																		X							
Carcinoma																					X				
Parathyroid gland	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
None																									
Genital System																									
Coagulating gland										M						+	+		+					+	
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+		+								+							+						
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, hepatocellular carcinoma, metastatic, liver	X																								
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland		X																							
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																						X			
Histiocytic sarcoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma					X																				
Histiocytic sarcoma																									
Thymus	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	M	M
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma																				X					
Subcutaneous tissue, melanoma malignant										X															

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	7 4 3 1	7 4 5 1	7 4 6 1	7 4 8 1	7 5 3 1	2 2 3 1	2 2 5 1	2 2 6 1	2 1 2 1	2 1 3 1	2 1 5 1	2 1 9 1	2 2 1 1	2 2 2 1	7 3 3 1	7 3 5 1	7 3 6 1	7 4 1 1	7 4 2 1	7 4 9 1	7 5 0 1	7 5 1 1	7 5 2 1	7 5 4 1	7 5 5 1	**Total Tissues/ Tumors**
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma							X						X													4
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neuroblastoma benign																										1
Pheochromocytoma benign							X																			1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Carcinoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma			X																							1
General Body System																										
None																										
Genital System																										
Coagulating gland		+								+														+		7
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+		+	+				M				+			+		+									11
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma					X																					1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, hepatocellular carcinoma, metastatic, liver																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	I	+	48
Carcinoma, metastatic, harderian gland																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Hemangiosarcoma																										1
Histiocytic sarcoma					X																					1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																							X			2
Histiocytic sarcoma					X																					1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	M	+	+	+	43
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, melanoma malignant																										1

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	4 9 0	5 2 2	5 4 8	5 6 2	5 6 2	6 0 1	6 2 6	6 3 8	6 4 0	6 6 6	6 6 8	6 6 7	6 7 2	6 8 8	6 9 8	6 9 9	7 1 4	7 2 3	7 2 7	7 2 7	7 2 7	7 3 0	7 3 3	7 3 3	7 3 3
Carcass ID Number	2 3 0 1	2 3 1 1	2 1 7 1	7 3 7 1	7 4 0 1	2 1 6 1	2 1 8 1	7 3 1 1	7 3 4 1	7 4 4 1	2 2 0 1	2 2 8 1	7 3 2 1	7 3 9 1	2 1 1 1	2 2 7 1	2 3 3 1	7 3 8 1	2 1 4 1	2 2 4 1	2 3 2 1	7 4 7 1	2 2 9 1	2 3 4 1	2 3 5 1
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma			X		X															X			X		
Alveolar/bronchiolar adenoma, two, multiple																			X						
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, harderian gland		X																							
Hepatocellular carcinoma, metastatic, liver	X																			X					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland		X																							
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																			+						
Harderian gland		+									+								+						
Adenoma											X								X						
Carcinoma		X																							
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver	X																								
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Lymphoma malignant mixed						X								X											

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	7 4 3 1	7 4 5 1	7 4 6 1	7 4 8 1	7 5 3 1	2 2 3 1	2 2 5 1	2 2 6 1	2 1 2 1	2 1 3 1	2 1 5 1	2 1 9 1	2 2 1 1	2 2 2 1	7 3 3 1	7 3 5 1	7 3 6 1	7 4 1 1	7 4 2 1	7 4 9 1	7 5 0 1	7 5 1 1	7 5 2 1	7 5 4 1	7 5 5 1	**Total Tissues/ Tumors**
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X						X														X			X	8
Alveolar/bronchiolar adenoma, two, multiple				X																						2
Alveolar/bronchiolar carcinoma														X				X								2
Carcinoma, metastatic, harderian gland																										1
Hepatocellular carcinoma, metastatic, liver																										2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye																										1
Harderian gland																								+	+	5
Adenoma																								X		3
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic, liver																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma					X																					1
Lymphoma malignant mixed														X												3

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 140 ppm

Number of Days on Study	5 4 0	5 5 1	5 5 1	5 5 8	5 6 5	5 6 7	6 2 6	6 4 8	6 8 0	6 8 8	6 9 1	6 9 8	7 1 7	7 2 6	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	7 1 9 1	1 7 7 1	1 8 1 1	1 9 4 1	2 0 0 1	1 9 0 1	1 8 0 1	7 2 0 1	1 7 6 1	6 9 6 1	7 0 1 1	1 8 2 1	1 8 8 1	1 9 8 1	7 1 8 1	1 7 8 1	1 7 9 1	7 0 8 1	7 0 9 1	7 1 0 1	7 1 1 1	7 1 2 1	7 1 3 1	7 1 4 1	7 1 5 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma	X				X																				
Hepatocellular carcinoma		X		X			X	X			X			X	X								X		
Hepatocellular carcinoma, two, multiple																									
Hepatocellular adenoma					X					X					X	X					X		X	X	
Hepatocellular adenoma, two, multiple						X					X							X							
Hepatocellular adenoma, three, multiple																									
Hepatocellular adenoma, four, multiple																			X						
Mesentery								+																	
Hemangiosarcoma								X																	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																						X			
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth				+		+												+	+						
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									X
Capsule, adenoma																									
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	M	+	+	+	I	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, carcinoma			X																						
Follicular cell, adenoma																									

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	
Carcass ID Number	7 1 6 1	7 1 7 1	1 9 5 1	1 9 6 1	1 9 7 1	1 9 9 1	1 8 9 1	1 9 1 1	1 9 2 1	1 9 3 1	7 0 2 1	7 0 3 1	7 0 4 1	7 0 5 1	7 0 6 1	7 0 7 1	1 8 3 1	1 8 4 1	1 8 5 1	1 8 6 1	1 8 7 1	6 9 8 1	6 9 9 1	6 9 7 1	7 0 0 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+		48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+		49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+		47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine small, ileum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Hemangiosarcoma																										2
Hepatocellular carcinoma							X													X			X			11
Hepatocellular carcinoma, two, multiple																			X							1
Hepatocellular adenoma								X													X				X	10
Hepatocellular adenoma, two, multiple				X					X							X	X	X		X			X	X		11
Hepatocellular adenoma, three, multiple							X				X			X	X											4
Hepatocellular adenoma, four, multiple			X																							2
Mesentery																		+								2
Hemangiosarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth									+										+							6
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Capsule, adenoma															X											1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	45
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, carcinoma																										1
Follicular cell, adenoma	X																	X								2

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	5 4 0	5 5 1	5 5 1	5 5 8	5 6 5	5 6 7	6 2 6	6 4 8	6 8 0	6 8 8	6 9 1	6 9 8	7 1 7	7 2 6	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	7 1 9 1	1 7 7 1	1 8 1 1	1 9 4 1	2 0 0 1	1 0 0 1	1 9 8 1	7 2 0 1	1 7 6 1	6 9 6 1	7 0 1 1	1 8 2 1	1 8 8 1	1 9 8 1	7 1 8 1	1 7 8 1	1 7 9 1	7 0 8 1	7 0 9 1	7 1 0 1	7 1 1 1	7 1 2 1	7 1 3 1	7 1 4 1	7 1 5 1
General Body System																									
None																									
Genital System																									
Coagulating gland																					+				+
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland			+			+	+			+						+						+	+		
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland			X																						
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	I	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma							X																		
Hemangiosarcoma								X																	
Thymus	+	+	M	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangiosarcoma								X																	
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma										X			X			X	X						X		X
Alveolar/bronchiolar adenoma, two, multiple							X																		
Alveolar/bronchiolar carcinoma				X					X									X							
Alveolar/bronchiolar carcinoma, three, multiple																								X	
Hepatocellular carcinoma, metastatic, liver														X											
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	
Carcass ID Number	7 1 6 1	7 1 7 1	1 1 5 1	1 1 6 1	1 1 7 1	1 1 9 1	1 1 9 1	1 1 1 1	1 1 2 1	1 1 3 1	7 0 2 1	7 0 3 1	7 0 4 1	7 0 5 1	7 0 6 1	7 0 7 1	1 1 3 1	1 1 4 1	1 1 5 1	1 1 6 1	1 1 7 1	6 6 8 1	6 6 9 1	6 6 9 1	7 0 0 1	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Coagulating gland														+		+				+				+		6
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+			+	+	+	+	+						+			+		+	+		+	+		20
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, thyroid gland																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	46
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, hemangiosarcoma																										1
Subcutaneous tissue, sarcoma																							X			1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma				X		X		X			X	X			X					X					X	14
Alveolar/bronchiolar adenoma, two, multiple																										1
Alveolar/bronchiolar carcinoma																						X	X			5
Alveolar/bronchiolar carcinoma, three, multiple																										1
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

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

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

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

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 275 ppm

Number of Days on Study	0 2 6	3 5 8	3 8 5	4 7 0	4 8 5	5 6 2	5 6 5	5 8 7	6 7 5	6 8 3	6 8 4	6 8 8	6 8 8	6 9 1	6 9 1	6 9 4	7 0 2	7 2 1	7 3 1	7 3 1	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4
Carcass ID Number	1 7 2 1	6 8 4 1	1 6 1 1	1 5 7 1	6 7 7 1	6 6 4 1	6 7 6 1	1 4 7 1	6 8 3 1	6 8 0 1	6 8 5 1	6 8 2 1	6 6 9 1	6 7 5 1	1 4 2 1	1 5 5 1	6 7 2 1	6 6 5 1	6 6 7 1	6 6 8 1	6 7 0 1	6 7 1 1	1 4 8 1	1 4 9 1	1 5 0 1	1 5 1 1
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	+	+	+	+	+	+	+	I	I	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	M	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma														X												
Intestine small, jejunum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																		X								X
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																							X			
Hepatocellular carcinoma		X	X	X					X	X	X	X													X	
Hepatocellular carcinoma, two, multiple					X									X												
Hepatocellular carcinoma, three, multiple							X						X													
Hepatocellular adenoma					X					X	X	X								X	X					X
Hepatocellular adenoma, two, multiple																							X			
Hepatocellular adenoma, three, multiple							X										X									
Hepatocellular adenoma, five, multiple																										
Mesentery				+																	+				+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																								X		
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Tooth				+				+											+		+			+		
Cardiovascular System																										
Blood vessel		+																								
Hemangioma		X																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Capsule, adenoma																X										
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																	X									

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	
Carcass ID Number	1 5 2 1	1 5 9 1	1 6 0 1	1 6 2 1	1 6 3 1	1 6 4 1	1 5 3 1	1 5 4 1	1 5 6 1	1 5 8 1	6 7 9 1	6 8 1 1	1 4 1 1	1 4 3 1	1 4 4 1	1 4 5 1	1 4 6 1	1 6 5 1	6 6 1 1	6 6 2 1	6 6 3 1	6 6 6 1	6 6 7 1	6 7 3 1	6 7 4 1	6 7 8 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma																										2
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hemangiosarcoma																										1
Hepatocellular carcinoma					X																	X				10
Hepatocellular carcinoma, two, multiple																										2
Hepatocellular carcinoma, three, multiple																										2
Hepatocellular adenoma		X	X			X	X	X			X		X											X		15
Hepatocellular adenoma, two, multiple				X										X		X			X							5
Hepatocellular adenoma, three, multiple										X		X														4
Hepatocellular adenoma, five, multiple									X																	1
Mesentery																										3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth									+													+				7
Cardiovascular System																										
Blood vessel																										1
Hemangioma																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma																X										1
Capsule, adenoma						X		X											X		X					5
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma malignant																										1

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	0 2 6	3 5 8	3 8 5	4 7 0	4 8 5	5 6 2	5 6 5	5 8 7	6 7 5	6 8 3	6 8 4	6 8 8	6 8 8	6 9 1	6 9 1	6 9 4	7 0 2	7 2 1	7 3 1	7 3 1	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4
Carcass ID Number	1 7 2 1	6 8 4 1	1 6 1 1	1 5 7 1	6 7 7 1	6 6 4 1	6 7 6 1	1 4 7 1	6 8 3 1	6 8 0 1	6 8 5 1	6 8 2 1	6 6 9 1	6 7 5 1	1 4 2 1	1 5 5 1	6 7 2 1	6 6 5 1	6 6 7 1	6 6 8 1	6 7 0 1	6 7 1 1	1 4 8 1	1 4 9 1	1 5 0 1	1 5 1 1
Endocrine System (continued)																											
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																											
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+
Pituitary gland	M	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																											
Tissue NOS															+												
Genital System																											
Coagulating gland								+											+								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland						+							+					+									
Squamous cell carcinoma						X																					
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, squamous cell carcinoma, metastatic, preputial gland						X																					
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																											
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																											
Mammary gland	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle						+																					
Squamous cell carcinoma, metastatic, preputial gland						X																					
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	
Carcass ID Number	1 5 2 1	1 5 9 1	1 6 0 1	1 6 2 1	1 6 3 1	1 6 4 1	1 5 3 1	1 5 4 1	1 5 6 1	1 5 8 1	1 7 9 1	6 8 1 1	6 7 1 1	1 4 4 1	1 4 4 1	1 4 4 1	1 4 5 1	1 4 6 1	1 6 5 1	6 6 1 1	6 6 2 1	6 6 3 1	6 6 6 1	6 7 3 1	6 7 4 1	6 7 8 1	**Total Tissues/ Tumors**
Endocrine System (continued)																										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma	X																									1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
General Body System																										
Tissue NOS																										1
Genital System																										
Coagulating gland								+														+				4
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland								+					+										+	+		7
Squamous cell carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Mediastinal, squamous cell carcinoma, metastatic, preputial gland																										1
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hemangioma		X																								1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	49
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Skeletal muscle																										1
Squamous cell carcinoma, metastatic, preputial gland																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51

Table E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	026	358	385	470	485	562	565	587	675	683	684	688	691	691	694	702	721	731	731	733	733	733	734	734	734	734
Carcass ID Number	1721	6841	1611	1571	6771	6641	6761	1471	6831	6801	6851	6821	6691	6751	1421	1551	6721	6651	6671	6681	6701	6711	1481	1491	1501	1511
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma				X			X			X						X	X		X			X	X			
Alveolar/bronchiolar carcinoma																				X		X				X
Alveolar/bronchiolar carcinoma, three, multiple																										
Carcinoma, metastatic, harderian gland									X																	
Hepatocellular carcinoma, metastatic, liver											X															
Squamous cell carcinoma, metastatic, preputial gland						X																				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Harderian gland									+																	
Carcinoma									X																	
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																										
Renal tubule, carcinoma																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed															X								X		X	

TABLE E2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	
Carcass ID Number	1 5 2 1	1 5 9 1	1 6 0 1	1 6 2 1	1 6 3 1	1 6 4 1	1 5 3 1	1 5 4 1	1 5 6 1	1 5 8 1	6 7 9 1	6 8 1 1	1 4 1 1	1 4 3 1	1 4 4 1	1 4 5 1	1 4 6 1	1 6 5 1	6 6 1 1	6 6 2 1	6 6 3 1	6 6 6 1	6 7 3 1	7 7 4 1	6 7 8 1	**Total Tissues/ Tumors**
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Alveolar/bronchiolar adenoma				X											X						X		X	X	13
Alveolar/bronchiolar carcinoma								X										X		X			X		7
Alveolar/bronchiolar carcinoma, three, multiple														X											1
Carcinoma, metastatic, harderian gland																									1
Hepatocellular carcinoma, metastatic, liver																									1
Squamous cell carcinoma, metastatic, preputial gland																									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																									
Harderian gland																									1
Carcinoma																									1
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Renal tubule, adenoma																						X			1
Renal tubule, carcinoma																								X	1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymphoma malignant mixed																						X			4

TABLE E3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Adrenal Cortex: Adenoma				
Overall rates[a]	5/50 (10%)	4/50 (8%)	2/50 (4%)	6/51 (12%)
Adjusted rates[b]	13.9%	12.4%	5.7%	18.0%
Terminal rates[c]	4/34 (12%)	2/28 (7%)	2/35 (6%)	5/32 (16%)
First incidence (days)	681	682	733 (T)	702
Life table tests[d]	P=0.424	P=0.599N	P=0.208N	P=0.464
Logistic regression tests[d]	P=0.407	P=0.537N	P=0.218N	P=0.471
Cochran-Armitage test[d]	P=0.433			
Fisher exact test[d]		P=0.500N	P=0.218N	P=0.514
Harderian Gland: Adenoma				
Overall rates	3/50 (6%)	3/50 (6%)	4/50 (8%)	0/51 (0%)
Adjusted rates	8.8%	8.9%	9.9%	0.0%
Terminal rates	3/34 (9%)	1/28 (4%)	2/35 (6%)	0/32 (0%)
First incidence (days)	733 (T)	668	558	–[e]
Life table tests	P=0.121N	P=0.583	P=0.508	P=0.131N
Logistic regression tests	P=0.113N	P=0.636	P=0.504	P=0.131N
Cochran-Armitage test	P=0.112N			
Fisher exact test		P=0.661N	P=0.500	P=0.118N
Harderian Gland: Adenoma or Carcinoma				
Overall rates	3/50 (6%)	4/50 (8%)	4/50 (8%)	1/51 (2%)
Adjusted rates	8.8%	10.8%	9.9%	2.3%
Terminal rates	3/34 (9%)	1/28 (4%)	2/35 (6%)	0/32 (0%)
First incidence (days)	733 (T)	522	558	675
Life table tests	P=0.219N	P=0.423	P=0.508	P=0.318N
Logistic regression tests	P=0.182N	P=0.513	P=0.504	P=0.318N
Cochran-Armitage test	P=0.205N			
Fisher exact test		P=0.500	P=0.500	P=0.301N
Liver: Hepatocellular Adenoma				
Overall rates	30/50 (60%)	29/50 (58%)	27/50 (54%)	25/51 (49%)
Adjusted rates	71.1%	75.7%	67.1%	63.3%
Terminal rates	22/34 (65%)	19/28 (68%)	22/35 (63%)	18/32 (56%)
First incidence (days)	558	562	565	485
Life table tests	P=0.184N	P=0.306	P=0.315N	P=0.320N
Logistic regression tests	P=0.196N	P=0.572	P=0.356N	P=0.263N
Cochran-Armitage test	P=0.136N			
Fisher exact test		P=0.500N	P=0.343N	P=0.182N
Liver: Hepatocellular Carcinoma				
Overall rates	12/50 (24%)	13/50 (26%)	12/50 (24%)	14/51 (27%)
Adjusted rates	26.9%	31.8%	27.7%	29.9%
Terminal rates	4/34 (12%)	4/28 (14%)	5/35 (14%)	3/32 (9%)
First incidence (days)	541	490	551	358
Life table tests	P=0.390	P=0.388	P=0.578N	P=0.389
Logistic regression tests	P=0.503N	P=0.585N	P=0.569N	P=0.568N
Cochran-Armitage test	P=0.406			
Fisher exact test		P=0.500	P=0.592N	P=0.433

TABLE E3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Liver: Hepatoblastoma or Hepatocellular Carcinoma				
Overall rates	13/50 (26%)	14/50 (28%)	12/50 (24%)	14/51 (27%)
Adjusted rates	28.7%	33.7%	27.7%	29.9%
Terminal rates	4/34 (12%)	4/28 (14%)	5/35 (14%)	3/32 (9%)
First incidence (days)	541	490	551	358
Life table tests	P=0.485	P=0.387	P=0.495N	P=0.466
Logistic regression tests	P=0.392N	P=0.581N	P=0.471N	P=0.473N
Cochran-Armitage test	P=0.515			
Fisher exact test		P=0.500	P=0.500N	P=0.524
Liver: Hepatocellular Adenoma, Hepatoblastoma, or Hepatocellular Carcinoma				
Overall rates	35/50 (70%)	38/50 (76%)	33/50 (66%)	34/51 (67%)
Adjusted rates	75.8%	84.1%	73.0%	74.9%
Terminal rates	23/34 (68%)	21/28 (75%)	23/35 (66%)	21/32 (66%)
First incidence (days)	541	490	551	358
Life table tests	P=0.384N	P=0.123	P=0.400N	P=0.520
Logistic regression tests	P=0.296N	P=0.320	P=0.415N	P=0.461N
Cochran-Armitage test	P=0.281N			
Fisher exact test		P=0.326	P=0.415N	P=0.442N
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	15/50 (30%)	10/50 (20%)	15/50 (30%)	13/51 (25%)
Adjusted rates	36.1%	29.4%	39.0%	33.1%
Terminal rates	9/34 (26%)	6/28 (21%)	12/35 (34%)	7/32 (22%)
First incidence (days)	541	548	626	470
Life table tests	P=0.515N	P=0.326N	P=0.558N	P=0.480N
Logistic regression tests	P=0.504N	P=0.158N	P=0.586	P=0.382N
Cochran-Armitage test	P=0.485N			
Fisher exact test		P=0.178N	P=0.586N	P=0.388N
Lung: Alveolar/bronchiolar Carcinoma				
Overall rates	8/50 (16%)	2/50 (4%)	6/50 (12%)	8/51 (16%)
Adjusted rates	20.7%	7.1%	15.4%	25.0%
Terminal rates	5/34 (15%)	2/28 (7%)	4/35 (11%)	8/32 (25%)
First incidence (days)	559	733 (T)	558	733 (T)
Life table tests	P=0.335	P=0.084N	P=0.380N	P=0.559
Logistic regression tests	P=0.315	P=0.051N	P=0.384N	P=0.577
Cochran-Armitage test	P=0.347			
Fisher exact test		P=0.046N	P=0.387N	P=0.590N
Lung: Alveolar/bronchiolar Adenoma or Alveolar/bronchiolar Carcinoma				
Overall rates	21/50 (42%)	12/50 (24%)	21/50 (42%)	19/51 (37%)
Adjusted rates	47.7%	35.8%	51.9%	49.1%
Terminal rates	12/34 (35%)	8/28 (29%)	16/35 (46%)	13/32 (41%)
First incidence (days)	541	548	558	470
Life table tests	P=0.450	P=0.144N	P=0.547N	P=0.505N
Logistic regression tests	P=0.444	P=0.038N	P=0.577N	P=0.412N
Cochran-Armitage test	P=0.483			
Fisher exact test		P=0.044N	P=0.580N	P=0.388N

TABLE E3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Small Intestine: Carcinoma				
Overall rates	1/50 (2%)	1/50 (2%)	0/50 (0%)	3/51 (6%)
Adjusted rates	2.9%	3.4%	0.0%	8.4%
Terminal rates	1/34 (3%)	0/28 (0%)	0/35 (0%)	1/32 (3%)
First incidence (days)	733 (T)	730	-	691
Life table tests	P=0.168	P=0.711	P=0.494N	P=0.292
Logistic regression tests	P=0.158	P=0.733	P=0.494N	P=0.291
Cochran-Armitage test	P=0.167			
Fisher exact test		P=0.753N	P=0.500N	P=0.316
All Organs: Hemangioma				
Overall rates	3/50 (6%)	0/50 (0%)	1/50 (2%)	2/51 (4%)
Adjusted rates	8.4%	0.0%	2.3%	5.1%
Terminal rates	2/34 (6%)	0/28 (0%)	0/35 (0%)	1/32 (3%)
First incidence (days)	730	-	626	358
Life table tests	P=0.550N	P=0.163N	P=0.305N	P=0.524N
Logistic regression tests	P=0.459N	P=0.146N	P=0.305N	P=0.442N
Cochran-Armitage test	P=0.541N			
Fisher exact test		P=0.121N	P=0.309N	P=0.491N
All Organs: Hemangiosarcoma				
Overall rates	3/50 (6%)	4/50 (8%)	3/50 (6%)	1/51 (2%)
Adjusted rates	8.8%	11.0%	6.4%	3.1%
Terminal rates	3/34 (9%)	1/28 (4%)	0/35 (0%)	1/32 (3%)
First incidence (days)	733 (T)	562	540	733 (T)
Life table tests	P=0.196N	P=0.422	P=0.655N	P=0.326N
Logistic regression tests	P=0.136N	P=0.510	P=0.646N	P=0.326N
Cochran-Armitage test	P=0.181N			
Fisher exact test		P=0.500	P=0.661N	P=0.301N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	6/50 (12%)	4/50 (8%)	4/50 (8%)	3/51 (6%)
Adjusted rates	17.0%	11.0%	8.5%	8.1%
Terminal rates	5/34 (15%)	1/28 (4%)	0/35 (0%)	2/32 (6%)
First incidence (days)	730	562	540	358
Life table tests	P=0.217N	P=0.477N	P=0.368N	P=0.273N
Logistic regression tests	P=0.130N	P=0.377N	P=0.353N	P=0.229N
Cochran-Armitage test	P=0.198N			
Fisher exact test		P=0.370N	P=0.370N	P=0.234N
All Organs: Histiocytic Sarcoma or Malignant Lymphoma				
Overall rates	0/50 (0%)	4/50 (8%)	3/50 (6%)	4/51 (8%)
Adjusted rates	0.0%	11.7%	8.6%	11.8%
Terminal rates	0/34 (0%)	2/28 (7%)	3/35 (9%)	3/32 (9%)
First incidence (days)	-	601	733 (T)	694
Life table tests	P=0.114	P=0.052	P=0.126	P=0.058
Logistic regression tests	P=0.106	P=0.066	P=0.126	P=0.058
Cochran-Armitage test	P=0.118			
Fisher exact test		P=0.059	P=0.121	P=0.061

TABLE E3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
All Organs: Malignant Lymphoma (Mixed or Undifferentiated Cell Type)				
Overall rates	0/50 (0%)	3/50 (6%)	3/50 (6%)	4/51 (8%)
Adjusted rates	0.0%	8.3%	8.6%	11.8%
Terminal rates	0/34 (0%)	1/28 (4%)	3/35 (9%)	3/32 (9%)
First incidence (days)	–	601	733 (T)	694
Life table tests	P=0.078	P=0.108	P=0.126	P=0.058
Logistic regression tests	P=0.072	P=0.132	P=0.126	P=0.058
Cochran-Armitage test	P=0.080			
Fisher exact test		P=0.121	P=0.121	P=0.061
All Organs: Benign Tumors				
Overall rates	39/50 (78%)	35/50 (70%)	37/50 (74%)	34/51 (67%)
Adjusted rates	84.6%	85.1%	83.9%	80.5%
Terminal rates	27/34 (79%)	22/28 (79%)	28/35 (80%)	24/32 (75%)
First incidence (days)	541	548	558	358
Life table tests	P=0.262N	P=0.437	P=0.382N	P=0.361N
Logistic regression tests	P=0.252N	P=0.302N	P=0.418N	P=0.205N
Cochran-Armitage test	P=0.160N			
Fisher exact test		P=0.247N	P=0.408N	P=0.147N
All Organs: Malignant Tumors				
Overall rates	22/50 (44%)	26/50 (52%)	20/50 (40%)	29/51 (57%)
Adjusted rates	47.9%	56.0%	42.5%	60.9%
Terminal rates	11/34 (32%)	9/28 (32%)	9/35 (26%)	14/32 (44%)
First incidence (days)	541	490	540	358
Life table tests	P=0.199	P=0.180	P=0.422N	P=0.135
Logistic regression tests	P=0.230	P=0.387	P=0.389N	P=0.189
Cochran-Armitage test	P=0.169			
Fisher exact test		P=0.274	P=0.420N	P=0.137
All Organs: Benign and Malignant Tumors				
Overall rates	42/50 (84%)	45/50 (90%)	44/50 (88%)	47/51 (92%)
Adjusted rates	87.4%	91.8%	89.7%	95.9%
Terminal rates	28/34 (82%)	24/28 (86%)	30/35 (86%)	30/32 (94%)
First incidence (days)	541	490	540	358
Life table tests	P=0.255	P=0.100	P=0.482	P=0.157
Logistic regression tests	P=0.142	P=0.304	P=0.392	P=0.111
Cochran-Armitage test	P=0.165			
Fisher exact test		P=0.277	P=0.387	P=0.169

(T)Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no tumors in animal group

TABLE E4
Historical Incidence of Renal Tubule Adenomas in Untreated Male B6C3F$_1$ Mice[a]

Study	Incidence in Controls
Historical Incidence at Southern Research Institute	
Feed	
Nitrofurantoin	0/50 (0%)
Rhodamine 6G	1/50 (2%)
Roxarsone	0/50 (0%)
Total	1/150 (1%)
Standard deviation	1.2%
Range	0%-2%
Water	
Chloramine	0/50 (0%)
Overall Historical Incidence	
Feed	
Total	1/563 (0.2%)
Standard deviation	0.6%
Range	0%-2%
Water	
Total	0/129 (0%)

[a] Data as of 15 September 1990

TABLE E5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	9
Early deaths				
Natural death	4	6	2	8
Moribund	12	16	13	10
Accidental death	0	0	0	1
Survivors				
Terminal sacrifice	34	27	35	32
Died last week of study	0	1	0	0
Animals examined microscopically	50	50	50	51
Alimentary System				
Gallbladder	(44)	(47)	(48)	(47)
Cyst		1 (2%)	1 (2%)	
Dilatation	1 (2%)			2 (4%)
Intestine large, colon	(49)	(49)	(47)	(51)
Diverticulum	1 (2%)			
Intestine small, duodenum	(49)	(50)	(50)	(50)
Hyperplasia, lymphoid	1 (2%)			
Metaplasia, squamous	1 (2%)			
Intestine small, ileum	(48)	(48)	(49)	(49)
Hyperplasia, lymphoid	1 (2%)			1 (2%)
Liver	(50)	(50)	(50)	(51)
Angiectasis		2 (4%)	1 (2%)	
Basophilic focus	3 (6%)	4 (8%)	3 (6%)	4 (8%)
Clear cell focus	11 (22%)	12 (24%)	15 (30%)	8 (16%)
Eosinophilic focus	1 (2%)			2 (4%)
Hematopoietic cell proliferation				1 (2%)
Hemorrhage		1 (2%)	1 (2%)	
Hepatodiaphragmatic nodule		1 (2%)		
Hyperplasia, focal	14 (28%)	18 (36%)	23 (46%)	13 (25%)
Hyperplasia, lymphoid	1 (2%)			
Inflammation, acute	1 (2%)			
Inflammation, chronic	2 (4%)	2 (4%)	3 (6%)	2 (4%)
Mineralization			1 (2%)	
Mixed cell focus	1 (2%)	2 (4%)	1 (2%)	
Bile duct, cyst				1 (2%)
Centrilobular, necrosis		1 (2%)	2 (4%)	1 (2%)
Hepatocyte, karyomegaly		2 (4%)		1 (2%)
Hepatocyte, vacuolization cytoplasmic	2 (4%)	4 (8%)	2 (4%)	1 (2%)
Kupffer cell, hyperplasia	4 (8%)	4 (8%)		1 (2%)
Kupffer cell, pigmentation			1 (2%)	2 (4%)
Lobules, necrosis	2 (4%)	8 (16%)	4 (8%)	3 (6%)
Mesentery	(7)	(3)	(2)	(3)
Accessory spleen		1 (33%)		
Fibrosis	1 (14%)			
Mineralization	1 (14%)			
Fat, necrosis	4 (57%)	1 (33%)		2 (67%)

TABLE E5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Alimentary System (continued)				
Pancreas	(50)	(50)	(50)	(51)
Atrophy	6 (12%)	4 (8%)	4 (8%)	2 (4%)
Cytoplasmic alteration	4 (8%)	1 (2%)		2 (4%)
Focal cellular change	2 (4%)	1 (2%)		1 (2%)
Inflammation, chronic	1 (2%)			
Salivary glands	(50)	(50)	(50)	(51)
Atrophy	1 (2%)			
Hyperplasia, lymphoid	18 (36%)	13 (26%)	13 (26%)	17 (33%)
Stomach, forestomach	(50)	(50)	(50)	(50)
Diverticulum				2 (4%)
Edema				1 (2%)
Erosion	1 (2%)			
Hyperkeratosis	1 (2%)			
Inflammation, subacute		1 (2%)		
Ulcer		1 (2%)		
Mucosa, hyperplasia	1 (2%)	2 (4%)	1 (2%)	
Stomach, glandular	(50)	(50)	(50)	(50)
Cyst	9 (18%)	5 (10%)	6 (12%)	8 (16%)
Edema				1 (2%)
Erosion		4 (8%)	1 (2%)	
Inflammation, subacute	1 (2%)		3 (6%)	3 (6%)
Metaplasia, squamous				1 (2%)
Mineralization	2 (4%)		4 (8%)	1 (2%)
Ulcer				1 (2%)
Mucosa, dysplasia	1 (2%)			
Mucosa, hyperplasia		2 (4%)	1 (2%)	
Tooth	(17)	(7)	(6)	(7)
Dysplasia	17 (100%)	7 (100%)	5 (83%)	6 (86%)
Cardiovascular System				
Heart	(50)	(50)	(50)	(51)
Epicardium, inflammation, chronic	2 (4%)			1 (2%)
Myocardium, fibrosis	1 (2%)			
Myocardium, inflammation, chronic	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(51)
Accessory adrenal cortical nodule	3 (6%)	7 (14%)	6 (12%)	5 (10%)
Basophilic focus	2 (4%)	2 (4%)	1 (2%)	
Clear cell focus	3 (6%)	6 (12%)	6 (12%)	9 (18%)
Cyst			1 (2%)	
Developmental malformation			2 (4%)	
Hyperplasia, diffuse	1 (2%)			
Hyperplasia, focal	28 (56%)	20 (40%)	26 (52%)	29 (57%)
Hypertrophy, focal	2 (4%)	1 (2%)		
Mineralization	1 (2%)			
Capsule, hyperplasia	10 (20%)	11 (22%)	4 (8%)	8 (16%)
Capsule, hyperplasia, focal				1 (2%)

TABLE E5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm		70 ppm		140 ppm		275 ppm	
Endocrine System (continued)								
Adrenal gland, medulla	(49)		(50)		(50)		(51)	
Developmental malformation							1	(2%)
Hyperplasia	3	(6%)					1	(2%)
Hyperplasia, focal							1	(2%)
Islets, pancreatic	(50)		(50)		(50)		(51)	
Hyperplasia	31	(62%)	26	(52%)	29	(58%)	21	(41%)
Parathyroid gland	(49)		(48)		(45)		(49)	
Cyst	1	(2%)			2	(4%)	2	(4%)
Pituitary gland	(48)		(49)		(49)		(49)	
Pars distalis, cyst	2	(4%)	1	(2%)	7	(14%)	2	(4%)
Pars distalis, hyperplasia	1	(2%)					5	(10%)
Thyroid gland	(50)		(50)		(50)		(51)	
Degeneration, cystic	12	(24%)	14	(28%)	13	(26%)	12	(24%)
Inflammation, subacute			3	(6%)				
Follicle, cyst			1	(2%)	1	(2%)	4	(8%)
Follicular cell, hyperplasia	5	(10%)	7	(14%)	4	(8%)	3	(6%)
General Body System								
None								
Genital System								
Coagulating gland	(8)		(7)		(6)		(4)	
Dilatation	8	(100%)	6	(86%)	5	(83%)	4	(100%)
Inflammation, suppurative	1	(13%)						
Epididymis	(50)		(50)		(50)		(51)	
Atypical cells							1	(2%)
Fibrosis					1	(2%)		
Granuloma sperm	1	(2%)						
Inflammation, chronic					1	(2%)	2	(4%)
Preputial gland	(4)		(11)		(20)		(7)	
Ectasia	4	(100%)	9	(82%)	18	(90%)	6	(86%)
Inflammation, chronic			1	(9%)	9	(45%)	3	(43%)
Inflammation, suppurative					1	(5%)		
Prostate	(50)		(49)		(50)		(51)	
Cyst	1	(2%)						
Hemorrhage					1	(2%)		
Inflammation, chronic			2	(4%)	2	(4%)		
Inflammation, suppurative	1	(2%)						
Seminal vesicle	(50)		(50)		(50)		(51)	
Dilatation	20	(40%)	22	(44%)	21	(42%)	14	(27%)
Fibrosis	1	(2%)	1	(2%)			1	(2%)
Hemorrhage			1	(2%)	1	(2%)		
Inflammation, chronic	1	(2%)	2	(4%)	2	(4%)		
Testes	(50)		(50)		(50)		(51)	
Mineralization	1	(2%)					1	(2%)
Interstitial cell, hyperplasia							1	(2%)
Seminiferous tubule, atrophy	2	(4%)	1	(2%)			3	(6%)

TABLE E5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(51)
Angiectasis	1 (2%)			1 (2%)
Hypercellularity	3 (6%)	2 (4%)	3 (6%)	4 (8%)
Necrosis	1 (2%)			
Lymph node	(50)	(50)	(50)	(51)
Bronchial, hyperplasia, lymphoid	1 (2%)			
Mediastinal, hemorrhage				1 (2%)
Mediastinal, hyperplasia, plasma cell	1 (2%)			
Lymph node, mandibular	(49)	(48)	(48)	(48)
Hyperplasia, lymphoid	2 (4%)	2 (4%)	1 (2%)	
Hyperplasia, plasma cell	3 (6%)	2 (4%)	1 (2%)	
Lymph node, mesenteric	(46)	(48)	(50)	(50)
Depletion	1 (2%)			
Hematopoietic cell proliferation	6 (13%)	6 (13%)	6 (12%)	1 (2%)
Hemorrhage	22 (48%)	20 (42%)	16 (32%)	15 (30%)
Hyperplasia, histiocyte	1 (2%)			
Hyperplasia, lymphoid	6 (13%)	1 (2%)	1 (2%)	4 (8%)
Hyperplasia, plasma cell		1 (2%)		
Inflammation, suppurative		1 (2%)		
Spleen	(50)	(50)	(50)	(51)
Angiectasis			1 (2%)	2 (4%)
Congestion				1 (2%)
Hematopoietic cell proliferation	9 (18%)	12 (24%)	7 (14%)	11 (22%)
Pigmentation, hemosiderin		1 (2%)		
Lymphoid follicle, atrophy		3 (6%)	1 (2%)	
Lymphoid follicle, hyperplasia	4 (8%)	2 (4%)	4 (8%)	
Red pulp, atrophy	2 (4%)		2 (4%)	1 (2%)
Red pulp, hyperplasia	3 (6%)	2 (4%)		1 (2%)
Thymus	(47)	(43)	(46)	(49)
Cyst	9 (19%)	8 (19%)	4 (9%)	9 (18%)
Depletion	11 (23%)	11 (26%)	5 (11%)	8 (16%)
Hyperplasia, lymphoid	1 (2%)			
Integumentary System				
Skin	(50)	(49)	(50)	(51)
Acanthosis			1 (2%)	
Inflammation, chronic		1 (2%)		
Ulcer			1 (2%)	
Fat, necrosis				1 (2%)
Subcutaneous tissue, edema			1 (2%)	
Subcutaneous tissue, fibrosis, focal				1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(51)
Hyperostosis		1 (2%)		1 (2%)

TABLE E5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Nervous System				
Brain	(50)	(50)	(50)	(51)
Cyst		1 (2%)		
Hemorrhage		2 (4%)		
Hydrocephalus	1 (2%)			
Metaplasia, osseous				1 (2%)
Thalamus, mineralization	41 (82%)	38 (76%)	43 (86%)	40 (78%)
Respiratory System				
Lung	(50)	(50)	(50)	(51)
Congestion	2 (4%)	2 (4%)	2 (4%)	3 (6%)
Hemorrhage	2 (4%)	3 (6%)	3 (6%)	2 (4%)
Hyperplasia, lymphoid	6 (12%)	3 (6%)	5 (10%)	2 (4%)
Infiltration cellular, histiocytic	16 (32%)	2 (4%)	6 (12%)	7 (14%)
Leukocytosis				1 (2%)
Metaplasia, osseous	1 (2%)			
Thrombus			1 (2%)	
Alveolar epithelium, hyperplasia	6 (12%)	2 (4%)	2 (4%)	4 (8%)
Nose	(50)	(50)	(50)	(51)
Exudate	8 (16%)	8 (16%)	2 (4%)	1 (2%)
Glands, hyperplasia, cystic	6 (12%)	4 (8%)	2 (4%)	4 (8%)
Trachea	(50)	(50)	(50)	(51)
Inflammation, suppurative				2 (4%)
Special Senses System				
Eye		(1)		
Cornea, inflammation, suppurative		1 (100%)		
Urinary System				
Kidney	(50)	(50)	(50)	(51)
Casts protein	6 (12%)	8 (16%)	10 (20%)	10 (20%)
Cyst	28 (56%)	24 (48%)	23 (46%)	25 (49%)
Glomerulosclerosis			4 (8%)	1 (2%)
Granuloma		1 (2%)	2 (4%)	4 (8%)
Hydronephrosis	2 (4%)		5 (10%)	1 (2%)
Hyperplasia, lymphoid	12 (24%)	10 (20%)	15 (30%)	18 (35%)
Inflammation, suppurative			1 (2%)	
Metaplasia, osseous	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Mineralization	48 (96%)	46 (92%)	44 (88%)	42 (82%)
Pigmentation, cholesterol		1 (2%)		
Papilla, necrosis		1 (2%)		
Renal tubule, atrophy	4 (8%)	16 (32%)	11 (22%)	7 (14%)
Renal tubule, dilatation		6 (12%)	5 (10%)	20 (39%)
Renal tubule, hyperplasia, focal		1 (2%)		2 (4%)
Renal tubule, necrosis	1 (2%)	2 (4%)		
Renal tubule, regeneration	45 (90%)	45 (90%)	49 (98%)	47 (92%)
Transitional epithelium, hyperplasia		3 (6%)	1 (2%)	
Urinary bladder	(50)	(50)	(50)	(51)
Dilatation	1 (2%)	1 (2%)		3 (6%)
Hemorrhage			1 (2%)	
Hyperplasia, lymphoid	4 (8%)	1 (2%)	2 (4%)	5 (10%)
Mucosa, hyperplasia				1 (2%)

APPENDIX F
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR CHLORINATED WATER STUDY

TABLE F1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	9	10	10
Early deaths				
Natural death	3	6	3	3
Moribund	13	14	19	12
Accidental death	1	0	0	0
Survivors				
Terminal sacrifice	33	31	27	35
Died last week of study	0	0	1	0
Animals examined microscopically	50	51	50	50
Alimentary System				
Gallbladder	(47)	(49)	(48)	(50)
Intestine large, cecum	(47)	(51)	(50)	(49)
Intestine small, ileum	(48)	(51)	(49)	(47)
Intestine small, jejunum	(48)	(51)	(49)	(50)
Hemangioma				1 (2%)
Liver	(50)	(51)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Chemodectoma malignant, metastatic, thyroid gland		1 (2%)		
Fibrous histiocytoma	1 (2%)		1 (2%)	
Hemangiosarcoma	1 (2%)			
Hepatoblastoma			1 (2%)	
Hepatocellular carcinoma	6 (12%)	6 (12%)	6 (12%)	5 (10%)
Hepatocellular carcinoma, two, multiple		1 (2%)		
Hepatocellular carcinoma, four, multiple			1 (2%)	
Hepatocellular adenoma	13 (26%)	11 (22%)	7 (14%)	18 (36%)
Hepatocellular adenoma, two, multiple	3 (6%)	6 (12%)	5 (10%)	4 (8%)
Hepatocellular adenoma, three, multiple	1 (2%)		4 (8%)	
Hepatocellular adenoma, four, multiple	1 (2%)	1 (2%)	2 (4%)	
Hepatocellular adenoma, five, multiple	1 (2%)			
Hepatocellular adenoma, greater than five, multiple		1 (2%)		1 (2%)
Histiocytic sarcoma		1 (2%)	1 (2%)	1 (2%)
Osteosarcoma, metastatic, bone				1 (2%)
Mesentery	(17)	(10)	(12)	(8)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (8%)	
Chemodectoma malignant	1 (6%)			
Fibrous histiocytoma			1 (8%)	
Hemangiosarcoma	1 (6%)			
Histiocytic sarcoma		1 (10%)		

TABLE F1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Alimentary System (continued)				
Pancreas	(50)	(50)	(49)	(50)
Fibrous histiocytoma	1 (2%)			
Hemangioma	1 (2%)			
Salivary glands	(49)	(51)	(50)	(50)
Stomach, forestomach	(50)	(51)	(50)	(50)
Hemangioma	1 (2%)			
Leiomyoma	1 (2%)			
Papilloma squamous				1 (2%)
Squamous cell carcinoma				1 (2%)
Stomach, glandular	(50)	(51)	(50)	(50)
Carcinoid tumor malignant		1 (2%)		
Cardiovascular System				
Blood vessel	(2)	(1)		(1)
Heart	(50)	(51)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Fibrous histiocytoma			1 (2%)	
Endocrine System				
Adrenal gland, cortex	(50)	(51)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Histiocytic sarcoma		1 (2%)		
Adrenal gland, medulla	(50)	(51)	(50)	(50)
Pheochromocytoma malignant				1 (2%)
Pheochromocytoma benign			1 (2%)	
Islets, pancreatic	(50)	(50)	(49)	(50)
Adenoma		1 (2%)	1 (2%)	1 (2%)
Pituitary gland	(48)	(50)	(48)	(50)
Pars distalis, adenoma	5 (10%)	8 (16%)	4 (8%)	6 (12%)
Pars intermedia, adenoma	1 (2%)			
Thyroid gland	(50)	(51)	(50)	(50)
Chemodectoma malignant		1 (2%)		
Follicular cell, adenoma	2 (4%)			2 (4%)
Follicular cell, carcinoma				1 (2%)
General Body System				
Tissue NOS			(1)	(1)

TABLE F1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Genital System				
Ovary	(46)	(46)	(48)	(46)
Adenoma	2 (4%)			
Cystadenocarcinoma				1 (2%)
Cystadenoma			1 (2%)	
Granulosa-theca tumor benign		1 (2%)		
Hemangioma	1 (2%)			
Teratoma benign	1 (2%)			
Uterus	(50)	(50)	(50)	(50)
Carcinoma		1 (2%)		
Histiocytic sarcoma		1 (2%)	1 (2%)	
Leiomyosarcoma	1 (2%)			
Polyp stromal			1 (2%)	3 (6%)
Sarcoma	1 (2%)			
Hematopoietic System				
Bone marrow	(50)	(51)	(50)	(50)
Fibrous histiocytoma	1 (2%)		1 (2%)	
Lymph node	(50)	(51)	(50)	(50)
Axillary, fibrosarcoma, metastatic, skin	1 (2%)			
Bronchial, alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Mediastinal, osteosarcoma, metastatic, bone				1 (2%)
Lymph node, mandibular	(46)	(49)	(50)	(49)
Carcinoma, metastatic, harderian gland			1 (2%)	
Fibrosarcoma, metastatic, skin			1 (2%)	
Lymph node, mesenteric	(49)	(47)	(48)	(48)
Renal, iliac, mediastinal, mandibular, fibrous histiocytoma	1 (2%)			
Spleen	(49)	(51)	(49)	(50)
Fibrous histiocytoma	1 (2%)		1 (2%)	
Hemangioma				1 (2%)
Hemangiosarcoma	1 (2%)	1 (2%)	1 (2%)	
Histiocytic sarcoma				1 (2%)
Thymus	(48)	(49)	(46)	(45)
Fibrous histiocytoma	1 (2%)		1 (2%)	
Thymoma benign	1 (2%)	2 (4%)		
Thymoma malignant			1 (2%)	
Integumentary System				
Mammary gland	(49)	(50)	(50)	(50)
Skin	(50)	(51)	(50)	(50)
Fibrosarcoma	1 (2%)			
Subcutaneous tissue, fibrosarcoma		2 (4%)	3 (6%)	1 (2%)
Subcutaneous tissue, hemangiosarcoma			1 (2%)	
Subcutaneous tissue, sarcoma	1 (2%)			

TABLE F1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Musculoskeletal System				
Bone	(50)	(51)	(50)	(50)
Fibrous histiocytoma			1 (2%)	
Osteosarcoma	1 (2%)		2 (4%)	1 (2%)
Skeletal muscle	(2)	(3)	(1)	(1)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (100%)	
Fibrosarcoma, metastatic, skin	1 (50%)	1 (33%)		
Histiocytic sarcoma		1 (33%)		
Osteosarcoma, metastatic, bone	1 (50%)			
Sarcoma				1 (100%)
Nervous System				
Brain	(49)	(51)	(50)	(50)
Fibrous histiocytoma			1 (2%)	
Respiratory System				
Lung	(50)	(51)	(50)	(50)
Alveolar/bronchiolar adenoma	4 (8%)	5 (10%)	2 (4%)	2 (4%)
Alveolar/bronchiolar carcinoma	1 (2%)	6 (12%)	5 (10%)	2 (4%)
Carcinoma, metastatic, harderian gland			1 (2%)	
Chemodectoma malignant, metastatic, thyroid gland		1 (2%)		
Fibrosarcoma, metastatic, skin	1 (2%)			
Fibrous histiocytoma			1 (2%)	
Hepatocellular carcinoma, metastatic, liver	1 (2%)		1 (2%)	2 (4%)
Histiocytic sarcoma		1 (2%)		
Osteosarcoma, metastatic, bone				1 (2%)
Special Senses System				
Harderian gland	(1)	(3)	(4)	(7)
Adenoma	1 (100%)		1 (25%)	3 (43%)
Carcinoma		1 (33%)	1 (25%)	
Urinary System				
Kidney	(50)	(51)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Fibrous histiocytoma	1 (2%)			
Histiocytic sarcoma			1 (2%)	
Osteosarcoma, metastatic, bone				1 (2%)
Urinary bladder	(49)	(50)	(49)	(50)
Histiocytic sarcoma				1 (2%)

TABLE F1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Systemic Lesions				
Multiple organs[a]	(50)	(51)	(50)	(50)
Histiocytic sarcoma		2 (4%)	1 (2%)	1 (2%)
Leukemia erythrocytic	1 (2%)			
Leukemia granulocytic		1 (2%)		
Lymphoma malignant lymphocytic	2 (4%)	3 (6%)	1 (2%)	2 (4%)
Lymphoma malignant mixed	7 (14%)	10 (20%)	7 (14%)	4 (8%)
Tumor Summary				
Total animals with primary neoplasms[b]	35	43	37	39
Total primary neoplasms	73	72	69	64
Total animals with benign neoplasms	26	27	23	33
Total benign neoplasms	40	36	29	43
Total animals with malignant neoplasms	23	30	25	19
Total malignant neoplasms	33	36	40	21
Total animals with secondary neoplasms[c]	3	2	4	3
Total secondary neoplasms	5	3	12	6

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 0 ppm

Number of Days on Study	0 1 6	4 5 2	5 1 0	5 1 8	5 3 6	5 6 1	5 8 1	5 8 8	6 5 3	6 5 9	6 8 1	6 8 8	6 9 4	6 9 5	6 9 5	6 9 8	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4
Carcass ID Number	7 7 1 1	7 8 9 1	7 7 3 1	7 8 4 1	7 7 7 1	2 4 8 1	2 4 7 1	2 5 9 1	7 7 8 1	2 6 2 1	7 6 7 1	7 6 6 1	2 6 1 1	2 6 6 1	2 6 8 1	2 5 3 1	7 7 4 1	7 7 2 1	7 7 5 1	7 7 6 1	7 8 0 1	7 8 1 1	7 9 0 1	2 5 8 1	2 6 0 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangiosarcoma																						X			
Hepatocellular carcinoma										X								X							
Hepatocellular adenoma						X					X								X					X	
Hepatocellular adenoma, two, multiple																		X							
Hepatocellular adenoma, three, multiple																									
Hepatocellular adenoma, four, multiple																									
Hepatocellular adenoma, five, multiple																				X					
Mesentery		+						+	+			+		+	+		+			+				+	
Chemodectoma malignant																									
Hemangiosarcoma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangioma																						X			
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Leiomyoma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel		+						+																	
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinate Water Study: 0 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	2 6 3 1	2 6 4 1	2 6 5 1	2 6 7 1	2 6 9 1	2 7 0 1	2 4 6 1	2 4 9 1	2 5 0 1	2 5 1 1	2 5 2 1	7 6 8 1	7 6 9 1	7 7 9 1	7 8 2 1	7 8 3 1	7 8 5 1	7 8 6 1	7 8 7 1	7 8 8 1	2 5 4 1	2 5 5 1	2 5 6 1	2 5 7 1	7 7 0 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma										X																1
Hemangiosarcoma																										1
Hepatocellular carcinoma	X				X							X								X						6
Hepatocellular adenoma	X			X	X									X				X		X		X	X		X	13
Hepatocellular adenoma, two, multiple													X											X		3
Hepatocellular adenoma, three, multiple															X											1
Hepatocellular adenoma, four, multiple												X														1
Hepatocellular adenoma, five, multiple																										1
Mesentery					+					+	+	+		+	+			+		+						17
Chemodectoma malignant																				X						1
Hemangiosarcoma												X														1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma										X																1
Hemangioma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma	X																									1
Leiomyoma																		X								1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel																										2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	0 1 6	4 5 2	5 1 0	5 1 8	5 3 6	5 6 1	5 8 1	5 8 8	6 5 3	6 5 9	6 8 1	6 8 8	6 9 4	6 9 5	6 9 5	6 9 8	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4
Carcass ID Number	7 7 1 1	7 8 9 1	7 7 3 1	7 8 4 1	7 7 7 1	2 4 8 1	2 4 7 1	2 5 9 1	7 7 8 1	2 6 2 1	7 6 7 1	7 6 6 1	2 6 1 1	2 6 6 1	2 6 8 1	2 5 3 1	7 7 4 1	7 7 2 1	7 7 5 1	7 7 6 1	7 8 0 1	8 8 1 1	7 9 0 1	2 5 8 1	2 6 0 1
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pituitary gland	M	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																X		X							
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																		X							
General Body System																									
None																									
Genital System																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Adenoma																									
Hemangioma																									
Teratoma benign																								X	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma						X																			
Sarcoma																								X	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Axillary, fibrosarcoma, metastatic, skin											X														
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	M	+	+	+
Lymph node, mesenteric	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal, iliac, mediastinal, mandibular, fibrous histiocytoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Fibrous histiocytoma																									
Hemangiosarcoma																								X	
Thymus	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Thymoma benign																				X					

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	2 6 3 1	2 6 4 1	2 6 5 1	2 6 7 1	2 6 9 1	2 7 0 1	2 4 6 1	2 4 9 1	2 5 0 1	2 5 1 1	2 5 2 1	7 6 8 1	7 6 9 1	7 7 9 1	7 8 2 1	7 8 3 1	7 8 5 1	7 8 6 1	7 8 7 1	7 8 8 1	2 5 4 1	2 5 5 1	2 5 6 1	2 5 7 1	7 7 0 1	**Total Tissues/ Tumors**
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma								X	X											X						5
Pars intermedia, adenoma			X																							1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma												X														2
General Body System																										
None																										
Genital System																										
Ovary	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	I	+	+	+	+	I	+	+	46
Adenoma					X										X											2
Hemangioma							X																			1
Teratoma benign																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma																										1
Sarcoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma										X																1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Axillary, fibrosarcoma, metastatic, skin																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	46
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Renal, iliac, mediastinal, mandibular, fibrous histiocytoma										X																1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrous histiocytoma										X																1
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibrous histiocytoma										X																1
Thymoma benign																										1

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	0 1 6	4 5 2	5 1 0	5 1 8	5 3 6	5 6 1	5 8 1	5 8 8	6 5 3	6 5 9	6 8 1	6 8 8	6 9 4	6 9 5	6 9 5	6 9 8	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4
Carcass ID Number	7 7 1 1	7 8 9 1	7 7 3 1	7 8 4 1	7 7 7 1	2 4 8 1	2 4 7 1	2 5 9 1	7 7 8 1	2 6 2 1	7 6 7 1	7 6 6 1	2 6 1 1	2 6 6 1	2 6 8 1	2 5 3 1	7 7 4 1	7 7 2 1	7 7 5 1	7 7 6 1	7 8 0 1	7 8 1 1	7 9 0 1	2 5 8 1	2 6 0 1
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma											X														
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																	X								
Skeletal muscle											+						+								
Fibrosarcoma, metastatic, skin											X														
Osteosarcoma, metastatic, bone																	X								
Nervous System																									
Brain	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma		X																							
Alveolar/bronchiolar carcinoma																				X					
Fibrosarcoma, metastatic, skin											X														
Hepatocellular carcinoma, metastatic, liver																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Ureter										+															
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia erythrocytic															X										
Lymphoma malignant lymphocytic		X										X													
Lymphoma malignant mixed									X							X						X	X		

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	2 6 3 1	2 6 4 1	2 6 5 1	2 6 7 1	2 6 9 1	2 7 0 1	2 4 6 1	2 4 9 1	2 5 0 1	2 5 1 1	2 5 2 1	7 6 8 1	7 6 9 1	7 7 9 1	7 8 2 1	7 8 3 1	7 8 5 1	7 8 6 1	7 8 7 1	7 8 8 1	2 5 4 1	2 5 5 1	2 5 6 1	2 5 7 1	7 7 0 1	**Total Tissues/ Tumors**
Integumentary System																										
Mammary gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma																										1
Subcutaneous tissue, sarcoma		X																								1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle																										2
Fibrosarcoma, metastatic, skin																										1
Osteosarcoma, metastatic, bone																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma													X	X						X						4
Alveolar/bronchiolar carcinoma																										1
Fibrosarcoma, metastatic, skin																										1
Hepatocellular carcinoma, metastatic, liver	X																									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland															+											1
Adenoma															X											1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma										X																1
Ureter																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia erythrocytic																										1
Lymphoma malignant lymphocytic																										2
Lymphoma malignant mixed							X				X											X				7

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 70 ppm

Number of Days on Study	2 1 1	3 5 1	5 0 1	5 3 3	5 5 2	5 6 4	5 8 9	6 1 6	6 2 2	6 4 0	6 4 2	6 6 6	6 7 3	6 8 4	7 0 7	7 0 8	7 1 7	7 2 1	7 3 0	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	1 0 0 7 1	0 4 7 1 1	0 9 8 3 1	0 4 6 1 1	0 4 7 8 1	1 0 0 1 1	0 4 6 7 1	0 4 5 8 1	0 4 8 0 1	0 9 7 9 1	0 9 9 8 1	0 4 5 7 1	0 4 6 5 1	0 9 8 4 1	0 9 9 6 1	0 9 7 1 1	0 9 8 1 1	0 9 7 7 1	0 9 9 3 1	0 9 8 9 1	0 4 5 9 1	0 4 4 4 1	0 4 5 7 1	0 4 4 6 1	0 4 4 7 1	0 4 4 9 1	9 9 4 1
Alimentary System																										+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Chemodectoma malignant, metastatic, thyroid gland		X																								X
Hepatocellular carcinoma						X					X							X			X					
Hepatocellular carcinoma, two, multiple																										X
Hepatocellular adenoma				X						X				X												
Hepatocellular adenoma, two, multiple											X															
Hepatocellular adenoma, four, multiple																										r
Hepatocellular adenoma, greater than five, multiple																										
Histiocytic sarcoma										X																
Mesentery				+	+					+											+			+		
Histiocytic sarcoma										X																+
Pancreas	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoid tumor malignant																										
Cardiovascular System																										
Blood vessel				+																						+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	9 9 5 1	9 9 6 1	9 9 7 1	9 9 9 1	4 6 2 1	4 6 3 1	4 6 4 1	4 6 6 1	4 6 8 1	4 7 0 1	4 7 2 1	4 7 3 1	4 5 6 1	4 6 0 1	4 6 9 1	9 7 8 1	9 8 0 1	9 8 8 1	9 9 0 1	9 9 1 1	9 9 2 1	9 8 2 1	9 8 5 1	9 8 6 1	9 8 7 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Chemodectoma malignant, metastatic, thyroid gland																										1
Hepatocellular carcinoma													X													6
Hepatocellular carcinoma, two, multiple																					X					1
Hepatocellular adenoma	X				X	X			X								X		X					X		11
Hepatocellular adenoma, two, multiple							X						X					X				X	X			6
Hepatocellular adenoma, four, multiple																					X					1
Hepatocellular adenoma, greater than five, multiple				X																						1
Histiocytic sarcoma																										1
Mesentery				+			+						+								+			+		10
Histiocytic sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Carcinoid tumor malignant	X																									1
Cardiovascular System																										
Blood vessel																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	2 1 1	3 5 1	5 0 1	5 3 3	5 5 2	5 6 4	5 8 9	6 1 6	6 2 2	6 4 0	6 4 2	6 6 6	6 7 3	6 8 4	7 0 7	7 0 8	7 1 7	7 2 1	7 3 0	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	1 0 0 7 1 1	0 4 7 1 1	0 9 8 3 1	0 4 6 1 1	0 4 7 8 1	1 0 0 1 1	0 4 6 7 1	0 4 5 8 1	0 4 8 0 1	0 4 7 9 1	0 9 9 8 1	0 9 5 7 1	0 4 6 5 1	0 4 8 4 1	0 9 7 6 1	0 9 8 1 1	0 9 7 7 1	0 9 7 3 1	0 9 8 9 1	0 4 5 9 1	0 4 7 4 1	0 4 7 5 1	0 4 7 6 1	0 4 7 7 1	0 4 7 9 1	0 4 4 1	9 9 4 1
Endocrine System																										+
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma										X																+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma																										+
Parathyroid gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X
Pars distalis, adenoma																	X									+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Chemodectoma malignant		X																								
General Body System																										
None																										
Genital System																										+
Ovary	+	+	+	+	+	+	M	+	+	+	+	+	+	+	I	+	+	+	+	+	+	M	+	+	M	
Granulosa-theca tumor benign																										+
Uterus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma																					X					
Histiocytic sarcoma																										
Hematopoietic System																										+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Hemangiosarcoma																										+
Thymus	+	+	+	+	+	+	+	+	+	+	I	+	+	M	+	+	+	+	+	+	+	+	+	+	+	
Thymoma benign																			X							
Integumentary System																										+
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Subcutaneous tissue, fibrosarcoma						X						X														
Musculoskeletal System																										+
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Skeletal muscle				+		+				+																
Fibrosarcoma, metastatic, skin						X																				
Histiocytic sarcoma										X																

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	9 9 5 1	9 9 6 1	9 9 7 1	9 9 9 1	4 6 2 1	4 6 3 1	4 6 4 1	4 6 6 1	4 6 8 1	4 7 0 1	4 7 2 1	4 7 3 1	4 5 6 1	4 6 0 1	4 6 9 1	9 7 8 1	9 8 0 1	9 8 8 1	9 9 0 1	9 9 1 1	9 9 2 1	9 8 2 1	9 8 5 1	9 8 6 1	9 8 7 1	**Total Tissues/ Tumors**
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																									X	1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X									X		X		X		X				X						8
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Chemodectoma malignant																										1
General Body System																										
None																										
Genital System																										
Ovary	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Granulosa-theca tumor benign																X										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Histiocytic sarcoma																		X								1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mandibular	+	M	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hemangiosarcoma			X																							1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymoma benign																					X					2
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Subcutaneous tissue, fibrosarcoma																										2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Skeletal muscle																										3
Fibrosarcoma, metastatic, skin																										1
Histiocytic sarcoma																										1

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	2 1 1	3 5 1	5 0 1	5 3 3	5 5 2	5 6 4	5 8 9	6 1 6	6 2 2	6 4 0	6 4 2	6 6 6	6 7 3	6 8 4	7 0 7	7 0 8	7 1 7	7 2 1	7 3 0	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	1 0 7 7 1	0 4 7 1 1	0 9 8 3 1	0 4 6 1 1	0 4 7 8 1	1 0 0 7 1	0 4 6 7 1	0 4 5 8 1	0 4 8 0 1	0 9 7 9 1	0 9 9 8 1	0 4 5 7 1	0 4 6 5 1	0 9 8 4 1	0 9 7 6 1	0 9 8 1 1	0 9 7 7 1	0 9 9 3 1	0 9 8 9 1	0 4 5 9 1	0 4 7 4 1	0 4 7 5 1	0 4 7 6 1	0 4 7 7 1	0 4 4 9 1	9 9 4 1
Nervous System																									+
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spinal cord												+													
Respiratory System																									+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Alveolar/bronchiolar adenoma																X									
Alveolar/bronchiolar carcinoma									X				X										X	X	
Chemodectoma malignant, metastatic, thyroid gland		X																							
Histiocytic sarcoma										X															+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Special Senses System																									
Harderian gland																			+						
Carcinoma																			X						
Urinary System																									+
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																									+
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma										X															
Leukemia granulocytic	X																								
Lymphoma malignant lymphocytic																	X		X						X
Lymphoma malignant mixed				X				X								X								X	

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 70 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	9 9 5 1	9 9 6 1	9 9 7 1	9 9 9 1	4 6 2 1	4 6 3 1	4 6 4 1	4 6 6 1	4 6 8 1	4 7 0 1	4 7 2 1	4 7 3 1	4 5 6 1	4 6 0 1	4 6 9 1	4 7 8 1	9 8 0 1	9 8 8 1	9 9 0 1	9 9 1 1	9 9 2 1	9 8 2 1	9 8 5 1	9 8 6 1	9 8 7 1	**Total Tissues/ Tumors**
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Spinal cord																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Alveolar/bronchiolar adenoma								X					X								X		X				5
Alveolar/bronchiolar carcinoma			X																				X				6
Chemodectoma malignant, metastatic, thyroid gland																											1
Histiocytic sarcoma																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																											
Harderian gland			+															+								3
Carcinoma																											1
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																		X									2
Leukemia granulocytic																											1
Lymphoma malignant lymphocytic																							X				3
Lymphoma malignant mixed							X				X						X		X	X							10

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 140 ppm

Number of Days on Study	2 6 8	3 1 0	3 6 2	4 5 3	5 1 7	5 5 7	5 5 7	5 5 8	5 6 1	5 7 5	6 5 8	6 6 1	6 8 1	7 1 6	7 1 6	7 2 6	7 2 8	7 3 0	7 3 0	7 3 1	7 3 1	7 3 2	7 3 3	7 3 4	7 3 4
Carcass ID Number	4 3 8 1	9 6 1 1	4 3 2 1	4 3 3 1	4 2 1 1	9 4 9 1	9 6 5 1	4 4 1 1	4 2 8 1	4 4 0 1	4 4 5 1	9 5 0 1	4 3 6 1	4 4 2 1	9 5 2 1	4 3 5 1	4 3 9 1	9 4 6 1	9 5 9 1	9 5 4 1	9 5 5 1	9 6 3 1	4 3 4 1	4 3 7 1	4 2 7 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung											X														
Fibrous histiocytoma		X																							
Hepatoblastoma																									
Hepatocellular carcinoma								X					X					X							
Hepatocellular carcinoma, four, multiple																	X								
Hepatocellular adenoma											X						X							X	
Hepatocellular adenoma, two, multiple															X										
Hepatocellular adenoma, three, multiple																					X				
Hepatocellular adenoma, four, multiple																			X						
Histiocytic sarcoma																									
Mesentery		+						+		+	+	+			+									+	
Alveolar/bronchiolar carcinoma, metastatic, lung											X														
Fibrous histiocytoma		X																							
Pancreas	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung											X														
Fibrous histiocytoma		X																							

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	
Carcass ID Number	4 3 0 1	4 3 1 1	4 2 9 1	4 4 3 1	4 4 4 1	9 4 8 1	4 2 2 1	4 2 3 1	4 2 4 1	4 2 5 1	4 2 6 1	9 4 1 1	9 4 2 1	9 4 3 1	9 4 4 1	9 4 5 1	9 4 7 1	9 5 1 1	9 5 3 1	9 5 6 1	9 5 7 1	9 5 8 1	9 6 0 1	9 6 2 1	9 6 4 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Fibrous histiocytoma																										1
Hepatoblastoma																					X					1
Hepatocellular carcinoma										X	X										X					6
Hepatocellular carcinoma, four, multiple																										1
Hepatocellular adenoma							X		X		X								X							7
Hepatocellular adenoma, two, multiple					X									X		X							X			5
Hepatocellular adenoma, three, multiple			X					X									X									4
Hepatocellular adenoma, four, multiple													X													2
Histiocytic sarcoma																					X					1
Mesentery		+			+					+			+				+									12
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Fibrous histiocytoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Fibrous histiocytoma																										1

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	2 6 8	3 1 0	3 6 2	4 5 3	5 1 7	5 5 7	5 5 7	5 5 8	5 6 1	5 7 5	6 5 8	6 6 1	6 8 1	7 1 6	7 1 6	7 2 6	7 2 8	7 3 0	7 3 0	7 3 1	7 3 1	7 3 2	7 3 3	7 3 3	7 3 4
Carcass ID Number	4 3 8 1	9 6 1 1	4 3 2 1	4 3 3 1	4 2 1 1	9 4 9 1	9 6 5 1	4 4 1 1	4 2 8 1	4 4 0 1	4 4 5 1	9 5 0 1	4 3 6 1	4 4 2 1	9 5 2 1	4 3 5 1	4 3 9 1	4 4 6 1	9 5 9 1	9 5 4 1	9 5 5 1	9 6 3 1	4 3 4 1	4 3 7 1	4 2 7 1
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung											X														
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Pars distalis, adenoma																								X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
Tissue NOS															+										
Genital System																									
Clitoral gland																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma																								X	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Polyp stromal									X																
Vagina																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma		X																							
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bronchial, alveolar/bronchiolar carcinoma, metastatic, lung											X														
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung											X														
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland																				X					
Fibrosarcoma, metastatic, skin				X																					
Lymph node, mesenteric	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma		X																							
Hemangiosarcoma																									
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	I	M	+	+	+	+	+	+	+
Fibrous histiocytoma		X																							
Thymoma malignant																									

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	
Carcass ID Number	4 3 0 1	4 3 1 1	4 2 9 1	4 4 3 1	4 4 4 1	9 4 8 1	4 2 2 1	4 2 3 1	4 2 4 1	4 2 5 1	4 2 6 1	4 4 1 1	9 4 2 1	9 4 4 1	9 4 3 1	9 4 4 1	9 4 5 1	9 5 7 1	9 5 1 1	9 5 3 1	9 5 6 1	9 5 7 1	9 5 8 1	9 6 0 1	9 6 2 1	9 6 4 1	**Total Tissues/ Tumors**
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign				X																						1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																									X	1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma											X			X						X						4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
Tissue NOS																										1
Genital System																										
Clitoral gland																						+		+		2
Ovary	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Cystadenoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																				X						1
Polyp stromal																										1
Vagina														+												1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bronchial, alveolar/bronchiolar carcinoma, metastatic, lung																										1
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland																										1
Fibrosarcoma, metastatic, skin																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrous histiocytoma																										1
Hemangiosarcoma															X											1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	46
Fibrous histiocytoma																										1
Thymoma malignant										X																1

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	2 6 8	3 1 0	3 6 2	4 5 3	5 1 7	5 5 7	5 5 7	5 5 8	5 6 1	5 7 5	6 5 8	6 6 1	6 8 1	7 1 6	7 1 6	7 2 6	7 2 8	7 3 0	7 3 0	7 3 1	7 3 1	7 3 2	7 3 3	7 3 3	7 3 4
Carcass ID Number	4 3 8 1	9 6 1 1	4 3 2 1	4 3 3 1	4 2 1 1	9 4 9 1	9 6 5 1	4 4 1 1	4 2 8 1	4 4 0 1	4 4 5 1	9 5 0 1	4 3 6 1	4 4 2 1	9 5 2 1	4 3 5 1	4 3 9 1	9 4 6 1	9 5 9 1	9 5 4 1	9 5 5 1	9 5 3 1	9 6 4 1	4 3 1 1	4 3 7 1	4 2 7 1
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma				X													X						X		
Subcutaneous tissue, hemangiosarcoma																		X							
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma		X																							
Osteosarcoma	X															X									
Skeletal muscle											+														
Alveolar/bronchiolar carcinoma, metastatic, lung											X														
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma		X																							
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma															X										
Alveolar/bronchiolar carcinoma											X			X											
Carcinoma, metastatic, harderian gland																				X					
Fibrous histiocytoma		X																							
Hepatocellular carcinoma, metastatic, liver																	X								
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																			+						
Harderian gland													+						+	+					
Adenoma													X												
Carcinoma																				X					
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung											X														
Histiocytic sarcoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed										X		X								X					

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 140 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	
Carcass ID Number	4 3 0 1	4 3 1 1	4 2 9 1	4 4 3 1	4 4 4 1	9 4 8 1	4 2 2 1	4 2 3 1	4 2 4 1	4 2 5 1	4 2 6 1	9 4 1 1	9 4 2 1	9 4 3 1	9 4 4 1	9 4 5 1	9 4 7 1	9 5 1 1	9 5 3 1	9 5 6 1	9 5 7 1	9 5 8 1	9 6 0 1	9 6 2 1	9 6 4 1	**Total Tissues/ Tumors**
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																									3
Subcutaneous tissue, hemangiosarcoma																									1
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																									1
Osteosarcoma																									2
Skeletal muscle																									1
Alveolar/bronchiolar carcinoma, metastatic, lung																									1
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																									1
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X																		2
Alveolar/bronchiolar carcinoma			X										X						X						5
Carcinoma, metastatic, harderian gland																									1
Fibrous histiocytoma																									1
Hepatocellular carcinoma, metastatic, liver																									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	49
Special Senses System																									
Eye																									1
Harderian gland		+																							4
Adenoma																									1
Carcinoma																									1
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																									1
Histiocytic sarcoma																					X				1
Urinary bladder	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																					X				1
Lymphoma malignant lymphocytic																									1
Lymphoma malignant mixed		X	X						X					X											7

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 275 ppm

Number of Days on Study	4 5 7	4 8 0	4 9 1	5 1 9	5 3 6	6 0 6	6 2 0	6 5 1	6 5 9	6 7 3	6 8 6	6 9 3	7 0 4	7 2 7	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4
Carcass ID Number	3 9 5 1	9 0 8 1	3 9 7 1	9 1 2 1	9 0 9 1	4 0 7 1	3 8 9 1	9 3 0 1	9 2 7 1	4 0 2 1	3 9 0 1	9 1 3 1	9 1 8 1	4 0 9 1	9 1 6 1	4 0 4 1	4 0 5 1	4 0 6 1	4 0 8 1	9 1 4 1	9 1 5 1	9 1 7 1	3 9 2 1	3 9 3 1	3 9 4 1
Alimentary System																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	A	I	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																								
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma														X	X									
Hepatocellular adenoma													X						X	X	X	X		X
Hepatocellular adenoma, two, multiple														X		X								
Hepatocellular adenoma, greater than five, multiple																								
Histiocytic sarcoma																X								
Osteosarcoma, metastatic, bone			X																					
Mesentery								+	+				+		+	+							+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																								
Squamous cell carcinoma																								
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																								
Blood vessel																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	3 9 6 1	3 9 8 1	3 9 9 1	4 0 0 1	4 0 1 1	4 0 3 1	4 1 0 1	3 8 6 1	3 8 7 1	3 8 8 1	3 9 1 1	9 0 6 1	9 0 7 1	9 0 0 1	9 1 1 1	9 1 9 1	9 1 0 1	9 2 0 1	9 2 1 1	9 2 2 1	9 2 3 1	9 2 4 1	9 2 5 1	9 2 6 1	9 2 8 1	9 2 9 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																					X					1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma		X	X																X							5
Hepatocellular adenoma			X	X	X	X	X	X	X						X				X		X	X		X		18
Hepatocellular adenoma, two, multiple		X																X								4
Hepatocellular adenoma, greater than five, multiple																				X						1
Histiocytic sarcoma																										1
Osteosarcoma, metastatic, bone																										1
Mesentery		+			+																					8
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous																				X						1
Squamous cell carcinoma									X																	1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel																				+						1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	4 5 7	4 8 0	4 9 1	5 1 9	5 3 6	6 0 6	6 2 0	6 5 1	6 5 9	6 7 3	6 8 6	6 9 3	7 0 4	7 2 7	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4
Carcass ID Number	3 9 5 1	9 0 8 1	3 9 7 1	9 1 2 1	9 0 9 1	4 0 7 1	3 8 9 1	9 3 0 1	9 2 7 1	4 0 2 1	3 9 0 1	9 1 3 1	9 1 8 1	4 0 9 1	9 1 6 1	4 0 4 1	4 0 5 1	4 0 6 1	4 0 8 1	9 1 4 1	9 1 5 1	9 1 7 1	3 9 2 1	3 9 3 1	3 9 4 1
Endocrine System																								
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																		X						
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma							X																	
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X															X								
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma													X											
Follicular cell, carcinoma																								
General Body System																								
Tissue NOS																		+						
Genital System																								
Clitoral gland	+																				+			
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+
Cystadenocarcinoma		X																						
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal						X				X							X							
Vagina									+															
Hematopoietic System																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, osteosarcoma, metastatic, bone			X																					
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	I	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																								
Histiocytic sarcoma																X								
Thymus	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Integumentary System																								
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma											X													

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	3 9 6 1	3 9 8 1	3 9 9 1	4 0 0 1	4 0 1 1	4 0 3 1	4 1 0 1	3 8 6 1	3 8 7 1	3 8 8 1	3 9 1 1	9 0 6 1	9 0 7 1	9 1 0 1	9 1 1 1	9 1 9 1	9 2 0 1	9 2 1 1	9 2 2 1	9 2 3 1	9 2 4 1	9 2 5 1	9 2 6 1	9 2 8 1	9 2 9 1	**Total Tissues/ Tumors**
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																									1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																									1
Parathyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma				X									X						X				X		6
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma											X														2
Follicular cell, carcinoma																								X	1
General Body System																									
Tissue NOS																									1
Genital System																									
Clitoral gland																									2
Ovary	+	+	+	+	+	+	+	+	+	+	M	+	M	M	+	+	+	+	+	+	+	+	+	+	46
Cystadenocarcinoma																									1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal																									3
Vagina																									1
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, osteosarcoma, metastatic, bone																									1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma				X																					1
Histiocytic sarcoma																									1
Thymus	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	45
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																									1

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	4 5 7	4 8 0	4 9 1	5 1 9	5 3 6	6 0 6	6 2 0	6 5 1	6 5 9	6 7 3	6 8 6	6 9 3	7 0 4	7 2 7	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4
Carcass ID Number	3 9 5 1	9 0 8 1	3 9 7 1	9 1 2 1	9 0 9 1	4 0 7 1	3 8 9 1	9 3 0 1	9 2 7 1	4 0 2 1	3 9 0 1	9 1 3 1	9 1 8 1	4 1 9 1	9 0 6 1	4 0 4 1	4 0 5 1	4 0 6 1	4 0 8 1	9 1 4 1	9 1 5 1	9 1 7 1	3 9 2 1	3 9 3 1	3 9 4 1
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma			X																					
Skeletal muscle				+																				
Sarcoma				X																				
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma				X																				
Alveolar/bronchiolar carcinoma										X														
Hepatocellular carcinoma, metastatic, liver														X										
Osteosarcoma, metastatic, bone			X																					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Eye						+																		
Harderian gland															+					+			+	
Adenoma															X					X			X	
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone			X																					
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X								
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X								
Lymphoma malignant lymphocytic																		X	X					
Lymphoma malignant mixed								X							X									

TABLE F2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chlorinated Water Study: 275 ppm (continued)

Number of Days on Study	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	3 9 6 1	3 9 8 1	3 9 9 1	4 0 0 1	4 0 1 1	4 0 3 1	4 1 0 1	3 8 6 1	3 8 7 1	3 8 8 1	3 9 1 1	9 0 6 1	9 0 7 1	9 1 0 1	9 1 1 1	9 1 9 1	9 2 0 1	9 2 1 1	9 2 2 1	9 2 3 1	9 2 4 1	9 2 5 1	9 2 6 1	9 2 8 1	9 2 9 1	**Total Tissues/ Tumors**
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																									1
Skeletal muscle																									1
Sarcoma																									1
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma											X														2
Alveolar/bronchiolar carcinoma																		X							2
Hepatocellular carcinoma, metastatic, liver																			X						2
Osteosarcoma, metastatic, bone																									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																									
Eye																					+				2
Harderian gland												+								+	+		+		7
Adenoma																									3
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic, bone																									1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																									1
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																									1
Lymphoma malignant lymphocytic																									2
Lymphoma malignant mixed							X															X			4

TABLE F3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Harderian Gland: Adenoma				
Overall rates[a]	1/50 (2%)	0/51 (0%)	1/50 (2%)	3/50 (6%)
Adjusted rates[b]	3.0%	0.0%	2.6%	8.3%
Terminal rates[c]	1/33 (3%)	0/31 (0%)	0/28 (0%)	2/35 (6%)
First incidence (days)	733 (T)	–[e]	681	731
Life table tests[d]	P=0.114	P=0.512N	P=0.736	P=0.328
Logistic regression tests[d]	P=0.103	P=0.512N	P=0.758	P=0.330
Cochran-Armitage test[d]	P=0.096			
Fisher exact test[d]		P=0.495N	P=0.753N	P=0.309
Harderian Gland: Adenoma or Carcinoma				
Overall rates	1/50 (2%)	1/51 (2%)	2/50 (4%)	3/50 (6%)
Adjusted rates	3.0%	3.0%	5.8%	8.3%
Terminal rates	1/33 (3%)	0/31 (0%)	0/28 (0%)	2/35 (6%)
First incidence (days)	733 (T)	730	681	731
Life table tests	P=0.188	P=0.750	P=0.465	P=0.328
Logistic regression tests	P=0.175	P=0.763	P=0.492	P=0.330
Cochran-Armitage test	P=0.162			
Fisher exact test		P=0.748N	P=0.500	P=0.309
Liver: Hepatocellular Adenoma				
Overall rates	19/50 (38%)	19/51 (37%)	18/50 (36%)	23/50 (46%)
Adjusted rates	53.8%	53.2%	53.7%	62.1%
Terminal rates	17/33 (52%)	15/31 (48%)	13/28 (46%)	21/35 (60%)
First incidence (days)	561	552	658	704
Life table tests	P=0.313	P=0.503	P=0.454	P=0.348
Logistic regression tests	P=0.261	P=0.568N	P=0.537N	P=0.323
Cochran-Armitage test	P=0.217			
Fisher exact test		P=0.551N	P=0.500N	P=0.272
Liver: Hepatocellular Carcinoma				
Overall rates	6/50 (12%)	7/51 (14%)	7/50 (14%)	5/50 (10%)
Adjusted rates	17.2%	19.5%	20.1%	13.5%
Terminal rates	5/33 (15%)	4/31 (13%)	3/28 (11%)	3/35 (9%)
First incidence (days)	659	589	558	727
Life table tests	P=0.365N	P=0.468	P=0.415	P=0.460N
Logistic regression tests	P=0.386N	P=0.510	P=0.483	P=0.470N
Cochran-Armitage test	P=0.406N			
Fisher exact test		P=0.515	P=0.500	P=0.500N
Liver: Hepatocellular Adenoma, Hepatoblastoma, or Hepatocellular Carcinoma				
Overall rates	20/50 (40%)	22/51 (43%)	23/50 (46%)	24/50 (48%)
Adjusted rates	54.9%	58.4%	63.0%	63.2%
Terminal rates	17/33 (52%)	16/31 (52%)	15/28 (54%)	21/35 (60%)
First incidence (days)	561	552	558	704
Life table tests	P=0.346	P=0.346	P=0.175	P=0.358
Logistic regression tests	P=0.272	P=0.439	P=0.290	P=0.322
Cochran-Armitage test	P=0.232			
Fisher exact test		P=0.453	P=0.343	P=0.273

TABLE F3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	4/50 (8%)	5/51 (10%)	2/50 (4%)	2/50 (4%)
Adjusted rates	10.9%	15.3%	6.2%	4.9%
Terminal rates	3/33 (9%)	4/31 (13%)	1/28 (4%)	1/35 (3%)
First incidence (days)	452	708	716	519
Life table tests	P=0.165N	P=0.474	P=0.386N	P=0.318N
Logistic regression tests	P=0.176N	P=0.512	P=0.338N	P=0.370N
Cochran-Armitage test	P=0.179N			
Fisher exact test		P=0.513	P=0.339N	P=0.339N
Lung: Alveolar/bronchiolar Carcinoma				
Overall rates	1/50 (2%)	6/51 (12%)	5/50 (10%)	2/50 (4%)
Adjusted rates	3.0%	17.1%	15.3%	5.2%
Terminal rates	1/33 (3%)	4/31 (13%)	3/28 (11%)	1/35 (3%)
First incidence (days)	733 (T)	622	658	673
Life table tests	P=0.511N	P=0.054	P=0.085	P=0.516
Logistic regression tests	P=0.533N	P=0.061	P=0.097	P=0.509
Cochran-Armitage test	P=0.547N			
Fisher exact test		P=0.059	P=0.102	P=0.500
Lung: Alveolar/bronchiolar Adenoma or Alveolar/bronchiolar Carcinoma				
Overall rates	5/50 (10%)	10/51 (20%)	7/50 (14%)	4/50 (8%)
Adjusted rates	13.9%	28.4%	20.9%	10.0%
Terminal rates	4/33 (12%)	7/31 (23%)	4/28 (14%)	2/35 (6%)
First incidence (days)	452	622	658	519
Life table tests	P=0.238N	P=0.118	P=0.314	P=0.471N
Logistic regression tests	P=0.258N	P=0.139	P=0.368	P=0.521N
Cochran-Armitage test	P=0.268N			
Fisher exact test		P=0.141	P=0.380	P=0.500N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	5/48 (10%)	8/50 (16%)	4/48 (8%)	6/50 (12%)
Adjusted rates	14.6%	24.8%	14.8%	16.0%
Terminal rates	4/33 (12%)	7/31 (23%)	4/27 (15%)	5/35 (14%)
First incidence (days)	698	717	733 (T)	457
Life table tests	P=0.495N	P=0.246	P=0.608N	P=0.541
Logistic regression tests	P=0.514N	P=0.275	P=0.518N	P=0.529
Cochran-Armitage test	P=0.521N			
Fisher exact test		P=0.304	P=0.500N	P=0.529
Skin (Subcutaneous Tissue): Fibrosarcoma				
Overall rates	0/50 (0%)	2/51 (4%)	3/50 (6%)	1/50 (2%)
Adjusted rates	0.0%	4.6%	8.4%	2.5%
Terminal rates	0/33 (0%)	0/31 (0%)	1/28 (4%)	0/35 (0%)
First incidence (days)	-	564	453	686
Life table tests	P=0.450	P=0.245	P=0.113	P=0.505
Logistic regression tests	P=0.401	P=0.231	P=0.121	P=0.499
Cochran-Armitage test	P=0.433			
Fisher exact test		P=0.252	P=0.121	P=0.500

TABLE F3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Skin (Subcutaneous Tissue): Fibrosarcoma or Sarcoma				
Overall rates	1/50 (2%)	2/51 (4%)	3/50 (6%)	1/50 (2%)
Adjusted rates	3.0%	4.6%	8.4%	2.5%
Terminal rates	1/33 (3%)	0/31 (0%)	1/28 (4%)	0/35 (0%)
First incidence (days)	733 (T)	564	453	686
Life table tests	P=0.562N	P=0.498	P=0.277	P=0.751N
Logistic regression tests	P=0.599	P=0.504	P=0.307	P=0.757N
Cochran-Armitage test	P=0.583N			
Fisher exact test		P=0.508	P=0.309	P=0.753N
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rates	2/50 (4%)	0/51 (0%)	0/50 (0%)	3/50 (6%)
Adjusted rates	6.1%	0.0%	0.0%	8.2%
Terminal rates	2/33 (6%)	0/31 (0%)	0/28 (0%)	2/35 (6%)
First incidence (days)	733 (T)	-	-	704
Life table tests	P=0.276	P=0.252N	P=0.275N	P=0.531
Logistic regression tests	P=0.264	P=0.252N	P=0.275N	P=0.522
Cochran-Armitage test	P=0.248			
Fisher exact test		P=0.243N	P=0.247N	P=0.500
Uterus: Stromal Polyp				
Overall rates	0/50 (0%)	0/51 (0%)	1/50 (2%)	3/50 (6%)
Adjusted rates	0.0%	0.0%	2.4%	7.3%
Terminal rates	0/33 (0%)	0/31 (0%)	0/28 (0%)	1/35 (3%)
First incidence (days)	-	-	561	606
Life table tests	P=0.024	-	P=0.486	P=0.133
Logistic regression tests	P=0.016	-	P=0.491	P=0.112
Cochran-Armitage test	P=0.020			
Fisher exact test		-	P=0.500	P=0.121
All Organs: Hemangioma				
Overall rates	3/50 (6%)	0/51 (0%)	0/50 (0%)	2/50 (4%)
Adjusted rates	9.1%	0.0%	0.0%	5.7%
Terminal rates	3/33 (9%)	0/31 (0%)	0/28 (0%)	2/35 (6%)
First incidence (days)	733 (T)	-	-	733 (T)
Life table tests	P=0.498N	P=0.132N	P=0.151N	P=0.473N
Logistic regression tests	P=0.498N	P=0.132N	P=0.151N	P=0.473N
Cochran-Armitage test	P=0.522N			
Fisher exact test		P=0.118N	P=0.121N	P=0.500N
All Organs: Hemangiosarcoma				
Overall rates	3/50 (6%)	1/51 (2%)	2/50 (4%)	0/50 (0%)
Adjusted rates	9.1%	3.2%	6.5%	0.0%
Terminal rates	3/33 (9%)	1/31 (3%)	1/28 (4%)	0/35 (0%)
First incidence (days)	733 (T)	733 (T)	730	-
Life table tests	P=0.100N	P=0.327N	P=0.562N	P=0.110N
Logistic regression tests	P=0.092N	P=0.327N	P=0.500N	P=0.110N
Cochran-Armitage test	P=0.104N			
Fisher exact test		P=0.301N	P=0.500N	P=0.121N

TABLE F3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	5/50 (10%)	1/51 (2%)	2/50 (4%)	2/50 (4%)
Adjusted rates	15.2%	3.2%	6.5%	5.7%
Terminal rates	5/33 (15%)	1/31 (3%)	1/28 (4%)	2/35 (6%)
First incidence (days)	733 (T)	733 (T)	730	733 (T)
Life table tests	P=0.201N	P=0.116N	P=0.278N	P=0.191N
Logistic regression tests	P=0.204N	P=0.116N	P=0.215N	P=0.191N
Cochran-Armitage test	P=0.219N			
Fisher exact test		P=0.098N	P=0.218N	P=0.218N
All Organs: Histiocytic Sarcoma or Malignant Lymphoma				
Overall rates	9/50 (18%)	15/51 (29%)	9/50 (18%)	7/50 (14%)
Adjusted rates	23.2%	39.3%	26.5%	18.6%
Terminal rates	5/33 (15%)	9/31 (29%)	5/28 (18%)	5/35 (14%)
First incidence (days)	452	533	575	651
Life table tests	P=0.154N	P=0.120	P=0.508	P=0.359N
Logistic regression tests	P=0.163N	P=0.132	P=0.594	P=0.381N
Cochran-Armitage test	P=0.175N			
Fisher exact test		P=0.133	P=0.602N	P=0.393N
All Organs: Malignant Lymphoma (Lymphocytic or Mixed)				
Overall rates	9/50 (18%)	13/51 (25%)	8/50 (16%)	6/50 (12%)
Adjusted rates	23.2%	35.0%	23.3%	15.9%
Terminal rates	5/33 (15%)	8/31 (26%)	4/28 (14%)	4/35 (11%)
First incidence (days)	452	533	575	651
Life table tests	P=0.122N	P=0.224	P=0.583N	P=0.264N
Logistic regression tests	P=0.126N	P=0.250	P=0.508N	P=0.280N
Cochran-Armitage test	P=0.135N			
Fisher exact test		P=0.252	P=0.500N	P=0.288N
All Organs: Benign Tumors				
Overall rates	26/50 (52%)	27/51 (53%)	23/50 (46%)	33/50 (66%)
Adjusted rates	69.8%	70.6%	64.8%	76.5%
Terminal rates	22/33 (67%)	20/31 (65%)	16/28 (57%)	25/35 (71%)
First incidence (days)	452	552	561	457
Life table tests	P=0.199	P=0.405	P=0.558	P=0.201
Logistic regression tests	P=0.115	P=0.527	P=0.392N	P=0.132
Cochran-Armitage test	P=0.097			
Fisher exact test		P=0.542	P=0.345N	P=0.111
All Organs: Malignant Tumors				
Overall rates	23/50 (46%)	30/51 (59%)	25/50 (50%)	19/50 (38%)
Adjusted rates	54.2%	65.8%	57.9%	43.4%
Terminal rates	14/33 (42%)	16/31 (52%)	11/28 (39%)	11/35 (31%)
First incidence (days)	452	211	268	480
Life table tests	P=0.121N	P=0.136	P=0.296	P=0.245N
Logistic regression tests	P=0.129N	P=0.138	P=0.420	P=0.266N
Cochran-Armitage test	P=0.120N			
Fisher exact test		P=0.138	P=0.421	P=0.272N

TABLE F3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
All Organs: Benign and Malignant Tumors				
Overall rates	35/50 (70%)	43/51 (84%)	37/50 (74%)	39/50 (78%)
Adjusted rates	83.1%	89.4%	83.6%	82.8%
Terminal rates	26/33 (79%)	26/31 (84%)	21/28 (75%)	27/35 (77%)
First incidence (days)	452	211	268	457
Life table tests	P=0.496N	P=0.078	P=0.195	P=0.426
Logistic regression tests	P=0.394	P=0.068	P=0.375	P=0.293
Cochran-Armitage test	P=0.362			
Fisher exact test		P=0.069	P=0.412	P=0.247

(T)Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no tumors in animal group

TABLE F4
Historical Incidence of Uterine Neoplasms in Untreated Female B6C3F$_1$ Mice[a]

Study	Incidence in Controls		
	Stromal Polyp	Stromal Sarcoma	Stromal Polyp or Stromal Sarcoma
Historical Incidence at Southern Research Institute			
Feed			
Nitrofurantoin	2/50 (4%)	0/50 (0%)	2/50 (4%)
Rhodamine 6G	1/50 (2%)	1/50 (2%)	2/50 (4%)
Roxarsone	1/50 (2%)	0/50 (0%)	1/50 (2%)
Total	4/150 (3%)	1/150 (1%)	5/150 (3%)
Standard deviation	1.2%	1.2%	1.2%
Range	2%-4%	0%-2%	2%-4%
Water			
Chloramine	0/50 (0%)	0/50 (0%)	0/50 (0%)
Overall Historical Incidence			
Feed			
Total	14/570 (2%)	3/570 (1%)	17/570 (3%)
Standard deviation	1.9%	0.9%	2.0%
Range	0%-6%	0%-2%	0%-6%
Water			
Total	2/130 (2%)	0/130 (0%)	2/130 (2%)
Standard deviation	2.1%		2.1%
Range	0%-3%		0%-3%

[a] Data as of 15 September 1990

TABLE F5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chlorinated Water Study

	0 ppm	70 ppm	140 ppm	275 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	9	10	10
Early deaths				
Natural death	3	6	3	3
Moribund	13	14	19	12
Accidental death	1	0	0	0
Survivors				
Terminal sacrifice	33	31	27	35
Died last week of study	0	0	1	0
Animals examined microscopically	50	51	50	50
Alimentary System				
Gallbladder	(47)	(49)	(48)	(50)
Cyst	3 (6%)	1 (2%)	1 (2%)	1 (2%)
Dilatation		1 (2%)	1 (2%)	
Hyperplasia, lymphoid			1 (2%)	
Necrosis			1 (2%)	
Intestine large, cecum	(47)	(51)	(50)	(49)
Edema	2 (4%)		3 (6%)	
Intestine large, rectum	(47)	(50)	(50)	(49)
Erosion		1 (2%)		
Intestine small, duodenum	(48)	(51)	(50)	(50)
Erosion		1 (2%)		
Ulcer			1 (2%)	
Intestine small, ileum	(48)	(51)	(49)	(47)
Artery, jejunum, necrosis, fibrinoid	1 (2%)			
Liver	(50)	(51)	(50)	(50)
Angiectasis		1 (2%)		1 (2%)
Basophilic focus	2 (4%)	2 (4%)	2 (4%)	4 (8%)
Clear cell focus	1 (2%)	4 (8%)	4 (8%)	4 (8%)
Eosinophilic focus		1 (2%)		
Hematopoietic cell proliferation	5 (10%)	2 (4%)	5 (10%)	1 (2%)
Hemorrhage			1 (2%)	1 (2%)
Hyperplasia, focal	12 (24%)	11 (22%)	4 (8%)	12 (24%)
Hyperplasia, lymphoid	6 (12%)	3 (6%)		7 (14%)
Inflammation, chronic				1 (2%)
Inflammation, subacute	2 (4%)	9 (18%)	4 (8%)	4 (8%)
Mineralization	1 (2%)			1 (2%)
Mixed cell focus	1 (2%)	1 (2%)		
Artery, necrosis, fibrinoid	1 (2%)			
Centrilobular, necrosis		1 (2%)	1 (2%)	
Hepatocyte, cytomegaly				1 (2%)
Hepatocyte, karyomegaly	1 (2%)			2 (4%)
Hepatocyte, nuclear alteration				1 (2%)
Hepatocyte, vacuolization cytoplasmic	2 (4%)	1 (2%)	6 (12%)	3 (6%)
Kupffer cell, hyperplasia	1 (2%)	5 (10%)	3 (6%)	3 (6%)
Kupffer cell, pigmentation	1 (2%)	2 (4%)		1 (2%)
Lobules, necrosis	6 (12%)	3 (6%)	8 (16%)	7 (14%)

TABLE F5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Alimentary System (continued)				
Mesentery	(17)	(10)	(12)	(8)
Edema	1 (6%)			
Artery, necrosis, fibrinoid	1 (6%)			
Fat, inflammation, suppurative	1 (6%)			
Fat, necrosis	14 (82%)	7 (70%)	7 (58%)	6 (75%)
Pancreas	(50)	(50)	(49)	(50)
Atrophy	3 (6%)	1 (2%)	1 (2%)	3 (6%)
Cyst		1 (2%)	1 (2%)	
Cytoplasmic alteration	2 (4%)	5 (10%)	7 (14%)	3 (6%)
Focal cellular change	1 (2%)		1 (2%)	1 (2%)
Hyperplasia, lymphoid	8 (16%)	6 (12%)	4 (8%)	4 (8%)
Inflammation, chronic active			1 (2%)	
Inflammation, subacute	1 (2%)			
Salivary glands	(49)	(51)	(50)	(50)
Hyperplasia, lymphoid	18 (37%)	11 (22%)	9 (18%)	17 (34%)
Acinus, hyperplasia, cystic	1 (2%)			
Stomach, forestomach	(50)	(51)	(50)	(50)
Cyst	1 (2%)			
Diverticulum	1 (2%)			1 (2%)
Edema	1 (2%)		1 (2%)	
Erosion				1 (2%)
Inflammation, suppurative	1 (2%)		2 (4%)	1 (2%)
Ulcer	1 (2%)		1 (2%)	
Mucosa, hyperplasia	2 (4%)	1 (2%)	6 (12%)	2 (4%)
Stomach, glandular	(50)	(51)	(50)	(50)
Cyst	7 (14%)	13 (25%)	9 (18%)	5 (10%)
Edema	2 (4%)		1 (2%)	
Erosion	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Inflammation, subacute	2 (4%)		1 (2%)	2 (4%)
Metaplasia, squamous			2 (4%)	
Mineralization	1 (2%)			
Ulcer		1 (2%)		
Mucosa, hyperplasia		1 (2%)		
Cardiovascular System				
Blood vessel	(2)	(1)		(1)
Hypertrophy				1 (100%)
Necrosis, fibrinoid	1 (50%)			
Thrombus	1 (50%)			
Heart	(50)	(51)	(50)	(50)
Myocardium, fibrosis			2 (4%)	
Myocardium, inflammation, subacute	1 (2%)			
Myocardium, mineralization	1 (2%)	1 (2%)		1 (2%)

TABLE F5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm		70 ppm		140 ppm		275 ppm	
Endocrine System								
Adrenal gland, cortex	(50)		(51)		(50)		(50)	
Accessory adrenal cortical nodule	10	(20%)	18	(35%)	8	(16%)	11	(22%)
Basophilic focus	3	(6%)						
Clear cell focus	1	(2%)	2	(4%)				
Cyst					1	(2%)	1	(2%)
Developmental malformation					1	(2%)		
Hematopoietic cell proliferation					2	(4%)		
Hyperplasia, focal	2	(4%)	4	(8%)	5	(10%)	3	(6%)
Necrosis							1	(2%)
Capsule, hyperplasia	2	(4%)	3	(6%)				
X-zone, degeneration, fatty			1	(2%)			1	(2%)
Adrenal gland, medulla	(50)		(51)		(50)		(50)	
Hyperplasia	1	(2%)			3	(6%)	3	(6%)
Islets, pancreatic	(50)		(50)		(49)		(50)	
Hyperplasia	3	(6%)	5	(10%)	8	(16%)	8	(16%)
Hyperplasia, lymphoid	1	(2%)						
Parathyroid gland	(47)		(50)		(48)		(48)	
Cyst					4	(8%)	1	(2%)
Hyperplasia	1	(2%)						
Pituitary gland	(48)		(50)		(48)		(50)	
Pars distalis, angiectasis	3	(6%)	2	(4%)	2	(4%)	2	(4%)
Pars distalis, hyperplasia	8	(17%)	7	(14%)	9	(19%)	7	(14%)
Thyroid gland	(50)		(51)		(50)		(50)	
Degeneration, cystic	24	(48%)	26	(51%)	25	(50%)	27	(54%)
Hyperplasia, lymphoid			3	(6%)				
Inflammation, subacute	2	(4%)	2	(4%)	1	(2%)	2	(4%)
Follicle, cyst	3	(6%)	1	(2%)	3	(6%)		
Follicular cell, hyperplasia	12	(24%)	17	(33%)	8	(16%)	14	(28%)
General Body System								
None								
Genital System								
Clitoral gland					(2)		(2)	
Ectasia					2	(100%)	2	(100%)
Ovary	(46)		(46)		(48)		(46)	
Angiectasis	11	(24%)	15	(33%)	10	(21%)	7	(15%)
Cyst	12	(26%)	14	(30%)	16	(33%)	15	(33%)
Hemorrhage					1	(2%)		
Hyperplasia	1	(2%)					2	(4%)
Artery, necrosis, fibrinoid	1	(2%)						
Interstitial cell, hyperplasia					1	(2%)	1	(2%)
Uterus	(50)		(50)		(50)		(50)	
Angiectasis	5	(10%)	4	(8%)	7	(14%)	3	(6%)
Hydrometra	18	(36%)	18	(36%)	22	(44%)	21	(42%)
Hyperplasia, cystic	49	(98%)	49	(98%)	46	(92%)	48	(96%)
Hyperplasia, histiocyte			1	(2%)				
Hyperplasia, lymphoid	1	(2%)	3	(6%)	2	(4%)	1	(2%)
Inflammation, suppurative	1	(2%)			4	(8%)	2	(4%)
Metaplasia, squamous	1	(2%)	1	(2%)	3	(6%)	3	(6%)
Myometrium, fibrosis					1	(2%)		

TABLE F5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Hematopoietic System				
Bone marrow	(50)	(51)	(50)	(50)
Angiectasis				1 (2%)
Hypercellularity	7 (14%)	5 (10%)	9 (18%)	6 (12%)
Myelofibrosis				1 (2%)
Lymph node	(50)	(51)	(50)	(50)
Artery, necrosis, fibrinoid	1 (2%)			
Iliac, angiectasis	2 (4%)			
Iliac, hematopoietic cell proliferation			1 (2%)	1 (2%)
Iliac, hemorrhage			1 (2%)	
Iliac, hyperplasia, plasma cell	2 (4%)		1 (2%)	
Iliac, lymphatic, dilatation			1 (2%)	
Mediastinal, hematopoietic cell proliferation			1 (2%)	
Renal, hematopoietic cell proliferation				1 (2%)
Renal, hyperplasia, plasma cell	1 (2%)			1 (2%)
Lymph node, mandibular	(46)	(49)	(50)	(49)
Hematopoietic cell proliferation			1 (2%)	
Hyperplasia, lymphoid	5 (11%)	4 (8%)	2 (4%)	1 (2%)
Hyperplasia, plasma cell		1 (2%)	1 (2%)	
Lymph node, mesenteric	(49)	(47)	(48)	(48)
Hematopoietic cell proliferation	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Hemorrhage	2 (4%)	4 (9%)	5 (10%)	1 (2%)
Hyperplasia, lymphoid	4 (8%)	2 (4%)	1 (2%)	1 (2%)
Hyperplasia, plasma cell	2 (4%)	1 (2%)		
Lymphatic, dilatation		2 (4%)		
Spleen	(49)	(51)	(49)	(50)
Angiectasis				1 (2%)
Congestion		1 (2%)		2 (4%)
Hematopoietic cell proliferation	21 (43%)	17 (33%)	19 (39%)	22 (44%)
Hemorrhage	1 (2%)	1 (2%)		
Necrosis	1 (2%)			
Pigmentation, hemosiderin	5 (10%)	3 (6%)		4 (8%)
Lymphoid follicle, atrophy	1 (2%)	1 (2%)	1 (2%)	4 (8%)
Lymphoid follicle, hyperplasia	4 (8%)	6 (12%)	6 (12%)	5 (10%)
Red pulp, hyperplasia	3 (6%)	2 (4%)	2 (4%)	3 (6%)
Thymus	(48)	(49)	(46)	(45)
Angiectasis	3 (6%)	1 (2%)	5 (11%)	2 (4%)
Cyst	7 (15%)	5 (10%)	6 (13%)	6 (13%)
Depletion	3 (6%)	10 (20%)	9 (20%)	4 (9%)
Ectopic parathyroid gland	1 (2%)			
Hyperplasia, lymphoid	3 (6%)			
Artery, necrosis, fibrinoid	1 (2%)			
Epithelial cell, hyperplasia				1 (2%)
Integumentary System				
Mammary gland	(49)	(50)	(50)	(50)
Hyperplasia, cystic		3 (6%)	4 (8%)	2 (4%)
Skin	(50)	(51)	(50)	(50)
Acanthosis	1 (2%)	3 (6%)		1 (2%)
Exudate		1 (2%)		
Inflammation, chronic		4 (8%)		1 (2%)
Ulcer		1 (2%)		1 (2%)
Subcutaneous tissue, edema	2 (4%)	3 (6%)		

TABLE F5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm		70 ppm		140 ppm		275 ppm	
Musculoskeletal System								
Bone	(50)		(51)		(50)		(50)	
Fibrous osteodystrophy	1	(2%)						
Hyperostosis	6	(12%)	7	(14%)	6	(12%)	7	(14%)
Nervous System								
Brain	(49)		(51)		(50)		(50)	
Compression							1	(2%)
Cyst					1	(2%)		
Hemorrhage					1	(2%)	1	(2%)
Hydrocephalus					1	(2%)	1	(2%)
Inflammation, chronic			1	(2%)	1	(2%)		
Necrosis					2	(4%)		
Thalamus, mineralization	41	(84%)	45	(88%)	44	(88%)	26	(52%)
Respiratory System								
Lung	(50)		(51)		(50)		(50)	
Congestion	2	(4%)	3	(6%)	2	(4%)	3	(6%)
Edema	1	(2%)						
Fibrosis					2	(4%)		
Hemorrhage	2	(4%)	4	(8%)	2	(4%)	5	(10%)
Hyperplasia, lymphoid	10	(20%)	9	(18%)	15	(30%)	13	(26%)
Infiltration cellular, histiocytic	3	(6%)	7	(14%)	5	(10%)	7	(14%)
Leukocytosis					1	(2%)		
Thrombus			1	(2%)	1	(2%)		
Alveolar epithelium, hyperplasia	1	(2%)	1	(2%)	1	(2%)	2	(4%)
Nose	(50)		(51)		(50)		(50)	
Exudate	3	(6%)	5	(10%)	3	(6%)	5	(10%)
Glands, hyperplasia, cystic	5	(10%)	7	(14%)	6	(12%)	5	(10%)
Trachea	(50)		(51)		(49)		(50)	
Inflammation, suppurative					1	(2%)		
Special Senses System								
Eye					(1)		(2)	
Cataract					1	(100%)	1	(50%)
Cornea, inflammation, chronic					1	(100%)		
Retina, atrophy							1	(50%)
Harderian gland	(1)		(3)		(4)		(7)	
Cyst					1	(25%)		
Hyperplasia							1	(14%)
Hyperplasia, focal			2	(67%)	1	(25%)	3	(43%)

TABLE F5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chlorinated Water Study (continued)

	0 ppm	70 ppm	140 ppm	275 ppm
Urinary System				
Kidney	(50)	(51)	(50)	(50)
Casts protein	12 (24%)	10 (20%)	8 (16%)	7 (14%)
Cyst		6 (12%)		5 (10%)
Glomerulosclerosis	2 (4%)	3 (6%)	2 (4%)	
Hemorrhage		1 (2%)	1 (2%)	1 (2%)
Hydronephrosis	3 (6%)	2 (4%)	1 (2%)	
Hyperplasia, lymphoid	21 (42%)	15 (29%)	15 (30%)	18 (36%)
Inflammation, suppurative	1 (2%)			
Metaplasia, osseous	1 (2%)	2 (4%)	2 (4%)	2 (4%)
Mineralization	22 (44%)	6 (12%)	13 (26%)	13 (26%)
Interstitium, pigmentation		1 (2%)	2 (4%)	1 (2%)
Papilla, necrosis	1 (2%)			1 (2%)
Renal tubule, atrophy	4 (8%)	4 (8%)	7 (14%)	10 (20%)
Renal tubule, cytoplasmic alteration		1 (2%)	1 (2%)	
Renal tubule, dilatation	5 (10%)	3 (6%)	4 (8%)	1 (2%)
Renal tubule, necrosis	1 (2%)		2 (4%)	
Renal tubule, pigmentation			1 (2%)	2 (4%)
Renal tubule, regeneration	34 (68%)	34 (67%)	32 (64%)	27 (54%)
Transitional epithelium, hyperplasia	2 (4%)		1 (2%)	
Ureter	(1)			
Dilatation	1 (100%)			
Inflammation, suppurative	1 (100%)			
Urinary bladder	(49)	(50)	(49)	(50)
Dilatation	1 (2%)	1 (2%)		
Edema		1 (2%)	1 (2%)	
Hyperplasia, lymphoid	23 (47%)	18 (36%)	23 (47%)	18 (36%)
Inflammation, chronic		1 (2%)		
Inflammation, subacute	2 (4%)			
Mucosa, hyperplasia	2 (4%)			

APPENDIX G
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR CHLORAMINATED WATER STUDY

TABLE G1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	9
Early deaths				
Natural death	4	3	3	4
Moribund	12	24	13	10
Survivors				
Terminal sacrifice	34	23	34	37
Animals examined microscopically	50	50	50	51
Alimentary System				
Gallbladder	(44)	(50)	(48)	(50)
Papilloma		1 (2%)		
Intestine small, ileum	(48)	(49)	(48)	(49)
Carcinoma	1 (2%)	1 (2%)		
Intestine small, jejunum	(49)	(50)	(50)	(48)
Carcinoma		2 (4%)	3 (6%)	2 (4%)
Hemangiosarcoma		1 (2%)		
Liver	(50)	(50)	(50)	(51)
Hemangioma		1 (2%)		
Hemangiosarcoma	1 (2%)	1 (2%)	4 (8%)	2 (4%)
Hepatoblastoma	1 (2%)			1 (2%)
Hepatocellular carcinoma	9 (18%)	13 (26%)	14 (28%)	10 (20%)
Hepatocellular carcinoma, two, multiple	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Hepatocellular carcinoma, three, multiple	1 (2%)			
Hepatocellular adenoma	8 (16%)	15 (30%)	14 (28%)	11 (22%)
Hepatocellular adenoma, two, multiple	10 (20%)	10 (20%)	1 (2%)	6 (12%)
Hepatocellular adenoma, three, multiple	9 (18%)	7 (14%)	5 (10%)	1 (2%)
Hepatocellular adenoma, four, multiple	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Hepatocellular adenoma, five, multiple			1 (2%)	
Hepatocellular adenoma, greater than five, multiple	1 (2%)		1 (2%)	
Sarcoma	1 (2%)			
Mesentery	(7)	(6)	(2)	(3)
Alveolar/bronchiolar carcinoma, metastatic, lung		1 (17%)		
Fibrosarcoma, metastatic, skeletal muscle	1 (14%)			
Hemangioma		1 (17%)		
Hepatoblastoma, metastatic, liver	1 (14%)			
Salivary glands	(50)	(50)	(50)	(51)
Sarcoma	1 (2%)			

TABLE G1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Alimentary System (continued)				
Stomach, forestomach	(50)	(48)	(50)	(51)
Hepatoblastoma, metastatic, liver	1 (2%)			
Papilloma squamous	1 (2%)			
Stomach, glandular	(50)	(48)	(50)	(51)
Alveolar/bronchiolar carcinoma, metastatic, lung		1 (2%)		
Cardiovascular System				
Heart	(50)	(50)	(50)	(51)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Hemangiosarcoma		1 (2%)		
Sarcoma	1 (2%)			
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(51)
Hepatoblastoma, metastatic, liver	1 (2%)			
Capsule, adenoma	5 (10%)	4 (8%)	4 (8%)	1 (2%)
Adrenal gland, medulla	(49)	(50)	(50)	(51)
Pheochromocytoma benign	1 (2%)		1 (2%)	1 (2%)
Islets, pancreatic	(50)	(50)	(50)	(51)
Adenoma		1 (2%)	1 (2%)	
Thyroid gland	(50)	(49)	(49)	(50)
Follicular cell, adenoma	1 (2%)	2 (4%)	1 (2%)	3 (6%)
General Body System				
Tissue NOS		(1)		
Genital System				
Epididymis	(50)	(50)	(50)	(51)
Testes	(50)	(50)	(50)	(51)
Hemangioma		1 (2%)		
Interstitial cell, adenoma	1 (2%)	1 (2%)	2 (4%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(51)
Hemangiosarcoma	1 (2%)	1 (2%)	1 (2%)	
Lymph node	(50)	(50)	(50)	(51)
Inguinal, renal, popliteal, sarcoma	1 (2%)			
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung		1 (2%)	1 (2%)	
Mediastinal, hepatoblastoma, metastatic, liver	1 (2%)			
Mediastinal, hepatocellular carcinoma, metastatic, liver	1 (2%)			1 (2%)

TABLE G1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Hematopoietic System (continued)				
Lymph node, mandibular	(49)	(46)	(50)	(48)
Lymph node, mesenteric	(46)	(50)	(50)	(50)
Spleen	(50)	(50)	(50)	(51)
Hemangioma	1 (2%)			
Hemangiosarcoma	3 (6%)		1 (2%)	
Hepatoblastoma, metastatic, liver	1 (2%)			
Thymus	(47)	(41)	(46)	(48)
Hemangioma	1 (2%)			
Integumentary System				
Skin	(50)	(50)	(50)	(51)
Neoplasm NOS			1 (2%)	
Subcutaneous tissue, fibrosarcoma				1 (2%)
Subcutaneous tissue, hemangiosarcoma		1 (2%)	1 (2%)	
Subcutaneous tissue, lipoma			1 (2%)	
Musculoskeletal System				
Skeletal muscle	(3)			(1)
Fibrosarcoma	1 (33%)			
Hemangiosarcoma				1 (100%)
Hepatoblastoma, metastatic, liver	1 (33%)			
Sarcoma	1 (33%)			
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(51)
Alveolar/bronchiolar adenoma	14 (28%)	9 (18%)	10 (20%)	4 (8%)
Alveolar/bronchiolar adenoma, two, multiple	1 (2%)	1 (2%)	1 (2%)	
Alveolar/bronchiolar carcinoma	8 (16%)	7 (14%)	7 (14%)	3 (6%)
Alveolar/bronchiolar carcinoma, two, multiple		2 (4%)		
Fibrosarcoma, metastatic, skeletal muscle	1 (2%)			
Hepatoblastoma, metastatic, liver	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	3 (6%)	3 (6%)	2 (4%)	2 (4%)
Sarcoma	1 (2%)			
Mediastinum, hemangioma	1 (2%)	1 (2%)		
Special Senses System				
Harderian gland	(3)	(1)	(1)	(6)
Adenoma	3 (100%)	1 (100%)	1 (100%)	5 (83%)

TABLE G1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Urinary System				
Kidney	(50)	(50)	(50)	(51)
Hepatoblastoma, metastatic, liver	1 (2%)			
Hepatocellular carcinoma, metastatic, liver				1 (2%)
Sarcoma	1 (2%)			
Renal tubule, adenoma				2 (4%)
Systemic Lesions				
Multiple organs[a]	(50)	(50)	(50)	(51)
Lymphoma malignant lymphocytic		2 (4%)		
Lymphoma malignant mixed		3 (6%)	3 (6%)	2 (4%)
Tumor Summary				
Total animals with primary neoplasms[b]	42	49	41	37
Total primary neoplasms	95	95	81	58
Total animals with benign neoplasms	39	38	32	27
Total benign neoplasms	60	58	45	35
Total animals with malignant neoplasms	22	28	28	19
Total malignant neoplasms	35	37	35	23
Total animals with secondary neoplasms[c]	4	4	3	2
Total secondary neoplasms	14	6	4	4
Total animals with neoplasms uncertain-Benign or malignant			1	
Total uncertain neoplasms			1	

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 0 ppm

Number of Days on Study	5 4 1	5 5 1	5 5 8	5 5 9	5 7 9	6 2 5	6 5 7	6 6 1	6 7 1	6 8 1	6 9 1	6 9 1	7 2 7	7 3 0	7 3 0	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	0 0 3 1	0 2 0 1	0 0 7 1	0 2 3 1	5 3 3 1	0 3 9 1	5 0 4 1	5 2 6 1	5 3 2 1	5 2 8 1	0 1 3 1	5 2 3 1	0 1 9 1	5 4 2 1	5 4 3 1	5 3 5 1	0 0 1 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	5 2 7 1	5 2 9 1	5 3 0 1	5 3 1 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Intestine small, jejunum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Hepatoblastoma											X														
Hepatocellular carcinoma	X	X			X		X			X						X			X						
Hepatocellular carcinoma, two, multiple			X																						
Hepatocellular carcinoma, three, multiple														X											
Hepatocellular adenoma					X											X							X		
Hepatocellular adenoma, two, multiple			X								X		X						X						X
Hepatocellular adenoma, three, multiple									X	X					X		X	X				X			
Hepatocellular adenoma, four, multiple																									
Hepatocellular adenoma, greater than five, multiple																									
Sarcoma							X																		
Mesentery	+									+	+											+			
Fibrosarcoma, metastatic, skeletal muscle	X																								
Hepatoblastoma, metastatic, liver											X														
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatoblastoma, metastatic, liver											X														
Papilloma squamous											X														
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth					+	+		+	+	+		+						+	+	+					

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

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 1 1	0 2 1 1	0 8 1 1	0 1 1 1	0 1 1 1	0 1 2 1	0 1 4 1	0 1 5 1	0 1 6 1	0 1 7 1	0 1 8 1	0 2 4 1	0 2 5 1	0 3 4 1	5 3 6 1	5 3 7 1	5 3 8 1	5 4 4 1	5 4 5 1	5 3 9 1	5 4 1 1	5 2 1 1	5 2 2 1	5 2 4 1	5 2 5 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	44
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma		X																								1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																		X								1
Hepatoblastoma																										1
Hepatocellular carcinoma													X	X												9
Hepatocellular carcinoma, two, multiple						X																				2
Hepatocellular carcinoma, three, multiple																										1
Hepatocellular adenoma		X							X			X									X	X				8
Hepatocellular adenoma, two, multiple					X		X			X	X				X											10
Hepatocellular adenoma, three, multiple				X		X													X							9
Hepatocellular adenoma, four, multiple													X										X			2
Hepatocellular adenoma, greater than five, multiple																	X									1
Sarcoma																										1
Mesentery						+				+														+		7
Fibrosarcoma, metastatic, skeletal muscle																										1
Hepatoblastoma, metastatic, liver																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatoblastoma, metastatic, liver																										1
Papilloma squamous																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth	+	+		+		+				+			+				+							+		17

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	5 4 1	5 5 1	5 5 1	5 5 1	5 7 1	6 2 1	6 5 1	6 6 1	6 7 1	6 8 1	6 9 1	6 9 1	7 2 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	0 0 3 1	0 2 0 1	0 0 7 1	0 2 3 1	5 3 3 1	0 3 9 1	5 4 0 1	5 2 6 1	5 3 2 1	5 2 8 1	0 1 3 1	5 2 3 1	0 1 9 1	5 4 2 1	5 4 3 1	5 3 5 1	0 0 1 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	5 2 7 1	5 2 9 1	5 3 0 1	5 3 1 1
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatoblastoma, metastatic, liver											X														
Capsule, adenoma										X															
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma											X														
General Body System																									
None																									
Genital System																									
Coagulating gland								+					+		+			+	+						
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland																						+		+	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma									X																
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Inguinal, renal, popliteal, sarcoma							X																		
Mediastinal, hepatoblastoma, metastatic, liver											X														
Mediastinal, hepatocellular carcinoma, metastatic, liver	X																								
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma														X											
Hemangiosarcoma																									
Hepatoblastoma, metastatic, liver											X														
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 1 1	0 2 1 1	0 2 8 1	0 1 0 1	0 1 1 1	0 1 2 1	0 1 4 1	0 1 5 1	0 1 6 1	0 1 7 1	0 1 8 1	0 2 4 1	0 2 5 1	0 3 4 1	5 3 6 1	5 3 7 1	5 3 8 1	5 4 4 1	5 4 5 1	5 3 9 1	5 4 1 1	5 2 1 1	5 2 2 1	5 2 4 1	5 2 5 1	**Total Tissues/ Tumors**
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																										1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatoblastoma, metastatic, liver																										1
Capsule, adenoma							X	X							X							X				5
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign																						X				1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	48
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																										1
General Body System																										
None																										
Genital System																										
Coagulating gland					+		+										+									8
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland		+									I					+										4
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell, adenoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																						X				1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Inguinal, renal, popliteal, sarcoma																										1
Mediastinal, hepatoblastoma, metastatic, liver																										1
Mediastinal, hepatocellular carcinoma, metastatic, liver																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	49
Lymph node, mesenteric	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Hemangiosarcoma																		X	X			X				3
Hepatoblastoma, metastatic, liver																										1
Thymus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Hemangioma		X																								1

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	5 4 1	5 5 1	5 5 1	5 5 1	5 7 1	6 2 1	6 5 1	6 6 1	6 7 1	6 8 1	6 9 1	6 9 1	7 2 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	0 0 3 1	0 2 0 1	0 0 7 1	0 2 3 1	5 3 3 1	0 3 9 1	5 4 0 1	5 2 6 1	5 3 2 1	5 2 8 1	0 1 3 1	5 2 3 1	0 1 9 1	5 4 2 1	5 4 3 1	5 3 5 1	0 0 1 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	5 2 7 1	5 2 9 1	5 3 0 1	5 3 1 1
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+						+				+														
Fibrosarcoma	X																								
Hepatoblastoma, metastatic, liver											X														
Sarcoma							X																		
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma	X	X	X			X								X		X	X								X
Alveolar/bronchiolar adenoma, two, multiple																									
Alveolar/bronchiolar carcinoma				X						X			X				X								
Fibrosarcoma, metastatic, skeletal muscle	X																								
Hepatoblastoma, metastatic, liver											X														
Hepatocellular carcinoma, metastatic, liver	X	X	X																						
Sarcoma							X																		
Mediastinum, hemangioma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatoblastoma, metastatic, liver											X														
Sarcoma							X																		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 2 1 1	0 2 2 1	0 0 8 1	0 1 0 1	0 1 1 1	0 1 2 1	0 1 4 1	0 1 5 1	0 1 6 1	0 1 7 1	0 1 8 1	0 2 4 1	0 2 5 1	0 3 4 1	5 3 6 1	5 3 7 1	5 3 8 1	5 4 4 1	5 4 5 1	5 4 9 1	5 3 1 1	5 4 1 1	5 2 1 1	5 2 2 1	5 2 4 1	5 2 5 1	**Total Tissues/ Tumors**
Integumentary System																											
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																											3
Fibrosarcoma																											1
Hepatoblastoma, metastatic, liver																											1
Sarcoma																											1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma										X	X		X	X							X			X		14
Alveolar/bronchiolar adenoma, two, multiple																										X	1
Alveolar/bronchiolar carcinoma								X					X		X					X							8
Fibrosarcoma, metastatic, skeletal muscle																											1
Hepatoblastoma, metastatic, liver																											1
Hepatocellular carcinoma, metastatic, liver																											3
Sarcoma																											1
Mediastinum, hemangioma								X																			1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																											
Harderian gland						+									+							+					3
Adenoma						X									X							X					3
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatoblastoma, metastatic, liver																											1
Sarcoma																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 50 ppm

Number of Days on Study	4 9 0	5 5 8	5 5 9	5 5 9	5 6 5	6 3 1	6 3 6	6 5 2	6 7 5	6 8 1	6 8 6	6 8 6	6 9 1	6 9 1	6 9 8	6 9 8	6 9 8	7 0 2	7 2 6	7 2 7	7 2 7	7 2 8	7 3 1	7 3 2	7 3 2
Carcass ID Number	1 1 6 1	1 2 0 1	1 0 7 1	1 0 8 1	6 4 6 1	6 4 2 1	6 3 0 1	1 2 9 1	6 3 1 1	6 4 8 1	1 2 4 1	1 2 7 1	6 2 6 1	6 4 0 1	1 0 6 1	1 2 6 1	1 2 6 1	6 2 8 1	1 1 5 1	1 1 0 1	1 1 7 1	1 1 4 1	6 4 1 1	6 2 7 1	6 3 2 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma																									
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									X
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma					X										X										
Hemangiosarcoma																X									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma													X												
Hemangiosarcoma																									X
Hepatocellular carcinoma		X		X					X			X			X	X		X		X					
Hepatocellular carcinoma, two, multiple																	X				X				
Hepatocellular adenoma									X				X			X		X			X		X		
Hepatocellular adenoma, two, multiple							X															X		X	X
Hepatocellular adenoma, three, multiple				X							X									X					
Hepatocellular adenoma, four, multiple																									
Mesentery					+			+	+	+															
Alveolar/bronchiolar carcinoma, metastatic, lung									X																
Hemangioma										X															
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung									X																
Tooth			+		+	+							+						+			+			
Cardiovascular System																									
Blood vessel														+											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma											X														

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 2	7 3 2	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	
Carcass ID Number	6 4 3 1	6 4 4 1	6 4 5 1	6 4 7 1	6 4 9 1	1 1 8 1	1 1 9 1	1 2 1 1	1 2 2 1	1 2 3 1	1 1 2 1	1 1 3 1	1 1 0 1	1 2 5 1	6 3 3 1	6 3 4 1	6 3 5 1	6 3 6 1	6 3 7 1	6 5 0 1	1 0 9 1	1 1 1 1	6 3 8 1	6 3 9 1	6 2 9 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+		49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Papilloma																				X						1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+		48
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+		49
Carcinoma																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Carcinoma																										2
Hemangiosarcoma																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Hemangioma																										1
Hemangiosarcoma																										1
Hepatocellular carcinoma		X		X		X										X						X				13
Hepatocellular carcinoma, two, multiple																										2
Hepatocellular adenoma	X	X			X	X	X			X				X								X		X		15
Hepatocellular adenoma, two, multiple			X	X					X	X		X			X											10
Hepatocellular adenoma, three, multiple																X			X	X	X					7
Hepatocellular adenoma, four, multiple													X				X									2
Mesentery										+						+										6
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Hemangioma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+		48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+		48
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+		48
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Tooth					+			+		+		+										+				11
Cardiovascular System																										
Blood vessel																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Hemangiosarcoma																										1

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	4 9 0	5 5 8	5 5 9	5 5 9	5 6 5	6 3 1	6 3 6	6 5 2	6 7 5	6 8 1	6 8 6	6 8 6	6 9 1	6 9 1	6 9 1	6 9 8	6 9 8	6 9 8	7 0 2	7 2 6	7 2 7	7 2 7	7 2 8	7 3 1	7 3 2	7 3 2
Carcass ID Number	1 1 6 1	1 2 0 1	1 0 7 1	1 0 8 1	6 4 6 1	6 4 2 1	6 3 0 1	1 2 9 1	6 3 1 1	6 4 8 1	1 2 4 1	1 2 7 1	6 2 6 1	6 4 0 1	1 0 6 1	1 2 6 1	1 2 8 1	1 2 8 1	6 2 5 1	1 1 0 1	1 1 7 1	1 1 4 1	6 4 1 1	6 2 7 1	6 3 2 1	
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma								X														X				
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																										
General Body System																										
Tissue NOS																			+							
Genital System																										
Coagulating gland						+													+			+				
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland				+		+	+	+							+											
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																										
Interstitial cell, adenoma																										
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																										X
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung								X																		
Lymph node, mandibular	+	I	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	M	+	+	M	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	M

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 2	7 3 2	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	
Carcass ID Number	6 4 3 1	6 4 4 1	6 4 5 1	6 4 7 1	6 4 9 1	1 1 8 1	1 1 9 1	1 2 1 1	1 2 2 1	1 2 3 1	1 1 2 1	1 1 3 1	1 3 0 1	1 2 5 1	6 3 3 1	6 3 4 1	6 3 5 1	6 3 6 1	6 3 7 1	6 5 0 1	6 0 9 1	1 1 1 1	6 3 8 1	6 3 9 1	6 2 9 1	**Total Tissues/ Tumors**
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma										X														X		4
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma													X													1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	M	+		47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	I		45
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+		49
Follicular cell, adenoma											X	X														2
General Body System																										
Tissue NOS																										1
Genital System																										
Coagulating gland	+							+			+				+								+			8
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland			+		+						+					+									+	10
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma		X																								1
Interstitial cell, adenoma																		X								1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	46
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	M	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	41

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	4 9 0	5 5 8	5 5 9	5 5 9	5 6 5	6 3 1	6 3 6	6 5 2	6 7 5	6 8 1	6 8 6	6 8 6	6 9 1	6 9 1	6 9 8	6 9 8	6 9 8	7 0 2	7 2 6	7 2 7	7 2 7	7 2 8	7 3 1	7 3 2	7 3 2
Carcass ID Number	1 1 6 1	1 2 0 1	1 0 7 1	1 0 8 1	6 4 6 1	6 4 2 1	6 3 0 1	1 2 9 1	6 3 1 1	6 4 8 1	1 2 4 1	1 2 7 1	6 2 6 1	6 4 0 1	1 0 6 1	1 2 6 1	1 2 8 1	6 2 8 1	1 2 5 1	1 1 0 1	1 1 7 1	1 1 4 1	6 4 1 1	6 2 7 1	6 3 2 1
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangiosarcoma																									X
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																				X			X		
Alveolar/bronchiolar adenoma, two, multiple																									X
Alveolar/bronchiolar carcinoma	X							X			X			X							X			X	
Alveolar/bronchiolar carcinoma, two, multiple																									
Hepatocellular carcinoma, metastatic, liver									X		X										X				
Mediastinum, hemangioma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																				+					
Adenoma																				X					
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic						X	X																		
Lymphoma malignant mixed																			X						

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 2	7 3 2	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	
Carcass ID Number	6 4 3 1	6 4 4 1	6 4 5 1	6 4 7 1	6 4 9 1	1 1 8 1	1 1 9 1	1 2 1 1	1 2 2 1	1 2 3 1	1 1 2 1	1 1 3 1	1 3 0 1	1 2 5 1	6 3 3 1	6 3 4 1	6 3 5 1	6 3 6 1	6 3 7 1	6 5 0 1	1 0 9 1	1 1 1 1	6 3 8 1	6 3 9 1	6 2 9 1	**Total Tissues/ Tumors**
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, hemangiosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X		X	X	X										X	X	X								9
Alveolar/bronchiolar adenoma, two, multiple																										1
Alveolar/bronchiolar carcinoma																									X	7
Alveolar/bronchiolar carcinoma, two, multiple	X																						X			2
Hepatocellular carcinoma, metastatic, liver																										3
Mediastinum, hemangioma																X										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland																										1
Adenoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										2
Lymphoma malignant mixed			X					X																		3

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 100 ppm

Number of Days on Study	5 6 2	5 6 5	5 8 1	6 1 8	6 3 8	6 7 7	6 7 7	6 8 1	6 9 1	6 9 1	6 9 8	6 9 9	7 2 7	7 2 7	7 3 0	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 5	7 3 5	7 3 5
Carcass ID Number	6 0 9 1	6 0 8 1	0 8 0 1	0 7 8 1	5 9 7 1	0 7 4 1	0 8 1 1	0 8 7 1	6 0 1 1	6 0 7 1	0 7 5 1	0 7 6 1	0 7 7 1	0 8 2 1	6 1 2 1	5 9 3 1	0 9 5 1	6 0 3 1	6 0 4 1	6 0 5 1	6 0 6 1	6 1 5 1	0 8 3 1	0 8 4 1	0 8 5 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Gallbladder	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma			X							X															
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma				X							X		X												
Hepatocellular carcinoma	X	X				X			X	X		X			X	X						X			
Hepatocellular carcinoma, two, multiple								X																	
Hepatocellular adenoma					X		X				X					X		X				X			X
Hepatocellular adenoma, two, multiple																									
Hepatocellular adenoma, three, multiple										X					X										
Hepatocellular adenoma, four, multiple																									
Hepatocellular adenoma, five, multiple																			X						
Hepatocellular adenoma, greater than five, multiple																					X				
Mesentery	+																								
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth											+								+		+				
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung					X																				

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 8 6 1	0 8 1 1	0 7 9 1	0 8 9 1	0 9 0 1	0 9 1 1	0 9 2 1	0 9 3 1	0 9 4 1	0 9 8 1	5 9 9 1	6 0 0 1	6 0 2 1	6 1 0 1	6 1 1 1	6 1 3 1	6 1 4 1	0 7 1 1	0 7 2 1	0 7 3 1	5 9 1 1	5 9 2 1	5 9 4 1	5 9 5 1	5 9 6 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma										X																3
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma											X															4
Hepatocellular carcinoma		X	X	X			X							X												14
Hepatocellular carcinoma, two, multiple																										1
Hepatocellular adenoma		X				X							X								X		X	X	X	14
Hepatocellular adenoma, two, multiple											X															1
Hepatocellular adenoma, three, multiple													X						X			X				5
Hepatocellular adenoma, four, multiple												X														1
Hepatocellular adenoma, five, multiple																										1
Hepatocellular adenoma, greater than five, multiple																										1
Mesentery												+														2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth							+					+														5
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	5 6 2	5 6 5	5 6 1	6 1 8	6 3 8	6 7 7	6 7 7	6 8 1	6 9 1	6 9 1	6 9 8	6 9 9	7 2 7	7 2 7	7 3 0	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 5	7 3 5	7 3 5
Carcass ID Number	6 0 9 1	6 0 8 1	0 0 1 1	0 8 1 1	5 9 7 1	0 7 4 1	0 8 1 1	0 8 7 1	6 0 1 1	6 0 7 1	0 7 5 1	0 7 6 1	0 7 7 1	0 7 7 1	6 8 2 1	5 1 2 1	0 9 3 1	6 9 5 1	6 0 3 1	6 0 4 1	6 0 5 1	6 0 6 1	6 1 5 1	0 8 3 1	0 8 4 1	0 8 5 1
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma													X							X					
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma						X																			
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Follicular cell, adenoma																	X								
General Body System																									
None																									
Genital System																									
Coagulating gland														+					+						
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland								+					+							+					
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma											X														
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																						X			
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung					X																				
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm NOS													X												
Subcutaneous tissue, hemangiosarcoma																						X			
Subcutaneous tissue, lipoma																			X						

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 8 6 1	0 8 8 1	0 7 9 1	0 8 9 1	0 9 0 1	0 9 1 1	0 9 2 1	0 9 3 1	0 9 4 1	0 9 8 1	5 9 9 1	5 9 0 1	6 0 0 1	6 0 2 1	6 1 0 1	6 1 1 1	6 1 3 1	6 1 4 1	0 7 1 1	0 7 2 1	0 7 3 1	5 9 1 1	5 9 2 1	5 9 4 1	5 9 5 1	5 9 6 1	**Total Tissues/ Tumors**
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma						X														X							4
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																			X								1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																											1
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell, adenoma																											1
General Body System																											
None																											
Genital System																											
Coagulating gland					+		+								+												5
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+																		+	+							6
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell, adenoma																										X	2
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																											1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, alveolar/bronchiolar carcinoma, metastatic, lung																											1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																											1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	46
Integumentary System																											
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplasm NOS																											1
Subcutaneous tissue, hemangiosarcoma																											1
Subcutaneous tissue, lipoma																											1

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	5 6 2	5 6 5	5 8 1	6 1 8	6 3 8	6 7 7	6 7 7	6 8 1	6 9 1	6 9 1	6 9 8	6 9 9	7 2 7	7 2 7	7 3 0	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 5	7 3 5	7 3 5
Carcass ID Number	6 0 9 1	6 0 8 1	0 8 0 1	0 8 7 1	5 9 7 1	0 7 4 1	0 8 1 1	0 8 7 1	6 0 1 1	6 0 7 1	0 7 5 1	0 7 6 1	0 7 7 1	0 7 8 1	6 1 2 1	5 9 2 1	0 9 3 1	6 0 5 1	6 0 3 1	6 0 4 1	6 0 5 1	6 0 6 1	6 1 5 1	0 8 3 1	0 8 4 1	0 8 5 1
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma									X									X			X				
Alveolar/bronchiolar adenoma, two, multiple																									
Alveolar/bronchiolar carcinoma	X				X		X											X			X				
Hepatocellular carcinoma, metastatic, liver						X		X																	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed										X									X						

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 8 6 1	0 8 8 1	0 7 9 1	0 8 9 1	0 9 0 1	0 9 1 1	0 9 2 1	0 9 3 1	0 9 4 1	0 9 8 1	5 9 9 1	5 9 0 1	6 0 0 1	6 0 2 1	6 0 0 1	6 1 1 1	6 1 3 1	6 1 4 1	6 0 1 1	0 7 2 1	0 7 3 1	5 9 1 1	5 9 2 1	5 9 4 1	5 9 5 1	5 9 6 1	**Total Tissues/ Tumors**
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X	X			X	X															X	X		X		10
Alveolar/bronchiolar adenoma, two, multiple												X															1
Alveolar/bronchiolar carcinoma													X	X													7
Hepatocellular carcinoma, metastatic, liver																											2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																											
Harderian gland								+																			1
Adenoma								X																			1
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed			X																								3

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 200 ppm

Number of Days on Study	3 5 3	4 2 6	4 4 3	5 8 6	5 8 6	6 2 5	6 3 8	6 6 6	6 7 5	7 2 6	7 2 6	7 2 7	7 3 1	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	0 6 8 1	0 3 7 1	0 5 6 1	5 5 8 1	5 6 3 1	0 4 1 1	5 6 7 1	0 5 9 1	5 6 8 1	0 3 8 1	0 4 6 1	0 5 7 1	5 7 2 1	5 6 2 1	0 6 0 1	5 6 4 1	5 6 5 1	5 6 6 1	5 6 8 1	0 8 0 1	0 5 4 1	0 5 5 1	0 5 8 1	0 4 2 1	0 4 3 1	0 4 4 1	0 4 5 1
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	M	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	M	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma													X		X											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma					X				X																	
Hepatoblastoma													X													
Hepatocellular carcinoma			X	X			X												X		X			X		X
Hepatocellular carcinoma, two, multiple									X																	
Hepatocellular adenoma	X		X			X			X						X				X							
Hepatocellular adenoma, two, multiple														X		X										
Hepatocellular adenoma, three, multiple								X																		
Hepatocellular adenoma, four, multiple																										
Mesentery										+																
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth									+																	
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																										
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																						X				
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Pituitary gland	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Follicular cell, adenoma																						X				

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	0 4 7 1	0 4 8 1	0 4 9 1	0 5 0 1	0 5 1 1	0 5 2 1	0 5 3 1	0 3 9 1	0 4 0 1	0 3 6 1	5 5 6 1	5 5 7 1	5 5 9 1	5 6 0 1	5 6 1 1	5 6 9 1	5 7 0 1	5 7 1 1	5 7 3 1	5 7 4 1	5 7 5 1	5 7 6 1	5 7 7 1	5 7 8 1	5 7 9 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Gallbladder	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma																										2
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hemangiosarcoma																										2
Hepatoblastoma																										1
Hepatocellular carcinoma			X				X								X											10
Hepatocellular carcinoma, two, multiple																										1
Hepatocellular adenoma					X		X										X	X						X		11
Hepatocellular adenoma, two, multiple								X					X			X									X	6
Hepatocellular adenoma, three, multiple																										1
Hepatocellular adenoma, four, multiple																			X							1
Mesentery			+				+																			3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tooth														+		+										3
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Capsule, adenoma																X										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma						X															X					3

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	3 5 3	4 2 6	4 4 3	5 8 6	5 8 6	6 2 5	6 3 8	6 6 6	6 7 5	7 2 6	7 2 6	7 2 7	7 3 1	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	0 6 8 1	0 3 7 1	0 5 6 1	5 5 8 1	5 6 3 1	0 4 1 1	5 6 7 1	0 5 9 1	5 6 8 1	0 3 8 1	0 4 6 1	0 5 7 1	5 7 2 1	5 6 2 1	0 6 0 1	5 6 4 1	5 6 5 1	5 6 6 1	5 6 8 1	5 8 0 1	0 5 4 1	0 5 5 1	0 5 8 1	0 4 2 1	0 4 3 1	0 4 4 1	0 4 5 1
General Body System																										
None																										
Genital System																										
Coagulating gland																			+							
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland				+															+		+					
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																										
Blood																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, hepatocellular carcinoma, metastatic, liver							X																			
Lymph node, mandibular	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Lymph node, mesenteric	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma						X																				
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle				+																						
Hemangiosarcoma				X																						
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	0 4 7 1	0 4 8 1	0 4 9 1	0 5 0 1	0 5 1 1	0 5 2 1	0 5 3 1	0 3 9 1	0 4 0 1	0 3 6 1	5 5 6 1	5 5 7 1	5 5 9 1	5 6 0 1	5 6 1 1	5 6 9 1	5 7 0 1	5 7 1 1	5 7 3 1	5 7 4 1	5 7 5 1	5 7 6 1	5 7 7 1	5 7 8 1	5 7 9 1	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Coagulating gland																		+								2
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland							+		+					+					+							7
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hematopoietic System																										
Blood																			+							1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Mediastinal, hepatocellular carcinoma, metastatic, liver																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	M	+	48
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Subcutaneous tissue, fibrosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Skeletal muscle																										1
Hemangiosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	3 5 3	4 2 6	4 4 3	5 8 6	5 8 6	6 2 5	6 3 8	6 6 6	6 7 5	7 2 6	7 2 6	7 2 7	7 3 1	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	0 6 8 1	0 3 7 1	0 5 6 1	5 5 8 1	5 6 3 1	0 4 1 1	5 6 7 1	0 5 9 1	5 6 8 1	0 3 8 1	0 4 6 1	0 5 7 1	5 7 2 1	5 6 2 1	0 6 0 1	5 6 4 1	5 6 5 1	5 6 6 1	5 8 0 1	0 5 4 1	0 5 5 1	0 5 4 1	0 4 2 1	0 4 3 1	0 4 4 1	0 4 5 1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma						X		X																		
Alveolar/bronchiolar carcinoma										X					X											
Hepatocellular carcinoma, metastatic, liver				X			X																			
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Harderian gland													+			+		+								
Adenoma													X			X		X								
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver							X																			
Renal tubule, adenoma															X											
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed												X														

TABLE G2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	0 4 7 1	0 4 8 1	0 4 9 1	0 5 0 1	0 5 1 1	0 5 2 1	0 5 3 1	0 3 9 1	0 4 0 1	0 3 6 1	5 5 6 1	5 5 7 1	5 5 9 1	5 6 0 1	5 6 1 1	5 6 9 1	5 7 0 1	5 7 1 1	5 7 3 1	5 7 4 1	5 7 5 1	5 7 6 1	5 7 7 1	5 7 8 1	5 7 9 1	**Total Tissues/ Tumors**
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Alveolar/bronchiolar adenoma															X								X			4
Alveolar/bronchiolar carcinoma						X																				3
Hepatocellular carcinoma, metastatic, liver																										2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																										
Harderian gland					+				+													+				6
Adenoma									X													X				5
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular carcinoma, metastatic, liver																										1
Renal tubule, adenoma													X													2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymphoma malignant mixed								X																		2

TABLE G3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Adrenal Cortex: Adenoma				
Overall rates[a]	5/50 (10%)	4/50 (8%)	4/50 (8%)	1/51 (2%)
Adjusted rates[b]	13.9%	13.9%	11.2%	2.7%
Terminal rates[c]	4/34 (12%)	2/23 (9%)	3/34 (9%)	1/37 (3%)
First incidence (days)	681	652	727	733 (T)
Life table tests[d]	P=0.057N	P=0.598	P=0.497N	P=0.089N
Logistic regression tests[d]	P=0.069N	P=0.523N	P=0.483N	P=0.095N
Cochran-Armitage test[d]	P=0.076N			
Fisher exact test[d]		P=0.500N	P=0.500N	P=0.098N
Harderian Gland: Adenoma				
Overall rates	3/50 (6%)	1/50 (2%)	1/50 (2%)	5/51 (10%)
Adjusted rates	8.8%	3.2%	2.9%	13.1%
Terminal rates	3/34 (9%)	0/23 (0%)	1/34 (3%)	4/37 (11%)
First incidence (days)	733 (T)	727	733 (T)	731
Life table tests	P=0.238	P=0.435N	P=0.304N	P=0.405
Logistic regression tests	P=0.216	P=0.365N	P=0.304N	P=0.404
Cochran-Armitage test	P=0.169			
Fisher exact test		P=0.309N	P=0.309N	P=0.369
Liver: Hepatocellular Adenoma				
Overall rates	30/50 (60%)	34/50 (68%)	23/50 (46%)	19/51 (37%)
Adjusted rates	71.1%	89.2%	57.0%	43.4%
Terminal rates	22/34 (65%)	19/23 (83%)	17/34 (50%)	13/37 (35%)
First incidence (days)	558	559	638	353
Life table tests	P<0.001N	P=0.017	P=0.131N	P=0.019N
Logistic regression tests	P=0.002N	P=0.197	P=0.087N	P=0.019N
Cochran-Armitage test	P=0.002N			
Fisher exact test		P=0.266	P=0.115N	P=0.018N
Liver: Hepatocellular Carcinoma				
Overall rates	12/50 (24%)	15/50 (30%)	15/50 (30%)	11/51 (22%)
Adjusted rates	26.9%	39.6%	33.8%	25.7%
Terminal rates	4/34 (12%)	4/23 (17%)	6/34 (18%)	7/37 (19%)
First incidence (days)	541	558	562	443
Life table tests	P=0.269N	P=0.199	P=0.367	P=0.448N
Logistic regression tests	P=0.335N	P=0.368	P=0.237	P=0.431N
Cochran-Armitage test	P=0.359N			
Fisher exact test		P=0.326	P=0.326	P=0.478N
Liver: Hepatoblastoma or Hepatocellular Carcinoma				
Overall rates	13/50 (26%)	15/50 (30%)	15/50 (30%)	12/51 (24%)
Adjusted rates	28.7%	39.6%	33.8%	27.6%
Terminal rates	4/34 (12%)	4/23 (17%)	6/34 (18%)	7/37 (19%)
First incidence (days)	541	558	562	443
Life table tests	P=0.284N	P=0.262	P=0.446	P=0.444N
Logistic regression tests	P=0.358N	P=0.460	P=0.318	P=0.435N
Cochran-Armitage test	P=0.380N			
Fisher exact test		P=0.412	P=0.412	P=0.477N

TABLE G3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Liver: Hepatocellular Adenoma, Hepatoblastoma, or Hepatocellular Carcinoma				
Overall rates	35/50 (70%)	39/50 (78%)	33/50 (66%)	26/51 (51%)
Adjusted rates	75.8%	90.5%	71.4%	56.0%
Terminal rates	23/34 (68%)	19/23 (83%)	21/34 (62%)	17/37 (46%)
First incidence (days)	541	558	562	353
Life table tests	P=0.006N	P=0.025	P=0.411N	P=0.053N
Logistic regression tests	P=0.007N	P=0.225	P=0.424N	P=0.037N
Cochran-Armitage test	P=0.007N			
Fisher exact test		P=0.247	P=0.415N	P=0.040N
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	15/50 (30%)	10/50 (20%)	11/50 (22%)	4/51 (8%)
Adjusted rates	36.1%	36.1%	31.1%	9.6%
Terminal rates	9/34 (26%)	6/23 (26%)	10/34 (29%)	2/37 (5%)
First incidence (days)	541	727	691	625
Life table tests	P=0.003N	P=0.464N	P=0.252N	P=0.006N
Logistic regression tests	P=0.005N	P=0.182N	P=0.254N	P=0.004N
Cochran-Armitage test	P=0.005N			
Fisher exact test		P=0.178N	P=0.247N	P=0.004N
Lung: Alveolar/bronchiolar Carcinoma				
Overall rates	8/50 (16%)	9/50 (18%)	7/50 (14%)	3/51 (6%)
Adjusted rates	20.7%	25.8%	17.3%	7.7%
Terminal rates	5/34 (15%)	2/23 (9%)	4/34 (12%)	2/37 (5%)
First incidence (days)	559	490	562	726
Life table tests	P=0.041N	P=0.325	P=0.482N	P=0.086N
Logistic regression tests	P=0.052N	P=0.514	P=0.531N	P=0.096N
Cochran-Armitage test	P=0.054N			
Fisher exact test		P=0.500	P=0.500N	P=0.094N
Lung: Alveolar/bronchiolar Adenoma or Alveolar/bronchiolar Carcinoma				
Overall rates	21/50 (42%)	19/50 (38%)	17/50 (34%)	7/51 (14%)
Adjusted rates	47.7%	54.5%	43.5%	16.8%
Terminal rates	12/34 (35%)	8/23 (35%)	13/34 (38%)	4/37 (11%)
First incidence (days)	541	490	562	625
Life table tests	P<0.001N	P=0.362	P=0.275N	P=0.003N
Logistic regression tests	P<0.001N	P=0.410N	P=0.297N	P=0.001N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.419N	P=0.268N	P=0.001N
Small Intestine: Carcinoma				
Overall rates	1/50 (2%)	3/50 (6%)	3/50 (6%)	2/51 (4%)
Adjusted rates	2.9%	8.4%	7.2%	5.2%
Terminal rates	1/34 (3%)	0/23 (0%)	1/34 (3%)	1/37 (3%)
First incidence (days)	733 (T)	565	581	731
Life table tests	P=0.543	P=0.251	P=0.318	P=0.532
Logistic regression tests	P=0.501	P=0.318	P=0.276	P=0.530
Cochran-Armitage test	P=0.486			
Fisher exact test		P=0.309	P=0.309	P=0.508

TABLE G3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Small Intestine (Jejunum): Carcinoma				
Overall rates	0/50 (0%)	2/50 (4%)	3/50 (6%)	2/51 (4%)
Adjusted rates	0.0%	4.9%	7.2%	5.2%
Terminal rates	0/34 (0%)	0/23 (0%)	1/34 (3%)	1/37 (3%)
First incidence (days)	-[e]	565	581	731
Life table tests	P=0.288	P=0.234	P=0.131	P=0.261
Logistic regression tests	P=0.270	P=0.262	P=0.093	P=0.255
Cochran-Armitage test	P=0.244			
Fisher exact test		P=0.247	P=0.121	P=0.252
Thyroid Gland (Follicular Cell): Adenoma				
Overall rates	1/50 (2%)	2/49 (4%)	1/49 (2%)	3/50 (6%)
Adjusted rates	2.5%	9.1%	3.0%	8.3%
Terminal rates	0/34 (0%)	2/22 (9%)	1/33 (3%)	3/36 (8%)
First incidence (days)	691	733 (T)	733 (T)	733 (T)
Life table tests	P=0.302	P=0.394	P=0.758N	P=0.326
Logistic regression tests	P=0.260	P=0.476	P=0.760	P=0.307
Cochran-Armitage test	P=0.240			
Fisher exact test		P=0.492	P=0.747	P=0.309
All Organs: Hemangioma				
Overall rates	3/50 (6%)	4/50 (8%)	0/50 (0%)	0/51 (0%)
Adjusted rates	8.4%	12.4%	0.0%	0.0%
Terminal rates	2/34 (6%)	1/23 (4%)	0/34 (0%)	0/37 (0%)
First incidence (days)	730	675	-	-
Life table tests	P=0.025N	P=0.372	P=0.125N	P=0.110N
Logistic regression tests	P=0.027N	P=0.479	P=0.118N	P=0.106N
Cochran-Armitage test	P=0.029N			
Fisher exact test		P=0.500	P=0.121N	P=0.118N
All Organs: Hemangiosarcoma				
Overall rates	3/50 (6%)	3/50 (6%)	5/50 (10%)	3/51 (6%)
Adjusted rates	8.8%	8.7%	12.6%	6.4%
Terminal rates	3/34 (9%)	0/23 (0%)	2/34 (6%)	0/37 (0%)
First incidence (days)	733 (T)	686	618	586
Life table tests	P=0.532N	P=0.546	P=0.366	P=0.627N
Logistic regression tests	P=0.563	P=0.644	P=0.362	P=0.628N
Cochran-Armitage test	P=0.549			
Fisher exact test		P=0.661N	P=0.357	P=0.652N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	6/50 (12%)	7/50 (14%)	5/50 (10%)	3/51 (6%)
Adjusted rates	17.0%	20.2%	12.6%	6.4%
Terminal rates	5/34 (15%)	1/23 (4%)	2/34 (6%)	0/37 (0%)
First incidence (days)	730	675	618	586
Life table tests	P=0.110N	P=0.327	P=0.496N	P=0.215N
Logistic regression tests	P=0.137N	P=0.469	P=0.486N	P=0.225N
Cochran-Armitage test	P=0.139N			
Fisher exact test		P=0.500	P=0.500N	P=0.234N

TABLE G3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
All Organs: Malignant Lymphoma				
Overall rates	0/50 (0%)	5/50 (10%)	3/50 (6%)	2/51 (4%)
Adjusted rates	0.0%	15.5%	8.1%	5.1%
Terminal rates	0/34 (0%)	2/23 (9%)	2/34 (6%)	1/37 (3%)
First incidence (days)	-	631	691	727
Life table tests	P=0.526	P=0.022	P=0.126	P=0.255
Logistic regression tests	P=0.466	P=0.035	P=0.124	P=0.251
Cochran-Armitage test	P=0.466			
Fisher exact test		P=0.028	P=0.121	P=0.252
All Organs: Benign Tumors				
Overall rates	39/50 (78%)	38/50 (76%)	32/50 (64%)	27/51 (53%)
Adjusted rates	84.6%	97.4%	74.2%	60.9%
Terminal rates	27/34 (79%)	22/23 (96%)	23/34 (68%)	20/37 (54%)
First incidence (days)	541	559	638	353
Life table tests	P<0.001N	P=0.062	P=0.140N	P=0.012N
Logistic regression tests	P=0.002N	P=0.561N	P=0.073N	P=0.007N
Cochran-Armitage test	P=0.002N			
Fisher exact test		P=0.500N	P=0.093N	P=0.007N
All Organs: Malignant Tumors				
Overall rates	22/50 (44%)	28/50 (56%)	28/50 (56%)	19/51 (37%)
Adjusted rates	47.9%	62.0%	56.8%	40.6%
Terminal rates	11/34 (32%)	7/23 (30%)	13/34 (38%)	10/37 (27%)
First incidence (days)	541	490	562	443
Life table tests	P=0.123N	P=0.070	P=0.242	P=0.290N
Logistic regression tests	P=0.187N	P=0.199	P=0.107	P=0.292N
Cochran-Armitage test	P=0.175N			
Fisher exact test		P=0.159	P=0.159	P=0.313N
All Organs: Benign and Malignant Tumors				
Overall rates	42/50 (84%)	49/50 (98%)	41/50 (82%)	37/51 (73%)
Adjusted rates	87.4%	100.0%	83.6%	75.4%
Terminal rates	28/34 (82%)	23/23 (100%)	26/34 (76%)	25/37 (68%)
First incidence (days)	541	490	562	353
Life table tests	P=0.015N	P=0.004	P=0.468N	P=0.141N
Logistic regression tests	P=0.012N	P=0.020	P=0.525N	P=0.121N
Cochran-Armitage test	P=0.011N			
Fisher exact test		P=0.015	P=0.500N	P=0.124N

(T)Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no tumors in animal group

TABLE G4
Historical Incidence of Renal Tubule Adenomas in Untreated Male B6C3F$_1$ Mice[a]

Studies	Incidence in Controls
Historical Incidence at Southern Research Institute	
Feed	
Nitrofurantoin	0/50 (0%)
Rhodamine 6G	1/50 (2%)
Roxarsone	0/50 (0%)
Total	1/150 (1%)
Standard deviation	1.2%
Range	0%-2%
Water	
Chloramine	0/50 (0%)
Overall Historical Incidence	
Feed	
Total	1/563 (0.2%)
Standard deviation	0.6%
Range	0%-2%
Water	
Total	0/129 (0%)

[a] Data as of 15 September 1990

TABLE G5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	9
Early deaths				
Natural death	4	3	3	4
Moribund	12	24	13	10
Survivors				
Terminal sacrifice	34	23	34	37
Animals examined microscopically	50	50	50	51
Alimentary System				
Gallbladder	(44)	(50)	(48)	(50)
Cyst				1 (2%)
Dilatation	1 (2%)	1 (2%)		2 (4%)
Intestine large, cecum	(50)	(49)	(49)	(51)
Hyperplasia, lymphoid				1 (2%)
Intestine large, colon	(49)	(50)	(50)	(51)
Diverticulum	1 (2%)			
Intestine small, duodenum	(49)	(50)	(49)	(49)
Hyperplasia, lymphoid	1 (2%)			
Metaplasia, squamous	1 (2%)			
Intestine small, ileum	(48)	(49)	(48)	(49)
Hyperplasia, lymphoid	1 (2%)			
Liver	(50)	(50)	(50)	(51)
Basophilic focus	3 (6%)	4 (8%)	3 (6%)	5 (10%)
Clear cell focus	11 (22%)	11 (22%)	13 (26%)	4 (8%)
Eosinophilic focus	1 (2%)		2 (4%)	
Hematopoietic cell proliferation			1 (2%)	1 (2%)
Hyperplasia, focal	14 (28%)	21 (42%)	12 (24%)	4 (8%)
Hyperplasia, lymphoid	1 (2%)	1 (2%)		1 (2%)
Infarct				1 (2%)
Inflammation, acute	1 (2%)			
Inflammation, chronic	2 (4%)	2 (4%)	2 (4%)	2 (4%)
Metaplasia, osseous				1 (2%)
Mineralization				1 (2%)
Mixed cell focus	1 (2%)	1 (2%)	3 (6%)	3 (6%)
Centrilobular, necrosis		1 (2%)	2 (4%)	1 (2%)
Hepatocyte, cytomegaly				1 (2%)
Hepatocyte, karyomegaly			1 (2%)	2 (4%)
Hepatocyte, vacuolization cytoplasmic	2 (4%)	1 (2%)	4 (8%)	3 (6%)
Kupffer cell, hyperplasia	4 (8%)	3 (6%)	2 (4%)	4 (8%)
Kupffer cell, pigmentation		3 (6%)	2 (4%)	1 (2%)
Lobules, necrosis	2 (4%)	7 (14%)	6 (12%)	6 (12%)
Mesentery	(7)	(6)	(2)	(3)
Fibrosis	1 (14%)			
Hemorrhage			1 (50%)	
Mineralization	1 (14%)			
Fat, necrosis	4 (57%)	4 (67%)	1 (50%)	3 (100%)

TABLE G5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm		50 ppm		100 ppm		200 ppm	
Alimentary System (continued)								
Pancreas	(50)		(50)		(50)		(51)	
Atrophy	6	(12%)	3	(6%)	5	(10%)	1	(2%)
Cyst					1	(2%)		
Cytoplasmic alteration	4	(8%)			2	(4%)	2	(4%)
Focal cellular change	2	(4%)						
Hyperplasia, lymphoid					2	(4%)		
Inflammation, chronic	1	(2%)						
Salivary glands	(50)		(50)		(50)		(51)	
Atrophy	1	(2%)						
Hyperplasia, lymphoid	18	(36%)	13	(26%)	15	(30%)	10	(20%)
Stomach, forestomach	(50)		(48)		(50)		(51)	
Edema			1	(2%)				
Erosion	1	(2%)						
Hyperkeratosis	1	(2%)						
Inflammation, suppurative					2	(4%)	1	(2%)
Mucosa, hyperplasia	1	(2%)	1	(2%)	2	(4%)	2	(4%)
Stomach, glandular	(50)		(48)		(50)		(51)	
Cyst	9	(18%)	11	(23%)	8	(16%)	9	(18%)
Inflammation, subacute	1	(2%)	2	(4%)	1	(2%)	1	(2%)
Metaplasia, squamous			1	(2%)			1	(2%)
Mineralization	2	(4%)	5	(10%)	3	(6%)	6	(12%)
Mucosa, dysplasia	1	(2%)	1	(2%)				
Tooth	(17)		(11)		(5)		(3)	
Dysplasia	17	(100%)	11	(100%)	5	(100%)	3	(100%)
Cardiovascular System								
Blood vessel			(1)					
Hypertrophy			1	(100%)				
Inflammation, chronic			1	(100%)				
Heart	(50)		(50)		(50)		(51)	
Epicardium, inflammation, chronic	2	(4%)			1	(2%)		
Myocardium, fibrosis	1	(2%)						
Myocardium, inflammation, chronic	3	(6%)					1	(2%)
Myocardium, mineralization			2	(4%)				
Endocrine System								
Adrenal gland, cortex	(50)		(50)		(50)		(51)	
Accessory adrenal cortical nodule	3	(6%)	4	(8%)	7	(14%)	7	(14%)
Atrophy					1	(2%)		
Basophilic focus	2	(4%)					2	(4%)
Clear cell focus	3	(6%)	7	(14%)	3	(6%)	3	(6%)
Cyst			1	(2%)				
Developmental malformation					1	(2%)		
Hyperplasia, diffuse			1	(2%)				
Hyperplasia, focal	28	(56%)	24	(48%)	31	(62%)	20	(39%)
Hypertrophy, focal	2	(4%)	1	(2%)	1	(2%)	1	(2%)
Mineralization	1	(2%)						
Capsule, hyperplasia	10	(20%)	11	(22%)	6	(12%)	4	(8%)
Adrenal gland, medulla	(49)		(50)		(50)		(51)	
Atrophy					1	(2%)		
Hyperplasia	3	(6%)			1	(2%)		

TABLE G5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm		50 ppm		100 ppm		200 ppm	
Endocrine System (continued)								
Islets, pancreatic	(50)		(50)		(50)		(51)	
Cyst			1	(2%)				
Hyperplasia	31	(62%)	27	(54%)	26	(52%)	15	(29%)
Parathyroid gland	(49)		(47)		(46)		(46)	
Cyst	1	(2%)	2	(4%)			1	(2%)
Pituitary gland	(48)		(45)		(49)		(50)	
Pars distalis, cyst	2	(4%)	3	(7%)	6	(12%)	3	(6%)
Pars distalis, hyperplasia	1	(2%)			2	(4%)		
Thyroid gland	(50)		(49)		(49)		(50)	
Degeneration, cystic	12	(24%)	17	(35%)	15	(31%)	11	(22%)
Ectopic thymus					1	(2%)		
Inflammation, subacute							1	(2%)
Follicle, cyst			3	(6%)	4	(8%)	3	(6%)
Follicular cell, hyperplasia	5	(10%)	2	(4%)	6	(12%)	8	(16%)
General Body System								
None								
Genital System								
Coagulating gland	(8)		(8)		(5)		(2)	
Dilatation	8	(100%)	8	(100%)	5	(100%)	2	(100%)
Inflammation, suppurative	1	(13%)						
Epididymis	(50)		(50)		(50)		(51)	
Atypical cells			2	(4%)	1	(2%)		
Granuloma sperm	1	(2%)					1	(2%)
Hyperplasia, lymphoid			1	(2%)				
Inflammation, chronic			2	(4%)	1	(2%)	1	(2%)
Spermatocele			1	(2%)				
Preputial gland	(4)		(10)		(6)		(7)	
Ectasia	4	(100%)	9	(90%)	6	(100%)	7	(100%)
Inflammation, chronic			2	(20%)	2	(33%)	1	(14%)
Prostate	(50)		(50)		(50)		(51)	
Cyst	1	(2%)						
Inflammation, chronic					1	(2%)		
Inflammation, suppurative	1	(2%)					1	(2%)
Epithelium, hyperplasia			1	(2%)				
Seminal vesicle	(50)		(50)		(50)		(51)	
Dilatation	20	(40%)	18	(36%)	18	(36%)	8	(16%)
Fibrosis	1	(2%)						
Hemorrhage			1	(2%)				
Inflammation, chronic	1	(2%)						
Testes	(50)		(50)		(50)		(51)	
Congestion			1	(2%)				
Hemorrhage			1	(2%)				
Infarct					1	(2%)		
Mineralization	1	(2%)						
Seminiferous tubule, atrophy	2	(4%)	4	(8%)	1	(2%)	4	(8%)

TABLE G5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(51)
Angiectasis	1 (2%)	1 (2%)	1 (2%)	
Hypercellularity	3 (6%)	4 (8%)	2 (4%)	1 (2%)
Necrosis	1 (2%)			
Lymph node	(50)	(50)	(50)	(51)
Bronchial, hyperplasia, lymphoid	1 (2%)			
Mediastinal, hematopoietic cell proliferation		1 (2%)		
Mediastinal, hyperplasia, lymphoid		1 (2%)		1 (2%)
Mediastinal, hyperplasia, plasma cell	1 (2%)			1 (2%)
Lymph node, mandibular	(49)	(46)	(50)	(48)
Hyperplasia, lymphoid	2 (4%)	1 (2%)		1 (2%)
Hyperplasia, plasma cell	3 (6%)	1 (2%)		
Lymph node, mesenteric	(46)	(50)	(50)	(50)
Depletion	1 (2%)			
Hematopoietic cell proliferation	6 (13%)	3 (6%)	1 (2%)	3 (6%)
Hemorrhage	22 (48%)	15 (30%)	12 (24%)	13 (26%)
Hyperplasia, histiocyte	1 (2%)			
Hyperplasia, lymphoid	6 (13%)	2 (4%)	3 (6%)	1 (2%)
Hyperplasia, plasma cell		2 (4%)		1 (2%)
Spleen	(50)	(50)	(50)	(51)
Angiectasis		2 (4%)		
Congestion				1 (2%)
Hematopoietic cell proliferation	9 (18%)	13 (26%)	15 (30%)	11 (22%)
Pigmentation, hemosiderin		2 (4%)		
Lymphoid follicle, atrophy		2 (4%)	1 (2%)	1 (2%)
Lymphoid follicle, hyperplasia	4 (8%)	4 (8%)	2 (4%)	1 (2%)
Red pulp, atrophy	2 (4%)		1 (2%)	1 (2%)
Red pulp, hyperplasia	3 (6%)			
Thymus	(47)	(41)	(46)	(48)
Cyst	9 (19%)	5 (12%)	3 (7%)	7 (15%)
Depletion	11 (23%)	9 (22%)	2 (4%)	7 (15%)
Hyperplasia, lymphoid	1 (2%)			
Integumentary System				
Skin	(50)	(50)	(50)	(51)
Acanthosis		1 (2%)		1 (2%)
Cyst epithelial inclusion			1 (2%)	
Inflammation, chronic		1 (2%)	1 (2%)	1 (2%)
Hair follicle, cyst			1 (2%)	
Subcutaneous tissue, edema				1 (2%)
Musculoskeletal System				
None				
Nervous System				
Brain	(50)	(50)	(50)	(51)
Hydrocephalus	1 (2%)			
Thalamus, mineralization	41 (82%)	38 (76%)	44 (88%)	42 (82%)

TABLE G5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Respiratory System				
Lung	(50)	(50)	(50)	(51)
Congestion	2 (4%)	1 (2%)		1 (2%)
Embolus			1 (2%)	
Hemorrhage	2 (4%)	3 (6%)	4 (8%)	1 (2%)
Hyperplasia, lymphoid	6 (12%)	4 (8%)	2 (4%)	3 (6%)
Infiltration cellular, histiocytic	16 (32%)	9 (18%)	8 (16%)	7 (14%)
Inflammation, chronic				1 (2%)
Metaplasia, osseous	1 (2%)			
Alveolar epithelium, hyperplasia	6 (12%)	2 (4%)		3 (6%)
Alveolar epithelium, hyperplasia, focal			1 (2%)	
Nose	(50)	(50)	(50)	(51)
Exudate	8 (16%)	5 (10%)	1 (2%)	4 (8%)
Foreign body			1 (2%)	
Glands, hyperplasia, cystic	6 (12%)	3 (6%)	1 (2%)	2 (4%)
Special Senses System				
None				
Urinary System				
Kidney	(50)	(50)	(50)	(51)
Casts protein	6 (12%)	17 (34%)	14 (28%)	12 (24%)
Cyst	28 (56%)	24 (48%)	24 (48%)	18 (35%)
Glomerulosclerosis		2 (4%)		
Granuloma		1 (2%)		3 (6%)
Hydronephrosis	2 (4%)	3 (6%)	1 (2%)	
Hyperplasia, lymphoid	12 (24%)	18 (36%)	18 (36%)	12 (24%)
Metaplasia, osseous	1 (2%)	1 (2%)	1 (2%)	
Mineralization	48 (96%)	44 (88%)	44 (88%)	47 (92%)
Renal tubule, atrophy	4 (8%)	16 (32%)	8 (16%)	13 (25%)
Renal tubule, dilatation		4 (8%)	15 (30%)	20 (39%)
Renal tubule, hyperplasia, focal		1 (2%)	2 (4%)	1 (2%)
Renal tubule, necrosis	1 (2%)		2 (4%)	2 (4%)
Renal tubule, regeneration	45 (90%)	48 (96%)	47 (94%)	49 (96%)
Transitional epithelium, hyperplasia		1 (2%)		
Urinary bladder	(50)	(50)	(50)	(51)
Dilatation	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Hemorrhage		1 (2%)		
Hyperplasia, lymphoid	4 (8%)	4 (8%)	4 (8%)	5 (10%)

APPENDIX H
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR CHLORAMINATED WATER STUDY

TABLE H1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	10
Early deaths				
Natural death	3	3	6	3
Moribund	13	14	9	5
Accidental death	1	1	0	0
Survivors				
Terminal sacrifice	33	32	35	42
Animals examined microscopically	50	50	50	50
Alimentary System				
Gallbladder	(47)	(49)	(48)	(49)
Intestine small, duodenum	(48)	(46)	(48)	(49)
Fibrous histiocytoma		1 (2%)		
Intestine small, ileum	(48)	(50)	(49)	(47)
Histiocytic sarcoma				1 (2%)
Intestine small, jejunum	(48)	(49)	(49)	(48)
Liver	(50)	(50)	(50)	(50)
Fibrous histiocytoma	1 (2%)	1 (2%)		1 (2%)
Hemangiosarcoma	1 (2%)			
Hepatocellular carcinoma	6 (12%)	8 (16%)	4 (8%)	3 (6%)
Hepatocellular carcinoma, two, multiple		3 (6%)	2 (4%)	
Hepatocellular adenoma	13 (26%)	10 (20%)	18 (36%)	11 (22%)
Hepatocellular adenoma, two, multiple	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Hepatocellular adenoma, three, multiple	1 (2%)	1 (2%)	1 (2%)	
Hepatocellular adenoma, four, multiple	1 (2%)	2 (4%)	1 (2%)	
Hepatocellular adenoma, five, multiple	1 (2%)			
Histiocytic sarcoma, metastatic				1 (2%)
Mesentery	(17)	(8)	(8)	(2)
Chemodectoma malignant	1 (6%)			
Hemangiosarcoma	1 (6%)			
Pancreas	(50)	(50)	(49)	(50)
Fibrous histiocytoma	1 (2%)	1 (2%)		
Hemangioma	1 (2%)			
Salivary glands	(49)	(50)	(50)	(50)
Stomach, forestomach	(50)	(50)	(50)	(49)
Hemangioma	1 (2%)			
Leiomyoma	1 (2%)			
Stomach, glandular	(50)	(50)	(50)	(49)
Fibrous histiocytoma		1 (2%)		
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)

TABLE H1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Adenoma			1 (2%)	
Capsule, adenoma				1 (2%)
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Pheochromocytoma benign			1 (2%)	1 (2%)
Islets, pancreatic	(50)	(50)	(48)	(50)
Adenoma			2 (4%)	1 (2%)
Carcinoma			1 (2%)	
Pituitary gland	(48)	(50)	(47)	(50)
Pars distalis, adenoma	5 (10%)	11 (22%)	4 (9%)	2 (4%)
Pars distalis, carcinoma				1 (2%)
Pars intermedia, adenoma	1 (2%)			
Thyroid gland	(50)	(49)	(50)	(49)
Follicular cell, adenoma	2 (4%)	1 (2%)	1 (2%)	
Follicular cell, carcinoma			1 (2%)	
General Body System				
None				
Genital System				
Ovary	(46)	(46)	(48)	(47)
Adenoma	2 (4%)			1 (2%)
Cystadenoma		1 (2%)	1 (2%)	1 (2%)
Hemangioma	1 (2%)		1 (2%)	
Teratoma benign	1 (2%)			
Uterus	(50)	(50)	(50)	(50)
Carcinoma		1 (2%)	1 (2%)	
Hemangiosarcoma				1 (2%)
Histiocytic sarcoma			1 (2%)	2 (4%)
Leiomyosarcoma	1 (2%)			
Polyp stromal		3 (6%)	2 (4%)	1 (2%)
Sarcoma	1 (2%)			
Sarcoma stromal		1 (2%)		
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Fibrous histiocytoma	1 (2%)			1 (2%)
Hemangiosarcoma				1 (2%)
Lymph node	(50)	(50)	(50)	(50)
Axillary, fibrosarcoma, metastatic, skin	1 (2%)			
Renal, fibrous histiocytoma		1 (2%)		
Lymph node, mandibular	(46)	(49)	(47)	(50)
Lymph node, mesenteric	(49)	(50)	(48)	(46)
Fibrous histiocytoma		1 (2%)		
Renal, iliac, mediastinal, mandibular, fibrous histiocytoma	1 (2%)			

TABLE H1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Hematopoietic System (continued)				
Spleen	(49)	(50)	(50)	(50)
Fibrous histiocytoma	1 (2%)	1 (2%)		1 (2%)
Hemangioma				1 (2%)
Hemangiosarcoma	1 (2%)			1 (2%)
Thymus	(48)	(47)	(47)	(43)
Fibrous histiocytoma	1 (2%)			
Thymoma benign	1 (2%)	1 (2%)		1 (2%)
Integumentary System				
Mammary gland	(49)	(50)	(49)	(50)
Skin	(50)	(50)	(49)	(48)
Fibrosarcoma	1 (2%)			
Mast cell tumor benign		1 (2%)		
Subcutaneous tissue, sarcoma	1 (2%)			1 (2%)
Subcutaneous tissue, schwannoma malignant		2 (4%)		1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma	1 (2%)			
Skeletal muscle	(2)			
Fibrosarcoma, metastatic, skin	1 (50%)			
Osteosarcoma, metastatic, bone	1 (50%)			
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	4 (8%)	3 (6%)	2 (4%)	2 (4%)
Alveolar/bronchiolar adenoma, two, multiple				1 (2%)
Alveolar/bronchiolar carcinoma	1 (2%)	2 (4%)	2 (4%)	
Fibrosarcoma, metastatic, skin	1 (2%)			
Fibrous histiocytoma		1 (2%)		1 (2%)
Hepatocellular carcinoma, metastatic, liver	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Schwannoma malignant, metastatic, skin		1 (2%)		
Nose	(50)	(50)	(50)	(50)
Glands, carcinoma			1 (2%)	
Special Senses System				
Harderian gland	(1)	(1)	(1)	(5)
Adenoma	1 (100%)	1 (100%)		3 (60%)
Carcinoma			1 (100%)	

TABLE H1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Fibrous histiocytoma	1 (2%)	1 (2%)		
Renal tubule, carcinoma		1 (2%)		
Urinary bladder	(49)	(49)	(49)	(50)
Systemic Lesions				
Multiple organs[a]	(50)	(50)	(50)	(50)
Histiocytic sarcoma			1 (2%)	2 (4%)
Leukemia erythrocytic	1 (2%)		1 (2%)	
Lymphoma malignant lymphocytic	2 (4%)		1 (2%)	3 (6%)
Lymphoma malignant mixed	7 (14%)	5 (10%)	4 (8%)	11 (22%)
Lymphoma malignant undifferentiated cell		1 (2%)		
Tumor Summary				
Total animals with primary neoplasms[b]	35	40	35	31
Total primary neoplasms	73	69	57	58
Total animals with benign neoplasms	26	28	28	21
Total benign neoplasms	40	36	37	29
Total animals with malignant neoplasms	23	21	16	21
Total malignant neoplasms	33	33	20	29
Total animals with secondary neoplasms[c]	3	3	1	2
Total secondary neoplasms	5	3	1	2

[a] The number in parentheses is the number of animals with any tissue examined microscopically.
[b] Primary tumors: all tumors except metastatic tumors
[c] Secondary tumors: metastatic tumors or tumors invasive to an adjacent organ

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 0 ppm

Number of Days on Study	0161	0452	0510	0518	0536	0561	0581	0588	0653	0659	0681	0688	0694	0705	0709	0729	0731	0733	0733	0733	0733	0733	0733	0734	0734
Carcass ID Number	7711	7819	7731	7841	7741	2418	2441	2459	7708	2621	7761	7761	2661	2661	2668	2653	7741	7712	7755	7766	7780	8811	7901	2581	2601
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangiosarcoma																						X			
Hepatocellular carcinoma										X							X								
Hepatocellular adenoma						X					X							X						X	
Hepatocellular adenoma, two, multiple																	X								
Hepatocellular adenoma, three, multiple																									
Hepatocellular adenoma, four, multiple																									
Hepatocellular adenoma, five, multiple																			X						
Mesentery		+						+	+			+		+	+		+			+					+
Chemodectoma malignant																									
Hemangiosarcoma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangioma																						X			
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Leiomyoma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel		+						+																	
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

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

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	2 6 3 1	2 6 4 1	2 6 5 1	2 6 7 1	2 6 9 1	2 7 0 1	2 4 6 1	2 4 9 1	2 5 0 1	2 5 1 1	2 5 2 1	7 6 8 1	7 6 9 1	7 7 9 1	7 8 2 1	7 8 3 1	7 8 5 1	7 8 6 1	7 8 7 1	7 8 8 1	2 5 4 1	2 5 5 1	2 5 6 1	2 5 7 1	7 7 0 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma										X																1
Hemangiosarcoma																										1
Hepatocellular carcinoma	X				X							X								X						6
Hepatocellular adenoma	X			X	X									X				X		X		X	X		X	13
Hepatocellular adenoma, two, multiple													X											X		3
Hepatocellular adenoma, three, multiple															X											1
Hepatocellular adenoma, four, multiple												X														1
Hepatocellular adenoma, five, multiple																										1
Mesentery					+					+	+	+		+	+			+		+						17
Chemodectoma malignant																				X						1
Hemangiosarcoma												X														1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma										X																1
Hemangioma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma	X																									1
Leiomyoma																		X								1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Blood vessel																										2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	0 1 6	4 5 2	5 1 0	5 1 8	5 3 6	5 6 1	5 8 1	5 8 8	6 5 3	6 5 9	6 8 1	6 8 8	6 9 4	6 9 5	6 9 5	6 9 8	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4
Carcass ID Number	7 7 1 1	7 8 9 1	7 7 3 1	7 8 4 1	7 7 7 1	2 4 8 1	2 4 7 1	2 5 9 1	7 7 8 1	2 6 2 1	7 6 7 1	7 6 6 1	2 6 1 1	2 6 6 1	2 6 8 1	2 5 3 1	7 7 4 1	7 7 2 1	7 7 5 1	7 7 6 1	7 8 0 1	7 8 1 1	7 9 0 1	2 5 8 1	2 6 0 1
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pituitary gland	M	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																X		X							
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																		X							
General Body System																									
None																									
Genital System																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Adenoma																									
Hemangioma																									
Teratoma benign																								X	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma						X																			
Sarcoma																								X	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Axillary, fibrosarcoma, metastatic, skin											X														
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	M	+	+	+
Lymph node, mesenteric	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal, iliac, mediastinal, mandibular, fibrous histiocytoma																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Fibrous histiocytoma																									
Hemangiosarcoma																								X	
Thymus	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Thymoma benign																			X						

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	2 6 3 1	2 6 4 1	2 6 5 1	2 6 7 1	2 6 9 1	2 7 0 1	2 4 6 1	2 4 9 1	2 5 0 1	2 5 1 1	2 5 2 1	7 6 8 1	7 6 9 1	7 7 9 1	7 8 2 1	7 8 3 1	7 8 5 1	7 8 6 1	7 8 7 1	7 8 8 1	7 5 4 1	2 5 5 1	2 5 6 1	2 5 7 1	7 7 0 1	**Total Tissues/ Tumors**
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma								X	X											X						5
Pars intermedia, adenoma			X																							1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma												X														2
General Body System																										
None																										
Genital System																										
Ovary	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	I	+	+	+	+	I	+	+	46
Adenoma					X										X											2
Hemangioma							X																			1
Teratoma benign																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma																										1
Sarcoma																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma										X																1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Axillary, fibrosarcoma, metastatic, skin																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	46
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Renal, iliac, mediastinal, mandibular, fibrous histiocytoma										X																1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrous histiocytoma										X																1
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibrous histiocytoma										X																1
Thymoma benign																										1

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	0 1 6	4 5 2	5 1 0	5 1 8	5 3 6	5 6 1	5 8 1	5 8 8	6 5 3	6 5 9	6 8 1	6 8 8	6 9 4	6 9 5	6 9 5	6 9 8	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4
Carcass ID Number	7 7 1 1	7 8 9 1	7 7 3 1	7 8 4 1	7 7 7 1	2 4 8 1	2 4 7 1	2 5 9 1	7 7 8 1	2 6 2 1	7 6 7 1	7 6 6 1	2 6 1 1	2 6 6 1	2 6 8 1	2 5 3 1	7 7 4 1	7 7 2 1	7 7 5 1	7 7 6 1	7 8 0 1	8 8 1 1	9 0 1 1	5 8 1 1	2 6 0 1
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma											X														
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																	X								
Skeletal muscle											+						+								
Fibrosarcoma, metastatic, skin											X														
Osteosarcoma, metastatic, bone																	X								
Nervous System																									
Brain	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma		X																							
Alveolar/bronchiolar carcinoma																				X					
Fibrosarcoma, metastatic, skin											X														
Hepatocellular carcinoma, metastatic, liver																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Ureter										+															
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia erythrocytic															X										
Lymphoma malignant lymphocytic		X										X													
Lymphoma malignant mixed									X							X						X	X		

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 0 ppm (continued)

Number of Days on Study	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	2 6 3 1	2 6 4 1	2 6 5 1	2 6 7 1	2 6 9 1	2 7 0 1	2 4 6 1	2 4 9 1	2 5 0 1	2 5 1 1	2 5 2 1	7 6 8 1	7 6 9 1	7 7 9 1	7 8 2 1	7 8 3 1	7 8 5 1	7 8 6 1	7 8 7 1	7 8 8 1	2 5 4 1	2 5 5 1	2 5 6 1	2 5 7 1	7 0 1	**Total Tissues/ Tumors**
Integumentary System																											
Mammary gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Fibrosarcoma																										1	
Subcutaneous tissue, sarcoma		X																								1	
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Osteosarcoma																										1	
Skeletal muscle																										2	
Fibrosarcoma, metastatic, skin																										1	
Osteosarcoma, metastatic, bone																										1	
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Alveolar/bronchiolar adenoma													X	X						X						4	
Alveolar/bronchiolar carcinoma																										1	
Fibrosarcoma, metastatic, skin																										1	
Hepatocellular carcinoma, metastatic, liver	X																									1	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Special Senses System																											
Harderian gland															+											1	
Adenoma															X											1	
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Fibrous histiocytoma										X																1	
Ureter																										1	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	49	
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Leukemia erythrocytic																										1	
Lymphoma malignant lymphocytic																										2	
Lymphoma malignant mixed							X				X											X				7	

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 50 ppm

Number of Days on Study	3 9 7	5 4 7	5 6 4	5 7 9	5 8 5	5 9 0	6 2 8	6 3 2	6 4 8	6 6 1	6 7 2	6 7 7	6 9 8	7 1 7	7 2 6	7 3 0	7 3 0	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	8 7 8 1	8 7 6 1	8 7 3 1	3 5 3 1	8 8 1 1	3 6 1 1	3 5 9 1	3 6 4 1	8 8 9 1	8 8 5 1	3 5 1 1	3 6 3 1	8 9 5 1	8 9 4 1	3 7 3 1	8 8 6 1	8 8 8 1	8 8 2 1	3 5 7 1	3 5 8 1	3 6 0 1	3 6 2 1	3 6 9 1	3 7 0 1	3 7 1 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	M	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	I	+	+	+	+
Fibrous histiocytoma																		X							
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																		X							
Hepatocellular carcinoma					X	X		X									X						X		
Hepatocellular carcinoma, two, multiple									X				X	X											
Hepatocellular adenoma														X			X					X	X		X
Hepatocellular adenoma, two, multiple																									
Hepatocellular adenoma, three, multiple																									
Hepatocellular adenoma, four, multiple																									
Mesentery							+	+						+		+					+				
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																		X							
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																		X							
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X														X	X	X			X			X		
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
None																									

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	3 7 2 1	3 7 4 1	8 7 1 1	8 7 2 1	8 7 4 1	8 7 5 1	8 8 3 1	8 8 4 1	8 8 7 1	3 7 5 1	3 5 2 1	3 5 4 1	3 5 5 1	3 5 6 1	8 9 0 1	8 9 1 1	8 9 2 1	8 9 3 1	3 6 5 1	3 6 6 1	3 6 7 1	3 6 8 1	8 7 7 1	8 7 9 1	8 8 0 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Fibrous histiocytoma																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																										1
Hepatocellular carcinoma													X								X		X			8
Hepatocellular carcinoma, two, multiple																										3
Hepatocellular adenoma	X							X										X	X			X				10
Hepatocellular adenoma, two, multiple					X																					1
Hepatocellular adenoma, three, multiple																							X			1
Hepatocellular adenoma, four, multiple										X	X															2
Mesentery		+	+					+																		8
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X	X							X								X					X				11
Thyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell, adenoma															X											1
General Body System																										
None																										

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	3 9 7	5 4 7	5 6 4	5 7 9	5 8 5	5 9 0	6 2 8	6 3 2	6 4 8	6 6 1	6 7 2	6 7 7	6 9 8	7 1 7	7 2 6	7 3 0	7 3 0	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	8 7 8 1	8 7 6 1	8 7 3 1	3 5 3 1	8 8 1 1	3 6 1 1	3 5 9 1	3 6 4 1	8 8 9 1	8 8 5 1	3 5 1 1	3 6 3 1	8 9 5 1	8 9 4 1	3 7 3 1	8 8 6 1	8 8 8 1	8 8 2 1	3 5 7 1	3 5 8 1	3 6 0 1	3 6 2 1	3 6 9 1	3 7 0 1	3 7 1 1
Genital System																									
Clitoral gland																								+	
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Cystadenoma																			X						
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Polyp stromal									X															X	
Sarcoma stromal										X															
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal, fibrous histiocytoma																		X							
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																		X							
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																		X							
Thymus	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Thymoma benign			X																						
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mast cell tumor benign																									
Subcutaneous tissue, schwannoma malignant				X										X											
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																			X						
Alveolar/bronchiolar carcinoma																									
Fibrous histiocytoma																		X							
Hepatocellular carcinoma, metastatic, liver						X								X											
Schwannoma malignant, metastatic, skin				X																					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	3 7 2 1	3 7 4 1	8 7 1 1	8 7 2 1	8 7 4 1	8 7 5 1	8 7 3 1	8 8 4 1	8 8 7 1	3 7 5 1	3 5 2 1	3 5 4 1	3 5 5 1	3 5 6 1	8 9 0 1	8 9 1 1	8 9 2 1	8 9 3 1	3 6 5 1	3 6 6 1	3 6 7 1	3 6 8 1	8 7 7 1	8 7 9 1	8 8 0 1	**Total Tissues/ Tumors**
Genital System																											
Clitoral gland																											1
Ovary	+	+	+	+	+	+	M	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+		46
Cystadenoma																											1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Carcinoma													X														1
Polyp stromal				X																							3
Sarcoma stromal																											1
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Renal, fibrous histiocytoma																											1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Fibrous histiocytoma																											1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Fibrous histiocytoma																											1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+		47
Thymoma benign																											1
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Mast cell tumor benign																	X										1
Subcutaneous tissue, schwannoma malignant																											2
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Alveolar/bronchiolar adenoma	X							X																			3
Alveolar/bronchiolar carcinoma																							X		X		2
Fibrous histiocytoma																											1
Hepatocellular carcinoma, metastatic, liver																											2
Schwannoma malignant, metastatic, skin																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	3 9 7	5 4 7	5 6 4	5 7 9	5 8 5	5 9 0	6 2 8	6 3 2	6 4 8	6 6 1	6 7 2	6 7 7	6 9 8	7 1 7	7 2 6	7 3 0	7 3 0	7 3 1	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	8 7 8 1	8 7 6 1	8 7 3 1	3 5 3 1	8 8 1 1	3 6 1 1	3 5 9 1	3 6 4 1	8 8 9 1	8 8 5 1	3 5 1 1	3 6 3 1	8 9 5 1	8 9 4 1	3 7 3 1	8 8 6 1	8 8 8 1	8 8 2 1	3 5 7 1	3 5 8 1	3 6 0 1	3 6 2 1	3 6 9 1	3 7 0 1	3 7 1 1
Special Senses System																									
Eye																									
Harderian gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																		X							
Renal tubule, carcinoma																								X	
Urinary bladder	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																X					X				
Lymphoma malignant undifferentiated cell type													X												

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 50 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	3 7 2 1	3 7 4 1	8 7 1 1	8 7 2 1	8 7 4 1	8 7 5 1	8 8 3 1	8 8 4 1	8 8 7 1	3 7 5 1	3 5 2 1	3 5 4 1	3 5 5 1	3 5 6 1	8 9 0 1	8 9 1 1	8 9 2 1	8 9 3 1	3 6 5 1	3 6 6 1	3 6 7 1	3 6 8 1	8 7 7 1	8 7 9 1	8 8 0 1	**Total Tissues/ Tumors**
Special Senses System																										
Eye																+										1
Harderian gland																+										1
Adenoma																X										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma																										1
Renal tubule, carcinoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed	X					X				X																5
Lymphoma malignant undifferentiated cell type																										1

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 100 ppm

Number of Days on Study	3 8 5	5 0 9	5 0 9	6 2 8	6 6 9	6 7 1	6 7 9	6 8 1	6 8 8	7 2 1	7 2 8	7 3 0	7 3 1	7 3 2	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 5
Carcass ID Number	3 3 4 1	3 2 7 1	3 3 5 1	3 3 8 1	3 3 0 1	3 1 8 1	3 2 9 1	8 5 8 1	8 4 3 1	8 4 1 1	3 2 6 1	8 5 2 1	8 3 9 1	8 4 2 1	8 5 6 1	3 2 2 1	3 2 3 1	3 2 4 1	3 2 5 1	3 3 6 1	3 3 7 1	3 3 9 1	3 4 0 1	8 5 4 1	8 5 5 1
Alimentary System																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Gallbladder	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma	X																			X				
Hepatocellular carcinoma, two, multiple											X													
Hepatocellular adenoma				X	X		X				X			X	X			X					X	X	X
Hepatocellular adenoma, two, multiple																			X					
Hepatocellular adenoma, three, multiple																								
Hepatocellular adenoma, four, multiple									X															
Mesentery							+	+																+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																								
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign													X											
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X				X															
Carcinoma																								
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																								
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																								
Follicular cell, carcinoma										X														

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	8 5 7 1	8 5 9 1	8 6 0 1	3 2 8 1	3 3 1 1	3 3 2 1	3 3 3 1	8 4 4 1	8 4 5 1	8 4 6 1	8 4 7 1	8 5 0 1	3 1 6 1	3 1 7 1	3 1 9 1	3 2 0 1	3 2 1 1	8 3 6 1	8 3 7 1	8 3 8 1	8 4 0 1	8 4 4 1	8 4 9 1	8 5 1 1	8 5 3 1	**Total Tissues/ Tumors**
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma					X									X											4
Hepatocellular carcinoma, two, multiple													X												2
Hepatocellular adenoma					X	X		X					X	X	X			X						X	18
Hepatocellular adenoma, two, multiple									X																2
Hepatocellular adenoma, three, multiple																				X					1
Hepatocellular adenoma, four, multiple																									1
Mesentery								+			+			+	+								+		8
Pancreas	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X																								1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																									1
Islets, pancreatic	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	48
Adenoma																									2
Carcinoma																						X			1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma		X				X										X					X				4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell, adenoma																				X					1
Follicular cell, carcinoma																									1

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	385	500	599	628	669	671	719	768	818	821	728	730	731	732	733	733	733	733	733	733	733	733	733	733
Carcass ID Number	34411	32711	35311	38311	33011	31811	32911	38511	34811	34111	32611	32911	33911	34211	34511	32211	32311	34411	35511	33311	33911	34011	34511	35511
General Body System																								
None																								
Genital System																								
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Cystadenoma																			X					
Hemangioma																	X							
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																								X
Histiocytic sarcoma																								X
Polyp stromal													X											
Hematopoietic System																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	I	+	+	I	+	+
Lymph node, mesenteric	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Integumentary System																								
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																		X						
Alveolar/bronchiolar carcinoma																		X		X				
Hepatocellular carcinoma, metastatic, liver	X																							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glands, carcinoma																								
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Harderian gland																								
Carcinoma																								
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																								X
Leukemia erythrocytic							X																	
Lymphoma malignant lymphocytic																	X							
Lymphoma malignant mixed								X																

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 100 ppm (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 3	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	8 5 7 1	8 5 9 1	8 6 0 1	3 2 8 1	3 3 1 1	3 3 2 1	3 3 3 1	3 4 4 1	4 4 5 1	4 4 6 1	4 4 7 1	8 5 0 1	3 1 6 1	3 1 7 1	3 1 9 1	3 2 0 1	3 2 1 1	8 3 6 1	8 3 7 1	8 3 8 1	8 4 0 1	8 4 8 1	8 4 9 1	8 5 1 1	8 5 3 1	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Ovary	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cystadenoma																										1
Hemangioma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Histiocytic sarcoma																										1
Polyp stromal														X												2
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+		47
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																				X						2
Alveolar/bronchiolar carcinoma																										2
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glands, carcinoma											X															1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland																		+								1
Carcinoma																		X								1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia erythrocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed														X				X					X			4

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 200 ppm

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

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	2 9 4 1	2 9 5 1	2 9 8 1	3 0 5 1	8 0 1 1	8 1 1 1	8 1 2 1	2 1 8 1	2 2 8 1	2 2 8 1	2 2 8 1	2 2 8 1	2 2 8 1	8 0 7 1	8 1 3 1	8 1 4 1	8 1 6 1	8 1 7 1	8 1 8 1	8 1 1 1	8 0 2 1	8 0 3 1	8 0 4 1	8 0 5 1	8 0 6 1	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Histiocytic sarcoma																	X									1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma															X											1
Hepatocellular carcinoma															X											3
Hepatocellular adenoma	X	X					X	X								X	X			X						11
Hepatocellular adenoma, two, multiple			X																			X				2
Histiocytic sarcoma, metastatic																										1
Mesentery																			+							2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth																										1
Cardiovascular System																										
Blood vessel																			+							2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign														X												1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma																	X			X						2
Pars distalis, carcinoma	X																									1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
None																										

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	0 6 3	5 7 9	6 4 7	6 6 1	6 7 5	6 9 1	6 9 8	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 6
Carcass ID Number	2 8 8 1	2 9 2 1	8 1 5 1	8 0 8 1	8 0 9 1	8 2 3 1	2 9 6 1	2 9 7 1	8 1 9 1	8 2 0 1	8 2 1 1	8 2 2 1	8 2 4 1	8 2 5 1	2 8 7 1	2 8 9 1	2 9 0 1	2 9 1 1	2 9 9 1	3 0 0 1	3 0 1 1	3 0 2 1	3 0 3 1	3 0 4 1	2 9 3 1
Genital System																									
Ovary	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Adenoma														X											
Cystadenoma																					X				
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma					X																				
Histiocytic sarcoma																					X				
Polyp stromal																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangiosarcoma					X																				
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	M	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma																									
Hemangioma																									
Hemangiosarcoma					X																				
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Thymoma benign												X													
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, sarcoma																	X								
Subcutaneous tissue, schwannoma malignant																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	2 9 4 1	2 9 5 1	2 9 8 1	3 0 5 1	8 1 0 1	8 1 1 1	8 1 2 1	2 1 8 1	2 2 8 1	2 2 8 1	2 2 8 1	2 2 8 1	2 2 8 1	2 8 0 1	8 0 7 1	8 1 3 1	8 1 4 1	8 1 6 1	8 1 7 1	8 1 8 1	8 1 0 1	8 0 1 1	8 0 2 1	8 0 3 1	8 0 4 1	8 0 5 1	8 0 6 1	**Total Tissues/ Tumors**
Genital System																											
Ovary	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																											1
Cystadenoma																											1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																		X									1
Histiocytic sarcoma																											2
Polyp stromal																				X							1
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma															X												1
Hemangiosarcoma																											1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma															X												1
Hemangioma																					X						1
Hemangiosarcoma																											1
Thymus	+	+	+	M	M	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	M	+	43
Thymoma benign																											1
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	48
Subcutaneous tissue, sarcoma																											1
Subcutaneous tissue, schwannoma malignant																									X		1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	0 6 3	5 7 9	6 4 7	6 6 1	6 7 5	6 9 1	6 9 8	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 6
Carcass ID Number	2 8 8 1	2 9 2 1	8 1 5 1	8 0 8 1	8 0 9 1	8 2 3 1	2 9 6 1	2 9 7 1	8 1 9 1	8 2 0 1	8 2 1 1	8 2 2 1	8 2 4 1	8 2 5 1	2 8 7 1	2 8 9 1	2 9 0 1	2 9 1 1	2 9 9 1	3 0 0 1	3 0 1 1	3 0 2 1	3 0 3 1	3 0 4 1	2 9 3 1
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma								X																	
Alveolar/bronchiolar adenoma, two, multiple												X													
Fibrous histiocytoma																									
Hepatocellular carcinoma, metastatic, liver						X																			
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Harderian gland							+							+											
Adenoma							X							X											
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																					X				
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed									X	X															X

TABLE H2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Chloraminated Water Study: 200 ppm (continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	2 9 4 1	2 9 5 1	2 9 8 1	3 0 5 1	8 1 0 1	8 1 1 1	8 1 2 1	2 8 1 1	2 8 2 1	2 8 3 1	2 8 4 1	2 8 5 1	2 8 6 1	2 8 7 1	8 0 1 1	8 1 3 1	8 1 4 1	8 1 6 1	8 1 7 1	8 1 8 1	8 1 1 1	8 0 2 1	8 0 3 1	8 0 4 1	8 0 5 1	8 0 6 1	**Total Tissues/ Tumors**
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X																			2
Alveolar/bronchiolar adenoma, two, multiple																										1
Fibrous histiocytoma															X											1
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Ear																								+		1
Harderian gland									+					+			+									5
Adenoma														X												3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																		X								2
Lymphoma malignant lymphocytic						X											X						X			3
Lymphoma malignant mixed	X											X		X	X					X	X	X		X		11

TABLE H3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Harderian Gland: Adenoma				
Overall rates[a]	1/50 (2%)	1/50 (2%)	0/50 (0%)	3/50 (6%)
Adjusted rates[b]	3.0%	3.1%	0.0%	6.9%
Terminal rates[c]	1/33 (3%)	1/32 (3%)	0/35 (0%)	2/42 (5%)
First incidence (days)	733 (T)	733 (T)	-[e]	698
Life table tests[d]	P=0.227	P=0.755	P=0.488N	P=0.394
Logistic regression tests[d]	P=0.194	P=0.755	P=0.488N	P=0.350
Cochran-Armitage test[d]	P=0.160			
Fisher exact test[d]		P=0.753N	P=0.500N	P=0.309
Harderian Gland: Adenoma or Carcinoma				
Overall rates	1/50 (2%)	1/50 (2%)	1/50 (2%)	3/50 (6%)
Adjusted rates	3.0%	3.1%	2.9%	6.9%
Terminal rates	1/33 (3%)	1/32 (3%)	1/35 (3%)	2/42 (5%)
First incidence (days)	733 (T)	733 (T)	733 (T)	698
Life table tests	P=0.238	P=0.755	P=0.749N	P=0.394
Logistic regression tests	P=0.204	P=0.755	P=0.749N	P=0.350
Cochran-Armitage test	P=0.163			
Fisher exact test		P=0.753N	P=0.753N	P=0.309
Liver: Hepatocellular Adenoma				
Overall rates	19/50 (38%)	14/50 (28%)	22/50 (44%)	13/50 (26%)
Adjusted rates	53.8%	40.9%	51.9%	29.4%
Terminal rates	17/33 (52%)	12/32 (38%)	15/35 (43%)	11/42 (26%)
First incidence (days)	561	717	628	675
Life table tests	P=0.044N	P=0.211N	P=0.454	P=0.032N
Logistic regression tests	P=0.090N	P=0.157N	P=0.471	P=0.065N
Cochran-Armitage test	P=0.210N			
Fisher exact test		P=0.198N	P=0.342	P=0.142N
Liver: Hepatocellular Carcinoma				
Overall rates	6/50 (12%)	11/50 (22%)	6/50 (12%)	3/50 (6%)
Adjusted rates	17.2%	26.6%	15.4%	6.9%
Terminal rates	5/33 (15%)	4/32 (13%)	4/35 (11%)	2/42 (5%)
First incidence (days)	659	585	385	691
Life table tests	P=0.044N	P=0.160	P=0.570N	P=0.150N
Logistic regression tests	P=0.093N	P=0.148	P=0.619N	P=0.195N
Cochran-Armitage test	P=0.088N			
Fisher exact test		P=0.143	P=0.620N	P=0.243N
Liver: Hepatocellular Adenoma or Hepatocellular Carcinoma				
Overall rates	20/50 (40%)	21/50 (42%)	24/50 (48%)	15/50 (30%)
Adjusted rates	54.9%	52.8%	55.2%	34.0%
Terminal rates	17/33 (52%)	14/32 (44%)	16/35 (46%)	13/42 (31%)
First incidence (days)	561	585	385	675
Life table tests	P=0.031N	P=0.477	P=0.389	P=0.049N
Logistic regression tests	P=0.111N	P=0.549	P=0.343	P=0.104N
Cochran-Armitage test	P=0.165N			
Fisher exact test		P=0.500	P=0.273	P=0.201N

TABLE H3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	4/50 (8%)	3/50 (6%)	2/50 (4%)	3/50 (6%)
Adjusted rates	10.9%	9.4%	5.7%	7.0%
Terminal rates	3/33 (9%)	3/32 (9%)	2/35 (6%)	2/42 (5%)
First incidence (days)	452	733 (T)	733 (T)	732
Life table tests	P=0.301N	P=0.514N	P=0.315N	P=0.388N
Logistic regression tests	P=0.402N	P=0.498N	P=0.347N	P=0.505N
Cochran-Armitage test	P=0.420N			
Fisher exact test		P=0.500N	P=0.339N	P=0.500N
Lung: Alveolar/bronchiolar Adenoma or Alveolar/bronchiolar Carcinoma				
Overall rates	5/50 (10%)	5/50 (10%)	3/50 (6%)	3/50 (6%)
Adjusted rates	13.9%	15.6%	8.6%	7.0%
Terminal rates	4/33 (12%)	5/32 (16%)	3/35 (9%)	2/42 (5%)
First incidence (days)	452	733 (T)	733 (T)	732
Life table tests	P=0.141N	P=0.614	P=0.328N	P=0.249N
Logistic regression tests	P=0.208N	P=0.618N	P=0.352N	P=0.354N
Cochran-Armitage test	P=0.240N			
Fisher exact test		P=0.630N	P=0.357N	P=0.357N
Pancreatic Islets: Adenoma or Carcinoma				
Overall rates	0/50 (0%)	0/50 (0%)	3/48 (6%)	1/50 (2%)
Adjusted rates	0.0%	0.0%	7.4%	2.1%
Terminal rates	0/33 (0%)	0/32 (0%)	1/33 (3%)	0/42 (0%)
First incidence (days)	-	-	669	647
Life table tests	P=0.299	-	P=0.137	P=0.527
Logistic regression tests	P=0.238	-	P=0.112	P=0.485
Cochran-Armitage test	P=0.247			
Fisher exact test		-	P=0.114	P=0.500
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	5/48 (10%)	11/50 (22%)	4/47 (9%)	2/50 (4%)
Adjusted rates	14.6%	29.8%	12.1%	4.8%
Terminal rates	4/33 (12%)	7/32 (22%)	4/33 (12%)	2/42 (5%)
First incidence (days)	698	397	733 (T)	733 (T)
Life table tests	P=0.023N	P=0.090	P=0.489N	P=0.133N
Logistic regression tests	P=0.041N	P=0.102	P=0.452N	P=0.152N
Cochran-Armitage test	P=0.050N			
Fisher exact test		P=0.100	P=0.514N	P=0.201N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rates	5/48 (10%)	11/50 (22%)	4/47 (9%)	3/50 (6%)
Adjusted rates	14.6%	29.8%	12.1%	7.1%
Terminal rates	4/33 (12%)	7/32 (22%)	4/33 (12%)	3/42 (7%)
First incidence (days)	698	397	733 (T)	733 (T)
Life table tests	P=0.050N	P=0.090	P=0.489N	P=0.235N
Logistic regression tests	P=0.083N	P=0.102	P=0.452N	P=0.263N
Cochran-Armitage test	P=0.100N			
Fisher exact test		P=0.100	P=0.514N	P=0.335N

TABLE H3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Uterus: Stromal Polyp				
Overall rates	0/50 (0%)	3/50 (6%)	2/50 (4%)	1/50 (2%)
Adjusted rates	0.0%	8.5%	5.4%	2.4%
Terminal rates	0/33 (0%)	2/32 (6%)	1/35 (3%)	1/42 (2%)
First incidence (days)	-	648	731	733 (T)
Life table tests	P=0.573N	P=0.119	P=0.259	P=0.548
Logistic regression tests	P=0.588	P=0.124	P=0.270	P=0.548
Cochran-Armitage test	P=0.556			
Fisher exact test		P=0.121	P=0.247	P=0.500
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rates	0/50 (0%)	4/50 (8%)	2/50 (4%)	1/50 (2%)
Adjusted rates	0.0%	10.7%	5.4%	2.4%
Terminal rates	0/33 (0%)	2/32 (6%)	1/35 (3%)	1/42 (2%)
First incidence (days)	-	648	731	733 (T)
Life table tests	P=0.483N	P=0.065	P=0.259	P=0.548
Logistic regression tests	P=0.563N	P=0.063	P=0.270	P=0.548
Cochran-Armitage test	P=0.577N			
Fisher exact test		P=0.059	P=0.247	P=0.500
All Organs: Hemangioma				
Overall rates	3/50 (6%)	0/50 (0%)	1/50 (2%)	1/50 (2%)
Adjusted rates	9.1%	0.0%	2.9%	2.4%
Terminal rates	3/33 (9%)	0/32 (0%)	1/35 (3%)	1/42 (2%)
First incidence (days)	733 (T)	-	733 (T)	733 (T)
Life table tests	P=0.228N	P=0.126N	P=0.284N	P=0.223N
Logistic regression tests	P=0.228N	P=0.126N	P=0.284N	P=0.223N
Cochran-Armitage test	P=0.296N			
Fisher exact test		P=0.121N	P=0.309N	P=0.309N
All Organs: Hemangiosarcoma				
Overall rates	3/50 (6%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
Adjusted rates	9.1%	0.0%	0.0%	2.2%
Terminal rates	3/33 (9%)	0/32 (0%)	0/35 (0%)	0/42 (0%)
First incidence (days)	733 (T)	-	-	675
Life table tests	P=0.200N	P=0.126N	P=0.110N	P=0.234N
Logistic regression tests	P=0.226N	P=0.126N	P=0.110N	P=0.273N
Cochran-Armitage test	P=0.247N			
Fisher exact test		P=0.121N	P=0.121N	P=0.309N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	5/50 (10%)	0/50 (0%)	1/50 (2%)	2/50 (4%)
Adjusted rates	15.2%	0.0%	2.9%	4.5%
Terminal rates	5/33 (15%)	0/32 (0%)	1/35 (3%)	1/42 (2%)
First incidence (days)	733 (T)	-	733 (T)	675
Life table tests	P=0.163N	P=0.035N	P=0.089N	P=0.137N
Logistic regression tests	P=0.186N	P=0.035N	P=0.089N	P=0.164N
Cochran-Armitage test	P=0.232N			
Fisher exact test		P=0.028N	P=0.102N	P=0.218N

TABLE H3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
All Organs: Histiocytic Sarcoma or Malignant Lymphoma				
Overall rates	9/50 (18%)	6/50 (12%)	6/50 (12%)	16/50 (32%)
Adjusted rates	23.2%	17.2%	16.3%	38.1%
Terminal rates	5/33 (15%)	4/32 (13%)	5/35 (14%)	16/42 (38%)
First incidence (days)	452	698	681	733 (T)
Life table tests	P=0.094	P=0.302N	P=0.250N	P=0.229
Logistic regression tests	P=0.036	P=0.276N	P=0.278N	P=0.109
Cochran-Armitage test	P=0.023			
Fisher exact test		P=0.288N	P=0.288N	P=0.083
All Organs: Malignant Lymphoma (Lymphocytic, Mixed, or Undifferentiated Cell Type)				
Overall rates	9/50 (18%)	6/50 (12%)	5/50 (10%)	14/50 (28%)
Adjusted rates	23.2%	17.2%	13.5%	33.3%
Terminal rates	5/33 (15%)	4/32 (13%)	4/35 (11%)	14/42 (33%)
First incidence (days)	452	698	681	733 (T)
Life table tests	P=0.203	P=0.302N	P=0.168N	P=0.364
Logistic regression tests	P=0.099	P=0.276N	P=0.189N	P=0.207
Cochran-Armitage test	P=0.072			
Fisher exact test		P=0.288N	P=0.194N	P=0.171
All Organs: Benign Tumors				
Overall rates	26/50 (52%)	28/50 (56%)	28/50 (56%)	21/50 (42%)
Adjusted rates	69.8%	71.3%	64.8%	44.7%
Terminal rates	22/33 (67%)	21/32 (66%)	20/35 (57%)	16/42 (38%)
First incidence (days)	452	397	628	647
Life table tests	P=0.014N	P=0.387	P=0.562	P=0.039N
Logistic regression tests	P=0.065N	P=0.481	P=0.567	P=0.124N
Cochran-Armitage test	P=0.141N			
Fisher exact test		P=0.421	P=0.421	P=0.212N
All Organs: Malignant Tumors				
Overall rates	23/50 (46%)	21/50 (42%)	16/50 (32%)	21/50 (42%)
Adjusted rates	54.2%	48.1%	39.0%	47.6%
Terminal rates	14/33 (42%)	10/32 (31%)	11/35 (31%)	19/42 (45%)
First incidence (days)	452	579	385	675
Life table tests	P=0.111N	P=0.441N	P=0.089N	P=0.145N
Logistic regression tests	P=0.321N	P=0.400N	P=0.097N	P=0.336N
Cochran-Armitage test	P=0.357N			
Fisher exact test		P=0.420N	P=0.109N	P=0.420N
All Organs: Benign and Malignant Tumors				
Overall rates	35/50 (70%)	40/50 (80%)	35/50 (70%)	31/50 (62%)
Adjusted rates	83.1%	86.8%	75.9%	65.9%
Terminal rates	26/33 (79%)	26/32 (81%)	24/35 (69%)	26/42 (62%)
First incidence (days)	452	397	385	647
Life table tests	P=0.006N	P=0.220	P=0.400N	P=0.029N
Logistic regression tests	P=0.055N	P=0.230	P=0.451N	P=0.114N
Cochran-Armitage test	P=0.109N			
Fisher exact test		P=0.178	P=0.586N	P=0.263N

TABLE H3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Chloraminated Water Study (continued)

(T)Terminal sacrifice
[a] Number of tumor-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, epididymis, gallbladder (mouse), heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated tumor incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the "0 ppm" column are the P values associated with the trend test. Beneath the dose group columns are the P values corresponding to pairwise comparisons between the controls and that dose group. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher Exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no tumors in animal group

TABLE H4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chloraminated Water Study

	0 ppm	50 ppm	100 ppm	200 ppm
Disposition Summary				
Animals initially in study	70	70	70	70
15-week interim evaluation	10	10	10	10
66-week interim evaluation	10	10	10	10
Early deaths				
Natural death	3	3	6	3
Moribund	13	14	9	5
Accidental death	1	1		
Survivors				
Terminal sacrifice	33	32	35	42
Animals examined microscopically	50	50	50	50
Alimentary System				
Gallbladder	(47)	(49)	(48)	(49)
Cyst	3 (6%)			
Dilatation			1 (2%)	
Intestine large, cecum	(47)	(47)	(50)	(49)
Edema	2 (4%)			
Intestine small, ileum	(48)	(50)	(49)	(47)
Artery, jejunum, necrosis, fibrinoid	1 (2%)			
Liver	(50)	(50)	(50)	(50)
Angiectasis			1 (2%)	
Basophilic focus	2 (4%)	3 (6%)	7 (14%)	
Clear cell focus	1 (2%)	2 (4%)	1 (2%)	
Hematopoietic cell proliferation	5 (10%)	4 (8%)		2 (4%)
Hemorrhage			1 (2%)	
Hyperplasia, focal	12 (24%)	11 (22%)	9 (18%)	8 (16%)
Hyperplasia, lymphoid	6 (12%)	2 (4%)	4 (8%)	9 (18%)
Inflammation, chronic		1 (2%)	1 (2%)	3 (6%)
Inflammation, subacute	2 (4%)	3 (6%)	7 (14%)	2 (4%)
Mineralization	1 (2%)			
Mixed cell focus	1 (2%)			1 (2%)
Artery, necrosis, fibrinoid	1 (2%)			
Centrilobular, necrosis		1 (2%)		
Hepatocyte, karyomegaly	1 (2%)	1 (2%)		
Hepatocyte, vacuolization cytoplasmic	2 (4%)	3 (6%)	1 (2%)	
Kupffer cell, hyperplasia	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Kupffer cell, pigmentation	1 (2%)			1 (2%)
Lobules, necrosis	6 (12%)	4 (8%)	10 (20%)	4 (8%)
Mesentery	(17)	(8)	(8)	(2)
Accessory spleen				1 (50%)
Edema	1 (6%)			
Artery, necrosis, fibrinoid	1 (6%)			
Fat, inflammation, suppurative	1 (6%)			
Fat, necrosis	14 (82%)	6 (75%)	6 (75%)	1 (50%)

TABLE H4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Alimentary System (continued)				
Pancreas	(50)	(50)	(49)	(50)
Atrophy	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Cyst			1 (2%)	1 (2%)
Cytoplasmic alteration	2 (4%)	2 (4%)	5 (10%)	1 (2%)
Focal cellular change	1 (2%)		1 (2%)	
Hyperplasia, lymphoid	8 (16%)	9 (18%)	5 (10%)	2 (4%)
Inflammation, subacute	1 (2%)			
Salivary glands	(49)	(50)	(50)	(50)
Hyperplasia, lymphoid	18 (37%)	15 (30%)	22 (44%)	14 (28%)
Necrosis		1 (2%)		
Acinus, hyperplasia, cystic	1 (2%)			
Stomach, forestomach	(50)	(50)	(50)	(49)
Cyst	1 (2%)			
Diverticulum	1 (2%)			2 (4%)
Edema	1 (2%)	1 (2%)		
Fibrosis		1 (2%)		
Inflammation, subacute			1 (2%)	
Inflammation, suppurative	1 (2%)		1 (2%)	
Ulcer	1 (2%)			
Mucosa, hyperplasia	2 (4%)	6 (12%)	2 (4%)	
Stomach, glandular	(50)	(50)	(50)	(49)
Cyst	7 (14%)	8 (16%)	7 (14%)	8 (16%)
Edema	2 (4%)	1 (2%)	1 (2%)	
Erosion	1 (2%)		1 (2%)	
Inflammation, subacute	2 (4%)	1 (2%)		3 (6%)
Metaplasia, squamous				1 (2%)
Mineralization	1 (2%)			
Mucosa, hyperplasia		1 (2%)		1 (2%)
Cardiovascular System				
Blood vessel	(2)			(2)
Hypertrophy				2 (100%)
Inflammation, chronic				1 (50%)
Necrosis, fibrinoid	1 (50%)			
Thrombus	1 (50%)			
Heart	(50)	(50)	(50)	(50)
Myocardium, inflammation, chronic			1 (2%)	
Myocardium, inflammation, subacute	1 (2%)			
Myocardium, mineralization	1 (2%)			
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule	10 (20%)	10 (20%)	9 (18%)	15 (30%)
Basophilic focus	3 (6%)		1 (2%)	1 (2%)
Clear cell focus	1 (2%)			1 (2%)
Cyst		2 (4%)	1 (2%)	2 (4%)
Hyperplasia, focal	2 (4%)		5 (10%)	
Capsule, hyperplasia	2 (4%)		1 (2%)	1 (2%)
X-zone, degeneration, fatty		2 (4%)	1 (2%)	
Zona reticularis, proliferation		1 (2%)		

TABLE H4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Endocrine System (continued)				
Adrenal gland, medulla	(50)	(50)	(50)	(50)
Hyperplasia	1 (2%)	1 (2%)	2 (4%)	
Islets, pancreatic	(50)	(50)	(48)	(50)
Cyst			1 (2%)	
Hyperplasia	3 (6%)	8 (16%)	6 (13%)	5 (10%)
Hyperplasia, lymphoid	1 (2%)		1 (2%)	
Parathyroid gland	(47)	(49)	(49)	(48)
Cyst		1 (2%)	1 (2%)	
Ectopic thymus			2 (4%)	1 (2%)
Hyperplasia	1 (2%)		1 (2%)	
Pituitary gland	(48)	(50)	(47)	(50)
Pars distalis, angiectasis	3 (6%)	3 (6%)	4 (9%)	1 (2%)
Pars distalis, cyst		1 (2%)	2 (4%)	1 (2%)
Pars distalis, hyperplasia	8 (17%)	6 (12%)	7 (15%)	7 (14%)
Pars distalis, hyperplasia, focal		1 (2%)		
Thyroid gland	(50)	(49)	(50)	(49)
Degeneration, cystic	24 (48%)	26 (53%)	23 (46%)	17 (35%)
Ectopic thymus			1 (2%)	
Hyperplasia, lymphoid		3 (6%)		
Inflammation, subacute	2 (4%)	3 (6%)	3 (6%)	1 (2%)
Follicle, cyst	3 (6%)		1 (2%)	3 (6%)
Follicular cell, hyperplasia	12 (24%)	10 (20%)	10 (20%)	9 (18%)
Follicular cell, hyperplasia, diffuse			1 (2%)	
Follicular cell, hyperplasia, focal			1 (2%)	
General Body System				
None				
Genital System				
Clitoral gland		(1)		
Ectasia		1 (100%)		
Ovary	(46)	(46)	(48)	(47)
Angiectasis	11 (24%)	13 (28%)	10 (21%)	15 (32%)
Cyst	12 (26%)	11 (24%)	17 (35%)	17 (36%)
Hyperplasia	1 (2%)			
Artery, necrosis, fibrinoid	1 (2%)			
Interstitial cell, hyperplasia			1 (2%)	
Uterus	(50)	(50)	(50)	(50)
Angiectasis	5 (10%)	4 (8%)	5 (10%)	4 (8%)
Granuloma			1 (2%)	
Hemorrhage				1 (2%)
Hydrometra	18 (36%)	13 (26%)	16 (32%)	14 (28%)
Hyperplasia, cystic	49 (98%)	49 (98%)	46 (92%)	46 (92%)
Hyperplasia, lymphoid	1 (2%)	2 (4%)	2 (4%)	
Inflammation, suppurative	1 (2%)	2 (4%)	3 (6%)	3 (6%)
Metaplasia, squamous	1 (2%)	2 (4%)	1 (2%)	3 (6%)

TABLE H4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hypercellularity	7 (14%)	6 (12%)	2 (4%)	4 (8%)
Lymph node	(50)	(50)	(50)	(50)
Artery, necrosis, fibrinoid	1 (2%)			
Iliac, angiectasis	2 (4%)			
Iliac, hyperplasia, lymphoid		1 (2%)		1 (2%)
Iliac, hyperplasia, plasma cell	2 (4%)			
Mediastinal, hyperplasia, lymphoid		1 (2%)		
Renal, hyperplasia, lymphoid				2 (4%)
Renal, hyperplasia, plasma cell	1 (2%)			
Lymph node, mandibular	(46)	(49)	(47)	(50)
Hemorrhage			1 (2%)	
Hyperplasia, lymphoid	5 (11%)	4 (8%)	1 (2%)	1 (2%)
Hyperplasia, plasma cell		1 (2%)		1 (2%)
Lymph node, mesenteric	(49)	(50)	(48)	(46)
Depletion		1 (2%)		
Hematopoietic cell proliferation	2 (4%)	1 (2%)		
Hemorrhage	2 (4%)	3 (6%)	1 (2%)	1 (2%)
Hyperplasia, lymphoid	4 (8%)	3 (6%)		
Hyperplasia, plasma cell	2 (4%)			1 (2%)
Spleen	(49)	(50)	(50)	(50)
Angiectasis		1 (2%)		
Congestion				1 (2%)
Hematopoietic cell proliferation	21 (43%)	19 (38%)	13 (26%)	18 (36%)
Hemorrhage	1 (2%)		1 (2%)	
Necrosis	1 (2%)			
Pigmentation, hemosiderin	5 (10%)	4 (8%)	1 (2%)	1 (2%)
Lymphoid follicle, atrophy	1 (2%)	2 (4%)		
Lymphoid follicle, hyperplasia	4 (8%)	7 (14%)	5 (10%)	8 (16%)
Red pulp, atrophy		1 (2%)		1 (2%)
Red pulp, hyperplasia	3 (6%)	2 (4%)	3 (6%)	4 (8%)
Thymus	(48)	(47)	(47)	(43)
Angiectasis	3 (6%)	1 (2%)	2 (4%)	1 (2%)
Cyst	7 (15%)	10 (21%)	4 (9%)	1 (2%)
Depletion	3 (6%)	6 (13%)	3 (6%)	2 (5%)
Ectopic parathyroid gland	1 (2%)	1 (2%)	1 (2%)	
Hyperplasia, lymphoid	3 (6%)	2 (4%)	1 (2%)	
Artery, necrosis, fibrinoid	1 (2%)			
Integumentary System				
Mammary gland	(49)	(50)	(49)	(50)
Hyperplasia, cystic			2 (4%)	2 (4%)
Hyperplasia, lobular		1 (2%)		1 (2%)
Skin	(50)	(50)	(49)	(48)
Acanthosis	1 (2%)	2 (4%)	2 (4%)	2 (4%)
Inflammation, chronic			1 (2%)	1 (2%)
Inflammation, chronic, focal		1 (2%)		
Ulcer		1 (2%)		
Subcutaneous tissue, edema	2 (4%)			1 (2%)

TABLE H4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Fibrous osteodystrophy	1 (2%)			
Hyperostosis	6 (12%)	9 (18%)	7 (14%)	7 (14%)
Nervous System				
Brain	(49)	(50)	(50)	(50)
Compression		1 (2%)	1 (2%)	1 (2%)
Hydrocephalus			1 (2%)	
Inflammation, chronic				1 (2%)
Necrosis		1 (2%)		
Parenchyma, vacuolization cytoplasmic, diffuse		1 (2%)		
Thalamus, mineralization	41 (84%)	27 (54%)	33 (66%)	35 (70%)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion	2 (4%)		5 (10%)	2 (4%)
Edema	1 (2%)			
Hemorrhage	2 (4%)	3 (6%)	2 (4%)	2 (4%)
Hyperplasia, lymphoid	10 (20%)	9 (18%)	12 (24%)	13 (26%)
Infiltration cellular, histiocytic	3 (6%)	3 (6%)	2 (4%)	9 (18%)
Leukocytosis		1 (2%)	1 (2%)	1 (2%)
Thrombus		2 (4%)		
Alveolar epithelium, hyperplasia	1 (2%)	2 (4%)		1 (2%)
Nose	(50)	(50)	(50)	(50)
Exudate	3 (6%)	2 (4%)		2 (4%)
Glands, hyperplasia, cystic	5 (10%)	3 (6%)	1 (2%)	4 (8%)
Special Senses System				
Eye		(1)		
Cornea, inflammation, chronic		1 (100%)		
Harderian gland	(1)	(1)	(1)	(5)
Cyst				1 (20%)
Hyperplasia, focal				1 (20%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Amyloid deposition				1 (2%)
Casts protein	12 (24%)	9 (18%)	6 (12%)	7 (14%)
Cyst		1 (2%)	1 (2%)	2 (4%)
Glomerulosclerosis	2 (4%)	1 (2%)		
Hemorrhage		1 (2%)	1 (2%)	2 (4%)
Hydronephrosis	3 (6%)	2 (4%)		
Hyperplasia, lymphoid	21 (42%)	14 (28%)	15 (30%)	17 (34%)
Inflammation, suppurative	1 (2%)			
Metaplasia, osseous	1 (2%)	1 (2%)	4 (8%)	1 (2%)
Mineralization	22 (44%)	9 (18%)	8 (16%)	13 (26%)

TABLE H4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Chloraminated Water Study (continued)

	0 ppm	50 ppm	100 ppm	200 ppm
Urinary System				
Kidney (continued)	(50)	(50)	(50)	(50)
Thrombus			1 (2%)	
Interstitium, pigmentation		1 (2%)	1 (2%)	
Papilla, necrosis	1 (2%)			
Renal tubule, atrophy	4 (8%)	7 (14%)	6 (12%)	8 (16%)
Renal tubule, dilatation	5 (10%)	4 (8%)	6 (12%)	
Renal tubule, necrosis	1 (2%)		1 (2%)	
Renal tubule, pigmentation		1 (2%)	1 (2%)	1 (2%)
Renal tubule, regeneration	34 (68%)	32 (64%)	35 (70%)	25 (50%)
Transitional epithelium, hyperplasia	2 (4%)	1 (2%)	1 (2%)	
Ureter	(1)			
Dilatation	1 (100%)			
Inflammation, suppurative	1 (100%)			
Urinary bladder	(49)	(49)	(49)	(50)
Angiectasis			1 (2%)	
Dilatation	1 (2%)			
Edema		1 (2%)		
Hyperplasia, lymphoid	23 (47%)	21 (43%)	27 (55%)	27 (54%)
Inflammation, subacute	2 (4%)			
Mucosa, hyperplasia	2 (4%)			

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

TABLE I1
Organ Weights for Rats at the 14-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	10	10
Necropsy body wt.	374 ± 9	385 ± 7	362 ± 6	363 ± 5
Brain	1.98 ± 0.01	1.99 ± 0.01	1.98 ± 0.02	1.96 ± 0.02
Kidney	1.09 ± 0.04	1.16 ± 0.02	1.11 ± 0.02	1.08 ± 0.03
Liver	12.90 ± 0.44[b]	13.68 ± 0.34	12.42 ± 0.28	12.08 ± 0.42
Thymus	0.40 ± 0.02	0.49 ± 0.03	0.40 ± 0.02	0.41 ± 0.04
Female				
n	10	10	10	10
Necropsy body wt.	206 ± 4	208 ± 3	203 ± 4	204 ± 2
Brain	1.82 ± 0.01	1.81 ± 0.02	1.81 ± 0.02	1.81 ± 0.01
Kidney	0.67 ± 0.01	0.62 ± 0.01*	0.64 ± 0.01	0.65 ± 0.01
Liver	6.18 ± 0.16	5.91 ± 0.10	5.84 ± 0.13	5.93 ± 0.10
Thymus	0.25 ± 0.02	0.25 ± 0.01	0.26 ± 0.01	0.25 ± 0.02

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
[a] Organ weights are given in grams. Mean ± standard error
[b] n=8

TABLE I2
Organ-Weight-to-Body-Weight Ratios for Rats at the 14-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	10	10
Necropsy body wt.	374 ± 9	385 ± 7	362 ± 6	363 ± 5
Brain	5.32 ± 0.11	5.20 ± 0.09	5.49 ± 0.07	5.40 ± 0.07
Kidney	2.91 ± 0.07	3.01 ± 0.05	3.07 ± 0.04	2.98 ± 0.04
Liver	34.6 ± 0.48[b]	35.5 ± 0.41	34.3 ± 0.39	33.2 ± 0.75
Thymus	1.08 ± 0.06	1.27 ± 0.07	1.11 ± 0.07	1.12 ± 0.09
Female				
n	10	10	10	10
Necropsy body wt.	206 ± 4	208 ± 3	203 ± 4	204 ± 2
Brain	8.88 ± 0.19	8.69 ± 0.16	8.93 ± 0.14	8.89 ± 0.10
Kidney	3.24 ± 0.09	2.98 ± 0.04*	3.13 ± 0.03	3.17 ± 0.07
Liver	30.0 ± 0.49	28.4 ± 0.48	28.7 ± 0.39	29.1 ± 0.56
Thymus	1.23 ± 0.09	1.22 ± 0.06	1.26 ± 0.06	1.22 ± 0.08

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error
[b] n=8

TABLE I3
Organ Weights for Rats at the 66-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	9	9	10	9
Necropsy body wt.	509 ± 6	511 ± 14	507 ± 7	505 ± 9
Brain	2.15 ± 0.01	2.11 ± 0.02	2.12 ± 0.01	2.14 ± 0.02
Kidney	1.55 ± 0.02	1.52 ± 0.05	1.57 ± 0.04	1.55 ± 0.04
Liver	16.94 ± 0.27	16.70 ± 0.78	16.23 ± 0.44	16.81 ± 0.41
Thymus	0.19 ± 0.02	0.22 ± 0.02	0.21 ± 0.02	0.19 ± 0.02
Female				
n	10	10	9	10
Necropsy body wt.	317 ± 8	332 ± 5	321 ± 10	317 ± 8
Brain	1.91 ± 0.01	1.90 ± 0.02	1.92 ± 0.01	1.88 ± 0.02
Kidney	0.91 ± 0.02	0.91 ± 0.01	0.91 ± 0.03	0.92 ± 0.03
Liver	9.01 ± 0.27	9.14 ± 0.17	9.24 ± 0.34	8.96 ± 0.24
Thymus	0.17 ± 0.02	0.17 ± 0.02	0.17 ± 0.02	0.20 ± 0.02

[a] Organ weights are given in grams. Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.

TABLE I4
Organ-Weight-to-Body-Weight Ratios for Rats at the 66-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	9	9	10	9
Necropsy body wt.	509 ± 6	511 ± 14	507 ± 7	505 ± 9
Brain	4.23 ± 0.06	4.15 ± 0.11	4.18 ± 0.06	4.25 ± 0.08
Kidney	3.05 ± 0.05	2.97 ± 0.06	3.11 ± 0.06	3.06 ± 0.06
Liver	33.3 ± 0.44	32.6 ± 0.82	32.0 ± 0.73	33.3 ± 0.62
Thymus	0.37 ± 0.05	0.45 ± 0.05	0.41 ± 0.04	0.38 ± 0.05
Female				
n	10	10	9	10
Necropsy body wt.	317 ± 8	332 ± 5	321 ± 10	317 ± 8
Brain	6.06 ± 0.15	5.74 ± 0.10	6.03 ± 0.20	5.96 ± 0.13
Kidney	2.88 ± 0.07	2.75 ± 0.05	2.86 ± 0.05	2.91 ± 0.06
Liver	28.5 ± 0.76	27.5 ± 0.45	28.8 ± 0.50	28.3 ± 0.58
Thymus	0.54 ± 0.05	0.51 ± 0.04	0.54 ± 0.05	0.61 ± 0.07

[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.

TABLE I5
Organ Weights for Rats at the 14-Week Interim Evaluations for Chloraminated Water Studies[a]

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	10
Necropsy body wt.	374 ± 9	365 ± 6	371 ± 7	341 ± 4**
Brain	1.98 ± 0.01	1.96 ± 0.02	1.97 ± 0.02	1.95 ± 0.02
Kidney	1.09 ± 0.04	1.09 ± 0.02	1.11 ± 0.03	1.07 ± 0.03
Liver	12.90 ± 0.44[b]	12.33 ± 0.31	12.55 ± 0.23	11.36 ± 0.26**
Thymus	0.40 ± 0.02	0.41 ± 0.03	0.41 ± 0.03	0.38 ± 0.03
Female				
n	10	10	10	10
Necropsy body wt.	206 ± 4	202 ± 3	206 ± 2	199 ± 3
Brain	1.82 ± 0.01	1.80 ± 0.01	1.77 ± 0.02	1.80 ± 0.02
Kidney	0.67 ± 0.01	0.62 ± 0.01	0.64 ± 0.02	0.68 ± 0.01
Liver	6.18 ± 0.16	5.83 ± 0.17	5.91 ± 0.11[c]	5.78 ± 0.11
Thymus	0.25 ± 0.02	0.25 ± 0.01	0.24 ± 0.01	0.27 ± 0.02

** Significantly different (P≤0.01) from the control group by Dunn's or Shirley's test
[a] Organ weights are given in grams. Mean ± standard error
[b] n=8
[c] n=9

TABLE I6
Organ-Weight-to-Body-Weight Ratios for Rats at the 14-Week Interim Evaluations for Chloraminated Water Studies[a]

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	10
Necropsy body wt.	374 ± 9	365 ± 6	371 ± 7	341 ± 4**
Brain	5.32 ± 0.11	5.39 ± 0.07	5.32 ± 0.09	5.73 ± 0.07**
Kidney	2.91 ± 0.07	2.98 ± 0.04	3.00 ± 0.05	3.15 ± 0.09*
Liver	34.6 ± 0.48[b]	33.7 ± 0.49	33.8 ± 0.28	33.3 ± 0.75
Thymus	1.08 ± 0.06	1.11 ± 0.07	1.11 ± 0.08	1.11 ± 0.09
Female				
n	10	10	10	10
Necropsy body wt.	206 ± 4	202 ± 3	206 ± 2	199 ± 3
Brain	8.88 ± 0.19	8.96 ± 0.14	8.60 ± 0.14	9.08 ± 0.11
Kidney	3.24 ± 0.09	3.09 ± 0.04	3.08 ± 0.08	3.42 ± 0.05*
Liver	30.0 ± 0.49	28.9 ± 0.69	28.7 ± 0.45[c]	29.1 ± 0.30
Thymus	1.23 ± 0.09	1.25 ± 0.07	1.18 ± 0.04	1.34 ± 0.09

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error
[b] n=8
[c] n=9

TABLE I7
Organ Weights for Rats at the 66-Week Interim Evaluations for Chloraminated Water Studies[a]

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	9	10	9	10
Necropsy body wt.	509 ± 6	498 ± 6	488 ± 11*	480 ± 6**
Brain	2.15 ± 0.01	2.14 ± 0.02	2.12 ± 0.02	2.12 ± 0.01
Kidney	1.55 ± 0.02	1.51 ± 0.02	1.50 ± 0.07	1.45 ± 0.03*
Liver	16.94 ± 0.27	16.12 ± 0.64	16.60 ± 0.83	14.79 ± 0.48*
Thymus	0.19 ± 0.02	0.21 ± 0.03	0.20 ± 0.03	0.22 ± 0.02
Female				
n	10	10	10	10
Necropsy body wt.	317 ± 8	321 ± 6	309 ± 8	292 ± 8*
Brain	1.91 ± 0.01	1.89 ± 0.01	1.88 ± 0.02	1.94 ± 0.02
Kidney	0.91 ± 0.02	0.93 ± 0.02	0.92 ± 0.03	0.94 ± 0.03
Liver	9.01 ± 0.27	9.22 ± 0.26	8.70 ± 0.22	8.31 ± 0.25
Thymus	0.17 ± 0.02	0.18 ± 0.02	0.18 ± 0.03	0.16 ± 0.02

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Organ weights are given in grams. Mean ± standard error

TABLE I8
Organ-Weight-to-Body-Weight Ratios for Rats at the 66-Week Interim Evaluations for Chloraminated Water Studies[a]

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	9	10	9	10
Necropsy body wt.	509 ± 6	498 ± 6	488 ± 11*	480 ± 6**
Brain	4.23 ± 0.06	4.31 ± 0.07	4.36 ± 0.07	4.43 ± 0.05*
Kidney	3.05 ± 0.05	3.05 ± 0.05	3.07 ± 0.08	3.03 ± 0.04
Liver	33.3 ± 0.44	32.4 ± 1.12	33.9 ± 0.98	30.8 ± 0.89
Thymus	0.37 ± 0.05	0.41 ± 0.06	0.41 ± 0.06	0.47 ± 0.04
Female				
n	10	10	10	10
Necropsy body wt.	317 ± 8	321 ± 6	309 ± 8	292 ± 8*
Brain	6.06 ± 0.15	5.92 ± 0.11	6.13 ± 0.14	6.69 ± 0.20*
Kidney	2.88 ± 0.07	2.90 ± 0.05	2.97 ± 0.09	3.21 ± 0.08**
Liver	28.5 ± 0.76	28.7 ± 0.49	28.3 ± 0.73	28.5 ± 0.46
Thymus	0.54 ± 0.05	0.57 ± 0.07	0.56 ± 0.08	0.54 ± 0.05

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error

TABLE I9
Organ Weights for Mice at the 15-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	10	10
Necropsy body wt.	38.3 ± 0.9	39.1 ± 1.1	39.0 ± 1.3	36.8 ± 1.2
Brain	0.47 ± 0.00	0.47 ± 0.01	0.47 ± 0.01	0.45 ± 0.00*
Kidney	0.31 ± 0.01	0.32 ± 0.01	0.30 ± 0.01	0.29 ± 0.01
Liver	1.50 ± 0.07	1.61 ± 0.09	1.57 ± 0.10[b]	1.54 ± 0.08
Thymus	0.06 ± 0.01[b]	0.06 ± 0.01	0.06 ± 0.01	0.05 ± 0.01
Female				
n	10	10	10	10
Necropsy body wt.	31.9 ± 1.5	32.3 ± 1.6	29.0 ± 0.9	29.2 ± 0.9
Brain	0.47 ± 0.01	0.47 ± 0.01	0.46 ± 0.01	0.47 ± 0.01
Kidney	0.21 ± 0.01	0.21 ± 0.01	0.19 ± 0.01[b]	0.21 ± 0.01
Liver	1.31 ± 0.07	1.31 ± 0.05	1.19 ± 0.05	1.20 ± 0.05
Thymus	0.06 ± 0.01	0.07 ± 0.01	0.07 ± 0.00	0.06 ± 0.00

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
[a] Organ weights are given in grams. Mean ± standard error
[b] n=9

TABLE I10
Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	10	10
Necropsy body wt.	38.3 ± 0.9	39.1 ± 1.1	39.0 ± 1.3	36.8 ± 1.2
Brain	12.3 ± 0.27	12.0 ± 0.26	12.1 ± 0.36	12.4 ± 0.38
Kidney	7.96 ± 0.24	8.16 ± 0.26	7.83 ± 0.18	7.87 ± 0.33
Liver	39.1 ± 1.45	41.0 ± 1.62	40.8 ± 1.77[b]	41.7 ± 1.49
Thymus	1.51 ± 0.13[b]	1.60 ± 0.14	1.62 ± 0.13	1.49 ± 0.15
Female				
n	10	10	10	10
Necropsy body wt.	31.9 ± 1.5	32.3 ± 1.6	29.0 ± 0.9	29.2 ± 0.9
Brain	15.1 ± 0.62	14.8 ± 0.69	16.0 ± 0.45	16.3 ± 0.57
Kidney	6.67 ± 0.33	6.42 ± 0.24	6.76 ± 0.36[b]	7.11 ± 0.19
Liver	40.9 ± 0.88	40.8 ± 1.53	41.2 ± 1.43	41.1 ± 1.23
Thymus	1.99 ± 0.16	2.25 ± 0.13	2.34 ± 0.12	2.14 ± 0.11

[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.
[b] n=9

TABLE I11
Organ Weights for Mice at the 66-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	10	9
Necropsy body wt.	51.1 ± 0.6	48.6 ± 1.1	49.1 ± 1.1	47.3 ± 1.0**
Brain	0.46 ± 0.01	0.46 ± 0.00	0.46 ± 0.00	0.46 ± 0.01
Kidney	0.42 ± 0.01	0.41 ± 0.01	0.42 ± 0.01	0.40 ± 0.01
Liver	3.02 ± 0.37	2.57 ± 0.31	2.64 ± 0.32	2.13 ± 0.11*
Thymus	0.06 ± 0.01	0.06 ± 0.01	0.05 ± 0.01	0.05 ± 0.00
Female				
n	10	9	10	10
Necropsy body wt.	48.3 ± 3.4	56.8 ± 2.1	51.6 ± 2.7	48.3 ± 1.9
Brain	0.47 ± 0.00	0.48 ± 0.00*	0.48 ± 0.00	0.48 ± 0.01
Kidney	0.23 ± 0.01	0.27 ± 0.01	0.25 ± 0.01	0.25 ± 0.01
Liver	1.69 ± 0.10	1.95 ± 0.09	1.76 ± 0.09	1.60 ± 0.07
Thymus	0.05 ± 0.00	0.05 ± 0.00	0.05 ± 0.00	0.05 ± 0.01

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Organ weights are given in grams. Mean ± standard error

TABLE I12
Organ-Weight-to-Body-Weight Ratios for Mice at the 66-Week Interim Evaluations for Chlorinated Water Studies[a]

	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	10	9
Necropsy body wt.	51.1 ± 0.6	48.6 ± 1.1	49.1 ± 1.1	47.3 ± 1.0**
Brain	8.94 ± 0.13	9.50 ± 0.26	9.42 ± 0.24	9.77 ± 0.25**
Kidney	8.15 ± 0.24	8.53 ± 0.37	8.58 ± 0.25	8.53 ± 0.18
Liver	59.4 ± 7.67	53.4 ± 6.77	54.2 ± 7.00	44.9 ± 1.65
Thymus	1.08 ± 0.17	1.25 ± 0.15	0.96 ± 0.09	1.13 ± 0.08
Female				
n	10	9	10	10
Necropsy body wt.	48.3 ± 3.4	56.8 ± 2.1	51.6 ± 2.7	48.3 ± 1.9
Brain	10.1 ± 0.83	8.50 ± 0.40	9.40 ± 0.45	10.0 ± 0.43
Kidney	5.01 ± 0.28	4.75 ± 0.35	4.96 ± 0.21	5.17 ± 0.21
Liver	35.4 ± 1.08	34.3 ± 1.86	34.4 ± 1.52	33.4 ± 1.18
Thymus	0.95 ± 0.07	0.87 ± 0.11	0.97 ± 0.07	1.01 ± 0.09

** Significantly different (P≤0.01) from the control group by Dunn's or Shirley's test
[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error

TABLE I13
Organ Weights for Mice at the 15-Week Interim Evaluations for Chloraminated Water Studies[a]

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	10
Necropsy body wt.	38.3 ± 0.9	36.9 ± 1.3	37.0 ± 1.0	34.7 ± 0.6*
Brain	0.47 ± 0.00	0.46 ± 0.01	0.46 ± 0.00	0.45 ± 0.00**
Kidney	0.31 ± 0.01	0.29 ± 0.01	0.30 ± 0.01	0.30 ± 0.01[b]
Liver	1.50 ± 0.07	1.46 ± 0.07	1.44 ± 0.06	1.43 ± 0.03[b]
Thymus	0.06 ± 0.01[b]	0.06 ± 0.00	0.06 ± 0.01	0.06 ± 0.01
Female				
n	10	10	10	10
Necropsy body wt.	31.9 ± 1.5	32.2 ± 1.1	30.9 ± 1.1	26.7 ± 0.7**
Brain	0.47 ± 0.01	0.47 ± 0.01	0.46 ± 0.01	0.47 ± 0.01
Kidney	0.21 ± 0.01	0.21 ± 0.01	0.21 ± 0.01	0.20 ± 0.01
Liver	1.31 ± 0.07	1.31 ± 0.06	1.20 ± 0.05	1.07 ± 0.03**
Thymus	0.06 ± 0.01	0.07 ± 0.00	0.07 ± 0.01	0.05 ± 0.00

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Organ weights are given in grams. Mean ± standard error
[b] n=9

TABLE I14
Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Week Interim Evaluations for Chloraminated Water Studies[a]

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	10
Necropsy body wt.	38.3 ± 0.9	36.9 ± 1.3	37.0 ± 1.0	34.7 ± 0.6*
Brain	12.3 ± 0.27	12.5 ± 0.40	12.5 ± 0.47	13.0 ± 0.20
Kidney	7.96 ± 0.24	7.92 ± 0.23	8.24 ± 0.25	8.66 ± 0.19*[b]
Liver	39.1 ± 1.45	39.6 ± 1.32	38.9 ± 1.13	41.0 ± 0.64[b]
Thymus	1.51 ± 0.13[b]	1.69 ± 0.13	1.70 ± 0.15	1.72 ± 0.17
Female				
n	10	10	10	10
Necropsy body wt.	31.9 ± 1.5	32.2 ± 1.1	30.9 ± 1.1	26.7 ± 0.7**
Brain	15.1 ± 0.62	14.7 ± 0.41	15.2 ± 0.52	17.7 ± 0.42**
Kidney	6.67 ± 0.33	6.51 ± 0.11	6.73 ± 0.15	7.44 ± 0.21**
Liver	40.9 ± 0.88	40.8 ± 1.37	38.8 ± 1.21	40.1 ± 0.89
Thymus	1.99 ± 0.16	2.20 ± 0.12	2.11 ± 0.18	2.03 ± 0.12

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error
[b] n=9

TABLE I15
Organ Weights for Mice at the 66-Week Interim Evaluations for Chloraminated Water Studies[a]

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	9
Necropsy body wt.	51.1 ± 0.6	49.6 ± 1.0	46.3 ± 1.3**	46.4 ± 0.9**
Brain	0.46 ± 0.01	0.47 ± 0.00	0.46 ± 0.01	0.46 ± 0.01
Kidney	0.42 ± 0.01	0.43 ± 0.02	0.43 ± 0.01	0.43 ± 0.01
Liver	3.02 ± 0.37	2.40 ± 0.19	2.07 ± 0.17**	1.99 ± 0.07**
Thymus	0.06 ± 0.01	0.05 ± 0.01	0.05 ± 0.00	0.05 ± 0.01
Female				
n	10	10	10	10
Necropsy body wt.	48.3 ± 3.4	46.7 ± 2.5	49.5 ± 2.2	42.0 ± 2.3
Brain	0.47 ± 0.00	0.47 ± 0.01	0.47 ± 0.01	0.48 ± 0.01
Kidney	0.23 ± 0.01	0.26 ± 0.01	0.26 ± 0.01	0.26 ± 0.01
Liver	1.69 ± 0.10	1.64 ± 0.07	1.70 ± 0.13	1.48 ± 0.06
Thymus	0.05 ± 0.00	0.04 ± 0.00	0.05 ± 0.01	0.04 ± 0.00

** Significantly different (P≤0.01) from the control group by Dunn's or Shirley's test
[a] Organ weights are given in grams. Mean ± standard error

TABLE I16
Organ-Weight-to-Body-Weight Ratios for Mice at the 66-Week Interim Evaluations [a] for Chloraminated Water Studies

	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	9
Necropsy body wt.	51.1 ± 0.6	49.6 ± 1.0	46.3 ± 1.3**	46.4 ± 0.9**
Brain	8.94 ± 0.13	9.46 ± 0.18	9.93 ± 0.28**	10.03 ± 0.22**
Kidney	8.15 ± 0.24	8.72 ± 0.20*	9.20 ± 0.19**	9.29 ± 0.18**
Liver	59.4 ± 7.67	48.4 ± 3.76	44.5 ± 3.20*	42.8 ± 1.09*
Thymus	1.08 ± 0.17	1.00 ± 0.17	1.07 ± 0.10	1.00 ± 0.11
Female				
n	10	10	10	10
Necropsy body wt.	48.3 ± 3.4	46.7 ± 2.5	49.5 ± 2.2	42.0 ± 2.3
Brain	10.1 ± 0.83	10.3 ± 0.49	9.60 ± 0.47	11.7 ± 0.69*
Kidney	5.01 ± 0.28	5.65 ± 0.28	5.35 ± 0.17	6.34 ± 0.24**
Liver	35.4 ± 1.08	35.6 ± 1.46	34.1 ± 1.57	35.6 ± 0.86
Thymus	0.95 ± 0.07	0.94 ± 0.10	1.04 ± 0.09	1.02 ± 0.09

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Organ-weight-to-body-weight ratios given as mg organ weight/g body weight. Mean ± standard error

APPENDIX J
HEMATOLOGY RESULTS AT THE 14-WEEK/15-WEEK AND 66-WEEK INTERIM EVALUATIONS

TABLE J1
Hematology Data for Rats at the 14-Week Interim Evaluations in the 2-Year Chlorinated Water Studies[a]

Analysis	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	9	10
Hematocrit (%)	37.6 ± 1.4	38.6 ± 0.8	39.1 ± 0.9	38.1 ± 0.5
Hemoglobin (g/dL)	13.4 ± 0.4	13.9 ± 0.2	14.0 ± 0.2	13.6 ± 0.1
Erythrocytes ($10^6/\mu L$)	8.35 ± 0.24	8.71 ± 0.06	8.79 ± 0.16	8.59 ± 0.06
Mean cell volume (μ^3)	45.0 ± 0.9	44.2 ± 0.7	44.7 ± 0.6	44.5 ± 0.6
Mean cell hemoglobin (pg)	16.1 ± 0.1	15.9 ± 0.1	15.9 ± 0.1	15.9 ± 0.1
Mean cell hemoglobin concentration (g/dL)	35.9 ± 0.7	36.0 ± 0.5	35.9 ± 0.5	35.8 ± 0.5
Platelets ($10^3/\mu L$)	534.3 ± 15.1	518.1 ± 24.4	488.3 ± 23.2	498.3 ± 17.1
Reticulocytes (%)	2.5 ± 0.6	1.5 ± 0.3	1.2 ± 0.2	1.4 ± 0.2
Leukocytes ($10^3/\mu L$)	3.43 ± 0.16	3.19 ± 0.25	3.58 ± 0.15	3.35 ± 0.15
Segmented neutrophils (%)	19.10 ± 1.70	16.80 ± 2.48	20.56 ± 3.44	21.90 ± 2.54
Bands (%)	0.20 ± 0.13	0.20 ± 0.20	0.33 ± 0.24	0.00 ± 0.00
Lymphocytes (%)	79.50 ± 1.96	82.00 ± 2.56	77.89 ± 3.36	76.90 ± 2.42
Atypical lymphocytes (%)	0.40 ± 0.31	-[b]	0.33 ± 0.24	0.20 ± 0.13
Monocytes (%)	0.10 ± 0.10	0.30 ± 0.30	0.33 ± 0.17	0.50 ± 0.22
Eosinophils (%)	0.70 ± 0.26	0.70 ± 0.26	0.56 ± 0.29	0.50 ± 0.17
Nucleated erythrocytes (/100 leukocytes)	0.70 ± 0.42	0.20 ± 0.13	0.67 ± 0.24	0.10 ± 0.10
Female				
n	10	9	10	10
Hematocrit (%)	37.4 ± 1.0	38.2 ± 0.8	37.9 ± 0.7	38.6 ± 0.5
Hemoglobin (g/dL)	13.4 ± 0.4	13.8 ± 0.3	13.8 ± 0.1	13.7 ± 0.1
Erythrocytes ($10^6/\mu L$)	7.81 ± 0.20	8.04 ± 0.15	8.03 ± 0.06	8.02 ± 0.08
Mean cell volume (μ^3)	47.9 ± 0.6	47.6 ± 0.7	47.3 ± 0.6	48.2 ± 0.5
Mean cell hemoglobin (pg)	17.2 ± 0.1	17.1 ± 0.1	17.2 ± 0.1	17.1 ± 0.1
Mean cell hemoglobin concentration (g/dL)	35.9 ± 0.5	36.1 ± 0.5	36.5 ± 0.7	35.5 ± 0.2
Platelets ($10^3/\mu L$)	514.9 ± 15.2[c]	511.4 ± 28.4	531.7 ± 12.0[c]	539.0 ± 32.8
Reticulocytes (%)	1.5 ± 0.3	1.3 ± 0.2	1.4 ± 0.2	1.4 ± 0.2
Leukocytes ($10^3/\mu L$)	2.21 ± 0.23	2.52 ± 0.17	2.59 ± 0.18	2.66 ± 0.15
Segmented neutrophils (%)	21.40 ± 1.93	23.44 ± 2.53	22.10 ± 2.93	23.40 ± 1.84
Bands (%)	0.20 ± 0.13	0.33 ± 0.24	0.40 ± 0.31	0.20 ± 0.13
Lymphocytes (%)	77.30 ± 2.04	75.56 ± 2.58	76.40 ± 2.89	74.50 ± 2.05
Atypical lymphocytes (%)	0.10 ± 0.10	0.11 ± 0.11	0.10 ± 0.10	0.30 ± 0.21
Monocytes (%)	0.20 ± 0.20	0.00 ± 0.00	0.30 ± 0.21	0.50 ± 0.31
Eosinophils (%)	0.80 ± 0.25	0.56 ± 0.24	0.70 ± 0.37	1.10 ± 0.23
Nucleated erythrocytes (/100 leukocytes)	0.20 ± 0.20	0.22 ± 0.22	0.30 ± 0.15	-

[a] Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.
[b] Insufficient data
[c] n=8

TABLE J2
Hematology Data for Rats at the 66-Week Interim Evaluations in the 2-Year Chlorinated Water Studies[a]

Analysis	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	8	9	10	9
Hematocrit (%)	44.8 ± 1.3	45.4 ± 1.6	43.9 ± 0.8	43.9 ± 0.5
Hemoglobin (g/dL)	15.4 ± 0.4	15.7 ± 0.5	15.3 ± 0.2	15.0 ± 0.2
Erythrocytes ($10^6/\mu L$)	9.23 ± 0.23	9.37 ± 0.27	9.04 ± 0.16	8.86 ± 0.18
Mean cell volume (μ^3)	48.6 ± 0.4	48.0 ± 0.2	48.7 ± 0.6	49.7 ± 0.7
Mean cell hemoglobin (pg)	16.7 ± 0.1	16.7 ± 0.1	16.9 ± 0.2	17.0 ± 0.2
Mean cell hemoglobin concentration (g/dL)	34.3 ± 0.2	34.6 ± 0.2	34.9 ± 0.3	34.2 ± 0.2
Platelets ($10^3/\mu L$)	547.1 ± 37.6	581.4 ± 31.7	603.1 ± 18.5	562.3 ± 23.3
Reticulocytes (%)	0.5 ± 0.1	0.5 ± 0.0	0.5 ± 0.0	0.6 ± 0.0
Leukocytes ($10^3/\mu L$)	4.06 ± 0.29	4.87 ± 0.40	4.57 ± 0.25	4.38 ± 0.20
Segmented neutrophils (%)	29.88 ± 1.96	36.89 ± 3.19	38.20 ± 2.43	33.67 ± 2.30
Bands (%)	0.00 ± 0.00	0.11 ± 0.11	0.00 ± 0.00	0.11 ± 0.11
Lymphocytes (%)	65.88 ± 2.02	58.78 ± 3.28	57.70 ± 2.43	62.44 ± 1.80
Atypical lymphocytes (%)	0.88 ± 0.40	1.00 ± 0.37	1.20 ± 0.49	0.22 ± 0.22
Monocytes (%)	2.00 ± 0.57	1.89 ± 0.31	1.80 ± 0.39	1.78 ± 0.66
Eosinophils (%)	1.25 ± 0.56	1.33 ± 0.33	1.10 ± 0.28	1.78 ± 0.52
Nucleated erythrocytes (/100 leukocytes)	2.50 ± 0.78	1.78 ± 0.52	2.00 ± 0.63	3.11 ± 0.95
Female				
n	10	10	9	9
Hematocrit (%)	44.2 ± 1.1	44.0 ± 0.5	42.8 ± 0.6	43.6 ± 1.0
Hemoglobin (g/dL)	15.3 ± 0.4	15.2 ± 0.1	15.0 ± 0.2	15.2 ± 0.3
Erythrocytes ($10^6/\mu L$)	8.54 ± 0.20	8.42 ± 0.09	8.37 ± 0.10	8.34 ± 0.20
Mean cell volume (μ^3)	51.8 ± 0.3	52.2 ± 0.1	51.2 ± 0.3	52.4 ± 0.4
Mean cell hemoglobin (pg)	17.9 ± 0.2	18.0 ± 0.1	17.9 ± 0.1	18.2 ± 0.1
Mean cell hemoglobin concentration (g/dL)	34.7 ± 0.3	34.5 ± 0.1	35.1 ± 0.3	34.9 ± 0.2
Platelets ($10^3/\mu L$)	443.5 ± 30.0	507.8 ± 11.3	408.7 ± 13.0	511.3 ± 28.2
Reticulocytes (%)	0.5 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	0.5 ± 0.1
Leukocytes ($10^3/\mu L$)	2.44 ± 0.27	2.62 ± 0.15	2.28 ± 0.07	2.37 ± 0.19
Segmented neutrophils (%)	34.20 ± 4.24	35.80 ± 3.66	32.56 ± 1.84	30.44 ± 3.44
Bands (%)	0.10 ± 0.10	0.00 ± 0.00	0.00 ± 0.00	0.11 ± 0.11
Lymphocytes (%)	61.20 ± 4.55	60.50 ± 3.88	63.89 ± 2.62	65.89 ± 3.42
Atypical lymphocytes (%)	1.60 ± 0.40	1.30 ± 0.40	1.44 ± 1.00	1.11 ± 0.31
Monocytes (%)	1.40 ± 0.60	1.10 ± 0.43	0.67 ± 0.33	0.78 ± 0.47
Eosinophils (%)	1.50 ± 0.34	1.30 ± 0.40	1.44 ± 0.41	1.67 ± 0.50
Nucleated erythrocytes (/100 leukocytes)	3.10 ± 0.60	1.80 ± 0.39	2.56 ± 0.60	2.44 ± 0.50

[a] Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.

TABLE J3
Hematology Data for Rats at the 14-Week Interim Evaluations in the 2-Year Chloraminated Water Studies[a]

Analysis	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	10
Hematocrit (%)	37.6 ± 1.4	38.5 ± 0.5	38.9 ± 0.9	39.3 ± 0.9
Hemoglobin (g/dL)	13.4 ± 0.4	13.8 ± 0.1	13.9 ± 0.2	13.9 ± 0.2
Erythrocytes ($10^6/\mu L$)	8.35 ± 0.24	8.64 ± 0.08	8.69 ± 0.11	8.72 ± 0.10
Mean cell volume (μ^3)	45.0 ± 0.9	44.7 ± 0.8	44.8 ± 0.7	45.1 ± 0.8
Mean cell hemoglobin (pg)	16.1 ± 0.1	16.0 ± 0.1	15.9 ± 0.1	15.9 ± 0.1
Mean cell hemoglobin concentration (g/dL)	35.9 ± 0.7	35.9 ± 0.4	35.7 ± 0.5	35.5 ± 0.6
Platelets ($10^3/\mu L$)	534.3 ± 15.1	514.2 ± 14.2	511.2 ± 17.1	481.6 ± 12.6**
Reticulocytes (%)	2.5 ± 0.6	1.7 ± 0.3	1.4 ± 0.2	1.5 ± 0.2
Leukocytes ($10^3/\mu L$)	3.43 ± 0.16	3.49 ± 0.14	3.20 ± 0.13	3.68 ± 0.17
Segmented neutrophils (%)	19.10 ± 1.70	18.20 ± 1.60	19.00 ± 0.67	18.10 ± 1.81
Bands (%)	0.20 ± 0.13	0.40 ± 0.16	0.10 ± 0.10	0.10 ± 0.10
Lymphocytes (%)	79.50 ± 1.96	79.40 ± 1.75	79.30 ± 0.98	80.50 ± 1.78
Atypical lymphocytes (%)	0.40 ± 0.31	0.10 ± 0.10	0.10 ± 0.10	0.20 ± 0.13
Monocytes (%)	0.10 ± 0.10	0.60 ± 0.31	0.40 ± 0.16	0.40 ± 0.16
Eosinophils (%)	0.70 ± 0.26	1.30 ± 0.37	1.10 ± 0.48	0.70 ± 0.26
Nucleated erythrocytes (/100 leukocytes)	0.70 ± 0.42	0.40 ± 0.27	0.20 ± 0.13	0.30 ± 0.21
Female				
n	10	8	9	10
Hematocrit (%)	37.4 ± 1.0	38.2 ± 0.9	37.4 ± 0.6	38.6 ± 0.8
Hemoglobin (g/dL)	13.4 ± 0.4	13.7 ± 0.1	13.6 ± 0.1	13.8 ± 0.2
Erythrocytes ($10^6/\mu L$)	7.81 ± 0.20	8.06 ± 0.10	7.92 ± 0.09	8.13 ± 0.09
Mean cell volume (μ^3)	47.9 ± 0.6	47.4 ± 0.8	47.2 ± 0.7	47.5 ± 0.8
Mean cell hemoglobin (pg)	17.2 ± 0.1	17.1 ± 0.1	17.2 ± 0.1	17.0 ± 0.1
Mean cell hemoglobin concentration (g/dL)	35.9 ± 0.5	36.1 ± 0.7	36.5 ± 0.6	35.9 ± 0.5
Platelets ($10^3/\mu L$)	514.9 ± 15.2[b]	498.4 ± 25.0	479.6 ± 30.6	496.0 ± 28.4[b]
Reticulocytes (%)	1.5 ± 0.3	1.4 ± 0.2	1.7 ± 0.2	1.5 ± 0.2
Leukocytes ($10^3/\mu L$)	2.21 ± 0.23	2.33 ± 0.16	2.57 ± 0.13	2.49 ± 0.14
Segmented neutrophils (%)	21.40 ± 1.93	26.13 ± 1.73	21.22 ± 1.48	27.90 ± 2.11*
Bands (%)	0.20 ± 0.13	0.63 ± 0.38	0.11 ± 0.11	0.40 ± 0.31
Lymphocytes (%)	77.30 ± 2.04	71.13 ± 1.77	76.33 ± 1.69	70.20 ± 2.28
Atypical lymphocytes (%)	0.10 ± 0.10	0.13 ± 0.13	0.11 ± 0.11	0.10 ± 0.10
Monocytes (%)	0.20 ± 0.20	0.88 ± 0.48	0.11 ± 0.11	0.10 ± 0.10
Eosinophils (%)	0.80 ± 0.25	1.13 ± 0.44	2.11 ± 0.42	1.30 ± 0.34
Nucleated erythrocytes (/100 leukocytes)	0.20 ± 0.20	0.25 ± 0.16	–[c]	0.10 ± 0.10

* Significantly different ($P \le 0.05$) from the control group by Dunn's or Shirley's test
** $P \le 0.01$
[a] Mean ± standard error.
[b] n=8
[c] Insufficient data

TABLE J4
Hematology Data for Rats at the 66-Week Interim Evaluations in the 2-Year Chloraminated Water Studies[a]

Analysis	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	8	10	8	9
Hematocrit (%)	44.8 ± 1.3	45.1 ± 0.6	44.0 ± 0.8	44.1 ± 0.8
Hemoglobin (g/dL)	15.4 ± 0.4	15.5 ± 0.2	15.1 ± 0.3	15.2 ± 0.3
Erythrocytes ($10^6/\mu L$)	9.23 ± 0.23	9.26 ± 0.15	9.08 ± 0.23	8.93 ± 0.17
Mean cell volume (μ^3)	48.6 ± 0.4	48.6 ± 0.6	48.5 ± 0.3	49.1 ± 0.5
Mean cell hemoglobin (pg)	16.7 ± 0.1	16.8 ± 0.2	16.6 ± 0.1	16.9 ± 0.3
Mean cell hemoglobin concentration (g/dL)	34.3 ± 0.2	34.4 ± 0.2	34.2 ± 0.2	34.3 ± 0.3
Platelets ($10^3/\mu L$)	547.1 ± 37.6	566.3 ± 17.8	577.7 ± 32.4	546.4 ± 20.3
Reticulocytes (%)	0.5 ± 0.1	0.5 ± 0.0	0.5 ± 0.0	0.5 ± 0.1
Leukocytes ($10^3/\mu L$)	4.06 ± 0.29	4.61 ± 0.38	4.48 ± 0.28	4.48 ± 0.25
Segmented neutrophils (%)	29.88 ± 1.96	39.10 ± 3.44	32.25 ± 3.66	35.44 ± 2.48
Bands (%)	0.00 ± 0.00	0.20 ± 0.13	0.00 ± 0.00	0.11 ± 0.11
Lymphocytes (%)	65.88 ± 2.02	55.70 ± 4.23	64.63 ± 3.56	61.44 ± 2.30
Atypical lymphocytes (%)	0.88 ± 0.40	1.00 ± 0.37	0.25 ± 0.16	0.89 ± 0.61
Monocytes (%)	2.00 ± 0.57	2.20 ± 1.18	1.75 ± 0.49	0.89 ± 0.26
Eosinophils (%)	1.25 ± 0.56	1.80 ± 0.29	1.13 ± 0.35	1.22 ± 0.55
Nucleated erythrocytes (/100 leukocytes)	2.50 ± 0.78	2.10 ± 0.57	0.25 ± 0.16*	1.56 ± 0.63
Female				
n	10	8	10	10
Hematocrit (%)	44.2 ± 1.1	44.9 ± 1.4	45.4 ± 1.5	43.5 ± 0.9
Hemoglobin (g/dL)	15.3 ± 0.4	15.6 ± 0.5	15.8 ± 0.5	15.0 ± 0.3
Erythrocytes ($10^6/\mu L$)	8.54 ± 0.20	8.63 ± 0.25	8.75 ± 0.28	8.28 ± 0.16
Mean cell volume (μ^3)	51.8 ± 0.3	52.0 ± 0.4	51.8 ± 0.2	52.3 ± 0.3
Mean cell hemoglobin (pg)	17.9 ± 0.2	18.0 ± 0.1	18.1 ± 0.1	18.2 ± 0.1
Mean cell hemoglobin concentration (g/dL)	34.7 ± 0.3	34.7 ± 0.2	34.8 ± 0.2	34.6 ± 0.2
Platelets ($10^3/\mu L$)	443.5 ± 30.0	450.1 ± 30.4	463.8 ± 32.2	483.8 ± 26.2
Reticulocytes (%)	0.5 ± 0.0	0.5 ± 0.0	0.4 ± 0.0	0.4 ± 0.0
Leukocytes ($10^3/\mu L$)	2.44 ± 0.27	2.23 ± 0.10	2.42 ± 0.19	2.34 ± 0.10
Segmented neutrophils (%)	34.20 ± 4.24	27.75 ± 2.38	33.20 ± 2.55	29.30 ± 2.74
Bands (%)	0.10 ± 0.10	0.13 ± 0.13	0.00 ± 0.00	0.20 ± 0.13
Lymphocytes (%)	61.20 ± 4.55	68.13 ± 2.63	61.70 ± 2.86	67.30 ± 3.21
Atypical lymphocytes (%)	1.60 ± 0.40	0.63 ± 0.38	1.90 ± 0.61	0.40 ± 0.27*
Monocytes (%)	1.40 ± 0.60	1.75 ± 0.77	1.80 ± 0.42	1.10 ± 0.41
Eosinophils (%)	1.50 ± 0.34	1.63 ± 0.46	1.40 ± 0.31	1.70 ± 0.47
Nucleated erythrocytes (/100 leukocytes)	3.10 ± 0.60	3.00 ± 0.80	1.80 ± 0.47	2.00 ± 0.49

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
[a] Mean ± standard error.

TABLE J5
Hematology Data for Mice at the 15-Week Interim Evaluations in the 2-Year Chlorinated Water Studies[a]

Analysis	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	7	8	10	10
Hematocrit (%)	37.8 ± 0.8	37.6 ± 0.9	38.5 ± 0.5	36.7 ± 0.8
Hemoglobin (g/dL)	12.9 ± 0.4	12.9 ± 0.4	13.4 ± 0.2	12.6 ± 0.4
Erythrocytes ($10^6/\mu L$)	8.69 ± 0.17	8.69 ± 0.21	9.01 ± 0.09	8.57 ± 0.20
Mean cell volume (μ^3)	43.6 ± 0.4	43.3 ± 0.4	42.7 ± 0.6	42.7 ± 0.4
Mean cell hemoglobin (pg)	14.8 ± 0.2	14.8 ± 0.1	14.9 ± 0.1	14.7 ± 0.2
Mean cell hemoglobin concentration (g/dL)	34.1 ± 0.6	34.2 ± 0.5	34.9 ± 0.5	34.3 ± 0.5
Platelets ($10^3/\mu L$)	598.0 ± 40.7	648.5 ± 50.7	686.4 ± 36.5	570.7 ± 61.9[b]
Reticulocytes (%)	1.2 ± 0.2	1.5 ± 0.2[c]	1.2 ± 0.1	1.4 ± 0.1
Leukocytes ($10^3/\mu L$)	1.47 ± 0.30	1.31 ± 0.37	1.52 ± 0.41	1.47 ± 0.22
Segmented neutrophils (%)	16.57 ± 1.90	19.13 ± 2.75	22.40 ± 4.58	23.20 ± 2.54
Bands (%)	0.29 ± 0.29	0.25 ± 0.16	0.60 ± 0.34	0.60 ± 0.34
Lymphocytes (%)	79.29 ± 1.27	77.25 ± 2.77	73.10 ± 4.34	73.40 ± 2.72
Atypical lymphocytes ($10^3/\mu L$)	2.14 ± 0.88	2.50 ± 0.73	2.40 ± 0.56	1.50 ± 0.60
Monocytes (%)	0.14 ± 0.14	0.25 ± 0.16	0.80 ± 0.25	0.20 ± 0.20
Eosinophils (%)	1.57 ± 0.72	0.63 ± 0.18	0.70 ± 0.30	1.10 ± 0.57
Female				
n	10	9	10	10
Hematocrit (%)	35.6 ± 1.2	36.2 ± 1.4[d]	34.1 ± 1.0	35.9 ± 0.6
Hemoglobin (g/dL)	12.4 ± 0.5	12.7 ± 0.5[d]	12.1 ± 0.3	12.6 ± 0.2
Erythrocytes ($10^6/\mu L$)	8.24 ± 0.30	8.46 ± 0.33[d]	8.01 ± 0.21	8.39 ± 0.11
Mean cell volume (μ^3)	43.3 ± 0.4	42.8 ± 0.3[d]	42.5 ± 0.5	42.6 ± 0.6
Mean cell hemoglobin (pg)	15.1 ± 0.2	15.0 ± 0.2[d]	15.1 ± 0.2	15.0 ± 0.2
Mean cell hemoglobin concentration (g/dL)	34.9 ± 0.5	35.1 ± 0.5[d]	35.4 ± 0.4	35.2 ± 0.3
Platelets ($10^3/\mu L$)	598.7 ± 37.3	624.5 ± 41.8[d]	657.1 ± 22.6[d]	598.4 ± 37.0
Reticulocytes (%)	1.4 ± 0.2	1.4 ± 0.2	1.4 ± 0.2	2.7 ± 0.9
Leukocytes ($10^3/\mu L$)	1.04 ± 0.11	1.11 ± 0.11[d]	1.06 ± 0.09	1.39 ± 0.18
Segmented neutrophils (%)	18.10 ± 2.42	22.00 ± 5.65	19.60 ± 3.48	14.90 ± 2.08
Bands (%)	0.40 ± 0.22	0.00 ± 0.00	0.30 ± 0.21	0.00 ± 0.00
Lymphocytes (%)	77.10 ± 2.75	74.89 ± 5.65	77.50 ± 3.41	80.20 ± 2.57
Atypical lymphocytes ($10^3/\mu L$)	2.60 ± 0.73	1.44 ± 0.53	1.90 ± 0.66	2.60 ± 0.99
Monocytes (%)	0.20 ± 0.20	0.11 ± 0.11	0.20 ± 0.13	1.00 ± 0.52
Eosinophils (%)	1.60 ± 0.69	1.56 ± 0.63	0.50 ± 0.27	1.30 ± 0.40

[a] Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.
[b] n=9
[c] n=7
[d] n=8

TABLE J6
Hematology Data for Mice at the 66-Week Interim Evaluations in the 2-Year Chlorinated Water Studies[a]

Analysis	0 ppm	70 ppm	140 ppm	275 ppm
Male				
n	10	10	10	9
Hematocrit (%)	35.6 ± 1.2	33.1 ± 0.9	33.2 ± 1.7	34.2 ± 0.5
Hemoglobin (g/dL)	14.1 ± 0.4	13.3 ± 0.3	13.3 ± 0.7	13.6 ± 0.2
Erythrocytes ($10^6/\mu L$)	9.49 ± 0.45	8.89 ± 0.26	8.85 ± 0.58	9.04 ± 0.11
Mean cell volume (μ^3)	37.8 ± 0.7	37.4 ± 0.8	38.0 ± 0.8	37.9 ± 0.6
Mean cell hemoglobin (pg)	15.0 ± 0.3	15.0 ± 0.2	15.1 ± 0.3	15.1 ± 0.2
Mean cell hemoglobin concentration (g/dL)	39.7 ± 0.4	40.2 ± 0.4	40.0 ± 0.4	39.9 ± 0.3
Platelets ($10^3/\mu L$)	1,103 ± 59	1,209 ± 76	1,177 ± 56	1,159 ± 59
Reticulocytes ($10^6/\mu L$)	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.1[b]	0.4 ± 0.0
Leukocytes ($10^3/\mu L$)	2.04 ± 0.38	1.52 ± 0.18	1.40 ± 0.36	1.72 ± 0.33
Segmented neutrophils (%)	31.30 ± 3.84	34.90 ± 4.50	35.10 ± 5.03	36.56 ± 2.39
Bands (%)	0.00 ± 0.00	0.40 ± 0.40	0.10 ± 0.10	0.44 ± 0.29
Lymphocytes (%)	67.50 ± 3.53	64.10 ± 4.47	64.20 ± 5.00	62.11 ± 2.39
Atypical lymphocytes (%)	0.60 ± 0.43	0.10 ± 0.10	0.20 ± 0.13	0.33 ± 0.17
Monocytes (%)	0.10 ± 0.10	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Eosinophils (%)	0.50 ± 0.22	0.40 ± 0.22	0.40 ± 0.16	0.56 ± 0.18
Female				
n	10	9	10	10
Hematocrit (%)	34.5 ± 0.5	35.9 ± 0.8	34.0 ± 0.5	34.3 ± 1.1
Hemoglobin (g/dL)	13.7 ± 0.2	13.9 ± 0.2	13.5 ± 0.3	13.4 ± 0.3
Erythrocytes ($10^6/\mu L$)	9.01 ± 0.10	8.94 ± 0.12	8.70 ± 0.21	8.78 ± 0.26
Mean cell volume (μ^3)	38.4 ± 0.3	40.1 ± 0.6	39.1 ± 0.5	39.0 ± 0.5
Mean cell hemoglobin (pg)	15.3 ± 0.2	15.5 ± 0.1	15.5 ± 0.1	15.3 ± 0.2
Mean cell hemoglobin concentration (g/dL)	39.8 ± 0.4	38.8 ± 0.5	39.7 ± 0.4	39.3 ± 0.8
Platelets ($10^3/\mu L$)	868.0 ± 30.4	873.6 ± 26.6	908.3 ± 37.2	854.4 ± 35.5
Reticulocytes ($10^6/\mu L$)	0.4 ± 0.0	0.4 ± 0.0[b]	0.4 ± 0.0[b]	0.4 ± 0.0[b]
Leukocytes ($10^3/\mu L$)	1.06 ± 0.12	1.19 ± 0.24	0.83 ± 0.04	1.10 ± 0.25
Segmented neutrophils (%)	25.80 ± 4.90	30.11 ± 4.38	34.40 ± 3.77	25.80 ± 2.49
Bands (%)	0.30 ± 0.15	0.22 ± 0.22	0.00 ± 0.00	0.20 ± 0.20
Lymphocytes (%)	71.80 ± 4.87	68.33 ± 4.21	64.50 ± 3.72	73.10 ± 2.41
Atypical lymphocytes (%)	1.20 ± 0.53	0.67 ± 0.33	0.60 ± 0.40	0.50 ± 0.22
Monocytes (%)	0.10 ± 0.10	0.00 ± 0.00	0.10 ± 0.10	0.00 ± 0.00
Eosinophils (%)	0.80 ± 0.29	0.67 ± 0.29	0.40 ± 0.16	0.40 ± 0.16

[a] Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.
[b] n=8

TABLE J7
Hematology Data for Mice at the 15-Week Interim Evaluations in the 2-Year Chloraminated Water Studies[a]

Analysis	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	7	9	10	9
Hematocrit (%)	37.8 ± 0.8	34.9 ± 1.1	34.8 ± 1.2	37.4 ± 0.5
Hemoglobin (g/dL)	12.9 ± 0.4	12.0 ± 0.6	12.2 ± 0.5	12.9 ± 0.2
Erythrocytes ($10^6/\mu L$)	8.69 ± 0.17	8.20 ± 0.27	8.18 ± 0.28	8.75 ± 0.09
Mean cell volume (μ^3)	43.6 ± 0.4	42.7 ± 0.5	42.6 ± 0.4	42.8 ± 0.3
Mean cell hemoglobin (pg)	14.8 ± 0.2	14.5 ± 0.4	14.9 ± 0.2	14.8 ± 0.2
Mean cell hemoglobin concentration (g/dL)	34.1 ± 0.6	34.2 ± 1.1	35.0 ± 0.6	34.5 ± 0.3
Platelets ($10^3/\mu L$)	598.0 ± 40.7	637.7 ± 38.0	650.6 ± 31.3	662.1 ± 47.7
Reticulocytes (%)	1.2 ± 0.2	1.2 ± 0.1	1.6 ± 0.3[b]	1.3 ± 0.2[c]
Leukocytes ($10^3/\mu L$)	1.47 ± 0.30	0.92 ± 0.17	1.01 ± 0.17	1.09 ± 0.20
Segmented neutrophils (%)	16.57 ± 1.90	24.89 ± 4.24	25.60 ± 4.29	19.78 ± 3.47
Bands (%)	0.29 ± 0.29	0.33 ± 0.17	0.30 ± 0.21	0.67 ± 0.24
Lymphocytes (%)	79.29 ± 1.27	71.44 ± 3.80	70.70 ± 3.89	77.78 ± 3.23
Atypical lymphocytes ($10^3/\mu L$)	2.14 ± 0.88	1.78 ± 0.52	2.10 ± 0.89	1.22 ± 0.55
Monocytes (%)	0.14 ± 0.14	0.67 ± 0.33	0.30 ± 0.15	0.11 ± 0.11
Eosinophils (%)	1.57 ± 0.72	0.89 ± 0.26	1.00 ± 0.68	0.44 ± 0.24
Female				
n	10	10	9	9
Hematocrit (%)	35.6 ± 1.2	37.5 ± 0.9	37.6 ± 0.5	33.3 ± 1.7
Hemoglobin (g/dL)	12.4 ± 0.5	13.1 ± 0.4	13.2 ± 0.2	11.7 ± 0.7
Erythrocytes ($10^6/\mu L$)	8.24 ± 0.30	8.55 ± 0.23	8.75 ± 0.12	7.76 ± 0.39
Mean cell volume (μ^3)	43.3 ± 0.4	43.8 ± 0.5	43.1 ± 0.4	42.9 ± 0.4
Mean cell hemoglobin (pg)	15.1 ± 0.2	15.3 ± 0.2	15.0 ± 0.1	15.1 ± 0.2
Mean cell hemoglobin concentration (g/dL)	34.9 ± 0.5	34.9 ± 0.5	35.0 ± 0.5	35.1 ± 0.5
Platelets ($10^3/\mu L$)	598.7 ± 37.3	676.3 ± 22.2	586.7 ± 64.0	577.9 ± 50.9
Reticulocytes (%)	1.4 ± 0.2	1.9 ± 0.2	1.8 ± 0.2	1.5 ± 0.2
Leukocytes ($10^3/\mu L$)	1.04 ± 0.11	1.12 ± 0.17	1.00 ± 0.12	1.02 ± 0.14
Segmented neutrophils (%)	18.10 ± 2.42	12.40 ± 1.20	11.78 ± 1.50	21.11 ± 2.60
Bands (%)	0.40 ± 0.22	0.40 ± 0.31	0.33 ± 0.17	0.22 ± 0.15
Lymphocytes (%)	77.10 ± 2.75	83.70 ± 1.25	84.11 ± 2.18	74.67 ± 2.35
Atypical lymphocytes ($10^3/\mu L$)	2.60 ± 0.73	2.00 ± 0.60	2.44 ± 0.85	1.44 ± 0.34
Monocytes (%)	0.20 ± 0.20	0.60 ± 0.27	0.44 ± 0.24	0.89 ± 0.66
Eosinophils (%)	1.60 ± 0.69	0.90 ± 0.23	0.89 ± 0.46	1.67 ± 0.44

[a] Mean ± standard error. Differences from the control group are not significant by Dunn's or Shirley's test.
[b] n=9
[c] n=8

TABLE J8
Hematology Data for Mice at the 66-Week Interim Evaluations in the 2-Year Chloraminated Water Studies[a]

Analysis	0 ppm	50 ppm	100 ppm	200 ppm
Male				
n	10	10	10	9
Hematocrit (%)	35.6 ± 1.2	34.9 ± 1.2	33.9 ± 0.6	34.2 ± 0.7
Hemoglobin (g/dL)	14.1 ± 0.4	13.9 ± 0.5	13.7 ± 0.2	13.6 ± 0.3
Erythrocytes ($10^6/\mu L$)	9.49 ± 0.45	9.16 ± 0.47	8.92 ± 0.16	8.79 ± 0.18
Mean cell volume (μ^3)	37.8 ± 0.7	38.3 ± 0.8	38.2 ± 0.5	39.0 ± 0.5
Mean cell hemoglobin (pg)	15.0 ± 0.3	15.2 ± 0.2	15.3 ± 0.2	15.5 ± 0.1
Mean cell hemoglobin concentration (g/dL)	39.7 ± 0.4	39.8 ± 0.4	40.3 ± 0.3	39.9 ± 0.5
Platelets ($10^3/\mu L$)	1,103 ± 59	1,057 ± 37	1,046 ± 34	1,139 ± 37
Reticulocytes (%)	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0
Leukocytes ($10^3/\mu L$)	2.04 ± 0.38	1.79 ± 0.23	1.06 ± 0.22	1.61 ± 0.25
Segmented neutrophils (%)	31.30 ± 3.84	25.20 ± 3.17	33.40 ± 5.43	34.56 ± 6.62
Bands (%)	0.00 ± 0.00	0.20 ± 0.13	0.30 ± 0.30	0.33 ± 0.24
Lymphocytes (%)	67.50 ± 3.53	73.40 ± 3.06	65.80 ± 5.52	63.78 ± 6.55
Atypical lymphocytes (%)	0.60 ± 0.43	0.60 ± 0.27	0.30 ± 0.15	0.56 ± 0.24
Monocytes (%)	0.10 ± 0.10	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Eosinophils (%)	0.50 ± 0.22	0.60 ± 0.22	0.20 ± 0.13	0.78 ± 0.22
Female				
n	10	9	9	10
Hematocrit (%)	34.5 ± 0.5	34.5 ± 0.8	34.7 ± 0.5	35.0 ± 0.9
Hemoglobin (g/dL)	13.7 ± 0.2	13.6 ± 0.2	13.6 ± 0.2	13.8 ± 0.3
Erythrocytes ($10^6/\mu L$)	9.01 ± 0.10	8.70 ± 0.11	8.84 ± 0.10	8.98 ± 0.17
Mean cell volume (μ^3)	38.4 ± 0.3	39.7 ± 0.7	39.3 ± 0.6	38.9 ± 0.5
Mean cell hemoglobin (pg)	15.3 ± 0.2	15.6 ± 0.1	15.4 ± 0.2	15.4 ± 0.1
Mean cell hemoglobin concentration (g/dL)	39.8 ± 0.4	39.4 ± 0.8	39.2 ± 0.6	39.5 ± 0.5
Platelets ($10^3/\mu L$)	868.0 ± 30.4	873.3 ± 29.1	879.9 ± 84.3	869.2 ± 23.4
Reticulocytes (%)	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0
Leukocytes ($10^3/\mu L$)	1.06 ± 0.12	1.22 ± 0.15	0.91 ± 0.15	1.35 ± 0.18
Segmented neutrophils (%)	25.80 ± 4.90	33.11 ± 6.86	25.44 ± 3.15	27.10 ± 2.52
Bands (%)	0.30 ± 0.15	0.11 ± 0.11	0.00 ± 0.00	0.00 ± 0.00*
Lymphocytes (%)	71.80 ± 4.87	66.00 ± 6.86	73.56 ± 3.20	70.90 ± 2.71
Atypical lymphocytes (%)	1.20 ± 0.53	0.44 ± 0.18	0.67 ± 0.44	0.80 ± 0.36
Monocytes (%)	0.10 ± 0.10	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Eosinophils (%)	0.80 ± 0.29	0.33 ± 0.24	0.33 ± 0.24	1.20 ± 0.36

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
[a] Mean ± standard error.

APPENDIX K
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION

PROCUREMENT AND CHARACTERIZATION OF CHLORINE

Two 18.1 kg cylinders of chlorine gas from the same lot (lot no. A081584) and a third cylinder from a different lot (lot no. 12152-5) were obtained from Air Products (Lenexa, KS). Purity and identity analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (MRI), Kansas City, MO.

The chemical was identified as chlorine by infrared spectroscopy and physical appearance. The infrared spectrum was consistent with those expected for the structure of chlorine and with an available literature reference, *Sadtler Standard Spectra*, (Figure K1). Gas chromatography indicated that hexachloroethane and hexachlorobenzene, possible impurities, were not present at a concentration greater than 0.01%. Purity determinations on these samples of chlorine were similar and were consistent with those of batches of chlorine previously analyzed by MRI (99.5% pure).

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

Dose formulations for chlorinated and chloraminated water were prepared from a stock solution of buffered sodium hypochlorite. This stock solution was prepared by bubbling chlorine gas into charcoal filtered, deionized water until the solution obtained a deep greenish-yellow color. The concentration of available atomic chlorine in the solution was determined by titration with 0.0028 N ferrous ammonium sulfate (FAS) using N,N-diethyl-*p*-phenyldiamine (DPD) as an indicator and adding an equivalent weight of sodium hydroxide. The solution was then buffered to approximately pH 9 with bicarbonate-carbonate buffer solution (Table K1). The buffers were 0.045 M in carbonate.

Chlorinated dose formulations, as sodium hypochlorite (NaOCl) solutions, were prepared by mixing the appropriate volume of the buffered sodium hypochlorite stock solution with sodium chloride and bicarbonate-carbonate buffer solutions, then diluting with charcoal filtered, deionized water to a final concentration of 0.022 M in carbonate and 0.035 M in sodium at pH 9. Dose concentrations were expressed as ppm of available atomic chlorine. Chloraminated dose formulations were prepared by mixing the appropriate volume of the buffered sodium hypochlorite stock solution with sodium chloride and bicarbonate-carbonate buffer solutions, and adding the resulting solution to a dilute ammonium hydroxide solution to generate monochloramine. The final solution was 0.022 M in carbonate and 0.035 M in sodium at pH 9. Dose concentrations were expressed as ppm of chloramine. Monochloramine and dichloramine concentrations were then confirmed by titration with FAS using potassium iodide as an indicator. Control drinking water was prepared by diluting the sodium chloride and bicarbonate-carbonate buffer solutions with charcoal filtered, deionized water to final concentrations of 0.022 M in carbonate and 0.035 M in sodium and a pH of approximately 9.

Stability studies performed by the analytical chemistry laboratory on buffered hypochlorite stock solution indicated approximately 96% retention of the original concentration after storage of the solution for 7 days at 5° C. For chlorinated water, dose levels of approximately 70, 140, and 275 ppm available atomic chlorine retained respective averages of 95%, 90%, 85%, and 85% of their original concentrations after 1, 2, 3, and 4 days storage in rat-cage water bottles. Based on these findings, the buffered hypochlorite stock solution was stored at 5° C for no longer than 7 days and the dose formulations were stored at room temperature for no longer than 48 hours. For chloraminated water, dose levels of approximately 50, 100, and 200 ppm chloramine retained 95% to 97% of the original concentration after 24 hours and 91% to 94% after 48 hours. A stability study was also performed at the study laboratory and verified that the dose formulations were stable under the storage conditions used in the toxicology studies.

Chlorinated dose formulations were analyzed for available atomic chlorine after each mixing by titration with 0.0028 N FAS using DPD as an indicator. The concentration of available atomic chlorine (ppm) was determined using the following equation:

$$\text{available atomic chlorine (ppm)} = \frac{\text{mL FAS x N of FAS x 35.45 x 1000.}}{\text{sample volume (mL)}}$$

Chloraminated dose formulations and buffered deionized water control solutions were analyzed for available atomic chlorine after each mixing by titration with 0.0028 N FAS using DPD as an indicator, and for monochloramine and dichloramine by FAS titration using potassium iodide (KI) as an indicator. The concentration of chloramine (ppm) was determined using the following equation:

$$\text{chloramine (ppm)} = \frac{\text{mL FAS x N of FAS x 51.48 x 1000.}}{\text{sample volume (mL)}}$$

Results of analyses were within the acceptable range (within 10% of the target concentrations), with the exception of a 50 ppm chloramine solution analyzed on April 17, 1985, at 112% of the target concentration, and a 70 ppm chlorine solution released for study on April 19, 1985, at 114% of target concentration. Monthly averages are shown in Tables K2 and K3. Animal room samples from each chlorine group were analyzed for available atomic chlorine and trihalomethanes (Tables K4, K5, K8, and K9). Animal room samples from each chloramine dose group and the buffered deionized water control group were analyzed monthly in duplicate for available atomic chlorine, monochloramine, dichloramine, and trihalomethanes (Tables K6, K7, K10, and K11). The method for trihalomethane determination involved extraction of the animal room drinking water samples with pentane or isooctane and injection of the extracts into a gas chromatograph equipped with an electron capture detector. A 1.8 m × 2.0 mm ID glass column packed with 1% SP-1000 on Carbopack B, a column temperature of 120° C, and a N_2 carrier flow rate of 30 mL/minute were used.

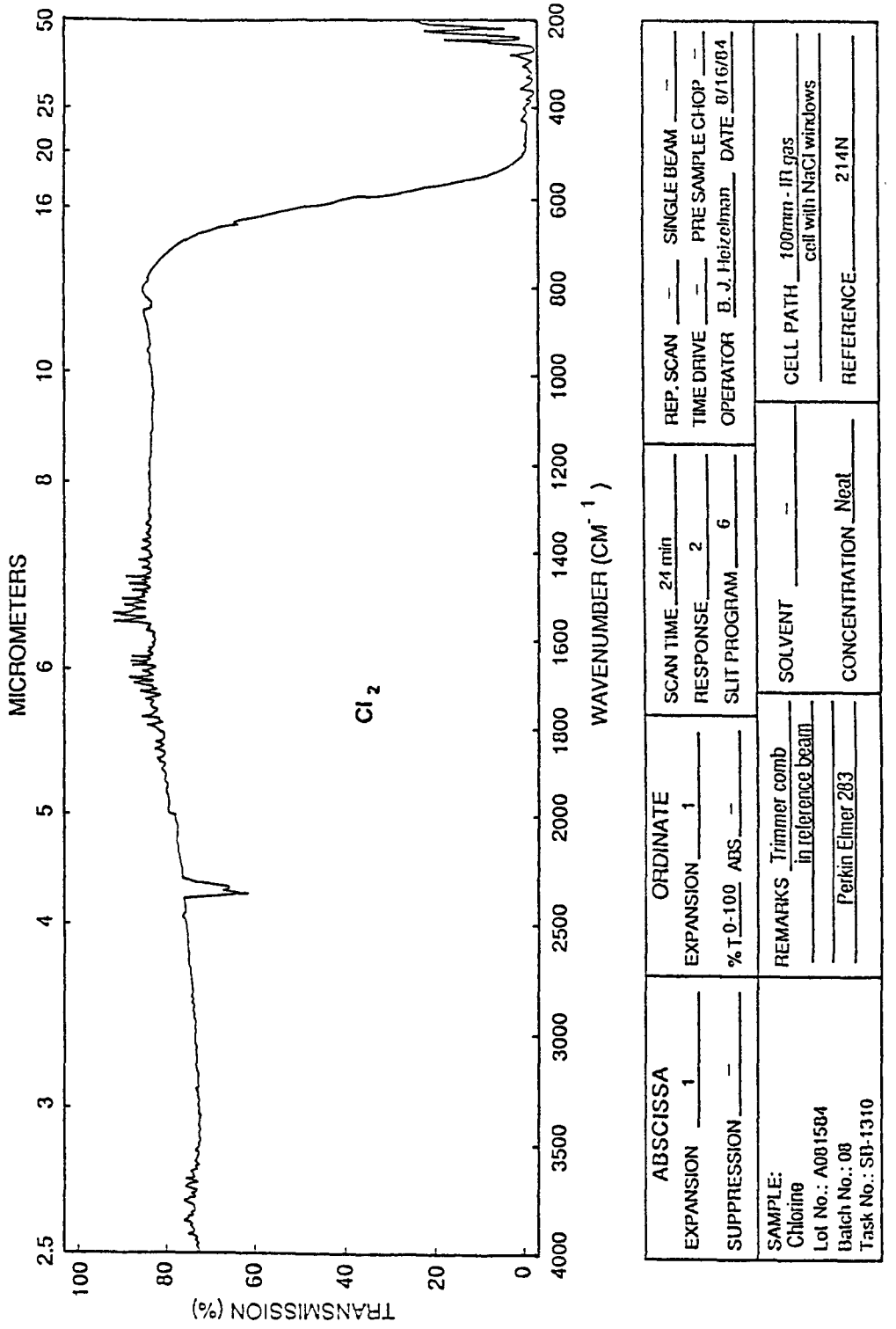

FIGURE K1
Infrared Spectrum of Chlorine

TABLE K1
Preparation and Storage of Dose Formulations in the Chlorinated and Chloraminated Water Studies

Preparation of Stock Solution
Buffered sodium hypochlorite stock solution was prepared by bubbling chlorine gas into charcoal filtered, deionized water until saturation (the appearance of a deep greenish-yellow color). The concentration of available atomic chlorine was determined by titration with 0.0028 N ferrous ammonium sulfate (FAS) using N,N-diethyl-*p*-phenyldiamine (DPD) as indicator, and an equivalent weight of sodium hydroxide was added. Sodium bicarbonate and sodium carbonate monohydrate were added to a molar concentration of 0.045 and the preparation was stirred until the added reagents were in solution. The sodium hypochlorite stock solution was stored at approximately 5° C until preparation of the chloramine and chlorine dose formulations.

Preparation of Dose Formulations
The concentration of available atomic chlorine in the sodium hypochlorite stock solution was determined by titration with 0.0028 N FAS using DPD as indicator prior to preparation of the dose formulations. Chlorinated dose formulations were prepared by diluting the stock solution to the desired available atomic chlorine concentrations with sodium chloride and bicarbonate-carbonate buffer solutions and charcoal filtered, deionized water. The available atomic chlorine concentrations were again determined by titration with FAS and DPD prior to use. Chloraminated dose formulations were prepared by diluting the stock solution with sodium chloride and bicarbonate-carbonate buffer solutions and charcoal filtered, deionized water. To the resulting solution was added a dilute solution of ammonium hydroxide to generate monochloramine. Monochloramine concentration was then confirmed by FAS titration using potassium iodide as an indicator. All final dose formulations were 0.022 M in carbonate and 0.035 M in sodium at pH 9.

Concentration
Chlorine: 70 ppm (2 mM chlorine), 140 ppm (4 mM chlorine), or 275 ppm (8 mM chlorine).
Chloramine: 50 ppm (1 mM chlorine), 100 ppm (2 mM chlorine), or 200 ppm (4 mM chlorine).
Control groups received charcoal filtered, deionized water with 0.022 M in carbonate and 0.035 M in sodium buffered at pH 9.

Storage Conditions
Polypropylene bottles at room temperature

Maximum Storage Time
48 hours

Study Laboratory
Southern Research Institute
Birmingham, AL

Referee Laboratory
Midwest Research Institute, Kansas City, MO

TABLE K2
Results of Analysis of Chlorinated Water Dose Formulations for Rats and Mice in the 2-Year Chlorinated and Chloraminated Water Studies[a]

Target Dose Concentration (ppm)	Chlorinated Water[b] Samples (n)	Mean ± S.E.	Range
December 1984			
70	19	70.0 ± 0.32	66.8 – 72.8
140	19	139.9 ± 0.60	135.0 – 146.1
275	19	271.0 ± 0.88	266.0 – 280.4
January 1985			
70	17	68.5 ± 0.39	66.3 – 71.1
140	17	137.3 ± 0.82	133.0 – 143.0
275	17	263.6 ± 1.36	255.0 – 277.0
February 1985			
70	16	70.7 ± 0.58	66.7 – 74.1
140	16	140.5 ± 1.05	133.0 – 147.0
275	16	272.2 ± 1.95	259.0 – 283.0
March 1985			
70	18	70.5 ± 0.55	67.6 – 75.0
140	18	139.3 ± 0.93	134.0 – 147.0
275	18	268.9 ± 1.52	255.0 – 281.0
April 1985			
70	17	71.0 ± 0.82	66.9 – 79.7
140	17	138.9 ± 1.32	132.0 – 152.0
275	17	270.3 ± 2.14	254.0 – 287.0
May 1985			
70	18	70.6 ± 0.39	67.9 – 72.5
140	18	139.9 ± 0.81	135.0 – 147.0
275	18	273.6 ± 1.19	265.0 – 282.0
June 1985			
70	17	68.7 ± 0.55	64.8 – 72.0
140	17	137.1 ± 0.94	129.0 – 145.0
275	17	268.8 ± 2.09	250.0 – 286.0
July 1985			
70	18	70.4 ± 0.48	66.6 – 73.5
140	18	140.1 ± 0.95	134.0 – 147.0
275	18	272.3 ± 2.13	257.0 – 285.0
August 1985			
70	18	72.3 ± 0.27	68.9 – 74.0
140	18	143.4 ± 0.66	136.0 – 147.0
275	18	278.6 ± 1.59	254.0 – 286.0

TABLE K2
Results of Analysis of Chlorinated Water Dose Formulations for Rats and Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Target Dose Concentration (ppm)	Chlorinated Water		
	Samples (n)	Mean ± S.E.	Range
September 1985			
70	17	72.5 ± 0.29	70.9 - 75.0
140	17	144.3 ± 0.65	141.0 - 150.0
275	17	277.9 ± 1.45	267.0 - 290.0
October 1985			
70	17	72.6 ± 0.29	70.5 - 75.0
140	17	144.5 ± 0.72	140.0 - 149.0
275	17	278.9 ± 1.62	260.0 - 288.0
November 1985			
70	18	72.5 ± 0.36	70.0 - 75.5
140	18	143.7 ± 0.85	138.0 - 151.0
275	18	281.9 ± 1.45	274.0 - 296.0
December 1985			
70	17	72.5 ± 0.33	70.5 - 75.4
140	17	143.0 ± 0.72	139.0 - 149.0
275	17	278.6 ± 1.08	272.0 - 286.0
January 1986			
70	18	72.2 ± 0.51	65.0 - 74.5
140	18	142.7 ± 0.57	139.0 - 150.0
275	18	280.1 ± 1.39	270.0 - 292.0
February 1986			
70	16	72.9 ± 0.43	69.3 - 75.0
140	16	142.7 ± 0.44	140.0 - 145.0
275	16	284.3 ± 1.62	273.0 - 294.0
March 1986			
70	18	73.0 ± 0.54	69.2 - 76.0
140	18	144.1 ± 1.02	138.0 - 154.0
275	18	295.6 ± 5.66	278.0 - 388.0
April 1986			
70	17	72.1 ± 0.32	69.9 - 74.5
140	17	144.0 ± 0.82	137.0 - 149.0
275	17	286.4 ± 1.06	280.0 - 297.0
May 1986			
70	18	71.7 ± 0.26	69.4 - 74.0
140	18	143.1 ± 0.72	138.0 - 149.0
275	18	285.8 ± 1.36	274.0 - 296.0

TABLE K2
Results of Analysis of Chlorinated Water Dose Formulations for Rats and Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Target Dose Concentration (ppm)	Chlorinated Water		
	Samples (n)	Mean ± S.E.	Range
June 1986			
70	17	72.5 ± 0.49	67.9 – 76.1
140	17	143.5 ± 1.05	135.0 – 153.0
275	17	283.4 ± 1.83	272.0 – 296.0
July 1986			
70	17	73.5 ± 0.41	71.0 – 75.6
140	17	144.4 ± 0.85	138.0 – 153.0
275	17	283.9 ± 1.88	275.0 – 301.0
August 1986			
70	18	72.4 ± 0.36	69.7 – 74.5
140	18	143.3 ± 0.68	137.0 – 148.0
275	18	287.6 ± 1.34	278.0 – 296.0
September 1986			
70	17	72.9 ± 0.44	69.2 – 76.1
140	17	144.2 ± 1.08	135.0 – 151.0
275	17	286.2 ± 1.58	272.0 – 296.0
October 1986			
70	18	71.9 ± 0.47	68.4 – 75.0
140	18	143.6 ± 1.12	135.0 – 150.0
275	18	281.8 ± 1.53	272.0 – 291.0
November 1986			
70	17	72.9 ± 0.30	70.9 – 75.0
140	17	144.9 ± 0.87	138.0 – 152.0
275	17	285.9 ± 1.74	271.0 – 302.0
December 1986			
70	18	73.5 ± 0.38	70.3 – 76.1
140	18	143.6 ± 0.87	137.0 – 149.0
275	18	283.0 ± 1.81	272.0 – 299.0
January 1987			
70	19	72.7 ± 0.44	68.9 – 75.5
140	19	143.1 ± 0.89	137.0 – 150.0
275	19	282.2 ± 1.14	273.0 – 291.0

[a] The analysis of dose formulations for rats and mice began on 28 January 1985 and ended on 2 February 1987. A total of 2,670 analyses were performed to determine chlorine concentrations of the dose formulations given to the rats on these studies. This table presents monthly averages for dose formulation samples obtained prior to administration. The NTP Archives maintain the complete data for dose formulation analyses performed during the 2-year studies.

[b] The concentrations are reported as ppm of available atomic chlorine.

TABLE K3
Results of Analysis of Chloraminated Water Dose Formulations for Rats and Mice in the 2-Year Chlorinated and Chloraminated Water Studies[a]

Target Dose Concentration (ppm)	Monochloramine (ppm)			Dichloramine (ppm)		
	Samples (n)	Mean ± S.E.	Range	Samples (n)	Mean ± S.E.	Range
December 1984						
50	19	51.0 ± 0.29	49.4 – 54.4	19	2.53 ± 0.20	1.10 – 4.20
100	19	99.7 ± 0.48	96.9 – 104.5	19	2.97 ± 0.16	2.10 – 4.40
200	19	195.9 ± 1.39	187.0 – 214.0	19	3.07 ± 0.23	1.10 – 4.40
January 1985						
50	17	50.4 ± 0.34	47.9 – 52.6	17	2.41 ± 0.24	0.00 – 4.20
100	17	98.6 ± 0.55	94.1 – 104.0	17	2.49 ± 0.13	2.10 – 3.20
200	17	190.7 ± 1.06	184.0 – 201.0	17	2.49 ± 0.18	1.10 – 3.20
February 1985						
50	16	51.6 ± 0.39	48.1 – 53.2	16	1.28 ± 0.14	0.00 – 2.10
100	16	101.1 ± 0.84	95.0 – 106.0	16	1.28 ± 0.14	0.00 – 2.10
200	16	194.7 ± 1.63	180.0 – 205.0	16	1.53 ± 0.23	0.00 – 3.20
March 1985						
50	18	52.6 ± 0.35	50.0 – 55.1	18	0.97 ± 0.15	0.00 – 2.10
100	18	101.3 ± 0.53	97.5 – 107.0	18	1.20 ± 0.14	0.00 – 2.10
200	18	194.9 ± 1.07	187.0 – 206.0	18	1.14 ± 0.13	0.00 – 2.10
April 1985						
50	17	51.3 ± 0.68	47.0 – 56.0	17	1.14 ± 0.20	0.00 – 2.50
100	17	100.6 ± 1.10	93.4 – 109.0	17	1.42 ± 0.16	0.00 – 2.50
200	17	196.2 ± 1.71	185.0 – 209.0	17	1.58 ± 0.18	0.00 – 2.50
May 1985						
50	18	51.6 ± 0.43	47.9 – 53.7	18	1.13 ± 0.07	0.00 – 1.20
100	18	100.3 ± 0.77	94.2 – 105.0	18	1.34 ± 0.10	1.20 – 2.50
200	18	197.7 ± 1.19	187.0 – 206.0	18	1.48 ± 0.21	1.20 – 4.90
June 1985						
50	17	50.5 ± 0.55	46.7 – 54.1	17	1.14 ± 0.07	0.00 – 1.30
100	17	99.5 ± 0.86	94.9 – 107.0	17	1.15 ± 0.13	0.00 – 2.50
200	17	193.1 ± 1.51	183.0 – 203.0	17	1.08 ± 0.10	0.00 – 1.30
July 1985						
50	18	51.0 ± 0.33	48.8 – 53.3	18	0.94 ± 0.14	0.00 – 1.30
100	18	101.3 ± 0.58	97.5 – 105.0	18	1.08 ± 0.12	0.00 – 1.30
200	18	197.7 ± 1.60	187.0 – 209.0	18	1.23 ± 0.07	0.00 – 1.30
August 1985						
50	18	52.5 ± 0.28	50.4 – 54.9	18	1.24 ± 0.01	1.20 – 1.30
100	18	104.8 ± 0.61	96.4 – 107.0	18	1.24 ± 0.01	1.20 – 1.30
200	18	204.3 ± 1.31	188.0 – 213.0	18	1.24 ± 0.01	1.20 – 1.30

TABLE K3
Results of Analysis of Chloraminated Water Dose Formulations for Rats and Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Target Dose Concentration (ppm)	Monochloramine (ppm)			Dichloramine (ppm)		
	Samples (n)	Mean ± S.E.	Range	Samples (n)	Mean ± S.E.	Range
September 1985						
50	17	52.5 ± 0.28	50.8 – 54.5	17	1.09 ± 0.10	0.00 – 1.30
100	17	105.1 ± 0.42	102.0 – 107.0	17	1.16 ± 0.07	0.00 – 1.30
200	17	206.8 ± 1.10	199.0 – 218.0	17	1.23 ± 0.01	1.20 – 1.30
October 1985						
50	17	52.7 ± 0.39	48.6 – 54.5	17	1.28 ± 0.08	1.20 – 2.50
100	17	104.6 ± 0.69	97.9 – 109.0	17	1.20 ± 0.00	1.20 – 1.20
200	17	205.0 ± 1.02	194.0 – 211.0	17	1.20 ± 0.00	1.20 – 1.20
November 1985						
50	18	52.6 ± 0.40	49.3 – 55.2	18	1.08 ± 0.09	0.00 – 1.30
100	18	105.0 ± 0.79	98.5 – 109.0	18	1.16 ± 0.07	0.00 – 1.30
200	18	202.7 ± 1.18	197.0 – 216.0	18	1.16 ± 0.07	0.00 – 1.30
December 1985						
50	17	51.9 ± 0.37	49.6 – 55.1	17	1.22 ± 0.08	0.00 – 1.30
100	17	103.7 ± 0.57	98.5 – 108.0	17	1.30 ± 0.00	1.30 – 1.30
200	17	202.6 ± 1.28	191.0 – 211.0	17	1.30 ± 0.00	1.30 – 1.30
January 1986						
50	18	52.9 ± 0.24	50.7 – 54.5	18	1.06 ± 0.12	0.00 – 1.30
100	18	104.6 ± 0.52	99.9 – 108.0	18	1.13 ± 0.10	0.00 – 1.30
200	18	202.9 ± 1.00	196.0 – 213.0	18	1.20 ± 0.07	0.00 – 1.30
February 1986						
50	16	52.0 ± 0.31	49.7 – 53.7	16	0.61 ± 0.16	0.00 – 1.30
100	16	103.1 ± 0.64	97.9 – 107.0	16	0.76 ± 0.15	0.00 – 1.30
200	16	202.6 ± 1.34	195.0 – 216.0	16	0.76 ± 0.15	0.00 – 1.30
March 1986						
50	18	52.2 ± 0.34	49.3 – 54.5	18	0.47 ± 0.14	0.00 – 1.30
100	18	102.9 ± 0.48	101.0 – 109.0	18	0.47 ± 0.14	0.00 – 1.20
200	18	202.4 ± 1.02	195.0 – 213.0	18	0.54 ± 0.15	0.00 – 1.30
April 1986						
50	17	51.7 ± 0.32	48.9 – 53.4	17	0.49 ± 0.15	0.00 – 1.20
100	17	101.9 ± 0.53	97.1 – 105.0	17	0.56 ± 0.15	0.00 – 1.20
200	17	202.5 ± 1.41	188.0 – 211.0	17	0.56 ± 0.15	0.00 – 1.20
May 1986						
50	18	51.3 ± 0.46	48.2 – 54.5	18	0.81 ± 0.14	0.00 – 1.30
100	18	101.6 ± 0.54	97.9 – 107.0	18	0.54 ± 0.15	0.00 – 1.30
200	18	200.8 ± 1.26	190.0 – 215.0	18	0.54 ± 0.15	0.00 – 1.30
June 1986						
50	17	52.3 ± 0.26	50.4 – 54.1	17	0.81 ± 0.14	0.00 – 1.30
100	17	102.9 ± 0.71	98.5 – 109.0	17	0.54 ± 0.15	0.00 – 1.30
200	17	202.8 ± 1.28	192.0 – 209.0	17	0.36 ± 0.14	0.00 – 1.30

TABLE K3
Results of Analysis of Chloraminated Water Dose Formulations for Rats and Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Target Dose Concentration (ppm)	Monochloramine (ppm)			Dichloramine (ppm)		
	Samples (n)	Mean ± S.E.	Range	Samples (n)	Mean ± S.E.	Range
July 1986						
50	17	52.2 ± 0.27	50.4 – 54.9	17	0.58 ± 0.15	0.00 – 1.30
100	17	103.2 ± 0.61	99.3 – 108.0	17	0.57 ± 0.15	0.00 – 1.30
200	17	203.6 ± 1.34	192.0 – 218.0	17	0.36 ± 0.14	0.00 – 1.30
August 1986						
50	18	52.4 ± 0.36	49.9 – 54.5	18	0.36 ± 0.14	0.00 – 1.30
100	18	103.1 ± 0.47	100.0 – 107.0	18	0.36 ± 0.14	0.00 – 1.30
200	18	205.6 ± 1.82	188.0 – 219.0	18	0.14 ± 0.10	0.00 – 1.30
September 1986						
50	17	52.6 ± 0.43	48.2 – 54.9	17	0.29 ± 0.13	0.00 – 1.30
100	17	102.9 ± 0.60	100.0 – 107.0	17	0.64 ± 0.15	0.00 – 1.30
200	17	205.0 ± 1.55	193.0 – 215.0	17	0.29 ± 0.13	0.00 – 1.30
October 1986						
50	18	51.6 ± 0.38	48.2 – 54.9	18	0.54 ± 0.18	0.00 – 2.50
100	18	102.4 ± 0.77	94.1 – 107.0	18	0.47 ± 0.14	0.00 – 1.20
200	18	203.8 ± 1.58	187.0 – 215.0	18	0.40 ± 0.14	0.00 – 1.20
November 1986						
50	17	52.7 ± 0.41	49.6 – 54.9	17	0.37 ± 0.14	0.00 – 1.30
100	17	103.0 ± 0.45	99.3 – 107.0	17	0.45 ± 0.15	0.00 – 1.30
200	17	203.4 ± 1.14	194.0 – 213.0	17	0.29 ± 0.17	0.00 – 2.50
December 1986						
50	18	52.1 ± 0.34	50.1 – 55.2	18	0.36 ± 0.14	0.00 – 1.30
100	18	103.1 ± 0.41	101.0 – 107.0	18	0.50 ± 0.15	0.00 – 1.30
200	18	201.4 ± 1.24	192.0 – 213.0	18	0.57 ± 0.18	0.00 – 2.50
January 1987						
50	19	51.8 ± 0.37	50.1 – 54.5	19	0.38 ± 0.16	0.00 – 2.50
100	19	101.8 ± 0.42	99.4 – 106.0	19	0.32 ± 0.12	0.00 – 1.20
200	19	201.4 ± 1.19	189.0 – 212.0	19	0.38 ± 0.13	0.00 – 1.20

[a] The analysis of dose formulations for rats and mice began on 28 January 1985 and ended on 2 February 1987. A total of 2,670 analyses were performed to determine monochloramine and dichloramine concentrations of the dose formulations. This table presents monthly averages for dose formulation samples obtained prior to administration. The NTP Archives maintain the complete data for dose formulation analyses performed during the 2-year studies.

TABLE K4
Results of Analysis of Chlorinated Water Dose Formulations from Rat Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies[a]

Date Prepared	Date Analyzed	Target Concentration[b] (ppm)	Determined Concentration (ppm)	% Difference from Target
11 February 1985	13 February 1985	70	65.8	−6
		140	134	−4
		275	269	−2
16 March 1985	18 March 1985	70	65.4	−7
		140	133	−5
		275	264	−4
13 April 1985	15 April 1985	70	66.4	−5
		140	135	−4
		275	251	−9
11 May 1985	13 May 1985	70	64.9	−7
		140	131	−6
		275	268	−3
8 June 1985	10 June 1985	70	56.7	−19
		140	135	−4
		275	266	−3
6 July 1985	8 July 1985	70	60.3	−14
		140	130	−7
		275	253	−8
17 August 1985	19 August 1985	70	71.5	+2
		140	141	<+1
		275	278	+1
14 September 1985	16 September 1985	70	70.9	+1
		140	132	−6
		275	270	−2
12 October 1985	14 October 1985	70	61.7	−12
		140	137	−2
		275	269	−2
9 November 1985	11 November 1985	70	64.4	−8
		140	137	−2
		275	274	−1
7 December 1985	9 December 1985	70	66.7	−5
		140	144	+3
		275	280	+2
11 January 1986	13 January 1986	70	67.2	−4
		140	134	−4
		275	270	−2

TABLE K4
Results of Analysis of Chlorinated Water Dose Formulations from Rat Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	% Difference from Target
8 February 1986	10 February 1986	70	72.5	+4
		140	140	0
		275	273	−1
8 March 1986	10 March 1986	70	68.3	−2
		140	137	−2
		275	280	+2
12 April 1986	14 April 1986	70	70.0	0
		140	137	−2
		275	277	+1
10 May 1986	12 May 1986	70	69.9	−1
		140	137	−2
		275	282	+3
7 June 1986	9 June 1986	70	67.3	−4
		140	137	−2
		275	267	−3
12 July 1986	14 July 1986	70	72.0	+3
		140	140	0
		275	276	+1
9 August 1986	11 August 1986	70	69.7	−1
		140	136	−3
		275	278	+1
6 September 1986	8 September 1986	70	71.3	+2
		140	142	+1
		275	279	+1
11 October 1986	13 October 1986	70	71.5	+2
		140	147	+5
		275	290	+5
15 November 1986	17 November 1986	70	71.9	+3
		140	142	+1
		275	286	+4
6 December 1986	8 December 1986	70	69.9	−1
		140	137	−2
		275	271	−1
10 January 1987	12 January 1987	70	71.0	+1
		140	143	+2
		275	278	+1

[a] Results of all vehicle analyses were below the limit of detection and are not included in the table.
[b] Concentrations are reported as ppm of available atomic chlorine.

TABLE K5
Results of Trihalomethane Analysis[a] from Chlorinated Water Animal-Room Samples for Rats in the 2-Year Chlorinated and Chloraminated Water Studies

Date Mixed	Date Analyzed	Target Conc.[b]	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
11 February 1985	15 February 1985	Control	1.1	<1.0	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	91.5	2.4	ND	ND
		140 ppm	111.5	2.0	ND	ND
		275 ppm	74.5	ND	ND	ND
16 March 1985	19 March 1985	Control	<1.0	ND	ND	ND
		Vehicle[c]	<1.0	ND	ND	ND
		70 ppm	48.5	ND	ND	ND
		140 ppm	42.0	ND	ND	ND
		275 ppm	70.0	ND	ND	ND
13 April 1985	16 April 1985	Control	ND	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	23.5	1.9	<1.0	ND
		140 ppm	35.5	2.9	1.3	ND
		275 ppm	42.0	3.6	1.2	ND
11 May 1985	14 May 1985	Control	<1.0	ND	ND	ND
		Vehicle[c]	<1.0	ND	ND	ND
		70 ppm	36.5	1.5	<1.0	ND
		140 ppm	45.5	1.5	<1.0	ND
		275 ppm	35.0	<1.0	ND	ND
8 June 1985	12 June 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	56.0	2.6	<1.0	ND
		140 ppm	19.5	<1.0	<1.0	ND
		275 ppm	44.0	1.4	<1.0	ND
6 July 1985	9 July 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	22.0	<1.0	ND	ND
		140 ppm	31.5	<1.0	ND	ND
		275 ppm	53.0	<1.0	ND	ND
17 August 1985	22 August 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	27.4	2.9	<1.0	ND
		140 ppm	22.1	1.1	ND	ND
		275 ppm	22.2	1.1	ND	ND
14 September 1985	17-18 September 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	47.4	2.1	ND	ND
		140 ppm	62.0	1.7	ND	ND
		275 ppm	46.7	<1.0	ND	ND

TABLE K5
Results of Trihalomethane Analysis from Chlorinated Water Animal-Room Samples for Rats in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
12 October 1985	17-18 October 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	56.2	1.3	ND	ND
		140 ppm	49.0	<1.0	ND	ND
		275 ppm	45.0	<1.0	ND	ND
9 November 1985	13-15 November 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	100.8	4.8	<1.0	ND
		140 ppm	39.1	3.4	<1.0	ND
		275 ppm	37.0	2.7	ND	ND
7 December 1985	10-11 December 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	39.4	2.7	ND	ND
		140 ppm	62.1	2.6	<1.0	ND
		275 ppm	74.3	2.3	ND	ND
11 January 1986	15-16 January 1986	Control	1.8	1.2	<3.0	<5.0
		Vehicle	1.1	1.2	<3.0	<5.0
		70 ppm	176.3	7.1	<3.0	<5.0
		140 ppm	137.8	5.3	<3.0	<5.0
		275 ppm	157.9	5.5	<3.0	<5.0
8 February 1986	11-12 February 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	88.6	4.7	ND	ND
		140 ppm	135.8	5.2	ND	ND
		275 ppm	98.9	3.6	ND	ND
8 March 1986	11-12 March 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	149.5	3.7	ND	ND
		140 ppm	175.0	3.0	ND	ND
		275 ppm	213.3	2.4	ND	ND
12 April 1986	15 April 1986	Control	1.8	ND	ND	ND
		Vehicle	1.4	ND	ND	ND
		70 ppm	97.4	1.6	ND	ND
		140 ppm	103.7	1.3	<1.0	ND
		275 ppm	91.3	<1.0	ND	ND
10 May 1986	13-14 May 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	43.4	1.3	ND	ND
		140 ppm	34.7	<1.0	ND	ND
		275 ppm	44.1	<1.0	ND	ND

TABLE K5
Results of Trihalomethane Analysis from Chlorinated Water Animal-Room Samples for Rats in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
7 June 1986	12-13 June 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	48.6	2.4	<1.0	ND
		140 ppm	54.6	1.7	ND	ND
		275 ppm	80.9	1.6	ND	ND
12 July 1986	15-16 July 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	48.6	1.9	<1.0	ND
		140 ppm	125.0	2.4	1.5	ND
		275 ppm	57.9	1.6	1.9	ND
9 August 1986	12-13 August 1986	Control	1.1	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	35.6	2.4	ND	ND
		140 ppm	46.2	2.2	ND	ND
		275 ppm	43.4	1.9	ND	ND
6 September 1986	9-10 September 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	24.1	1.5	<1.0	ND
		140 ppm	14.9	<1.0	ND	ND
		275 ppm	11.5	<1.0	ND	ND
11 October 1986	14-15 October 1986	Control	<1.0	ND	1.7	ND
		Vehicle	<1.0	ND	1.8	ND
		70 ppm	50.9	1.7	1.8	ND
		140 ppm	58.3	1.7	1.8	ND
		275 ppm	36.2	<1.0	1.8	ND
15 November 1986	18-21 November 1986	Control	1.2	<1.0	10.9	3.3
		Vehicle	<1.0	<1.0	6.3	2.0
		70 ppm	70.9	2.4	2.4	1.0
		140 ppm	133.5	2.8	2.7	1.0
		275 ppm	65.4	<1.0	1.9	<1.0
6 December 1986	12-13 December 1986	Control	7.5	ND	1.0	ND
		Vehicle	5.2	ND	<1.0	4.4
		70 ppm	126.8	4.6	1.1	ND
		140 ppm	164.5	3.3	ND	ND
		275 ppm	134.5	2.5	<1.0	ND
10 January 1987	14 January 1987	Control	<1.0	<1.0	ND	ND
		Vehicle	<1.0	ND	ND	<1.0
		70 ppm	136.0	6.4	1.1	<1.0
		140 ppm	109.0	4.1	<1.0	<1.0
		275 ppm	83.5	2.7	<1.0	<1.0

ND Not detected
[a] Results of duplicate analyses except where noted
[b] Control sample was deionized water and represents an analysis control, not an animal-room sample. Vehicle was deionized water that was used in the animal room. Concentrations are reported as ppm of available atomic chlorine.
[c] n=1

TABLE K6
Results of Analysis of Chloraminated Water Dose Formulations from Rat Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies[a]

Date Prepared	Date Analyzed	Target Concentration[b] (ppm)	Determined Concentration[c] (ppm)	
			Monochloramine	Dichloramine
11 February 1985	13 February 1985	50	48.1 (+4)	1.1
		100	95.0 (−5)	1.1
		200	179 (−11)	2.1
16 March 1985	18 March 1985	50	49.4 (−1)	2.1
		100	98.8 (−1)	1.1
		200	182 (−9)	1.1
13 April 1985	15 April 1985	50	46.0 (−8)	0.0
		100	96.4 (−4)	1.2
		200	172 (−14)	1.2
11 May 1985	13 May 1985	50	46.4 (−7)	1.2
		100	91.3 (−9)	1.2
		200	176 (−12)	1.2
8 June 1985	10 June 1985	50	48.9 (−2)	0.0
		100	92.7 (−7)	1.2
		200	174 (−13)	1.2
6 July 1985	8 July 1985	50	44.2 (−12)	1.3
		100	92.2 (−8)	1.3
		200	174 (−13)	1.3
17 August 1985	19 August 1985	50	50.4 (+1)	1.2
		100	97.9 (−2)	1.2
		200	190 (−5)	1.2
14 September 1985	16 September 1985	50	50.8 (+2)	1.2
		100	102 (+2)	1.2
		200	195 (−3)	1.2
12 October 1985	14 October 1985	50	48.5 (−3)	1.2
		100	99.3 (−1)	1.2
		200	187 (−7)	1.2
9 November 1985	11 November 1985	50	49.3 (−1)	0.0
		100	95.7 (−4)	1.2
		200	180 (−10)	1.2
7 December 1985	9 December 1985	50	52.0 (+4)	1.3
		100	100 (0)	1.3
		200	193 (−4)	1.3
11 January 1986	13 January 1986	50	49.2 (−2)	1.3
		100	96.9 (−3)	1.3
		200	182 (−9)	1.3

TABLE K6
Results of Analysis of Chloraminated Water Dose Formulations from Rat Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	
			Monochloramine	Dichloramine
8 February 1986	10 February 1986	50	47.4 (−5)	1.2
		100	93.4 (−7)	1.2
		200	192 (−4)	1.2
8 March 1986	10 March 1986	50	46.2 (−8)	0.0
		100	93.8 (−6)	0.0
		200	172 (−14)	0.0
12 April 1986	14 April 1986	50	44.3 (−11)	0.0
		100	90.0 (−10)	1.2
		200	182 (−9)	0.0
10 May 1986	12 May 1986	50	50.4 (+1)	1.2
		100	95.6 (−4)	0.0
		200	188 (−6)	0.0
7 June 1986	9 June 1986	50	48.9 (−2)	1.3
		100	94.0 (−6)	1.3
		200	179 (−11)	1.3
12 July 1986	14 July 1986	50	49.7 (−1)	0.0
		100	101 (+1)	0.0
		200	202 (+1)	0.0
9 August 1986	11 August 1986	50	45.3 (−9)	0.0
		100	95.1 (−5)	0.0
		200	198 (−1)	0.0
6 September 1986	8 September 1986	50	51.4 (+3)	0.0
		100	97.4 (−3)	0.0
		200	195 (−2)	0.0
11 October 1986	13 October 1986	50	48.9 (−2)	0.0
		100	100 (0)	0.0
		200	204 (+2)	0.0
15 November 1986	17 November 1986	50	49.6 (−1)	1.3
		100	98.5 (−1)	1.3
		200	186 (−7)	1.3
6 December 1986	8 December 1986	50	49.6 (−1)	1.3
		100	98.5 (−2)	1.3
		200	179 (−11)	1.3
10 January 1987	12 January 1987	50	48.6 (−3)	0.0
		100	100 (0)	0.0
		200	187 (−7)	0.0

[a] Results of all vehicle analyses were below the limit of detection and are not included in the table.
[b] Concentrations are reported as ppm chloramine.
[c] The numbers in parentheses are the percent differences from target concentration.

TABLE K7
Results of Trihalomethane Analysis[a] from Chloraminated Water Animal-Room Samples for Rats in the 2-Year Chlorinated and Chloraminated Water Studies

Date Mixed	Date Analyzed	Target Conc.[b]	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
11 February 1985	15 February 1985	Control	1.1	<1.0	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	2.2	ND	ND	ND
		100 ppm	2.5	ND	ND	ND
		200 ppm	3.2	ND	ND	ND
16 March 1985	19 March 1985	Control	<1.0	ND	ND	ND
		Vehicle[c]	<1.0	ND	ND	ND
		50 ppm[d]	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
13 April 1985	16 April 1985	Control	ND	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
11 May 1985	14 May 1985	Control	<1.0	ND	ND	ND
		Vehicle[c]	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
8 June 1985	12 June 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
6 July 1985	9 July 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
17 August 1985	22 August 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	1.2	ND	ND	ND
		200 ppm	2.0	ND	ND	ND
14 September 1985	17-18 September 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	1.2	ND	ND	ND

TABLE K7
Results of Trihalomethane Analysis from Chloraminated Water Animal-Room Samples for Rats in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
12 October 1985	17-18 October 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	1.7	ND	ND	ND
		100 ppm	2.6	ND	ND	ND
		200 ppm	3.1	ND	ND	ND
9 November 1985	13-15 November 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	<1.0	ND	ND
7 December 1985	10-11 December 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	1.3	ND	ND	ND
		200 ppm	1.8	ND	ND	ND
11 January 1986	15-16 January 1986	Control	1.8	1.2	<3.0	<5.0
		Vehicle	1.1	1.2	<3.0	<5.0
		50 ppm	1.2	1.2	<3.0	<5.0
		100 ppm	1.3	1.2	<3.0	<5.0
		200 ppm	2.1	<1.0	ND	<5.0
8 February 1986	11-12 February 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	1.5	ND	ND	ND
8 March 1986	11-12 March 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	1.2	ND	ND	ND
		200 ppm	2.7	ND	ND	ND
12 April 1986	15 April 1986	Control	1.8	ND	ND	ND
		Vehicle	1.4	ND	ND	ND
		50 ppm	2.0	ND	ND	ND
		100 ppm	2.1	ND	ND	ND
		200 ppm	2.8	<1.0	ND	ND
10 May 1986	13-14 May 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	2.9	ND	ND	ND
		100 ppm	2.1	ND	ND	ND
		200 ppm	2.8	ND	ND	ND

TABLE K7
Results of Trihalomethane Analysis from Choraminated Water Animal-Room Samples for Rats in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
7 June 1986	12-13 June 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
12 July 1986	15-16 July 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
9 August 1986	12-13 August 1986	Control	1.1	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	1.4	ND	ND	ND
		100 ppm	2.0	ND	ND	ND
		200 ppm	1.9	ND	ND	ND
6 September 1986	9-10 September 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
11 October 1986	14-15 October 1986	Control	<1.0	ND	1.7	ND
		Vehicle	<1.0	ND	1.8	ND
		50 ppm	<1.0	ND	1.8	ND
		100 ppm	1.1	ND	2.4	ND
		200 ppm	2.2	ND	ND	ND
15 November 1986	18-21 November 1986	Control	1.2	<1.0	10.9	3.3
		Vehicle	<1.0	<1.0	6.3	2.0
		50 ppm	<1.0	<1.0	2.5	1.1
		100 ppm	1.1	<1.0	2.4	1.3
		200 ppm	1.4	<1.0	2.4	1.1
6 December 1986	12-13 December 1986	Control	7.5	ND	1.0	ND
		Vehicle	5.2	ND	<1.0	4.4
		50 ppm	5.1	ND	ND	<1.0
		100 ppm	5.7	<1.0	ND	ND
		200 ppm	7.7	<1.0	ND	ND
10 January 1987	14 January 1987	Control	<1.0	<1.0	ND	ND
		Vehicle	<1.0	ND	ND	<1.0
		50 ppm	1.3	<1.0	ND	<1.0
		100 ppm	2.2	ND	ND	<1.0
		200 ppm	3.9	<1.0	ND	<1.0

ND Not detected
[a] Results of duplicate analyses except where noted
[b] Control sample was deionized water and represents an analysis control, not an animal-room sample. Vehicle was deionized water that was used in the animal room. Concentrations are reported as ppm chloramine.
[c] n=1
[d] The samples were pooled.

TABLE K8
Results of Analysis of Chlorinated Water Dose Formulations from Mouse Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies[a]

Date Prepared	Date Analyzed	Target Concentration[b] (ppm)	Determined Concentration (ppm)	% Difference from Target
26 December 1984	28 December 1984	70	43.6	−38
		140	134	−4
		275	259	−6
31 December 1984	2 January 1985	70[c]	48.8	−30
		70	67.7	−3
		70	65.5	-6
		70	63.7	−9
		70	66.8	−5
		70	67.7	−3
14 January 1985	16 January 1985	70	62.8	−10
		140	132	−6
		275	273	−1
11 February 1985	13 February 1985	70[d]	56.2	−20
		70	64.1	−8
		140	136	−3
		275	264	−4
16 March 1985	18 March 1985	70	68.5	−2
		140	133	−5
		275	254	−8
13 April 1985	15 April 1985	70	66.9	−4
		140	134	−4
		275	255	−7
11 May 1985	13 May 1985	70	60.3	−14
		140	132	−6
		275	272	−1
8 June 1985	10 June 1985	70	62.3	−11
		140	135	−4
		275	263	−4
6 July 1985	8 July 1985	70	55.1	−21
		140	128	−9
		275	251	−9
17 August 1985	19 August 1985	70	69.9	−1
		140	143	+2
		275	280	+2
14 September 1985	16 September 1985	70	72.0	+3
		140	137	−2
		275	271	−1
12 October 1985	14 October 1985	70	66.3	−5
		140	137	−2
		275	269	−2
9 November 1985	11 November 1985	70	67.9	−3
		140	128	−9
		275	271	−1

TABLE K8
Results of Analysis of Chlorinated Water Dose Formulations from Mouse Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration[a] (ppm)	% Difference from Target
7 December 1985	9 December 1985	70	72.1	+3
		140	143	+2
		275	283	+3
11 January 1986	13 January 1986	70	67.7	−3
		140	135	−4
		275	271	−1
8 February 1986	10 February 1986	70	71.0	+1
		140	139	−1
		275	274	−1
8 March 1986	10 March 1986	70	68.3	−2
		140	136	−3
		275	278	+1
12 April 1986	14 April 1986	70	69.0	−1
		140	145	+4
		275	280	+2
10 May 1986	12 May 1986	70	69.9	−1
		140	135	−4
		275	282	+3
7 June 1986	9 June 1986	70	66.8	−5
		140	137	−2
		275	268	−3
12 July 1986	14 July 1986	70	69.9	−1
		140	138	−1
		275	274	−1
9 August 1986	11 August 1986	70	67.6	−3
		140	133	−5
		275	280	+2
6 September 1986	8 September 1986	70	70.3	+1
		140	144	+3
		275	279	+1
11 October 1986	13 October 1986	70	71.0	+1
		140	146	+4
		275	289	+5
15 November 1986	17 November 1986	70	71.9	+3
		140	138	−1
		275	288	+5

[a] Results of all vehicle analyses were below the limit of detection and are not included in the table.
[b] Concentrations are reported as ppm of available atomic chlorine.
[c] Samples from the 70 ppm chlorine dose level were reanalyzed due to previous low values.
[d] Sample was reanalyzed due to low value.

TABLE K9
Results of Trihalomethane Analysis[a] from Chlorinated Water Animal-Room Samples for Mice in the 2-Year Chlorinated and Chloraminated Water Studies

Date Mixed	Date Analyzed	Target Conc.[b]	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
26 December 1984	29 December 1984	Control	<1.0	<1.0	ND	ND
		Vehicle	<1.0	<1.0	ND	ND
		70 ppm	NA	NA	NA	ND
		140 ppm	NA	NA	NA	ND
		275 ppm	NA	NA	NA	ND
14 January 1985	22 January 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	256.0	5.2	2.8	ND
		140 ppm	386.0	4.5	<1.0	ND
		275 ppm	415.0	2.8	ND	ND
11 February 1985	15 February 1985	Control	1.1	<1.0	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	59.0	1.7[c]	<1.0[c]	ND[c]
		140 ppm	51.5	1.1	<1.0	ND
		275 ppm	62.5	<1.0	<1.0	ND
16 March 1985	19 March 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	29.5	ND	ND	ND
		140 ppm	28.5	ND	ND	ND
		275 ppm	28.5	ND	ND	ND
13 April 1985	16 April 1985	Control	ND	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm[d]	24.0	1.8	1.2	ND
		140 ppm	24.5	1.8	ND	ND
		275 ppm	35.0	1.9	ND	ND
11 May 1985	14 May 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	63.0	<1.0	<1.0	ND
		140 ppm	25.5	<1.0	<1.0	ND
		275 ppm	26.0	ND	ND	ND
8 June 1985	12 June 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	39.5	1.8	<1.0	ND
		140 ppm	26.0	<1.0	<1.0	ND
		275 ppm	29.5	<1.0	<1.0	ND
6 July 1985	9 July 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	19.5	<1.0	ND	ND
		140 ppm	26.0	<1.0	ND	ND
		275 ppm	22.5	<1.0	ND	ND
17 August 1985	22 August 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	17.9	1.4	ND	ND
		140 ppm	16.2	1.2	ND	ND
		275 ppm	15.5	<1.0	ND	ND

TABLE K9
Results of Trihalomethane Analysis from Chlorinated Water Animal-Room Samples for Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
14 September 1985	17-18 September 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	33.4	1.2	ND	ND
		140 ppm	30.5	<1.0	ND	ND
		275 ppm	24.0	<1.0	ND	ND
12 October 1985	17-18 October 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	22.7	<1.0	ND	ND
		140 ppm	21.7	<1.0	ND	ND
		275 ppm	17.8	<1.0	ND	ND
9 November 1985	13-15 November 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	<1.0	ND	ND
		70 ppm	23.7	1.8	<1.0	ND
		140 ppm	25.8	2.0	<1.0	ND
		275 ppm	21.4	1.7	ND	ND
7 December 1985	10-11 December 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	10.7	1.6	ND	ND
		140 ppm	18.6	1.7	ND	ND
		275 ppm	18.2	<1.0	ND	ND
11 January 1986	15-16 January 1986	Control	1.8	1.2	<3.0	<5.0
		Vehicle	<1.0	1.1	<3.0	<5.0
		70 ppm	69.5	2.4	<3.0	<5.0
		140 ppm	70.3	2.2	<3.0	<5.0
		275 ppm	52.8	2.1	ND	<5.0
8 February 1986	11-12 February 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	40.2	3.4	ND	ND
		140 ppm	47.8	3.1	ND	ND
		275 ppm	40.6	2.9	ND	ND
8 March 1986	11-12 March 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	70.6	2.5	ND	ND
		140 ppm	69.2	2.3	ND	ND
		275 ppm	96.9	2.2	ND	ND
12 April 1986	15 April 1986	Control	1.8	ND	ND	ND
		Vehicle	1.4	ND	ND	ND
		70 ppm	51.8	<1.0	ND	ND
		140 ppm	40.6	<1.0	<1.0	ND
		275 ppm	43.9	<1.0	ND	ND

TABLE K9
Results of Trihalomethane Analysis from Chlorinated Water Animal-Room Samples for Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
10 May 1986	13-14 May 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	31.5	1.2	ND	ND
		140 ppm	25.9	<1.0	ND	ND
		275 ppm	35.0	<1.0	ND	ND
7 June 1986	12-13 June 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	25.3	1.7	<1.0	ND
		140 ppm	28.4	1.4	ND	ND
		275 ppm	38.9	1.2	ND	ND
12 July 1986	15-16 July 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	40.5	1.7	1.5	ND
		140 ppm	44.5	1.5	<1.0	ND
		275 ppm	35.5	1.4	1.5	ND
9 August 1986	12-13 August 1986	Control	1.1	ND	ND	ND
		Vehicle	1.1	ND	ND	ND
		70 ppm	25.1	2.2	ND	ND
		140 ppm	33.2	1.9	ND	ND
		275 ppm	28.5	1.7	ND	ND
6 September 1986	9-10 September 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		70 ppm	8.7	<1.0	<1.0	ND
		140 ppm	7.8	<1.0	ND	ND
		275 ppm	10.0	<1.0	ND	ND
11 October 1986	14-15 October 1986	Control	<1.0	ND	1.7	ND
		Vehicle	<1.0	ND	2.0	ND
		70 ppm	26.8	1.4	1.8	ND
		140 ppm	36.1	1.2	1.7	ND
		275 ppm	23.1	<1.0	1.7	ND
15 November 1986	18-21 November 1986	Control	1.2	<1.0	10.9	3.3
		Vehicle	<1.0	<1.0	7.1	3.2
		70 ppm	45.5	1.5	2.4	1.1
		140 ppm	47.3	1.1	2.3	1.1
		275 ppm	56.6	<1.0	2.4	1.0

NA Not Analyzed
ND Not Detected
[a] Results of duplicate analyses except where noted
[b] Control sample was deionized water and represents an analysis control, not an animal-room sample. Vehicle was deionized water that was used in the animal room. Concentrations are reported as ppm of available atomic chlorine.
[c] n=1; the second sample was spilled during dilution process.
[d] n=1; the second sample was lost during extraction.

TABLE K10
Results of Analysis of Chloraminated Water Dose Formulations from Mouse Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies[a]

Date Prepared	Date Analyzed	Target Concentration[b] (ppm)	Determined Concentration[c] (ppm)	
			Monochloramine	Dichloramine
26 December 1984	28 December 1984	50	45.6 (−9)	2.1
		100	89.9 (−10)	2.1
		200	169.0 (−16)	2.1
14 January 1985	16 January 1985	50	48.8 (−2)	2.1
		100	95.6 (−4)	2.1
		200	175.0 (−13)	3.2
11 February 1985	13 February 1985	50	50.0 (−0)	1.1
		100	93.7 (−6)	1.1
		200	175 (−13)	1.1
16 March 1985	18 March 1985	50	49.4 (−1)	1.1
		100	95.6 (−4)	1.1
		200	178 (−11)	1.1
13 April 1985	15 April 1985	50	45.2 (−10)	1.2
		100	95.6 (−4)	2.5
		200	167 (−17)	1.2
11 May 1985	13 May 1985	50	45.6 (−9)	1.2
		100	90.5 (−10)	1.2
		200	172 (−14)	1.2
8 June 1985	10 June 1985	50	48.2 (−4)	0.0
		100	91.2 (−9)	1.2
		200	171 (−15)	1.2
6 July 1985	8 July 1985	50	45.0 (−10)	1.3
		100	89.9 (−10)	1.3
		200	169 (−15)	1.3
17 August 1985	19 August 1985	50	48.9 (−2)	1.2
		100	96.4 (−4)	1.2
		200	189 (−6)	1.2
14 September 1985	16 September 1985	50	50.0 (0)	1.2
		100	101 (+1)	1.2
		200	192 (−4)	1.2
12 October 1985	14 October 1985	50	47.0 (−6)	1.2
		100	97.0 (−3)	1.2
		200	181 (−10)	1.2
9 November 1985	11 November 1985	50	47.9 (−4)	0.0
		100	95.7 (−4)	1.2
		200	179 (−11)	1.2
7 December 1985	9 December 1985	50	51.2 (+2)	1.3
		100	101 (+1)	1.3
		200	187 (−7)	1.3

TABLE K10
Results of Analysis of Chloraminated Water Dose Formulations from Mouse Animal-Room Samples in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	
			Monochloramine	Dichloramine
11 January 1986	13 January 1986	50	49.2 (−2)	1.3
		100	87.8 (−12)	1.3
		200	176 (−12)	1.3
8 February 1986	10 February 1986	50	47.4 (−5)	1.2
		100	95.6 (−4)	1.2
		200	190 (−5)	1.2
8 March 1986	10 March 1986	50	46.2 (−8)	0.0
		100	91.6 (−8)	0.0
		200	170 (−15)	0.0
12 April 1986	14 April 1986	50	48.6 (−3)	1.2
		100	88.6 (−11)	1.2
		200	179 (−10	1.2
10 May 1986	12 May 1986	50	50.4 (+1)	0.0
		100	92.7 (−7)	1.2
		200	183 (−8)	1.2
7 June 1986	9 June 1986	50	48.1 (−4)	1.3
		100	94.7 (−5)	1.3
		200	177 (−12)	1.3
12 July 1986	14 July 1986	50	48.9 (−2)	1.2
		100	98.6 (−1)	0.0
		200	199 (−1)	0.0
9 August 1986	11 August 1986	50	45.3 (−9)	0.0
		100	95.1 (−5)	0.0
		200	192 (−4)	0.0
6 September 1986	8 September 1986	50	52.1 (+4)	0.0
		100	98.1 (−2)	0.0
		200	196 (−2)	0.0
11 October 1986	13 October 1986	50	49.7 (−1)	0.0
		100	99.3 (−1)	1.2
		200	202 (+1)	1.2
15 November 1986	17 November 1986	50	48.1 (−4)	1.3
		100	96.2 (−4)	1.3
		200	185 (−7)	1.3

[a] Numbers specify 50, 100, and 200 ppm chloramine. Results of all vehicle analyses were below the limit of detection and are not included in the table.
[b] Concentrations are reported as ppm of chloramine
[c] The numbers in parentheses are the percent differences from target concentration

TABLE K11
Results of Trihalomethane Analysis[a] from Chloraminated Water Animal-Room Samples for Mice in the 2-Year Chlorinated and Chloraminated Water Studies

Date Mixed	Date Analyzed	Target Conc.[b]	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodichloromethane	Chlorodibromomethane	Bromoform
26 December 1984	29 December 1984	Control	<1.0	<1.0	ND	ND
		Vehicle	<1.0	<1.0	ND	ND
		50 ppm	<1.0	<1.0	ND	ND
		100 ppm	<1.0	<1.0	ND	ND
		200 ppm	<1.0	<1.0	ND	ND
14 January 1985	22 January 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	1.6	ND	ND	ND
		200 ppm	2.3	ND	ND	ND
11 February 1985	15 February 1985	Control	1.1	<1.0	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	1.2	ND	ND	ND
		200 ppm	1.3	ND	ND	ND
16 March 1985	19 March 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
13 April 1985	16 April 1985	Control	ND	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
11 May 1985	14 May 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
8 June 1985	12 June 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
6 July 1985	9 July 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND

TABLE K11
Results of Trihalomethane Analysis from Chloraminated Water Animal-Room Samples for Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
17 August 1985	22 August 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	1.2	ND	ND	ND
14 September 1985	17-18 September 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
12 October 1985	17-18 October 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	1.5	ND	ND	ND
		200 ppm	2.3	ND	ND	ND
9 November 1985	13-15 November 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	<1.0	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	<1.0	ND	ND
7 December 1985	10-11 December 1985	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
11 January 1986	15-16 January 1986	Control	1.8	1.2	<3.0	<5.0
		Vehicle	<1.0	1.1	<3.0	<5.0
		50 ppm	<1.0	1.2	<3.0	<5.0
		100 ppm	<1.0	1.2	<3.0	<5.0
		200 ppm	1.1	<1.0	ND	<5.0
8 February 1986	11-12 February 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
8 March 1986	11-12 March 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND

TABLE K11
Results of Trihalomethane Analysis from Chloraminated Water Animal-Room Samples for Mice in the 2-Year Chlorinated and Chloraminated Water Studies (continued)

Date Mixed	Date Analyzed	Target Conc.	Trihalomethane Concentration (ppb)			
			Chloroform	Bromodi-chloromethane	Chlorodi-bromomethane	Bromoform
12 April 1986	15 April 1986	Control	1.8	ND	ND	ND
		Vehicle	1.4	ND	ND	ND
		50 ppm	1.8	ND	ND	ND
		100 ppm	2.1	<1.0	ND	ND
		200 ppm	2.3	ND	ND	ND
10 May 1986	13-14 May 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	1.3	ND	ND	ND
		200 ppm	2.5	ND	ND	ND
7 June 1986	12-13 June 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
12 July 1986	15-16 July 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
9 August 1986	12-13 August 1986	Control	1.1	ND	ND	ND
		Vehicle	1.1	ND	ND	ND
		50 ppm	1.1	ND	ND	ND
		100 ppm	1.5	ND	ND	ND
		200 ppm	1.7	ND	ND	ND
6 September 1986	9-10 September 1986	Control	<1.0	ND	ND	ND
		Vehicle	<1.0	ND	ND	ND
		50 ppm	<1.0	ND	ND	ND
		100 ppm	<1.0	ND	ND	ND
		200 ppm	<1.0	ND	ND	ND
11 October 1986	14-15 October 1986	Control	<1.0	ND	1.7	ND
		Vehicle	<1.0	ND	2.0	ND
		50 ppm	<1.0	ND	<1.0	ND
		100 ppm	<1.0	ND	<1.0	ND
		200 ppm	1.1	ND	<1.0	ND
15 November 1986	18-21 November 1986	Control	1.2	<1.0	10.9	3.3
		Vehicle	<1.0	<1.0	7.1	3.2
		50 ppm	<1.0	<1.0	2.4	1.2
		100 ppm	<1.0	<1.0	2.5	1.2
		200 ppm	<1.0	<1.0	2.4	1.2

ND Not Detected
[a] Results of duplicate analyses except where noted
[b] Control sample was deionized water and represents an analysis control, not an animal-room sample. Vehicle was deionized water that was used in the animal room. Concentrations are reported as ppm chloramine.

APPENDIX L
WATER AND COMPOUND CONSUMPTION BY RATS AND MICE IN THE 2-YEAR DRINKING WATER STUDIES

TABLE L1
Water and Compound Consumption by Male Rats[a] in the 2-Year Chlorinated Water Studies

Week	0 ppm		70 ppm			140 ppm			275 ppm		
	Water (g/day)[b]	Body Wt. (g)	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]
1	20.0	119.4	18.8	120.4	10.9	17.1	119.2	20.1	15.5	116.7	36.6
2	23.1	159.1	21.7	161.6	9.4	19.4	159.4	17.0	17.7	157.8	30.8
3	23.7	194.5	22.1	198.8	7.8	19.5	194.4	14.0	17.6	193.0	25.0
4	24.1	221.6	22.4	226.5	6.9	20.3	224.5	12.6	18.8	220.3	23.5
5	25.2	249.7	22.0	252.8	6.1	21.6	250.5	12.0	20.2	245.2	22.7
6	22.7	270.2	21.2	275.6	5.4	20.9	270.4	10.8	18.0	265.5	18.6
7	22.2	288.5	20.7	293.0	5.0	19.6	290.1	9.4	17.1	283.9	16.6
8	22.8	303.1	20.4	305.5	4.7	19.9	303.2	9.2	17.9	299.0	16.5
9	23.4	317.8	21.1	322.5	4.6	20.7	317.6	9.1	18.6	312.0	16.4
10	21.6	330.8	19.5	334.5	4.1	18.7	330.3	7.9	18.0	323.5	15.3
11	20.8	340.3	18.3	344.3	3.7	18.4	337.3	7.6	17.5	332.4	14.5
12	21.6	349.4	18.5	352.8	3.7	17.9	350.1	7.2	16.9	344.4	13.5
13	20.7	359.0	19.5	362.2	3.8	18.3	359.5	7.1	17.2	353.0	13.4
17	21.0	387.7	19.1	394.0	3.4	18.3	391.3	6.5	17.8	382.0	12.8
21	20.9	402.9	18.8	407.3	3.2	18.3	408.1	6.3	16.9	396.0	11.7
25	20.0	422.8	19.6	427.1	3.2	17.9	427.8	5.9	17.8	416.7	11.7
29	21.8	434.9	18.8	442.2	3.0	18.3	439.5	5.8	16.3	433.1	10.4
33	19.5	450.3	18.6	454.8	2.9	17.1	454.6	5.3	16.9	443.2	10.5
37	20.9	457.0	17.7	463.3	2.7	17.4	460.2	5.3	16.7	447.4	10.3
41	19.7	465.2	18.8	468.1	2.8	18.5	468.8	5.5	17.3	459.3	10.3
45	22.2	468.3	20.9	474.9	3.1	19.4	474.2	5.7	17.9	463.1	10.7
49	21.6	474.7	20.2	484.0	2.9	18.8	482.3	5.5	17.5	473.5	10.1
53	20.9	480.1	19.4	485.4	2.8	18.1	483.0	5.2	17.9	472.2	10.4
57	22.6	489.0	20.7	493.9	2.9	19.2	495.1	5.4	18.0	480.0	10.3
61	23.1	492.0	21.0	495.2	3.0	18.7	495.1	5.3	16.7	485.9	9.4
65	23.4	495.7	22.4	498.1	3.1	20.2	498.4	5.7	18.1	490.1	10.1
69	26.1	492.8	23.1	491.9	3.3	19.9	489.7	5.7	18.4	483.2	10.5
73	27.2	490.7	26.6	489.3	3.8	22.2	495.1	6.3	21.3	481.0	12.2
77	28.3	493.0	26.4	487.8	3.8	23.5	492.5	6.7	23.5	483.8	13.4
81	30.4	487.1	28.2	468.0	4.2	25.1	480.5	7.3	24.9	485.4	14.1
85	32.8	486.1	32.2	454.5	5.0	27.0	472.8	8.0	26.8	471.8	15.6
89	34.3	473.2	37.6	449.7	5.8	29.4	458.5	9.0	24.2	469.2	14.2
93	39.0	469.1	42.9	443.3	6.8	30.8	444.0	9.7	28.4	457.1	17.1
97	38.5	463.0	52.7	428.6	8.6	33.3	439.2	10.6	32.1	450.7	19.6
101	44.5	470.6	54.8	425.1	9.0	38.6	422.8	12.8	37.5	431.5	23.9
Mean for Weeks											
1-13	22.4	269.5	20.5	273.1	5.8	19.4	269.7	11.1	17.8	265.1	20.3
14-52	20.8	440.4	19.2	446.2	3.0	18.2	445.2	5.8	17.2	434.9	10.9
53-101	30.1	483.3	31.4	470.1	4.8	25.1	474.4	7.5	23.7	472.5	13.9

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of available atomic chlorine consumed per day per kilogram of body weight

TABLE L2
Water and Compound Consumption by Female Rats[a] in the 2-Year Chlorinated Water Studies

Week	0 ppm		70 ppm			140 ppm			275 ppm		
	Water (g/day)[b]	Body Wt. (g)	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]
1	17.9	100.2	15.9	98.4	11.3	14.9	98.9	21.1	13.0	99.0	36.1
2	19.4	128.0	17.6	129.0	9.5	15.9	128.5	17.3	13.9	128.7	29.6
3	18.7	145.4	16.1	143.6	7.8	14.9	142.0	14.7	13.2	144.1	25.1
4	18.1	155.9	17.1	154.7	7.7	15.2	154.9	13.7	12.8	154.0	22.8
5	18.1	165.4	16.2	164.1	6.9	14.8	164.0	12.6	12.9	163.4	21.7
6	18.7	173.2	15.2	171.6	6.2	14.3	171.4	11.7	12.6	170.0	20.4
7	17.3	181.3	15.2	180.4	5.9	14.1	180.0	11.0	12.2	178.0	18.8
8	16.9	186.3	15.0	185.5	5.7	13.8	184.4	10.5	12.4	183.3	18.5
9	15.9	191.8	14.5	190.1	5.3	13.6	188.8	10.1	11.9	187.9	17.5
10	15.8	195.2	14.0	195.6	5.0	12.9	193.9	9.3	11.7	191.6	16.7
11	15.1	198.4	13.6	199.2	4.8	12.9	197.6	9.1	12.0	195.1	16.9
12	15.3	201.6	13.5	203.2	4.7	12.7	200.2	8.9	11.8	198.0	16.3
13	14.7	203.8	13.7	204.9	4.7	13.1	203.2	9.0	12.0	199.7	16.6
17	14.4	218.1	13.5	219.8	4.3	12.6	217.6	8.1	11.5	213.6	14.8
21	15.2	225.9	14.1	226.5	4.4	13.1	224.1	8.2	11.7	220.9	14.5
25	14.7	233.5	13.8	234.0	4.1	13.8	231.9	8.3	12.2	227.8	14.7
29	15.4	245.8	13.6	245.4	3.9	12.9	244.3	7.4	11.5	237.7	13.3
33	15.0	249.5	13.2	250.8	3.7	12.5	247.2	7.1	11.6	244.3	13.1
37	14.3	256.6	14.7	255.8	4.0	13.2	252.9	7.3	11.3	246.8	12.6
41	15.7	259.9	13.8	263.7	3.7	13.1	261.4	7.0	12.1	253.9	13.1
45	15.2	271.4	14.8	271.9	3.8	13.4	270.9	6.9	12.3	261.0	13.0
49	15.6	281.4	14.6	281.2	3.6	14.1	279.2	7.1	12.8	269.0	13.1
53	15.1	283.3	14.9	289.4	3.6	14.0	286.3	6.9	13.1	277.6	12.9
57	16.5	299.0	15.7	298.2	3.7	14.5	298.4	6.8	13.6	287.8	13.0
61	15.7	306.1	14.7	306.9	3.4	13.4	307.6	6.1	12.7	296.5	11.8
65	16.7	317.9	15.6	314.6	3.5	14.2	317.1	6.3	13.5	306.9	12.1
69	18.0	326.8	15.8	323.4	3.4	15.6	327.7	6.7	14.2	312.3	12.5
73	18.5	327.1	17.5	332.3	3.7	16.0	335.6	6.7	14.4	320.1	12.4
77	19.7	339.3	17.5	337.6	3.6	16.1	341.7	6.6	14.5	323.7	12.3
81	20.7	343.6	18.2	344.2	3.7	17.1	347.0	6.9	16.6	330.3	13.8
85	22.3	347.1	18.7	342.1	3.8	16.4	345.1	6.7	16.4	329.9	13.7
89	23.0	346.0	17.5	347.7	3.5	18.2	348.1	7.3	16.1	330.3	13.4
93	22.5	339.1	20.3	350.7	4.0	17.5	348.7	7.0	17.0	332.4	14.0
97	25.6	352.2	22.9	352.5	4.5	19.4	351.7	7.7	18.7	336.5	15.3
101	25.8	347.6	23.3	352.7	4.6	18.8	351.6	7.5	17.8	335.3	14.6
Mean for Weeks											
1-13	17.1	171.3	15.2	170.8	6.6	14.1	169.8	12.2	12.5	168.7	21.3
14-52	15.1	249.1	14.0	249.9	3.9	13.2	247.7	7.5	11.9	241.7	13.6
53-101	20.0	328.9	17.9	330.2	3.8	16.3	331.3	6.9	15.3	316.9	13.2

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of available atomic chlorine consumed per day per kilogram of body weight

TABLE L3
Water and Compound Consumption by Male Rats[a] in the 2-Year Chloraminated Water Studies

Week	0 ppm		50 ppm			100 ppm			200 ppm		
	Water (g/day)[b]	Body Wt. (g)	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]
1	20.0	119.4	16.5	116.1	7.1	12.6	118.7	10.6	8.4	118.5	14.1
2	23.1	159.1	19.2	159.0	6.0	16.5	156.4	10.5	13.4	144.9	18.6
3	23.7	194.5	20.0	193.7	5.2	16.3	190.8	8.6	13.9	176.7	15.7
4	24.1	221.6	19.6	223.1	4.4	17.0	218.1	7.8	15.1	203.7	14.8
5	25.2	249.7	21.3	248.7	4.3	17.5	244.3	7.2	14.9	228.5	13.0
6	22.7	270.2	20.3	267.3	3.8	17.3	265.4	6.5	14.1	249.3	11.3
7	22.2	288.5	18.7	288.7	3.2	16.0	283.8	5.6	14.3	266.2	10.7
8	22.8	303.1	19.3	302.4	3.2	17.1	296.9	5.8	15.3	282.2	10.9
9	23.4	317.8	20.0	315.5	3.2	17.4	311.7	5.6	15.1	295.3	10.2
10	21.6	330.8	19.2	328.0	2.9	17.1	323.6	5.3	15.1	305.8	9.9
11	20.8	340.3	18.9	337.9	2.8	16.8	334.6	5.0	14.8	316.7	9.3
12	21.6	349.4	19.0	348.6	2.7	16.8	344.1	4.9	14.5	325.7	8.9
13	20.7	359.0	18.6	357.4	2.6	17.3	352.5	4.9	15.2	333.4	9.1
17	21.0	387.7	18.5	388.0	2.4	17.9	381.3	4.7	15.1	362.5	8.3
21	20.9	402.9	18.2	405.0	2.2	16.7	395.2	4.2	15.5	379.3	8.2
25	20.0	422.8	18.7	424.3	2.2	17.2	418.8	4.1	15.4	397.0	7.8
29	21.8	434.9	19.0	437.8	2.2	17.5	431.4	4.1	15.6	413.4	7.5
33	19.5	450.3	18.3	453.0	2.0	16.7	447.1	3.7	14.7	424.8	6.9
37	20.9	457.0	18.8	456.3	2.1	16.2	453.5	3.6	14.1	431.0	6.6
41	19.7	465.2	18.7	467.8	2.0	16.8	462.1	3.6	15.6	441.5	7.1
45	22.2	468.3	19.8	474.5	2.1	17.6	466.8	3.8	15.4	444.1	7.0
49	21.6	474.7	19.3	479.7	2.0	17.5	475.3	3.7	15.6	450.5	6.9
53	20.9	480.1	18.9	484.4	2.0	17.4	480.3	3.6	15.8	454.9	7.0
57	22.6	489.0	19.4	489.1	2.0	18.7	491.1	3.8	16.0	466.5	6.9
61	23.1	492.0	18.9	490.9	1.9	17.8	490.6	3.6	15.5	469.8	6.6
65	23.4	495.7	19.8	497.0	2.0	18.8	498.9	3.8	17.6	473.8	7.4
69	26.1	492.8	21.6	493.9	2.2	20.5	493.8	4.1	16.8	466.2	7.2
73	27.2	490.7	22.1	503.1	2.2	20.7	498.3	4.2	17.8	466.1	7.6
77	28.3	493.0	24.9	490.5	2.5	22.6	488.6	4.6	18.2	467.3	7.8
81	30.4	487.1	23.1	485.1	2.4	22.6	479.5	4.7	19.9	459.6	8.7
85	32.8	486.1	26.8	479.5	2.8	24.5	477.6	5.1	20.1	451.7	8.9
89	34.3	473.2	32.4	465.5	3.5	29.0	464.6	6.2	22.1	437.7	10.1
93	39.0	469.1	34.4	455.2	3.8	30.2	457.4	6.6	22.3	434.7	10.3
97	38.5	463.0	33.7	449.1	3.8	30.4	448.1	6.8	23.4	428.7	10.9
101	44.5	470.6	36.2	441.8	4.1	33.0	431.1	7.6	31.5	415.4	15.2
Mean for Weeks											
1-13	22.4	269.5	19.3	268.2	4.0	16.6	264.7	6.8	14.2	249.8	12.1
14-52	20.8	440.4	18.8	442.9	2.1	17.1	436.8	3.9	15.2	416.0	7.4
53-101	30.1	483.3	25.6	478.9	2.7	23.6	476.9	5.0	19.8	453.3	8.8

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of chloramine consumed per day per kilogram of body weight

TABLE L4
Water and Compound Consumption by Female Rats[a] in the 2-Year Chloraminated Water Studies

Week	0 ppm		50 ppm			100 ppm			200 ppm		
	Water (g/day)[b]	Body Wt. (g)	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]	Water (g/day)[b]	Body Wt. (g)	Dose/ Day[c]
1	17.9	100.2	13.2	98.2	6.7	10.2	99.0	10.4	7.0	99.3	14.2
2	19.4	128.0	15.3	127.6	6.0	12.8	125.5	10.2	10.9	121.1	18.0
3	18.7	145.4	14.8	143.5	5.1	11.9	141.3	8.4	10.2	136.1	15.0
4	18.1	155.9	14.6	153.1	4.8	12.2	152.6	8.0	10.6	147.5	14.3
5	18.1	165.4	14.6	162.7	4.5	12.5	162.0	7.7	10.8	156.8	13.8
6	18.7	173.2	13.8	170.2	4.1	12.2	169.9	7.2	10.3	164.4	12.5
7	17.3	181.3	13.7	178.8	3.8	11.7	178.6	6.6	9.7	171.5	11.3
8	16.9	186.3	13.6	184.4	3.7	12.0	184.9	6.5	10.0	176.4	11.3
9	15.9	191.8	13.1	188.9	3.5	11.7	189.0	6.2	9.8	181.3	10.8
10	15.8	195.2	12.6	194.7	3.2	11.6	193.5	6.0	10.0	186.3	10.8
11	15.1	198.4	12.5	197.7	3.2	11.6	196.9	5.9	10.1	190.5	10.6
12	15.3	201.6	12.5	201.6	3.1	11.3	199.0	5.7	9.8	192.5	10.2
13	14.7	203.8	12.8	203.6	3.1	12.0	202.0	5.9	10.0	195.6	10.2
17	14.4	218.1	12.5	218.5	2.9	11.5	216.2	5.3	9.9	206.2	9.6
21	15.2	225.9	12.8	226.6	2.8	12.7	223.2	5.7	9.8	213.7	9.1
25	14.7	233.5	12.5	235.0	2.7	11.6	232.0	5.0	10.1	221.7	9.1
29	15.4	245.8	12.5	245.4	2.5	11.9	242.5	4.9	10.4	228.1	9.1
33	15.0	249.5	12.7	250.0	2.5	12.2	245.6	5.0	10.2	234.0	8.7
37	14.3	256.6	12.4	255.9	2.4	11.8	252.4	4.7	10.3	235.8	8.7
41	15.7	259.9	13.0	263.2	2.5	11.9	257.4	4.6	10.7	244.1	8.8
45	15.2	271.4	13.6	270.4	2.5	12.9	266.2	4.8	10.9	250.2	8.7
49	15.6	281.4	14.5	279.2	2.6	12.9	274.0	4.7	12.3	255.9	9.7
53	15.1	283.3	13.9	288.0	2.4	13.2	280.7	4.7	12.3	267.1	9.2
57	16.5	299.0	14.7	298.2	2.5	13.6	293.7	4.6	12.6	275.1	9.2
61	15.7	306.1	13.8	307.8	2.2	12.9	300.8	4.3	11.1	282.7	7.9
65	16.7	317.9	15.3	318.0	2.4	14.7	309.3	4.7	13.2	292.7	9.0
69	18.0	326.8	15.3	330.9	2.3	14.1	319.6	4.4	12.5	294.8	8.5
73	18.5	327.1	15.8	339.1	2.3	15.0	327.4	4.6	13.1	303.0	8.6
77	19.7	339.3	16.1	342.1	2.4	15.2	336.4	4.5	12.7	309.4	8.2
81	20.7	343.6	17.5	349.0	2.5	16.0	340.4	4.7	13.7	313.3	8.7
85	22.3	347.1	17.4	348.8	2.5	16.5	339.2	4.9	14.1	316.4	8.9
89	23.0	346.0	16.7	347.0	2.4	16.8	343.6	4.9	14.0	310.6	9.0
93	22.5	339.1	19.0	347.5	2.7	19.5	339.6	5.7	14.9	310.6	9.6
97	25.6	352.2	19.3	359.2	2.7	19.8	340.0	5.8	15.5	307.3	10.1
101	25.8	347.6	20.5	363.2	2.8	21.7	345.7	6.3	18.4	307.0	12.0
Mean for Weeks											
1-13	17.1	171.3	13.6	169.6	4.2	11.8	168.8	7.3	9.9	163.0	12.5
14-52	15.1	249.1	12.9	249.4	2.6	12.1	245.5	5.0	10.5	232.2	9.0
53-101	20.0	328.9	16.5	333.8	2.5	16.1	324.3	4.9	13.7	299.2	9.1

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of chloramine consumed per day per kilogram of body weight

TABLE L5
Water and Compound Consumption by Male Mice[a] in the 2-Year Chlorinated Water Studies

	0 ppm		70 ppm			140 ppm			275 ppm		
Week	Water (g/day)[b]	Body Weight (g)	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]
1	4.6	22.2	4.0	21.8	12.8	4.0	21.9	25.7	3.5	21.7	44.5
2	4.7	24.4	4.2	24.3	12.1	3.9	24.5	22.1	3.5	23.8	40.2
3	4.9	25.5	4.6	25.5	12.6	4.2	25.8	22.8	4.1	25.1	44.8
4	4.3	26.6	4.3	26.9	11.3	4.2	26.8	21.8	3.8	25.9	40.0
5	4.7	27.8	4.4	27.7	11.0	4.1	28.1	20.5	3.7	27.0	37.5
6	5.1	29.3	4.5	29.2	10.7	4.3	29.4	20.3	3.8	28.3	36.6
7	4.8	30.5	4.7	30.3	10.8	4.3	30.3	19.9	3.6	29.4	34.0
8	4.9	31.5	4.7	31.2	10.5	4.3	31.3	19.4	3.9	30.0	35.9
9	4.5	31.9	4.6	32.2	10.0	4.2	32.0	18.3	3.5	31.0	30.8
10	4.4	33.0	4.5	33.6	9.3	4.2	33.3	17.7	3.5	32.0	29.9
11	4.6	34.2	4.4	34.6	8.9	4.1	34.4	16.8	3.8	33.0	31.3
12	4.7	35.1	4.5	35.3	8.9	4.1	35.1	16.4	3.5	33.6	28.8
13	4.3	36.4	4.2	36.5	8.1	4.0	36.4	15.2	3.4	34.8	27.1
17	4.2	39.4	4.0	39.9	7.0	3.8	39.5	13.6	3.4	38.0	24.9
21	4.5	42.4	4.1	42.4	6.7	3.8	42.4	12.5	3.6	40.9	24.3
25	4.2	45.0	4.2	44.8	6.6	3.7	44.8	11.5	3.3	43.6	21.1
29	4.4	46.1	4.2	45.8	6.5	3.9	45.9	12.0	3.3	44.5	20.7
33	4.3	46.2	4.1	45.8	6.2	3.8	45.8	11.5	3.1	44.5	19.5
37	4.3	46.7	4.1	45.9	6.3	3.7	45.8	11.3	3.6	45.0	21.8
41	4.6	46.9	4.3	46.5	6.5	3.9	46.2	11.8	3.4	45.3	20.8
45	4.6	48.1	4.5	47.6	6.7	4.0	47.2	12.0	3.5	46.0	21.0
49	4.7	48.4	4.5	47.6	6.6	4.1	47.5	12.2	3.4	46.1	20.4
53	5.0	49.0	4.7	48.0	6.9	4.3	47.8	12.6	3.8	46.4	22.2
57	5.0	49.9	4.9	48.6	7.1	4.7	48.2	13.8	3.8	47.6	21.9
61	5.2	49.8	5.2	48.2	7.5	4.6	48.0	13.3	3.7	46.7	21.6
65	5.2	50.2	4.7	48.4	6.8	4.7	48.3	13.5	3.6	47.3	21.0
69	5.1	50.9	4.6	48.7	6.6	4.9	48.2	14.3	3.7	47.4	21.3
73	6.2	50.4	4.9	48.1	7.2	5.4	47.3	16.1	3.4	47.4	19.9
77	5.7	50.3	5.0	49.0	7.1	4.8	47.5	14.1	3.9	47.4	22.6
81	5.3	50.9	4.4	49.4	6.3	4.5	48.2	13.1	3.6	47.5	21.1
85	5.4	50.6	5.2	48.6	7.5	4.6	48.4	13.3	4.0	47.4	23.3
89	5.5	50.2	4.7	48.0	6.8	4.6	48.3	13.3	3.9	46.8	22.8
93	5.7	49.6	5.2	48.7	7.5	5.1	47.8	14.9	4.0	46.5	23.7
97	6.0	48.8	5.3	47.4	7.9	5.0	47.5	14.8	4.4	45.2	26.8
101	6.8	48.8	5.3	47.0	7.9	4.9	47.0	14.7	4.0	44.9	24.7
Mean for Weeks											
1-13	4.6	29.9	4.4	29.9	10.5	4.1	29.9	19.8	3.7	28.9	35.5
14-52	4.4	45.5	4.2	45.1	6.6	3.9	45.0	12.0	3.4	43.8	21.6
53-101	5.5	50.0	4.9	48.3	7.2	4.8	47.9	14.0	3.8	46.8	22.5

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of available atomic chlorine consumed per day per kilogram of body weight

TABLE L6
Water and Compound Consumption by Female Mice[a] in the 2-Year Chlorinated Water Studies

Week	0 ppm		70 ppm			140 ppm			275 ppm		
	Water (g/day)[b]	Body Weight (g)	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]
1	4.3	18.0	3.9	17.8	15.3	3.7	17.5	29.7	3.3	17.7	51.8
2	4.9	19.9	4.3	19.7	15.3	3.9	19.5	27.8	3.4	19.5	48.3
3	5.2	20.6	5.1	20.8	17.2	4.8	20.5	32.6	4.1	20.5	55.0
4	4.6	22.0	4.4	22.0	14.1	4.2	21.6	27.5	3.7	21.7	47.5
5	5.1	23.1	4.8	22.9	14.6	4.4	22.8	26.9	3.6	22.6	44.4
6	5.0	23.7	4.7	24.0	13.8	4.4	23.4	26.0	3.9	23.1	46.0
7	5.0	24.4	4.8	24.7	13.7	4.4	24.1	25.5	3.7	23.9	42.6
8	5.3	25.5	4.8	25.5	13.1	4.5	25.0	25.5	3.9	24.7	43.8
9	5.0	26.3	4.8	26.3	12.8	4.3	25.6	23.6	3.6	25.1	39.0
10	4.7	27.4	4.8	27.6	12.1	4.1	26.5	21.9	3.8	26.2	40.3
11	4.8	28.2	4.6	28.6	11.3	4.2	27.7	21.5	3.7	27.1	37.2
12	5.0	28.9	4.7	29.2	11.3	4.3	28.3	21.3	3.8	27.8	37.1
13	4.8	30.0	4.5	30.2	10.5	4.1	29.2	19.6	3.6	28.7	34.3
17	4.7	33.3	4.3	33.4	9.0	4.0	33.2	16.9	3.6	32.4	30.2
21	4.3	36.7	4.3	37.1	8.1	3.9	36.6	14.9	3.4	35.5	26.2
25	4.4	39.5	4.1	39.5	7.3	3.8	39.2	13.5	3.4	38.2	24.2
29	4.4	41.6	4.3	41.1	7.3	3.9	41.1	13.1	3.4	39.7	23.3
33	4.4	41.5	4.0	42.0	6.7	3.7	41.5	12.6	3.2	40.5	21.6
37	4.4	43.0	4.4	42.8	7.2	3.8	42.5	12.4	3.2	41.5	21.5
41	4.7	44.2	4.3	44.3	6.9	3.8	43.5	12.2	3.4	42.4	22.4
45	4.4	46.4	4.1	46.0	6.3	3.8	45.2	11.7	3.2	43.9	20.3
49	4.7	47.2	4.3	47.1	6.4	3.8	46.2	11.6	3.3	44.9	20.4
53	4.9	51.0	4.5	50.0	6.2	4.0	48.4	11.7	3.5	48.2	20.0
57	4.8	50.6	4.7	50.7	6.5	4.2	49.8	11.8	3.2	48.1	18.3
61	4.8	50.7	4.8	51.0	6.6	4.2	50.1	11.7	3.7	48.3	20.8
65	4.7	51.8	4.5	52.3	6.0	4.3	50.3	12.0	3.5	49.4	19.6
69	4.7	53.9	4.4	52.6	5.9	4.2	51.6	11.5	3.6	51.2	19.1
73	5.5	53.7	4.8	52.1	6.4	5.5	51.3	14.9	3.7	50.8	20.2
77	5.2	55.5	4.5	53.2	5.9	4.3	52.6	11.5	3.7	52.3	19.5
81	4.7	55.2	4.3	53.3	5.6	4.4	52.4	11.6	3.8	52.2	19.8
85	4.7	56.9	4.7	53.3	6.2	4.3	52.9	11.5	3.5	53.0	18.3
89	5.0	56.3	4.2	53.7	5.5	4.3	53.3	11.2	3.5	53.2	18.3
93	5.4	55.7	4.8	53.4	6.3	4.7	52.6	12.5	3.7	52.5	19.6
97	5.2	55.8	5.2	51.8	7.0	4.5	52.6	12.0	4.2	51.7	22.2
101	5.8	54.7	5.3	49.6	7.5	4.7	50.5	13.0	4.1	50.8	22.1
Mean for Weeks											
1-13	4.9	24.5	4.6	24.6	13.5	4.3	24.0	25.3	3.7	23.7	43.6
14-52	4.5	41.5	4.3	41.5	7.3	3.8	41.0	13.2	3.3	39.9	23.3
53-101	5.0	54.0	4.7	52.1	6.3	4.4	51.4	12.1	3.7	50.9	19.8

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of available atomic chlorine consumed per day per kilogram of body weight

TABLE L7
Water and Compound Consumption by Male Mice[a] in the 2-Year Chloraminated Water Studies

Week	0 ppm		50 ppm			100 ppm			200 ppm		
	Water (g/day)[b]	Body Weight (g)	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]
1	4.6	22.2	3.9	21.7	9.1	3.3	21.6	15.1	2.4	22.2	21.4
2	4.7	24.4	4.0	24.3	8.3	3.5	23.9	14.5	2.7	23.3	23.0
3	4.9	25.5	4.2	25.7	8.2	3.7	25.1	14.8	2.8	24.6	22.5
4	4.3	26.6	3.9	27.0	7.2	3.5	26.1	13.4	2.8	25.5	21.6
5	4.7	27.8	4.2	27.9	7.5	3.8	27.5	13.8	2.8	26.6	21.3
6	5.1	29.3	4.4	29.4	7.4	3.9	28.8	13.6	3.1	27.9	22.1
7	4.8	30.5	4.2	29.9	7.0	3.8	29.8	12.7	2.9	28.4	20.4
8	4.9	31.5	4.4	31.5	6.9	3.8	30.7	12.4	3.0	28.9	20.9
9	4.5	31.9	4.1	32.2	6.3	3.8	31.5	12.0	3.1	29.9	20.5
10	4.4	33.0	4.2	33.5	6.3	3.8	32.5	11.6	3.0	30.8	19.2
11	4.6	34.2	4.1	34.2	5.9	3.7	33.3	11.1	2.9	31.6	18.2
12	4.7	35.1	4.2	35.1	6.0	3.8	34.0	11.1	3.1	32.2	19.2
13	4.3	36.4	3.9	36.0	5.4	3.7	35.2	10.6	2.9	33.2	17.2
17	4.2	39.4	3.8	39.4	4.8	3.6	38.3	9.4	3.0	35.5	17.1
21	4.5	42.4	4.0	41.9	4.8	3.5	40.9	8.6	3.3	39.1	17.1
25	4.2	45.0	3.9	44.6	4.4	3.7	43.4	8.6	3.4	41.3	16.4
29	4.4	46.1	3.9	45.8	4.3	3.5	44.2	8.0	3.2	42.5	14.9
33	4.3	46.2	3.8	45.7	4.1	3.3	43.9	7.6	3.0	42.1	14.1
37	4.3	46.7	3.7	45.8	4.1	3.5	44.3	7.9	3.4	42.0	16.1
41	4.6	46.9	4.1	46.1	4.4	3.6	44.8	8.1	3.2	42.3	15.0
45	4.6	48.1	4.1	47.3	4.4	3.6	45.6	8.0	3.4	42.7	15.7
49	4.7	48.4	4.0	47.5	4.2	3.6	45.9	7.9	3.1	42.9	14.4
53	5.0	49.0	4.4	48.0	4.6	3.9	46.5	8.4	3.1	43.5	14.4
57	5.0	49.9	4.4	48.5	4.5	3.9	47.0	8.2	3.4	44.1	15.6
61	5.2	49.8	4.6	48.2	4.7	3.9	47.0	8.2	3.2	43.7	14.5
65	5.2	50.2	4.3	48.5	4.5	4.0	47.4	8.4	3.4	44.5	15.4
69	5.1	50.9	4.4	48.8	4.5	3.7	48.0	7.7	2.9	44.8	13.0
73	6.2	50.4	4.6	48.2	4.8	4.0	47.2	8.5	3.2	44.1	14.4
77	5.7	50.3	4.3	48.3	4.5	3.8	47.9	8.0	3.3	44.3	14.7
81	5.3	50.9	4.5	48.6	4.6	3.8	47.6	8.0	3.1	44.1	14.0
85	5.4	50.6	4.8	48.3	5.0	3.8	48.2	7.9	3.1	43.8	14.1
89	5.5	50.2	4.5	48.0	4.7	3.7	47.4	7.9	3.0	42.7	14.2
93	5.7	49.6	5.1	46.6	5.5	4.0	46.3	8.6	3.2	42.4	15.1
97	6.0	48.8	5.3	45.2	5.8	4.4	46.0	9.6	3.4	39.4	17.4
101	6.8	48.8	4.9	45.3	5.4	4.3	45.6	9.3	3.2	38.1	16.8
Mean for Weeks											
1-13	4.6	29.9	4.1	29.9	7.0	3.7	29.2	12.8	2.9	28.1	20.6
14-52	4.4	45.5	3.9	44.9	4.4	3.6	43.5	8.2	3.2	41.2	15.6
53-101	5.5	50.0	4.6	47.7	4.9	3.9	47.1	8.4	3.2	43.0	14.9

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of chloramine consumed per day per kilogram of body weight

TABLE L8
Water and Compound Consumption by Female Mice[a] in the 2-Year Chloraminated Water Studies

Week	0 ppm		50 ppm			100 ppm			200 ppm		
	Water (g/day)[b]	Body Weight (g)	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]	Water (g/day)[b]	Body Weight (g)	Dose/ Day[c]
1	4.3	18.0	3.6	17.6	10.3	3.1	17.5	17.8	2.1	17.7	24.2
2	4.9	19.9	4.1	19.7	10.4	3.3	19.6	16.8	2.5	18.8	27.1
3	5.2	20.6	4.1	20.6	9.9	3.6	20.4	17.9	2.6	19.5	27.1
4	4.6	22.0	3.9	21.8	9.0	3.6	21.6	16.7	2.6	20.6	25.4
5	5.1	23.1	4.2	22.9	9.1	3.8	22.7	16.5	2.8	21.5	25.6
6	5.0	23.7	4.3	23.4	9.1	3.7	22.9	16.3	3.0	22.0	27.3
7	5.0	24.4	4.1	23.9	8.6	3.7	23.8	15.6	2.8	22.5	24.7
8	5.3	25.5	4.4	24.7	8.9	3.9	24.6	16.0	2.9	22.9	25.5
9	5.0	26.3	4.1	25.5	8.1	3.7	25.3	14.7	2.8	23.4	23.8
10	4.7	27.4	4.1	26.5	7.8	3.8	26.2	14.4	2.8	24.1	23.5
11	4.8	28.2	4.0	27.3	7.4	3.7	27.2	13.6	2.9	24.5	23.3
12	5.0	28.9	4.1	27.9	7.4	3.8	27.7	13.8	2.9	24.7	23.6
13	4.8	30.0	4.0	28.9	6.9	3.7	28.7	13.0	2.7	25.6	21.0
17	4.7	33.3	3.7	32.3	5.7	3.4	31.9	10.6	2.7	27.8	19.5
21	4.3	36.7	3.8	35.1	5.4	3.3	35.4	9.4	3.0	31.0	19.4
25	4.4	39.5	3.6	37.6	4.8	3.5	38.2	9.2	2.9	33.4	17.3
29	4.4	41.6	3.6	39.4	4.6	3.3	39.7	8.4	2.8	35.0	15.9
33	4.4	41.5	3.4	40.1	4.3	3.2	40.0	8.0	2.7	35.1	15.2
37	4.4	43.0	3.5	40.6	4.3	3.0	40.3	7.4	2.6	35.3	14.9
41	4.7	44.2	3.7	42.0	4.4	3.3	41.2	8.0	2.7	35.3	15.5
45	4.4	46.4	3.7	43.8	4.2	3.4	42.4	7.9	3.0	36.3	16.4
49	4.7	47.2	3.7	44.4	4.2	3.3	43.4	7.7	2.9	37.0	15.5
53	4.9	51.0	3.8	46.6	4.1	3.5	47.4	7.5	2.9	40.3	14.4
57	4.8	50.6	4.1	47.2	4.3	3.6	46.0	7.8	3.2	38.9	16.7
61	4.8	50.7	3.8	47.8	4.0	3.7	46.2	8.0	3.1	38.7	16.2
65	4.7	51.8	4.2	48.7	4.3	3.6	46.6	7.8	3.3	39.3	16.6
69	4.7	53.9	4.1	49.7	4.1	3.5	47.1	7.5	2.8	39.3	14.4
73	5.5	53.7	4.4	49.5	4.4	3.7	46.6	7.9	3.0	38.6	15.4
77	5.2	55.5	3.8	50.3	3.8	3.6	47.6	7.6	3.1	39.5	15.9
81	4.7	55.2	3.9	50.5	3.9	3.6	48.5	7.4	3.1	39.5	15.7
85	4.7	56.9	4.0	51.4	3.9	3.5	48.9	7.2	2.8	39.9	13.9
89	5.0	56.3	3.8	51.4	3.7	3.4	49.0	6.9	2.7	39.2	13.8
93	5.4	55.7	4.2	51.5	4.0	3.6	48.5	7.4	3.0	38.1	15.5
97	5.2	55.8	4.5	50.9	4.4	4.0	47.2	8.4	3.2	36.7	17.4
101	5.8	54.7	4.5	48.2	4.7	3.9	44.5	8.8	3.0	35.3	17.2
Mean for Weeks											
1-13	4.9	24.5	4.1	23.9	8.7	3.7	23.7	15.6	2.7	22.1	24.8
14-52	4.5	41.5	3.6	39.5	4.6	3.3	39.2	8.5	2.8	34.0	16.6
53-101	5.0	54.0	4.1	49.5	4.1	3.6	47.2	7.7	3.0	38.7	15.6

[a] Includes interim evaluation animals
[b] Grams of water consumed per animal per day
[c] Estimated milligrams of chloramine consumed per day per kilogram of body weight

APPENDIX M
INGREDIENTS, NUTRIENT COMPOSITION, AND CONTAMINANT LEVELS IN FEED AND WATER

TABLE M1
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, 1976a; NIH, 1978
[b] Ingredients ground to pass through a U.S. Standard Screen No. 16 before being mixed

TABLE M2
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	
Pyroxidine	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 M3
Nutrient Composition of NIH-07 Rat and Mouse Ration

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	22.10 ± 0.47	21.1–23.1	26
Crude fat (% by weight)	5.63 ± 0.41	4.7–6.4	26
Crude fiber (% by weight)	3.39 ± 0.25	2.7–4.0	26
Ash (% by weight)	6.46 ± 0.24	6.1–7.0	26
Amino Acids (% of total diet)			
Arginine	1.320 ± 0.072	1.310–1.390	5
Cystine	0.319 ± 0.088	0.218–0.400	5
Glycine	1.146 ± 0.063	1.060–1.210	5
Histidine	0.571 ± 0.026	0.531–0.603	5
Isoleucine	0.914 ± 0.030	0.881–0.944	5
Leucine	1.946 ± 0.056	1.850–1.990	5
Lysine	1.280 ± 0.067	1.200–1.370	5
Methionine	0.436 ± 0.165	0.306–0.699	5
Phenylalanine	0.938 ± 0.158	0.665–1.050	5
Threonine	0.855 ± 0.035	0.824–0.898	5
Tryptophan	0.277 ± 0.221	0.156–0.671	5
Tyrosine	0.618 ± 0.086	0.564–0.769	5
Valine	1.108 ± 0.043	1.050–1.170	5
Essential Fatty Acids (% of total diet)			
Linoleic	2.290 ± 0.313	1.830–2.520	5
Linolenic	0.258 ± 0.040	0.210–0.308	5
Vitamins			
Vitamin A (IU/kg)	8,375 ± 2,725	4,700–15,000	26
Vitamin D (IU/kg)	4,450 ± 1,382	3,000–6,300	4
α-Tocopherol (ppm)	43.58 ± 6.92	31.1–48.0	5
Thiamine (ppm)	20.69 ± 2.00	17.0–26.0	26
Riboflavin (ppm)	7.60 ± 0.85	6.10–8.20	5
Niacin (ppm)	97.80 ± 31.68	65.0–150.0	5
Pantothenic acid (ppm)	30.06 ± 4.31	23.0–34.0	5
Pyridoxine (ppm)	7.68 ± 1.31	5.60–8.80	5
Folic acid (ppm)	2.62 ± 0.89	1.80–3.70	5
Biotin (ppm)	0.254 ± 0.053	0.19–0.32	5
Vitamin B_{12} (ppb)	24.21 ± 12.66	10.6–38.0	5
Choline (ppm)	3,122 ± 416.8	2,400–3,430	5
Minerals			
Calcium (%)	1.14 ± 0.09	0.98–1.41	26
Phosphorus (%)	0.92 ± 0.05	0.73–0.99	26
Potassium (%)	0.900 ± 0.098	0.772–0.971	3
Chloride (%)	0.513 ± 0.114	0.380–0.635	5
Sodium (%)	0.323 ± 0.043	0.258–0.371	5
Magnesium (%)	0.167 ± 0.012	0.151–0.181	5
Sulfur (%)	0.304 ± 0.064	0.268–0.420	5
Iron (ppm)	410.3 ± 94.04	262.0–523.0	5
Manganese (ppm)	90.29 ± 7.15	81.70–99.40	5
Zinc (ppm)	52.78 ± 4.94	46.10–58.20	5
Copper (ppm)	10.72 ± 2.76	8.090–15.39	5
Iodine (ppm)	2.95 ± 1.05	1.52–3.82	4
Chromium (ppm)	1.85 ± 0.25	1.44–2.09	5
Cobalt (ppm)	0.681 ± 0.14	0.490–0.780	4

TABLE M4
Contaminant Levels in NIH-07 Rat and Mouse Ration

	Mean ± Standard Deviation[a]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.72 ± 0.21	0.18–1.07	26
Cadmium (ppm)	<0.10	–	26
Lead (ppm)	0.46 ± 0.28	0.05–1.32	26
Mercury (ppm)	<0.05	–	26
Selenium (ppm)	0.35 ± 0.08	0.17–0.48	26
Aflatoxins (ppb)	<5.0	–	26
Nitrate nitrogen (ppm)	17.69 ± 7.62	0.10–41.0	26
Nitrite nitrogen (ppm)	0.41 ± 0.71	0.10–2.60	26
BHA (ppm)[b]	2.54 ± 1.03	2.00–5.00	26
BHT (ppm)[b]	1.62 ± 0.98	1.00–4.00	26
Aerobic plate count (CFU/g)[c]	34,760 ± 40,712	770–130,000	26
Coliform (MPN/g)[d]	5.81 ± 7.95	3.00–43.0	26
E. coli (MPN/g)[e]	3.04 ± 0.20	3.00–4.00	26
Total nitrosamines (ppb)[f]	8.05 ± 3.29	3.80–16.00	26
N-Nitrosodimethylamine (ppb)[f]	6.87 ± 3.10	2.80–15.00	26
N-Nitrosopyrrolidine (ppb)[f]	1.18 ± 0.55	1.00–3.40	26
Pesticides (ppm)			
α-BHC[g]	<0.01		26
β-BHC	<0.02		26
γ-BHC	<0.01		26
δ-BHC	<0.01		26
Heptachlor	<0.01		26
Aldrin	<0.01		26
Heptachlor epoxide	<0.01		26
DDE	<0.01		26
DDD	<0.01		26
DDT	<0.01		26
HCB	<0.01		26
Mirex	<0.01		26
Methoxychlor	<0.05		26
Dieldrin	<0.01		26
Endrin	<0.01		26
Telodrin	<0.01		26
Chlordane	<0.05		26
Toxaphene	<0.1		26
Estimated PCBs	<0.2		26
Ronnel	<0.01		26
Ethion	<0.02		26
Trithion	<0.05		26
Diazinon	<0.1		26
Methyl parathion	<0.02		26
Ethyl parathion	<0.02		26
Malathion[h]	0.10 ± 0.13	0.05–0.69	26
Endosulfan I	<0.01		26
Endosulfan II	<0.01		26
Endosulfan sulfate	<0.03		26

[a] For values less than the limit of detection, the detection limit is given for the mean.
[b] Source of contamination: soy oil and fish meal
[c] CFU = colony forming unit
[d] MPN = most probable number
[e] One lot milled 17 October 1984 had a value of 4.0 MPN.
[f] All values were corrected for percent recovery.
[g] BHC = hexachlorocyclohexane or benzene hexachloride
[h] Nine lots contained more than 0.05 ppm.

TABLE M5
Water Analyses[a] Performed During the 2-Year Chlorinated and Chloraminated Water Studies

Analysis	Levels
pH	7.9
Hardness, as calcium carbonate	83.0 mg/L
Alkalinity, as calcium carbonate	
Total	35 mg/L
Free carbon dioxide	0.4 mg/L
Total iron	0.01 mg/L
Manganese	<0.001 mg/L
Nitrate nitrogen	0.10 mg/L
Chloride	4 mg/L
Sulfate	45 mg/L
Fluoride	1.46 mg/L
Calcium	23 mg/L
Magnesium	4 mg/L
Sodium	5 mg/L
Copper	<0.1 mg/L
Zinc	0.01 mg/L
Cadmium	<0.01 mg/L
Arsenic	<0.001 mg/L
Chromium	<0.001 mg/L
Mercury	<0.0001 mg/L
Lead	<0.001 mg/L
Barium	<0.01 mg/L
Selenium	<0.001 mg/L
Silver	<0.001 mg/L
Chlorine residual[b]	1.20 mg/L
Trihalomethane[c]	0.019 mg/L
Chlorinated hydrocarbons	
Endrin	<0.0001 μg/L
Lindane	<0.001 μg/L
Methoxychlor	<0.01 μg/L
Toxaphene	<0.001 μg/L
Chlorophenoxys	
2,4-D (2,4-Dichlorophenoxy acetic acid)	<0.01 μg/L
2,4,5-TP silvex	<0.001 μg/L
Bacteria count[b]	
Coliform	0/100 mL
Other	0/1 mL

[a] Analyses were performed on water collected 23 April 1984 by the Alabama Department of Environmental Management, Water Supply Division (Lab ID: 20024), Montgomery, AL. Source of raw water was Cahaba River and Lake Purdy; purification facility was Shades Mountain Filter Plant.
[b] Analyses were performed by Birmingham Water Works (Lab ID: 30010), Birmingham, AL.
[c] Sample taken on 23 April 1984 at the grocery store in Shannon, AL, and analyzed by the Alabama Department of Environmental Management (Lab No. 84-667).

TABLE M5
Water Analyses[a] Performed During the 2-Year Chlorinated and Chloraminated Water Studies
(continued)

Analysis	Levels
pH	8.4
Hardness, as calcium carbonate	74.0 mg/L
Alkalinity, as calcium carbonate	
Total	46 mg/L
Free carbon dioxide	<0.1 mg/L
Total iron	0.01 mg/L
Manganese	<0.001 mg/L
Nitrate nitrogen	0.40 mg/L
Chloride	4 mg/L
Sulfate	40 mg/L
Fluoride	0.92 mg/L
Calcium	146 mg/L
Magnesium	31 mg/L
Sodium	5 mg/L
Copper	<0.1 mg/L
Zinc	<0.01 mg/L
Cadmium	<0.01 mg/L
Arsenic	<0.001 mg/L
Chromium	<0.001 mg/L
Mercury	<0.0001 mg/L
Lead	<0.001 mg/L
Barium	<0.01 mg/L
Selenium	<0.001 mg/L
Silver	<0.001 mg/L
Chlorine residual[b]	1.20 mg/L
Trihalomethane[c]	0.049 mg/L
Chlorinated hydrocarbons	
Endrin	<0.0001 µg/L
Lindane	<0.001 µg/L
Methoxychlor	<0.01 µg/L
Toxaphene	<0.001 µg/L
Chlorophenoxys	
2,4-D (2,4-Dichlorophenoxy acetic acid)	<0.01 µg/L
2,4,5-TP silvex	<0.001 µg/L
Bacteria count[b]	
Coliform	0/100 mL
Other	0/1 mL

[a] Analyses were performed on water collected 4 March 1985 by the Alabama Department of Environmental Management, Water Supply Division (Lab ID: 20024), Montgomery, AL. Source of raw water was Cahaba River and Lake Purdy; purification facility was Shades Mountain Filter Plant.
[b] Analyses were performed by Birmingham Water Works (Lab ID: 30010), Birmingham, AL.
[c] Sample taken on 30 May 1985 at the grocery store in Shannon, AL, and analyzed by the Alabama Department of Environmental Management (Lab No. 85-672).

APPENDIX N
FEED CONSUMPTION BY RATS AND MICE IN THE 2-YEAR DRINKING WATER STUDIES

TABLE N1
Feed Consumption[a] by Male Rats in the 2-Year Chlorinated Water Study

Study Week	0 ppm	70 ppm	140 ppm	275 ppm
1-4	16.0	16.5	16.0	16.1
	15.7[b]	16.0	16.0	15.7
5-8	17.9	18.2	18.4	18.1
	19.3[b]	18.4	16.3	17.1
9-12	19.9	19.7	20.1	19.8
	19.5[b]	21.2	18.7	18.3
13-16	17.7	17.5	17.5	16.9
	16.2[b]	20.2	17.5	15.9
17-20	19.0	17.9	17.5	17.6
21-24	17.7	18.1	17.6	17.3
25-28	17.9	18.6	17.5	18.6
29-32	17.5	17.1	17.6	16.5
33-36	17.2	17.5	17.1	17.4
37-40	17.7	18.1	17.8	18.5
41-44	17.9	18.4	17.7	17.2
45-48	16.7	16.2	16.3	16.7
49-52	18.9	18.3	17.5	17.0
53-56	18.5	18.4	18.3	18.6
57-60	18.3	18.7	18.2	18.7
61-64	18.4	19.2	18.5	18.5
65-68	17.5	17.8	16.8	16.8
69-72	18.0	16.8	17.1	16.7
73-76	18.0	18.1	17.1	17.6
77-80	17.7	17.7	17.4	17.1
81-84	16.9	17.2	18.1	17.4
85-88	17.0	17.7	16.3	17.0
89-92	19.0	18.0	16.9	16.1
93-96	19.4	18.1	16.9	17.0
97-100	16.6	18.2	15.9	17.4
101-104	18.1	19.9	16.1	17.8
Mean for weeks				
1-52	18.0	18.7	17.1	16.9
53-104	17.9	18.0	17.5	17.5

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

TABLE N2
Feed Consumption[a] by Female Rats in the 2-Year Chlorinated Water Study

Study Week	0 ppm	70 ppm	140 ppm	275 ppm
1-4	12.5	12.9	12.5	12.2
	12.8[b]	13.0	13.7	12.6
5-8	11.5	11.2	11.4	11.1
	12.1[b]	11.3	11.2	12.0
9-12	11.3	11.4	11.4	11.2
	11.4[b]	11.8	11.4	11.3
13-16	11.1	10.7	11.1	10.8
17-20	11.3	11.1	11.1	11.1
21-24	11.0	11.0	11.2	10.8
25-28	11.2	11.4	11.8	11.1
29-32	11.2	10.9	11.2	10.8
33-36	11.5	11.7	11.6	10.9
37-40	11.1	11.2	11.3	11.1
41-44	11.9	11.7	11.6	11.5
45-48	12.2	11.8	11.9	11.4
49-52	11.9	11.7	11.9	12.0
53-56	13.4	12.4	13.1	11.9
57-60	12.5	12.6	12.3	12.1
61-64	13.1	12.1	12.5	12.6
65-68	12.7	13.0	12.6	12.2
69-72	13.3	13.2	12.9	12.4
73-76	13.9	13.3	14.0	12.6
77-80	13.4	13.4	13.1	12.7
81-84	13.3	13.8	13.6	13.1
85-88	14.2	13.4	13.1	12.4
89-92	12.8	12.6	12.6	12.0
93-96	14.1	13.7	14.1	12.6
97-100	14.3	13.6	12.8	13.1
101-104	12.8	12.3	13.8	12.3
Mean for weeks				
1-52	11.9	11.9	11.9	11.9
53-104	12.3	12.1	12.2	11.8

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

TABLE N3
Feed Consumption[a] by Male Rats in the 2-Year Chloraminated Water Study

Study Week	0 ppm	50 ppm	100 ppm	200 ppm
1-4	16.0	16.4	15.7	13.7
	15.7[b]	16.0	16.5	13.4
5-8	17.9	18.1	17.4	16.1
	19.3[b]	18.0	17.6	17.8
9-12	19.9	19.1	18.6	18.7
	19.5[b]	17.7	20.3	18.1
13-16	17.7	17.7	16.7	16.7
	16.2[b]	17.0	16.7	14.3
17-20	19.0	18.0	18.1	17.2
21-24	17.7	17.3	17.0	17.5
25-28	17.9	18.6	17.3	17.2
29-32	17.5	17.6	16.7	17.1
33-36	17.2	17.5	17.1	16.7
37-40	17.7	18.2	17.7	17.5
41-44	17.9	17.8	17.4	17.3
45-48	16.7	15.8	15.1	14.8
49-52	18.9	18.2	17.5	17.3
53-56	18.5	18.3	18.2	18.2
57-60	18.3	18.6	17.9	17.9
61-64	18.4	17.9	18.4	17.5
65-68	17.5	17.5	16.7	17.1
69-72	18.0	18.1	17.6	16.8
73-76	18.0	17.2	16.9	17.2
77-80	17.7	17.6	17.4	15.3
81-84	16.9	16.7	17.3	16.7
85-88	17.0	16.6	16.6	16.8
89-92	19.0	17.7	16.7	16.8
93-96	19.4	17.8	17.5	16.8
97-100	16.6	17.8	16.2	16.1
101-104	18.1	18.1	16.3	18.7
Mean for weeks				
1-52	18.0	17.2	18.0	16.2
53-104	17.9	17.7	17.2	16.9

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

TABLE N4
Feed Consumption[a] by Female Rats in the 2-Year Chloraminated Water Study

Study Week	0 ppm	50 ppm	100 ppm	200 ppm
1-4	12.5	12.7	12.1	12.2
	12.8[b]	12.2	13.7	12.8
5-8	11.5	11.4	11.3	11.2
	12.1[b]	11.8	11.7	11.7
9-12	11.3	11.5	11.4	10.9
	11.4[b]	11.2	11.3	11.0
13-16	11.1	11.3	10.8	10.4
17-20	11.3	11.5	11.0	11.0
21-24	11.0	11.0	10.9	10.6
25-28	11.2	11.3	11.1	10.9
29-32	11.2	11.0	10.4	10.8
33-36	11.5	11.5	11.6	11.1
37-40	11.1	11.2	11.2	11.5
41-44	11.9	11.6	11.5	11.4
45-48	12.2	12.0	11.9	11.4
49-52	11.9	12.1	12.0	11.8
53-56	13.4	12.3	12.6	12.1
57-60	12.5	12.7	12.3	12.0
61-64	13.1	12.6	12.7	11.3
65-68	12.7	13.2	12.5	12.0
69-72	13.3	12.9	14.0	12.1
73-76	13.9	13.0	13.1	12.1
77-80	13.4	12.5	13.0	12.8
81-84	13.3	13.3	12.7	11.9
85-88	14.2	13.7	12.8	11.8
89-92	12.8	11.3	12.7	11.4
93-96	14.1	13.0	13.9	14.2
97-100	14.3	13.2	14.0	12.2
101-104	12.8	12.9	11.4	11.6
Mean for weeks				
1-52	11.9	11.7	12.1	11.7
53-104	12.3	12.1	12.0	11.6

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

TABLE N5
Feed Consumption[a] by Male Mice in the 2-Year Chlorinated Water Study

Study Week	0 ppm	70 ppm	140 ppm	275 ppm
1-4	5.0	5.0	5.1	5.1
	4.5[b]	4.8	4.4	4.8
5-8	4.7	4.8	4.9	4.8
	4.7[b]	4.8	5.6	5.4
9-12	4.8	5.0	4.8	5.0
	5.0[b]	5.1	5.1	5.0
13-16	5.3	5.3	5.2	5.3
	4.5[b]	5.4	4.9	5.5
17-20	4.8	4.7	4.8	4.8
21-24	5.8	5.9	5.7	5.7
25-28	5.3	5.4	5.4	5.2
29-32	5.1	4.9	5.1	5.0
33-36	5.0	5.1	5.1	4.9
37-40	5.5	5.7	5.5	6.1
41-44	5.3	5.3	5.2	5.2
45-48	5.3	5.3	5.2	5.2
49-52	5.4	5.4	5.4	5.3
53-56	5.1	5.3	5.2	5.3
57-60	5.2	5.2	5.2	5.0
61-64	5.4	5.7	5.4	5.3
65-68	5.2	5.5	5.3	5.4
69-72	5.6	5.7	5.7	5.8
73-76	5.5	5.7	5.5	5.5
77-80	5.4	5.5	5.4	5.4
81-84	5.5	5.5	5.5	5.5
85-88	5.5	5.7	5.7	5.7
89-92	5.5	5.4	5.5	5.4
93-96	5.4	5.5	5.7	5.6
97-100	5.6	5.6	5.6	5.3
101-104	5.6	5.5	5.6	5.2
Mean for weeks				
1-52	4.7	5.0	4.9	5.1
53-104	5.3	5.4	5.3	5.3

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

TABLE N6
Feed Consumption[a] by Female Mice in the 2-Year Chlorinated Water Study

Study Week	0 ppm	70 ppm	140 ppm	275 ppm
1-4	4.4	4.5	4.2	4.7
	4.4[b]	4.2	4.7	4.1
5-8	4.6	4.6	4.4	4.6
	4.6[b]	4.7	4.4	4.2
9-12	4.5	4.6	4.5	4.5
	4.6[b]	4.5	4.3	4.2
13-16	5.1	5.0	4.8	5.0
	5.2[b]	5.1	4.6	4.4
17-20	4.9	4.8	4.7	4.8
21-24	5.2	5.3	5.4	5.1
25-28	5.6	5.3	5.3	5.4
29-32	5.0	5.2	5.1	5.1
33-36	5.2	5.3	5.1	5.0
37-40	5.0	5.2	4.9	4.8
41-44	5.5	5.3	5.3	5.3
45-48	5.2	5.1	5.1	5.0
49-52	5.4	5.4	5.2	5.4
53-56	5.8	5.7	5.6	5.4
57-60	5.3	5.5	5.4	5.2
61-64	5.6	5.4	5.4	5.5
65-68	5.6	5.5	5.5	5.7
69-72	6.0	6.0	5.8	6.0
73-76	5.6	5.6	5.8	5.4
77-80	6.1	5.9	5.8	5.9
81-84	6.1	5.7	5.9	6.0
85-88	6.2	5.9	6.0	6.0
89-92	6.0	5.8	5.8	5.8
93-96	6.4	6.1	6.4	6.3
97-100	5.8	5.6	5.7	5.8
101-104	5.9	5.8	5.6	5.8
Mean for weeks				
1-52	4.6	4.5	4.5	4.2
53-104	5.4	5.3	5.3	5.3

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

TABLE N7
Feed Consumption[a] by Male Mice in the 2-Year Chloraminated Water Study

Study Week	0 ppm	50 ppm	100 ppm	200 ppm
1-4	5.0	4.8	5.1	4.5
	4.5[b]	5.4	4.9	4.6
5-8	4.7	4.8	4.9	4.9
	4.7[b]	5.8	4.7	4.8
9-12	4.8	4.8	4.8	4.6
	5.0[b]	4.8	5.5	4.3
13-16	5.3	5.2	5.3	4.7
	4.5[b]	5.1	4.6	4.9
17-20	4.8	4.8	4.6	4.6
21-24	5.8	6.1	5.6	5.7
25-28	5.3	5.4	5.3	5.1
29-32	5.1	5.0	4.9	4.6
33-36	5.0	5.0	4.9	4.7
37-40	5.5	5.6	5.7	5.4
41-44	5.3	5.2	5.1	4.8
45-48	5.3	5.2	5.2	4.9
49-52	5.4	5.2	5.3	5.0
53-56	5.1	5.1	5.1	4.9
57-60	5.2	5.1	5.1	4.8
61-64	5.4	5.3	5.4	5.0
65-68	5.2	5.4	5.3	5.2
69-72	5.6	5.5	5.5	5.3
73-76	5.5	5.3	5.2	5.1
77-80	5.4	5.3	5.3	5.3
81-84	5.5	5.5	5.4	5.0
85-88	5.5	5.7	5.5	5.2
89-92	5.5	5.5	5.4	5.1
93-96	5.4	5.6	5.3	5.0
97-100	5.6	5.5	5.4	5.1
101-104	5.6	5.4	5.3	4.8
Mean for weeks				
1-52	4.7	5.2	5.0	4.6
53-104	5.3	5.3	5.2	5.0

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

TABLE N8
Feed Consumption[a] by Female Mice in the 2-Year Chloraminated Water Study

Study Week	0 ppm	50 ppm	100 ppm	200 ppm
1-4	4.4	4.5	4.4	4.0
	4.4[b]	5.0	4.2	4.2
5-8	4.6	4.5	4.4	4.4
	4.6[b]	4.7	4.7	4.2
9-12	4.5	4.4	4.4	4.1
	4.6[b]	4.6	4.6	4.1
13-16	5.1	5.0	4.8	4.5
	5.2[b]	4.8	4.5	4.3
17-20	4.9	4.7	4.8	4.4
21-24	5.2	5.3	5.5	4.8
25-28	5.6	5.3	5.3	5.1
29-32	5.0	4.9	4.9	4.7
33-36	5.2	5.1	5.0	4.6
37-40	5.0	5.1	5.0	4.7
41-44	5.5	5.2	5.2	4.7
45-48	5.2	5.1	4.9	4.5
49-52	5.4	5.2	5.2	4.8
53-56	5.8	5.5	5.4	5.2
57-60	5.3	5.2	5.0	4.6
61-64	5.6	5.3	5.2	4.9
65-68	5.6	5.6	5.3	4.9
69-72	6.0	5.8	5.5	5.1
73-76	5.6	5.5	5.4	4.9
77-80	6.1	5.6	5.3	5.0
81-84	6.1	5.8	5.5	5.1
85-88	6.2	5.7	5.6	5.2
89-92	6.0	5.7	5.4	5.2
93-96	6.4	6.1	5.5	5.2
97-100	5.8	5.8	5.3	4.7
101-104	5.9	5.7	5.2	4.5
Mean for weeks				
1-52	4.6	4.7	4.5	4.2
53-104	5.4	5.2	5.1	4.7

[a] Feed consumption is given in grams per animal day for the given time period.
[b] Interim evaluation animals

APPENDIX O
SENTINEL ANIMAL PROGRAM

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 are untreated and are subject to environmental conditions identical to the study animals. The sentinel animals come from the same production source and weanling groups as the animals used for the studies of chemical compounds.

Because of the large number of animals needed for these studies and because of restrictions on animal availability, each study was conducted in two parts, separated by an interval of 2 weeks. The group of animals used in each half of the studies were housed in separate rooms. Upon arrival, 5 male and 5 female rats and 5 male and 5 female mice in each room were sacrificed for the evaluation of the health status of the animals. In addition, special health checks were conducted on 5 males and 5 females in each room. The health checks indicated that no ectoparasites or endoparasites were present; however, gross abnormalities were found in several of the rats and in one mouse. Only animals with a generally healthy appearance were used in the studies.

Fifteen F344/N rats of each sex per room were selected at the time of randomization and allocation of the animals to the various study groups to serve as sentinel animals. Similarly, 15 B6C3F$_1$ mice of each sex per room were designated as sentinel animals. Five animals of each designated sentinel group were killed at 6, 12, and 18 months on study. Blood processed from rats during the 14- and 66-week interim evaluations was also used for serological screening. Data from animals surviving 24 months were collected from 5/50 randomly selected control animals of each sex. The blood from each animal was collected and clotted, and the serum was separated. The serum was cooled on ice and shipped to Microbiological Associates' Comprehensive Animal Diagnostic Service for determination of the antibody titers. The following tests were performed:

RATS

Test	Time of Analysis
ELISA	
RCV/SDA (sialodacryoadenitis virus)	0, 3, 6, 12, 15, 18, and 24 months
PVM (pneumonia virus of mice)	0, 3, 6, 12, 15, 18, and 24 months
Sendai virus	0, 3, 6, 12, 15, 18, and 24 months
Mycoplasma pulmonis	0, 3, 6, 12, 15, 18, and 24 months
Mycoplasma arthriditis	0, 3, 6, 12, 15, 18, and 24 months
CARB (cilia-associated respiratory bacillus)	18 months
Hemagglutination Inhibition	
KRV (Kilham rat virus)	0, 3, 6, 12, 15, 18, and 24 months
H-1 (Toolan's H-1 virus)	0, 3, 6, 12, 15, 18, and 24 months

MICE

Test	Time of Analysis
Complement Fixation	
LCM (lymphocytic choriomeningitis virus)	6, 12, and 18 months
ELISA	
Reovirus type 3	6, 12, 18, and 24 months
M. Ad. (mouse adenoma virus)	6, 12, 18, and 24 months
Mycoplasma pulmonis	6, 12, 18, and 24 months
Mycoplasma arthritidis	6, 12, 18, and 24 months
PVM (pneumonia virus of mice)	6, 12, 18, and 24 months
Sendai virus	6, 12, 18, and 24 months
MHV (mouse hepatitis virus)	6, 12, 18, and 24 months
Ectromelia virus	6, 12, 18, and 24 months
GDVII (mouse encephalomyelitis virus)	6, 12, 18, and 24 months
Hemagglutination Inhibition	
K (papovavirus)	6, 12, 18, and 24 months
Polyoma virus	6, 12, 18, and 24 months
MVM (minute virus of mice)	6, 12, 18, and 24 months
Immunofluorescence Assay	
PVM	12 months
EDIM (Epizootic diarrhea of infant mice)	6, 12, 18, and 24 months
LCM	24 months

RESULTS

The serology results for sentinel animals are presented in Table O1.

TABLE O1
Murine Virus Antibody Determinations for Rats and Mice in the 2-Year Chlorinated and Chloraminated Water Studies

	Interval (months)	Number of Animals	Positive Serologic Reaction for
Rats			
	0	0/20	-
	2	0/1[a]	-
	3[b]	0/140	-
	6	2/20	KRV
		2/20	H-1
	12	1/20	*M. arthritidis*[c]
	15[d]	0/129	-
	18	2/20	*M. arthritidis*[c]
	24	2/18	*M. arthritidis*[c]
Mice			
	6	0/16	-
	12	2/18	PVM[e]
	18	0/19	-
	24	0/19	-

[a] Rat FM-745.
[b] 14-week interim evaluation.
[c] These results possibly represented reactivity of the serum with an antigen cross reactive to *M. arthritidis*. These results may be considered false positive.
[d] 66-week interim evaluation.
[e] Sera from both of these mice reacted with control antigen in the IFA tests for both PVM and EDIM. These results may be considered false positive.

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TR No.	CHEMICAL
201	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Dermal)
206	1,2-Dibromo-3-chloropropane
207	Cytembena
208	FD & C Yellow No. 6
209	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Gavage)
210	1,2-Dibromoethane
211	C.I. Acid Orange 10
212	Di(2-ethylhexyl)adipate
213	Butyl Benzyl Phthalate
214	Caprolactam
215	Bisphenol A
216	11-Aminoundecanoic Acid
217	Di(2-ethylhexyl)phthalate
219	2,6-Dichloro-p-phenylenediamine
220	C.I. Acid Red 14
221	Locust Bean Gum
222	C.I. Disperse Yellow 3
223	Eugenol
224	Tara Gum
225	D & C Red No. 9
226	C.I. Solvent Yellow 14
227	Gum Arabic
228	Vinylidene Chloride
229	Guar Gum
230	Agar
231	Stannous Chloride
232	Pentachloroethane
233	2-Biphenylamine Hydrochloride
234	Allyl Isothiocyanate
235	Zearalenone
236	*D*-Mannitol
237	1,1,1,2-Tetrachloroethane
238	Ziram
239	Bis(2-chloro-1-methylethyl)ether
240	Propyl Gallate
242	Diallyl Phthalate (Mice)
243	Trichloroethylene (Rats and Mice)
244	Polybrominated Biphenyl Mixture
245	Melamine
246	Chrysotile Asbestos (Hamsters)
247	L-Ascorbic Acid
248	4,4'-Methylenedianiline Dihydrochloride
249	Amosite Asbestos (Hamsters)
250	Benzyl Acetate
251	2,4- & 2,6-Toluene Diisocyanate
252	Geranyl Acetate
253	Allyl Isovalerate
254	Dichloromethane (Methylene Chloride)
255	1,2-Dichlorobenzene
257	Diglycidyl Resorcinol Ether
259	Ethyl Acrylate
261	Chlorobenzene
263	1,2-Dichloropropane
266	Monuron
267	1,2-Propylene Oxide
269	Telone II® (1,3-Dichloropropene)
271	HC Blue No. 1
272	Propylene
273	Trichloroethylene (Four Rat Strains)
274	Tris(2-ethylhexyl)phosphate
275	2-Chloroethanol
276	8-Hydroxyquinoline
277	Tremolite
278	2,6-Xylidine
279	Amosite Asbestos
280	Crocidolite Asbestos
281	HC Red No. 3
282	Chlorodibromomethane
284	Diallylphthalate (Rats)
285	C.I. Basic Red 9 Monohydrochloride
287	Dimethyl Hydrogen Phosphite
288	1,3-Butadiene
289	Benzene
291	Isophorone
293	HC Blue No. 2
294	Chlorinated Trisodium Phosphate
295	Chrysotile Asbestos (Rats)
296	Tetrakis(hydroxymethyl) phosphonium Sulfate & Tetrakis(hydroxymethyl) phosphonium Chloride
298	Dimethyl Morpholinophosphoramidate
299	C.I. Disperse Blue 1
300	3-Chloro-2-methylpropene
301	*o*-Phenylphenol
303	4-Vinylcyclohexene
304	Chlorendic Acid
305	Chlorinated Paraffins (C_{23}, 43% chlorine)
306	Dichloromethane (Methylene Chloride)
307	Ephedrine Sulfate
308	Chlorinated Paraffins (C_{12}, 60% chlorine)
309	Decabromodiphenyl Oxide
310	Marine Diesel Fuel and JP-5 Navy Fuel
311	Tetrachloroethylene (Inhalation)
312	*n*-Butyl Chloride
313	Mirex
314	Methyl Methacrylate
315	Oxytetracycline Hydrochloride
316	1-Chloro-2-methylpropene
317	Chlorpheniramine Maleate
318	Ampicillin Trihydrate
319	1,4-Dichlorobenzene
320	Rotenone
321	Bromodichloromethane
322	Phenylephrine Hydrochloride
323	Dimethyl Methylphosphonate
324	Boric Acid
325	Pentachloronitrobenzene
326	Ethylene Oxide
327	Xylenes (Mixed)
328	Methyl Carbamate
329	1,2-Epoxybutane
330	4-Hexylresorcinol
331	Malonaldehyde, Sodium Salt
332	2-Mercaptobenzothiazole
333	*N*-Phenyl-2-naphthylamine
334	2-Amino-5-nitrophenol
335	C.I. Acid Orange 3
336	Penicillin VK
337	Nitrofurazone

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338	Erythromycin Stearate
339	2-Amino-4-nitrophenol
340	Iodinated Glycerol
341	Nitrofurantoin
342	Dichlorvos
343	Benzyl Alcohol
344	Tetracycline Hydrochloride
345	Roxarsone
346	Chloroethane
347	D-Limonene
348	*a*-Methyldopa Sesquihydrate
349	Pentachlorophenol
350	Tribromomethane
351	*p*-Chloroaniline Hydrochloride
352	N-Methylolacrylamide
353	2,4-Dichlorophenol
354	Dimethoxane
355	Diphenhydramine Hydrochloride
356	Furosemide
357	Hydrochlorothiazide
358	Ochratoxin A
359	8-Methoxypsoralen
360	N,N-Dimethylaniline
361	Hexachloroethane
362	4-Vinyl-1-Cyclohexene Diepoxide
363	Bromoethane (Ethyl Bromide)
364	Rhodamine 6G (C.I. Basic Red 1)
365	Pentaerythritol Tetranitrate
366	Hydroquinone
367	Phenylbutazone
368	Nalidixic Acid
369	Alpha-Methylbenzyl Alcohol
370	Benzofuran
371	Toluene
372	3,3'-Dimethoxybenzidine Dihydrochloride
373	Succinic Anhydride
374	Glycidol
375	Vinyl Toluene
376	Allyl Glycidyl Ether
377	*o*-Chlorobenzalmalononitrile
378	Benzaldehyde
379	2-Chloroacetophenone
380	Epinephrine Hydrochloride
381	*d*-Carvone
382	Furfural
386	Tetranitromethane
387	Amphetamine Sulfate
389	Sodium Azide
390	3,3'-Dimethylbenzidine Dihydrochloride
391	Tris(2-chloroethyl) Phosphate
393	Sodium Fluoride
395	Probenecid
396	Monochloroacetic Acid
399	Titanocene Dichloride
405	C.I. Acid Red 114
415	Polysorbate 80

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