NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES OF SODIUM CHLORATE

(CAS NO. 7775-09-9)

IN F344/N RATS AND B6C3F$_1$ MICE

(DRINKING WATER STUDIES)

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

December 2005

NTP TR 517

NIH Publication No. 06-4457

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

FOREWORD

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

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

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

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

Details about ongoing and completed NTP studies, abstracts of all NTP Technical Reports, and full versions of the completed reports are available at the NTP's World Wide Web site: http://ntp.niehs.nih.gov. In addition, printed copies of these reports are available from NTP as supplies last by contacting (919) 541-3419.

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SUMMARY

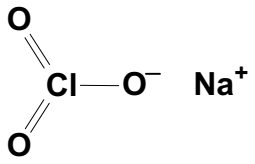
Background
Sodium chlorate occurs when drinking water is disinfected by chlorine dioxide. We studied the effects of sodium chlorate in rats and mice to identify potential toxic or carcinogenic hazards to humans.

Methods
We gave groups of male and female rats drinking water containing 125, 1,000, or 2,000 milligrams (mg) of sodium chlorate per liter (L) of water for two years. Male and female mice received 500, 1,000, or 2,000 mg/L. Other groups of animals received plain tap water and served as the control groups. At the end of the study, tissues from more than 40 sites were examined for every animal.

Results
Male and female rats receiving sodium chlorate had higher rates of follicular cell hypertrophy of the thyroid gland, and the groups receiving 2,000 mg/L had higher rates of thyroid gland cancer, compared with the control groups. Female mice exposed to sodium chlorate had a few pancreatic islet cell tumors.

Conclusions
We conclude that sodium chlorate caused some thyroid gland neoplasms in male and female rats. The pancreatic islet cell tumors in female mice may have been related to sodium chlorate exposure.

ABSTRACT



SODIUM CHLORATE

CAS No. 7775-09-9

Chemical Formula: $NaClO_3$ Molecular Weight: 106.44

Synonyms: Chlorate of soda; chloric acid, sodium salt; soda chlorate
Trade names: Atlacide, Chlorax, Defol, De-Fol-Ate, Dervan, Drop-Leaf, Fall, Harvest-Aid, Kusatol, Leafex, Shed-A-Leaf 'L', Tumbleaf

Sodium chlorate is used as an oxidizing agent and bleach for paper pulp; to make chlorine dioxide used in water disinfection; in ore processing; in the manufacture of matches and explosives; in dye making and the printing and dyeing of fabrics; in leather finishing and tanning; to make perchlorates; in toothpaste and mouthwash; and as a nonselective herbicide, defoliant, and harvest aid. Chlorate is found as a stable by-product in drinking water that has been disinfected with chlorine dioxide. Sodium chlorate was nominated for study by the United States Environmental Protection Agency because of widespread consumer exposure to treated drinking water and lack of carcinogenicity data. Male and female F344/N rats and B6C3F_1 mice were exposed to sodium chlorate (at least 99% pure) in drinking water for 3 weeks and 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium* and mouse peripheral blood erythrocytes.

3-Week Study in Rats

Groups of 10 male and 10 female rats were exposed to drinking water containing 0, 125, 250, 500, 1,000, or 2,000 mg/L sodium chlorate for 3 weeks (equivalent to average daily doses of approximately 20, 35, 75, 170, and 300 mg sodium chlorate/kg body weight per day for males and 20, 40, 75, 150, and 340 mg/kg per day for females). All rats survived to the end of the study. Mean body weights of exposed groups were similar to those of control groups. Water consumption by exposed rats was generally similar to that by control groups throughout the study. An exposure concentration-related decrease in segmented neutrophil counts occurred in male and female rats on days 4 and 22. Heart weights were significantly decreased in 2,000 mg/L males. The incidences of minimal to mild thyroid gland follicular cell hypertrophy were significantly increased in males and females exposed to 500 mg/L or greater.

3-Week Study in Mice

Groups of 10 male and 10 female mice were exposed to drinking water containing 0, 125, 250, 500, 1,000, or 2,000 mg/L sodium chlorate for 3 weeks (equivalent to average daily doses of approximately 20, 45, 90, 175, and 350 mg/kg per day for male mice and 20, 45, 95,

190, and 365 mg/kg per day for female mice). All mice survived to the end of the study. Mean body weights of exposed groups were generally similar to those of control groups. Water consumption by exposed mice was generally similar to that by control groups throughout the study. No exposure-related lesions occurred in male or female mice.

2-Year Study in Rats

Groups of 50 male and 50 female rats were exposed to drinking water containing 0, 125, 1,000, or 2,000 mg/L sodium chlorate for 2 years (equivalent to average daily doses of approximately 5, 35, and 75 mg/kg per day for male rats and 5, 45, and 95 mg/kg per day for female rats). Survival of exposed rats was similar to that of the control groups. Mean body weights of all exposed groups were similar to those of the control groups throughout the study. Water consumption by exposed rats was generally similar to that by controls throughout the study.

Serum concentrations of thyroxine and triiodothyronine were significantly reduced in 1,000 and 2,000 mg/L males and females on day 4 and in 2,000 mg/L males and females at week 3. Serum concentrations of thyroid stimulating hormone were significantly increased in 1,000 and 2,000 mg/L males on day 4 and at week 3, in 1,000 and 2,000 mg/L females on day 4, in 2,000 mg/L females at week 3, and in 2,000 mg/L males and females at week 14.

All special study rats in the 1,000 and 2,000 mg/L groups had thyroid gland follicular cell hypertrophy at 3 and 14 weeks. There were positive trends in the incidences of thyroid gland follicular cell carcinoma in male rats and of thyroid gland follicular cell adenoma or carcinoma (combined) in males and females. The incidences of thyroid gland follicular cell hypertrophy were significantly increased in all exposed groups of males and in 1,000 and 2,000 mg/L females. Thyroid gland focal follicle mineralization occurred in most 1,000 and 2,000 mg/L female rats. The incidences of hematopoietic cell proliferation in the spleen of 2,000 mg/L males and bone marrow hyperplasia in 1,000 and 2,000 mg/L males were significantly greater than those in the controls.

2-Year Study in Mice

Groups of 50 male and 50 female mice were exposed to drinking water containing 0, 500, 1,000, or 2,000 mg/L sodium chlorate for 2 years (equivalent to average daily doses of approximately 40, 80, and 160 mg/kg per day for male mice and 30, 60, and 120 mg/kg per day for female mice). Survival of exposed mice was similar to that of the control groups. Mean body weights of exposed females were generally less than those of the control groups after week 84 of the study. Water consumption by exposed mice was generally similar to that by controls throughout the study.

There was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) in female mice. Thyroid gland follicular cell hypertrophy was significantly increased in 2,000 mg/L females. The incidences of bone marrow hyperplasia were significantly increased in all exposed groups of females.

Genetic Toxicology

Sodium chlorate was not mutagenic in *Salmonella typhimurium* strains TA97, TA98, TA100, TA102, TA104, or TA1535; all tests were conducted with and without exogenous metabolic activation (induced rat or hamster liver S9 enzymes). *In vivo*, no increases in the frequencies of micronucleated normochromatic erythrocytes were seen in peripheral blood samples from male and female B6C3F$_1$ mice exposed to sodium chlorate in drinking water for 3 weeks.

Conclusions

Under the conditions of this 2-year drinking water study, there was *some evidence of carcinogenic activity** of sodium chlorate in male and female F344/N rats based on increased incidences of thyroid gland neoplasms. There was *no evidence of carcinogenic activity* of sodium chlorate in male B6C3F$_1$ mice exposed to 500, 1,000, or 2,000 mg/L. There was *equivocal evidence of carcinogenic activity* of sodium chlorate in female B6C3F$_1$ mice based on marginally increased incidences of pancreatic islet neoplasms.

Exposure to sodium chlorate resulted in nonneoplastic lesions in the thyroid gland of male and female rats and female mice, bone marrow of male rats and female mice, and spleen of male rats.

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

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Sodium Chlorate

	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Concentrations in drinking water	0, 125, 1,000 or 2,000 mg/L	0, 125, 1,000 or 2,000 mg/L	0, 500, 1,000, or 2,000 mg/L	0, 500, 1,000, or 2,000 mg/L
Body weights	Exposed groups similar to the control group	Exposed groups similar to the control group	Exposed groups similar to the control group	Exposed groups less than the control group
Survival rates	36/50, 27/50, 31/50, 28/50	37/50, 36/50, 33/50, 41/50	38/50, 41/50, 41/50, 33/50	36/49, 35/50, 31/49, 35/50
Nonneoplastic effects	Thyroid gland: follicular cell hypertrophy (4/47, 13/44, 33/43, 40/47) Spleen: hematopoietic cell proliferation (2/48, 6/49, 4/49, 11/50) Bone marrow: hyperplasia (28/48, 35/48, 41/50, 40/49)	Thyroid gland: follicular cell hypertrophy (3/47, 7/47, 27/43, 42/46); follicular cell mineralization (25/47, 26/47, 40/43, 44/46)	None	Thyroid gland: follicular cell hypertrophy (3/48, 2/50, 5/49, 14/50) Bone marrow: hyperplasia (14/50, 28/50, 29/50, 31/50)
Neoplastic effects	Thyroid gland: follicular cell carcinoma (0/47, 0/44, 0/43, 4/47); follicular cell adenoma or carcinoma (1/47, 0/44, 0/43, 6/47)	Thyroid gland: follicular cell adenoma or carcinoma (1/47, 0/47, 1/43, 4/46)	None	None
Equivocal findings	None	None	None	Pancreatic islets: adenoma or carcinoma (0/46, 2/47, 2/49, 4/49)
Level of evidence of carcinogenic activity	Some evidence	Some evidence	No evidence	Equivocal evidence
Genetic toxicology				
Salmonella typhimurium gene mutations:	Negative in strains TA97, TA98, TA100, TA102, TA104, and TA1535 with and without S9			
Micronucleated erythrocytes Mouse peripheral blood *in vivo*:	Negative in male and female mice			

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

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

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

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

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

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

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

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS
TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the draft NTP Technical Report on sodium chlorate on December 9, 2004, are listed below. Subcommittee members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, subcommittee members have five major responsibilities in reviewing the NTP studies:

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

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SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On December 9, 2004, the draft Technical Report on the toxicology and carcinogenesis studies of sodium chlorate received public review by the National Toxicology Program's Board of Scientific Counselors' Technical Reports Review Subcommittee. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. M.J. Hooth, NIEHS, introduced the toxicology and carcinogenesis studies of sodium chlorate by describing its use as a bleach and occurrence after water disinfection, the design of the drinking water studies, and the toxic and neoplastic responses in the study animals. The proposed conclusions were *some evidence of carcinogenic activity* of sodium chlorate in male and female F344/N rats, *no evidence of carcinogenic activity* of sodium chlorate in male $B6C3F_1$ mice, and *equivocal evidence of carcinogenic activity* of sodium chlorate in female $B6C3F_1$ mice.

Dr. Birt, the first principal reviewer, thought the study was designed and reported well, and she agreed with the proposed conclusions.

Dr. Gasiewicz, the second principal reviewer, agreed with most of the proposed conclusions but thought the pancreatic islet neoplasms merited a conclusion of *some evidence* rather than *equivocal evidence*.

Dr. Vore, the third principal reviewer, agreed with the proposed conclusions and inquired about the presence of chlorate in the tap water.

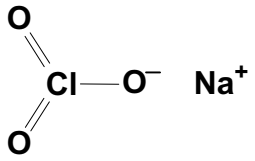
Dr. Hooth replied that no chlorate was found above the level of detection (0.11 parts per million) in any of the water samples assayed. She explained that the pancreatic islet neoplasms were considered *equivocal evidence* because they were seen only in one sex of one species, and the decreased incidences of hyperplasia were not supportive of an effect. She noted that the NTP had never made a call of carcinogenicity in mice based on pancreatic islet neoplasms.

Dr. C. Capen, representing EKA Chemical Company, spoke about the perturbation of thyroid hormone economy by sodium chlorate above a certain threshold as a possible link to the genesis of the observed thyroid gland neoplasms.

Dr. Birt moved and Dr. Vore seconded that the proposed conclusions be accepted as written. The motion was carried unanimously with nine votes.

Dr. W.T. Allaben, NCTR, asked if the concept of a threshold effect in the thyroid gland would be added to the discussion. Drs. Birt and Gasiewicz replied that this was a hypothesis that required more testing, and they did not feel the data yet supported their inclusion in the discussion.

INTRODUCTION



SODIUM CHLORATE

CAS No. 7775-09-9

Chemical Formula: $NaClO_3$ Molecular Weight: 106.44

Synonyms: Chlorate of soda; chloric acid, sodium salt; soda chlorate
Trade names: Atlacide, Chlorax, Defol, De-Fol-Ate, Dervan, Drop-Leaf, Fall, Harvest-Aid, Kusatol, Leafex, Shed-A-Leaf 'L', Tumbleaf

CHEMICAL AND PHYSICAL PROPERTIES

Sodium chlorate occurs as colorless, odorless crystals or white granules with a salty taste (*Merck Index*, 1996; HSDB, 2003). It has a melting point of 248° C, a boiling point of 300° C, and a density of 2.49 g/mL. It is soluble in water, liquid ammonia, glycerin, and alcohol (*Merck Index*, 1996; HSDB, 2003). Sodium chlorate decomposes on heating above 300° C, producing oxygen and chlorine. It is a strong oxidant and reacts with combustible, reducing, and organic materials, causing fire and explosion hazards.

PRODUCTION, USE, AND HUMAN EXPOSURE

Sodium chlorate is manufactured from sodium chloride by electrolysis (HSDB, 2003). The production capacities of the United States and Canada in 1999 were 946,000 and 1,193,000 short tons per year, respectively (Chemical Market Reporter, 1999). The demand for sodium chlorate from the United States and Canada was 1.75 million tons in 1997 and 1.85 million tons in 1998 and was estimated to be 2.35 million tons in 2002 (Chemical Market Reporter, 1999). United States production for 1991 was 639,000 metric tons; imports and exports in 1984 equaled 124,000 and 1,720 metric tons, respectively (HSDB, 2003). Between the years 1983 and 1990, the commercial use of sodium chlorate in North America was estimated to be 565,000 to 967,000 tons per year (Mendiratta and Duncan, 1993), and 28,583 workers were estimated to have been occupationally exposed in 1983 (Perry *et al.*, 1994).

Sodium chlorate is used as an oxidizing agent and bleach for paper pulp, to make chlorine dioxide used in water disinfection, in ore processing (especially uranium ore), in the manufacture of matches and explosives, in dye making and the printing and dyeing of fabrics, in leather finishing and tanning, to make perchlorates, and in toothpaste and mouthwash (*Merck Index*, 1996; HSDB, 2003). The consumption pattern for sodium chlorate in the United States in the 1990s indicated 95% was used for wood pulp bleaching in the paper industry; 3% for

the production of other chlorates, perchlorates, and chlorites; and 2% for other uses, including herbicides, water treatment, and uranium mining (HSDB, 2003).

Sodium chlorate has been widely used as a nonselective herbicide, defoliant, and harvest aid (Sheahan *et al.*, 1971; Perry *et al.*, 1994; HSDB, 2003). It is considered phytotoxic to all green plant parts and can kill through root absorption. Sodium chlorate may be used to control morning glory, Canada thistle, Johnson grass, and St. John's wort (EXTOXNET, 1995). It is used as a total weed control on noncrop land where it is applied at up to 600 kg/hectare (HSDB, 2003). Sodium chlorate is also used as a defoliant and desiccant for cotton, safflower, corn, flax, peppers, soybeans, grain sorghum, southern peas, dry beans, rice, and sunflowers. Sodium chlorate may be used in combination with other herbicides, including atrazine, 2,4-D, bromacil, diuron, and sodium metaborate (EXTOXNET, 1995; HSDB, 2003). The total estimated annual agricultural use of sodium chlorate in the United States in 1992 for eight crops was over 5,200,000 pounds applied. Use of sodium chlorate on crops of cotton and dry beans accounted for greater than 98% of the national agricultural use (USGS, 1992).

Chlorate is also found as a stable by-product in drinking water that has been disinfected with chlorine dioxide (Condie, 1986; Pfaff and Brockhoff, 1990; Singer, 1993). Chlorine dioxide is more effective than chlorine for killing most microorganisms, produces fewer chlorinated by-products, and does not produce significant levels of trihalomethanes (Richardson, 1998). Chlorate may be formed by inefficient chlorine dioxide generation, if the pH of the reaction mixture has not been adjusted properly, or as a result of the reaction between residual chlorite in finished water and free chlorine in the distribution system (Singer, 1993; Gallagher *et al.*, 1994). In addition, chlorine dioxide disproportionates to form chlorite and chlorate in alkaline solutions and decomposes to form chlorate in acidic solutions with exposure to sunlight (Condie, 1986).

In the United States, between 500 and 900 drinking water treatment facilities used chlorine dioxide either seasonally or year-round, and as many as 25 million people may be drinking water treated with chlorine dioxide (Gallagher *et al.*, 1994). Laboratory studies estimate that 10% to 30% of the chlorine dioxide added to water is converted to chlorate (Moore *et al.*, 1978; Michael *et al.*, 1981). For water treatment plants using chlorine dioxide, chlorate concentrations in four treated water samples ranged from 21 to 330 µg/L, with a mean of 200 µg/L (USEPA, 1994). Evaluation of a United States public water supply, which was disinfected solely by chlorine dioxide, indicated average weekly chlorate levels in treated water of 0.34 to 1.13 mg/L (Michael *et al*., 1981). For water treatment systems that used hypochlorite for disinfection, chlorate concentrations ranged from 11 to 660 µg/L (USEPA, 1994). Chlorate has been detected in source waters and may result from commercial wastewater from paper and pulp mills, from the use of chlorate salts as herbicides, and from the use of free chlorine to disinfect wastewater prior to its release to receiving waters (Bolyard *et al.*, 1993). High levels of chlorate (0.2 to 42 g/L) have also been found in hypochlorite solutions used for drinking water disinfection (Bolyard and Fair, 1992). In addition, swimming pool water has been found to contain an average concentration of 16 mg/L chlorate, with a maximum of 124 mg/L (Beech *et al.*, 1980).

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Experimental Animals

Most of the data on the absorption, distribution, metabolism, and excretion of chlorine dioxide, chlorite, and chlorate have been published by Abdel-Rahman *et al.* (1980a, 1982, 1984). These investigators utilized ^{36}Cl as a tracer for the chlorine and utilized a fractionation method to separate the ^{36}Cl compounds in various body fluids. In the rat, chlorine dioxide is metabolized to chloride, chlorite, and chlorate. Abdel-Rahman *et al.* (1984) administered 0.065 mg/kg $^{36}ClO_3$ (0.85 µCi) in 3 mL of a 5 mg/L solution orally to male Sprague-Dawley rats. The radiolabeled chlorate was rapidly absorbed from the gastrointestinal tract. A peak ^{36}Cl plasma level of 185 ng/mL was reached at 30 minutes. Distribution of radioactivity at 72 hours after administration indicated that the highest concentrations were in the plasma, followed by whole blood, stomach, testes, lung, kidney, skin, duodenum, spleen, brain, packed cells, ileum, carcass, liver, and bone marrow. Elimination from the plasma occurred in two phases; the half-life for the rapid elimination phase was about 6 hours, followed by a slower phase that had a half-life of 36.7 hours. Radioactivity first appeared in the urine, and urinary excretion accounted for up to 42% of the total initial dose in 72 hours. Approximately 2% to 4% of the initial dose was excreted in the feces at 72 hours postdosing. Chlorate was metabolized, and 20%, 4%,

and 13% of the initial dose was excreted as chloride, chlorite, and chlorate, respectively. Daily administration of 100 mg/L chlorate to male rats in drinking water for 1 year resulted in an increase in the chloroform concentration in the liver but not in the blood (Abdel-Rahman *et al.*, 1982).

Steffen and Wetzel (1993) administered 1 g/kg sodium chlorate to rabbits by gavage and determined serum and urine concentrations of chlorate. The highest serum concentrations were observed 90 minutes after dosing and remained high (10 to 20 mM) for at least 12 hours. Peak concentrations of chlorate (246 ± 99 mM) were observed in the urine at 6 hours; the elimination half-life was approximately 20 hours.

Humans

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

TOXICITY

Experimental Animals

The oral LD_{50} for sodium chlorate is reported to be 8,350 mg/kg in mice, 1,200 mg/kg in rats, 1,350 mg/kg in cats, 7,200 mg/kg in rabbits, and 700 mg/kg in dogs (Lewis, 1996; HSDB, 2003). In laboratory studies, the LD_{50} for intravenous administration of sodium chlorate to male and female Sprague-Dawley rats was 2,229 mg chlorate/kg (1,743 to 2,638 mg/kg) (Jeng and Woodworth, 1990).

Chlorate toxicosis has been reported in horses, pigs, cows, sheep, chickens, and dogs and is caused primarily by accidental ingestion through the inadequate handling or disposal of herbicides or through accidental inclusion in animal feed (Gregory *et al.*, 1993). Ingestion of chlorates causes local irritation of the gastrointestinal tract. Hemolysis and methemoglobin formation, followed by intravascular coagulation, are also frequently observed. The kidney is a target organ, with the renal tubules being most susceptible. Clinical signs in animals have included vomiting, ataxia, dyspnea, cyanosis, hematuria, hemoglobinuria, and hemoglobinemia. Anuria, coma, and death can follow. Animals that survive chlorate poisoning may die from chronic renal failure.

Male Sprague-Dawley rats were given 10 or 100 mg/L chlorate per day in drinking water for 4 months (Abdel-Rahman *et al.*, 1980b). At 2 months, blood glutathione levels were decreased significantly in both exposed groups. At 4 months, blood osmotic fragility was decreased significantly in the 100 mg/L group, and abnormal erythrocyte morphology, including the presence of codocytes and echinocytes, was observed in both exposed groups.

Couri and Abdel-Rahman (1980) studied the glutathione-dependent enzyme system in the erythrocytes of male Sprague-Dawley rats after exposure to chlorate in drinking water at 0, 10, or 100 mg/L for up to 12 months. At 6 months, rats exhibited no change in glutathione reductase activity, an increase in glutathione peroxidase at 100 mg/L, a decrease in catalase activity at 100 mg/L, and a decrease in glutathione concentration at both 10 and 100 mg/L. After 12 months of treatment, there were no significant differences in the activity of glutathione reductase, glutathione peroxidase, or catalase in either exposed group, and the glutathione concentration was significantly higher in both exposed groups.

Male Sprague-Dawley rats were exposed to drinking water containing 0, 10, or 100 mg chlorate/L for up to 1 year (Couri *et al.*, 1982; Abdel-Rahman *et al.*, 1985). Mean body weights were significantly decreased (10% to 20%) in both treatment groups throughout the experiment. Blood osmotic fragility was significantly decreased in both exposed groups after 7 or 9 months of treatment. Reduced fragility of red blood cells was attributed to cross-linking of membrane components with hemoglobin and subsequent precipitation of hemoglobin. Reductions in blood glutathione levels were observed in the 100 mg/L group after 7 and 9 months of treatment and in the 10 mg/L group after 9 months of treatment. After 9 months of treatment, red blood cell count, hematocrit, and hemoglobin content were all significantly decreased at both 10 and 100 mg/L. Evaluation of ^{3}H-thymidine incorporation into the organs of rats exposed to 10 mg/L chlorate for 3 months indicated a decrease in incorporation in the testes but not in the liver, kidney, or intestinal mucosa.

McCauley *et al.* (1995) conducted a subchronic (90-day) study on sodium chlorate in male and female Sprague-Dawley rats. Animals were exposed to 3, 12, or 48 mM (250, 1,001, or 4,005 mg/L, respectively) sodium chlorate in the drinking water, resulting in doses of 30 to 512 mg/kg per day for males and 42 to 801 mg/kg per day for females. There were no compound-related

deaths, but males and females in the highest exposure group had significantly lower weights (76% and 84% of that of control values, respectively). Significant decreases in heart, kidney, and liver relative weights were observed in 4,005 mg/L males, whereas significant decreases in adrenal, thymus, and spleen relative weights were observed in 4,005 mg/L females. Red blood cell counts and percent hematocrit were decreased in 4,005 mg/L males and females. Microscopic evaluation of tissues revealed treatment-related changes in the pituitary and thyroid glands. The severity, but not the incidence, of pituitary gland vacuolization was increased in 4,005 mg/L males, whereas both the incidence and severity were increased in 4,005 mg/L females. Thyroid gland colloid depletion was present in both sexes; males and females in the 1,001 and 4,005 mg/L groups exhibited 100% incidence with moderate to marked severity. No-observed-adverse-effect-levels of 0.36 mM/kg per day (30 mg/kg per day) and 0.50 mM/kg per day (42 mg/kg per day) were established in male and female Sprague-Dawley rats, respectively.

Bercz *et al.* (1982) exposed 12 African green monkeys to drinking water containing 25, 50, 100, 200, or 400 mg chlorine dioxide equivalent/L (about 4, 8, 16, 31, or 62 mg chlorate/kg per day, respectively, based on water intake of 125 mL/kg per day) in a rising dose protocol using 30 to 60 day exposures for each concentration. Chlorate did not induce significant changes in hematological parameters or thyroid hormone levels.

Bio/dynamics, Inc. (cited in USEPA, 1994), gave Sprague-Dawley rats (14/sex per dose) sodium chlorate at doses of 0, 7.8, 78, or 784 mg/kg per day by gavage for up to 3 months. No treatment-related effects were observed in mortality, physical appearance or behavior, body weight, food consumption, clinical chemistry, gross necropsy, or organ histopathology. In the 784 mg/kg group, hematological changes indicative of anemia included decreases in erythrocyte count, hemoglobin concentration, and percent hematocrit.

Steffen and Wetzel (1993) administered 1 g/kg sodium chlorate to New Zealand white rabbits by gavage. No methemoglobin was detected in the blood. No changes in serum values of urea, creatinine, aspartate, or alanine aminotransferase were observed. No adverse histopathological effects were observed in the kidneys 7 days after dosing.

Heywood *et al.* (1972) repeatedly administered 200 to 326 mg sodium chlorate/kg per day to four male and four female beagle dogs by gavage over a 5-day period. Two animals receiving more than 300 mg/kg displayed loss of appetite and body weight and had blood in their urine or feces, and one died after 4 days of exposure. The surviving animal was allowed a 7-day recovery period. Postmortem examination of both animals revealed classic signs of chlorate poisoning, including cyanotic kidney surface and evidence of hemolysis in the liver. Dogs receiving less than 300 mg/kg sodium chlorate survived the exposure period and were allowed a week of recovery before necropsy. Some of these dogs exhibited extramedullary hematopoiesis in the spleen and evidence of hemolysis in the liver. Packed cell volume, hemoglobin content, and red blood cell count were all reduced in animals treated with greater than 200 mg/kg compared to pretreatment values for each animal.

Bio/dynamics, Inc. (cited in USEPA, 1994), exposed beagle dogs (four/sex per dose) by gavage to sodium chlorate at doses of 0, 10, 60, or 360 mg/kg per day for 3 months. There was no significant effect at any dose concentration on body weight, food consumption, clinical chemistry, organ weights, gross necropsy, or tissue histopathology.

Most of the potential adverse health effects of sodium chlorate exposure are associated with blood oxidation, including increased methemoglobin formation, decreased hematocrit, red blood cell membrane damage, and reduction in red blood cell glutathione levels. Incubation of human and rabbit erythrocytes with sodium chlorate induces a concentration-dependent oxidation of hemoglobin (Steffen and Wetzel, 1993). *In vitro*, rabbit erythrocytes are less sensitive to methemoglobin formation than human erythrocytes; approximately twice as much sodium chlorate is required to mimic the time course of methemoglobin formation observed for human erythrocytes. At 30 mM sodium chlorate, significant concentrations of methemoglobin were formed in rabbit erythrocytes 1 hour later than human erythrocytes incubated with the same concentration of sodium chlorate.

Sodium chlorate is known to be an inhibitor of sulfation (Baeuerle and Huttner, 1986; Humphries and Silbert, 1988; Roy *et al.*, 1988) and has been used as a research tool to elucidate molecular mechanisms in which sulfation, specifically proteoglycan sulfation, appears to play an important role. Davies *et al.* (1995) used sodium chlorate, an inhibitor of glycosaminoglycan sulfation, to study the morphological development of the urinary-collecting ducts and nephrons in mouse

embryonic kidneys. Sodium chlorate has been shown to inhibit fibroblast-growth-factor-mediated cardiogenesis in chick heart precardiac mesoderm (Zhu *et al.*, 1996) and to inhibit extracellular matrix deposition during skeletal muscle differentiation (Melo *et al.*, 1996). Sodium chlorate also inhibits tyrosine sulfation (Beinfeld, 1994; Mintz *et al.*, 1994).

Humans

The oral LD_{50} in adult women is reported to be 800 mg/kg (Lewis, 1996). Concern about the acute toxicity of sodium chlorate to humans stemmed from reports of death or illness resulting from accidental or intentional ingestion of large amounts of herbicides containing sodium chlorate (Timperman and Maes, 1966; Stoodley and Rowe, 1970; Jansen and Zeldenrust, 1972; Oliver *et al.*, 1972; Vakili, 1977; Stavrou *et al.*, 1978; Bloxham *et al.*, 1979; Helliwell and Nunn, 1979; Proudfoot *et al.*, 1979; Steffen and Seitz, 1981; Cunningham, 1982; Casey and Vale, 1994). Sodium chlorate ingestion has been associated with more than 100 cases of fatal poisoning in humans (Singelmann *et al.*, 1984). Chlorate toxicity after ingestion can be characterized primarily by gastrointestinal irritation, massive intravascular hemolysis, disseminated intravascular coagulation, cyanosis, and renal failure. Gastrointestinal irritation appears to be the result of a direct effect of the chlorate ion on the gastrointestinal mucosa. The intravascular hemolysis occurs subsequent to the formation of methemoglobin in exposed erythrocytes, eventually resulting in cyanosis. In addition, chlorate exerts a direct toxic effect on the proximal tubule of the kidney, causing necrosis and preventing the formation of urine and subsequent elimination of chlorate from the blood stream, thus prolonging exposure of the erythrocytes. Supportive management aimed at removing or deactivating the chlorate ion includes gastric lavage, administration of activated charcoal, and oral or intravascular administration of sodium thiosulfate. Reversal of hemoglobinemia may be accomplished with methylene blue during the very early stages of poisoning (Proudfoot *et al.*, 1979; Steffen and Seitz, 1981). Transfusions, bicarbonate infusion containing sodium thiosulfate, anticoagulation with heparin, and substitution of clotting factors may be called for to counteract the oxidizing effects of the chlorate on the erythrocytes (Steffen and Seitz, 1981). Peritoneal dialysis or hemodialysis is effective in treating renal failure. Death has been most frequently associated with doses of 20 g or greater, although recovery has been noted in patients who ingested as much as 200 g.

Human epidemiology studies investigating doses of chlorate more relevant to those found in drinking water have not identified any significant exposure-related effects (Michael *et al.*, 1981; Lubbers *et al.*, 1982, 1984a,b; Lubbers and Bianchine, 1984). A prospective epidemiology study was conducted on 197 volunteers during a 12-week period when the primary water disinfectant in the community was changed from chlorine to chlorine dioxide. Chlorate levels obtained from 42 samples ranged from 0.17 to 1.79 ppm, with a mean of 0.73 ppm (Michael *et al.*, 1981), and chlorate exposure was estimated to be 0.010 to 0.032 mg/kg per day (USEPA, 1994). Thyroid function, as measured by serum thyroxine levels, did not appear to be altered in the human population (Bercz *et al.*, 1982).

Chlorine dioxide and its by-products were also administered to normal, healthy, adult-male volunteers in controlled clinical studies to determine the physiological effects of chronic ingestion of these compounds. A three-phase study was conducted to characterize the effects of chronically ingested chlorate in drinking water (Lubbers *et al.*, 1982, 1984a,b; Lubbers and Bianchine, 1984). In Phase I, tolerance of a rising dose of chlorate in drinking water was evaluated through serum chemistry, blood counts, urinalysis, clinical chemistry, and a physical examination. Ten normal, healthy, male volunteers drank two 500-mL aliquots of chlorate-treated water 4 hours apart. A control group received the same volume of untreated water. A physical examination was conducted on each of the 2 days following water consumption. The 3-day study was repeated using successively higher doses of chlorate. Concentrations of 0.01, 0.1, 0.5, 1.0, 1.8, and 2.4 mg chlorate/L yielded total intakes equivalent to 0.143, 1.43, 7.14, 14.3, 25.7, and 34.3 µg/kg for a 70 kg man. No adverse health effects were noted.

In Phase II, 10 healthy male volunteers ingested a daily aliquot of 500 mL of drinking water containing 5 mg chlorate/L (35.7 µg/kg) for 12 weeks. Physical examinations and laboratory measurements were made on a weekly basis during the treatment period and for 8 weeks following cessation of treatment. There was no effect of chlorate treatment on any parameter measured. Phase III used the treatment protocol of Phase II to

evaluate the effect of chlorate ingestion on three glucose-6-phosphate dehydrogenase-deficient subjects. No adverse effects were noted.

Incubation of human erythrocytes with 30 mM sodium chlorate resulted in methemoglobin formation and a dramatic increase in filtration time, beginning after 2 hours of exposure (Steffen and Singelmann, 1983). The increase in filtration time, indicating increased rigidity of the cells, suggests an explanation for the hemolysis, disseminated intravascular coagulation, and renal failure observed in humans after chlorate poisoning, since erythrocyte rigidity may lead to impairment of the microcirculation and to the destruction of the red cells by the spleen. Further study of the effect of sodium chlorate on human erythrocytes revealed that sodium chlorate indirectly induces methemoglobinemia by inactivating glucose-6-phosphate dehydrogenase (Singelmann *et al.*, 1984; Steffen and Wetzel, 1993).

Reproductive and Developmental Toxicology

Experimental Animals

Female Sprague-Dawley rats were given 0, 1, or 10 mg chlorate/L daily in the drinking water for 2.5 months prior to mating with untreated males (Suh *et al.*, 1983). Administration of the treated water to pregnant females (six to nine per group) continued until gestation day 20, when they were killed and evaluated for status of uterine implants. Live fetuses were weighed, measured (crown-rump length), and evaluated for external malformations. Fetuses were then examined for visceral and skeletal malformations. All animals survived to scheduled necropsy. Maternal body weight was not affected by treatment. There was no statistically significant effect on pregnancy rate, total number of implantations per dam, or the number of live, resorbed, or dead fetuses. Fetal body weight was not adversely affected by treatment. Crown-rump length was significantly increased in male fetuses exposed to 10 mg/L. There was no statistically significant increase in the incidence of external, visceral, or skeletal anomalies.

Pregnant Sprague-Dawley (CD) rats were given 0, 10, 100, or 1,000 mg sodium chlorate/kg per day in distilled water by gavage on gestation days 6 through 15 (Bio/dynamics, Inc., 1987). Females were killed and evaluated on gestation day 20. There were no maternal deaths in treated animals. No treatment-related effects were evident in maternal body weight or weight gain, food consumption, physical observations, number of uterine implantations, or gross necropsy. Examination of fetuses on day 20 revealed no effects on fetal body weight or sex ratio, and no treatment-related effects on external, visceral, or skeletal abnormalities were detected.

Due to the absence of nonrodent toxicity data in the literature, the National Toxicology Program conducted developmental toxicity studies of sodium chlorate in rabbits. Female New Zealand white (NZW) rabbits (24/group) were given 100, 250, or 475 mg sodium chlorate/kg per day by gavage or vehicle (deionized/distilled water) on gestation days 6 through 29 (NTP, 2002). Dams were necropsied on gestation day 30. One maternal death occurred in each dose group, but these were not considered to be treatment related. Transient changes in maternal food intake, urine color, and/or output were noted at doses of 100 mg/kg per day and greater, but clear evidence of maternal toxicity was observed only at doses greater than 475 mg/kg per day in the screening study (NTP, 1998). Sodium chlorate exposure did not affect resorptions, fetal viability, fetal body weight, or fetal external, visceral, or skeletal alterations. Sodium chlorate did not cause any significant treatment-related developmental toxicity under the conditions of this study.

Sodium chlorate was negative in the mouse sperm head abnormality assay (Meier *et al.*, 1985). Sodium chlorate was administered by gavage at doses of 8, 20, or 40 mg/kg per day for 5 days to male $B6C3F_1$ mice (10/group). The animals were sacrificed at 1, 3, and 5 weeks after the last dose, and the sperm were examined for abnormal shapes in the head region. No evidence of an increased incidence of abnormal sperm heads was found at any dose or time of sacrifice.

Humans

No reproductive or developmental toxicity studies of sodium chlorate in humans were found in the literature.

Carcinogenicity

Experimental Animals

Sodium chlorate was tested in male F344 rats (15/group) for potential promoting effects in two-stage rat renal carcinogenesis studies (Kurokawa *et al.*, 1985). Renal carcinogenesis was initiated with 0.05% N-ethyl-N-hydroxyethylnitrosamine in the drinking water three

times per week for 2 weeks. Control animals received distilled water. Rats were then treated with 1% sodium chlorate (1 g/100 mL; mean consumption; 686 mg/kg per day) in the drinking water for 25 weeks. No animals died during the course of the experiment. Animals were necropsied at 27 weeks. Sodium chlorate showed no promoting effect on the incidences of renal neoplastic lesions, including dysplastic foci and renal cell tumors.

Humans

No epidemiology studies of sodium chlorate in humans were found in the literature.

GENETIC TOXICITY

The published data from investigations of sodium chlorate genetic toxicity are limited. Gocke *et al.* (1981), reporting results from a large screening study, listed sodium chlorate (12 µmoles per plate) as positive in a *Salmonella* mutagenicity assay (strain TA1535 with S9), weakly positive in a *Drosophila* sex-linked recessive lethal assay (0.25 M solution administered by feeding), and negative in an acute bone marrow micronucleus test in NMRI mice (2,100 mg/kg intraperitoneal or 4,200 mg/kg gavage). The report did not include data tables, and the methods and results presentations lacked detail. However, the authors pointed out that the *S. typhimurium* TA1535 strain that demonstrated the mutagenic response was obtained several years prior to the experiment, and that replicate trials in a more recently acquired sample of TA1535 did not demonstrate the same strength of response. In addition, the mutagenic response observed in TA1535 occurred in cultures grown on "ZLM" medium, a modified *Escherichia coli* medium with different salt concentrations than the standard Vogel Bonner medium typically used in Ames testing. *Salmonella* cultured on the standard Vogel Bonner medium did not demonstrate a pronounced reversion. Moriya *et al*. (1983) observed no mutagenicity with sodium chlorate in several strains of *Salmonella*, including TA1535, or in *E. coli* strain WP2 *hcr*; Vogel Bonner medium was used in these *Salmonella* assays. A publication of results from *in vivo* cytogenetics tests with several drinking water disinfectants reported a lack of activity with sodium chlorate (up to 40 mg/kg by gavage for 5 days) in tests for induction of micronuclei or chromosomal aberrations in bone marrow cells of male and female CD-1 Swiss mice (Meier *et al.*, 1985). The concentrations of test chemicals used in these experiments were below the maximum tolerated dose. Therefore, the tests may be considered inadequate indicators of the absence of genetic toxicity.

Further evidence in support of a lack of mutagenic activity for sodium chlorate *in vivo* and *in vitro* is provided by several industry reports from Life Science Research, Suffolk, England, cited in an Environmental Protection Agency criteria document (USEPA, 1994). Negative results were reported for gene reversion in *S. typhimurium* tester strains, with and without S9 activation enzymes, at sodium chlorate doses up to 5,000 µg/plate. No induction of unscheduled DNA synthesis (an indicator of DNA damage repair) was observed in cultured HeLa cells in the presence or absence of S9 liver enzymes. No consistent, reproducible induction of gene mutations at the HGPRT locus of cultured Chinese hamster V79 lung cells exposed to sodium chlorate (up to 5,000 µg/mL) was reported. However, lethality, an indicator of induced primary DNA damage, was seen in repair deficient *E. coli* strains WP67 and CM871, but not in the repair proficient strain WP2, with and without S9, at sodium chlorate doses of 1,000 µg/mL and higher. Results of *in vivo* studies demonstrated no induction of micronuclei in bone marrow erythrocytes of male and female CD-1 mice treated with up to 5,000 mg/kg sodium chlorate.

STUDY RATIONALE

Sodium chlorate was nominated for toxicity and carcinogenicity studies by the United States Environmental Protection Agency and by the American Water Works Association and Research Council based on the presence of sodium chlorate in drinking water disinfected with chlorine dioxide. A large segment of the United States population is potentially exposed to sodium chlorate in the drinking water and from its use as a herbicide. The 3-week and 2-year studies were performed in male and female F344/N rats and B6C3F$_1$ mice to evaluate the toxicity and carcinogenicity of sodium chlorate. Drinking water was chosen as the route of exposure because it is the most likely route of human exposure.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF SODIUM CHLORATE

A single lot of sodium chlorate (14019PQ) was obtained from Aldrich Chemical Company, Inc. (Milwaukee, WI), by the analytical chemistry laboratory, Battelle Columbus (Columbus, OH), and provided to the study laboratory, Southern Research Institute (Birmingham, AL). Lot 14019PQ was used in the 3-week and 2-year studies. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory and the study laboratory. Reports on analyses performed in support of the sodium chlorate studies are on file at the National Institute of Environmental Health Sciences.

Lot 14019PQ, a white crystalline solid, was identified as sodium chlorate by infrared spectroscopy and melting point determination. The purity of lot 14019PQ was determined by argentimetric titration, anion exchange ion chromatography (IC), and elemental analysis. Karl Fischer titration indicated a moisture content of less than 0.05%. Elemental analysis for chlorine was in agreement with the theoretical value for sodium chlorate. However, elemental analysis for sodium was higher (108%) than the theoretical value. Argentimetric titration indicated a purity of 99.7%. IC indicated one major peak with no reportable impurities by one system and a relative purity of 101% based on major peak comparison with a frozen reference standard of the same lot by a second system. Major peak area percent by the second system indicated a purity of 100%. The overall purity of lot 14019PQ was determined to be greater than 99%.

Stability studies of the bulk chemical were performed by the analytical chemistry laboratory using IC. These studies indicated that sodium chlorate was stable as a bulk chemical for 15 days when stored under a minimal headspace protected from light at temperatures up to 60° C. To ensure stability, the bulk chemical was stored at room temperature in amber glass containers with Teflon®-lined lids and protected from light. Stability was monitored by the study laboratory during the 2-year studies with IC. No degradation of the bulk chemical was detected.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared once during the 3-week studies and every 4 weeks during the 2-year studies by mixing sodium chlorate with tap water (Table H1). Homogeneity studies of 125 and 2,000 mg/L dose formulations were performed by the study laboratory using IC. Stability studies of a 2 mg/L dose formulation were performed by the analytical chemistry laboratory using IC. Homogeneity was confirmed. Stability was confirmed for at least 44 days for dose formulations stored in sealed NALGENE® containers at temperatures up to 25° C and for at least 7 days when stored in drinking water bottles under simulated animal room conditions.

Periodic analyses of the dose formulations of sodium chlorate were conducted by the study laboratory using IC. During the 3-week studies, the dose formulations were analyzed once; all five of the dose formulations for rats and mice were within 10% of the target concentrations (Table H2). During the 2-year studies, the dose formulations were analyzed approximately every 10 weeks (Table H3). Of the dose formulations used for rats and mice, 40 of 42 were within 10% of the target concentrations; one dose formulation for rats and one dose formulation for mice were inadvertently used at 14% and 11% of target, respectively.

3-WEEK STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Taconic Laboratory Animals and Services (Germantown, NY). On receipt, the rats and mice were 3 to 4 weeks old. Rats were quarantined for 11 (males)

or 12 (females) days, and mice were quarantined for 13 (males) or 14 (females) days; animals were 5 to 6 weeks old on the first day of the studies. Groups of 10 male and 10 female core study rats and mice and groups of 10 male and 10 female clinical pathology study rats were exposed to drinking water containing 0, 125, 250, 500, 1,000, or 2,000 mg/L sodium chlorate for 22 days. Feed and water were available *ad libitum*. Rats and female mice were housed five per cage; male mice were housed individually. Clinical findings were recorded weekly for core study rats and mice. Water consumption by core and special study animals was recorded weekly by cage until day 22. The animals were weighed initially, weekly, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 1.

Blood was collected from the retroorbital sinus of clinical pathology study rats on day 4 and from core study rats and mice at the end of the 3-week studies for hematology (rats and mice) and clinical chemistry (rats) analyses. Animals were anesthetized with a CO_2/O_2 mixture. The parameters measured are listed in Table 1. Blood samples for hematology analyses were placed in tubes containing EDTA. Erythrocyte, platelet, and leukocyte counts; hematocrit values; hemoglobin concentrations; and mean cell volume, hemoglobin, and hemoglobin concentration were determined using a Technicon H-1™ (Bayer HealthCare LLC, Tarrytown, NY) with reagents from R&D Systems, Inc. (Minneapolis, MN), Bayer, Inc. (Tustin, CA), and Fisher Scientific (Norcross, GA). Reticulocytes were counted using a Coulter Model Elite Flow Cytometer (Coulter Corp., Miami, FL) with reagents supplied by the manufacturer and Molecular Probes (Eugene, OR). Methemoglobin concentration was determined using a spectrophotometric method and reagents from J.T. Baker, Inc. (Phillipsburg, NJ) and Fisher Scientific. Samples for clinical chemistry analyses were placed in tubes with no anticoagulant. Samples were analyzed using a Hitachi 911 clinical chemistry analyzer (Roche Diagnostics Corporation, Indianapolis, IN) with reagents from Boehringer Mannheim Biochemicals (Indianapolis, IN) and Sigma Chemical Co. (St. Louis, MO), except sorbitol dehydrogenase was measured using a Cobas Fara chemistry analyzer (Roche) with reagents from Sigma Chemical Co. after serum was frozen at –20° C.

Necropsies were performed on all core study rats and mice. The heart, right kidney, liver, lungs, right testis, and thymus were weighed. Histopathologic examinations were performed on core study vehicle control and 2,000 mg/L rats and mice. Table 1 lists the tissues and organs examined to the no-effect level.

2-YEAR STUDIES

Study Design

Groups of 50 male and 50 female rats were exposed to drinking water containing 0, 125, 1,000, or 2,000 mg/L sodium chlorate for 105 to 106 weeks. Additional groups of 20 male and 20 female special study rats were exposed to the same concentrations for up to 14 weeks for thyroid hormone evaluations and histopathology. Groups of 50 male and 50 female mice were exposed to drinking water containing 0, 500, 1,000, or 2,000 mg/L sodium chlorate for 105 to 106 weeks.

Source and Specification of Animals

Male and female F344/N rats and $B6C3F_1$ mice were obtained from Taconic Laboratory Animals and Services for use in the 2-year studies. Rats and mice were quarantined for 13 days before the beginning of the studies. Five male and five female core study rats and mice and five male and five female special study rats were randomly selected for parasite evaluation and gross observation of disease. Rats and mice were approximately 6 weeks old at the beginning of the studies. The health of the animals was monitored during the studies according to the protocols of the NTP Sentinel Animal Program (Appendix K).

Animal Maintenance

Male rats were housed three per cage. Female rats and mice were housed five per cage. Male mice were housed individually. Feed and water were available *ad libitum*. Water consumption was recorded every 4 weeks by cage. Cages and racks were rotated every two weeks. Further details of animal maintenance are given in Table 1. Information on feed composition and contaminants is provided in Appendix J.

Clinical Examinations and Pathology

All animals were observed twice daily. Clinical findings were recorded every 4 weeks. Body weights were recorded initially, every 4 weeks, and at the end of the studies.

Ten male and 10 female special study rats per exposure group were designated for thyroid hormone evaluations at day 4 and week 3. Additional groups of 10 male and

10 female special study rats were designated for thyroid hormone evaluation at week 14. Rats were anesthetized with CO_2/O_2 for each blood collection. Blood was taken from the retroorbital sinus and collected into tubes containing no anticoagulant. The blood samples were processed for serum, and the serum was aliquoted into clean tubes and stored frozen (approximately –70° C or below) until analyzed for thyroid hormones. Rats bled at week 3 or week 14 were sacrificed and necropsied, and the thyroid gland was examined histopathologically. See Table 1 for a list of the parameters measured.

Complete necropsies and microscopic examinations were performed on all core study rats and mice. At necropsy, all organs and tissues were examined for grossly visible lesions, and all major tissues were fixed and preserved in 10% neutral buffered formalin (except eyes), processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 µm, and stained with hematoxylin and eosin for microscopic examination. For all paired organs (e.g., adrenal gland, kidney, ovary), samples from each organ were examined. See Table 1 for a list of the tissues examined microscopically.

Microscopic evaluations were completed by the study laboratory pathologist, and the pathology data were entered into the Toxicology Data Management System. The slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit. The slides, individual animal data records, and pathology tables were evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy; the slide and tissue counts were verified; and the histotechnique was evaluated. For the 2-year studies, a quality assessment pathologist evaluated slides from all tumors and all potential target organs, which included the thyroid gland of male and female rats and female mice; the forestomach of male and female mice; the bone marrow, liver, preputial gland, and spleen of male rats; the liver and pancreas of female rats; and the bone marrow, mammary gland, ovary, and pancreatic islets of female mice.

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

TABLE 1
Experimental Design and Materials and Methods in the Drinking Water Studies of Sodium Chlorate

3-Week Studies	2-Year Studies
Study Laboratory	
Southern Research Institute (Birmingham, AL)	Southern Research Institute (Birmingham, AL)
Strain and Species	
F344/N rats $B6C3F_1$ mice	F344/N rats $B6C3F_1$ mice
Animal Source	
Taconic Laboratory Animals and Services (Germantown, NY)	Taconic Laboratory Animals and Services (Germantown, NY)
Time Held Before Studies	
Rats: 11 days (males) or 12 days (females) Mice: 13 days (males) or 14 days (females)	13 days
Average Age When Studies Began	
6 weeks	6 weeks
Date of First Exposure	
Rats: May 18 (males) or 19 (females), 1998 Mice: May 20 (males) or 21 (females), 1998	Rats: September 16, 1998 Mice: September 30, 1998
Duration of Exposure	
22 (core study) or 27 (special study) days	105 to 106 weeks
Date of Last Exposure	
Rats: June 8 (males) or 9 (females), 1998 Mice: June 10 (males) or 11 (females), 1998	Rats: September 21, 2000 Mice: October 5, 2000
Necropsy Dates	
Rats: June 8 (males) or 9 (females), 1998 Mice: June 10 (males) or 11 (females), 1998	Rats: September 13-21, 2000 Mice: September 27 to October 5, 2000
Average Age at Necropsy	
9 weeks	110-111 weeks
Size of Study Groups	
10 males and 10 females	50 males and 50 females
Method of Distribution	
Animals were distributed randomly into groups of approximately equal initial mean body weights.	Animals were distributed randomly into groups of approximately equal initial mean body weights.
Animals per Cage	
Rats: 5 Mice: 1 (males) or 5 (females)	Rats: 3 (males) or 5 (females) Mice: 1 (males) or 5 (females)
Method of Animal Identification	
Tail tattoo	Tail tattoo

TABLE 1
Experimental Design and Materials and Methods in the Drinking Water Studies of Sodium Chlorate

3-Week Studies	2-Year Studies
Diet	
NTP-2000 irradiated pelleted diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*, changed weekly	NTP-2000 irradiated wafer rodent feed (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*, changed weekly
Water	
Tap water (Birmingham municipal supply) via amber glass water bottles with stainless steel screw caps (Kerr Glass Manufacturing Corp., Plainfield, IL), available *ad libitum*, changed twice weekly	Tap water (Birmingham municipal supply) via amber glass water bottles with Teflon®-lined plastic screw caps (Wheaton Scientific Products, Millville, NJ), available *ad libitum*, changed twice weekly
Cages	
Solid-bottom polycarbonate (Lab Products, Maywood, NJ), changed twice weekly (rats and female mice) or weekly (male mice)	Same as 3-week studies
Bedding	
Irradiated hardwood chips (mice) or heat-treated irradiated hardwood chips (rats) (P.J. Murphy Forest Products Corp., Montville, NJ), changed once (male mice) or twice (rats and female mice) weekly	Heat-treated irradiated hardwood chips (P.J. Murphy Forest Products Corp., Montville, NJ), changed once (male mice) or twice (rats and female mice) weekly
Rack Filters	
Reemay® spun bonded polyester (Andico, Birmingham, AL), changed every 2 weeks	Same as 3-week studies
Racks	
Stainless steel (Lab Products, Inc., Maywood, NJ), changed every 2 weeks	Same as 3-week studies
Animal Room Environment	
Temperature: 72° ± 3° F Relative humidity: 50% ± 15% Room fluorescent light: 12 hours/day Room air changes: 10/hour	Temperature: 72° ± 3° F Relative humidity: 50% ± 15% Room fluorescent light: 12 hours/day Room air changes: 10/hour
Exposure Concentrations	
0, 125, 250, 500, 1,000, or 2,000 mg/L in water, available *ad libitum*	Rats: 0, 125, 1,000, or 2,000 mg/L in drinking water, available *ad libitum* Mice: 0, 500, 1,000, or 2,000 mg/L in drinking water, available *ad libitum*
Type and Frequency of Observation	
Observed twice daily and clinical findings recorded weekly. Water consumption was recorded weekly by cage for core and special study animals until day 22. Animals were weighed initially, weekly, and at the end of the studies.	Observed twice daily; clinical findings and water consumption by cage were recorded every 4 weeks; core study animals were weighed initially, every 4 weeks, and at the end of the studies.

TABLE 1
Experimental Design and Materials and Methods in the Drinking Water Studies of Sodium Chlorate

3-Week Studies	2-Year Studies
Method of Sacrifice	
Carbon dioxide asphyxiation	Same as 3-week studies
Necropsy	
Necropsies were performed on all core study animals. Organs weighed were heart, right kidney, liver, lungs, right testis, and thymus of core study animals and liver of special study animals.	Necropsies were performed on all animals.
Clinical Pathology	
Blood was collected from the retroorbital sinus of special study rats on day 4 and from all core study animals at the end of the studies for hematology (rats and mice) and clinical chemistry (rats). ***Hematology:*** hematocrit; hemoglobin concentration; erythrocyte, reticulocyte, and platelet counts; erythrocyte morphology; mean cell volume; mean cell hemoglobin; mean cell hemoglobin concentration; and leukocyte count and differentials ***Clinical chemistry:*** urea nitrogen, creatinine, total protein, albumin, alanine aminotransferase, alkaline phosphatase, creatine kinase, sorbitol dehydrogenase, and bile acids	None
Histopathology	
Complete histopathology was performed on all core study control and 2,000 mg/L rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined to the no-effect level: adrenal gland, bone with marrow, brain, clitoral gland, esophagus, gallbladder (mice), heart and aorta, large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, ileum), kidney, liver, lung, lymph nodes (mandibular and mesenteric), mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, seminal vesicle, skin, spleen, stomach (forestomach and glandular), testis (with epididymis), thymus, thyroid gland, trachea, urinary bladder, and uterus.	Complete histopathology was performed on all core study rats and mice. In addition to gross lesions and tissue masses, the following tissues were examined: adrenal gland, bone with marrow, brain, clitoral gland, esophagus, gallbladder (mice), harderian gland, heart and aorta, large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, ileum), kidney, liver, lung, lymph nodes (mandibular and mesenteric), mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, seminal vesicle, skin, spleen, stomach (forestomach and glandular), testis (with epididymis), thymus, thyroid gland, trachea, urinary bladder, and uterus. In addition, the thyroid gland of special study rats was examined at 3 and 14 weeks.
Thyroid Hormone Analysis	
None	At 4 days, 3 weeks, and 14 weeks, blood was collected from the retroorbital sinus of up to 10 special study male and female rats per group for determinations of thyroid stimulating hormone (TSH), triiodothyronine (T_3), and thyroxine (T_4).

STATISTICAL METHODS

Survival Analyses

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

Calculation of Incidence

The incidences of neoplasms or nonneoplastic lesions are presented in Tables A1, A5, B1, B5, C1, C4, D1, and D5 as the numbers of animals bearing such lesions at a specific anatomic site and the numbers of animals with that site examined microscopically. For calculation of statistical significance, the incidences of most neoplasms (Tables A3, B3, C3, and D3) and all nonneoplastic lesions are given as the numbers of animals affected at each site examined microscopically. However, when macroscopic examination was required to detect neoplasms in certain tissues (i.e., harderian gland, intestine, mammary gland, and skin) before microscopic evaluation, or when neoplasms had multiple potential sites of occurrence (e.g., leukemia or lymphoma), the denominators consist of the number of animals on which a necropsy was performed. Tables A3, B3, C3, and D3 also give the survival-adjusted neoplasm rate for each group and each site-specific neoplasm. This survival-adjusted rate (based on the Poly-3 method described below) accounts for differential mortality by assigning a reduced risk of neoplasm, proportional to the third power of the fraction of time on study, only to site-specific, lesion-free animals that do not reach terminal sacrifice.

Analysis of Neoplasm and Nonneoplastic Lesion Incidences

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

This method yields a lesion prevalence rate that depends only upon the choice of a shape parameter for a Weibull hazard function describing cumulative lesion incidence over time (Bailer and Portier, 1988). Unless otherwise specified, a value of k=3 was used in the analysis of site-specific lesions. This value was recommended by Bailer and Portier (1988) following an evaluation of neoplasm onset time distributions for a variety of site-specific neoplasms in control F344 rats and B6C3F$_1$ mice (Portier *et al.,* 1986). Bailer and Portier (1988) showed that the Poly-3 test gave valid results if the true value of k was anywhere in the range from 1 to 5. A further advantage of the Poly-3 method is that it does not require lesion lethality assumptions. Variation introduced by the use of risk weights, which reflect differential mortality, was accommodated by adjusting the variance of the Poly-3 statistic as recommended by Bieler and Williams (1993).

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

Analysis of Continuous Variables

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

were analyzed using the nonparametric multiple comparison methods of Shirley (1977) (as modified by Williams, 1986) and Dunn (1964). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of the dose-related trends and to determine whether a trend-sensitive test (Williams' or Shirley's test) was more appropriate for pairwise comparisons than a test that does not assume a monotonic dose-related trend (Dunnett's or Dunn's test). Prior to statistical analysis, extreme values identified by the outlier test of Dixon and Massey (1957) were examined by NTP personnel, and implausible values were eliminated from the analysis. Average severity values were analyzed for significance with the Mann-Whitney U test (Hollander and Wolfe, 1973).

Historical Control Data

The concurrent control group represents the most valid comparison to the treated groups and is the only control group analyzed statistically in NTP bioassays. However, historical control data are often helpful in interpreting potential treatment-related effects, particularly for uncommon or rare neoplasm types. For meaningful comparisons, the conditions for studies in the historical database must be generally similar. One significant factor affecting the background incidence of neoplasms at a variety of sites is diet. In 1995, the NTP incorporated a new diet (NTP-2000) that contains less protein and more fiber and fat than the NIH-07 diet previously used in toxicity and carcinogenicity studies (Rao, 1996, 1997). The current NTP historical database contains all 23 studies that use the NTP-2000 diet with histopathology findings completed up to the present. A second potential source of variability is route of administration. In general, the historical database for a given study will include studies using the same route of administration, and the overall incidences of neoplasms for all routes of administration are included for comparison.

Quality Assurance Methods

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

Genetic Toxicology

The genetic toxicity of sodium chlorate was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium* and increases in the frequency of micronucleated erythrocytes in mouse peripheral blood. The protocols for these studies and the results are given in Appendix E.

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

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

The predictivity for carcinogenicity of a positive response in acute *in vivo* bone marrow chromosome aberration or micronucleus tests appears to be less than that in the *Salmonella* test (Shelby *et al.,* 1993; Shelby and Witt, 1995). However, clearly positive results in long-term peripheral blood micronucleus tests have high

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

RESULTS

RATS

3-WEEK STUDY

All rats survived to the end of the study (Table 2). Final mean body weights and body weight gains of all exposed groups were similar to those of the control groups. Water consumption by exposed rats was generally similar to that by control groups throughout the study. Drinking water concentrations of 125, 250, 500, 1,000, and 2,000 mg/L resulted in average daily doses of approximately 20, 35, 75, 170, and 300 mg sodium chlorate/kg body weight per day for male rats and 20, 40, 75, 150, and 340 mg/kg per day for female rats. No clinical findings attributed to sodium chlorate exposure were observed.

The hematology and clinical chemistry data are shown in Table F1. An exposure concentration-related decrease in segmented neutrophil counts occurred in male and female rats on days 4 and 22. In 2,000 mg/L rats, segmented neutrophil counts were decreased by approximately 64% in males and 51% in females on day 22. The cause of the decrease is unknown, but the decrease

TABLE 2
Survival, Body Weights, and Water Consumption of Rats in the 3-Week Drinking Water Study of Sodium Chlorate

Concentration (mg/L)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Week 1	Week 3
Male							
0	10/10	87 ± 1	149 ± 3	61 ± 2		14	19
125	10/10	87 ± 1	148 ± 3	60 ± 2	99	14	21
250	10/10	88 ± 2	153 ± 4	65 ± 3	103	15	20
500	10/10	85 ± 1	149 ± 3	64 ± 2	100	15	20
1,000	10/10	85 ± 1	146 ± 2	61 ± 2	98	17	20
2,000	10/10	86 ± 1	144 ± 2	57 ± 2	97	16	19
Female							
0	10/10	81 ± 1	118 ± 1	36 ± 1		12	15
125	10/10	82 ± 1	118 ± 1	36 ± 2	100	13	20
250	10/10	81 ± 1	118 ± 1	37 ± 1	100	13	18
500	10/10	80 ± 1	117 ± 2	38 ± 2	100	12	16
1,000	10/10	82 ± 2	118 ± 2	35 ± 2	100	13	16
2,000	10/10	81 ± 2	117 ± 2	36 ± 1	99	14	20

[a] Number of animals surviving at 22 days/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Differences from the control group are not significant by Dunnett's test.
[c] Water consumption is expressed as grams per animal per day.

may represent a redistribution of the neutrophils from the circulating pool to the marginal neutrophil pool. At day 22, there were minimal decreases (approximately 6%) in the hematocrit value, hemoglobin concentration, and erythrocyte count in the 2,000 mg/L males. No chemical-related changes in clinical chemistry parameters occurred.

Absolute and relative heart weights of 2,000 mg/L males were significantly less than those of the control group (Table G1).

Significantly increased incidences of minimal to mild thyroid gland follicular cell hypertrophy occurred in males and females receiving 500 mg/L or greater (males: 0 mg/L, 0/10; 125 mg/L, 0/10; 250 mg/L, 1/10; 500 mg/L, 5/10; 1,000 mg/L, 10/10; 2,000 mg/L, 10/10; females: 0/10, 0/10, 1/10, 8/10, 6/10, 10/10).

Exposure Concentration Selection Rationale: Because there were no effects of sodium chlorate on survival or body weights of male or female F344/N rats, the highest exposure concentration selected for the 2-year study was 2,000 mg/L. Although follicular cell hypertrophy was observed at 1,000 and 2,000 mg/L, it was not considered a potential threat to the health of the rats during a 2-year study. A low dose of 125 mg/L was selected because it was anticipated to be a no-observed-adverse-effect level for thyroid gland effects.

2-YEAR STUDY

Survival

Estimates of 2-year survival probabilities for male and female rats are shown in Table 3 and in the Kaplan-Meier survival curves (Figure 1). Survival of exposed rats was similar to that of the control groups.

Body Weights, Water and Compound Consumption, and Clinical Findings

The mean body weights of all exposed groups were similar to those of the control groups throughout the study (Figure 2; Tables 4 and 5). Water consumption by exposed rats was generally similar to that by controls throughout the study (Tables I1 and I2). Drinking water concentrations of 125, 1,000, and 2,000 mg/L resulted in average daily doses of approximately 5, 35, and 75 mg/kg per day for male rats and 5, 45, and 95 mg/kg per day for female rats. No clinical findings were attributed to sodium chlorate exposure.

TABLE 3
Survival of Rats in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Male				
Animals initially in study	50	50	50	50
Accidental death[a]	1	0	0	0
Moribund	10	13	11	14
Natural deaths	3	10	8	8
Animals surviving to study termination	36	27	31	28
Percent probability of survival at end of study[b]	74	54	62	56
Mean survival (days)[c]	687	693	688	689
Survival analysis[d]	P=0.412	P=0.108	P=0.353	P=0.146
Female				
Animals initially in study	50	50	50	50
Moribund	10	11	11	4
Natural deaths	3	3	6	5
Animals surviving to study termination	37	36[e]	33[f]	41[f]
Percent probability of survival at end of study	74	72	66	82
Mean survival (days)	695	687	687	711
Survival analysis	P=0.368N	P=0.945	P=0.498	P=0.426N

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

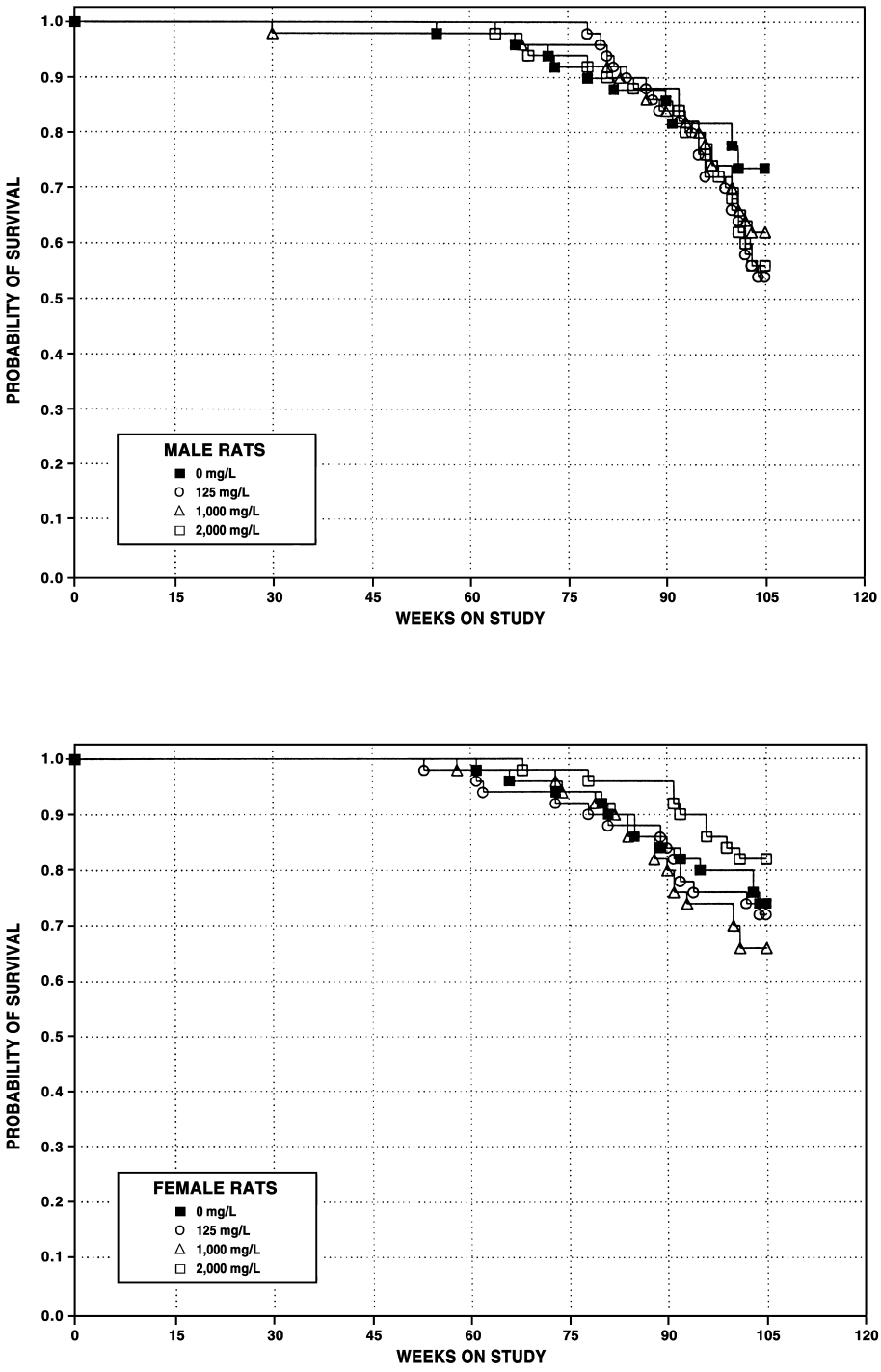


FIGURE 1
Kaplan-Meier Survival Curves for Male and Female Rats Exposed to Sodium Chlorate in Drinking Water for 2 Years

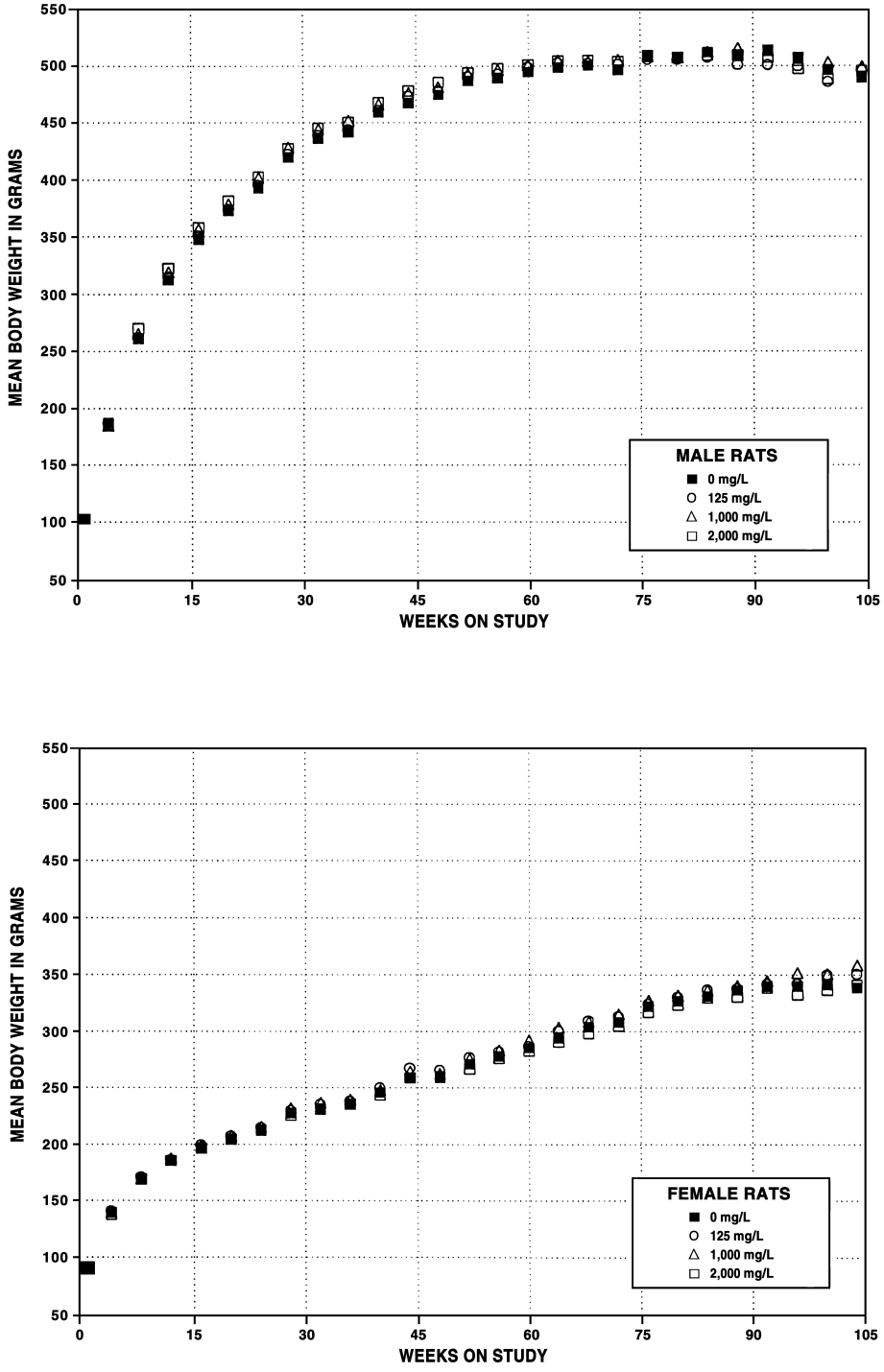


FIGURE 2
Growth Curves for Male and Female Rats Exposed to Sodium Chlorate in Drinking Water for 2 Years

TABLE 4
Mean Body Weights and Survival of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate

Weeks on Study	0 mg/L		125 mg/L			1,000 mg/L			2,000 mg/L		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	102	50	103	101	50	103	101	50	103	101	50
4	187	50	187	100	50	185	99	50	186	99	50
8	261	50	263	101	50	266	102	50	270	104	50
12	312	50	315	101	50	319	102	50	322	103	50
16	348	50	351	101	50	357	103	50	358	103	50
20	373	50	374	100	50	379	102	50	382	102	50
24	393	50	396	101	50	402	102	50	403	103	50
28	420	50	423	101	50	429	102	50	428	102	50
32	437	50	439	101	50	445	102	49	446	102	50
36	442	50	445	101	50	452	102	49	451	102	50
40	459	50	461	100	50	466	102	49	468	102	50
44	467	50	474	101	50	477	102	49	478	102	50
48	475	50	479	101	50	482	102	49	486	102	50
52	487	50	491	101	50	493	101	49	494	101	50
56	489	49	493	101	50	497	102	49	498	102	50
60	495	49	499	101	50	501	101	49	501	101	50
64	499	48	503	101	50	505	101	49	505	101	50
68	500	47	503	101	50	504	101	49	505	101	48
72	497	47	502	101	50	506	102	48	504	102	47
76	508	45	506	100	50	508	100	48	509	100	47
80	508	44	506	100	49	507	100	48	508	100	46
84	512	43	508	99	45	513	100	45	510	100	45
88	509	43	501	99	44	516	101	43	510	100	44
92	514	40[a]	501	98	41	514	100	42	508	99	43
96	507	40	500	99	38	505	100	40	498	98	40
100	497	40	486	98	35	504	101	37	488	98	36
104	490	36	497	101	28	500	102	31	496	101	28
Mean for weeks											
1-13	216		217	101		218	101		220	102	
14-52	430		433	101		438	102		439	102	
53-104	502		500	100		506	101		503	100	

[a] Number of animals weighed is less than the number of animals surviving.

TABLE 5
Mean Body Weights and Survival of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate

Weeks on Study	0 mg/L		125 mg/L			1,000 mg/L			2,000 mg/L		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	91	50	91	99	50	91	100	50	89	98	50
4	140	50	141	101	50	140	100	50	138	99	50
8	169	50	171	101	50	170	101	50	169	100	50
12	186	50	187	101	50	188	101	50	186	100	50
16	197	50	200	101	50	199	101	50	196	100	50
20	205	50	208	101	50	208	101	50	204	100	50
24	213	50	215	101	50	216	101	50	212	100	50
28	228	50	230	101	50	232	102	50	226	99	50
32	232	50	236	102	50	237	102	50	231	100	50
36	235	50	239	101	50	240	102	50	236	100	50
40	246	50	250	102	50	248	101	50	244	99	50
44	259	50	268	103	50	265	102	50	259	100	50
48	260	50	266	102	50	263	101	50	259	100	50
52	271	50	277	102	50	276	102	50	267	98	50
56	278	50	283	102	49	284	102	50	276	99	50
60	285	50	287	101	49	293	103	49	283	99	50
64	294	49	301	102	47	304	103	49	291	99	50
68	304	48	310	102	47	309	102	49	298	98	50
72	308	48	313	102	47	316	102	49	305	99	49
76	322	47	325	101	46	328	102	47	317	98	49
80	327	46	331	101	45	332	102	46	323	99	48
84	331	45	337	102	44	337	102	45	330	100	48
88	337	43	338	101	44	341	101	43	331	98	48
92	340	42	342	101	40	345	102	38	339	100	46
96	340	40	343	101	38	352	104	37	332	98	45
100	342	40	350	103	38	351	103	37	337	99	42
104	339	38	351	104	37	359	106	33	341	101	41
Mean for weeks											
1-13	147		148	101		147	101		146	99	
14-52	235		239	102		238	102		233	100	
53-104	319		324	102		327	103		316	99	

Thyroid Hormone Concentrations

Assays for thyroxine (T_4), triiodothyronine (T_3), and thyroid stimulating hormone (TSH) were conducted using special study rats on day 4, at week 3, and at week 14 (Table 6). Serum concentrations of T_4 and T_3 were significantly reduced in 1,000 and 2,000 mg/L males and females on day 4 and in 2,000 mg/L males and females at week 3. Serum concentrations of TSH generally increased with exposure concentration and were significantly increased in 1,000 and 2,000 mg/L males on day 4 and at week 3, in 1,000 and 2,000 mg/L females on day 4, in 2,000 mg/L females at week 3, and in 2,000 mg/L males and females at week 14.

TABLE 6
Serum Concentrations of Thyroid Hormones in Rats in the 2-Year Drinking Water Study of Sodium Chlorate[a]

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
n	10	10	10	10
Male				
Day 4				
T_4 (µg/dL)	4.67 ± 0.17	5.13 ± 0.20	3.60 ± 0.12**	2.62 ± 0.17**
T_3 (ng/dL)	124.60 ± 3.70	136.40 ± 4.67	95.800 ± 2.33**	80.50 ± 4.26**
TSH (ng/mL)	3.33 ± 0.14	2.75 ± 0.15	7.47 ± 0.81**	12.09 ± 0.63**
Week 3				
T_4 (µg/dL)	4.63 ± 0.17	4.54 ± 0.21	4.08 ± 0.18	2.71 ± 0.12**
T_3 (ng/dL)	88.10 ± 4.47	84.20 ± 4.15	77.80 ± 3.63	55.60 ± 3.16**
TSH (ng/mL)	3.34 ± 0.29[b]	2.58 ± 0.24	7.77 ± 1.21**	31.03 ± 4.72**
Week 14				
T_4 (µg/dL)	4.81 ± 0.23	4.63 ± 0.20	4.81 ± 0.15	4.89 ± 0.18
T_3 (ng/dL)	103.60 ± 5.82	99.70 ± 6.13	99.80 ± 5.33	96.80 ± 3.16
TSH (ng/mL)	2.75 ± 0.29	3.41 ± 0.36	3.64 ± 0.49	5.22 ± 0.60**
Female				
Day 4				
T_4 (µg/dL)	4.12 ± 0.19	4.41 ± 0.13	3.41 ± 0.11**	2.13 ± 0.21**
T_3 (ng/dL)	113.10 ± 2.97	120.20 ± 2.95	95.90 ± 2.82**	76.30 ± 4.26**
TSH (ng/mL)	2.46 ± 0.22	2.67 ± 0.19	4.57 ± 0.40**	10.96 ± 1.14**
Week 3				
T_4 (µg/dL)	3.87 ± 0.27	3.63 ± 0.15	3.79 ± 0.17[b]	2.35 ± 0.14**
T_3 (ng/dL)	88.00 ± 6.27[c]	84.20 ± 2.90	80.22 ± 3.60[b]	60.00 ± 2.95**
TSH (ng/mL)	1.99 ± 0.20	1.75 ± 0.13	2.85 ± 0.37	13.77 ± 1.79**
Week 14				
T_4 (µg/dL)	3.63 ± 0.20	3.87 ± 0.15	3.60 ± 0.28	3.19 ± 0.22
T_3 (ng/dL)	100.90 ± 2.70	106.80 ± 4.43	102.70 ± 7.18	94.60 ± 3.32
TSH (ng/mL)	2.10 ± 0.32	2.71 ± 0.26	2.38 ± 0.32	3.74 ± 0.61*

* Significantly different ($P \leq 0.05$) from the control group by Shirley's test
** $P \leq 0.01$
[a] Data are presented as mean ± standard error. Statistical tests were performed on unrounded data. T_4=thyroxine; T_3=triiodothyronine; TSH=thyroid stimulating hormone
[b] n=9
[c] n=7

Pathology and Statistical Analyses

This section describes the statistically significant or biologically noteworthy changes in the incidences of mononuclear cell leukemia and neoplasms and/or nonneoplastic lesions of the thyroid gland, spleen, and bone marrow. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group, and the historical incidences for the neoplasms mentioned in this section are presented in Appendix A for male rats and Appendix B for female rats.

Thyroid Gland: Slightly enlarged thyroid glands were observed in 1,000 and 2,000 mg/L special study male rats and 2,000 mg/L special study female rats at 14 weeks. All special study rats in the 1,000 and 2,000 mg/L groups had follicular cell hypertrophy at 3 and 14 weeks; this lesion did not occur in control rats (Table 7).

There were positive trends in the incidences of follicular cell carcinoma in male rats and in follicular cell adenoma or carcinoma (combined) in males and females (Tables 8, A3, and B3). The incidences of follicular cell adenoma, follicular cell carcinoma, and follicular cell adenoma or carcinoma (combined) in 2,000 mg/L males and females exceeded the historical ranges for drinking water controls (Tables 8, A4, and B4). Microscopically, adenomas were well demarcated, focal, expansile masses consisting of well-differentiated thyroid follicular epithelial cells forming follicular structures with central colloid. Increased cell density occasionally led to the formation of papillary projections into the lumens of the follicle (Plate 1). Histologically, carcinomas were less well demarcated and less well differentiated and consisted of glandular to solid hypercellular masses of pleomorphic thyroid epithelial cells (Plate 2). Occasionally, invasion into the peripheral thyroid was noted.

The incidences of follicular cell hypertrophy in all exposed groups of males and in 1,000 and 2,000 mg/L females at 2 years were significantly greater than those in the control groups and the severity was increased in 2,000 mg/L males and females (Tables 8, A5, and B5). Histologically, the normal thyroid gland is composed of variably-sized follicles containing eosinophilic material (colloid) within the lumens (Plate 3). These follicles range in size from very small (approximately

TABLE 7
Incidences of Thyroid Gland Follicular Cell Hypertrophy in Special Study Rats at Week 3 and Week 14 in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Male				
Number Examined Microscopically	10	10	10	10
Week 3[a,b]	0	0	10** (2.0)[c]	10** (2.0)
Week 14	0	0	10** (2.0)	10** (2.0)
Female				
Number Examined Microscopically	10	10	10	10
Week 3[b]	0	0	10** (2.0)	10** (2.0)
Week 14	0	0	10** (1.0)	10** (2.0)

** Significantly different ($P \leq 0.01$) from the control group by the Fisher exact test
[a] Number of animals with lesion
[b] In Hooth *et al.* (2001), thyroid gland follicular cell hyperplasia was diagnosed.
[c] Average severity grade of lesions of affected animals: 1=minimal, 2=mild

TABLE 8
Incidences of Neoplasms and Nonneoplastic Lesions of the Thyroid Gland in Rats in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Male				
Number Examined Microscopically	47	44	43	47
Follicular Cell, Hypertrophy[a]	4 (1.3)[b]	13* (1.2)	33** (1.5)	40** (2.0)
Follicular Cell, Adenoma[c]	1	0	0	2
Follicular Cell, Carcinoma[d]				
Overall rate[e]	0/47 (0%)	0/44 (0%)	0/43 (0%)	4/47 (9%)
Adjusted rate[f]	0.0%	0.0%	0.0%	9.6%
Terminal rate[g]	0/36 (0%)	0/27 (0%)	0/31 (0%)	4/28 (14%)
First incidence (days)	—[h]	—	—	729 (T)
Poly-3 test[i]	P=0.003	—[j]	—	P=0.058
Follicular Cell, Adenoma or Carcinoma[k]				
Overall rate	1/47 (2%)	0/44 (0%)	0/43 (0%)	6/47 (13%)
Adjusted rate	2.4%	0.0%	0.0%	14.4%
Terminal rate	0/36 (0%)	0/27 (0%)	0/31 (0%)	6/28 (21%)
First incidence (days)	705	—	—	729 (T)
Poly-3 test	P=0.002	P=0.512N	P=0.513N	P=0.052
Female				
Number Examined Microscopically	47	47	43	46
Follicular Cell, Hypertrophy	3 (1.3)	7 (1.0)	27** (1.2)	42** (1.8)
Follicular Cell, Mineralization	25 (1.0)	26 (1.0)	40** (1.3)	44** (2.1)
Follicular Cell, Adenoma[l]	0	0	0	2
Follicular Cell, Carcinoma[m]	1	0	1	2
Follicular Cell, Adenoma or Carcinoma[n]				
Overall rate	1/47 (2%)	0/47 (0%)	1/43 (2%)	4/46 (9%)
Adjusted rate	2.3%	0.0%	2.6%	9.1%
Terminal rate	1/36 (3%)	0/36 (0%)	0/32 (0%)	2/40 (5%)
First incidence (days)	729 (T)	—	703	644
Poly-3 test	P=0.026	P=0.503N	P=0.741	P=0.189

* Significantly different ($P \leq 0.05$) from the control group by the Poly-3 test
** $P \leq 0.01$
(T) Terminal sacrifice
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked
[c] Historical incidence for 2-year drinking water studies with controls given NTP-2000 diet (mean ± standard deviation): 3/139 (2.2% ± 0.3%), range 2%
[d] Historical incidence: 1/139 (1.0% ± 1.4%), range 0%-2%
[e] Number of animals with neoplasm per number of animals with thyroid gland examined microscopically
[f] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[g] Observed incidence at terminal kill
[h] Not applicable; no neoplasms in animal group
[i] Beneath the control incidence is the P value associated with the trend test. Beneath the exposed group incidences are the P values corresponding to pairwise comparisons between the controls and that exposed group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice. A lower incidence in an exposed group is indicated by **N**.
[j] Value of statistic cannot be computed.
[k] Historical incidence: 4/139 (3.2% ± 1.1%), range 2%-4%
[l] Historical incidence: 1/142 (1.0% ± 1.4%), range 0%-2%
[m] Historical incidence: 3/142 (2.1% ± 0.2%), range 2%
[n] Historical incidence: 4/142 (3.1% ± 1.3%), range 2%-4%

50 microns) containing little colloid to relatively large (several hundred microns) filled with colloid. In smaller follicles, the epithelium is generally cuboidal, while more attenuated in glands distended with colloid. Following sodium chlorate administration, there was an exposure concentration-related increase in the percentage of smaller follicles, and these follicles contained sparse amounts of generally pale, often vacuolated appearing colloid (colloid depletion). The lining epithelium of affected glands appeared more prominent, ranging from cuboidal to somewhat columnar (Plate 4).

The incidences of focal follicle mineralization in 1,000 and 2,000 mg/L females were significantly greater than that in the control group (Tables 8 and B5), and the severity was increased in the 2,000 mg/L group. This lesion consisted of basophilic, ovoid-shaped bodies in the colloid of some of the thyroid follicles. This is a common aging change, but the increased incidences may have been exacerbated by exposure to sodium chlorate.

Spleen: The incidence of hematopoietic cell proliferation was significantly increased in 2,000 mg/L males when compared to the control group (0 mg/L, 2/48, severity grade 2.5; 125 mg/L, 6/49, severity grade 2.3; 1,000 mg/L, 4/49, severity grade 2.5; 2,000 mg/L, 11/50, severity grade 2.5; Table A5). Histologically, this lesion was characterized by an increase in erythroid and myeloid cells within the red pulp. While the increase in hematopoietic cell proliferation was modest and not observed in the 3-week study, this finding is consistent with hematological effects observed in humans and other animal species administered sodium chlorate.

Bone Marrow: The incidences of bone marrow hyperplasia were significantly increased in 1,000 and 2,000 mg/L males when compared to the control group (0 mg/L, 28/48; 125 mg/L, 35/48; 1,000 mg/L, 41/50; 2,000 mg/L, 40/49; Table A5). The severity grades of this lesion were greater in all treatment groups when compared to controls (1.9, 2.3, 2.4, 2.7). Microscopically, bone marrow hyperplasia was characterized by an increase of hematopoietic cells in the marrow cavity. Though histological evaluation of bone marrow sections is generally a crude assessment of erythroid and/or myeloid response, the increases in hyperplasia incidence and severity suggest this was a treatment-related effect.

Mononuclear Cell Leukemia: The incidence of mononuclear cell leukemia was significantly increased in the male 2,000 mg/L group when compared to controls (13/50, 21/50, 16/50, 23/50; Table A3). However, the incidences of this lesion in all exposed groups fell within the historical range in controls (all routes) [514/1,159 (43.1% ± 12.8%), range 22% to 68%]. Because the incidence of mononuclear cell leukemia in the control group was at the low end of the historical control range and near average in the exposed groups, this lesion was not attributed to sodium chlorate administration.

MICE

3-WEEK STUDY

All mice survived to the end of the study (Table 9). Final mean body weights and body weight gains (except body weight gain of 500 mg/L females) of all exposed groups of mice were similar to those of the control groups. Water consumption by exposed mice was generally similar to that by the control groups throughout the study. Drinking water concentrations of 125, 250, 500, 1,000, and 2,000 mg/L resulted in average daily doses of approximately 20, 45, 90, 175, and 350 mg/kg per day for male mice and 20, 45, 95, 190, and 365 mg/kg per day for female mice. No clinical findings attributed to sodium chlorate exposure were observed.

At the exposure concentrations selected, no chemical-related changes in hematology parameters occurred (Table F2). There were no significant differences in organ weights between control and exposed groups (Table G2). No exposure-related lesions occurred in male or female mice.

Exposure Concentration Selection Rationale: Because sodium chlorate produced no biologically significant changes in any of the parameters examined in male or female B6C3F$_1$ mice, exposure concentrations of 500, 1,000, and 2,000 mg/L were selected for the 2-year study in B6C3F$_1$ mice.

TABLE 9
Survival, Body Weights, and Water Consumption of Mice in the 3-Week Drinking Water Study of Sodium Chlorate

Concentration (mg/L)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Week 1	Week 3
Male							
0	10/10	24.5 ± 0.2	27.7 ± 0.3	3.3 ± 0.2		4.6	4.9
125	10/10	24.2 ± 0.3	28.0 ± 0.3	3.8 ± 0.2	101	4.6	4.7
250	10/10	24.4 ± 0.2	28.0 ± 0.4	3.7 ± 0.2	101	4.6	4.5
500	10/10	23.9 ± 0.4	28.0 ± 0.3	4.1 ± 0.5	101	4.6	4.6
1,000	10/10	24.2 ± 0.3	27.5 ± 0.3	3.3 ± 0.2	99	4.4	4.7
2,000	10/10	24.3 ± 0.3	27.9 ± 0.4	3.6 ± 0.2	101	4.3	5.0
Female							
0	10/10	19.1 ± 0.2	21.3 ± 0.3	2.2 ± 0.3		2.8	3.6
125	10/10	18.9 ± 0.3	21.3 ± 0.2	2.4 ± 0.3	100	2.8	3.5
250	10/10	18.8 ± 0.3	20.9 ± 0.1	2.1 ± 0.2	98	3.3	3.7
500	10/10	19.1 ± 0.1	20.4 ± 0.2	1.3 ± 0.2*	96	3.0	4.7
1,000	10/10	19.0 ± 0.3	21.1 ± 0.3	2.1 ± 0.2	99	3.5	4.8
2,000	10/10	18.3 ± 0.2	20.7 ± 0.3	2.3 ± 0.3	97	2.7	3.8

* Significantly different ($P \le 0.05$) from the control group by Dunnett's test
[a] Number of animals surviving at 22 days/number initially in group
[b] Weights and weight changes are given as mean ± standard error.
[c] Water consumption is expressed as grams per animal per day.

2-YEAR STUDY

Survival

Estimates of 2-year survival probabilities for male and female mice are shown in Table 10 and in the Kaplan-Meier survival curves (Figure 3). Survival of exposed mice was similar to that of the control groups.

TABLE 10
Survival of Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Male				
Animals initially in study	50	50	50	50
Moribund	5	5	4	10
Natural deaths	7	4	5	7
Animals surviving to study termination	38	41	41	33
Percent probability of survival at end of study[a]	76	82	82	66
Mean survival (days)[b]	694	712	708	689
Survival analysis[c]	P=0.192	P=0.538N	P=0.577N	P=0.423
Female				
Animals initially in study	50	50	50	50
Accidental death[d]	1	0	0	0
Other[d]	0	0	1	0
Moribund	3	5	6	8
Natural deaths	10	10	12	7
Animals surviving to study termination	36	35[e]	31	35
Percent probability of survival at end of study	74	70	63	70
Mean survival (days)	687	700	679	682
Survival analysis	P=0.728	P=0.937	P=0.426	P=0.871

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

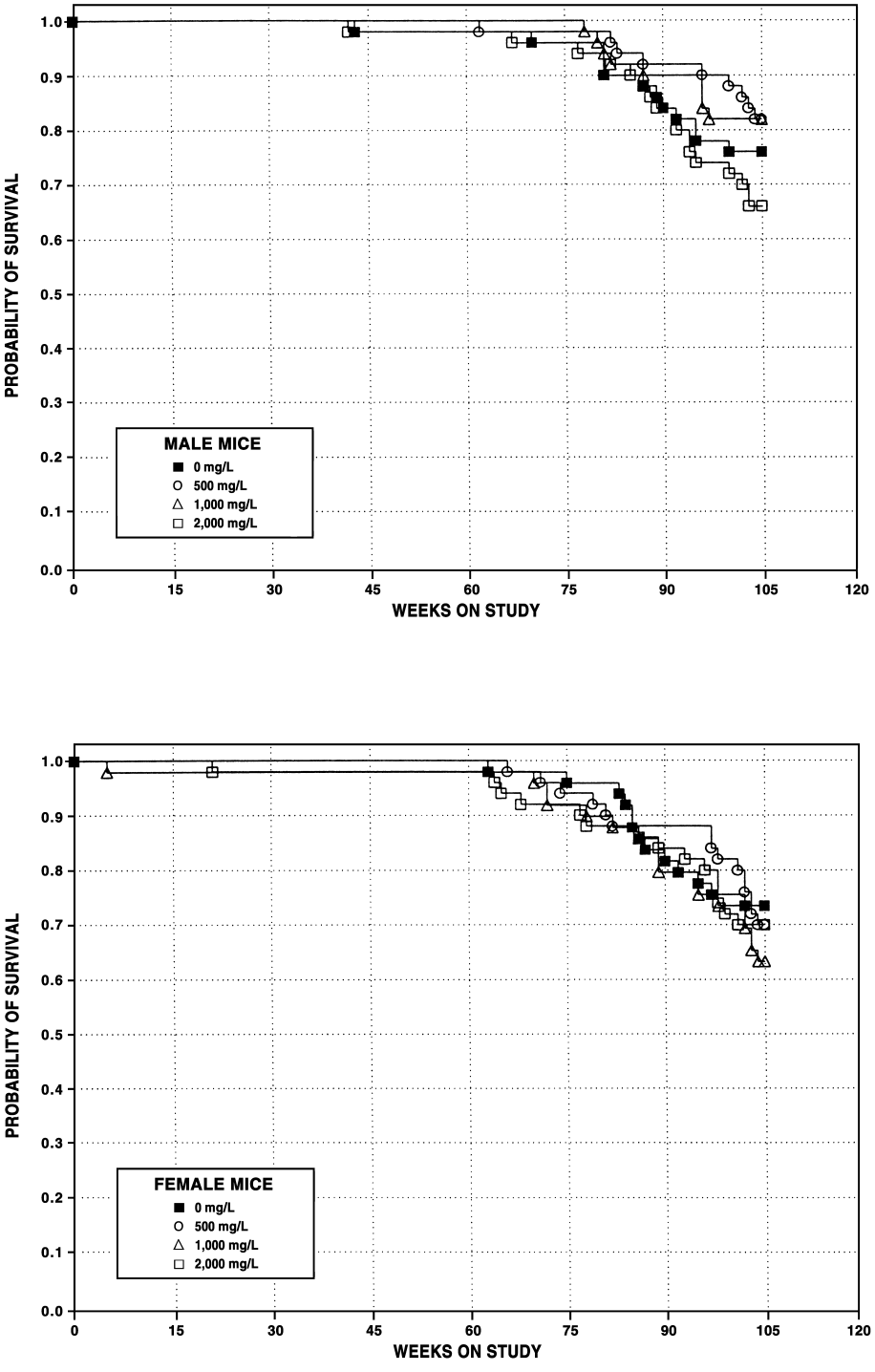


FIGURE 3
Kaplan-Meier Survival Curves for Male and Female Mice Exposed to Sodium Chlorate in Drinking Water for 2 Years

Body Weights, Water and Compound Consumption, and Clinical Findings

The mean body weights of exposed groups of males were similar to those of the control group throughout the study (Table 11 and Figure 4). Body weights of 500 and 1,000 mg/L females were less than those of the controls after week 84, and those of 2,000 mg/L females were less after week 88 of the study (Table 12 and Figure 4).

Water consumption by exposed mice was generally similar to that by controls throughout the study (Tables I3 and I4). Drinking water concentrations of 500, 1,000, and 2,000 mg/L resulted in average daily doses of approximately 40, 80, and 160 mg/kg per day for male mice and 30, 60, and 120 mg/kg per day for female mice. No clinical findings related to sodium chlorate exposure were observed.

TABLE 11
Mean Body Weights and Survival of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate

Weeks on Study	0 mg/L		500 mg/L			1,000 mg/L			2,000 mg/L		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	22	50	22	101	50	22	100	50	22	101	50
4	28	50	28	99	50	28	100	50	28	100	50
8	34	50	33	98	50	34	99	50	34	100	50
12	39	50	38	99	50	38	99	50	39	100	50
16	44	50	43	99	50	44	100	50	44	100	50
20	47	50	47	99	50	47	101	50	47	100	50
24	50	50	49	99	50	49	99	50	50	100	50
28	51	50	50	99	50	50	99	50	50	99	50
32	51	50	50	98	50	50	98	50	50	99	50
36	51	50	51	99	50	51	99	50	51	100	50
40	52	50	51	99	50	51	99	50	52	100	50
44	52	49	51	98	50	51	98	50	52	100	49
48	53	49	52	98	50	52	98	50	53	100	49
52	53	49	52	99	50	52	99	50	53	101	49
56	53	49	52	99	50	52	99	50	53	100	49
60	53	49	52	99	50	53	99	50	53	100	49
64	53	49	53	100	49	53	99	50	53	100	49
68	53	49	54	101	49	53	100	50	55	102	48
72	54	48	53	99	49	53	98	50	54	100	48
76	54	48	53	99	49	52	97	50	54	101	48
80	53	48	52	100	49	52	99	49	53	101	47
84	53	45	52	99	47	53	100	46	52	98	46
88	52	44	51	99	46	52	101	45	51	98	44
92	51	41	51	99	46	51	101	45	50	97	42
96	51	39	50	98	45	50	99	44	50	98	37
100	49	39	47	97	45	48	99	41	48	99	36
104	47	38	45	97	41	47	100	41	49	104	33
Mean for weeks											
1-13	31		30	99		31	100		31	100	
14-52	50		50	99		50	99		50	100	
53-104	52		51	99		51	99		52	100	

TABLE 12
Mean Body Weights and Survival of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

Weeks on Study	0 mg/L		500 mg/L			1,000 mg/L			2,000 mg/L		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	18	50	18	99	50	18	100	50	18	100	50
4	22	50	22	100	50	22	100	50	22	99	50
8	27	50	27	97	50	27	99	48	26	96	50
12	32	50	31	98	50	32	99	48	30	94	50
16	37	50	36	98	50	36	99	48	35	96	50
20	42	50	42	99	50	42	100	48	41	97	50
24	47	50	47	99	50	47	100	48	45	96	49
28	50	50	50	100	50	50	101	48	49	97	49
32	53	50	52	99	50	53	100	48	51	98	49
36	54	50	54	100	50	54	100	48	53	97	49
40	58	49	58	100	50	57	99	48	56	97	49
44	58	49	59	100	50	57	98	48	57	97	49
48	60	49	60	99	50	59	97	48	59	98	49
52	61	49	61	100	50	60	98	48	61	99	49
56	61	49	61	100	50	60	98	48	61	100	49
60	62	49	61	98	50	61	98	48	62	100	49
64	63	48	62	99	50	63	100	48	62	99	49
68	63	48	62	98	49	63	99	48	64	101	47
72	64	48	62	96	48	63	98	47	65	101	46
76	65	47	64	98	47	64	99	45	65	99	46
80	67	47	65	97	46	65	98	44	65	98	44
84	66	46	65	99	44	64	98	43	65	99	44
88	66	41	63	95	44	62	94	42	64	97	43
92	65	39	60	93	44	62	96	39	62	95	42
96	64	38	58	90	44	60	94	37	59	91	41
100	63	37	56	89	41	57	91	36	59	93	36
104	61	36	54	88	36	55	90	31	55	90	35
Mean for weeks											
1-13	25		25	99		25	100		24	97	
14-52	52		52	99		52	99		51	97	
53-104	64		61	95		61	96		62	97	

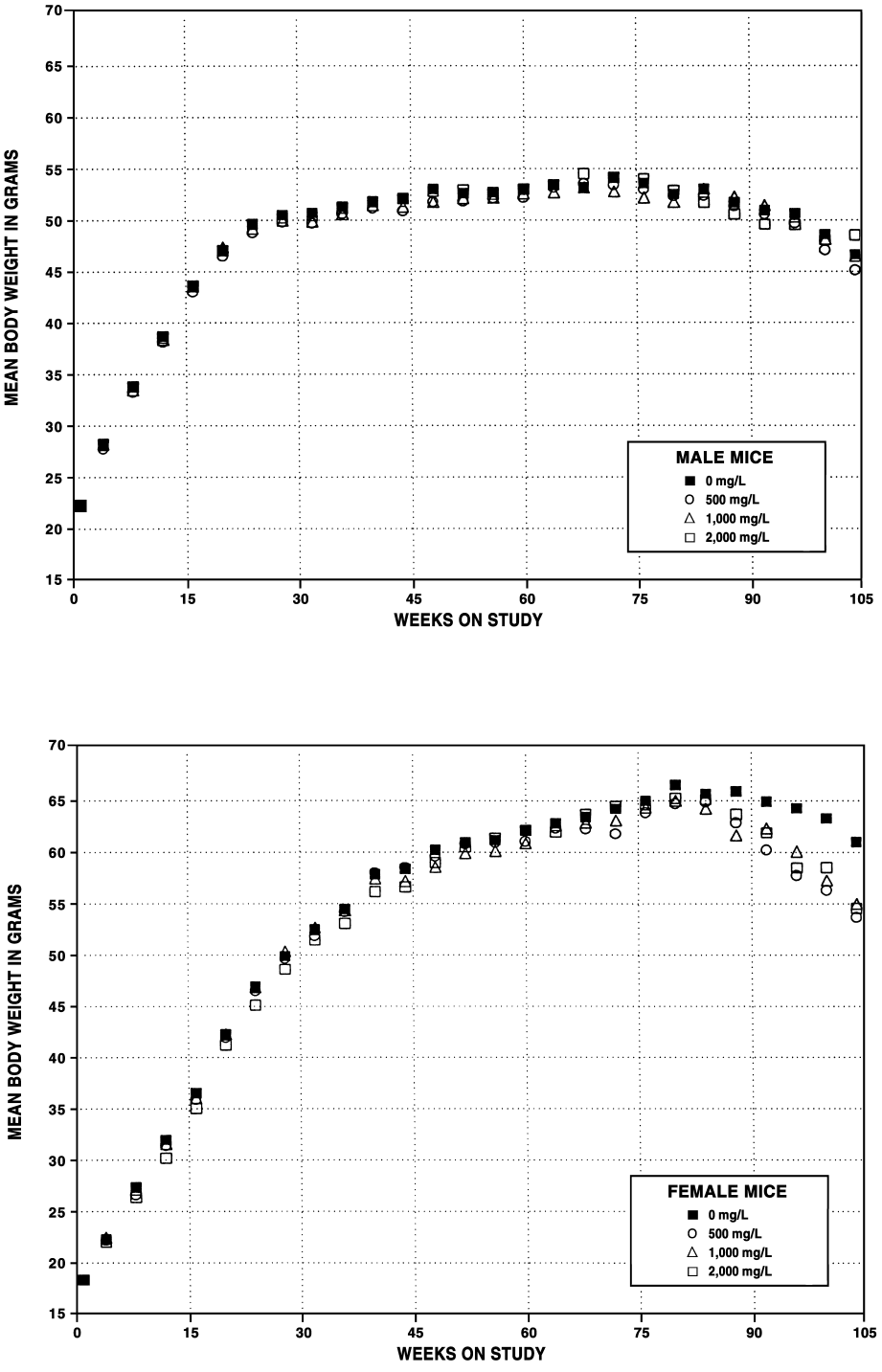


FIGURE 4
Growth Curves for Male and Female Mice Exposed to Sodium Chlorate in Drinking Water for 2 Years

Pathology and Statistical Analyses

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

Pancreatic Islets: There was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) (Tables 13, D1, and D3) in female mice that was composed primarily of adenomas (three of four neoplasms in the 2,000 mg/L group). The incidences of pancreatic islet adenoma and adenoma or carcinoma (combined) in 2,000 mg/L females exceeded the historical ranges for drinking water controls (Tables 13, D1, D3, and D4a). The incidences of hyperplasia decreased with increasing exposure concentration. Histologically, islet cell adenomas were characterized by enlarged islets composed of focal accumulations of well-differentiated islet cells with variable stromal components that compressed the adjacent parenchyma. On occasion, normal acinar cells were entrapped within the tumor. Because size is often considered an important criterion for discerning adenomas of endocrine organs, including the islets, it was noted that adenomas diagnosed in this study were significantly larger than those considered to be hyperplastic. In general, the hyperplastic lesions were smaller, affected multiple islets, and did not compress surrounding acinar tissue.

Liver: The incidences of hepatocellular carcinoma were significantly greater in 500 and 1,000 mg/L females than in the control group (0 mg/L, 3/49; 500 mg/L, 13/50; 1,000 mg/L, 15/49; 2,000 mg/L, 9/50; Tables D1 and D3). Although not statistically significant, the incidence in 2,000 mg/L females was also increased. The incidences in all exposed groups of females exceeded the historical range for drinking water controls [12/149 (8%), range 4% to 14%; Table D4b]. Microscopically, these neoplasms were not well demarcated, primarily trabecular in growth pattern, and characterized by cords of atypical hepatocytes. When incidences of hepatocellular adenoma (30/49, 19/50, 26/49, 23/50) and carcinoma were combined (31/49, 26/50, 31/49, 26/50), there was no chemical effect. Due to this fact and because the increases were not exposure concentration-related, these carcinomas were not considered to be induced by sodium chlorate.

Thyroid Gland: The incidence of minimal follicular cell hypertrophy was significantly increased in 2,000 mg/L female mice when compared to the control group (0 mg/L, 3/48, severity grade 1.3; 500 mg/L, 2/50, severity grade 2.0; 1,000 mg/L, 5/49, severity grade 1.0; 2,000 mg/L, 14/50, severity grade 1.4; Table D5). Histologically, affected follicles appeared small and were lined by slightly enlarged epithelial cells. The lumens of these follicles contained sparse amounts of generally pale colloid.

The incidence of thyroid gland cystic degeneration was significantly increased in 1,000 mg/L females when compared to the control group (25/48, 28/50, 34/49, 32/50; Table D5). Microscopically, there were variations in follicle size, often with coalescence of contiguous, large follicles to form multilocular cysts. These cysts were usually lined by flattened epithelial cells, separated by variable amounts of connective tissue, and filled with pale colloid. Thyroid gland cystic degeneration was considered an aging change and not related to sodium chlorate administration.

Bone Marrow: The incidences of bone marrow hyperplasia were significantly increased in all exposed groups of female mice when compared to the control group (14/50, 28/50, 29/50, 31/50; Table D5). The severity of this lesion in exposed females was slightly greater than in the controls (2.4, 2.6, 2.9, 2.7). Microscopically, bone marrow hyperplasia was characterized by an increase of hematopoietic cells in the marrow cavity. As in the rat, the increases in incidence and severity suggest a treatment-related effect.

Ovary: The incidence of granulosa cell hyperplasia of the ovary was significantly increased in 2,000 mg/L female mice when compared to the control group (0/45, 0/45, 3/47, 7/50; Table D5). Microscopically, granulosa cell hyperplasia was characterized by one or more foci or a diffuse increase in the number of granulosa or luteal cells as pure or mixed populations. It was often difficult to discern focal hyperplastic changes from enlarged copora lutea. In general, these were not considered to be preneoplastic lesions.

TABLE 13
Incidences of Neoplasms and Nonneoplastic Lesions of the Pancreatic Islets in Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Male				
Number Examined Microscopically	48	50	50	50
Hyperplasia[a]	31 (2.4)[b]	25 (2.3)	28 (2.5)	23 (2.3)
Female				
Number Examined Microscopically	46	47	49	49
Hyperplasia	9 (1.7)	6 (2.0)	4 (2.3)	3 (2.0)
Adenoma[c]				
Overall rate[d]	0/46 (0%)	2/47 (4%)	2/49 (4%)	3/49 (6%)
Adjusted rate[e]	0.0%	4.5%	4.8%	6.8%
Terminal rate[f]	0/36 (0%)	1/35 (3%)	2/31 (7%)	1/35 (3%)
First incidence (days)	—[g]	706	729 (T)	475
Poly-3 test[h]	P=0.112	P=0.248	P=0.235	P=0.125
Adenoma or Carcinoma[c]				
Overall rate	0/46 (0%)	2/47 (4%)	2/49 (4%)	4/49 (8%)
Adjusted rate	0.0%	4.5%	4.8%	9.1%
Terminal rate	0/36 (0%)	1/35 (3%)	2/31 (7%)	2/35 (6%)
First incidence (days)	—	706	729 (T)	475
Poly-3 test	P=0.045	P=0.248	P=0.235	P=0.065

(T) Terminal sacrifice
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked
[c] Historical incidence for 2-year drinking water studies with controls given NTP-2000 diet (mean ± standard deviation): 2/146 (1.4% ± 2.3%), range 0%-4%.
[d] Number of animals with neoplasm per number of animals with pancreatic islets examined microscopically
[e] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[f] Observed incidence at terminal kill
[g] Not applicable; no neoplasms in animal group
[h] Beneath the control incidence is the P value associated with the trend test. Beneath the exposed group incidences are the P values corresponding to pairwise comparisons between the controls and that exposed group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice.

GENETIC TOXICOLOGY

Sodium chlorate (100 to 10,000 µg/plate) was not mutagenic in *Salmonella typhimurium* strains TA97, TA98, TA100, TA102, TA104, and TA1535, with or without induced rat or hamster liver S9 enzymes. *In viv*o, no increases in the frequencies of micronucleated normochromatic erythrocytes (NCEs) were seen in peripheral blood samples from male and female $B6C3F_1$ mice exposed to concentrations of 125 to 2,000 mg/L sodium chlorate in drinking water for 3 weeks. The abbreviated exposure duration of 3 weeks may not have allowed steady state to be reached in the circulating NCE population, but the data are clearly negative, with no indication of an exposure concentration-related increase in NCEs. Steady state is usually established by day 35 of continuous exposure.

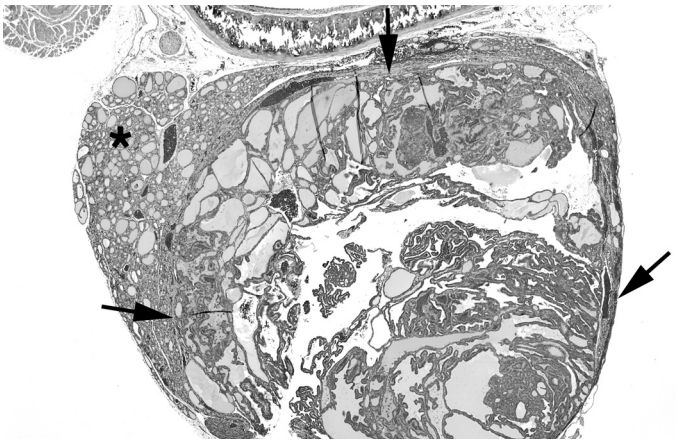


PLATE 1
Follicular cell adenoma (arrows) in the thyroid gland of a male F344/N rat exposed to 2,000 mg/L sodium chlorate in drinking water for 2 years. Note the normal portion of the thyroid gland to the upper left (asterisk). H&E; 4×

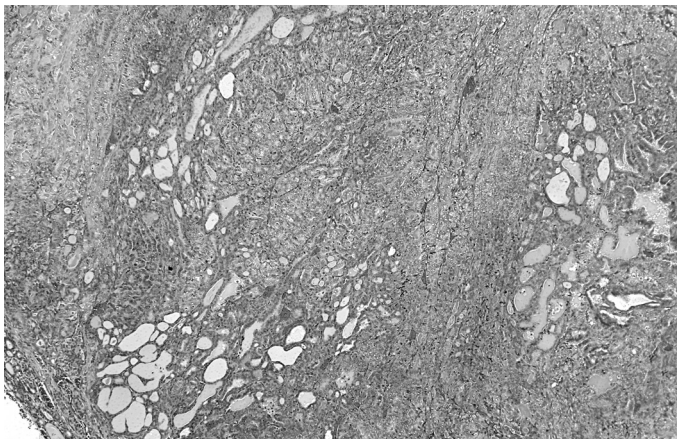


PLATE 2
Follicular cell carcinoma in the thyroid gland of a male F344/N rat exposed to 2,000 mg/L sodium chlorate in drinking water for 2 years. H&E; 8×

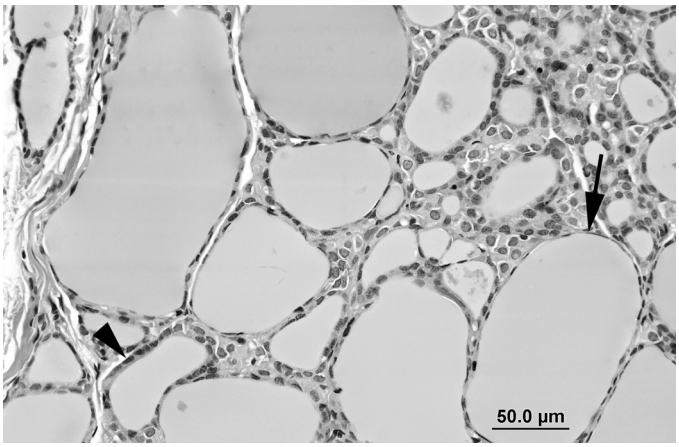


PLATE 3
Thyroid gland of a control male F344/N rat in the 2-year drinking water study of sodium chlorate. Note the variably-sized follicles lined by cuboidal (arrowhead) to attenuated (arrow) epithelium. H&E; 40×

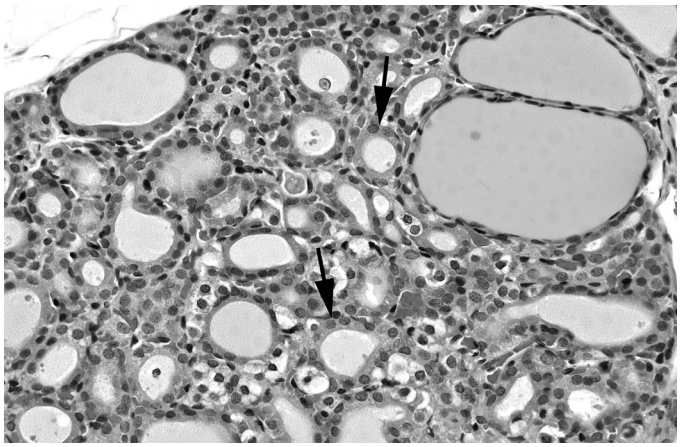


PLATE 4
Follicular cell hypertrophy in the thyroid gland of a male F344/N rat exposed to 2,000 mg/L sodium chlorate in drinking water for 2 years. Note the predominance of small follicles lined by enlarged epithelial cells (arrows) when compared to follicles in Plate 3. H&E; 40×

DISCUSSION AND CONCLUSIONS

Sodium chlorate is found as a stable by-product in drinking water that has been disinfected with chlorine dioxide. Disinfection with chlorine dioxide, a strong oxidant, is being considered as an alternative to chlorine, which produces trihalomethanes in finished drinking water. Chlorine dioxide is more effective than chlorine for killing most microorganisms, produces fewer chlorinated by-products, and does not produce significant levels of trihalomethanes (Richardson, 1998). However, sodium chlorate has been identified as a by-product of chlorine dioxide disinfection. Sodium chlorate was nominated for study by the United States Environmental Protection Agency (USEPA) because of widespread consumer exposure to treated drinking water and a lack of carcinogenicity data.

In the 3-week and 2-year rat studies, there were no chemical-related deaths. Administration of sodium chlorate did not produce any clinical findings of toxicity and had no significant effect on body weights or water consumption of rats of either sex. The thyroid gland was considered to be a target organ for sodium chlorate toxicity in the 3-week study because of the significantly increased incidences of thyroid gland follicular cell hypertrophy in 500 mg/L or greater males and females.

Administration of sodium chlorate to male and female rats caused significant exposure concentration-related decreases in serum concentrations of triiodothyronine (T_3) and thyroxine (T_4) and significant increases in serum concentrations of thyroid stimulating hormone (TSH) that were evident by day 4 and persisted through week 3 of the 2-year study. The higher concentrations of circulating TSH appear to have effectively restored T_3 and T_4 concentrations nearly to control levels by week 14 in all exposed groups. By week 14, serum TSH concentrations in 2,000 mg/L rats had declined significantly from the peak levels observed at week 3 but remained slightly elevated compared to control animals. Hormone levels may return to normal because of a homeostatic compensatory increase in cell proliferation with subsequent thyroid hormone production. Hood *et al.* (1999) demonstrated that small increases in serum TSH (between 10 and 20 ng/mL) can be sufficient to stimulate thyroid cell proliferation and thyroid gland growth. In fact, several special study rats had enlarged thyroid glands at the 14-week evaluation, indicating increased cellular growth. Although thyroid hormone levels were not measured after week 14, chronic stimulation of the thyroid gland by TSH has been shown to increase the susceptibility of rats to follicular-cell-derived tumors in long-term bioassays (Capen, 1997).

Significant changes in serum hormone levels were observed within a few days of exposure, providing early evidence that sodium chlorate disrupts the hypothalamic-thyroid-pituitary axis. Bercz *et al*. (1982) reported that exposure of African green monkeys to chlorine dioxide, but not chlorate, resulted in decreased serum T_4 levels. In a subsequent study, Harrington *et al.* (1986) noted a decrease in T_4 levels in both Sprague-Dawley rats and African green monkeys exposed to drinking water containing 0.1 g/L chlorine dioxide. Decreased T_4 levels were associated with increased binding of dietary iodide to gastrointestinal tissue and contents. These observations led to the hypothesis that chlorine dioxide oxidizes iodide in food to a reactive species that binds to tissues of the digestive tract, preventing absorption of dietary iodide. This effect produces a functional state of iodine deficiency that promotes increased iodide uptake by the thyroid gland.

In the 2-year rat study, there were positive trends in the incidences of thyroid gland follicular cell carcinoma in males and in follicular cell adenoma or carcinoma (combined) in males and females. The incidences of follicular cell adenoma, carcinoma, and adenoma or carcinoma (combined) in 2,000 mg/L males and females exceeded the historical ranges for drinking water controls. Additional thyroid gland effects were observed, including alterations in thyroid hormone levels, follicular cell hypertrophy in males and females in the 3-week study, follicular cell hypertrophy at 3 and 14 weeks in special study rats, and increased incidences of follicular cell hypertrophy in all exposed groups of males and in

1,000 and 2,000 mg/L females in the 2-year study. Furthermore, the incidence of follicular cell hypertrophy was significantly increased in 2,000 mg/L female mice. Based on these data, the increased incidences of thyroid gland neoplasms were considered to be related to sodium chlorate exposure.

Chlorate is chemically similar to perchlorate and bromate; both are thyroid gland toxicants and chemical oxidants. Perchlorate (ClO_4^-) is an anion that originates as a contaminant in groundwater and surface water from the dissolution of its ammonium, potassium, magnesium, or sodium salt. The primary target tissue for perchlorate toxicity is the thyroid gland, as indicated by perturbations of T_3, T_4, and TSH and by histopathology. Benign tumors and follicular cell carcinomas have been reported in the thyroid gland of male Wistar rats and female BALB/c mice after repeated high exposures (2 years at 1,339 mg/kg per day and 46 weeks at 2,147 mg/kg per day, respectively) of potassium perchlorate in drinking water (Kessler and Krunkemper, 1966; Pajer and Kalisnik, 1991). The mode-of-action for perchlorate toxicity is the competitive inhibition of iodide anion uptake by the sodium-iodide symporter, a carrier protein responsible for the active transport of iodide across the basolateral membrane of the thyroid gland epithelial cells (Wolff, 1998). Thyroid hormone synthesis is inhibited, resulting in decreased levels of T_3 and T_4, increased TSH levels, and stimulation of thyroid cell proliferation.

Bromate is one of the most prevalent water disinfection by-products associated with ozonation (Glaze, 1986; Cavanagh *et al.*, 1992). Potassium bromate is carcinogenic in the rat thyroid gland, producing adenomas and carcinomas at water concentrations as low as 0.02 g/L (20 ppm; 1.5 mg/kg/day; DeAngelo *et al*., 1998; Wolf *et al.*, 1998). The mechanism by which potassium bromate induces thyroid gland tumors is not known. Bromide binds to the sodium-iodide symporter of the thyroid gland with low affinity (Van Sande *et al.*, 2003). High levels of bromide result in a decrease in iodide accumulation in the thyroid gland and a rise in iodide excretion by the kidneys, resulting in decreased thyroid hormone synthesis and stimulation of thyroid cell proliferation (Pavelka, 2004).

The mechanism by which sodium chlorate induces thyroid gland follicular cell adenomas and carcinomas has not been determined. Chlorate may interfere with iodide uptake indirectly or directly, in a similar manner to chlorine dioxide or perchlorate, respectively, resulting in stimulation of thyroid follicular cell proliferation mediated by TSH secondary to decreases in T_3 and T_4. Sodium chlorate was not mutagenic in several strains of *Salmonella typhimurium*, with or without exogenous metabolic activation, and did not induce chromosomal aberrations in the bone marrow of CD-1 mice (Meier *et al*., 1985) or micronucleated erythrocytes in peripheral blood of $B6C3F_1$ mice (Table E2). Therefore, it is unlikely that sodium chlorate induces thyroid gland follicular cell tumors through a direct genotoxic mechanism. However, sodium chlorate could potentially alter genes via oxidative damage.

Investigators at USEPA conducted a 90-day study on sodium chlorate administered in the drinking water to male F344 rats and $B6C3F_1$ mice (Hooth *et al*., 2001). However, hematology and clinical chemistry were not included in this study. For this reason, a 3-week study of sodium chlorate was initiated by NTP for the collection of hematology and clinical chemistry data on days 4 and 22, the early time points for these data collections in NTP 13-week toxicity studies. Hematotoxicity, primarily methemoglobin formation, is a characteristic symptom of chlorate poisoning in humans and animals, including horses, pigs, cows, sheep, chickens, and dogs (Gregory *et al*., 1993). Sodium chlorate is a potent oxidizing agent and oxidizes ferrous hemoglobin (Fe^{2+}) to ferric-hemoglobin (Fe^{3+} or methemoglobin), which is unable to bind oxygen. The formation of methemoglobin is prevented by reduction of Fe^{3+} to Fe^{2+} by methemoglobin reductase. There were minimal effects on hematological parameters in rats in the 3-week sodium chlorate study. The effects were similar to those reported previously (Couri *et al.*, 1982; Abdel-Rahman *et al.*, 1985; McCauley *et al.*, 1995). However, there were no effects on methemoglobin formation in rats or mice in the 3-week studies. Rat and mouse erythrocytes have high rates of methemoglobin reductase compared to human erythrocytes (Smith, 1996), with the mouse having 9.5-fold activity relative to that in human erythrocytes. There was also no evidence of the subsequent kidney damage described in other species, including humans, poisoned with sodium chlorate.

Although hematological effects were not observed in the 3-week studies, nonneoplastic lesions of the hematopoietic system were evident in the 2-year rat and mouse studies. The incidences of bone marrow hyperplasia were significantly increased in 1,000 and 2,000 mg/L male rats and all exposed groups of female mice when

compared to the control groups. Hematopoietic cell proliferation of the spleen was significantly increased in 2,000 mg/L male rats. Although the severities were minimal to mild, these lesions were considered to be related to sodium chlorate administration and indicated potential hematotoxicity.

In the 3-week and 2-year studies in mice, there were no chemical-related deaths. Administration of sodium chlorate did not produce any clinical findings of toxicity and had no significant effect on body weights of males or water consumption by mice of either sex. Male mice may have been able to tolerate slightly higher exposure concentrations. Target organs for sodium chlorate toxicity in the 2-year study included the pancreatic islets and thyroid gland in female mice. The thyroid gland was considered to be a target organ for sodium chlorate toxicity because of the increases in the incidences of follicular cell hypertrophy in 1,000 and 2,000 mg/L female mice; the incidence was significantly increased at 2,000 mg/L. There was no evidence of thyroid gland effects in male or female mice after 3 weeks of exposure.

Several arguments support an association of pancreatic islet neoplasms with sodium chlorate administration. Spontaneous pancreatic islet cell tumors are rare in the $B6C3F_1$ mouse (Boorman and Sills, 1999). In the 2-year mouse study, there was a positive trend in the incidences of pancreatic islet cell adenoma or carcinoma (combined) in females. The incidences of adenoma and adenoma or carcinoma (combined) in the 2,000 mg/L group exceeded the NTP historical range for drinking water controls. However, the incidences of these lesions were not increased in male mice. Furthermore, the incidences of pancreatic islet hyperplasia were not increased significantly in exposed mice of either sex. Based on these data, the pancreatic islet cell response in female mice was considered an equivocal finding. Only one other NTP study, 2,4- and 2,6-toluene diisocyanate (NTP, 1986), demonstrated clear or some evidence of carcinogenicity in female rats based on an increased incidence of pancreatic islet adenomas.

CONCLUSIONS

Under the conditions of this 2-year drinking water study, there was *some evidence of carcinogenic activity** of sodium chlorate in male and female F344/N rats based on increased incidences of thyroid gland neoplasms. There was *no evidence of carcinogenic activity* of sodium chlorate in male $B6C3F_1$ mice exposed to 500, 1,000, or 2,000 mg/L. There was *equivocal evidence of carcinogenic activity* of sodium chlorate in female $B6C3F_1$ mice based on marginally increased incidences of pancreatic islet neoplasms.

Exposure to sodium chlorate resulted in nonneoplastic lesions in the thyroid gland of male and female rats and female mice, bone marrow of male rats and female mice, and spleen of male rats.

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

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APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF SODIUM CHLORATE

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental death	1			
Moribund	10	13	11	14
Natural deaths	3	10	8	8
Survivors				
Terminal sacrifice	36	27	31	28
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(48)	(47)	(44)	(49)
Intestine large, cecum	(47)	(46)	(43)	(47)
Intestine small, duodenum	(49)	(46)	(46)	(47)
Intestine small, jejunum	(47)	(46)	(42)	(44)
Intestine small, ileum	(47)	(46)	(42)	(47)
Liver	(50)	(50)	(48)	(50)
Hemangiosarcoma		1 (2%)		
Hepatocellular adenoma		3 (6%)		
Histiocytic sarcoma	1 (2%)	1 (2%)		
Mesentery	(19)	(20)	(19)	(23)
Carcinoma, metastatic, pancreas		1 (5%)		
Hemangiosarcoma, metastatic, liver		1 (5%)		
Histiocytic sarcoma	1 (5%)	1 (5%)		
Osteosarcoma	1 (5%)			
Pancreas	(49)	(49)	(49)	(50)
Hemangiosarcoma, metastatic, liver		1 (2%)		
Acinus, adenoma		2 (4%)	1 (2%)	
Acinus, adenoma, multiple		1 (2%)		
Acinus, carcinoma		1 (2%)		
Salivary glands	(49)	(50)	(50)	(50)
Fibrosarcoma			1 (2%)	
Stomach, forestomach	(50)	(50)	(50)	(50)
Schwannoma malignant	1 (2%)			
Squamous cell papilloma				1 (2%)
Stomach, glandular	(49)	(48)	(48)	(50)
Tongue	(1)	(1)	(1)	(1)
Sarcoma			1 (100%)	
Squamous cell carcinoma		1 (100%)		
Squamous cell papilloma				1 (100%)
Cardiovascular System				
Blood vessel	(1)		(2)	
Aorta, osteosarcoma	1 (100%)			
Heart	(50)	(50)	(50)	(50)
Carcinoma, metastatic, Zymbal's gland				1 (2%)
Schwannoma benign			1 (2%)	

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Endocrine System				
Adrenal cortex	(49)	(49)	(50)	(50)
Carcinoma				1 (2%)
Osteosarcoma, metastatic, bone	1 (2%)			
Adrenal medulla	(49)	(49)	(50)	(50)
Ganglioneuroma		1 (2%)		
Pheochromocytoma malignant	3 (6%)		1 (2%)	1 (2%)
Pheochromocytoma benign	6 (12%)	3 (6%)	3 (6%)	5 (10%)
Bilateral, ganglioneuroma				1 (2%)
Bilateral, pheochromocytoma benign		1 (2%)		3 (6%)
Islets, pancreatic	(50)	(49)	(49)	(50)
Adenoma	3 (6%)	4 (8%)	3 (6%)	5 (10%)
Carcinoma	2 (4%)	1 (2%)		2 (4%)
Pituitary gland	(48)	(50)	(49)	(50)
Pars distalis, adenoma	16 (33%)	15 (30%)	20 (41%)	15 (30%)
Pars intermedia, adenoma		1 (2%)		1 (2%)
Thyroid gland	(47)	(44)	(43)	(47)
Bilateral, C-cell, adenoma, multiple			1 (2%)	
C-cell, adenoma	9 (19%)	9 (20%)	5 (12%)	9 (19%)
C-cell, carcinoma	2 (4%)	2 (5%)		1 (2%)
Follicular cell, adenoma	1 (2%)			2 (4%)
Follicular cell, carcinoma				4 (9%)
General Body System				
Peritoneum		(1)	(1)	
Tissue NOS	(5)	(6)	(2)	(7)
Abdominal, paraganglioma	1 (20%)			
Mediastinum, carcinoma, metastatic, Zymbal's gland		1 (17%)		
Mediastinum, squamous cell carcinoma, metastatic, lung		1 (17%)		
Pelvic, leiomyoma	1 (20%)			
Thoracic, fibroma				1 (14%)
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Preputial gland	(48)	(49)	(50)	(50)
Adenoma	1 (2%)	6 (12%)	5 (10%)	5 (10%)
Carcinoma	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Prostate	(50)	(49)	(50)	(50)
Seminal vesicle	(50)	(49)	(50)	(50)
Testes	(50)	(50)	(50)	(50)
Bilateral, interstitial cell, adenoma				1 (2%)
Bilateral, interstitial cell, adenoma, multiple	40 (80%)	43 (86%)	42 (84%)	39 (78%)
Interstitial cell, adenoma	2 (4%)	1 (2%)		2 (4%)
Interstitial cell, adenoma, multiple	3 (6%)	5 (10%)	2 (4%)	3 (6%)
Hematopoietic System				
Bone marrow	(48)	(48)	(50)	(49)
Lymph node	(34)	(24)	(26)	(34)
Histiocytic sarcoma	1 (3%)			
Deep cervical, histiocytic sarcoma	1 (3%)			
Mediastinal, carcinoma, metastatic, Zymbal's gland		1 (4%)		
Lymph node, mandibular	(3)	(2)	(3)	(4)

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Hematopoietic System (continued)				
Lymph node, mesenteric	(49)	(50)	(49)	(50)
Spleen	(48)	(49)	(49)	(50)
Histiocytic sarcoma	1 (2%)			
Capsule, carcinoma, metastatic, pancreas		1 (2%)		
Thymus	(48)	(48)	(49)	(47)
Carcinoma, metastatic, Zymbal's gland		1 (2%)		
Thymoma benign			1 (2%)	
Integumentary System				
Mammary gland	(45)	(43)	(47)	(44)
Carcinoma		1 (2%)	1 (2%)	
Fibroadenoma	2 (4%)	1 (2%)	4 (9%)	4 (9%)
Skin	(50)	(50)	(50)	(50)
Basal cell carcinoma		1 (2%)		2 (4%)
Basal cell carcinoma, multiple		1 (2%)		
Keratoacanthoma	4 (8%)	2 (4%)	1 (2%)	1 (2%)
Trichoepithelioma	1 (2%)			
Subcutaneous tissue, fibroma	9 (18%)	9 (18%)	4 (8%)	7 (14%)
Subcutaneous tissue, fibroma, multiple		1 (2%)	1 (2%)	1 (2%)
Subcutaneous tissue, fibrosarcoma	1 (2%)	2 (4%)		
Subcutaneous tissue, histiocytic sarcoma		1 (2%)		
Subcutaneous tissue, lipoma		1 (2%)		
Subcutaneous tissue, neural crest tumor	1 (2%)			
Subcutaneous tissue, osteosarcoma				1 (2%)
Subcutaneous tissue, sarcoma			1 (2%)	
Subcutaneous tissue, schwannoma malignant			1 (2%)	1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma	1 (2%)			
Periosteum, cranium, fibrosarcoma, metastatic, skin		1 (2%)		
Nervous System				
Brain	(50)	(50)	(50)	(50)
Carcinoma, metastatic, Zymbal's gland				1 (2%)
Glioma malignant		1 (2%)		
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	1 (2%)	2 (4%)	
Alveolar/bronchiolar carcinoma	2 (4%)	2 (4%)		1 (2%)
Alveolar/bronchiolar carcinoma, multiple	1 (2%)			
Carcinoma, metastatic, Zymbal's gland				1 (2%)
Histiocytic sarcoma, metastatic, uncertain primary site	1 (2%)			
Osteosarcoma, metastatic, bone	1 (2%)			
Squamous cell carcinoma		1 (2%)		
Nose	(49)	(49)	(49)	(50)
Trachea	(50)	(49)	(50)	(50)

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Special Senses System				
Eye	(50)	(48)	(46)	(50)
Retrobulbar, fibrosarcoma, metastatic, skin		1 (2%)		
Harderian gland	(49)	(49)	(49)	(50)
Carcinoma	1 (2%)			
Zymbal's gland		(1)	(1)	(3)
Carcinoma		1 (100%)	1 (100%)	1 (33%)
Urinary System				
Kidney	(47)	(46)	(49)	(49)
Lipoma		1 (2%)		1 (2%)
Mesenchymal tumor benign			1 (2%)	
Renal tubule, adenoma		1 (2%)		
Urinary bladder	(48)	(49)	(47)	(50)
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma	1 (2%)	1 (2%)		
Leukemia mononuclear	13 (26%)	21 (42%)	16 (32%)	23 (46%)
Lymphoma malignant	1 (2%)			
Mesothelioma malignant		1 (2%)	2 (4%)	2 (4%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	49	50	50	50
Total primary neoplasms	135	152	124	150
Total animals with benign neoplasms	48	49	47	47
Total benign neoplasms	100	112	97	108
Total animals with malignant neoplasms	27	32	24	32
Total malignant neoplasms	34	40	27	42
Total animals with metastatic neoplasms	2	5		1
Total metastatic neoplasms	3	10		3
Total animals with malignant neoplasms of uncertain primary site	1			
Total animals with uncertain neoplasms benign or malignant	1			
Total uncertain neoplasms	1			

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

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	3 8 1	4 2 3	4 6 9	5 0 3	5 1 1	5 4 5	5 7 4	6 3 0	6 3 6	6 3 6	6 9 5	6 9 9	7 0 5	7 0 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 1 2	0 3 9	0 3 1	0 2 0	0 3 8	0 3 2	0 0 7	0 4 5	0 2 6	0 4 0	0 2 4	0 5 0	0 4 1	0 4 6	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 0 1	0 0 2	0 0 3	0 0 8	0 0 9
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Mesentery		+	+	+	+	+	+								+	+							+	+	
Histiocytic sarcoma				X																					
Osteosarcoma			X																						
Pancreas	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma malignant			X																						
Stomach, glandular	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Cardiovascular System																									
Blood vessel													+												
Aorta, osteosarcoma													X												
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone														X											
Adrenal medulla	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																						X			
Pheochromocytoma benign															X										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma															X										
Carcinoma																									
Parathyroid gland	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma								X			X			X	X										
Thyroid gland	+	A	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma									X		X						X		X			X			X
C-cell, carcinoma																									
Follicular cell, adenoma													X												
General Body System																									
Tissue NOS										+										+					+
Abdominal, paraganglioma																				X					
Pelvic, leiomyoma																									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 Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	731	731	731	731	731	733	734	734	734	734	734	
Carcass ID Number	02525	02727	03033	04049	01010	01111	01919	02021	02208	02209	03030	03304	03505	03606	03707	04202	04303	04404	04407	04808	00404	00505	00606	02202	02303	Total Tissues/ Tumors
Alimentary System																												
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																												1
Mesentery					+		+	+					+		+		+	+	+		+							19
Histiocytic sarcoma																												1
Osteosarcoma																												1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma malignant																												1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue									+																			1
Cardiovascular System																												
Blood vessel																												1
Aorta, osteosarcoma																												1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																												
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Osteosarcoma, metastatic, bone																												1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant											X											X						3
Pheochromocytoma benign		X								X					X		X				X							6
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma								X	X																			3
Carcinoma	X																			X								2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma		X	X	X			X		X				X					X	X	X		X	X	X				16
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
C-cell, adenoma							X																	X	X			9
C-cell, carcinoma																	X					X						2
Follicular cell, adenoma																												1
General Body System																												
Tissue NOS																	+								+			5
Abdominal, paraganglioma																												1
Pelvic, leiomyoma																												1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	3 8 1	4 2 3	4 6 9	5 0 3	5 1 1	5 4 5	5 7 4	6 3 0	6 3 6	6 3 6	6 9 5	6 9 9	7 0 5	7 0 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 1 2	0 3 9	0 3 1	0 2 0	0 3 8	0 3 2	0 0 7	0 4 5	0 2 6	0 4 0	0 2 4	0 5 0	0 4 1	0 4 6	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 0 1	0 0 2	0 0 3	0 0 8	0 0 9
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma					X																X				
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma, multiple					X	X	X		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Interstitial cell, adenoma				X																					
Interstitial cell, adenoma, multiple			X							X															
Hematopoietic System																									
Bone marrow		+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node			+	+	+	+	+	+	+	+	+		+	+	+		+	+	+			+			+
Histiocytic sarcoma				X																					
Deep cervical, histiocytic sarcoma				X																					
Lymph node, mandibular	M	M	M	M	+	+	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M
Lymph node, mesenteric	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Thymus	+	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma									X				X				X								
Trichoepithelioma																X									
Subcutaneous tissue, fibroma											X	X				X		X							X
Subcutaneous tissue, fibrosarcoma	X																								
Subcutaneous tissue, neural crest tumor																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma														X											
Skeletal muscle																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve								+			+														
Spinal cord								+			+														

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	731	731	731	731	734	734	734	734	734	
Carcass ID Number	00225	00227	00233	00249	00310	00311	00319	00321	00228	00229	00230	00330	00334	00335	00336	00337	00342	00343	00344	00347	00348	00404	00405	00406	00422	00423	Total Tissues/ Tumors
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	48
Adenoma																X											1
Carcinoma																						X					3
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma, multiple	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X			X	X		X	X	40
Interstitial cell, adenoma																				X							2
Interstitial cell, adenoma, multiple																					X						3
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node		+	+	+	+		+		+			+	+	+		+		+	+	+	+	+			+	+	34
Histiocytic sarcoma																											1
Deep cervical, histiocytic sarcoma																											1
Lymph node, mandibular	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	3
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																											1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																											
Mammary gland	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Fibroadenoma					X				X																		2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma			X																								4
Trichoepithelioma																											1
Subcutaneous tissue, fibroma				X		X						X														X	9
Subcutaneous tissue, fibrosarcoma																											1
Subcutaneous tissue, neural crest tumor													X														1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																											1
Skeletal muscle										+																	1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																											2
Spinal cord																											2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	3 8 1	4 2 3	4 6 9	5 0 3	5 1 1	5 4 5	5 7 4	6 3 0	6 3 6	6 3 6	6 9 5	6 9 9	7 0 5	7 0 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 1 2	0 3 9	0 3 1	0 2 0	0 3 8	0 3 2	0 0 7	0 4 5	0 2 6	0 4 0	0 2 4	0 5 0	0 4 1	0 4 6	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 0 1	0 0 2	0 0 3	0 0 8	0 0 9
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Alveolar/bronchiolar carcinoma, multiple																									
Histiocytic sarcoma, metastatic, uncertain primary site				X																					
Osteosarcoma, metastatic, bone														X											
Nose	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Urinary System																									
Kidney	+	A	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma				X																					
Leukemia mononuclear						X	X		X	X		X						X				X	X		
Lymphoma malignant																	X								

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	0 2 5	0 2 7	0 3 3	0 4 9	0 1 0	0 1 1	0 1 9	0 2 1	0 2 8	0 2 9	0 3 0	0 3 4	0 3 5	0 3 6	0 3 7	0 4 2	0 4 3	0 4 4	0 4 7	0 4 8	0 4 4	0 0 5	0 0 6	0 2 2	0 2 3	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma						X																				1
Alveolar/bronchiolar carcinoma																						X			X	2
Alveolar/bronchiolar carcinoma, multiple																	X									1
Histiocytic sarcoma, metastatic, uncertain primary site																										1
Osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma												X														1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear										X				X			X				X			X		13
Lymphoma malignant																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	542	555	562	574	582	605	614	619	638	652	660	663	668	672	693	695	699	703	714	711	714	712	726	729	729
Carcass ID Number	05 52	08 55	07 71	07 78	09 92	08 33	06 66	06 62	05 54	06 64	05 55	06 65	08 50	09 01	05 11	09 99	08 44	05 58	08 88	08 89	09 94	06 43	06 69	05 53	05 57
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	A	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	A	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	A	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	A	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Hepatocellular adenoma																									X
Histiocytic sarcoma																									
Mesentery					+			+			+	+		+		+	+		+				+	+		+
Carcinoma, metastatic, pancreas																									
Hemangiosarcoma, metastatic, liver																									
Histiocytic sarcoma																									
Pancreas	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma, metastatic, liver																									
Acinus, adenoma																								X	X
Acinus, adenoma, multiple																									
Acinus, carcinoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																			+						
Squamous cell carcinoma																			X						
Tooth		+																							
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ganglioneuroma													X												
Pheochromocytoma benign		X																							
Bilateral, pheochromocytoma benign																								X	
Islets, pancreatic	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma												X			X									X	
Carcinoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma										X				X				X					X		
Pars intermedia, adenoma															X										
Thyroid gland	+	+	A	+	A	+	A	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+
C-cell, adenoma								X			X													X	
C-cell, carcinoma																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	
Carcass ID Number	05 59	07 72	07 73	07 74	08 81	08 82	08 87	09 00	09 03	09 05	05 66	06 67	06 68	07 05	07 66	07 67	09 66	09 67	09 68	10 00	06 00	06 01	07 10	07 09	08 06	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																X										1
Hepatocellular adenoma			X								X															3
Histiocytic sarcoma																			X							1
Mesentery		+	+		+	+		+			+					+			+			+				20
Carcinoma, metastatic, pancreas					X																					1
Hemangiosarcoma, metastatic, liver																X										1
Histiocytic sarcoma																			X							1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma, metastatic, liver																X										1
Acinus, adenoma																										2
Acinus, adenoma, multiple																			X							1
Acinus, carcinoma					X																					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Tongue																										1
Squamous cell carcinoma																										1
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Ganglioneuroma																										1
Pheochromocytoma benign																							X		X	3
Bilateral, pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																			X							4
Carcinoma				X																						1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X	X				X					X	X				X	X	X				X		X	X	15
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
C-cell, adenoma	X	X													X			X			X				X	9
C-cell, carcinoma											X						X									2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	5 4 2	5 5 5	5 6 2	5 7 4	5 8 2	6 0 5	6 1 4	6 1 9	6 3 8	6 5 2	6 6 0	6 6 3	6 6 8	6 7 2	6 9 3	6 9 5	6 9 9	7 0 3	7 1 4	7 1 4	7 1 4	7 2 1	7 2 6	7 2 9	7 2 9
Carcass ID Number	0 5 2	0 8 5	0 7 1	0 7 8	0 9 2	0 8 3	0 6 6	0 6 2	0 5 4	0 6 4	0 5 5	0 6 5	0 8 0	0 9 1	0 5 1	0 9 9	0 8 4	0 5 8	0 8 8	0 8 9	0 9 4	0 6 3	0 6 9	0 5 3	0 5 7
General Body System																									
Peritoneum											+														
Tissue NOS			+					+	+			+									+	+			
Mediastinum, carcinoma, metastatic, Zymbal's gland																					X				
Mediastinum, squamous cell carcinoma, metastatic, lung			X																						
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis																						+			
Preputial gland	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma	X																								
Carcinoma																									
Prostate	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma, multiple	X			X	X		X	X	X	X	X	X	X		X	X	X	X	X	X			X	X	X
Interstitial cell, adenoma		X																							
Interstitial cell, adenoma, multiple						X								X							X	X			
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+		+		+		+				+			+		+		+	+	+	+		+	+
Mediastinal, carcinoma, metastatic, Zymbal's gland																					X				
Lymph node, mandibular	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, carcinoma, metastatic, Pancreas																									
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	I	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, Zymbal's gland																					X				
Integumentary System																									
Mammary gland	+	M	+	M	A	M	M	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+
Carcinoma																							X		
Fibroadenoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Basal cell carcinoma, multiple																									
Keratoacanthoma																X					X				
Subcutaneous tissue, fibroma		X					X												X						
Subcutaneous tissue, fibroma, multiple						X																			
Subcutaneous tissue, fibrosarcoma										X															
Subcutaneous tissue, histiocytic sarcoma																									
Subcutaneous tissue, lipoma																	X								

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	
Carcass ID Number	059	072	073	074	081	082	087	090	093	095	056	067	068	075	076	077	096	097	098	100	060	061	070	079	086	Total Tissues/ Tumors
General Body System																										
Peritoneum																										1
Tissue NOS																										6
Mediastinum, carcinoma, metastatic, Zymbal's gland																										1
Mediastinum, squamous cell carcinoma, metastatic, lung																										1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Penis												+														2
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma									X		X			X										X	X	6
Carcinoma			X																							1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma, multiple	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	43
Interstitial cell, adenoma																										1
Interstitial cell, adenoma, multiple									X																	5
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node	+		+	+		+		+			+			+		+			+			+				24
Mediastinal, carcinoma, metastatic, Zymbal's gland																										1
Lymph node, mandibular	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	2
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Capsule, carcinoma, metastatic, Pancreas					X																					1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, Zymbal's gland																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Carcinoma																										1
Fibroadenoma		X																								1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma			X																							1
Basal cell carcinoma, multiple																			X							1
Keratoacanthoma																										2
Subcutaneous tissue, fibroma			X				X								X		X	X		X						9
Subcutaneous tissue, fibroma, multiple																										1
Subcutaneous tissue, fibrosarcoma								X																		2
Subcutaneous tissue, histiocytic sarcoma																			X							1
Subcutaneous tissue, lipoma																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	5 4 2	5 5 5	5 6 2	5 7 4	5 8 2	6 0 5	6 1 4	6 1 9	6 3 8	6 5 2	6 6 0	6 6 3	6 6 8	6 7 2	6 9 3	6 9 5	6 9 9	7 0 3	7 1 4	7 1 4	7 1 4	7 2 1	7 2 6	7 2 9	7 2 9
Carcass ID Number	0 5 2	0 8 5	0 7 1	0 7 8	0 9 2	0 8 3	0 6 6	0 6 2	0 5 4	0 6 4	0 5 5	0 6 5	0 8 0	0 9 1	0 5 1	0 9 9	0 8 4	0 5 8	0 8 8	0 8 9	0 9 4	0 6 3	0 6 9	0 5 3	0 5 7
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Periosteum, cranium, fibrosarcoma, metastatic, skin										X															
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant															X										
Peripheral nerve																	+								
Spinal cord																	+								
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									X
Squamous cell carcinoma			X																						
Nose	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Retrobulbar, fibrosarcoma, metastatic, skin										X															
Harderian gland	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lacrimal gland															+										
Zymbal's gland																					+				
Carcinoma																					X				
Urinary System																									
Kidney	+	+	+	+	+	+	A	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+
Lipoma																									
Renal tubule, adenoma											X														
Urinary bladder	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Leukemia mononuclear				X	X		X	X	X			X				X	X	X	X	X		X	X		X
Mesothelioma malignant											X														

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

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	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	
	9	9	9	9	9	9	9	9	9	9	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	Total
Carcass ID Number	5	7	7	7	8	8	8	9	9	9	5	6	6	7	7	7	9	9	9	0	6	6	7	7	8	Tissues/
	9	2	3	4	1	2	7	0	3	5	6	7	8	5	6	7	6	7	8	0	0	1	0	9	6	Tumors
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Periosteum, cranium, fibrosarcoma, metastatic, skin																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Glioma malignant																										1
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma					X																					1
Alveolar/bronchiolar carcinoma														X												2
Squamous cell carcinoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Retrobulbar, fibrosarcoma, metastatic, skin																										1
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lacrimal gland																										1
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lipoma																				X						1
Renal tubule, adenoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																			X							1
Leukemia mononuclear	X		X				X	X						X							X			X		21
Mesothelioma malignant																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	209	475	561	566	576	605	607	626	647	660	667	673	675	695	698	703	703	714	721	729	729	729	729	729	729
Carcass ID Number	10406	14505	10407	11012	13636	14444	12425	14848	10404	10002	11515	11919	13434	11017	10818	11616	13030	10303	10021	12222	12323	12424	12428	12429	14043
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	A	A	+	A	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	A	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	A	+	A	+	A	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	+	+	A	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	A	A	+	+	A	A	A	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	A	A	A	+	A	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+
Liver	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery		+		+			+	+	+	+	+		+						+		+	+			
Pancreas	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma																					X				
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue		+																							
Sarcoma		X																							
Tooth																									
Cardiovascular System																									
Blood vessel	+			+																					
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma benign																						X			
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant											X														
Pheochromocytoma benign															X						X				
Islets, pancreatic	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																		X							
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X	X			X		X					X	X		X	X					X	X	X
Thyroid gland	+	A	A	A	+	+	A	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+
Bilateral, C-cell, adenoma, multiple																									
C-cell, adenoma										X				X								X			
General Body System																									
Peritoneum													+												
Tissue NOS																			+						
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma								X							X							X			
Carcinoma																			X					X	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	11013	11014	11031	11032	11033	11035	11040	11041	11042	11049	11050	11051	11059	11090	11101	11111	11181	12001	12021	12026	12071	13031	13038	13039	14046	14047	Total Tissues/ Tumors
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Mesentery			+	+			+			+			+		+				+	+							19
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinus, adenoma																											1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma													X														1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Tongue																											1
Sarcoma																											1
Tooth																									+		1
Cardiovascular System																											
Blood vessel																											2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma benign																											1
Endocrine System																											
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																											1
Pheochromocytoma benign		X																									3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma								X														X					3
Parathyroid gland	M	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma		X									X			X			X	X	X	X	X	X					20
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Bilateral, C-cell, adenoma, multiple	X																										1
C-cell, adenoma													X			X											5
General Body System																											
Peritoneum																											1
Tissue NOS																		+									2
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma												X	X														5
Carcinoma																											2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	2 0 9	4 7 5	5 6 1	5 6 6	5 7 6	6 0 5	6 0 7	6 2 6	6 4 7	6 6 0	6 6 7	6 7 3	6 7 5	6 9 5	6 9 8	7 0 3	7 0 3	7 1 4	7 2 1	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	1 0 0 6	1 4 5	1 0 7	1 1 2	1 3 6	1 4 4	1 2 5	1 4 8	1 0 4	1 0 2	1 1 5	1 1 9	1 3 4	1 1 7	1 0 8	1 1 6	1 3 0	1 0 3	1 0 1	1 2 2	1 2 3	1 2 4	1 2 8	1 2 9	1 4 3
Genital System (continued)																									
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma, multiple			X		X	X		X	X	X	X	X			X	X	X	X	X	X	X	X	X	X	X
Interstitial cell, adenoma, multiple														X											
Hematopoietic system																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+		+			+	+		+	+	+		+	+	+	+	+		+	+		+			
Lymph node, mandibular	M	M	M	M	+	M	M	M	M	+	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																									
Integumentary system																									
Mammary gland	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Fibroadenoma				X																				X	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Subcutaneous tissue, fibroma							X													X					
Subcutaneous tissue, fibroma, multiple																X									
Subcutaneous tissue, sarcoma	X																								
Subcutaneous tissue, schwannoma malignant			X																						
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve									+		+		+	+											
Spinal cord									+		+		+	+											
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																							X		
Nose	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	M	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lacrimal gland											+														
Zymbal's gland										+															
Carcinoma										X															

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

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 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	1 1 3	1 1 4	1 3 1	1 3 2	1 3 3	1 3 5	1 4 0	1 4 1	1 4 2	1 4 9	1 5 0	1 5 5	1 0 9	1 1 0	1 1 1	1 1 8	1 2 0	1 2 1	1 2 6	1 2 7	1 3 7	1 3 8	1 3 9	1 4 6	1 4 7	Total Tissues/ Tumors
Genital System (continued)																									
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma, multiple	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X		X	X	X	X	42
Interstitial cell, adenoma, multiple																				X					2
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+		+			+		+				+	+	+				+		+	+			26
Lymph node, mandibular	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	3
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymoma benign								X																	1
Integumentary System																									
Mammary gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Carcinoma					X																				1
Fibroadenoma																				X		X			4
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma								X																	1
Subcutaneous tissue, fibroma		X								X															4
Subcutaneous tissue, fibroma, multiple																									1
Subcutaneous tissue, sarcoma																									1
Subcutaneous tissue, schwannoma malignant																									1
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																+									1
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																									4
Spinal cord								+																	5
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X																							2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lacrimal gland																									1
Zymbal's gland																									1
Carcinoma																									1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	209	245	261	266	267	605	627	626	647	660	667	673	675	699	698	703	703	714	721	729	729	729	729	729	729
Carcass ID Number	106	145	107	121	136	144	245	248	040	002	125	119	134	117	108	161	130	103	101	122	123	124	128	129	143
Urinary System																									
Kidney	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenchymal tumor benign												X													
Urinary bladder	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X			X		X			X				X	X	X		X	X	X		X		
Mesothelioma malignant							X						X												

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	11013	11014	11031	11032	11033	11035	11040	11041	11042	11049	11050	11050	11055	11059	11090	11111	11118	11120	11221	11226	11227	11233	11238	11239	11246	11247	Total Tissues/ Tumors
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesenchymal tumor benign																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear				X						X	X											X				X	16
Mesothelioma malignant																											2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	443	446	448	545	552	560	639	644	651	655	671	672	678	681	699	699	701	703	710	710	711	718	720	722	729	729
Carcass ID Number	19 2	18 4	15 7	18 7	16 7	16 9	15 5	15 4	15 9	16 1	17 3	19 9	17 1	16 5	15 8	18 6	15 1	15 2	17 6	18 5	17 8	17 4	16 0	16 2	16 3
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	A	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Intestine small, jejunum	A	+	A	+	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+
Intestine small, ileum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery		+	+	+	+	+	+	+			+			+	+	+		+			+	+	+	+		
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																										
Squamous cell papilloma																										
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, Zymbal's gland																				X						
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																										
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																										
Pheochromocytoma benign															X						X					
Bilateral, ganglioneuroma	X																									
Bilateral, pheochromocytoma benign																		X								
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma														X												
Carcinoma																	X									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma								X	X	X			X			X		X		X			X	X	
Pars intermedia, adenoma																								X		
Thyroid gland	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	
C-cell, adenoma																					X					
C-cell, carcinoma																							X			
Follicular cell, adenoma																										
Follicular cell, carcinoma																								X		
General Body System																										
Tissue NOS				+	+			+					+									+				
Thoracic, fibroma																										

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	164	172	181	182	183	190	191	196	197	198	170	179	180	188	189	153	156	166	168	175	177	193	194	195	200	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery		+	+		+		+	+		+												+				23
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																X										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue																				+						1
Squamous cell papilloma																				X						1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, Zymbal's gland																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																		X								1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant							X																			1
Pheochromocytoma benign		X											X		X											5
Bilateral, ganglioneuroma																										1
Bilateral, pheochromocytoma benign	X				X																					3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X		X							X			X												5
Carcinoma																		X								2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma					X				X			X			X			X					X			15
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
C-cell, adenoma				X		X								X		X					X	X	X		X	9
C-cell, carcinoma																										1
Follicular cell, adenoma		X																			X					2
Follicular cell, carcinoma				X	X																				X	4
General Body System																										
Tissue NOS	+									+																7
Thoracic, fibroma										X																1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	4 4 3	4 6 5	4 8 2	5 4 5	5 6 2	5 9 0	6 3 9	6 4 4	6 5 1	6 5 1	6 7 1	6 7 2	6 7 8	6 8 1	6 9 9	6 9 9	7 0 1	7 0 3	7 0 3	7 1 0	7 1 8	7 2 0	7 2 9	7 2 9
Carcass ID Number	1 9 2	1 8 4	1 5 7	1 8 7	1 6 7	1 6 9	1 5 5	1 5 4	1 5 9	1 6 1	1 7 3	1 7 9	1 7 1	1 6 5	1 5 8	1 8 6	1 5 1	1 5 2	1 7 6	1 8 5	1 8 8	1 7 4	1 6 0	1 6 2	1 6 3
Genital System																								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma		X											X											
Carcinoma						X																		
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma																								
Bilateral, interstitial cell, adenoma, multiple					X		X	X	X	X		X	X		X	X		X	X	X	X	X	X	X	X
Interstitial cell, adenoma		X		X																				
Interstitial cell, adenoma, multiple	X													X										
Hematopoietic System																								
Bone marrow	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node		+	+	+	+		+	+	+		+	+	+	+	+	+	+	+		+	+	+	+	
Lymph node, mandibular	M	M	+	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+
Integumentary system																								
Mammary gland	+	+	+	+	+	+	+	M	+	+	+	+	M	+	M	M	+	+	M	+	+	+	+	+	+
Fibroadenoma																					X				
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Keratoacanthoma																					X				
Subcutaneous tissue, fibroma										X		X				X									
Subcutaneous tissue, fibroma, multiple																									
Subcutaneous tissue, osteosarcoma																									X
Subcutaneous tissue, schwannoma malignant																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, Zymbal's gland																				X					
Peripheral nerve			+																	+	+				
Spinal cord			+																	+	+				
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, Zymbal's gland																				X					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	164	172	181	182	183	190	191	196	197	198	170	179	180	188	189	153	156	166	168	175	177	193	194	195	200	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma											X													X	X	5
Carcinoma																									X	2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma																				X						1
Bilateral, interstitial cell, adenoma, multiple		X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	39
Interstitial cell, adenoma																										2
Interstitial cell, adenoma, multiple	X																									3
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+		+						+		+		+		+		+	+	34
Lymph node, mandibular	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	4
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	44
Fibroadenoma				X																	X		X			4
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma							X												X							2
Keratoacanthoma																										1
Subcutaneous tissue, fibroma			X			X				X								X								7
Subcutaneous tissue, fibroma, multiple					X																					1
Subcutaneous tissue, osteosarcoma																										1
Subcutaneous tissue, schwannoma malignant															X											1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, Zymbal's gland																										1
Peripheral nerve																										3
Spinal cord						+	+																			5
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma							X																			1
Carcinoma, metastatic, Zymbal's gland																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	443	465	482	545	562	590	639	644	651	651	671	672	678	681	699	699	701	703	703	710	718	720	729	729	729
Carcass ID Number	192	184	157	187	167	169	155	154	159	161	173	179	171	165	158	186	151	152	176	185	178	174	160	162	163
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lacrimal gland																									+
Zymbal's gland			+					+												+					
Carcinoma																				X					
Urinary System																									
Kidney	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lipoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X	X	X	X		X	X			X		X		X	X		X			X	X			X
Mesothelioma malignant																									

Table A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	729	729	729	729	729	729	729	729	729	729	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	164	172	181	182	183	190	191	196	197	198	170	179	180	188	189	153	156	166	168	175	177	193	194	195	200	Total Tissues/ Tumors
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lacrimal gland																										1
Zymbal's gland																										3
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lipoma						X																				1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X		X	X					X	X	X				X		X								X	23
Mesothelioma malignant			X							X																2

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	6/49 (12%)	4/49 (8%)	3/50 (6%)	8/50 (16%)
Adjusted rate[b]	13.8%	9.1%	6.8%	18.3%
Terminal rate[c]	6/36 (17%)	3/27 (11%)	2/31 (7%)	5/28 (18%)
First incidence (days)	729 (T)	555	698	699
Poly-3 test[d]	P=0.229	P=0.364N	P=0.236N	P=0.391
Adrenal Medulla: Malignant Pheochromocytoma				
Overall rate	3/49 (6%)	0/49 (0%)	1/50 (2%)	1/50 (2%)
Adjusted rate	6.9%	0.0%	2.3%	2.3%
Terminal rate	3/36 (8%)	0/27 (0%)	0/31 (0%)	1/28 (4%)
First incidence (days)	729 (T)	—[e]	667	729 (T)
Poly-3 test	P=0.404N	P=0.119N	P=0.300N	P=0.305N
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rate	9/49 (18%)	4/49 (8%)	4/50 (8%)	9/50 (18%)
Adjusted rate	20.7%	9.1%	9.1%	20.6%
Terminal rate	9/36 (25%)	3/27 (11%)	2/31 (7%)	6/28 (21%)
First incidence (days)	729 (T)	555	667	699
Poly-3 test	P=0.331	P=0.110N	P=0.107N	P=0.598N
Liver: Hepatocellular Adenoma				
Overall rate	0/50 (0%)	3/50 (6%)	0/48 (0%)	0/50 (0%)
Adjusted rate	0.0%	6.9%	0.0%	0.0%
Terminal rate	0/36 (0%)	3/27 (11%)	0/31 (0%)	0/28 (0%)
First incidence (days)	—	729 (T)	—[f]	—
Poly-3 test	P=0.141N	P=0.119	—	—
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	3/50 (6%)	2/50 (4%)	0/50 (0%)	1/50 (2%)
Adjusted rate	6.9%	4.6%	0.0%	2.3%
Terminal rate	3/36 (8%)	2/27 (7%)	0/31 (0%)	1/28 (4%)
First incidence (days)	729 (T)	729 (T)	—	729 (T)
Poly-3 test	P=0.159N	P=0.499N	P=0.118N	P=0.307N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	4/50 (8%)	3/50 (6%)	2/50 (4%)	1/50 (2%)
Adjusted rate	9.2%	6.9%	4.6%	2.3%
Terminal rate	4/36 (11%)	3/27 (11%)	2/31 (7%)	1/28 (4%)
First incidence (days)	729 (T)	729 (T)	729 (T)	729 (T)
Poly-3 test	P=0.119N	P=0.499N	P=0.337N	P=0.180N
Mammary Gland: Fibroadenoma				
Overall rate	2/50 (4%)	1/50 (2%)	4/50 (8%)	4/50 (8%)
Adjusted rate	4.6%	2.3%	9.0%	9.2%
Terminal rate	2/36 (6%)	1/27 (4%)	3/31 (10%)	3/28 (11%)
First incidence (days)	729 (T)	729 (T)	566	718
Poly-3 test	P=0.118	P=0.499N	P=0.343	P=0.334
Mammary Gland: Fibroadenoma or Carcinoma				
Overall rate	2/50 (4%)	2/50 (4%)	5/50 (10%)	4/50 (8%)
Adjusted rate	4.6%	4.6%	11.3%	9.2%
Terminal rate	2/36 (6%)	1/27 (4%)	4/31 (13%)	3/28 (11%)
First incidence (days)	729 (T)	726	566	718
Poly-3 test	P=0.173	P=0.693N	P=0.221	P=0.334

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Pancreas: Adenoma				
Overall rate	0/49 (0%)	3/49 (6%)	1/49 (2%)	0/50 (0%)
Adjusted rate	0.0%	6.9%	2.3%	0.0%
Terminal rate	0/36 (0%)	3/27 (11%)	1/31 (3%)	0/28 (0%)
First incidence (days)	—	729 (T)	729 (T)	—
Poly-3 test	P=0.214N	P=0.118	P=0.500	—
Pancreas: Adenoma or Carcinoma				
Overall rate	0/49 (0%)	4/49 (8%)	1/49 (2%)	0/50 (0%)
Adjusted rate	0.0%	9.3%	2.3%	0.0%
Terminal rate	0/36 (0%)	4/27 (15%)	1/31 (3%)	0/28 (0%)
First incidence (days)	—	729 (T)	729 (T)	—
Poly-3 test	P=0.138N	P=0.059	P=0.500	—
Pancreatic Islets: Adenoma				
Overall rate	3/50 (6%)	4/49 (8%)	3/49 (6%)	5/50 (10%)
Adjusted rate	6.9%	9.2%	6.9%	11.5%
Terminal rate	3/36 (8%)	2/27 (7%)	2/31 (7%)	4/28 (14%)
First incidence (days)	729 (T)	663	714	681
Poly-3 test	P=0.335	P=0.498	P=0.661	P=0.355
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	5/50 (10%)	5/49 (10%)	3/49 (6%)	7/50 (14%)
Adjusted rate	11.4%	11.5%	6.9%	16.0%
Terminal rate	5/36 (14%)	3/27 (11%)	2/31 (7%)	5/28 (18%)
First incidence (days)	729 (T)	663	714	681
Poly-3 test	P=0.331	P=0.629	P=0.358N	P=0.379
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	16/48 (33%)	15/50 (30%)	20/49 (41%)	15/50 (30%)
Adjusted rate	37.2%	33.8%	43.8%	33.6%
Terminal rate	13/36 (36%)	11/27 (41%)	12/31 (39%)	8/28 (29%)
First incidence (days)	630	652	561	651
Poly-3 test	P=0.516N	P=0.457N	P=0.337	P=0.449N
Preputial Gland: Adenoma				
Overall rate	1/48 (2%)	6/49 (12%)	5/50 (10%)	5/50 (10%)
Adjusted rate	2.4%	13.7%	11.3%	11.3%
Terminal rate	1/35 (3%)	5/27 (19%)	3/31 (10%)	3/28 (11%)
First incidence (days)	729 (T)	542	626	465
Poly-3 test	P=0.287	P=0.060	P=0.111	P=0.111
Preputial Gland: Carcinoma				
Overall rate	3/48 (6%)	1/49 (2%)	2/50 (4%)	2/50 (4%)
Adjusted rate	7.0%	2.3%	4.6%	4.6%
Terminal rate	2/35 (6%)	1/27 (4%)	1/31 (3%)	1/28 (4%)
First incidence (days)	511	729 (T)	721	590
Poly-3 test	P=0.555N	P=0.304N	P=0.492N	P=0.491N
Preputial Gland: Adenoma or Carcinoma				
Overall rate	4/48 (8%)	7/49 (14%)	7/50 (14%)	6/50 (12%)
Adjusted rate	9.3%	16.0%	15.8%	13.4%
Terminal rate	3/35 (9%)	6/27 (22%)	4/31 (13%)	3/28 (11%)
First incidence (days)	511	542	626	465
Poly-3 test	P=0.461	P=0.270	P=0.276	P=0.395

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Skin: Keratoacanthoma				
Overall rate	4/50 (8%)	2/50 (4%)	1/50 (2%)	1/50 (2%)
Adjusted rate	9.1%	4.6%	2.3%	2.3%
Terminal rate	2/36 (6%)	0/27 (0%)	1/31 (3%)	0/28 (0%)
First incidence (days)	636	695	729 (T)	718
Poly-3 test	P=0.132N	P=0.338N	P=0.181N	P=0.183N
Skin: Keratoacanthoma, Trichoepithelioma, or Basal Cell Carcinoma				
Overall rate	5/50 (10%)	4/50 (8%)	1/50 (2%)	3/50 (6%)
Adjusted rate	11.3%	9.1%	2.3%	6.9%
Terminal rate	3/36 (8%)	2/27 (7%)	1/31 (3%)	2/28 (7%)
First incidence (days)	636	695	729 (T)	718
Poly-3 test	P=0.224N	P=0.502N	P=0.103N	P=0.364N
Skin: Fibroma				
Overall rate	9/50 (18%)	10/50 (20%)	5/50 (10%)	8/50 (16%)
Adjusted rate	20.5%	22.1%	11.3%	18.2%
Terminal rate	7/36 (19%)	6/27 (22%)	3/31 (10%)	5/28 (18%)
First incidence (days)	695	555	607	651
Poly-3 test	P=0.300N	P=0.528	P=0.187N	P=0.498N
Skin: Fibroma, Fibrosarcoma, or Sarcoma				
Overall rate	10/50 (20%)	12/50 (24%)	6/50 (12%)	8/50 (16%)
Adjusted rate	22.3%	26.4%	13.3%	18.2%
Terminal rate	7/36 (19%)	7/27 (26%)	3/31 (10%)	5/28 (18%)
First incidence (days)	381	555	209	651
Poly-3 test	P=0.180N	P=0.420	P=0.198N	P=0.412N
Testes: Adenoma				
Overall rate	45/50 (90%)	49/50 (98%)	44/50 (88%)	45/50 (90%)
Adjusted rate	93.8%	99.1%	93.3%	92.8%
Terminal rate	34/36 (94%)	27/27 (100%)	30/31 (97%)	27/28 (96%)
First incidence (days)	469	542	561	443
Poly-3 test	P=0.198N	P=0.164	P=0.644N	P=0.593N
Thyroid Gland (C-Cell): Adenoma				
Overall rate	9/47 (19%)	9/44 (20%)	6/43 (14%)	9/47 (19%)
Adjusted rate	21.1%	22.2%	15.0%	21.6%
Terminal rate	7/36 (19%)	7/27 (26%)	4/31 (13%)	8/28 (29%)
First incidence (days)	636	619	660	718
Poly-3 test	P=0.485N	P=0.553	P=0.334N	P=0.583
Thyroid Gland (C-Cell): Carcinoma				
Overall rate	2/47 (4%)	2/44 (5%)	0/43 (0%)	1/47 (2%)
Adjusted rate	4.7%	5.0%	0.0%	2.4%
Terminal rate	2/36 (6%)	2/27 (7%)	0/31 (0%)	1/28 (4%)
First incidence (days)	729 (T)	729 (T)	—	729 (T)
Poly-3 test	P=0.254N	P=0.673	P=0.251N	P=0.505N
Thyroid Gland (C-Cell): Adenoma or Carcinoma				
Overall rate	11/47 (23%)	11/44 (25%)	6/43 (14%)	10/47 (21%)
Adjusted rate	25.7%	27.2%	15.0%	23.9%
Terminal rate	9/36 (25%)	9/27 (33%)	4/31 (13%)	9/28 (32%)
First incidence (days)	636	619	660	718
Poly-3 test	P=0.339N	P=0.539	P=0.174N	P=0.524N

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Thyroid Gland (Follicular Cell): Carcinoma				
Overall rate	0/47 (0%)	0/44 (0%)	0/43 (0%)	4/47 (9%)
Adjusted rate	0.0%	0.0%	0.0%	9.6%
Terminal rate	0/36 (0%)	0/27 (0%)	0/31 (0%)	4/28 (14%)
First incidence (days)	—	—	—	729 (T)
Poly-3 test	P=0.003	—	—	P=0.058
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rate	1/47 (2%)	0/44 (0%)	0/43 (0%)	6/47 (13%)
Adjusted rate	2.4%	0.0%	0.0%	14.4%
Terminal rate	0/36 (0%)	0/27 (0%)	0/31 (0%)	6/28 (21%)
First incidence (days)	705	—	—	729 (T)
Poly-3 test	P=0.002	P=0.512N	P=0.513N	P=0.052
All Organs: Mononuclear Cell Leukemia				
Overall rate	13/50 (26%)	21/50 (42%)	16/50 (32%)	23/50 (46%)
Adjusted rate	28.5%	45.0%	35.0%	48.4%
Terminal rate	8/36 (22%)	8/27 (30%)	8/31 (26%)	10/28 (36%)
First incidence (days)	545	574	561	465
Poly-3 test	P=0.111	P=0.074	P=0.328	P=0.036
All Organs: Osteosarcoma				
Overall rate	3/50 (6%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
Adjusted rate	6.7%	0.0%	0.0%	2.3%
Terminal rate	0/36 (0%)	0/27 (0%)	0/31 (0%)	1/28 (4%)
First incidence (days)	469	—	—	729 (T)
Poly-3 test	P=0.344N	P=0.122N	P=0.122N	P=0.315N
All Organs: Benign Neoplasms				
Overall rate	48/50 (96%)	49/50 (98%)	47/50 (94%)	47/50 (94%)
Adjusted rate	99.3%	99.1%	97.7%	96.3%
Terminal rate	36/36 (100%)	27/27 (100%)	31/31 (100%)	27/28 (96%)
First incidence (days)	469	542	561	443
Poly-3 test	P=0.128N	P=0.955N	P=0.608N	P=0.346N
All Organs: Malignant Neoplasms				
Overall rate	27/50 (54%)	32/50 (64%)	24/50 (48%)	32/50 (64%)
Adjusted rate	55.4%	66.7%	49.7%	66.5%
Terminal rate	16/36 (44%)	14/27 (52%)	11/31 (36%)	16/28 (57%)
First incidence (days)	381	562	209	465
Poly-3 test	P=0.365	P=0.175	P=0.360N	P=0.181

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
All Organs: Benign or Malignant Neoplasms				
Overall rate	49/50 (98%)	50/50 (100%)	50/50 (100%)	50/50 (100%)
Adjusted rate	99.6%	100.0%	100.0%	100.0%
Terminal rate	36/36 (100%)	27/27 (100%)	31/31 (100%)	28/28 (100%)
First incidence (days)	381	542	209	443
Poly-3 test	P=0.987	P=1.000	P=1.000	P=1.000

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

TABLE A4
Historical Incidence of Thyroid Gland Neoplasms in Control Male F344/N Rats[a]

Study	Incidence in Controls		
	Follicular Cell Adenoma	Follicular Cell Carcinoma	Follicular Cell Adenoma or Carcinoma
Historical Incidence in Drinking Water Controls Given NTP-2000 Diet			
Dipropylene glycol	1/42	0/42	1/42
Sodium chlorate	1/47	0/47	1/47
Sodium nitrite	1/50	1/50	2/50
Overall Historical Incidence: Drinking Water Studies			
Total (%)	3/139 (2.2%)	1/139 (0.7%)	4/139 (2.9%)
Mean ± standard deviation	2.2% ± 0.3%	1.0% ± 1.4%	3.2% ± 1.1%
Range	2%	0%-2%	2%-4%
Overall Historical Incidence: All Routes			
Total (%)	12/1,140 (1.1%)	11/1,140 (1.0%)	23/1,140 (2.0%)
Mean ± standard deviation	1.0% ± 1.3%	0.9% ± 1.2%	1.9% ± 1.5%
Range	0%-4%	0%-4%	0%-4%

[a] Data as of April 19, 2004

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental death	1			
Moribund	10	13	11	14
Natural death	3	10	8	8
Survivors				
Terminal sacrifice	36	27	31	28
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(48)	(47)	(44)	(49)
Edema				2 (4%)
Intestine large, rectum	(48)	(47)	(47)	(50)
Congestion				1 (2%)
Edema				1 (2%)
Hemorrhage				1 (2%)
Intestine large, cecum	(47)	(46)	(43)	(47)
Edema		1 (2%)		1 (2%)
Ulcer				1 (2%)
Intestine small, duodenum	(49)	(46)	(46)	(47)
Ulcer		1 (2%)		
Epithelium, hyperplasia				1 (2%)
Intestine small, jejunum	(47)	(46)	(42)	(44)
Epithelium, necrosis			1 (2%)	
Intestine small, ileum	(47)	(46)	(42)	(47)
Ulcer	1 (2%)			
Liver	(50)	(50)	(48)	(50)
Angiectasis, focal	2 (4%)	1 (2%)	1 (2%)	3 (6%)
Basophilic focus	27 (54%)	30 (60%)	33 (69%)	29 (58%)
Cholangiofibrosis	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Clear cell focus	21 (42%)	18 (36%)	29 (60%)	15 (30%)
Congestion		2 (4%)		
Degeneration, cystic, focal	13 (26%)	9 (18%)	12 (25%)	14 (28%)
Eosinophilic focus	2 (4%)	3 (6%)		2 (4%)
Fibrosis, focal		1 (2%)		1 (2%)
Hemorrhage, focal	1 (2%)			
Hepatodiaphragmatic nodule	6 (12%)	2 (4%)	3 (6%)	5 (10%)
Hyperplasia, focal, histiocytic	6 (12%)	2 (4%)	8 (17%)	5 (10%)
Hyperplasia, focal, lymphoid			1 (2%)	1 (2%)
Infarct	1 (2%)			
Infiltration cellular, mixed cell	36 (72%)	29 (58%)	33 (69%)	28 (56%)
Mixed cell focus	13 (26%)	11 (22%)	3 (6%)	8 (16%)
Bile duct, hyperplasia	48 (96%)	49 (98%)	46 (96%)	50 (100%)
Centrilobular, congestion		1 (2%)		
Hepatocyte, necrosis, focal		1 (2%)		2 (4%)
Hepatocyte, vacuolization cytoplasmic, diffuse	3 (6%)	3 (6%)		4 (8%)
Hepatocyte, vacuolization cytoplasmic, focal	26 (52%)	15 (30%)	14 (29%)	18 (36%)
Hepatocyte, periportal, necrosis		1 (2%)		

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

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Alimentary System (continued)				
Liver (continued)	(50)	(50)	(48)	(50)
Hepatocyte, periportal, vacuolization cytoplasmic		1 (2%)	1 (2%)	
Hepatocyte, centrilobular, atrophy				1 (2%)
Hepatocyte, centrilobular, necrosis	1 (2%)	3 (6%)	6 (13%)	4 (8%)
Hepatocyte, centrilobular, vacuolization cytoplasmic	4 (8%)	9 (18%)	12 (25%)	11 (22%)
Hepatocyte, midzonal, necrosis	1 (2%)			
Hepatocyte, midzonal, vacuolization cytoplasmic	6 (12%)	1 (2%)		1 (2%)
Hepatocyte, midzonal, vacuolization cytoplasmic, focal		1 (2%)		
Portal, fibrosis		1 (2%)		
Portal, hemorrhage		1 (2%)		
Mesentery	(19)	(20)	(19)	(23)
Angiectasis		1 (5%)		
Hemorrhage	1 (5%)		1 (5%)	
Inflammation, chronic			1 (5%)	
Inflammation, chronic, focal				1 (4%)
Fat, necrosis	2 (11%)		2 (11%)	2 (9%)
Fat, necrosis, focal	12 (63%)	10 (50%)	13 (68%)	14 (61%)
Pancreas	(49)	(49)	(49)	(50)
Inflammation, chronic	1 (2%)			
Acinus, atrophy, diffuse				1 (2%)
Acinus, atrophy, focal	23 (47%)	23 (47%)	27 (55%)	15 (30%)
Acinus, hyperplasia, focal	1 (2%)	1 (2%)		
Duct, cyst, focal			1 (2%)	1 (2%)
Duct, cyst, focal, multiple	15 (31%)	13 (27%)	18 (37%)	15 (30%)
Salivary glands	(49)	(50)	(50)	(50)
Atrophy				1 (2%)
Hyperplasia, focal, histiocytic				1 (2%)
Stomach, forestomach	(50)	(50)	(50)	(50)
Edema	1 (2%)	1 (2%)		4 (8%)
Erosion			1 (2%)	
Inflammation, chronic		4 (8%)		1 (2%)
Inflammation, chronic, focal			1 (2%)	
Inflammation, focal		1 (2%)	1 (2%)	
Ulcer	1 (2%)	5 (10%)	2 (4%)	4 (8%)
Epithelium, cyst	1 (2%)			
Epithelium, hyperplasia	2 (4%)	8 (16%)	1 (2%)	7 (14%)
Epithelium, hyperplasia, focal			1 (2%)	
Stomach, glandular	(49)	(48)	(48)	(50)
Erosion	3 (6%)	2 (4%)	4 (8%)	4 (8%)
Perforation				1 (2%)
Pigmentation, focal		1 (2%)	1 (2%)	
Ulcer	1 (2%)			3 (6%)
Epithelium, hyperplasia, focal		1 (2%)		
Tongue	(1)	(1)	(1)	(1)
Epithelium, hyperplasia	1 (100%)			
Tooth		(1)	(1)	
Malformation			1 (100%)	
Peridontal tissue, hyperplasia, squamous		1 (100%)		

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	6 (12%)	3 (6%)	7 (14%)	10 (20%)
Infiltration cellular, mixed cell	2 (4%)	1 (2%)		2 (4%)
Inflammation, chronic, focal				1 (2%)
Thrombosis	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Artery, inflammation, chronic, focal	1 (2%)			
Endocardium, valve, inflammation, chronic, focal	1 (2%)			
Endocrine System				
Adrenal cortex	(49)	(49)	(50)	(50)
Accessory adrenal cortical nodule	1 (2%)	7 (14%)	4 (8%)	3 (6%)
Atrophy			1 (2%)	
Cytoplasmic alteration, focal	3 (6%)	3 (6%)	2 (4%)	4 (8%)
Degeneration, cystic, focal			2 (4%)	
Hyperplasia, diffuse			1 (2%)	
Infiltration cellular, mixed cell				1 (2%)
Necrosis, focal			1 (2%)	
Vacuolization cytoplasmic, diffuse		1 (2%)		
Vacuolization cytoplasmic, focal	12 (24%)	8 (16%)	7 (14%)	6 (12%)
Capsule, fibrosis, focal		1 (2%)		
Adrenal medulla	(49)	(49)	(50)	(50)
Hyperplasia, focal	5 (10%)	12 (24%)	9 (18%)	13 (26%)
Islets, pancreatic	(50)	(49)	(49)	(50)
Hyperplasia		2 (4%)		
Hyperplasia, focal	1 (2%)	1 (2%)		
Parathyroid gland	(49)	(50)	(47)	(49)
Hyperplasia, focal				1 (2%)
Pituitary gland	(48)	(50)	(49)	(50)
Angiectasis	2 (4%)	4 (8%)	1 (2%)	3 (6%)
Hemorrhage		1 (2%)		
Hemorrhage, focal				1 (2%)
Pars distalis, cyst	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Pars distalis, cytoplasmic alteration, focal	3 (6%)	7 (14%)	3 (6%)	8 (16%)
Pars distalis, degeneration, cystic, focal	2 (4%)	2 (4%)		
Pars distalis, hemorrhage, focal	2 (4%)	2 (4%)	1 (2%)	3 (6%)
Pars distalis, hyperplasia, focal	4 (8%)	2 (4%)	3 (6%)	1 (2%)
Pars distalis, pars nervosa, hemorrhage, focal			1 (2%)	
Pars intermedia, hemorrhage, focal			1 (2%)	
Rathke's cleft, cyst				1 (2%)
Rathke's cleft, hemorrhage	1 (2%)		2 (4%)	2 (4%)
Rathke's cleft, hyperplasia, cystic		1 (2%)		
Thyroid gland	(47)	(44)	(43)	(47)
C-cell, hyperplasia	45 (96%)	42 (95%)	41 (95%)	44 (94%)
C-cell, hyperplasia, focal			1 (2%)	
Follicle, cyst	1 (2%)		1 (2%)	2 (4%)
Follicle, degeneration, cystic, focal	2 (4%)			
Follicle, mineralization, focal	45 (96%)	43 (98%)	42 (98%)	42 (89%)
Follicular cell, hypertrophy	4 (9%)	13 (30%)	33 (77%)	40 (85%)
Follicular cell, hypertrophy, focal	1 (2%)			

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
General Body System				
Tissue NOS	(5)	(6)	(2)	(7)
Abdominal, fibrosis			1 (50%)	
Mediastinum, hemorrhage		1 (17%)		
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Fibrosis				1 (2%)
Inflammation, chronic	1 (2%)	1 (2%)		2 (4%)
Penis		(2)		
Thrombosis		1 (50%)		
Preputial gland	(48)	(49)	(50)	(50)
Atrophy				1 (2%)
Cyst		1 (2%)	1 (2%)	
Degeneration, cystic		2 (4%)	1 (2%)	2 (4%)
Hyperplasia, cystic		1 (2%)		1 (2%)
Inflammation, chronic	22 (46%)	12 (24%)	18 (36%)	20 (40%)
Necrosis				1 (2%)
Prostate	(50)	(49)	(50)	(50)
Inflammation, chronic	21 (42%)	23 (47%)	29 (58%)	30 (60%)
Mineralization, focal	3 (6%)	2 (4%)	3 (6%)	4 (8%)
Epithelium, hyperplasia, focal	11 (22%)	4 (8%)	2 (4%)	11 (22%)
Testes	(50)	(50)	(50)	(50)
Atrophy	4 (8%)	10 (20%)	9 (18%)	6 (12%)
Bilateral, atrophy		1 (2%)		
Germinal epithelium, atrophy				1 (2%)
Germinal epithelium, degeneration	1 (2%)			
Interstitial cell, hyperplasia, focal	1 (2%)	1 (2%)	1 (2%)	3 (6%)
Hematopoietic System				
Bone marrow	(48)	(48)	(50)	(49)
Angiectasis		1 (2%)		
Atrophy				1 (2%)
Fibrosis	2 (4%)			
Hyperplasia	28 (58%)	35 (73%)	41 (82%)	40 (82%)
Myeloid cell, erythroid cell, hyperplasia	2 (4%)			
Lymph node	(34)	(24)	(26)	(34)
Ectasia	1 (3%)			
Hemorrhage				1 (3%)
Deep cervical, hemorrhage			1 (4%)	
Deep cervical, hyperplasia, plasma cell	1 (3%)			
Mediastinal, angiectasis			1 (4%)	
Mediastinal, ectasia	5 (15%)	7 (29%)	5 (19%)	3 (9%)
Mediastinal, hemorrhage	3 (9%)	2 (8%)	2 (8%)	1 (3%)
Mediastinal, hyperplasia, histiocytic		3 (13%)	2 (8%)	1 (3%)
Mediastinal, hyperplasia, lymphoid	1 (3%)		1 (4%)	3 (9%)
Mediastinal, hyperplasia, plasma cell	1 (3%)		2 (8%)	
Mediastinal, infiltration cellular, polymorphonuclear		1 (4%)		
Mediastinal, inflammation, chronic active				1 (3%)
Mediastinal, inflammation, suppurative		1 (4%)		
Pancreatic, angiectasis	2 (6%)			
Pancreatic, ectasia	3 (9%)	3 (13%)	3 (12%)	6 (18%)
Pancreatic, hemorrhage	5 (15%)	3 (13%)	1 (4%)	1 (3%)

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Hematopoietic System (continued)				
Lymph node (continued)	(34)	(24)	(26)	(34)
Pancreatic, hyperplasia, histiocytic	8 (24%)	5 (21%)	9 (35%)	6 (18%)
Pancreatic, hyperplasia, lymphoid	1 (3%)	1 (4%)		
Pancreatic, pigmentation	1 (3%)	1 (4%)	1 (4%)	
Renal, hemorrhage			1 (4%)	
Renal, hyperplasia, focal, histiocytic		1 (4%)		
Renal, hyperplasia, lymphoid		1 (4%)		
Lymph node, mesenteric	(49)	(50)	(49)	(50)
Amyloid deposition				1 (2%)
Ectasia	1 (2%)	1 (2%)	1 (2%)	3 (6%)
Hemorrhage		2 (4%)	3 (6%)	
Hyperplasia, focal, histiocytic	1 (2%)			
Hyperplasia, histiocytic	3 (6%)	3 (6%)		1 (2%)
Hyperplasia, lymphoid	2 (4%)	1 (2%)		1 (2%)
Spleen	(48)	(49)	(49)	(50)
Amyloid deposition		1 (2%)		
Angiectasis, focal		2 (4%)	1 (2%)	3 (6%)
Atrophy				1 (2%)
Congestion	1 (2%)			1 (2%)
Fibrosis, focal		2 (4%)	2 (4%)	4 (8%)
Hematopoietic cell proliferation	2 (4%)	6 (12%)	4 (8%)	11 (22%)
Hemorrhage	1 (2%)	1 (2%)		
Hyperplasia, focal, histiocytic	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Infarct, multiple				1 (2%)
Metaplasia, focal, lipocyte			1 (2%)	
Necrosis	1 (2%)			
Pigmentation				1 (2%)
Pigmentation, focal			1 (2%)	
Capsule, accessory spleen, focal	1 (2%)			
Capsule, fibrosis, focal				1 (2%)
Lymphoid follicle, atrophy		1 (2%)		
Thymus	(48)	(48)	(49)	(47)
Angiectasis			1 (2%)	
Cyst		1 (2%)		
Hemorrhage	1 (2%)	2 (4%)	3 (6%)	
Hyperplasia, lymphoid			2 (4%)	1 (2%)
Integumentary System				
Mammary gland	(45)	(43)	(47)	(44)
Cyst				1 (2%)
Dilatation	7 (16%)	7 (16%)	7 (15%)	2 (5%)
Hyperplasia		1 (2%)	2 (4%)	2 (5%)
Inflammation, chronic, focal	1 (2%)			1 (2%)
Skin	(50)	(50)	(50)	(50)
Cyst epithelial inclusion	3 (6%)	1 (2%)	3 (6%)	1 (2%)
Fibrosis, focal		2 (4%)		
Hyperkeratosis, focal	1 (2%)		1 (2%)	
Inflammation, chronic, focal		2 (4%)		
Ulcer		1 (2%)		
Artery, subcutaneous tissue, thrombosis		1 (2%)		
Epidermis, hyperplasia, focal	1 (2%)			
Lip, inflammation, chronic, focal		1 (2%)		
Subcutaneous tissue, cyst		1 (2%)		

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Integumentary System (continued)				
Skin (continued)	(50)	(50)	(50)	(50)
Subcutaneous tissue, cyst epithelial inclusion			1 (2%)	
Subcutaneous tissue, hyperplasia, focal, histiocytic				1 (2%)
Subcutaneous tissue, inflammation, chronic, focal		1 (2%)		
Subcutaneous tissue, inflammation, chronic, focal, suppurative			1 (2%)	
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Cranium, hyperostosis		1 (2%)		
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression, focal	6 (12%)	6 (12%)	7 (14%)	6 (12%)
Hemorrhage, focal	2 (4%)	2 (4%)	4 (8%)	6 (12%)
Cerebrum, ventricle, hydrocephalus		1 (2%)		
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion	2 (4%)	1 (2%)	3 (6%)	
Foreign body, focal	1 (2%)			
Hemorrhage			1 (2%)	
Hemorrhage, focal	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Hyperplasia, focal, histiocytic		1 (2%)	1 (2%)	
Hyperplasia, histiocytic	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Infiltration cellular, mixed cell	1 (2%)	3 (6%)	1 (2%)	2 (4%)
Inflammation, chronic, focal	5 (10%)	2 (4%)	3 (6%)	3 (6%)
Inflammation, focal, suppurative		1 (2%)		
Alveolar epithelium, hyperplasia, focal	8 (16%)	5 (10%)	3 (6%)	4 (8%)
Alveolar epithelium, metaplasia, squamous		1 (2%)		
Alveolus, edema, focal			1 (2%)	
Alveolus, hyperplasia, focal, histiocytic	1 (2%)			
Interstitium, edema		1 (2%)		1 (2%)
Mediastinum, edema		1 (2%)	1 (2%)	
Nose	(49)	(49)	(49)	(50)
Foreign body		1 (2%)	2 (4%)	1 (2%)
Inflammation, chronic	1 (2%)			
Inflammation, suppurative	1 (2%)	1 (2%)	6 (12%)	1 (2%)
Nasolacrimal duct, inflammation	1 (2%)	3 (6%)		1 (2%)
Olfactory epithelium, hyperplasia, focal			1 (2%)	
Respiratory epithelium, hyperplasia, focal			1 (2%)	
Trachea	(50)	(49)	(50)	(50)
Peritracheal tissue, edema		1 (2%)		
Special Senses System				
Eye	(50)	(48)	(46)	(50)
Atrophy				2 (4%)
Cataract		2 (4%)	1 (2%)	2 (4%)
Exudate		1 (2%)		
Cornea, inflammation, chronic			1 (2%)	
Cornea, retrobulbar, inflammation, chronic active				1 (2%)
Retina, degeneration		2 (4%)	1 (2%)	2 (4%)

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Special Senses System (continued)				
Harderian gland	(49)	(49)	(49)	(50)
Fibrosis, focal				1 (2%)
Hyperplasia, focal, histiocytic		1 (2%)	1 (2%)	1 (2%)
Inflammation, chronic, focal		1 (2%)	1 (2%)	1 (2%)
Inflammation, chronic active, diffuse				1 (2%)
Epithelium, hyperplasia, focal	1 (2%)			
Urinary System				
Kidney	(47)	(46)	(49)	(49)
Cyst			1 (2%)	
Cyst, multiple		1 (2%)		
Hydronephrosis		1 (2%)		
Infarct			1 (2%)	
Infarct, multiple	1 (2%)	1 (2%)		
Metaplasia, focal, lipocyte		1 (2%)		
Nephropathy	45 (96%)	44 (96%)	48 (98%)	47 (96%)
Cortex, medulla, atrophy		1 (2%)		
Pelvis, infiltration cellular, mixed cell				1 (2%)
Pelvis, transitional epithelium, hyperplasia		1 (2%)	1 (2%)	
Renal tubule, accumulation, hyaline droplet		1 (2%)	4 (8%)	2 (4%)
Renal tubule, hyperplasia, focal		1 (2%)		
Renal tubule, pigmentation	4 (9%)	4 (9%)	1 (2%)	4 (8%)
Urinary bladder	(48)	(49)	(47)	(50)
Calculus microscopic observation only		1 (2%)		
Edema				2 (4%)
Hemorrhage			2 (4%)	
Inflammation, chronic			1 (2%)	
Serosa, inflammation, focal				1 (2%)
Transitional epithelium, hyperplasia, diffuse	1 (2%)			

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF SODIUM CHLORATE

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	10	11	11	4
Natural deaths	3	3	6	5
Survivors				
Died last week of study		2	1	1
Terminal sacrifice	37	34	32	40
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(50)	(48)	(46)	(49)
Leiomyosarcoma	1 (2%)			
Intestine small, jejunum	(49)	(47)	(44)	(45)
Leiomyoma		1 (2%)		
Liver	(50)	(50)	(50)	(50)
Cholangiocarcinoma		1 (2%)		
Histiocytic sarcoma		1 (2%)		
Histiocytic sarcoma, metastatic, skeletal muscle		1 (2%)		
Mesentery	(18)	(10)	(13)	(16)
Carcinoma				1 (6%)
Oral mucosa			(1)	(1)
Squamous cell carcinoma				1 (100%)
Pancreas	(50)	(49)	(49)	(49)
Acinus, adenoma	2 (4%)			
Salivary glands	(50)	(50)	(50)	(50)
Stomach, forestomach	(50)	(50)	(50)	(50)
Tooth		(2)	(2)	(1)
Odontoma		1 (50%)		
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Adrenal medulla	(50)	(50)	(50)	(50)
Pheochromocytoma malignant		1 (2%)		1 (2%)
Pheochromocytoma complex				1 (2%)
Pheochromocytoma benign	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Islets, pancreatic	(50)	(49)	(49)	(50)
Adenoma	2 (4%)	1 (2%)		
Carcinoma	1 (2%)	1 (2%)		1 (2%)
Pituitary gland	(49)	(49)	(50)	(50)
Pars distalis, adenoma	23 (47%)	18 (37%)	17 (34%)	24 (48%)
Pars distalis, adenoma, multiple				1 (2%)
Pars distalis, carcinoma	1 (2%)	3 (6%)		
Pars intermedia, adenoma	1 (2%)	1 (2%)		1 (2%)
Thyroid gland	(47)	(47)	(43)	(46)
Bilateral, C-cell, adenoma	1 (2%)	2 (4%)		
C-cell, adenoma	11 (23%)	8 (17%)	11 (26%)	9 (20%)
C-cell, carcinoma	1 (2%)	3 (6%)	1 (2%)	3 (7%)
Follicular cell, adenoma				2 (4%)
Follicular cell, carcinoma	1 (2%)		1 (2%)	2 (4%)

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
General Body System				
Tissue NOS	(1)	(2)	(4)	(6)
Mediastinum, carcinoma, metastatic, thyroid gland		1 (50%)		
Mediastinum, carcinoma, metastatic, Zymbal's gland			1 (25%)	
Mediastinum, histiocytic sarcoma			1 (25%)	
Mediastinum, sarcoma				1 (17%)
Genital System				
Clitoral gland	(49)	(50)	(50)	(49)
Adenoma	11 (22%)	5 (10%)	12 (24%)	4 (8%)
Carcinoma	3 (6%)	1 (2%)		
Sarcoma				1 (2%)
Ovary	(50)	(50)	(49)	(50)
Granulosa cell tumor benign	1 (2%)			
Sarcoma				1 (2%)
Oviduct			(2)	
Uterus	(50)	(50)	(49)	(50)
Carcinoma, metastatic, mesentery				1 (2%)
Sarcoma stromal	1 (2%)			
Endometrium, polyp stromal	8 (16%)	8 (16%)	7 (14%)	7 (14%)
Endometrium, polyp stromal, multiple	1 (2%)		2 (4%)	
Endometrium, sarcoma				1 (2%)
Hematopoietic System				
Bone marrow	(50)	(49)	(50)	(50)
Lymph node	(36)	(34)	(30)	(39)
Mediastinal, histiocytic sarcoma			1 (3%)	
Mediastinal, sarcoma				1 (3%)
Lymph node, mandibular	(4)	(6)	(4)	(5)
Lymph node, mesenteric	(50)	(49)	(49)	(50)
Spleen	(50)	(50)	(50)	(50)
Sarcoma				1 (2%)
Thymus	(49)	(48)	(48)	(48)
Sarcoma				1 (2%)
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Adenoma	3 (6%)			2 (4%)
Carcinoma	2 (4%)	1 (2%)		2 (4%)
Carcinoma, multiple	1 (2%)			
Fibroadenoma	23 (46%)	26 (52%)	23 (46%)	27 (54%)
Fibroadenoma, multiple	10 (20%)	3 (6%)	8 (16%)	6 (12%)
Histiocytic sarcoma, metastatic, skeletal muscle		1 (2%)		
Skin	(50)	(50)	(50)	(50)
Basal cell carcinoma	1 (2%)			
Keratoacanthoma				1 (2%)
Trichoepithelioma	2 (4%)			
Pinna, neural crest tumor	1 (2%)			
Subcutaneous tissue, carcinoma, metastatic, mammary gland		1 (2%)		
Subcutaneous tissue, fibroma	4 (8%)	1 (2%)	1 (2%)	1 (2%)

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Integumentary System (continued)				
Skin (continued)	(50)	(50)	(50)	(50)
Subcutaneous tissue, fibrosarcoma		1 (2%)		
Subcutaneous tissue, histiocytic sarcoma		1 (2%)		
Subcutaneous tissue, histiocytic sarcoma, metastatic, skeletal muscle		1 (2%)		
Subcutaneous tissue, lipoma	1 (2%)			
Subcutaneous tissue, sarcoma				1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma		1 (2%)		
Skeletal muscle		(2)	(1)	(1)
Histiocytic sarcoma		1 (50%)		
Rhabdomyosarcoma		1 (50%)		
Nervous System				
Brain	(49)	(50)	(50)	(50)
Carcinoma, metastatic, pituitary gland		2 (4%)		
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	1 (2%)		
Alveolar/bronchiolar carcinoma	1 (2%)			
Carcinoma, metastatic, mammary gland	1 (2%)			
Histiocytic sarcoma		1 (2%)		
Histiocytic sarcoma, metastatic, skeletal muscle		1 (2%)		
Sarcoma				1 (2%)
Nose	(50)	(50)	(50)	(50)
Special Senses System				
Eye	(50)	(49)	(47)	(50)
Harderian gland	(50)	(50)	(50)	(50)
Histiocytic sarcoma		1 (2%)		
Squamous cell carcinoma, metastatic, oral mucosa				1 (2%)
Zymbal's gland	(1)		(1)	(1)
Carcinoma			1 (100%)	
Urinary System				
Kidney	(50)	(49)	(47)	(47)
Sarcoma				1 (2%)
Urinary bladder	(50)	(48)	(50)	(50)
Transitional epithelium, papilloma				1 (2%)
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma		2 (4%)	1 (2%)	
Leukemia mononuclear	11 (22%)	9 (18%)	13 (26%)	9 (18%)
Lymphoma malignant			1 (2%)	
Mesothelioma malignant			1 (2%)	

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Neoplasm Summary				
Total animals with primary neoplasms[c]	49	48	46	48
Total primary neoplasms	133	102	101	118
Total animals with benign neoplasms	46	42	44	47
Total benign neoplasms	107	77	82	87
Total animals with malignant neoplasms	21	22	19	22
Total malignant neoplasms	25	25	19	31
Total animals with metastatic neoplasms	1	5	2	2
Total metastatic neoplasms	1	8	2	2
Total animals with uncertain neoplasms-benign or malignant	1			
Total uncertain neoplasms	1			

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	4 2 3	4 6 2	5 1 1	5 5 5	5 6 6	5 9 4	5 9 5	6 2 3	6 4 4	6 6 1	7 1 7	7 1 8	7 2 7	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 4	7 3 4
Carcass ID Number	2 4 2	2 1 8	2 1 0	2 0 3	2 4 5	2 3 6	2 4 7	2 2 7	2 4 6	2 0 5	2 4 0	2 3 0	2 1 1	2 0 1	2 0 2	2 0 4	2 1 2	2 1 3	2 1 4	2 1 5	2 2 1	2 2 2	2 2 3	2 2 4	2 2 5
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery	+		+		+	+			+		+	+			+		+	+					+	+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma																X									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Pars distalis, adenoma			X	X			X	X		X		X	X			X				X		X	X	X	X
Pars distalis, carcinoma									X																
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Bilateral, C-cell, adenoma																									
C-cell, adenoma										X			X				X	X					X		
C-cell, carcinoma																						X			
Follicular cell, carcinoma																									
General Body System																									
Tissue NOS						+																			
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma							X									X					X		X		
Carcinoma																			X						
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor benign											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 Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	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 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	2 3 3 7	2 3 3 8	2 3 3 9	2 4 4 8	2 4 4 9	2 5 0 0	2 2 2 6	2 2 2 8	2 2 2 9	2 0 0 6	2 0 0 7	2 0 0 8	2 0 0 9	2 1 1 6	2 1 1 7	2 1 9	2 2 0	2 3 0 1	2 3 2	2 3 3	2 3 4	2 3 5	2 4 1	2 4 3	2 4 4	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma				X																						1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery			+						+						+						+	+			+	18
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinus, adenoma													X													2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign												X									X					2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma									X										X							2
Carcinoma																					X					1
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma				X		X		X						X			X			X	X	X	X		X	23
Pars distalis, carcinoma																										1
Pars intermedia, adenoma											X															1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Bilateral, C-cell, adenoma																							X			1
C-cell, adenoma		X				X			X								X					X		X		11
C-cell, carcinoma																										1
Follicular cell, carcinoma													X													1
General Body System																										
Tissue NOS																										1
Genital System																										
Clitoral gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma						X	X							X						X		X	X		X	11
Carcinoma													X					X								3
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granulosa cell tumor benign																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	4 2 3	4 6 2	5 1 1	5 5 5	5 6 6	5 9 4	5 9 5	6 2 3	6 4 4	6 6 1	7 1 7	7 1 8	7 2 7	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 4	7 3 4
Carcass ID Number	2 4 2	2 1 8	2 1 0	2 0 3	2 4 5	2 3 6	2 4 7	2 2 7	2 4 6	2 0 5	2 4 0	2 3 0	2 1 1	2 0 1	2 0 2	2 0 4	2 1 2	2 1 3	2 1 4	2 1 5	2 2 1	2 2 2	2 2 3	2 2 4	2 2 5
Genital System (continued)																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma stromal																									
Endometrium, polyp stromal									X									X							
Endometrium, polyp stromal, multiple																									X
Vagina				+					+		+		+												
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+		+		+	+	+	+			+	+	+	+	+			+	+	+	+	+		+	+
Lymph node, mandibular	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																							X		
Carcinoma		X							X																
Carcinoma, multiple			X																						
Fibroadenoma	X				X		X		X							X	X	X	X		X				
Fibroadenoma, multiple								X				X	X	X	X								X		
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																			X						
Trichoepithelioma																							X		
Pinna, neural crest tumor				X																					
Subcutaneous tissue, fibroma								X																	
Subcutaneous tissue, lipoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve												+													
Spinal cord												+													
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, mammary gland		X																							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Zymbal's gland																+									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	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 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	
Carcass ID Number	2 3 7	2 3 8	2 3 9	2 4 8	2 4 9	2 5 0	2 2 6	2 2 8	2 2 9	2 0 6	2 0 7	2 0 8	2 0 9	2 1 6	2 1 7	2 1 9	2 2 0	2 3 1	2 3 2	2 3 3	2 3 4	2 3 5	2 4 1	2 4 3	2 4 4	Total Tissues/ Tumors
Genital System (continued)																										
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma stromal																	X									1
Endometrium, polyp stromal						X				X					X						X		X		X	8
Endometrium, polyp stromal, multiple																										1
Vagina							+	+																		6
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+		+	+	+	+	+	+		+			+		+	+	+		+	+		+	+	+	36
Lymph node, mandibular	M	M	M	M	M	+	M	M	M	M	M	M	M	M	+	M	M	M	M	M	+	M	M	M	M	4
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																					X	X				3
Carcinoma																										2
Carcinoma, multiple																										1
Fibroadenoma			X	X	X	X	X		X	X	X					X		X	X		X		X		X	23
Fibroadenoma, multiple		X													X		X			X						10
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma																										1
Trichoepithelioma																		X								2
Pinna, neural crest tumor																										1
Subcutaneous tissue, fibroma			X											X								X				4
Subcutaneous tissue, lipoma						X																				1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma														X												1
Alveolar/bronchiolar carcinoma								X																		1
Carcinoma, metastatic, mammary gland																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Zymbal's gland																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	4 2 3	4 6 2	5 1 1	5 5 5	5 6 6	5 9 4	5 9 5	6 2 3	6 4 4	6 6 1	7 1 7	7 1 8	7 2 7	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 4	7 3 4	7 3 4
Carcass ID Number	2 4 2	2 1 8	2 1 0	2 0 3	2 4 5	2 3 6	2 4 7	2 2 7	2 4 6	2 0 5	2 4 0	2 3 0	2 1 1	2 0 1	2 0 2	2 0 4	2 1 2	2 1 3	2 1 4	2 1 5	2 2 1	2 2 2	2 2 3	2 2 4	2 2 5
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 Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	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 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	
Carcass ID Number	2 3 7	2 3 8	2 3 9	2 4 8	2 4 9	2 5 0	2 2 6	2 2 8	2 2 9	2 0 6	2 0 7	2 0 8	2 0 9	2 1 6	2 1 7	2 1 9	2 2 0	2 3 1	2 3 2	2 3 3	2 3 4	2 3 5	2 4 1	2 4 3	2 4 4	Total Tissues/ Tumors
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Leukemia mononuclear							X						X										X			11	

Table B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	365	423	433	511	541	563	623	626	636	639	644	657	714	727	733	734	734	734	734	734	734	734	734	735	735
Carcass ID Number	265	290	286	276	287	258	281	254	295	282	252	260	271	278	257	251	253	255	261	262	263	264	299	266	267
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																						X			
Intestine small, ileum	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma																							X		
Histiocytic sarcoma										X															
Histiocytic sarcoma, metastatic, skeletal muscle																									
Mesentery				+	+		+		+						+							+		+	
Pancreas	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth		+																					+		
Odontoma		X																							
Cardiovascular System																									
Blood vessel										+															
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant					X																				
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma								X				X	X			X				X	X				X
Pars distalis, carcinoma									X		X														
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, C-cell, adenoma																									
C-cell, adenoma											X	X		X											X
C-cell, carcinoma								X													X				
General Body System																									
Tissue NOS								+																	
Mediastinum, carcinoma, metastatic, thyroid gland								X																	

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	735	735	735	735	735	735	735	735	735	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	
Carcass ID Number	26808	26909	27080	28088	28089	29091	29092	29093	29094	25056	25059	27072	27073	27074	27075	27077	27079	28080	28083	28084	28085	29096	29097	29098	30100	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Leiomyoma																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cholangiocarcinoma																										1
Histiocytic sarcoma																										1
Histiocytic sarcoma, metastatic, skeletal muscle																X										1
Mesentery								+	+						+											10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth																										2
Odontoma																										1
Cardiovascular System																										
Blood vessel																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Pheochromocytoma benign									X																	1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma					X																					1
Carcinoma										X																1
Parathyroid gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma			X		X				X				X	X	X		X	X			X			X	X	18
Pars distalis, carcinoma	X																									3
Pars intermedia, adenoma			X																							1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Bilateral, C-cell, adenoma													X			X										2
C-cell, adenoma						X		X		X								X								8
C-cell, carcinoma																		X								3
General Body System																										
Tissue NOS															+											2
Mediastinum, carcinoma, metastatic, thyroid gland																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	3 6 5	4 2 3	4 3 3	5 1 1	5 4 1	5 6 3	6 2 3	6 2 6	6 3 6	6 3 9	6 4 4	6 5 7	7 1 4	7 2 7	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
Carcass ID Number	2 6 5	2 9 0	2 8 6	2 7 6	2 8 7	2 5 8	2 8 1	2 5 4	2 9 5	2 8 2	2 5 2	2 6 0	2 7 1	2 7 8	2 5 7	2 5 1	2 5 3	2 5 5	2 6 1	2 6 2	2 6 3	2 6 4	2 9 9	2 6 6	2 6 7
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																		X			X					
Carcinoma																	X									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrium, polyp stromal									X											X						
Vagina						+														+						
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node		+	+	+	+		+		+	+		+	+	+	+	+		+	+	+	+	+	+	+		
Lymph node, mandibular	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	+	+	M	M	M	M	M	M	M	M	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma					X																					
Fibroadenoma	X			X				X							X	X		X	X	X	X	X		X	
Fibroadenoma, multiple													X													
Histiocytic sarcoma, metastatic, skeletal muscle																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, carcinoma, metastatic, mammary gland					X																					
Subcutaneous tissue, fibroma													X													
Subcutaneous tissue, fibrosarcoma														X												
Subcutaneous tissue, histiocytic sarcoma										X																
Subcutaneous tissue, histiocytic sarcoma, metastatic, skeletal muscle																										
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma						X																				
Skeletal muscle																										
Histiocytic sarcoma																										
Rhabdomyosarcoma																										
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland											X															
Peripheral nerve											+	+														
Spinal cord											+	+														

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

Number of Days on Study	735	735	735	735	735	735	735	735	735	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	
Carcass ID Number	26688	26699	27070	28088	28899	29091	29092	29093	29094	25056	25059	27072	27073	27074	27075	27077	27079	28080	28083	28084	28085	29096	29097	29098	30100	Total Tissues/ Tumors
Genital System																											
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma					X																	X			X		5
Carcinoma																											1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrium, polyp stromal				X									X	X		X			X	X							8
Vagina																+											3
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node			+	+		+		+		+			+	+	+		+	+	+	+	+			+	+		34
Lymph node, mandibular	M	M	+	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	+	M	M		6
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Carcinoma																											1
Fibroadenoma	X	X			X			X	X		X	X	X		X		X	X		X	X	X			X		26
Fibroadenoma, multiple																							X	X			3
Histiocytic sarcoma, metastatic, skeletal muscle																X											1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Subcutaneous tissue, carcinoma, metastatic, mammary gland																											1
Subcutaneous tissue, fibroma																											1
Subcutaneous tissue, fibrosarcoma																											1
Subcutaneous tissue, histiocytic sarcoma																											1
Subcutaneous tissue, histiocytic sarcoma, metastatic, skeletal muscle																X											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Osteosarcoma																											1
Skeletal muscle																+									+		2
Histiocytic sarcoma																X											1
Rhabdomyosarcoma																									X		1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Carcinoma, metastatic, pituitary gland	X																										2
Peripheral nerve		+																									3
Spinal cord		+																									3

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 125 mg/L

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 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 7	7 3 7	7 3 7	
Carcass ID Number	2 6 8	2 6 9	2 7 0	2 8 8	2 8 9	2 9 1	2 9 2	2 9 3	2 9 4	2 5 6	2 5 9	2 7 2	2 7 3	2 7 4	2 7 5	2 7 7	2 7 9	2 8 0	2 8 3	2 8 4	2 8 5	2 9 6	2 9 7	2 9 8	3 0 0	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma								X																		1
Histiocytic sarcoma																										1
Histiocytic sarcoma, metastatic, skeletal muscle																X										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																X										2
Leukemia mononuclear					X					X		X			X								X			9

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	401	511	514	547	573	587	587	615	611	625	636	636	651	699	699	703	703	734	734	734	734	734	734	734	734
Carcass ID Number	350	328	304	318	324	335	341	325	349	334	306	309	320	311	346	312	338	326	227	299	330	336	337	379	340
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	A	+	+	+	A	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	A	+	+	+	A	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	A	A	+	+	A	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	A	+	+	+	A	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	A	A	+	+	A	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+
Intestine small, ileum	+	+	+	A	A	+	+	A	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery		+			+							+	+	+	+	+			+				+	
Oral mucosa			+																						
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth						+	+																		
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X		X		X	X		X	X	X						X		X						
Thyroid gland	+	+	A	A	A	+	+	A	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+
C-cell, adenoma																				X	X	X	X		
C-cell, carcinoma						X																			
Follicular cell, carcinoma																	X								
General Body System																									
Tissue NOS							+						+		+								+		
Mediastinum, carcinoma, metastatic, Zymbal's gland							X																		
Mediastinum, histiocytic sarcoma																							X		
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma		X							X				X				X							X	X	X
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Oviduct			+													+									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Endometrium, polyp stromal			X		X			X																	
Endometrium, polyp stromal, multiple															X		X								
Vagina		+													+										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	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 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 4 4 2	3 4 4 3	3 4 4 4	3 4 4 5	3 4 4 7	3 4 4 8	3 3 1 1	3 3 1 2	3 3 3 3	3 3 0 1	3 3 0 2	3 3 0 3	3 3 0 5	3 3 1 6	3 3 1 7	3 3 1 9	3 3 2 1	3 3 2 2	3 3 2 3	3 3 0 7	3 3 0 8	3 3 1 0	3 3 1 3	3 3 1 4	3 3 1 5	Total Tissues Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery							+		+											+		+				13
Oral mucosa																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth																										2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																				X						1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma									X	X		X		X		X	X	X					X			17
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
C-cell, adenoma	X											X		X					X			X	X		X	11
C-cell, carcinoma																										1
Follicular cell, carcinoma																										1
General Body System																										
Tissue NOS																										4
Mediastinum, carcinoma, metastatic, Zymbal's gland																										1
Mediastinum, histiocytic sarcoma																										1
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma			X						X		X			X								X				12
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Oviduct																										2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endometrium, polyp stromal						X			X			X							X							7
Endometrium, polyp stromal, multiple																										2
Vagina					+																					3

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	401	511	514	547	573	587	587	615	611	625	636	636	635	651	699	699	703	703	734	744	733	734	733	734	733	734	734
Carcass ID Number	350	328	304	318	324	335	341	325	349	344	306	309	320	311	346	312	338	326	227	297	330	336	337	379	340		
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node		+	+	+	+	+	+	+	+				+	+		+	+	+			+	+	+		+	
Mediastinal, histiocytic sarcoma																							X				
Lymph node, mandibular	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M
Lymph node, mesenteric	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma						X			X					X	X		X	X		X	X	X			X	
Fibroadenoma, multiple				X												X			X					X	X	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma																								X			
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle					+																						
Mesothelioma malignant, metastatic, mesentery					X																						
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																											
Eye	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lacrimal gland																											
Zymbal's gland							+																				
Carcinoma							X																				
Urinary System																											
Kidney	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																							X				
Leukemia mononuclear								X	X			X	X		X	X		X	X								
Lymphoma malignant				X																							
Mesothelioma malignant					X																						

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	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 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 4 2	3 4 3	3 4 4	3 4 5	3 4 7	3 4 8	3 3 1	3 3 2	3 3 3	3 0 1	3 0 2	3 0 3	3 0 5	3 1 6	3 1 7	3 1 9	3 2 1	3 2 2	3 2 3	3 0 7	3 0 8	3 1 0	3 1 3	3 1 4	3 1 5	Total Tissues Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node			+		+	+			+		+		+		+	+				+	+	+	+		+	30
Mediastinal, histiocytic sarcoma																										1
Lymph node, mandibular	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	+	M	M	4
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroadenoma	X		X				X		X			X	X	X	X			X			X		X	X	X	23
Fibroadenoma, multiple										X						X						X				8
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibroma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Mesothelioma malignant, metastatic, mesentery																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve										+																1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lacrimal gland																								+		1
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Leukemia mononuclear			X	X		X											X						X			13
Lymphoma malignant																										1
Mesothelioma malignant																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	736	736	736	736	736	736	736	736	736	736	736	737	737	737	
Carcass ID Number	35 9	36 0	37 1	37 2	37 3	37 4	37 5	39 6	39 8	39 9	40 0	36 1	36 2	36 4	38 2	38 3	38 4	38 5	39 2	39 3	39 4	36 6	36 7	36 8	36 9	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery	+					+		+					+			+					+			+	+	16
Carcinoma																										1
Oral mucosa																										1
Squamous cell carcinoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										1
Cardiovascular System																										
Blood vessel															+											1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Pheochromocytoma complex																									X	1
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X		X		X		X			X									X	X	X	X	X	24
Pars distalis, adenoma, multiple																										1
Pars intermedia, adenoma		X																								1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
C-cell, adenoma		X							X	X		X											X		X	9
C-cell, carcinoma						X					X															3
Follicular cell, adenoma																										2
Follicular cell, carcinoma																			X							2
General Body System																										
Tissue NOS													+													6
Mediastinum, sarcoma																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	4 7 5	5 4 2	6 3 5	6 3 6	6 4 4	6 6 8	6 7 0	6 9 3	7 0 3	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 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	3 5 1	3 8 0	3 9 1	3 8 8	3 6 3	3 9 7	3 6 5	3 7 0	3 8 1	3 7 6	3 7 7	3 7 8	3 7 9	3 8 6	3 8 7	3 8 9	3 9 0	3 9 5	3 5 2	3 5 5 3	3 5 5 4	3 5 5 5	3 5 5 6	3 5 7	3 5 8
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									X
Sarcoma							X																		
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mesentery																	X								
Endometrium, polyp stromal			X				X					X	X	X											
Endometrium, sarcoma							X																		
Vagina																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+			+	+	
Mediastinal, sarcoma							X																		
Lymph node, mandibular	M	M	M	M	M	M	M	M	M	M	+	M	+	M	M	M	M	+	M	M	M	M	M	M	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Thymus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																X									
Fibroadenoma						X		X	X		X	X			X	X		X	X	X	X	X	X	X	
Fibroadenoma, multiple				X																					X
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma			X																						
Subcutaneous tissue, fibroma																	X								
Subcutaneous tissue, sarcoma							X																		
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+																								
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma							X																		
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	736	736	736	736	736	736	736	736	736	736	737	737	737	737	
Carcass ID Number	35 9	36 0	37 1	37 2	37 3	37 4	37 5	39 6	39 8	39 9	40 0	36 1	36 2	36 4	38 2	38 3	38 4	38 5	39 2	39 3	39 4	36 6	36 7	36 8	36 9	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma						X									X			X								4
Sarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, mesentery																										1
Endometrium, polyp stromal							X					X														7
Endometrium, sarcoma																										1
Vagina								+																		1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+		+			+	+	+	+		+	+	+		+	+		+		+	+	+	+	39
Mediastinal, sarcoma																										1
Lymph node, mandibular	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	5
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	48
Sarcoma																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma											X									X						2
Carcinoma																								X		2
Fibroadenoma	X	X		X				X	X			X	X		X	X		X			X	X			X	27
Fibroadenoma, multiple						X					X			X									X			6
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma																										1
Subcutaneous tissue, fibroma																										1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	4 7 5	5 4 2	6 3 5	6 3 6	6 4 4	6 6 8	6 7 0	6 9 3	7 0 3	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 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	3 5 1	3 8 0	3 9 1	3 8 8	3 6 3	3 9 7	3 6 5	3 7 0	3 8 1	3 7 6	3 7 7	3 7 8	3 7 9	3 8 6	3 8 7	3 8 9	3 9 0	3 9 5	3 5 2	3 5 3	3 5 4	3 5 5	3 5 6	3 5 7	3 5 8
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, oral mucosa			X																						
Lacrimal gland																							+		
Zymbal's gland			+																						
Urinary System																									
Kidney	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Sarcoma							X																		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional epithelium, papilloma																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X	X			X										X	X	X					

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	
Carcass ID Number	35 9	36 0	37 1	37 2	37 3	37 4	37 5	39 6	39 8	39 9	40 0	40 1	36 1	36 2	36 4	38 2	38 3	38 4	38 5	39 2	39 3	39 4	36 6	36 7	36 8	36 9		Total Tissues/ Tumors
Special Senses System																												
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Squamous cell carcinoma, metastatic, oral mucosa																												1
Lacrimal gland																						+						2
Zymbal's gland																												1
Urinary System																												
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Sarcoma																												1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Transitional epithelium, papilloma									X																			1
Systemic Lesions																												
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Leukemia mononuclear													X									X	X					9

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Adrenal Medulla: Benign, Complex, or Malignant Pheochromocytoma				
Overall rate[a]	2/50 (4%)	2/50 (4%)	1/50 (2%)	3/50 (6%)
Adjusted rate[b]	4.5%	4.5%	2.3%	6.4%
Terminal rate[c]	2/37 (5%)	1/36 (3%)	1/33 (3%)	3/41 (7%)
First incidence (days)	729 (T)	541	729 (T)	729 (T)
Poly-3 test[d]	P=0.430	P=0.690	P=0.512N	P=0.522
Clitoral Gland: Adenoma				
Overall rate	11/49 (22%)	5/50 (10%)	12/50 (24%)	4/49 (8%)
Adjusted rate	24.9%	11.4%	26.9%	8.7%
Terminal rate	10/36 (28%)	5/36 (14%)	8/33 (24%)	4/40 (10%)
First incidence (days)	595	729 (T)	511	729 (T)
Poly-3 test	P=0.131N	P=0.085N	P=0.512	P=0.035N
Clitoral Gland: Carcinoma				
Overall rate	3/49 (6%)	1/50 (2%)	0/50 (0%)	0/49 (0%)
Adjusted rate	6.9%	2.3%	0.0%	0.0%
Terminal rate	3/36 (8%)	1/36 (3%)	0/33 (0%)	0/40 (0%)
First incidence (days)	729 (T)	729 (T)	—[e]	—
Poly-3 test	P=0.054N	P=0.305N	P=0.120N	P=0.110N
Clitoral Gland: Adenoma or Carcinoma				
Overall rate	14/49 (29%)	6/50 (12%)	12/50 (24%)	4/49 (8%)
Adjusted rate	31.7%	13.7%	26.9%	8.7%
Terminal rate	13/36 (36%)	6/36 (17%)	8/33 (24%)	4/40 (10%)
First incidence (days)	595	729 (T)	511	729 (T)
Poly-3 test	P=0.036N	P=0.037N	P=0.395N	P=0.005N
Mammary Gland: Fibroadenoma				
Overall rate	33/50 (66%)	29/50 (58%)	31/50 (62%)	33/50 (66%)
Adjusted rate	69.8%	63.5%	68.7%	69.0%
Terminal rate	26/37 (70%)	25/36 (69%)	24/33 (73%)	29/41 (71%)
First incidence (days)	423	365	547	636
Poly-3 test	P=0.437	P=0.333N	P=0.544N	P=0.557N
Mammary Gland: Adenoma				
Overall rate	3/50 (6%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
Adjusted rate	6.7%	0.0%	0.0%	4.3%
Terminal rate	3/37 (8%)	0/36 (0%)	0/33 (0%)	2/41 (5%)
First incidence (days)	729 (T)	—	—	729 (T)
Poly-3 test	P=0.609	P=0.123N	P=0.125N	P=0.478N
Mammary Gland: Fibroadenoma or Adenoma				
Overall rate	35/50 (70%)	29/50 (58%)	31/50 (62%)	34/50 (68%)
Adjusted rate	74.0%	63.5%	68.7%	71.1%
Terminal rate	28/37 (76%)	25/36 (69%)	24/33 (73%)	30/41 (73%)
First incidence (days)	423	365	547	636
Poly-3 test	P=0.466	P=0.184N	P=0.362N	P=0.464N
Mammary Gland: Carcinoma				
Overall rate	3/50 (6%)	1/50 (2%)	0/50 (0%)	2/50 (4%)
Adjusted rate	6.5%	2.3%	0.0%	4.3%
Terminal rate	0/37 (0%)	0/36 (0%)	0/33 (0%)	2/41 (5%)
First incidence (days)	462	541	—	729 (T)
Poly-3 test	P=0.483N	P=0.323N	P=0.132N	P=0.495N

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Mammary Gland: Adenoma or Carcinoma				
Overall rate	6/50 (12%)	1/50 (2%)	0/50 (0%)	4/50 (8%)
Adjusted rate	12.9%	2.3%	0.0%	8.5%
Terminal rate	3/37 (8%)	0/36 (0%)	0/33 (0%)	4/41 (10%)
First incidence (days)	462	541	—	729 (T)
Poly-3 test	P=0.494N	P=0.064N	P=0.019N	P=0.362N
Mammary Gland: Fibroadenoma, Adenoma, or Carcinoma				
Overall rate	37/50 (74%)	30/50 (60%)	31/50 (62%)	35/50 (70%)
Adjusted rate	76.0%	64.9%	68.7%	73.2%
Terminal rate	28/37 (76%)	25/36 (69%)	24/33 (73%)	31/41 (76%)
First incidence (days)	423	365	547	636
Poly-3 test	P=0.466	P=0.161N	P=0.280N	P=0.466N
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	3/50 (6%)	2/49 (4%)	0/49 (0%)	1/50 (2%)
Adjusted rate	6.7%	4.7%	0.0%	2.1%
Terminal rate	3/37 (8%)	2/36 (6%)	0/32 (0%)	1/41 (2%)
First incidence (days)	729 (T)	729 (T)	—	729 (T)
Poly-3 test	P=0.153N	P=0.518N	P=0.129N	P=0.288N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	23/49 (47%)	18/49 (37%)	17/50 (34%)	25/50 (50%)
Adjusted rate	49.9%	41.0%	36.5%	51.3%
Terminal rate	16/36 (44%)	15/36 (42%)	9/33 (27%)	20/41 (49%)
First incidence (days)	511	626	511	475
Poly-3 test	P=0.367	P=0.261N	P=0.134N	P=0.526
Pituitary Gland (Pars Distalis): Carcinoma				
Overall rate	1/49 (2%)	3/49 (6%)	0/50 (0%)	0/50 (0%)
Adjusted rate	2.3%	6.8%	0.0%	0.0%
Terminal rate	0/36 (0%)	1/36 (3%)	0/33 (0%)	0/41 (0%)
First incidence (days)	644	636	—	—
Poly-3 test	P=0.074N	P=0.304	P=0.504N	P=0.487N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rate	24/49 (49%)	21/49 (43%)	17/50 (34%)	25/50 (50%)
Adjusted rate	51.7%	47.1%	36.5%	51.3%
Terminal rate	16/36 (44%)	16/36 (44%)	9/33 (27%)	20/41 (49%)
First incidence (days)	511	626	511	475
Poly-3 test	P=0.527N	P=0.409N	P=0.099N	P=0.566N
Skin: Trichoepithelioma or Basal Cell Carcinoma				
Overall rate	3/50 (6%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
Adjusted rate	6.7%	0.0%	0.0%	0.0%
Terminal rate	3/37 (8%)	0/36 (0%)	0/33 (0%)	0/41 (0%)
First incidence (days)	729 (T)	—	—	—
Poly-3 test	P=0.084N	P=0.123N	P=0.125N	P=0.110N
Skin: Keratoacanthoma, Trichoepithelioma, or Basal Cell Carcinoma				
Overall rate	3/50 (6%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
Adjusted rate	6.7%	0.0%	0.0%	2.1%
Terminal rate	3/37 (8%)	0/36 (0%)	0/33 (0%)	0/41 (0%)
First incidence (days)	729 (T)	—	—	635
Poly-3 test	P=0.337N	P=0.123N	P=0.125N	P=0.285N

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Skin: Fibroma				
Overall rate	4/50 (8%)	1/50 (2%)	1/50 (2%)	1/50 (2%)
Adjusted rate	8.9%	2.3%	2.3%	2.1%
Terminal rate	3/37 (8%)	0/36 (0%)	1/33 (3%)	1/41 (2%)
First incidence (days)	623	714	729 (T)	729 (T)
Poly-3 test	P=0.175N	P=0.188N	P=0.191N	P=0.167N
Skin: Fibroma, Fibrosarcoma, or Sarcoma				
Overall rate	4/50 (8%)	2/50 (4%)	1/50 (2%)	2/50 (4%)
Adjusted rate	8.9%	4.6%	2.3%	4.2%
Terminal rate	3/37 (8%)	0/36 (0%)	1/33 (3%)	1/41 (2%)
First incidence (days)	623	714	729 (T)	670
Poly-3 test	P=0.277N	P=0.351N	P=0.191N	P=0.316N
Thyroid Gland (C-Cell): Adenoma				
Overall rate	12/47 (26%)	9/47 (19%)	11/43 (26%)	9/46 (20%)
Adjusted rate	28.0%	21.2%	28.3%	20.6%
Terminal rate	10/36 (28%)	6/36 (17%)	11/32 (34%)	9/40 (23%)
First incidence (days)	661	644	729 (T)	729 (T)
Poly-3 test	P=0.368N	P=0.317N	P=0.585	P=0.292N
Thyroid Gland (C-Cell): Carcinoma				
Overall rate	1/47 (2%)	3/47 (6%)	1/43 (2%)	3/46 (7%)
Adjusted rate	2.3%	7.1%	2.5%	6.9%
Terminal rate	1/36 (3%)	2/36 (6%)	0/32 (0%)	3/40 (8%)
First incidence (days)	729 (T)	626	587	729 (T)
Poly-3 test	P=0.394	P=0.302	P=0.743	P=0.314
Thyroid Gland (C-Cell): Adenoma or Carcinoma				
Overall rate	13/47 (28%)	11/47 (23%)	12/43 (28%)	12/46 (26%)
Adjusted rate	30.3%	25.7%	30.5%	27.5%
Terminal rate	11/36 (31%)	7/36 (19%)	11/32 (34%)	12/40 (30%)
First incidence (days)	661	626	587	729 (T)
Poly-3 test	P=0.526N	P=0.406N	P=0.588	P=0.479N
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rate	1/47 (2%)	0/47 (0%)	1/43 (2%)	4/46 (9%)
Adjusted rate	2.3%	0.0%	2.6%	9.1%
Terminal rate	1/36 (3%)	0/36 (0%)	0/32 (0%)	2/40 (5%)
First incidence (days)	729 (T)	—	703	644
Poly-3 test	P=0.026	P=0.503N	P=0.741	P=0.189
Uterus: Stromal Polyp				
Overall rate	9/50 (18%)	8/50 (16%)	9/50 (18%)	7/50 (14%)
Adjusted rate	20.0%	18.2%	20.0%	14.7%
Terminal rate	8/37 (22%)	7/36 (19%)	4/33 (12%)	5/41 (12%)
First incidence (days)	644	636	514	635
Poly-3 test	P=0.318N	P=0.521N	P=0.603	P=0.347N
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rate	10/50 (20%)	8/50 (16%)	9/50 (18%)	7/50 (14%)
Adjusted rate	22.2%	18.2%	20.0%	14.7%
Terminal rate	9/37 (24%)	7/36 (19%)	4/33 (12%)	5/41 (12%)
First incidence (days)	644	636	514	635
Poly-3 test	P=0.255N	P=0.417N	P=0.501N	P=0.255N

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
All Organs: Mononuclear Cell Leukemia				
Overall rate	11/50 (22%)	9/50 (18%)	13/50 (26%)	9/50 (18%)
Adjusted rate	24.0%	20.4%	29.0%	18.8%
Terminal rate	7/37 (19%)	8/36 (22%)	7/33 (21%)	6/41 (15%)
First incidence (days)	594	623	615	636
Poly-3 test	P=0.408N	P=0.437N	P=0.385	P=0.359N
All Organs: Benign Neoplasms				
Overall rate	46/50 (92%)	42/50 (84%)	44/50 (88%)	47/50 (94%)
Adjusted rate	94.3%	88.7%	90.1%	95.1%
Terminal rate	35/37 (95%)	33/36 (92%)	29/33 (88%)	39/41 (95%)
First incidence (days)	423	365	511	475
Poly-3 test	P=0.319	P=0.248N	P=0.342N	P=0.609
All Organs: Malignant Neoplasms				
Overall rate	21/50 (42%)	22/50 (44%)	19/50 (38%)	22/50 (44%)
Adjusted rate	44.2%	47.3%	40.4%	45.5%
Terminal rate	14/37 (38%)	14/36 (39%)	8/33 (24%)	17/41 (42%)
First incidence (days)	462	541	547	635
Poly-3 test	P=0.497N	P=0.465	P=0.432N	P=0.533
All Organs: Benign or Malignant Neoplasms				
Overall rate	49/50 (98%)	48/50 (96%)	46/50 (92%)	48/50 (96%)
Adjusted rate	98.0%	97.5%	93.6%	97.1%
Terminal rate	36/37 (97%)	35/36 (97%)	30/33 (91%)	40/41 (98%)
First incidence (days)	423	365	511	475
Poly-3 test	P=0.429N	P=0.706N	P=0.271N	P=0.652N

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

TABLE B4
Historical Incidence of Thyroid Gland Neoplasms in Control Female F344/N Rats[a]

Study	Incidence in Controls		
	Follicular Cell Adenoma	Follicular Cell Carcinoma	Follicular Cell Adenoma or Carcinoma
Historical Incidence in Drinking Water Controls Given NTP-2000 Diet			
Dipropylene glycol	0/45	1/45	1/45
Sodium chlorate	0/47	1/47	1/47
Sodium nitrite	1/50	1/50	2/50
Overall Historical Incidence: Drinking Water Studies			
Total (%)	1/142 (0.7%)	3/142 (2.1%)	4/142 (2.8%)
Mean ± standard deviation	1.0% ± 1.4%	2.1% ± 0.2%	3.1% ± 1.3%
Range	0%-2%	2%	2%-4%
Overall Historical Incidence: All Routes			
Total (%)	3/1,192 (0.3%)	13/1,192 (1.1%)	16/1,192 (1.3%)
Mean ± standard deviation	0.2% ± 0.6%	1.2% ± 1.2%	1.5% ± 1.3%
Range	0%-2%	0%-4%	0%-4%

[a] Data as of April 19, 2004

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate[a]

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	10	11	11	4
Natural deaths	3	3	6	5
Survivors				
Died last week of study		2	1	1
Terminal sacrifice	37	34	32	40
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine small, duodenum	(50)	(49)	(45)	(49)
Amyloid deposition		1 (2%)		
Epithelium, cyst				1 (2%)
Liver	(50)	(50)	(50)	(50)
Angiectasis, focal			2 (4%)	
Basophilic focus	42 (84%)	44 (88%)	41 (82%)	42 (84%)
Cholangiofibrosis	1 (2%)		1 (2%)	3 (6%)
Clear cell focus	6 (12%)	16 (32%)	18 (36%)	10 (20%)
Congestion	6 (12%)	2 (4%)	2 (4%)	1 (2%)
Degeneration, cystic, focal	1 (2%)		1 (2%)	3 (6%)
Eosinophilic focus		1 (2%)	1 (2%)	2 (4%)
Fibrosis, focal				1 (2%)
Hemorrhage	1 (2%)			
Hepatodiaphragmatic nodule	7 (14%)	4 (8%)	8 (16%)	3 (6%)
Hyperplasia, focal, histiocytic	20 (40%)	19 (38%)	16 (32%)	23 (46%)
Hyperplasia, focal, regenerative	1 (2%)			1 (2%)
Hyperplasia, regenerative				2 (4%)
Infarct, multiple		1 (2%)		
Infiltration cellular, focal, polymorphonuclear			1 (2%)	
Infiltration cellular, polymorphonuclear		1 (2%)		
Infiltration cellular, mixed cell	39 (78%)	38 (76%)	35 (70%)	41 (82%)
Mixed cell focus	12 (24%)	6 (12%)	7 (14%)	8 (16%)
Thrombosis		1 (2%)		
Bile duct, cyst		1 (2%)		
Bile duct, hyperplasia	29 (58%)	24 (48%)	34 (68%)	26 (52%)
Capsule, cyst	1 (2%)			
Hepatocyte, karyomegaly		1 (2%)		
Hepatocyte, necrosis, focal		2 (4%)		1 (2%)
Hepatocyte, vacuolization cytoplasmic			2 (4%)	
Hepatocyte, vacuolization cytoplasmic, diffuse	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Hepatocyte, vacuolization cytoplasmic, focal	17 (34%)	10 (20%)	10 (20%)	10 (20%)
Hepatocyte, periportal, vacuolization cytoplasmic		2 (4%)		
Hepatocyte, periportal, centrilobular, vacuolization cytoplasmic			1 (2%)	
Hepatocyte, centrilobular, necrosis	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Hepatocyte, centrilobular, vacuolization cytoplasmic	5 (10%)	3 (6%)	8 (16%)	3 (6%)
Hepatocyte, midzonal, vacuolization cytoplasmic		2 (4%)		

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

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Alimentary System (continued)				
Mesentery	(18)	(10)	(13)	(16)
Inflammation, chronic, focal		1 (10%)		
Fat, necrosis	4 (22%)	2 (20%)	1 (8%)	
Fat, necrosis, focal	12 (67%)	5 (50%)	9 (69%)	13 (81%)
Pancreas	(50)	(49)	(49)	(49)
Lipomatosis				1 (2%)
Acinus, atrophy, diffuse				1 (2%)
Acinus, atrophy, focal	15 (30%)	8 (16%)	9 (18%)	16 (33%)
Duct, cyst, focal	1 (2%)	2 (4%)	4 (8%)	1 (2%)
Duct, cyst, focal, multiple	10 (20%)	14 (29%)	11 (22%)	18 (37%)
Duct, hyperplasia, focal				1 (2%)
Salivary glands	(50)	(50)	(50)	(50)
Atrophy, focal	2 (4%)			
Stomach, forestomach	(50)	(50)	(50)	(50)
Edema		1 (2%)	1 (2%)	1 (2%)
Erosion		1 (2%)		
Inflammation, chronic		2 (4%)	1 (2%)	
Inflammation, chronic, focal			1 (2%)	
Perforation			1 (2%)	
Ulcer	2 (4%)	7 (14%)		1 (2%)
Epithelium, hyperplasia	2 (4%)	4 (8%)	6 (12%)	1 (2%)
Stomach, glandular	(50)	(49)	(49)	(50)
Erosion	2 (4%)		2 (4%)	2 (4%)
Erosion, focal	1 (2%)			
Inflammation, chronic		1 (2%)		
Necrosis, focal		1 (2%)		
Pigmentation, focal	1 (2%)			
Ulcer		1 (2%)		
Tooth		(2)	(2)	(1)
Malformation			1 (50%)	
Dentine, malformation		1 (50%)		
Peridontal tissue, inflammation, chronic		1 (50%)	2 (100%)	
Peridontal tissue, inflammation, chronic, focal				1 (100%)
Cardiovascular System				
Blood vessel		(1)		(1)
Thrombosis		1 (100%)		
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	4 (8%)	2 (4%)		2 (4%)
Infiltration cellular, mixed cell		1 (2%)	1 (2%)	4 (8%)
Thrombosis	1 (2%)			
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule	2 (4%)	3 (6%)	5 (10%)	2 (4%)
Angiectasis	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Cytoplasmic alteration, focal	1 (2%)	2 (4%)	3 (6%)	2 (4%)
Degeneration, cystic, focal		1 (2%)		1 (2%)
Fibrosis, focal			1 (2%)	
Hematopoietic cell proliferation		1 (2%)		

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Endocrine System (continued)				
Adrenal cortex (continued)	(50)	(50)	(50)	(50)
Hemorrhage	1 (2%)	1 (2%)		2 (4%)
Infiltration cellular, mixed cell		1 (2%)		
Necrosis, focal		1 (2%)		
Vacuolization cytoplasmic, focal	7 (14%)	13 (26%)	7 (14%)	8 (16%)
Adrenal medulla	(50)	(50)	(50)	(50)
Angiectasis				1 (2%)
Hyperplasia, focal	3 (6%)	4 (8%)	1 (2%)	1 (2%)
Infiltration cellular, focal, lymphoid				1 (2%)
Islets, pancreatic	(50)	(49)	(49)	(50)
Hyperplasia, focal			1 (2%)	
Parathyroid gland	(47)	(47)	(48)	(47)
Hyperplasia, focal			1 (2%)	
Pituitary gland	(49)	(49)	(50)	(50)
Angiectasis	10 (20%)	6 (12%)	2 (4%)	13 (26%)
Pigmentation, focal	1 (2%)			
Pars distalis, angiectasis	1 (2%)	2 (4%)	2 (4%)	
Pars distalis, cyst	2 (4%)	2 (4%)	1 (2%)	2 (4%)
Pars distalis, cytoplasmic alteration, focal	3 (6%)	1 (2%)	2 (4%)	3 (6%)
Pars distalis, degeneration, cystic, focal	11 (22%)	14 (29%)	11 (22%)	3 (6%)
Pars distalis, hemorrhage, focal	9 (18%)	6 (12%)	10 (20%)	2 (4%)
Pars distalis, hyperplasia, focal	7 (14%)	5 (10%)	10 (20%)	4 (8%)
Pars distalis, infiltration cellular, focal			1 (2%)	
Pars nervosa, hyperplasia, atypical, focal		1 (2%)		
Rathke's cleft, cyst	1 (2%)	2 (4%)		
Rathke's cleft, hemorrhage	1 (2%)	2 (4%)	2 (4%)	6 (12%)
Rathke's cleft, hyperplasia, cystic			1 (2%)	
Thyroid gland	(47)	(47)	(43)	(46)
Congestion				1 (2%)
Ultimobranchial cyst	1 (2%)		1 (2%)	
C-cell, hyperplasia	43 (91%)	45 (96%)	43 (100%)	44 (96%)
Follicle, mineralization, focal	25 (53%)	26 (55%)	40 (93%)	44 (96%)
Follicular cell, hyperplasia, cystic, focal	1 (2%)			
Follicular cell, hypertrophy	3 (6%)	7 (15%)	27 (63%)	42 (91%)
General Body System				
Tissue NOS	(1)	(2)	(4)	(6)
Mediastinum, cyst			1 (25%)	
Mediastinum, thrombosis				1 (17%)
Oral, foreign body, focal				1 (17%)
Oral, necrosis, focal				1 (17%)
Genital System				
Clitoral gland	(49)	(50)	(50)	(49)
Cyst	1 (2%)			
Degeneration, cystic	5 (10%)	2 (4%)	6 (12%)	1 (2%)
Hyperplasia				1 (2%)
Hyperplasia, cystic	1 (2%)	4 (8%)	3 (6%)	1 (2%)
Hyperplasia, cystic, focal		1 (2%)		
Inflammation, chronic	6 (12%)	2 (4%)	1 (2%)	3 (6%)
Duct, inflammation, chronic	1 (2%)			

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Genital System (continued)				
Ovary	(50)	(50)	(49)	(50)
Cyst	5 (10%)	1 (2%)	1 (2%)	4 (8%)
Corpus luteum, hyperplasia				1 (2%)
Interstitial cell, hyperplasia		1 (2%)	1 (2%)	
Periovarian tissue, cyst	4 (8%)	4 (8%)	2 (4%)	1 (2%)
Uterus	(50)	(50)	(49)	(50)
Hemorrhage		1 (2%)		1 (2%)
Hydrometra	1 (2%)			
Inflammation, chronic			1 (2%)	
Inflammation, focal, suppurative				1 (2%)
Inflammation, suppurative		1 (2%)		1 (2%)
Ulcer, chronic active				1 (2%)
Endometrium, hyperplasia, cystic	16 (32%)	7 (14%)	16 (33%)	11 (22%)
Vagina	(6)	(3)	(3)	(1)
Cyst	2 (33%)	1 (33%)	1 (33%)	1 (100%)
Inflammation, chronic	1 (17%)			
Inflammation, suppurative		1 (33%)	1 (33%)	
Hematopoietic System				
Bone marrow	(50)	(49)	(50)	(50)
Angiectasis			1 (2%)	
Hemorrhage				1 (2%)
Hyperplasia	2 (4%)	1 (2%)	1 (2%)	
Hyperplasia, focal, histiocytic			2 (4%)	2 (4%)
Myeloid cell, hyperplasia	7 (14%)	3 (6%)	2 (4%)	6 (12%)
Myeloid cell, erythroid cell, hyperplasia		2 (4%)	2 (4%)	3 (6%)
Lymph node	(36)	(34)	(30)	(39)
Hyperplasia, plasma cell	1 (3%)			
Pigmentation				1 (3%)
Deep cervical, hemorrhage	1 (3%)			
Deep cervical, hyperplasia, lymphoid	1 (3%)			
Deep cervical, hyperplasia, plasma cell				1 (3%)
Mediastinal, angiectasis			1 (3%)	
Mediastinal, congestion	1 (3%)			
Mediastinal, ectasia	2 (6%)	4 (12%)	2 (7%)	4 (10%)
Mediastinal, hemorrhage	6 (17%)	6 (18%)	5 (17%)	3 (8%)
Mediastinal, hyperplasia, histiocytic	1 (3%)	4 (12%)	2 (7%)	3 (8%)
Mediastinal, hyperplasia, lymphoid	1 (3%)	2 (6%)	2 (7%)	3 (8%)
Mediastinal, hyperplasia, plasma cell		1 (3%)		
Mediastinal, infiltration cellular, mixed cell			1 (3%)	
Mediastinal, pigmentation			1 (3%)	
Pancreatic, angiectasis		1 (3%)		
Pancreatic, ectasia	1 (3%)			1 (3%)
Pancreatic, hemorrhage	5 (14%)	3 (9%)		5 (13%)
Pancreatic, hyperplasia, histiocytic	31 (86%)	22 (65%)	15 (50%)	25 (64%)
Pancreatic, hyperplasia, lymphoid			1 (3%)	
Pancreatic, pigmentation	1 (3%)	7 (21%)	3 (10%)	6 (15%)
Lymph node, mandibular	(4)	(6)	(4)	(5)
Ectasia		1 (17%)		

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Hematopoietic System (continued)				
Lymph node, mesenteric	(50)	(49)	(49)	(50)
Hemorrhage				1 (2%)
Hyperplasia, focal, histiocytic			1 (2%)	
Hyperplasia, histiocytic	2 (4%)	4 (8%)		4 (8%)
Hyperplasia, lymphoid	1 (2%)			
Spleen	(50)	(50)	(50)	(50)
Angiectasis, focal		1 (2%)		1 (2%)
Fibrosis, focal		1 (2%)		1 (2%)
Hematopoietic cell proliferation	16 (32%)	21 (42%)	8 (16%)	17 (34%)
Hemorrhage	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Hyperplasia, focal, histiocytic	2 (4%)	4 (8%)	2 (4%)	5 (10%)
Infarct				1 (2%)
Pigmentation, focal			1 (2%)	
Red pulp, fibrosis, diffuse				1 (2%)
Thymus	(49)	(48)	(48)	(48)
Angiectasis	2 (4%)	1 (2%)		
Cyst		1 (2%)		
Hemorrhage	1 (2%)		2 (4%)	1 (2%)
Hyperplasia, lymphoid	1 (2%)			1 (2%)
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Dilatation	37 (74%)	39 (78%)	34 (68%)	38 (76%)
Ectasia	4 (8%)	1 (2%)	3 (6%)	2 (4%)
Fibrosis	2 (4%)	1 (2%)	1 (2%)	4 (8%)
Fibrosis, focal	1 (2%)			
Hyperplasia	7 (14%)	11 (22%)	10 (20%)	9 (18%)
Hyperplasia, focal	1 (2%)			1 (2%)
Inflammation, chronic				1 (2%)
Skin	(50)	(50)	(50)	(50)
Inflammation, chronic, focal		1 (2%)		
Ulcer				1 (2%)
Subcutaneous tissue, fibrosis, focal	1 (2%)			
Musculoskeletal System				
None				
Nervous System				
Brain	(49)	(50)	(50)	(50)
Compression, focal	9 (18%)	9 (18%)	10 (20%)	9 (18%)
Hemorrhage, focal		4 (8%)	3 (6%)	2 (4%)
Necrosis, focal		1 (2%)		
Thalamus, mineralization, focal	1 (2%)			
Thalamus, necrosis, focal	1 (2%)			

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

	0 mg/L	125 mg/L	1,000 mg/L	2,000 mg/L
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion			2 (4%)	1 (2%)
Hemorrhage, focal	1 (2%)		1 (2%)	2 (4%)
Hyperplasia, focal, histiocytic	1 (2%)	1 (2%)		2 (4%)
Hyperplasia, histiocytic	4 (8%)	6 (12%)	5 (10%)	2 (4%)
Infiltration cellular, polymorphonuclear		1 (2%)		
Infiltration cellular, mixed cell	2 (4%)	3 (6%)	2 (4%)	1 (2%)
Inflammation, chronic, focal	2 (4%)		4 (8%)	2 (4%)
Metaplasia, focal, osseous			1 (2%)	
Alveolar epithelium, hyperplasia	1 (2%)			
Alveolar epithelium, hyperplasia, focal	4 (8%)	2 (4%)	3 (6%)	2 (4%)
Interstitium, edema				1 (2%)
Mediastinum, edema			1 (2%)	
Peribronchiolar, hyperplasia, lymphoid			1 (2%)	
Nose	(50)	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)	2 (4%)		
Nasolacrimal duct, inflammation		1 (2%)		1 (2%)
Respiratory epithelium, metaplasia, focal, squamous				1 (2%)
Special Senses System				
Eye	(50)	(49)	(47)	(50)
Atrophy	1 (2%)			
Cataract	2 (4%)	3 (6%)	1 (2%)	2 (4%)
Hemorrhage		1 (2%)		
Retinal detachment	1 (2%)			
Bilateral, atrophy				1 (2%)
Cornea, inflammation, chronic	1 (2%)	1 (2%)		
Cornea, necrosis, focal	1 (2%)			
Retina, degeneration	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Harderian gland	(50)	(50)	(50)	(50)
Hyperplasia, cystic, focal	1 (2%)			
Hyperplasia, focal				1 (2%)
Hyperplasia, focal, histiocytic	2 (4%)		1 (2%)	
Inflammation, chronic, focal		1 (2%)	1 (2%)	2 (4%)
Metaplasia, focal, squamous			1 (2%)	
Epithelium, hyperplasia, focal	1 (2%)			
Urinary System				
Kidney	(50)	(49)	(47)	(47)
Atrophy, diffuse		1 (2%)		
Atrophy, focal	1 (2%)			2 (4%)
Cyst			1 (2%)	1 (2%)
Hyperplasia, lymphoid			1 (2%)	
Infarct		1 (2%)	1 (2%)	
Infiltration cellular, polymorphonuclear		1 (2%)		
Inflammation, chronic	1 (2%)	2 (4%)		
Inflammation, chronic, focal, granulomatous				1 (2%)
Nephropathy	43 (86%)	41 (84%)	37 (79%)	38 (81%)
Pelvis, inflammation, chronic		1 (2%)		
Pelvis, transitional epithelium, hyperplasia		1 (2%)		
Renal tubule, accumulation, hyaline droplet	5 (10%)	12 (24%)	11 (23%)	5 (11%)
Renal tubule, pigmentation	2 (4%)	1 (2%)	4 (9%)	4 (9%)

APPENDIX C
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF SODIUM CHLORATE

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	5	5	4	10
Natural deaths	7	4	5	7
Survivors				
Terminal sacrifice	38	41	41	33
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(48)	(50)	(50)	(50)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Intestine large, cecum	(47)	(49)	(49)	(48)
Carcinoma				1 (2%)
Histiocytic sarcoma				1 (2%)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Intestine small, duodenum	(48)	(50)	(49)	(49)
Adenoma	1 (2%)			
Carcinoma				1 (2%)
Carcinoma, metastatic, islets, pancreatic				1 (2%)
Polyp adenomatous			2 (4%)	
Intestine small, jejunum	(47)	(49)	(50)	(50)
Adenoma			1 (2%)	1 (2%)
Carcinoma	2 (4%)	2 (4%)		2 (4%)
Liver	(48)	(50)	(50)	(50)
Carcinoma, metastatic, islets, pancreatic				1 (2%)
Cholangiocarcinoma	1 (2%)		1 (2%)	
Hemangioma			1 (2%)	
Hemangiosarcoma	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Hemangiosarcoma, metastatic, spleen			1 (2%)	
Hepatoblastoma	5 (10%)	3 (6%)	1 (2%)	3 (6%)
Hepatoblastoma, multiple	1 (2%)			
Hepatocellular carcinoma	14 (29%)	13 (26%)	14 (28%)	12 (24%)
Hepatocellular carcinoma, multiple	6 (13%)	1 (2%)	5 (10%)	1 (2%)
Hepatocellular adenoma	16 (33%)	15 (30%)	13 (26%)	14 (28%)
Hepatocellular adenoma, multiple	14 (29%)	17 (34%)	23 (46%)	16 (32%)
Histiocytic sarcoma	1 (2%)		2 (4%)	2 (4%)
Ito cell tumor malignant		1 (2%)		
Leiomyosarcoma, metastatic, mesentery	1 (2%)			
Mesentery	(9)	(10)	(10)	(8)
Cholangiocarcinoma, metastatic, liver	1 (11%)			
Hepatocellular carcinoma, metastatic, liver			1 (10%)	1 (13%)
Histiocytic sarcoma				2 (25%)
Histiocytic sarcoma, metastatic, liver	1 (11%)			
Ito cell tumor malignant, metastatic, liver		1 (10%)		
Leiomyosarcoma	1 (11%)			
Liposarcoma			1 (10%)	
Pancreas	(48)	(50)	(50)	(50)
Cholangiocarcinoma, metastatic, liver	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	1 (2%)		1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Salivary glands	(50)	(50)	(50)	(50)
Histiocytic sarcoma				1 (2%)

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Alimentary System (continued)				
Stomach, forestomach	(49)	(50)	(50)	(50)
Leiomyosarcoma, metastatic, mesentery	1 (2%)			
Squamous cell papilloma			2 (4%)	2 (4%)
Stomach, glandular	(48)	(50)	(50)	(50)
Adenoma		2 (4%)		
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Leiomyosarcoma, metastatic, mesentery	1 (2%)			
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cholangiocarcinoma, metastatic, liver	1 (2%)			
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Adenoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Hepatocellular carcinoma, metastatic, liver				1 (2%)
Bilateral, subcapsular, adenoma	1 (2%)			
Subcapsular, adenoma	1 (2%)	3 (6%)	4 (8%)	2 (4%)
Islets, pancreatic	(48)	(50)	(50)	(50)
Adenoma	1 (2%)			1 (2%)
Carcinoma				1 (2%)
Pituitary gland	(47)	(47)	(45)	(49)
Pars distalis, adenoma		1 (2%)		
General Body System				
None				
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Cholangiocarcinoma, metastatic, liver			1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Prostate	(50)	(50)	(50)	(50)
Seminal vesicle	(50)	(50)	(50)	(50)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Testes	(50)	(50)	(50)	(50)
Interstitial cell, adenoma				2 (4%)
Hematopoietic System				
Bone marrow	(49)	(50)	(50)	(50)
Hemangiosarcoma, metastatic, spleen			1 (2%)	
Histiocytic sarcoma				1 (2%)
Lymph node	(3)		(1)	(3)
Mediastinal, carcinoma, metastatic, harderian gland				1 (33%)
Mediastinal, hepatocellular carcinoma, metastatic, liver			1 (100%)	1 (33%)
Mediastinal, histiocytic sarcoma, metastatic, liver	1 (33%)			
Mediastinal, leiomyosarcoma, metastatic, mesentery	1 (33%)			
Pancreatic, hepatocellular carcinoma, metastatic, liver			1 (100%)	
Pancreatic, histiocytic sarcoma, metastatic, liver	1 (33%)			
Renal, hepatocellular carcinoma, metastatic, liver			1 (100%)	
Renal, histiocytic sarcoma, metastatic, liver	1 (33%)			
Renal, leiomyosarcoma, metastatic, mesentery	1 (33%)			

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Hematopoietic System (continued)				
Lymph node, mandibular	(49)	(48)	(45)	(49)
Histiocytic sarcoma				1 (2%)
Lymph node, mesenteric	(47)	(50)	(50)	(50)
Hepatocellular carcinoma, metastatic, liver	1 (2%)			
Histiocytic sarcoma				1 (2%)
Leiomyosarcoma, metastatic, mesentery	1 (2%)			
Spleen	(48)	(50)	(50)	(50)
Hemangiosarcoma			1 (2%)	
Histiocytic sarcoma			1 (2%)	1 (2%)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Leiomyosarcoma, metastatic, mesentery	1 (2%)			
Thymus	(43)	(43)	(40)	(44)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (3%)	
Hepatocellular carcinoma, metastatic, liver			1 (3%)	
Leiomyosarcoma, metastatic, mesentery	1 (2%)			
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Subcutaneous tissue, fibrous histiocytoma			1 (2%)	
Subcutaneous tissue, lipoma			1 (2%)	
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Carcinoma, metastatic, harderian gland			1 (2%)	
Skeletal muscle	(3)	(1)	(3)	(2)
Alveolar/bronchiolar carcinoma, metastatic, lung			2 (67%)	
Hepatocellular carcinoma, metastatic, liver				1 (50%)
Histiocytic sarcoma, metastatic, liver	1 (33%)			
Leiomyosarcoma, metastatic, mesentery	1 (33%)			
Rhabdomyosarcoma				1 (50%)
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	6 (12%)	4 (8%)	7 (14%)	6 (12%)
Alveolar/bronchiolar carcinoma	4 (8%)	5 (10%)	6 (12%)	4 (8%)
Alveolar/bronchiolar carcinoma, multiple			1 (2%)	
Carcinoma, metastatic, harderian gland				1 (2%)
Carcinoma, metastatic, kidney			1 (2%)	
Hemangiosarcoma				1 (2%)
Hepatoblastoma, metastatic, liver	1 (2%)	2 (4%)		
Hepatocellular carcinoma, metastatic, liver	9 (18%)	2 (4%)	4 (8%)	6 (12%)
Histiocytic sarcoma			1 (2%)	1 (2%)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Leiomyosarcoma, metastatic, mesentery	1 (2%)			

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Special Senses System				
Harderian gland	(50)	(50)	(50)	(49)
Adenoma	6 (12%)	4 (8%)	4 (8%)	6 (12%)
Carcinoma			1 (2%)	1 (2%)
Urinary System				
Kidney	(49)	(50)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic, lung			1 (2%)	
Hepatocellular carcinoma, metastatic, liver			1 (2%)	
Renal tubule, adenoma		1 (2%)		
Renal tubule, carcinoma			1 (2%)	
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma	1 (2%)		2 (4%)	3 (6%)
Lymphoma malignant	3 (6%)	1 (2%)		3 (6%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	45	45	47	45
Total primary neoplasms	86	76	95	87
Total animals with benign neoplasms	34	38	37	34
Total benign neoplasms	47	48	59	51
Total animals with malignant neoplasms	29	22	30	27
Total malignant neoplasms	39	28	36	36
Total animals with metastatic neoplasms	12	5	9	8
Total metastatic neoplasms	38	5	20	14

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	3 0 1	4 8 4	5 6 1	5 6 1	5 6 2	6 0 3	6 2 3	6 2 5	6 3 8	6 6 1	6 6 3	6 9 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 0 3 7	0 5 0	0 1 4	0 3 8	0 1 5	0 2 8	0 2 5	0 3 9	0 0 9	0 3 1	0 1 0	0 1 8	0 0 8	0 2 6	0 3 5	0 3 6	0 4 2	0 4 5	0 4 8	0 4 9	0 0 2	0 2 2	0 2 3	0 2 7	0 3 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	+	A	+	A	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver										X															
Intestine large, rectum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver										X															
Intestine small, duodenum	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Intestine small, jejunum	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Intestine small, ileum	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma								X																	
Hemangiosarcoma																									
Hepatoblastoma			X															X					X		
Hepatoblastoma, multiple																									
Hepatocellular carcinoma		X			X	X				X		X											X	X	
Hepatocellular carcinoma, multiple											X							X							
Hepatocellular adenoma		X	X	X				X					X				X				X	X			X
Hepatocellular adenoma, multiple						X								X	X	X							X		
Histiocytic sarcoma										X															
Leiomyosarcoma, metastatic, mesentery					X																				
Mesentery					+			+	+	+											+		+		
Cholangiocarcinoma, metastatic, liver								X																	
Histiocytic sarcoma, metastatic, liver										X															
Leiomyosarcoma					X																				
Pancreas	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma, metastatic, liver								X																	
Hepatocellular carcinoma, metastatic, liver											X														
Histiocytic sarcoma, metastatic, liver										X															
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma, metastatic, mesentery					X																				
Stomach, glandular	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver										X															
Leiomyosarcoma, metastatic, mesentery					X																				
Tooth				+																					
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma, metastatic, liver								X																	

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

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 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	0 4 4	0 4 7	0 0 1	0 0 3	0 0 4	0 0 5	0 0 6	0 1 2	0 1 3	0 1 6	0 1 7	0 1 9	0 2 0	0 2 1	0 2 9	0 3 4	0 3 7	0 4 0	0 4 6	0 4 1	0 2 4	0 3 0	0 3 3	0 4 1	0 4 3	Total Tissues/ Tumors
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma, metastatic, liver																											1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Histiocytic sarcoma, metastatic, liver																											1
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma					X																						1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Carcinoma								X														X					2
Intestine small, ileum	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cholangiocarcinoma																											1
Hemangiosarcoma																										X	1
Hepatoblastoma														X						X							5
Hepatoblastoma, multiple																		X									1
Hepatocellular carcinoma			X	X				X								X					X	X		X			14
Hepatocellular carcinoma, multiple		X																X	X				X				6
Hepatocellular adenoma	X	X		X			X	X											X				X				16
Hepatocellular adenoma, multiple					X				X	X	X	X		X						X	X					X	14
Histiocytic sarcoma																											1
Leiomyosarcoma, metastatic, mesentery																											1
Mesentery		+					+		+																		9
Cholangiocarcinoma, metastatic, liver																											1
Histiocytic sarcoma, metastatic, liver																											1
Leiomyosarcoma																											1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cholangiocarcinoma, metastatic, liver																											1
Hepatocellular carcinoma, metastatic, liver																											1
Histiocytic sarcoma, metastatic, liver																											1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leiomyosarcoma, metastatic, mesentery																											1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma, metastatic, liver																											1
Leiomyosarcoma, metastatic, mesentery																											1
Tooth					+																						2
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cholangiocarcinoma, metastatic, liver																											1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	3 0 1	4 8 4	5 6 1	5 6 1	5 6 2	6 0 3	6 2 3	6 2 5	6 3 8	6 6 1	6 6 3	6 9 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 0 3 7	0 5 0	0 1 4	0 3 8	0 1 5	0 2 8	0 2 5	0 3 9	0 0 9	0 3 1	0 1 0	0 1 8	0 0 8	0 2 6	0 3 5	0 3 6	0 4 2	0 4 5	0 4 8	0 4 9	0 0 2	0 2 2	0 2 3	0 2 7	0 3 2
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																					X				
Bilateral, subcapsular, adenoma													X												
Subcapsular, adenoma																									
Adrenal medulla	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	M	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+
Thyroid gland	I	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver										X															
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver										X															
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+				+					+															
Mediastinal, histiocytic sarcoma, metastatic, liver										X															
Mediastinal, leiomyosarcoma, metastatic, mesentery					X																				
Pancreatic, histiocytic sarcoma, metastatic, liver										X															
Renal, histiocytic sarcoma, metastatic, liver										X															
Renal, leiomyosarcoma, metastatic, mesentery					X																				
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	A	+	+	I	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver											X														
Leiomyosarcoma, metastatic, mesentery					X																				
Spleen	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver										X															
Leiomyosarcoma, metastatic, mesentery					X																				
Thymus	M	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Leiomyosarcoma, metastatic, mesentery					X																				

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

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 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	0 4 4	0 4 7	0 0 1	0 0 3	0 0 4	0 0 5	0 0 6	0 1 2	0 1 3	0 1 6	0 1 7	0 1 9	0 2 0	0 2 1	0 2 9	0 3 4	0 3 7	0 4 0	0 4 6	0 4 1	0 1 1	0 2 4	0 2 0	0 3 3	0 3 4	0 4 1	0 4 3	Total Tissues/ Tumors
Endocrine System																												
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																												1
Bilateral, subcapsular, adenoma																												1
Subcapsular, adenoma						X																						1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma									X																			1
Parathyroid gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
General Body System																												
None																												
Genital System																												
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma, metastatic liver																												1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma, metastatic, liver																												1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																												
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node																												3
Mediastinal, histiocytic sarcoma, metastatic, liver																												1
Mediastinal, leiomyosarcoma, metastatic, mesentery																												1
Pancreatic, histiocytic sarcoma, metastatic, liver																												1
Renal, histiocytic sarcoma, metastatic, liver																												1
Renal, leiomyosarcoma, metastatic, mesentery																												1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Hepatocellular carcinoma, metastatic, liver																												1
Leiomyosarcoma, metastatic, mesentery																												1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma, metastatic, liver																												1
Leiomyosarcoma, metastatic, mesentery																												1
Thymus	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+			43
Leiomyosarcoma, metastatic, mesentery																												1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

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 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	0 4 4	0 4 7	0 0 1	0 0 3	0 0 4	0 0 5	0 0 6	0 1 2	0 1 3	0 1 6	0 1 7	0 1 9	0 2 0	0 2 1	0 2 9	0 3 4	0 3 7	0 4 0	0 4 6	0 1 1	0 2 4	0 3 0	0 3 3	0 4 1	0 4 3	Total Tissues/ Tumors
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle						+																				3
Histiocytic sarcoma, metastatic, liver																										1
Leiomyosarcoma, metastatic, mesentery																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X			X									X						X	6
Alveolar/bronchiolar carcinoma																										4
Hepatoblastoma, metastatic, liver																		X								1
Hepatocellular carcinoma, metastatic, liver				X																		X				9
Histiocytic sarcoma, metastatic, liver																										1
Leiomyosarcoma, metastatic, mesentery																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma	X														X										X	6
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant	X																								X	3

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

Number of Days on Study	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 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	
Carcass ID Number	1 0 0	0 5 2	0 5 5	0 5 6	0 6 0	0 6 2	0 6 6	0 6 9	0 7 0	0 7 1	0 8 0	0 8 4	0 8 6	0 8 9	0 9 4	0 6 3	0 6 7	0 6 8	0 7 2	0 7 8	0 8 1	0 9 0	0 9 3	0 9 5	0 9 7	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	I	+	+	41
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma								X					X													2
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Hepatoblastoma												X														3
Hepatocellular carcinoma									X	X	X						X	X	X			X		X		13
Hepatocellular carcinoma, multiple														X												1
Hepatocellular adenoma		X		X		X		X						X			X		X	X			X	X	X	15
Hepatocellular adenoma, multiple			X		X		X					X	X		X	X										17
Ito cell tumor malignant																										1
Mesentery					+										+	+			+	+			+			10
Ito cell tumor malignant, metastatic, liver																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										2
Tooth				+		+																				4
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma				X																						1
Subcapsular, adenoma		X																								3
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	48
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	M	+	+	+	+	+	+	M	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma																							X			1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

Number of Days on Study	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 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	
Carcass ID Number	1 0 0 0	0 5 2	0 5 5	0 5 6	0 6 0	0 6 2	0 6 6	0 6 9	0 7 0	0 7 1	0 8 0	0 8 4	0 8 6	0 8 9	0 9 4	0 6 3	0 6 7	0 6 8	0 7 2	0 7 8	0 8 1	0 9 0	0 9 3	0 9 5	0 9 7	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	M	+	+	I	+	+	M	+	+	+	+	+	+	+	+	+	+	43
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma									X		X													X		4
Alveolar/bronchiolar carcinoma								X	X											X						5
Hepatoblastoma, metastatic, liver												X														2
Hepatocellular carcinoma, metastatic, liver														X												2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma										X													X			4
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenoma																			X							1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant																						X				1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	5 4 3	5 5 8	5 6 2	5 7 0	6 0 7	6 6 7	6 6 8	6 7 2	6 7 3	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0
Carcass ID Number	1 0 9	1 2 4	1 2 8	1 4 0	1 1 7	1 3 0	1 2 7	1 4 4	1 0 3	1 0 8	1 1 2	1 1 6	1 2 6	1 2 9	1 3 1	1 3 4	1 3 9	1 4 1	1 4 2	1 4 4	1 4 8	1 0 2	1 0 5	1 1 0	1 1 3
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	I	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp adenomatous																									
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma													X												
Hemangioma										X															
Hemangiosarcoma																								X	
Hemangiosarcoma, metastatic, spleen						X																			
Hepatoblastoma							X																		
Hepatocellular carcinoma		X	X					X					X	X				X		X				X	X
Hepatocellular carcinoma, multiple				X					X						X										
Hepatocellular adenoma	X							X			X	X				X	X						X		
Hepatocellular adenoma, multiple				X		X				X			X	X	X				X		X	X		X	
Histiocytic sarcoma																									X
Mesentery				+		+	+				+		+	+											
Hepatocellular carcinoma, metastatic, liver													X												
Liposarcoma				X																					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver													X												
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																						X			
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																									
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Subcapsular, adenoma																					X				
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Pituitary gland	+	+	M	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M

Table C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	734	734	734	734	734	734	734	734	
Carcass ID Number	115	120	123	132	136	145	146	147	101	107	111	119	122	135	137	149	150	106	114	118	121	125	133	138	143	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Polyp adenomatous		X			X																					2
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma													X													1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cholangiocarcinoma																										1
Hemangioma																										1
Hemangiosarcoma																										1
Hemangiosarcoma, metastatic, spleen																										1
Hepatoblastoma																										1
Hepatocellular carcinoma			X	X						X			X						X							14
Hepatocellular carcinoma, multiple																				X	X					5
Hepatocellular adenoma				X		X			X			X			X		X									13
Hepatocellular adenoma, multiple	X	X	X		X		X	X			X		X			X		X	X	X				X		23
Histiocytic sarcoma														X												2
Mesentery											+		+		+		+									10
Hepatocellular carcinoma, metastatic, liver																										1
Liposarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic, liver																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma								X																		2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth														+												1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma						X																				1
Subcapsular, adenoma					X							X			X											4
Adrenal medulla	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	45
Thyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48

Table C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	5	5	5	5	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	4	5	6	7	0	6	6	7	7	2	2	2	2	2	2	2	2	2	2	2	2	3	3	3	3
	3	8	2	0	7	7	8	2	3	9	9	9	9	9	9	9	9	9	9	9	9	0	0	0	0
Carcass ID Number	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	2	2	4	1	3	2	0	0	0	1	1	2	2	3	3	3	4	4	4	4	0	0	1	1
	9	4	8	0	7	0	7	4	3	8	2	6	6	9	1	4	9	1	2	4	8	2	5	0	3
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cholangiocarcinoma, metastatic, liver													X												
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma, metastatic, spleen						X																			
Lymph node													+												
Mediastinal, hepatocellular																									
Carcinoma, metastatic, liver													X												
Pancreatic, hepatocellular carcinoma, metastatic, liver													X												
Renal, hepatocellular carcinoma, metastatic, liver													X												
Lymph node, mandibular	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	M	M	M	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma						X																			
Histiocytic sarcoma																									X
Thymus	+	+	M	+	+	+	M	+	+	+	M	+	+	+	+	M	+	+	+	M	+	+	+	+	M
Alveolar/bronchiolar carcinoma, Metastatic, lung					X																				
Hepatocellular carcinoma, metastatic, liver													X												
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrous																									
Histiocytoma																									
Subcutaneous tissue, lipoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland																									
Skeletal muscle	+				+		+																		
Alveolar/bronchiolar carcinoma, Metastatic, lung	X				X																				

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

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 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	1 1 5	1 2 0	1 2 3	1 3 2	1 3 6	1 4 5	1 4 6	1 4 7	1 0 1	1 0 7	1 1 1	1 1 9	1 2 2	1 3 5	1 3 7	1 4 9	1 5 0	1 0 6	1 1 4	1 1 8	1 2 1	1 2 5	1 3 3	1 3 8	1 4 3	Total Tissues/ Tumors
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cholangiocarcinoma, metastatic, liver																									1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma, metastatic, spleen																									1
Lymph node																									1
Mediastinal, hepatocellular carcinoma, metastatic, liver																									1
Pancreatic, hepatocellular carcinoma, metastatic, liver																									1
Renal, hepatocellular carcinoma, metastatic, liver																									1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																									1
Histiocytic sarcoma																									1
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	M	+	+	+	40
Alveolar/bronchiolar carcinoma, metastatic, lung																									1
Hepatocellular carcinoma, metastatic, liver																									1
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrous Histiocytoma				X																					1
Subcutaneous tissue, lipoma																X									1
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, harderian gland											X														1
Skeletal muscle																									3
Alveolar/bronchiolar carcinoma, metastatic, lung																									2

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	543	558	562	570	607	667	688	722	733	729	729	729	729	729	729	729	729	729	729	729	729	729	730	730	730
Carcass ID Number	10209	12244	12288	14400	11417	13300	12327	10404	10003	10038	11212	11516	12266	12299	13191	13349	13939	14141	14422	14444	14848	10202	10025	11410	11113
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve					+		+																		
Spinal cord					+		+																		
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma				X						X				X											
Alveolar/bronchiolar carcinoma	X				X	X					X								X				X		
Alveolar/bronchiolar carcinoma, multiple																									
Carcinoma, metastatic, kidney																									
Hepatocellular carcinoma, metastatic, liver									X				X	X											
Histiocytic sarcoma																									X
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma	X								X																
Carcinoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung					X																				
Hepatocellular carcinoma, metastatic, liver													X												
Renal tubule, carcinoma																									
Urethra								+																	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									X

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

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 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	1 1 5	1 2 0	1 2 3	1 3 2	1 3 6	1 4 5	1 4 6	1 4 7	1 0 1	1 0 7	1 1 1	1 1 9	1 2 2	1 3 5	1 3 7	1 4 9	1 5 0	1 0 6	1 1 4	1 1 8	1 2 1	1 2 5	1 3 3	1 3 8	1 4 3	Total Tissues/ Tumors
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										2
Spinal cord																										2
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma									X			X						X	X							7
Alveolar/bronchiolar carcinoma																										6
Alveolar/bronchiolar carcinoma, multiple																		X								1
Carcinoma, metastatic, kidney					X																					1
Hepatocellular carcinoma, metastatic, liver																					X					4
Histiocytic sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X														X										4
Carcinoma											X															1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Hepatocellular carcinoma, metastatic, liver																										
Renal tubule, carcinoma					X																					1
Urethra																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma														X												2

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	2 8 8	4 6 5	5 3 5	5 7 0	5 9 5	6 0 5	6 1 6	6 1 8	6 4 0	6 4 0	6 5 2	6 5 7	6 6 4	6 9 4	7 1 1	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
Carcass ID Number	1 5 6	1 7 7	1 9 1	1 9 9	2 0 0	1 0 6 7	1 1 6 0	1 1 7 1	1 1 6 3	1 1 9 8	1 1 8 2	1 1 5 4	1 1 8 4	1 1 7 5	1 1 7 6	1 1 8 9	1 1 5 8	1 1 5 1	1 1 6 9	1 1 7 2	1 1 7 4	1 1 8 3	1 1 8 5	1 1 8 7	1 1 9 0
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	I	+	+	I	M	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Histiocytic sarcoma														X											
Intestine small, duodenum	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Carcinoma, metastatic, islets, pancreatic																									
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																		X							
Carcinoma				X											X										
Intestine small, ileum	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, islets, pancreatic																									
Hemangiosarcoma																									
Hepatoblastoma																X									
Hepatocellular carcinoma				X				X	X		X			X	X		X	X							X
Hepatocellular carcinoma, multiple													X												
Hepatocellular adenoma			X		X					X		X				X		X		X	X				X
Hepatocellular adenoma, multiple											X								X			X	X	X	
Histiocytic sarcoma					X									X											
Mesentery				+	+			+				+									+		+		
Hepatocellular carcinoma, metastatic, liver								X																	
Histiocytic sarcoma					X																				
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma								X														X			
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth		+																							
Cardiovascular System																									
Blood vessel																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Hepatocellular carcinoma, metastatic, liver				X																					
Subcapsular, adenoma																									X
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																X									
Carcinoma																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	1 9 2	1 9 6	1 5 7	1 6 1	1 7 0	1 8 0	1 8 1	1 9 3	1 9 5	1 5 2	1 6 2	1 6 4	1 6 6	1 7 3	1 7 8	1 7 9	1 8 8	1 9 7	1 5 3	1 5 5	1 5 9	1 6 5	1 6 8	1 8 6	1 9 4	Total Tissues/ Tumors
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	45
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma						X																			1
Histiocytic sarcoma																									1
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma														X											1
Carcinoma, metastatic, islets, pancreatic						X																			1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																									1
Carcinoma																									2
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, islets, pancreatic						X																			1
Hemangiosarcoma	X																				X				2
Hepatoblastoma								X																X	3
Hepatocellular carcinoma						X										X			X						12
Hepatocellular carcinoma, multiple																									1
Hepatocellular adenoma		X			X						X	X								X					14
Hepatocellular adenoma, multiple			X				X	X	X						X		X				X	X	X	X	X	16
Histiocytic sarcoma																									2
Mesentery																	+		+						8
Hepatocellular carcinoma, metastatic, liver																									1
Histiocytic sarcoma																	X								2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																									1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																									2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth				+						+															3
Cardiovascular System																									
Blood vessel																				+					1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X																							1
Hepatocellular carcinoma, metastatic, liver																									1
Subcapsular, adenoma			X																						2
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																									1
Carcinoma						X																			1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	2 8 8	4 6 5	5 3 5	5 7 0	5 9 5	6 0 5	6 1 6	6 1 8	6 4 0	6 4 0	6 5 2	6 5 7	6 6 4	6 9 4	7 1 1	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 2 9
Carcass ID Number	1 5 6	1 7 7	1 9 1	1 9 9	2 0 0	1 6 7	1 6 0	1 7 1	1 6 3	1 9 8	1 8 2	1 5 4	1 8 4	1 7 5	1 7 6	1 8 9	1 5 8	1 5 1	1 6 9	1 7 2	1 7 4	1 8 3	1 8 5	1 8 7	1 9 0
Endocrine System (continued)																									
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma																			X						
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Lymph node					+		+				+														
Mediastinal, carcinoma, metastatic, Harderian gland					X																				
Mediastinal, hepatocellular carcinoma, metastatic, liver											X														
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Thymus	+	+	+	+	+	M	+	+	+	I	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle			+	+																					
Hepatocellular carcinoma, metastatic, liver				X																					
Rhabdomyosarcoma			X																						
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve	+																								
Spinal cord	+																								

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	729	729	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	734	734	734	734	734	734	734	
Carcass ID Number	19292	19296	19557	19661	19710	19800	19881	19893	19895	19952	19962	19964	19966	19973	19978	19979	19988	19997	19973	19955	19965	19966	19968	19986	19994		Total Tissues/ Tumors
Endocrine System (continued)																											
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
General Body System																											
None																											
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Interstitial cell, adenoma											X																2
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Histiocytic sarcoma																											1
Lymph node																											3
Mediastinal, carcinoma, metastatic, Harderian gland																											1
Mediastinal, hepatocellular carcinoma metastatic, liver																											1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Histiocytic sarcoma																											1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Histiocytic sarcoma																											1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Histiocytic sarcoma																											1
Thymus	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+		44
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Skeletal muscle																											2
Hepatocellular carcinoma, metastatic, liver																											1
Rhabdomyosarcoma																											1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Peripheral nerve																											1
Spinal cord																											1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	1 1 9 2	1 1 9 6	1 1 5 7	1 1 6 1	1 1 7 0	1 1 8 0	1 1 8 1	1 1 9 3	1 1 9 5	1 1 5 2	1 1 6 2	1 1 6 4	1 1 6 6	1 1 7 3	1 1 7 8	1 1 7 9	1 1 8 8	1 1 9 7	1 1 5 3	1 1 5 5	1 1 5 9	1 1 6 5	1 1 6 8	1 1 8 6	1 1 9 4	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma					X				X																	6
Alveolar/bronchiolar carcinoma					X								X													4
Carcinoma, metastatic, harderian gland																										1
Hemangiosarcoma																					X					1
Hepatocellular carcinoma, metastatic, liver																										6
Histiocytic sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma											X	X			X											6
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																	X									3
Lymphoma malignant							X														X					3

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Adrenal Cortex: Adenoma				
Overall rate[a]	3/50 (6%)	4/50 (8%)	5/50 (10%)	3/50 (6%)
Adjusted rate[b]	6.7%	8.5%	10.8%	6.9%
Terminal rate[c]	3/38 (8%)	4/41 (10%)	5/41 (12%)	3/33 (9%)
First incidence (days)	729 (T)	729 (T)	729 (T)	729 (T)
Poly-3 test[d]	P=0.566	P=0.532	P=0.379	P=0.654
Harderian Gland: Adenoma				
Overall rate	6/50 (12%)	4/50 (8%)	4/50 (8%)	6/50 (12%)
Adjusted rate	13.2%	8.4%	8.5%	13.5%
Terminal rate	4/38 (11%)	3/41 (7%)	2/41 (5%)	3/33 (9%)
First incidence (days)	562	698	543	605
Poly-3 test	P=0.478	P=0.344N	P=0.345N	P=0.606
Harderian Gland: Adenoma or Carcinoma				
Overall rate	6/50 (12%)	4/50 (8%)	5/50 (10%)	7/50 (14%)
Adjusted rate	13.2%	8.4%	10.6%	15.6%
Terminal rate	4/38 (11%)	3/41 (7%)	3/41 (7%)	3/33 (9%)
First incidence (days)	562	698	543	595
Poly-3 test	P=0.335	P=0.344N	P=0.473N	P=0.491
Intestine Small (Duodenum or Jejunum): Carcinoma				
Overall rate	2/50 (4%)	2/50 (4%)	0/50 (0%)	3/50 (6%)
Adjusted rate	4.5%	4.2%	0.0%	6.8%
Terminal rate	2/38 (5%)	2/41 (5%)	0/41 (0%)	1/33 (3%)
First incidence (days)	729 (T)	729 (T)	—[e]	570
Poly-3 test	P=0.418	P=0.673N	P=0.228N	P=0.498
Intestine Small (Duodenum or Jejunum): Adenoma or Carcinoma				
Overall rate	3/50 (6%)	2/50 (4%)	1/50 (2%)	4/50 (8%)
Adjusted rate	6.7%	4.2%	2.2%	9.0%
Terminal rate	3/38 (8%)	2/41 (5%)	1/41 (2%)	2/33 (6%)
First incidence (days)	729 (T)	729 (T)	729 (T)	570
Poly-3 test	P=0.362	P=0.473N	P=0.291N	P=0.497
Liver: Hepatocellular Adenoma				
Overall rate	30/48 (63%)	32/50 (64%)	36/50 (72%)	30/50 (60%)
Adjusted rate	64.5%	67.6%	74.9%	65.5%
Terminal rate	25/38 (66%)	31/41 (76%)	32/41 (78%)	24/33 (73%)
First incidence (days)	484	722	543	535
Poly-3 test	P=0.478	P=0.459	P=0.184	P=0.546
Liver: Hepatocellular Carcinoma				
Overall rate	20/48 (42%)	14/50 (28%)	19/50 (38%)	13/50 (26%)
Adjusted rate	43.3%	28.6%	39.2%	28.4%
Terminal rate	14/38 (37%)	10/41 (24%)	14/41 (34%)	5/33 (15%)
First incidence (days)	484	431	558	570
Poly-3 test	P=0.159N	P=0.099N	P=0.421N	P=0.100N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	41/48 (85%)	42/50 (84%)	44/50 (88%)	40/50 (80%)
Adjusted rate	86.0%	85.8%	89.2%	84.2%
Terminal rate	32/38 (84%)	37/41 (90%)	37/41 (90%)	27/33 (82%)
First incidence (days)	484	431	543	535
Poly-3 test	P=0.477N	P=0.604N	P=0.434	P=0.517N

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Liver: Hepatoblastoma				
Overall rate	6/48 (13%)	3/50 (6%)	1/50 (2%)	3/50 (6%)
Adjusted rate	13.5%	6.3%	2.1%	6.8%
Terminal rate	5/38 (13%)	1/41 (2%)	0/41 (0%)	2/33 (6%)
First incidence (days)	561	577	668	719
Poly-3 test	P=0.179N	P=0.207N	P=0.048N	P=0.248N
Liver: Hepatocellular Carcinoma or Hepatoblastoma				
Overall rate	23/48 (48%)	16/50 (32%)	20/50 (40%)	16/50 (32%)
Adjusted rate	49.2%	32.7%	41.0%	34.9%
Terminal rate	16/38 (42%)	11/41 (27%)	14/41 (34%)	7/33 (21%)
First incidence (days)	484	431	558	570
Poly-3 test	P=0.180N	P=0.074N	P=0.276N	P=0.117N
Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma				
Overall rate	41/48 (85%)	43/50 (86%)	45/50 (90%)	40/50 (80%)
Adjusted rate	86.0%	87.7%	90.8%	84.2%
Terminal rate	32/38 (84%)	37/41 (90%)	37/41 (90%)	27/33 (82%)
First incidence (days)	484	431	543	535
Poly-3 test	P=0.448N	P=0.522	P=0.337	P=0.517N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	6/50 (12%)	4/50 (8%)	7/50 (14%)	6/50 (12%)
Adjusted rate	13.5%	8.4%	14.9%	13.7%
Terminal rate	6/38 (16%)	3/41 (7%)	6/41 (15%)	4/33 (12%)
First incidence (days)	729 (T)	604	570	711
Poly-3 test	P=0.423	P=0.328N	P=0.540	P=0.610
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	4/50 (8%)	5/50 (10%)	7/50 (14%)	4/50 (8%)
Adjusted rate	8.9%	10.6%	14.7%	9.1%
Terminal rate	2/38 (5%)	5/41 (12%)	4/41 (10%)	2/33 (6%)
First incidence (days)	638	729 (T)	543	640
Poly-3 test	P=0.534	P=0.528	P=0.293	P=0.631
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	10/50 (20%)	8/50 (16%)	13/50 (26%)	9/50 (18%)
Adjusted rate	22.1%	16.8%	27.0%	20.3%
Terminal rate	8/38 (21%)	7/41 (17%)	9/41 (22%)	5/33 (15%)
First incidence (days)	638	604	543	640
Poly-3 test	P=0.505	P=0.349N	P=0.383	P=0.520N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	1/50 (2%)	2/50 (4%)	3/50 (6%)	2/50 (4%)
Adjusted rate	2.2%	4.2%	6.4%	4.6%
Terminal rate	1/38 (3%)	2/41 (5%)	2/41 (5%)	2/33 (6%)
First incidence (days)	729 (T)	729 (T)	667	729 (T)
Poly-3 test	P=0.386	P=0.520	P=0.322	P=0.494
All Organs: Histiocytic Sarcoma				
Overall rate	1/50 (2%)	0/50 (0%)	2/50 (4%)	3/50 (6%)
Adjusted rate	2.2%	0.0%	4.3%	6.8%
Terminal rate	0/38 (0%)	0/41 (0%)	2/41 (5%)	1/33 (3%)
First incidence (days)	661	—	729 (T)	595
Poly-3 test	P=0.097	P=0.489N	P=0.512	P=0.301

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
All Organs: Malignant Lymphoma				
Overall rate	3/50 (6%)	1/50 (2%)	0/50 (0%)	3/50 (6%)
Adjusted rate	6.6%	2.1%	0.0%	6.8%
Terminal rate	2/38 (5%)	1/41 (2%)	0/41 (0%)	2/33 (6%)
First incidence (days)	301	729 (T)	—	616
Poly-3 test	P=0.514	P=0.292N	P=0.115N	P=0.649
All Organs: Benign Neoplasms				
Overall rate	34/50 (68%)	38/50 (76%)	37/50 (74%)	34/50 (68%)
Adjusted rate	70.7%	79.4%	76.7%	72.5%
Terminal rate	27/38 (71%)	35/41 (85%)	32/41 (78%)	24/33 (73%)
First incidence (days)	484	604	543	535
Poly-3 test	P=0.528N	P=0.223	P=0.330	P=0.515
All Organs: Malignant Neoplasms				
Overall rate	29/50 (58%)	22/50 (44%)	30/50 (60%)	27/50 (54%)
Adjusted rate	59.1%	44.9%	60.0%	56.7%
Terminal rate	19/38 (50%)	17/41 (42%)	21/41 (51%)	14/33 (42%)
First incidence (days)	301	431	543	535
Poly-3 test	P=0.435	P=0.113N	P=0.544	P=0.487N
All Organs: Benign or Malignant Neoplasms				
Overall rate	45/50 (90%)	45/50 (90%)	47/50 (94%)	45/50 (90%)
Adjusted rate	90.7%	91.0%	94.0%	93.1%
Terminal rate	34/38 (90%)	38/41 (93%)	38/41 (93%)	30/33 (91%)
First incidence (days)	301	431	543	535
Poly-3 test	P=0.355	P=0.618	P=0.402	P=0.470

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

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Moribund	5	5	4	10
Natural deaths	7	4	5	7
Survivors				
Terminal sacrifice	38	41	41	33
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, cecum	(47)	(49)	(49)	(48)
Edema	1 (2%)	3 (6%)	4 (8%)	2 (4%)
Inflammation, chronic		1 (2%)		1 (2%)
Intestine small, duodenum	(48)	(50)	(49)	(49)
Ulcer		1 (2%)	1 (2%)	
Epithelium, hyperplasia			1 (2%)	1 (2%)
Intestine small, jejunum	(47)	(49)	(50)	(50)
Epithelium, hyperplasia				2 (4%)
Intestine small, ileum	(47)	(49)	(49)	(49)
Cyst		1 (2%)		
Liver	(48)	(50)	(50)	(50)
Angiectasis	2 (4%)	2 (4%)		
Basophilic focus		2 (4%)	3 (6%)	4 (8%)
Clear cell focus	12 (25%)	19 (38%)	19 (38%)	13 (26%)
Cyst			1 (2%)	1 (2%)
Eosinophilic focus	11 (23%)	10 (20%)	5 (10%)	11 (22%)
Hematopoietic cell proliferation	1 (2%)			4 (8%)
Hemorrhage	1 (2%)	1 (2%)		
Hyperplasia, lymphoid		1 (2%)	1 (2%)	
Infarct			1 (2%)	
Infiltration cellular, mixed cell	2 (4%)	1 (2%)	1 (2%)	
Mixed cell focus	2 (4%)	9 (18%)	8 (16%)	7 (14%)
Necrosis, focal	4 (8%)	6 (12%)	7 (14%)	6 (12%)
Regeneration, focal			1 (2%)	
Tension lipidosis	1 (2%)		1 (2%)	
Bile duct, hyperplasia				2 (4%)
Centrilobular, necrosis	1 (2%)			2 (4%)
Hepatocyte, karyomegaly			1 (2%)	1 (2%)
Hepatocyte, vacuolization cytoplasmic	2 (4%)			3 (6%)
Kupffer cell, pigmentation	2 (4%)		1 (2%)	
Mesentery	(9)	(10)	(10)	(8)
Infarct			1 (10%)	
Inflammation, chronic	1 (11%)			2 (25%)
Fat, necrosis	3 (33%)	8 (80%)	6 (60%)	5 (63%)
Pancreas	(48)	(50)	(50)	(50)
Cyst				2 (4%)
Acinus, cytoplasmic alteration			1 (2%)	1 (2%)
Salivary glands	(50)	(50)	(50)	(50)
Atrophy			1 (2%)	2 (4%)
Hyperplasia, lymphoid	7 (14%)	3 (6%)	6 (12%)	4 (8%)

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

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Alimentary System (continued)				
Stomach, forestomach	(49)	(50)	(50)	(50)
Cyst	2 (4%)			
Diverticulum	1 (2%)	1 (2%)		2 (4%)
Erosion		1 (2%)		
Inflammation, chronic active	2 (4%)	2 (4%)	4 (8%)	2 (4%)
Ulcer	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Epithelium, hyperplasia	3 (6%)	7 (14%)	2 (4%)	4 (8%)
Stomach, glandular	(48)	(50)	(50)	(50)
Cyst	1 (2%)	2 (4%)	1 (2%)	
Ulcer				1 (2%)
Tooth	(2)	(4)	(1)	(3)
Malformation	2 (100%)	4 (100%)		2 (67%)
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy				2 (4%)
Inflammation, chronic	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Mineralization	1 (2%)			2 (4%)
Thrombosis			1 (2%)	1 (2%)
Endocrine System				
Adrenal cortex	(50)	(50)	(50)	(50)
Accessory adrenal cortical nodule	6 (12%)	5 (10%)	3 (6%)	5 (10%)
Degeneration, fatty	1 (2%)	1 (2%)		2 (4%)
Hyperplasia, focal	4 (8%)	6 (12%)	7 (14%)	9 (18%)
Hypertrophy	1 (2%)			
Hypertrophy, focal	9 (18%)	16 (32%)	11 (22%)	11 (22%)
Capsule, hyperplasia	5 (10%)	3 (6%)	1 (2%)	8 (16%)
Adrenal medulla	(49)	(48)	(49)	(49)
Hyperplasia	1 (2%)	1 (2%)	1 (2%)	
Islets, pancreatic	(48)	(50)	(50)	(50)
Hyperplasia	31 (65%)	25 (50%)	28 (56%)	23 (46%)
Parathyroid gland	(46)	(48)	(47)	(49)
Cyst		1 (2%)	2 (4%)	1 (2%)
Pituitary gland	(47)	(47)	(45)	(49)
Pars distalis, cyst	1 (2%)	1 (2%)	2 (4%)	5 (10%)
Pars intermedia, cyst	1 (2%)			
Thyroid gland	(48)	(50)	(48)	(50)
Degeneration, cystic	13 (27%)	17 (34%)	14 (29%)	15 (30%)
Follicular cell, hypertrophy	2 (4%)		1 (2%)	2 (4%)
General Body System				
None				
Genital System				
Epididymis	(50)	(50)	(50)	(50)
Atypia cellular	1 (2%)	6 (12%)	4 (8%)	3 (6%)
Granuloma sperm		1 (2%)		1 (2%)
Inflammation, chronic		1 (2%)	1 (2%)	1 (2%)

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Genital System (continued)				
Preputial gland	(50)	(50)	(50)	(50)
Cyst	22 (44%)	26 (52%)	15 (30%)	29 (58%)
Inflammation, chronic	28 (56%)	27 (54%)	18 (36%)	21 (42%)
Prostate	(50)	(50)	(50)	(50)
Inflammation, chronic	1 (2%)	4 (8%)	3 (6%)	5 (10%)
Seminal vesicle	(50)	(50)	(50)	(50)
Degeneration		1 (2%)		2 (4%)
Dilatation			1 (2%)	
Inflammation, chronic	3 (6%)		1 (2%)	
Testes	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)			1 (2%)
Atrophy		1 (2%)	1 (2%)	1 (2%)
Necrosis				1 (2%)
Germinal epithelium, atrophy	1 (2%)	5 (10%)	3 (6%)	4 (8%)
Hematopoietic System				
Bone marrow	(49)	(50)	(50)	(50)
Hyperplasia	21 (43%)	12 (24%)	13 (26%)	15 (30%)
Lymph node	(3)		(1)	(3)
Mediastinal, hemorrhage				1 (33%)
Lymph node, mandibular	(49)	(48)	(45)	(49)
Atrophy	1 (2%)			1 (2%)
Hyperplasia, lymphoid	14 (29%)	14 (29%)	16 (36%)	16 (33%)
Pigmentation	7 (14%)	10 (21%)	9 (20%)	9 (18%)
Lymph node, mesenteric	(47)	(50)	(50)	(50)
Atrophy	2 (4%)	1 (2%)		1 (2%)
Hematopoietic cell proliferation	2 (4%)		4 (8%)	1 (2%)
Hemorrhage	4 (9%)	6 (12%)	2 (4%)	4 (8%)
Hyperplasia, lymphoid	11 (23%)	6 (12%)	6 (12%)	9 (18%)
Spleen	(48)	(50)	(50)	(50)
Depletion lymphoid				1 (2%)
Hematopoietic cell proliferation	21 (44%)	17 (34%)	18 (36%)	21 (42%)
Hyperplasia, lymphoid	8 (17%)	9 (18%)	10 (20%)	8 (16%)
Pigmentation		3 (6%)	1 (2%)	1 (2%)
Lymphoid follicle, atrophy	1 (2%)		1 (2%)	3 (6%)
Thymus	(43)	(43)	(40)	(44)
Atrophy	11 (26%)	13 (30%)	4 (10%)	13 (30%)
Cyst	1 (2%)	3 (7%)	4 (10%)	4 (9%)
Hyperplasia, lymphoid	2 (5%)	1 (2%)		
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Cyst epithelial inclusion	1 (2%)			
Edema				3 (6%)
Inflammation, chronic			1 (2%)	1 (2%)
Ulcer	2 (4%)			
Epidermis, hyperplasia	1 (2%)			1 (2%)

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Fracture	1 (2%)	1 (2%)		2 (4%)
Hyperostosis	1 (2%)	1 (2%)		
Skeletal muscle	(3)	(1)	(3)	(2)
Atrophy		1 (100%)		
Infiltration cellular, lipocyte	1 (33%)			
Nervous System				
Peripheral nerve		(1)	(2)	(1)
Atrophy		1 (100%)		
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Edema	6 (12%)	11 (22%)	7 (14%)	8 (16%)
Foreign body	1 (2%)			1 (2%)
Hemorrhage	5 (10%)	3 (6%)	4 (8%)	5 (10%)
Hyperplasia, lymphoid	4 (8%)	5 (10%)	7 (14%)	6 (12%)
Infiltration cellular, histiocyte	8 (16%)	5 (10%)	9 (18%)	10 (20%)
Metaplasia, osseous		2 (4%)		
Alveolar epithelium, hyperplasia	2 (4%)	3 (6%)	1 (2%)	5 (10%)
Nose	(50)	(50)	(50)	(50)
Foreign body	1 (2%)	1 (2%)		2 (4%)
Inflammation, chronic	1 (2%)	2 (4%)	1 (2%)	5 (10%)
Respiratory epithelium, hyperplasia	1 (2%)	1 (2%)		
Special Senses System				
Eye	(49)	(50)	(50)	(50)
Cataract		1 (2%)		
Inflammation, chronic			3 (6%)	
Harderian gland	(50)	(50)	(50)	(49)
Hyperplasia, focal	1 (2%)			1 (2%)
Inflammation, chronic	1 (2%)	3 (6%)	3 (6%)	2 (4%)
Urinary System				
Kidney	(49)	(50)	(50)	(50)
Cyst	14 (29%)	10 (20%)	9 (18%)	10 (20%)
Hydronephrosis	1 (2%)	2 (4%)	2 (4%)	1 (2%)
Hyperplasia, lymphoid	8 (16%)	6 (12%)	4 (8%)	11 (22%)
Infarct	5 (10%)	1 (2%)	4 (8%)	5 (10%)
Inflammation, chronic		1 (2%)		1 (2%)
Metaplasia, osseous	7 (14%)	5 (10%)	3 (6%)	4 (8%)
Nephropathy	37 (76%)	42 (84%)	43 (86%)	36 (72%)
Renal tubule, accumulation, hyaline droplet		1 (2%)	1 (2%)	
Renal tubule, dilatation	1 (2%)	2 (4%)		3 (6%)
Renal tubule, hyperplasia	1 (2%)	1 (2%)		1 (2%)
Renal tubule, necrosis	1 (2%)			2 (4%)
Renal tubule, pigmentation		2 (4%)	1 (2%)	1 (2%)
Urethra			(1)	
Angiectasis			1 (100%)	

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Urinary System (continued)				
Urinary bladder	(49)	(50)	(50)	(50)
Edema	1 (2%)			1 (2%)
Hyperplasia, lymphoid		1 (2%)	1 (2%)	
Inflammation, chronic				1 (2%)
Transitional epithelium, hyperplasia		2 (4%)		1 (2%)

APPENDIX D
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF SODIUM CHLORATE

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental death	1			
Moribund sacrifice	3	5	6	8
Natural deaths	10	10	12	7
Survivors				
Died last week of study		1		
Terminal sacrifice	36	34	31	35
Other			1	
Animals examined microscopically	50	50	50	50
Alimentary System				
Esophagus	(49)	(50)	(50)	(50)
Gallbladder	(40)	(44)	(44)	(48)
Intestine large, cecum	(44)	(47)	(47)	(47)
Hemangioma			1 (2%)	
Intestine small, duodenum	(46)	(47)	(47)	(50)
Adenoma		1 (2%)		
Polyp adenomatous				1 (2%)
Intestine small, jejunum	(45)	(47)	(47)	(47)
Histiocytic sarcoma			1 (2%)	
Intestine small, ileum	(42)	(45)	(46)	(47)
Liver	(49)	(50)	(49)	(50)
Hemangioma	2 (4%)			
Hemangiosarcoma	1 (2%)	2 (4%)		
Hemangiosarcoma, metastatic, spleen		1 (2%)		
Hepatoblastoma	1 (2%)			
Hepatocellular carcinoma	2 (4%)	6 (12%)	11 (22%)	6 (12%)
Hepatocellular carcinoma, multiple	1 (2%)	7 (14%)	4 (8%)	3 (6%)
Hepatocellular adenoma	15 (31%)	9 (18%)	14 (29%)	8 (16%)
Hepatocellular adenoma, multiple	15 (31%)	10 (20%)	12 (24%)	15 (30%)
Histiocytic sarcoma			1 (2%)	1 (2%)
Mesentery	(30)	(32)	(27)	(24)
Fibrosarcoma			1 (4%)	
Fibrous histiocytoma	1 (3%)			
Hemangiosarcoma				1 (4%)
Hepatocellular carcinoma, metastatic, liver			1 (4%)	
Histiocytic sarcoma			1 (4%)	
Sarcoma, metastatic, skin				1 (4%)
Schwannoma malignant, metastatic, skin	1 (3%)			
Oral mucosa	(2)			(1)
Squamous cell carcinoma	1 (50%)			
Squamous cell papilloma				1 (100%)
Pancreas	(46)	(47)	(49)	(48)
Fibrosarcoma, metastatic, mesentery			1 (2%)	
Histiocytic sarcoma			1 (2%)	
Sarcoma, metastatic, skin				1 (2%)
Acinus, sarcoma			1 (2%)	
Salivary glands	(48)	(47)	(49)	(50)
Hepatocellular carcinoma, metastatic, liver			1 (2%)	
Histiocytic sarcoma			1 (2%)	

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Alimentary System (continued)				
Stomach, forestomach	(49)	(50)	(50)	(49)
Squamous cell carcinoma		1 (2%)	1 (2%)	
Squamous cell papilloma			1 (2%)	1 (2%)
Squamous cell papilloma, multiple			1 (2%)	
Stomach, glandular	(49)	(48)	(50)	(49)
Hepatocellular carcinoma, metastatic, liver			1 (2%)	
Tongue			(2)	
Cardiovascular System				
Heart	(49)	(50)	(49)	(50)
Hemangiosarcoma, metastatic, spleen		1 (2%)		
Hepatocellular carcinoma, metastatic, liver			1 (2%)	
Endocrine System				
Adrenal cortex	(50)	(49)	(49)	(50)
Histiocytic sarcoma			1 (2%)	
Osteosarcoma, metastatic, bone			1 (2%)	
Subcapsular, adenoma	1 (2%)			
Adrenal medulla	(50)	(49)	(49)	(50)
Pheochromocytoma malignant	2 (4%)			
Pheochromocytoma complex				1 (2%)
Pheochromocytoma benign	1 (2%)			1 (2%)
Islets, pancreatic	(46)	(47)	(49)	(49)
Adenoma		2 (4%)	2 (4%)	3 (6%)
Carcinoma				1 (2%)
Pituitary gland	(46)	(45)	(48)	(50)
Histiocytic sarcoma			1 (2%)	
Pars distalis, adenoma	3 (7%)	2 (4%)	4 (8%)	4 (8%)
Thyroid gland	(48)	(50)	(49)	(50)
Follicular cell, adenoma	1 (2%)			
General Body System				
None				
Genital System				
Clitoral gland	(47)	(47)	(47)	(49)
Ovary	(45)	(45)	(47)	(50)
Choriocarcinoma			2 (4%)	
Cystadenoma	1 (2%)	4 (9%)	1 (2%)	1 (2%)
Granulosa cell tumor malignant				1 (2%)
Granulosa cell tumor benign	1 (2%)	1 (2%)	1 (2%)	5 (10%)
Histiocytic sarcoma			2 (4%)	1 (2%)
Luteoma	3 (7%)		1 (2%)	
Yolk sac carcinoma				1 (2%)
Uterus	(50)	(50)	(50)	(50)
Hemangiosarcoma		1 (2%)		
Histiocytic sarcoma			2 (4%)	1 (2%)
Leiomyosarcoma			1 (2%)	
Polyp stromal	1 (2%)			3 (6%)
Yolk sac carcinoma, metastatic, ovary				1 (2%)

Table D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hemangiosarcoma	1 (2%)	1 (2%)	2 (4%)	
Histiocytic sarcoma				1 (2%)
Lymph node	(7)	(5)	(11)	(9)
Histiocytic sarcoma			1 (9%)	
Liposarcoma, metastatic, skin		1 (20%)		
Iliac, histiocytic sarcoma			2 (18%)	
Iliac, liposarcoma, metastatic, skin		1 (20%)		
Mediastinal, sarcoma, metastatic, pancreas			1 (9%)	
Pancreatic, histiocytic sarcoma			1 (9%)	
Renal, histiocytic sarcoma			1 (9%)	1 (11%)
Lymph node, mandibular	(46)	(46)	(49)	(49)
Histiocytic sarcoma			2 (4%)	
Squamous cell carcinoma, metastatic, uncertain primary site				1 (2%)
Lymph node, mesenteric	(47)	(49)	(49)	(49)
Histiocytic sarcoma		1 (2%)	2 (4%)	
Histiocytic sarcoma, metastatic, mesentery			1 (2%)	
Yolk sac carcinoma, metastatic, ovary				1 (2%)
Spleen	(49)	(48)	(49)	(50)
Hemangiosarcoma	2 (4%)	1 (2%)	1 (2%)	
Histiocytic sarcoma			2 (4%)	
Sarcoma, metastatic, skin				1 (2%)
Thymus	(48)	(44)	(48)	(48)
Hepatocellular carcinoma, metastatic, liver			1 (2%)	
Histiocytic sarcoma			1 (2%)	1 (2%)
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Adenoma			1 (2%)	
Carcinoma		1 (2%)		
Skin	(48)	(50)	(50)	(50)
Hemangioma		1 (2%)		
Squamous cell carcinoma			1 (2%)	
Subcutaneous tissue, fibrosarcoma		1 (2%)		2 (4%)
Subcutaneous tissue, hemangioma				1 (2%)
Subcutaneous tissue, hemangiosarcoma			1 (2%)	
Subcutaneous tissue, liposarcoma		1 (2%)		
Subcutaneous tissue, sarcoma				1 (2%)
Subcutaneous tissue, schwannoma malignant	3 (6%)	1 (2%)		1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma		1 (2%)	1 (2%)	2 (4%)
Sarcoma			1 (2%)	
Skeletal muscle		(2)	(4)	(6)
Histiocytic sarcoma, metastatic, mesentery			1 (25%)	
Rhabdomyosarcoma		1 (50%)	1 (25%)	2 (33%)
Sarcoma, metastatic, pancreas			1 (25%)	
Sarcoma, metastatic, skin				1 (17%)
Yolk sac carcinoma, metastatic, ovary				1 (17%)

Table D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Nervous System				
Brain	(50)	(50)	(50)	(50)
Osteosarcoma, metastatic, bone			1 (2%)	
Respiratory System				
Lung	(50)	(50)	(49)	(50)
Alveolar/bronchiolar adenoma	3 (6%)	1 (2%)		3 (6%)
Alveolar/bronchiolar carcinoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Alveolar/bronchiolar carcinoma, multiple			1 (2%)	
Hepatocellular carcinoma, metastatic, liver	1 (2%)	3 (6%)	5 (10%)	2 (4%)
Histiocytic sarcoma			1 (2%)	1 (2%)
Liposarcoma, metastatic, skin		1 (2%)		
Osteosarcoma, metastatic, bone			1 (2%)	
Sarcoma, metastatic, skin				1 (2%)
Nose	(50)	(50)	(50)	(50)
Carcinoma	1 (2%)			
Histiocytic sarcoma			1 (2%)	
Special Senses System				
Eye	(50)	(48)	(50)	(50)
Harderian gland	(50)	(50)	(50)	(49)
Adenoma	11 (22%)	9 (18%)	5 (10%)	6 (12%)
Carcinoma	1 (2%)	1 (2%)		
Histiocytic sarcoma			1 (2%)	
Urinary System				
Kidney	(50)	(49)	(49)	(50)
Hepatocellular carcinoma, metastatic, liver			1 (2%)	
Histiocytic sarcoma			1 (2%)	
Osteosarcoma, metastatic, bone			1 (2%)	
Urinary bladder	(49)	(50)	(50)	(50)
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Histiocytic sarcoma		1 (2%)	4 (8%)	2 (4%)
Leukemia granulocytic			1 (2%)	
Lymphoma malignant	23 (46%)	19 (38%)	28 (56%)	27 (54%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	47	45	46	47
Total primary neoplasms	99	87	108	105
Total animals with benign neoplasms	38	27	33	31
Total benign neoplasms	58	40	44	53
Total animals with malignant neoplasms	33	38	41	41
Total malignant neoplasms	41	47	64	52
Total animals with metastatic neoplasms	2	5	10	5
Total metastatic neoplasms	2	8	20	11

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	2 7 1	4 4 0	5 2 4	5 7 6	5 8 8	5 9 1	5 9 1	5 9 7	6 0 6	6 3 0	6 3 9	6 6 0	6 7 4	7 1 0	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	2 1 3	2 1 7	2 2 8	2 2 7	2 0 4	2 0 5	2 4 6	2 0 6	2 2 5	2 3 3	2 4 2	2 3 0	2 2 2	2 4 5	2 0 1	2 0 2	2 0 3	2 1 1	2 1 2	2 1 4	2 1 5	2 1 6	2 1 8	2 1 9	2 2 0
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	A	+	+	A	+	+	A	+	A	A	A	A	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	+	+	A	+	+	+	A	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	+	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	A	+	+	+	+	+	+	I	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	M	+	+	A	+	+	A	M	A	A	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Liver	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																				X					
Hemangiosarcoma																									
Hepatoblastoma																									
Hepatocellular carcinoma														X											
Hepatocellular carcinoma, multiple																									
Hepatocellular adenoma			X			X										X									X
Hepatocellular adenoma, multiple									X		X								X	X	X			X	
Mesentery	A	+	+	+	+	+	+	+		+	+	+	+	+			+			+	+	+	+	+		
Fibrous histiocytoma																									
Schwannoma malignant, metastatic, skin						X																			
Oral mucosa												+													+
Squamous cell carcinoma																									X
Pancreas	A	A	+	+	A	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel																									
Heart	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcapsular, adenoma																									
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant												X													
Pheochromocytoma benign																						X			
Islets, pancreatic	A	A	+	+	A	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	M	+	+	+	I	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Thyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	735	735	735	735	735	735	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	
Carcass ID Number	22026	22029	24047	24048	24049	25050	20007	20008	20009	21010	22021	22023	22024	23036	23037	23038	23039	24040	24041	24043	24044	23031	23032	23034	23035	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	40
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangioma			X																							2
Hemangiosarcoma						X																				1
Hepatoblastoma																				X						1
Hepatocellular carcinoma																					X					2
Hepatocellular carcinoma, multiple																	X									1
Hepatocellular adenoma	X		X			X		X				X		X			X				X	X	X	X	X	15
Hepatocellular adenoma, multiple		X		X	X		X		X		X		X					X		X						15
Mesentery		+	+	+	+	+		+				+	+				+			+	+	+				30
Fibrous histiocytoma				X																						1
Schwannoma malignant, metastatic, skin																										1
Oral mucosa																										2
Squamous cell carcinoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cardiovascular System																										
Blood vessel																					+					1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcapsular, adenoma																	X									1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant								X																		2
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Parathyroid gland	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	45
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	46
Pars distalis, adenoma		X					X											X								3
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	48
Follicular cell, adenoma																X										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

Number of Days on Study	2 7 1	4 4 0	5 2 4	5 7 6	5 8 8	5 9 1	5 9 1	5 9 7	6 0 6	6 3 0	6 3 9	6 6 0	6 7 4	7 1 0	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5
Carcass ID Number	2 1 3	2 1 7	2 2 8	2 2 7	2 0 4	2 0 5	2 4 6	2 0 6	2 2 5	2 3 3	2 4 2	2 3 0	2 2 2	2 4 5	2 0 1	2 0 2	2 0 3	2 1 1	2 1 2	2 1 4	2 1 5	2 1 6	2 1 8	2 1 9	2 2 0
General Body System																									
None																									
Genital System																									
Clitoral gland	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	I	M	+	+	+	+	+	+
Cystadenoma																									
Granulosa cell tumor benign																									
Luteoma													X											X	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma									X																
Lymph node		+					+																	+	+
Lymph node, mandibular	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+
Spleen	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma									X																
Thymus	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, schwannoma malignant						X											X								
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma										X															X
Alveolar/bronchiolar carcinoma																									
Hepatocellular carcinoma, metastatic, liver																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma								X																	
Trachea	I	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma				X											X			X				X			
Carcinoma																				X					

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

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 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 7	
Carcass ID Number	2 2 2 6	2 2 2 9	2 4 4 7	2 4 4 8	2 4 4 9	2 5 0 0	2 0 0 7	2 0 0 8	2 0 0 9	2 0 1 0	2 2 1 1	2 2 2 3	2 2 3 4	2 3 3 6	2 3 3 7	2 3 3 8	2 3 3 9	2 4 4 0	2 4 4 1	2 4 4 3	2 4 4 4	2 4 4 4	2 3 3 1	2 3 3 2	2 3 4 4	2 3 3 5	Total Tissues/ Tumors
General Body System																											
None																											
Genital System																											
Clitoral gland	+	M	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	45
Cystadenoma													X														1
Granulosa cell tumor benign																								X			1
Luteoma																X											3
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal										X																	1
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																											1
Lymph node								+						+						+							7
Lymph node, mandibular	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	46
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma					X																						2
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	48
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	48
Subcutaneous tissue, schwannoma malignant												X															3
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																				X							3
Alveolar/bronchiolar carcinoma						X																					1
Hepatocellular carcinoma, metastatic, liver																	X										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																											1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Special Senses System																											
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma				X			X			X				X	X		X	X									11
Carcinoma																											1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 0 mg/L

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 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 7	
Carcass ID Number	2 2 6	2 2 9	2 4 7	2 4 8	2 4 9	2 5 0	2 0 7	2 0 8	2 0 9	2 1 0	2 2 1	2 2 3	2 2 4	2 3 6	2 3 7	2 3 8	2 3 9	2 4 0	2 4 1	2 4 3	2 4 4	2 3 1	2 3 2	2 3 4	2 3 5	Total Tissues/ Tumors
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant	X		X	X	X			X			X				X	X		X		X	X				X	23

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

Number of Days on Study	461	492	513	552	561	568	673	674	682	706	713	714	717	719	727	733	734	734	734	734	734	734	734	734	735
Carcass ID Number	293	268	296	288	299	263	300	277	286	285	292	258	284	297	290	257	256	259	260	266	267	269	270	298	251
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	M	A	A	+	+	+	+	+	+	+	+	M	A	A	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Adenoma										X															
Intestine small, jejunum	+	+	+	A	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	A	A	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																				X					
Hemangiosarcoma, metastatic, spleen								X																	
Hepatocellular carcinoma									X						X									X	
Hepatocellular carcinoma, multiple												X	X					X							
Hepatocellular adenoma								X	X										X			X			
Hepatocellular adenoma, multiple																					X			X	
Mesentery	+			+	+		+		+	+	+	+	+	+	+			+		+	+	+			+
Pancreas	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	M	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Stomach, glandular	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Blood vessel					+		+							+											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma, metastatic, spleen								X																	
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Islets, pancreatic	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma										X															
Parathyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+
Pituitary gland	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Pars distalis, adenoma																X	X								
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Ovary	+	M	+	I	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma									X																
Granulosa cell tumor benign																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									X

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

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 5	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 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	
Carcass ID Number	2 5 2	2 5 3	2 5 4	2 5 5	2 7 6	2 7 8	2 7 9	2 8 0	2 8 1	2 8 2	2 8 3	2 9 1	2 9 4	2 9 5	2 7 1	2 7 2	2 7 3	2 7 4	2 7 5	2 8 7	2 8 9	2 6 1	2 6 2	2 6 4	2 6 5	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma						X																				2
Hemangiosarcoma, metastatic, spleen																										1
Hepatocellular carcinoma											X											X		X		6
Hepatocellular carcinoma, multiple								X											X				X		X	7
Hepatocellular adenoma							X		X							X						X	X			9
Hepatocellular adenoma, multiple	X			X		X		X		X					X				X	X						10
Mesentery			+		+	+	+	+	+		+		+		+		+	+		+	+	+	+		+	32
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma			X																							1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cardiovascular System																										
Blood vessel																										3
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma, metastatic, spleen																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma	X																									2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	45
Pars distalis, adenoma																										2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	47
Ovary	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Cystadenoma			X																X		X					4
Granulosa cell tumor benign	X																									1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1

Table D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

Number of Days on Study	4 6 1	4 9 2	5 1 3	5 5 2	5 6 1	5 6 8	6 7 3	6 7 4	6 8 2	7 0 6	7 1 3	7 1 4	7 1 7	7 1 9	7 2 7	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
Carcass ID Number	2 9 3	2 6 8	2 9 6	2 8 8	2 9 9	2 6 3	3 0 0	2 7 7	2 8 6	2 8 5	2 9 2	2 5 8	2 8 4	2 9 7	2 9 0	2 5 7	2 5 6	2 5 9	2 6 0	2 6 6	2 6 7	2 6 9	2 7 0	2 9 8	2 5 1
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									X
Lymph node		+									+					+		+							
Liposarcoma, metastatic, skin											X														
Iliac, liposarcoma, metastatic, skin											X														
Lymph node, mandibular	+	M	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Spleen	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma								X																	
Thymus	+	+	M	+	M	+	+	+	+	+	I	+	+	M	M	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																								X	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Subcutaneous tissue, fibrosarcoma			X																						
Subcutaneous tissue, liposarcoma											X														
Subcutaneous tissue, schwannoma malignant					X																				
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma														X											
Skeletal muscle	+	+																							
Rhabdomyosarcoma	X																								
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Hepatocellular carcinoma, metastatic, liver													X					X							
Liposarcoma, metastatic, skin											X														
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma							X							X										X	
Carcinoma						X																			

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

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 5	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 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	
Carcass ID Number	2 5 2	2 5 3	2 5 4	2 5 5	2 7 6	2 7 8	2 7 9	2 8 0	2 8 1	2 8 2	2 8 3	2 9 1	2 9 4	2 9 5	2 7 1	2 7 2	2 7 3	2 7 4	2 7 5	2 8 7	2 8 9	2 6 1	2 6 2	2 6 4	2 6 5	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Lymph node			+																							5
Liposarcoma, metastatic, skin																										1
Iliac, liposarcoma, metastatic, skin																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	46
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma	X																									1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hemangiosarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	44
Integumentary system																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																							X			1
Subcutaneous tissue, fibrosarcoma																										1
Subcutaneous tissue, liposarcoma																										1
Subcutaneous tissue, schwannoma malignant																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle																										2
Rhabdomyosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma															X											1
Alveolar/bronchiolar carcinoma																									X	1
Hepatocellular carcinoma, metastatic, liver																							X			3
Liposarcoma, metastatic, skin																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma				X		X		X		X								X			X					9
Carcinoma																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 500 mg/L

Number of Days on Study	735	735	735	735	735	735	735	735	735	735	735	735	735	735	736	736	736	736	736	736	736	737	737	737	737	
Carcass ID Number	25212	25523	25254	25255	25476	25778	25779	25880	25881	25882	25883	25991	25994	25995	27711	27712	27713	27714	27715	27887	27889	28061	28062	28064	28065	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma	X																									1
Lymphoma malignant		X					X	X		X		X								X	X	X	X		X	19

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	0 2 7	0 3 4	4 8 6	5 0 3	5 0 3	5 4 2	5 7 4	6 0 2	6 1 8	6 1 8	6 2 2	6 6 1	6 6 2	6 8 3	7 1 1	7 1 2	7 1 9	7 2 0	7 2 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4
Carcass ID Number	3 3 9	3 0 3	3 2 4	3 1 3	3 2 6	3 3 5	3 0 1	3 0 7	3 4 3	3 4 9	3 1 6	3 0 2	3 2 5	3 2 2	3 1 4	3 3 4	3 2 9	3 3 3	3 4 0	3 2 7	3 2 8	3 3 0	3 4 6	3 4 7	3 4 8
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	A	+	+	+	+	+	+	M	+	+	A	A	A	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	A	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Intestine small, duodenum	+	+	+	A	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Intestine small, ileum	+	+	+	A	+	+	+	+	+	+	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma															X	X				X		X			X
Hepatocellular carcinoma, multiple																	X								
Hepatocellular adenoma								X	X					X	X		X	X					X		
Hepatocellular adenoma, multiple													X								X				X
Histiocytic sarcoma																X									
Mesentery				+	+			+	+	+	+	+	+	+	+	+	+	+			+	+		+		+
Fibrosarcoma								X																	
Hepatocellular carcinoma, metastatic, liver																				X					
Histiocytic sarcoma				X																					
Pancreas	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic, mesentery								X																	
Histiocytic sarcoma																									
Acinus, sarcoma												X													
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver																	X								
Histiocytic sarcoma																									
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Squamous cell papilloma																									
Squamous cell papilloma, multiple							X																		
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver																	X								
Tongue				+						+															
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver																	X								
Endocrine System																									
Adrenal cortex	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Osteosarcoma, metastatic, bone											X														
Adrenal medulla	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

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 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	
Carcass ID Number	3 5 0	3 1 1	3 1 2	3 1 5	3 2 1	3 2 3	3 0 4	3 0 5	3 0 6	3 0 8	3 0 9	3 1 0	3 3 1	3 3 2	3 3 6	3 3 7	3 3 8	3 1 7	3 1 8	3 1 9	3 2 0	3 4 1	3 4 2	3 4 4	3 4 5	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	44
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Hemangioma	X																									1
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Histiocytic sarcoma															X											1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma										X		X						X		X			X		X	11
Hepatocellular carcinoma, multiple	X												X								X					4
Hepatocellular adenoma		X		X					X	X		X						X			X					14
Hepatocellular adenoma, multiple	X						X	X					X		X	X			X				X	X		12
Histiocytic sarcoma																										1
Mesentery	+									+	+				+		+	+	+		+		+	+		27
Fibrosarcoma																										1
Hepatocellular carcinoma, metastatic, liver																										1
Histiocytic sarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrosarcoma, metastatic, mesentery																										1
Histiocytic sarcoma															X											1
Acinus, sarcoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma, metastatic, liver																										1
Histiocytic sarcoma															X											1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																				X						1
Squamous cell papilloma						X																				1
Squamous cell papilloma, multiple																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic, liver																										1
Tongue																										2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma, metastatic, liver																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma															X											1
Osteosarcoma, metastatic, bone																										1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma			X													X										2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	0 2 7	0 3 4	4 8 6	5 0 3	5 0 3	5 4 2	5 7 4	6 0 2	6 1 8	6 1 8	6 2 2	6 6 1	6 6 2	6 8 3	7 1 1	7 1 2	7 1 9	7 2 0	7 2 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4
Carcass ID Number	3 3 9	3 0 3	3 2 4	3 1 3	3 2 6	3 3 5	3 0 1	3 0 7	3 4 3	3 4 9	3 1 6	3 0 2	3 2 5	3 2 2	3 1 4	3 3 4	3 2 9	3 3 3	3 4 0	3 2 7	3 2 8	3 3 0	3 4 6	3 4 7	3 4 8
Endocrine System (continued)																									
Pituitary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									
Pars distalis, adenoma																									
Thyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Choriocarcinoma														X											
Cystadenoma																					X				
Granulosa cell tumor benign																									
Histiocytic sarcoma																X									
Luteoma																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Leiomyosarcoma																									
Vagina																		+							
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma													X									X			
Lymph node					+				+		+					+			+					+	
Histiocytic sarcoma																									
Iliac, histiocytic sarcoma																X									
Mediastinal, sarcoma, metastatic, pancreas												X													
Pancreatic, histiocytic sarcoma																									
Renal, histiocytic sarcoma																									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Histiocytic sarcoma, metastatic, mesentery				X																					
Spleen	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																						X			
Histiocytic sarcoma																	X								
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver																	X								
Histiocytic sarcoma																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma															X										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Subcutaneous tissue, hemangiosarcoma																						X			

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

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 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	
Carcass ID Number	3 5 0	3 1 1	3 1 2	3 1 5	3 2 1	3 2 3	3 0 4	3 0 5	3 0 6	3 0 8	3 0 9	3 1 0	3 1 3	3 3 2	3 3 6	3 3 7	3 3 8	3 1 7	3 1 8	3 1 9	3 2 0	3 4 1	3 4 2	3 4 4	3 4 5	Total Tissues/ Tumors
Endocrine System (continued)																										
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma															X											1
Pars distalis, adenoma	X					X					X	X														4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	I	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	47
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	47
Choriocarcinoma																	X									2
Cystadenoma																										1
Granulosa cell tumor benign																						X				1
Histiocytic sarcoma															X											2
Luteoma							X																			1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma															X											2
Leiomyosarcoma																						X				1
Vagina																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										2
Lymph node	+										+				+					+			+			11
Histiocytic sarcoma															X											1
Iliac, histiocytic sarcoma															X											2
Mediastinal, sarcoma, metastatic, pancreas																										1
Pancreatic, histiocytic sarcoma															X											1
Renal, histiocytic sarcoma															X											1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma															X											2
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	49
Histiocytic sarcoma															X											2
Histiocytic sarcoma, metastatic, mesentery																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																										1
Histiocytic sarcoma															X											2
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	48
Hepatocellular carcinoma, metastatic, liver																										1
Histiocytic sarcoma															X											1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma		X																								1
Subcutaneous tissue, hemangiosarcoma																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 1,000 mg/L

Number of Days on Study	734	735	735	735	735	735	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	737	737	737	737	
Carcass ID Number	35010	31101	31102	31155	32101	32203	30104	30005	30006	30008	30009	31010	31301	33202	33306	33307	33308	31107	31108	31109	31200	34401	34402	34404	34405	Total Tissues/ Tumors
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Sarcoma																										1
Skeletal muscle											+															4
Histiocytic sarcoma, metastatic, mesentery																										1
Rhabdomyosarcoma											X															1
Sarcoma, metastatic, pancreas																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic, bone																										1
Peripheral nerve																										2
Spinal cord																										3
Respiratory System																										
Lung	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar carcinoma																										1
Alveolar/bronchiolar carcinoma, multiple							X																			1
Hepatocellular carcinoma, metastatic, liver																				X	X				X	5
Histiocytic sarcoma																										1
Osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma															X											1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																X		X								5
Histiocytic sarcoma															X											1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma, metastatic, liver																										1
Histiocytic sarcoma															X											1
Osteosarcoma, metastatic, bone																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma															X											4
Leukemia granulocytic																										1
Lymphoma malignant		X	X	X	X		X			X	X	X	X	X		X		X			X	X		X	X	X	28

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	735	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	737	737	737	737	737	737	737	
Carcass ID Number	39 0	36 2	36 4	36 5	37 7	37 8	38 1	38 2	38 3	38 4	38 5	39 1	39 3	39 4	35 6	35 7	35 8	37 1	37 2	37 3	37 4	37 5	39 6	39 8	40 0	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp adenomatous																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma									X			X						X			X					6
Hepatocellular carcinoma, multiple								X																		3
Hepatocellular adenoma											X	X			X				X							8
Hepatocellular adenoma, multiple			X	X	X	X		X	X	X				X										X	X		15
Histiocytic sarcoma																										1
Mesentery					+				+	+		+		+	+	+		+	+		+			+	+		24
Hemangiosarcoma														X												1
Sarcoma, metastatic, skin																					X					1
Oral mucosa																										1
Squamous cell papilloma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, skin																					X					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cardiovascular System																										
Blood vessel																							+			1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma complex																										1
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																X										3
Carcinoma						X																				1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X													X										4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	1 4 2	4 4 7	4 5 5	4 7 5	5 3 5	5 4 0	5 9 7	6 1 8	6 4 6	6 6 7	6 8 1	6 8 5	6 8 5	6 8 8	7 0 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 5
Carcass ID Number	3 5 2	3 5 9	3 9 2	3 9 9	3 9 7	3 8 9	3 7 6	3 6 0	3 9 5	3 6 3	3 8 8	3 7 9	3 8 0	3 6 1	3 6 8 7	3 5 1	3 5 1 3	3 5 3 4	3 5 5	3 6 6	3 6 6 7	3 6 7 8	3 6 9	3 7 0	3 8 6
Genital System																								
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma																								X
Granulosa cell tumor malignant	X																							
Granulosa cell tumor benign																								
Histiocytic sarcoma					X																			
Yolk sac carcinoma						X																		
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma					X																			
Polyp stromal																								
Yolk sac carcinoma, metastatic, ovary						X																		
Hematopoietic System																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma					X																			
Lymph node	+				+		+			+												+		
Renal, histiocytic sarcoma					X																			
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, uncertain primary site																								
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Yolk sac carcinoma, metastatic, ovary						X																		
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin																								
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X								
Integumentary System																								
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrosarcoma															X				X					
Subcutaneous tissue, hemangioma								X																
Subcutaneous tissue, sarcoma																								
Subcutaneous tissue, schwannoma malignant												X												
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma		X						X																
Skeletal muscle						+				+				+			+		+					
Rhabdomyosarcoma																	X		X					
Sarcoma, metastatic, skin																								
Yolk sac carcinoma, metastatic, ovary						X																		
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve										+				+										
Spinal cord										+				+										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	735	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	737	737	737	737	737	737	737	737	
Carcass ID Number	39 0	36 2	36 4	36 5	37 7	37 8	38 1	38 2	38 3	38 4	38 5	39 1	39 3	39 4	35 6	35 7	35 8	37 1	37 2	37 3	37 4	37 5	39 6	39 8	40 0	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	49
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma																										1
Granulosa cell tumor malignant																										1
Granulosa cell tumor benign					X		X			X				X									X			5
Histiocytic sarcoma																										1
Yolk sac carcinoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Polyp stromal								X							X	X										3
Yolk sac carcinoma, metastatic, ovary																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymph node	+									+								+	+							9
Renal, histiocytic sarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell carcinoma, metastatic, uncertain primary site										X																1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	49
Yolk sac carcinoma, metastatic, ovary																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skin																					X					1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																										2
Subcutaneous tissue, hemangioma																										1
Subcutaneous tissue, sarcoma																					X					1
Subcutaneous tissue, schwannoma malignant																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										2
Skeletal muscle																					+					6
Rhabdomyosarcoma																										2
Sarcoma, metastatic, skin																					X					1
Yolk sac carcinoma, metastatic, ovary																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										2
Spinal cord																										2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	1 4 2	4 4 7	4 5 5	4 7 5	5 3 5	5 4 0	5 9 7	6 1 8	6 4 6	6 6 7	6 8 1	6 8 5	6 8 5	6 8 8	7 0 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 5
Carcass ID Number	3 5 2	3 5 9	3 9 2	3 9 9	3 9 7	3 8 9	3 7 6	3 6 0	3 9 5	3 6 3	3 8 8	3 7 9	3 8 0	3 6 1	3 8 7	3 5 1	3 5 3	3 5 4	3 5 5	3 6 6	3 6 7	3 6 8	3 6 9	3 7 0	3 8 6
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																			X						
Alveolar/bronchiolar carcinoma																									
Hepatocellular carcinoma, metastatic, liver												X													
Histiocytic sarcoma					X																				
Sarcoma, metastatic, skin																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Harderian gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma							X									X					X				X
Urinary system																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma					X											X									
Lymphoma malignant		X					X	X		X			X					X	X	X	X	X	X		

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate: 2,000 mg/L

Number of Days on Study	735	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	737	737	737	737	737	737	737	
Carcass ID Number	39 0	36 2	36 4	36 5	37 7	37 8	38 1	38 2	38 3	38 4	38 5	39 1	39 3	39 4	35 6	35 7	35 8	37 1	37 2	37 3	37 4	37 5	39 6	39 8	40 0	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma					X										X											3
Alveolar/bronchiolar carcinoma		X																								1
Hepatocellular carcinoma, metastatic, liver								X																		2
Histiocytic sarcoma																										1
Sarcoma, metastatic, skin																					X					1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Harderian gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma															X							X				6
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										2
Lymphoma malignant	X		X	X	X	X			X	X	X	X	X	X	X	X			X	X		X				27

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Adrenal Medulla: Benign, Complex, or Malignant Pheochromocytoma				
Overall rate[a]	3/50 (6%)	0/49 (0%)	0/49 (0%)	2/50 (4%)
Adjusted rate[b]	6.8%	0.0%	0.0%	4.6%
Terminal rate[c]	2/36 (6%)	0/34 (0%)	0/31 (0%)	1/35 (3%)
First incidence (days)	660	—[e]	—	681
Poly-3 test[d]	P=0.538N	P=0.117N	P=0.126N	P=0.503N
Harderian Gland: Adenoma				
Overall rate	11/50 (22%)	9/50 (18%)	5/50 (10%)	6/50 (12%)
Adjusted rate	24.9%	19.7%	11.8%	13.7%
Terminal rate	10/36 (28%)	7/35 (20%)	4/31 (13%)	5/35 (14%)
First incidence (days)	576	673	712	597
Poly-3 test	P=0.093N	P=0.368N	P=0.095N	P=0.142N
Harderian Gland: Adenoma or Carcinoma				
Overall rate	12/50 (24%)	10/50 (20%)	5/50 (10%)	6/50 (12%)
Adjusted rate	27.2%	21.7%	11.8%	13.7%
Terminal rate	11/36 (31%)	7/35 (20%)	4/31 (13%)	5/35 (14%)
First incidence (days)	576	568	712	597
Poly-3 test	P=0.053N	P=0.358N	P=0.060N	P=0.094N
Liver: Hepatocellular Adenoma				
Overall rate	30/49 (61%)[f]	19/50 (38%)	26/49 (53%)	23/50 (46%)
Adjusted rate	66.1%	41.5%	59.9%	51.4%
Terminal rate	26/36 (72%)	17/35 (49%)	19/31 (61%)	20/35 (57%)
First incidence (days)	524	674	602	475
Poly-3 test	P=0.252N	P=0.013N	P=0.348N	P=0.108N
Liver: Hepatocellular Carcinoma				
Overall rate	3/49 (6%)	13/50 (26%)	15/49 (31%)	9/50 (18%)
Adjusted rate	6.9%	28.5%	35.6%	20.3%
Terminal rate	2/36 (6%)	9/35 (26%)	12/31 (39%)	7/35 (20%)
First incidence (days)	710	682	711	475
Poly-3 test	P=0.158	P=0.007	P<0.001	P=0.061
Liver: Hepatocellular Carcinoma or Hepatoblastoma				
Overall rate	4/49 (8%)	13/50 (26%)	15/49 (31%)	9/50 (18%)
Adjusted rate	9.2%	28.5%	35.6%	20.3%
Terminal rate	3/36 (8%)	9/35 (26%)	12/31 (39%)	7/35 (20%)
First incidence (days)	710	682	711	475
Poly-3 test	P=0.219	P=0.018	P=0.002	P=0.119
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	31/49 (63%)[f]	26/50 (52%)	31/49 (63%)	26/50 (52%)
Adjusted rate	68.1%	56.7%	71.3%	57.9%
Terminal rate	26/36 (72%)	21/35 (60%)	23/31 (74%)	22/35 (63%)
First incidence (days)	524	674	602	475
Poly-3 test	P=0.287N	P=0.174N	P=0.461	P=0.207N
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	3/50 (6%)	1/50 (2%)	0/49 (0%)	3/50 (6%)
Adjusted rate	6.8%	2.2%	0.0%	6.9%
Terminal rate	2/36 (6%)	1/35 (3%)	0/30 (0%)	3/35 (9%)
First incidence (days)	630	729 (T)	—	729 (T)
Poly-3 test	P=0.513	P=0.294N	P=0.130N	P=0.657

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	4/50 (8%)	2/50 (4%)	2/49 (4%)	4/50 (8%)
Adjusted rate	9.1%	4.4%	4.8%	9.2%
Terminal rate	3/36 (8%)	2/35 (6%)	1/30 (3%)	4/35 (11%)
First incidence (days)	630	729 (T)	712	729 (T)
Poly-3 test	P=0.482	P=0.323N	P=0.365N	P=0.636
Ovary: Cystadenoma				
Overall rate	1/45 (2%)	4/45 (9%)	1/47 (2%)	1/50 (2%)
Adjusted rate	2.5%	9.6%	2.5%	2.3%
Terminal rate	1/32 (3%)	3/34 (9%)	1/30 (3%)	1/35 (3%)
First incidence (days)	729 (T)	682	729 (T)	729 (T)
Poly-3 test	P=0.336N	P=0.196	P=0.757N	P=0.740N
Ovary: Benign Granulosa Cell Tumor				
Overall rate	1/45 (2%)	1/45 (2%)	1/47 (2%)	5/50 (10%)
Adjusted rate	2.5%	2.4%	2.5%	11.5%
Terminal rate	1/32 (3%)	1/34 (3%)	1/30 (3%)	5/35 (14%)
First incidence (days)	729 (T)	729 (T)	729 (T)	729 (T)
Poly-3 test	P=0.031	P=0.749N	P=0.757N	P=0.123
Ovary: Benign or Malignant Granulosa Cell Tumor				
Overall rate	1/45 (2%)	1/45 (2%)	1/47 (2%)	6/50 (12%)
Adjusted rate	2.5%	2.4%	2.5%	13.5%
Terminal rate	1/32 (3%)	1/34 (3%)	1/30 (3%)	5/35 (14%)
First incidence (days)	729 (T)	729 (T)	729 (T)	142
Poly-3 test	P=0.012	P=0.749N	P=0.757N	P=0.075
Ovary: Luteoma				
Overall rate	3/45 (7%)	0/45 (0%)	1/47 (2%)	0/50 (0%)
Adjusted rate	7.5%	0.0%	2.5%	0.0%
Terminal rate	2/32 (6%)	0/34 (0%)	1/30 (3%)	0/35 (0%)
First incidence (days)	674	—	729 (T)	—
Poly-3 test	P=0.079N	P=0.110N	P=0.300N	P=0.103N
Ovary: Benign Granulosa Cell Tumor, Malignant Granulosa Cell Tumor, or Luteoma				
Overall rate	4/45 (9%)	1/45 (2%)	2/47 (4%)	6/50 (12%)
Adjusted rate	10.1%	2.4%	5.0%	13.5%
Terminal rate	3/32 (9%)	1/34 (3%)	2/30 (7%)	5/35 (14%)
First incidence (days)	674	729 (T)	729 (T)	142
Poly-3 test	P=0.185	P=0.164N	P=0.331N	P=0.440
Pancreatic Islets: Adenoma				
Overall rate	0/46 (0%)	2/47 (4%)	2/49 (4%)	3/49 (6%)
Adjusted rate	0.0%	4.5%	4.8%	6.8%
Terminal rate	0/36 (0%)	1/35 (3%)	2/31 (7%)	1/35 (3%)
First incidence (days)	—	706	729 (T)	475
Poly-3 test	P=0.112	P=0.248	P=0.235	P=0.125
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	0/46 (0%)	2/47 (4%)	2/49 (4%)	4/49 (8%)
Adjusted rate	0.0%	4.5%	4.8%	9.1%
Terminal rate	0/36 (0%)	1/35 (3%)	2/31 (7%)	2/35 (6%)
First incidence (days)	—	706	729 (T)	475
Poly-3 test	P=0.045	P=0.248	P=0.235	P=0.065

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	3/46 (7%)	2/45 (4%)	4/48 (8%)	4/50 (8%)
Adjusted rate	7.2%	4.9%	9.8%	9.2%
Terminal rate	3/35 (9%)	2/32 (6%)	4/30 (13%)	3/35 (9%)
First incidence (days)	729 (T)	729 (T)	729 (T)	688
Poly-3 test	P=0.356	P=0.503N	P=0.489	P=0.526
Skin: Fibrosarcoma or Sarcoma				
Overall rate	0/50 (0%)	1/50 (2%)	0/50 (0%)	3/50 (6%)
Adjusted rate	0.0%	2.2%	0.0%	6.9%
Terminal rate	0/36 (0%)	0/35 (0%)	0/31 (0%)	2/35 (6%)
First incidence (days)	—	513	—	705
Poly-3 test	P=0.041	P=0.511	—[g]	P=0.118
Skin: Schwannoma Malignant				
Overall rate	3/50 (6%)	1/50 (2%)	0/50 (0%)	1/50 (2%)
Adjusted rate	6.8%	2.2%	0.0%	2.3%
Terminal rate	2/36 (6%)	0/35 (0%)	0/31 (0%)	0/35 (0%)
First incidence (days)	591	561	—	685
Poly-3 test	P=0.207N	P=0.291N	P=0.126N	P=0.309N
Stomach (Forestomach): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	0/50 (0%)	1/50 (2%)	3/50 (6%)	1/50 (2%)
Adjusted rate	0.0%	2.2%	7.0%	2.3%
Terminal rate	0/36 (0%)	1/35 (3%)	2/31 (7%)	1/35 (3%)
First incidence (days)	—	729 (T)	574	729 (T)
Poly-3 test	P=0.343	P=0.508	P=0.115	P=0.499
Uterus: Stromal Polyp				
Overall rate	1/50 (2%)	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted rate	2.3%	0.0%	0.0%	6.9%
Terminal rate	1/36 (3%)	0/35 (0%)	0/31 (0%)	3/35 (9%)
First incidence (days)	729 (T)	—	—	729 (T)
Poly-3 test	P=0.081	P=0.492N	P=0.506N	P=0.303
All Organs: Hemangiosarcoma				
Overall rate	3/50 (6%)	4/50 (8%)	2/50 (4%)	1/50 (2%)
Adjusted rate	6.8%	8.8%	4.7%	2.3%
Terminal rate	2/36 (6%)	3/35 (9%)	1/31 (3%)	1/35 (3%)
First incidence (days)	606	674	662	729 (T)
Poly-3 test	P=0.170N	P=0.518	P=0.515N	P=0.310N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	5/50 (10%)	5/50 (10%)	3/50 (6%)	2/50 (4%)
Adjusted rate	11.4%	11.0%	7.1%	4.6%
Terminal rate	4/36 (11%)	4/35 (11%)	2/31 (7%)	1/35 (3%)
First incidence (days)	606	674	662	618
Poly-3 test	P=0.134N	P=0.609N	P=0.375N	P=0.218N
All Organs: Histiocytic Sarcoma				
Overall rate	0/50 (0%)	1/50 (2%)	4/50 (8%)	2/50 (4%)
Adjusted rate	0.0%	2.2%	9.3%	4.6%
Terminal rate	0/36 (0%)	1/35 (3%)	1/31 (3%)	1/35 (3%)
First incidence (days)	—	729 (T)	503	535
Poly-3 test	P=0.163	P=0.508	P=0.058	P=0.239

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
All Organs: Malignant Lymphoma				
Overall rate	23/50 (46%)	19/50 (38%)	28/50 (56%)	27/50 (54%)
Adjusted rate	50.5%	41.0%	63.8%	59.5%
Terminal rate	19/36 (53%)	16/35 (46%)	23/31 (74%)	22/35 (63%)
First incidence (days)	440	492	503	447
Poly-3 test	P=0.089	P=0.238N	P=0.138	P=0.254
All Organs: Benign Neoplasms				
Overall rate	38/50 (76%)	27/50 (54%)	33/50 (66%)	31/50 (62%)
Adjusted rate	81.6%	58.6%	74.5%	67.9%
Terminal rate	31/36 (86%)	22/35 (63%)	24/31 (77%)	25/35 (71%)
First incidence (days)	524	673	574	475
Poly-3 test	P=0.234N	P=0.010N	P=0.273N	P=0.090N
All Organs: Malignant Neoplasms				
Overall rate	33/50 (66%)	38/50 (76%)	41/50 (82%)	41/50 (82%)
Adjusted rate	69.9%	76.9%	88.8%	84.1%
Terminal rate	24/36 (67%)	24/35 (69%)	27/31 (87%)	29/35 (83%)
First incidence (days)	440	461	503	142
Poly-3 test	P=0.041	P=0.289	P=0.018	P=0.073
All Organs: Benign or Malignant Neoplasms				
Overall rate	47/50 (94%)	45/50 (90%)	46/50 (92%)	47/50 (94%)
Adjusted rate	95.8%	91.0%	98.5%	95.4%
Terminal rate	34/36 (94%)	31/35 (89%)	31/31 (100%)	33/35 (94%)
First incidence (days)	440	461	503	142
Poly-3 test	P=0.439	P=0.288N	P=0.427	P=0.659N

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

TABLE D4a
Historical Incidence of Pancreatic Islet Neoplasms in Control Female B6C3F$_1$ Mice[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence in Drinking Water Controls Given NTP-2000 Diet			
Dipropylene glycol	2/50	0/50	2/50
Sodium chlorate	0/46	0/46	0/46
Sodium nitrite	0/50	0/50	0/50
Overall Historical Incidence: Drinking Water Studies			
Total (%)	2/146 (1.4%)	0/146	2/146 (1.4%)
Mean ± standard deviation	1.4% ± 2.3%		1.3% ± 2.3%
Range	0%-4%		0%-4%
Overall Historical Incidence: All Routes			
Total (%)	8/1,230 (0.7%)	1/1,230 (0.1%)	9/1,230 (0.7%)
Mean ± standard deviation	0.7% ± 1.2%	0.1% ± 0.4%	0.8% ± 1.2%
Range	0%-4%	0%-2%	0%-4%

[a] Data as of April 19, 2004

TABLE D4b
Historical Incidence of Liver Neoplasms in Control Female B6C3F$_1$ Mice[a]

Study	Incidence in Controls		
	Hepatocellular Adenoma	Hepatocellular Carcinoma	Hepatocellular Adenoma or Carcinoma
Historical Incidence in Drinking Water Controls Given NTP-2000 Diet			
Dipropylene glycol	11/50	7/50	17/50
Sodium chlorate	30/49	3/49	31/49
Sodium nitrite	9/50	2/50	10/50
Overall Historical Incidence: Drinking Water Studies			
Total (%)	50/149 (33.6%)	12/149 (8.1%)	58/149 (38.9%)
Mean ± standard deviation	20% ± 2.8%	9% ± 7.1%	27% ± 9.9%
Range	18%-61%	4%-14%	20%-63%
Overall Historical Incidence: All Routes			
Total (%)	214/1,251 (17.1%)	90/1,251 (7.2%)	286/1,251 (22.9%)
Mean ± standard deviation	18.0% ± 11.6%	7.6% ± 4.4%	24.1% ± 12.8%
Range	6%-61%	0%-16%	8%-63%

[a] Data as of April 19, 2004

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

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Disposition Summary				
Animals initially in study	50	50	50	50
Early deaths				
Accidental death	1			
Moribund	3	5	6	8
Natural death	10	10	12	7
Survivors				
Died last week of study		1		
Terminal sacrifice	36	34	31	35
Other			1	
Animals examined microscopically	50	50	50	50
Alimentary System				
Intestine large, colon	(48)	(49)	(48)	(49)
Hemorrhage	1 (2%)			
Intestine large, cecum	(44)	(47)	(47)	(47)
Edema	4 (9%)	6 (13%)	6 (13%)	6 (13%)
Hemorrhage	1 (2%)			
Inflammation, chronic			1 (2%)	
Ulcer			1 (2%)	
Intestine small, duodenum	(46)	(47)	(47)	(50)
Ulcer		1 (2%)	1 (2%)	
Epithelium, hyperplasia			2 (4%)	
Intestine small, ileum	(42)	(45)	(46)	(47)
Inflammation, chronic			1 (2%)	1 (2%)
Epithelium, hyperplasia			1 (2%)	1 (2%)
Liver	(49)	(50)	(49)	(50)
Angiectasis	2 (4%)		2 (4%)	1 (2%)
Basophilic focus	5 (10%)		4 (8%)	1 (2%)
Clear cell focus	3 (6%)		1 (2%)	
Eosinophilic focus	9 (18%)	9 (18%)	13 (27%)	7 (14%)
Hematopoietic cell proliferation	7 (14%)	4 (8%)	3 (6%)	8 (16%)
Hemorrhage			1 (2%)	
Hepatodiaphragmatic nodule		1 (2%)		
Hyperplasia, lymphoid	4 (8%)	7 (14%)	3 (6%)	5 (10%)
Infarct		1 (2%)		
Infiltration cellular, mixed cell	7 (14%)	7 (14%)	8 (16%)	7 (14%)
Mixed cell focus	7 (14%)	2 (4%)	3 (6%)	3 (6%)
Necrosis, focal	5 (10%)	1 (2%)	4 (8%)	1 (2%)
Tension lipidosis	2 (4%)	3 (6%)		1 (2%)
Centrilobular, necrosis	2 (4%)	2 (4%)	2 (4%)	2 (4%)
Hepatocyte, karyomegaly				3 (6%)
Hepatocyte, vacuolization cytoplasmic	4 (8%)	3 (6%)	6 (12%)	4 (8%)
Kupffer cell, hyperplasia		1 (2%)	1 (2%)	2 (4%)
Kupffer cell, pigmentation	3 (6%)	4 (8%)	4 (8%)	7 (14%)
Mesentery	(30)	(32)	(27)	(24)
Angiectasis	1 (3%)			1 (4%)
Hemorrhage	1 (3%)			
Inflammation, chronic				1 (4%)
Fat, necrosis	21 (70%)	24 (75%)	20 (74%)	16 (67%)

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

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Alimentary System (continued)				
Pancreas	(46)	(47)	(49)	(48)
Atrophy	2 (4%)	1 (2%)		1 (2%)
Cyst		1 (2%)	1 (2%)	
Acinus, hyperplasia, focal				1 (2%)
Salivary glands	(48)	(47)	(49)	(50)
Hyperplasia, lymphoid	16 (33%)	21 (45%)	15 (31%)	18 (36%)
Stomach, forestomach	(49)	(50)	(50)	(49)
Diverticulum	2 (4%)	1 (2%)	1 (2%)	2 (4%)
Edema			3 (6%)	
Erosion		1 (2%)	2 (4%)	2 (4%)
Hyperplasia	1 (2%)			
Inflammation, chronic active			2 (4%)	2 (4%)
Ulcer	2 (4%)		3 (6%)	3 (6%)
Epithelium, hyperplasia	3 (6%)	4 (8%)	9 (18%)	6 (12%)
Stomach, glandular	(49)	(48)	(50)	(49)
Erosion		1 (2%)	2 (4%)	
Ulcer			1 (2%)	
Cardiovascular System				
Blood vessel	(1)	(3)		(1)
Aorta, mineralization		1 (33%)		
Heart	(49)	(50)	(49)	(50)
Cardiomyopathy	1 (2%)	1 (2%)	1 (2%)	
Mineralization	1 (2%)		1 (2%)	2 (4%)
Endocrine System				
Adrenal cortex	(50)	(49)	(49)	(50)
Accessory adrenal cortical nodule	4 (8%)	2 (4%)	7 (14%)	7 (14%)
Hyperplasia, focal			1 (2%)	
Capsule, hyperplasia			1 (2%)	2 (4%)
Zona reticularis, vacuolization cytoplasmic			1 (2%)	1 (2%)
Adrenal medulla	(50)	(49)	(49)	(50)
Hyperplasia	2 (4%)		2 (4%)	1 (2%)
Islets, pancreatic	(46)	(47)	(49)	(49)
Hyperplasia	9 (20%)	6 (13%)	4 (8%)	3 (6%)
Parathyroid gland	(45)	(47)	(48)	(47)
Cyst	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Pituitary gland	(46)	(45)	(48)	(50)
Pars distalis, angiectasis	1 (2%)	2 (4%)	2 (4%)	
Pars distalis, cyst				1 (2%)
Pars distalis, hyperplasia, focal	3 (7%)	3 (7%)	3 (6%)	1 (2%)
Thyroid gland	(48)	(50)	(49)	(50)
Degeneration, cystic	25 (52%)	28 (56%)	34 (69%)	32 (64%)
Follicle, cyst	1 (2%)	1 (2%)		1 (2%)
Follicular cell, cyst				2 (4%)
Follicular cell, hypertrophy	3 (6%)	2 (4%)	5 (10%)	14 (28%)
General Body System				
None				

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Genital System				
Clitoral gland	(47)	(47)	(47)	(49)
Inflammation, chronic		2 (4%)		4 (8%)
Ovary	(45)	(45)	(47)	(50)
Angiectasis	3 (7%)	2 (4%)	4 (9%)	3 (6%)
Cyst	9 (20%)	14 (31%)	14 (30%)	13 (26%)
Cyst, hemorrhagic	1 (2%)			
Hemorrhage	1 (2%)			
Thrombosis	3 (7%)	1 (2%)	1 (2%)	
Bilateral, cyst		1 (2%)		
Follicle, hemorrhage	1 (2%)	4 (9%)	4 (9%)	9 (18%)
Granulosa cell, hyperplasia			3 (6%)	7 (14%)
Uterus	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)		2 (4%)	1 (2%)
Hyperplasia, atypical		1 (2%)		
Hyperplasia, cystic	45 (90%)	45 (90%)	40 (80%)	41 (82%)
Inflammation, chronic			2 (4%)	
Inflammation, suppurative	1 (2%)			
Metaplasia, squamous		2 (4%)	1 (2%)	
Endometrium, hyperplasia, atypical		1 (2%)		
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(50)
Hyperplasia	14 (28%)	28 (56%)	29 (58%)	31 (62%)
Myelofibrosis	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Lymph node	(7)	(5)	(11)	(9)
Iliac, hemorrhage			1 (9%)	
Iliac, hyperplasia, lymphoid	1 (14%)			1 (11%)
Mediastinal, hyperplasia, lymphoid	1 (14%)	1 (20%)	2 (18%)	
Mediastinal, pigmentation	1 (14%)			
Pancreatic, hemorrhage				1 (11%)
Renal, hemorrhage	1 (14%)			1 (11%)
Lymph node, mandibular	(46)	(46)	(49)	(49)
Atrophy		1 (2%)		1 (2%)
Hematopoietic cell proliferation		1 (2%)	1 (2%)	1 (2%)
Hyperplasia, lymphoid	12 (26%)	7 (15%)	7 (14%)	10 (20%)
Pigmentation	18 (39%)	16 (35%)	18 (37%)	15 (31%)
Lymph node, mesenteric	(47)	(49)	(49)	(49)
Atrophy	1 (2%)	1 (2%)		2 (4%)
Ectasia	2 (4%)			1 (2%)
Hematopoietic cell proliferation	2 (4%)	2 (4%)	1 (2%)	2 (4%)
Hemorrhage	4 (9%)	2 (4%)		1 (2%)
Hyperplasia, lymphoid	10 (21%)	8 (16%)	11 (22%)	6 (12%)
Pigmentation	1 (2%)	2 (4%)		
Spleen	(49)	(48)	(49)	(50)
Accessory spleen				1 (2%)
Hematopoietic cell proliferation	39 (80%)	39 (81%)	35 (71%)	39 (78%)
Hyperplasia, lymphoid	11 (22%)	10 (21%)	5 (10%)	9 (18%)
Pigmentation	28 (57%)	30 (63%)	28 (57%)	27 (54%)
Lymphoid follicle, atrophy	1 (2%)	2 (4%)	1 (2%)	2 (4%)
Thymus	(48)	(44)	(48)	(48)
Atrophy	5 (10%)	7 (16%)	5 (10%)	9 (19%)
Cyst	3 (6%)		1 (2%)	1 (2%)
Hyperplasia, lymphoid	5 (10%)	3 (7%)	4 (8%)	2 (4%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Integumentary System				
Mammary gland	(50)	(50)	(50)	(50)
Hyperplasia	5 (10%)	11 (22%)	8 (16%)	10 (20%)
Skin	(48)	(50)	(50)	(50)
Edema		1 (2%)		1 (2%)
Epidermis, hyperplasia	1 (2%)			1 (2%)
Subcutaneous tissue, edema			1 (2%)	2 (4%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Callus	1 (2%)			
Fracture			1 (2%)	1 (2%)
Hyperostosis	1 (2%)	1 (2%)	4 (8%)	3 (6%)
Cranium, osteopetrosis			1 (2%)	
Femur, osteopetrosis		1 (2%)	1 (2%)	
Skeletal muscle		(2)	(4)	(6)
Angiectasis				1 (17%)
Atrophy				1 (17%)
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression	1 (2%)		1 (2%)	1 (2%)
Inflammation, chronic				1 (2%)
Necrosis			1 (2%)	1 (2%)
Peripheral nerve			(2)	(2)
Atrophy			1 (50%)	2 (100%)
Respiratory System				
Lung	(50)	(50)	(49)	(50)
Edema	5 (10%)	8 (16%)	3 (6%)	5 (10%)
Foreign body	2 (4%)			
Hemorrhage	5 (10%)	8 (16%)	6 (12%)	4 (8%)
Hyperplasia, lymphoid	10 (20%)	8 (16%)	3 (6%)	9 (18%)
Infiltration cellular, polymorphonuclear		1 (2%)		
Infiltration cellular, histiocyte	1 (2%)	1 (2%)	3 (6%)	5 (10%)
Metaplasia, osseous		1 (2%)	2 (4%)	
Thrombosis	1 (2%)	4 (8%)	1 (2%)	
Alveolar epithelium, hyperplasia	2 (4%)	2 (4%)	1 (2%)	2 (4%)
Special Senses System				
Eye	(50)	(48)	(50)	(50)
Inflammation, chronic	3 (6%)	3 (6%)		
Cornea, hyperplasia	2 (4%)	1 (2%)		
Harderian gland	(50)	(50)	(50)	(49)
Cyst				1 (2%)
Hyperplasia, focal	1 (2%)	1 (2%)		1 (2%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

	0 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Urinary System				
Kidney	(50)	(49)	(49)	(50)
Hydronephrosis			1 (2%)	1 (2%)
Hyperplasia, lymphoid	8 (16%)	9 (18%)	6 (12%)	8 (16%)
Infarct	3 (6%)	2 (4%)	4 (8%)	5 (10%)
Metaplasia, osseous		1 (2%)	3 (6%)	2 (4%)
Nephropathy	14 (28%)	11 (22%)	14 (29%)	12 (24%)
Renal tubule, accumulation, hyaline droplet	2 (4%)	1 (2%)	2 (4%)	1 (2%)
Renal tubule, dilatation	1 (2%)			1 (2%)
Renal tubule, necrosis	1 (2%)			1 (2%)
Renal tubule, pigmentation	3 (6%)	1 (2%)		1 (2%)
Transitional epithelium, hyperplasia	1 (2%)			
Urinary bladder	(49)	(50)	(50)	(50)
Hyperplasia, lymphoid	4 (8%)	12 (24%)	4 (8%)	5 (10%)
Transitional epithelium, hyperplasia			1 (2%)	

APPENDIX E
GENETIC TOXICOLOGY

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GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST PROTOCOL

Testing was performed as reported by Zeiger *et al.* (1992). Sodium chlorate was sent to the laboratory as a coded aliquot. It was incubated with the *Salmonella typhimurium* tester strains TA97, TA98, TA100, TA102, TA104, and TA1535 either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver) for 20 minutes at 37° C. Top agar supplemented with L-histidine and d-biotin was added, and the contents of the tubes were mixed and poured onto the surfaces of minimal glucose agar plates. Histidine-independent mutant colonies arising on these plates were counted following incubation for 2 days at 37° C.

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

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

MOUSE PERIPHERAL BLOOD MICRONUCLEUS TEST PROTOCOL

A detailed discussion of this assay is presented by MacGregor *et al.* (1990). At the end of the 3-week toxicity study, peripheral blood samples were obtained from male and female mice. Smears were immediately prepared and fixed in absolute methanol. The methanol-fixed slides were stained with acridine orange and coded. Slides were scanned to determine the frequency of micronuclei in 2,000 normochromatic erythrocytes (NCEs) in each of 10 animals per exposure group. In addition, the percentage of polychromatic erythrocytes (PCEs) in a population of 1,000 erythrocytes was determined as a measure of bone marrow toxicity.

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

EVALUATION PROTOCOL

These are the basic guidelines for arriving at an overall assay result for assays performed by the National Toxicology Program. Statistical as well as biological factors are considered. For an individual assay, the statistical procedures for data analysis have been described in the preceding protocols. There have been instances, however,

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

RESULTS

Sodium chlorate (100 to 10,000 µg/plate) was not mutagenic in *S. typhimurium* strains TA97, TA98, TA100, TA102, TA104, or TA1535, with or without induced rat or hamster liver S9 enzymes. *In viv*o, no increases in the frequencies of micronucleated NCEs were seen in peripheral blood samples from male and female $B6C3F_1$ mice exposed to concentrations of 125 to 2,000 mg/L sodium chlorate in drinking water for 3 weeks. The abbreviated exposure duration of 3 weeks may not have allowed steady state to be reached in the circulating NCE population, but the data are clearly negative, with no indication of an exposure concentration-related increase in NCEs. Steady state is usually established by day 35 of continuous exposure.

TABLE E1
Mutagenicity of Sodium Chlorate in *Salmonella typhimurium*[a]

Strain	Dose (µg/plate)	Revertants/Plate[b]					
		–S9		hamster S9		rat S9	
		Trial 1	Trial 2	+ 10%	+ 30%	+ 10%	+ 30%
TA102	0	216 ± 5.2	233 ± 20.7	331 ± 9.8	264 ± 4.3	309 ± 27.7	275 ± 11.5
	100	210 ± 5.2	220 ± 16.4	359 ± 16.0	250 ± 3.3	340 ± 40.5	264 ± 23.0
	333	219 ± 3.3	225 ± 14.6	331 ± 7.2	259 ± 13.9	347 ± 31.0	254 ± 20.0
	1,000	233 ± 12.5	233 ± 16.9	305 ± 13.3	286 ± 5.8	357 ± 23.1	291 ± 9.6
	3,333	242 ± 22.7	238 ± 6.5	349 ± 4.5	291 ± 6.5	373 ± 34.6	274 ± 8.6
	10,000	209 ± 5.2	248 ± 19.3	392 ± 7.9	252 ± 20.8	322 ± 32.4	257 ± 11.6
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control[c]		737 ± 24.1	898 ± 41.7	1,211 ± 42.0	784 ± 15.3	1,110 ± 60.9	768 ± 24.3
TA104	0	298 ± 8.0	334 ± 16.8	430 ± 10.4	430 ± 11.2	397 ± 15.2	405 ± 10.0
	100	289 ± 29.1	328 ± 6.4	411 ± 2.7	432 ± 14.7	377 ± 25.2	411 ± 1.7
	333	285 ± 32.8	324 ± 26.7	426 ± 12.2	408 ± 11.4	368 ± 22.2	399 ± 7.5
	1,000	262 ± 18.1	364 ± 28.0	365 ± 2.3	406 ± 16.6	425 ± 20.0	398 ± 17.3
	3,333	314 ± 9.8	326 ± 16.2	363 ± 12.3	411 ± 3.8	427 ± 22.8	416 ± 9.8
	10,000	302 ± 8.2	342 ± 17.9	384 ± 40.0	407 ± 1.5	410 ± 4.9	412 ± 0.9
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		939 ± 17.9	921 ± 42.5	1,254 ± 25.9	974 ± 31.5	1,266 ± 29.0	826 ± 47.6
TA100	0	145 ± 6.9	137 ± 8.7	120 ± 7.3	126 ± 9.5	133 ± 5.2	122 ± 12.4
	100	125 ± 3.8	117 ± 4.4	130 ± 1.3	130 ± 9.3	162 ± 2.0	124 ± 9.5
	333	134 ± 7.3	127 ± 9.1	124 ± 0.0	135 ± 5.5	131 ± 3.3	148 ± 2.9
	1,000	131 ± 7.6	126 ± 9.1	137 ± 7.4	152 ± 8.5	134 ± 7.0	125 ± 2.0
	3,333	135 ± 8.7	121 ± 3.8	126 ± 11.2	134 ± 8.8	139 ± 13.4	134 ± 9.5
	10,000	144 ± 4.9	132 ± 5.5	128 ± 8.9	126 ± 10.1	122 ± 1.7	131 ± 12.5
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		900 ± 12.3	844 ± 5.1	695 ± 18.5	664 ± 21.1	635 ± 24.8	624 ± 15.4
TA1535	0	13 ± 2.4	11 ± 2.3	12 ± 0.9	12 ± 2.0	12 ± 1.5	13 ± 1.2
	100	11 ± 0.3	8 ± 1.2	10 ± 0.3	12 ± 0.7	13 ± 0.6	15 ± 2.0
	333	9 ± 0.6	11 ± 2.3	9 ± 1.2	15 ± 1.8	9 ± 0.0	10 ± 1.8
	1,000	12 ± 2.0	11 ± 1.3	10 ± 2.7	10 ± 1.2	7 ± 0.6	10 ± 1.2
	3,333	11 ± 1.7	7 ± 0.7	9 ± 0.6	12 ± 3.4	8 ± 0.7	10 ± 3.2
	10,000	9 ± 1.0	9 ± 1.7	10 ± 1.8	8 ± 0.7	6 ± 1.9	12 ± 2.7
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		938 ± 15.5	940 ± 16.2	126 ± 14.0	141 ± 5.0	130 ± 15.1	115 ± 6.9
TA97	0	128 ± 10.5	139 ± 9.5	146 ± 4.5	169 ± 3.3	154 ± 5.3	174 ± 6.3
	100	117 ± 11.1	147 ± 14.3	148 ± 18.1	151 ± 7.5	157 ± 9.8	191 ± 13.8
	333	127 ± 14.3	132 ± 10.8	157 ± 12.1	177 ± 10.4	132 ± 3.3	191 ± 14.0
	1,000	145 ± 11.4	126 ± 9.6	136 ± 5.2	155 ± 3.7	140 ± 15.5	167 ± 25.2
	3,333	121 ± 7.8	149 ± 10.6	138 ± 13.3	160 ± 6.6	158 ± 13.2	210 ± 9.3
	10,000	121 ± 6.1	125 ± 4.0	88 ± 45.6	142 ± 10.7	131 ± 8.2	173 ± 19.8
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		572 ± 16.9	640 ± 21.1	710 ± 8.9	660 ± 6.7	653 ± 15.0	650 ± 23.7

TABLE E1
Mutagenicity of Sodium Chlorate in *Salmonella typhimurium*

Strain	Dose (µg/plate)	Revertants/Plate –S9 Trial 1	–S9 Trial 2	hamster S9 + 10%	hamster S9 + 30%	rat S9 + 10%	rat S9 + 30%
TA98	0	12 ± 0.9	21 ± 2.7	18 ± 2.4	11 ± 1.5	30 ± 3.2	15 ± 2.6
	100	12 ± 1.5	22 ± 1.8	19 ± 5.0	13 ± 1.7	26 ± 1.8	10 ± 1.2
	333	10 ± 0.3	19 ± 4.1	24 ± 1.5	9 ± 2.6	23 ± 1.2	12 ± 1.2
	1,000	11 ± 2.1	21 ± 3.2	25 ± 0.7	14 ± 2.4	21 ± 2.0	8 ± 0.9
	3,333	12 ± 1.0	24 ± 4.3	26 ± 2.3	10 ± 1.9	30 ± 0.9	13 ± 1.9
	10,000	13 ± 1.5	21 ± 6.1	27 ± 1.7	10 ± 1.2	27 ± 4.3	13 ± 2.7
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		380 ± 8.3	443 ± 16.9	534 ± 11.4	478 ± 6.7	466 ± 15.8	431 ± 7.8

[a] Study performed at SRI International. The detailed protocol is presented by Zeiger *et al*. (1992). 0 µg/plate was the solvent control.
[b] Revertants are presented as mean ± standard error from three plates.
[c] The positive controls in the absence of metabolic activation were sodium azide (TA100 and TA1535), 9-aminoacridine (TA97), 4-nitro-*o*-phenylenediamine (TA98), mitomycin-C (TA102), and methyl methanesulfonate (TA104). The positive control for metabolic activation with all strains was 2-aminoanthracene, and 2-aminoanthracene or sterigmatocystin was used for TA102.

TABLE E2
Frequency of Micronuclei in Peripheral Blood Erythrocytes of Mice Following Administration of Sodium Chlorate in Drinking Water for 3 Weeks[a]

	Concentration (mg/L)	Number of Mice with Erythrocytes Scored	Micronucleated NCEs/ 1,000 NCEs[b]	P Value[c]	PCEs (%)
Male					
Tap water[d]		10	1.20 ± 0.20		2.510 ± 0.15
Sodium chlorate	125	10	1.25 ± 0.13	0.4432	2.350 ± 0.10
	250	10	1.10 ± 0.16	0.6160	2.190 ± 0.08
	500	10	0.75 ± 0.21	0.9253	2.260 ± 0.11
	1,000	10	1.05 ± 0.14	0.6727	2.080 ± 0.11
	2,000	10	1.25 ± 0.23	0.4432	2.040 ± 0.08
			P=0.406[e]		
Female					
Tap water		10	0.95 ± 0.16		1.890 ± 0.07
Sodium chlorate	125	10	1.05 ± 0.24	0.3759	1.820 ± 0.11
	250	10	1.00 ± 0.18	0.4364	1.750 ± 0.14
	500	10	0.65 ± 0.18	0.8557	1.680 ± 0.10
	1,000	10	0.85 ± 0.17	0.6306	1.840 ± 0.10
	2,000	10	1.15 ± 0.18	0.2684	2.040 ± 0.12
			P=0.285		

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

APPENDIX F
CLINICAL PATHOLOGY RESULTS

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TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Week Drinking Water Study of Sodium Chlorate[a]

	0 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Male						
Hematology						
n	10	10	10	10	10	10
Hematocrit (%)						
Day 4	42.7 ± 1.1	41.8 ± 0.8	42.4 ± 0.8	42.9 ± 1.2	42.5 ± 1.2	41.2 ± 0.8
Day 22	44.7 ± 0.5	44.8 ± 0.5	44.1 ± 0.7	43.3 ± 0.8	44.1 ± 0.5	42.1 ± 0.6**
Hemoglobin (g/dL)						
Day 4	14.1 ± 0.3	13.8 ± 0.2	14.1 ± 0.2	14.3 ± 0.4	14.1 ± 0.4	13.7 ± 0.2
Day 22	14.9 ± 0.2	15.1 ± 0.1	14.9 ± 0.2	14.7 ± 0.2	14.7 ± 0.2	14.0 ± 0.2**
Erythrocytes (10^6/µL)						
Day 4	7.22 ± 0.17	7.08 ± 0.13	7.24 ± 0.11	7.24 ± 0.18	7.21 ± 0.18	7.04 ± 0.14
Day 22	8.05 ± 0.09	8.05 ± 0.07	7.91 ± 0.14	7.80 ± 0.11	7.86 ± 0.09	7.53 ± 0.11**
Reticulocytes (10^6/µL)						
Day 4	0.76 ± 0.02	0.74 ± 0.02	0.73 ± 0.03	0.77 ± 0.03	0.77 ± 0.03	0.73 ± 0.02
Day 22	0.43 ± 0.01	0.44 ± 0.01	0.44 ± 0.01	0.46 ± 0.01	0.46 ± 0.01	0.41 ± 0.01
Mean cell volume (fL)						
Day 4	59.1 ± 0.4	59.0 ± 0.4	58.6 ± 0.3	59.3 ± 0.2	58.9 ± 0.3	58.5 ± 0.2
Day 22	55.5 ± 0.3	55.6 ± 0.2	55.7 ± 0.2	55.4 ± 0.4	56.1 ± 0.2	55.9 ± 0.2
Mean cell hemoglobin (pg)						
Day 4	19.6 ± 0.1	19.5 ± 0.1	19.5 ± 0.1	19.7 ± 0.1	19.6 ± 0.2	19.5 ± 0.1
Day 22	18.6 ± 0.1	18.7 ± 0.1	18.9 ± 0.1	18.9 ± 0.1	18.7 ± 0.1	18.6 ± 0.1
Mean cell hemoglobin concentration (g/dL)						
Day 4	33.1 ± 0.2	33.1 ± 0.1	33.3 ± 0.3	33.2 ± 0.2	33.3 ± 0.2	33.2 ± 0.2
Day 22	33.4 ± 0.3	33.7 ± 0.2	33.8 ± 0.3	34.1 ± 0.2	33.3 ± 0.2	33.3 ± 0.1
Platelets (10^3/µL)						
Day 4	850.4 ± 14.0	859.4 ± 15.7	820.7 ± 9.1	866.1 ± 20.0	888.2 ± 13.4	869.2 ± 20.5
Day 22	925.5 ± 16.4	958.0 ± 19.0	934.4 ± 18.7	954.9 ± 13.0	908.9 ± 19.7	837.3 ± 11.8**
Leukocytes (10^3/µL)						
Day 4	8.05 ± 0.39	7.91 ± 0.27	8.20 ± 0.21	7.89 ± 0.30	7.06 ± 0.45	7.71 ± 0.29
Day 22	10.82 ± 0.50	10.28 ± 0.14	9.73 ± 0.29	10.10 ± 0.25	9.52 ± 0.31	9.71 ± 0.33
Segmented neutrophils (10^3/µL)						
Day 4	1.09 ± 0.05	1.01 ± 0.04	0.91 ± 0.05*	0.63 ± 0.04**	0.48 ± 0.04**	0.47 ± 0.04**
Day 22	1.05 ± 0.04	0.85 ± 0.04**	0.70 ± 0.03**	0.66 ± 0.04**	0.54 ± 0.03**	0.38 ± 0.02**
Lymphocytes (10^3/µL)						
Day 4	6.69 ± 0.36	6.63 ± 0.26	7.01 ± 0.19	6.98 ± 0.30	6.34 ± 0.43	6.96 ± 0.26
Day 22	9.49 ± 0.47	9.15 ± 0.12	8.77 ± 0.26	9.20 ± 0.27	8.74 ± 0.30	9.10 ± 0.31
Activated lymphocytes (10^3/µL)						
Day 4	0.10 ± 0.01	0.11 ± 0.01	0.11 ± 0.01	0.12 ± 0.01	0.10 ± 0.01	0.14 ± 0.01*
Day 22	0.09 ± 0.02	0.08 ± 0.01	0.07 ± 0.01	0.08 ± 0.01	0.08 ± 0.01[b]	0.10 ± 0.01
Monocytes (10^3/µL)						
Day 4	0.12 ± 0.01	0.11 ± 0.00	0.12 ± 0.01	0.10 ± 0.01	0.10 ± 0.01	0.10 ± 0.01
Day 22	0.15 ± 0.02	0.15 ± 0.01	0.15 ± 0.02	0.12 ± 0.01	0.12 ± 0.01[b]	0.07 ± 0.01**
Basophils (10^3/µL)						
Day 4	0.005 ± 0.002	0.006 ± 0.002	0.008 ± 0.002	0.013 ± 0.004	0.007 ± 0.002	0.007 ± 0.002
Day 22	0.012 ± 0.003	0.012 ± 0.001	0.010 ± 0.001	0.010 ± 0.002	0.010 ± 0.002[b]	0.012 ± 0.001
Eosinophils (10^3/µL)						
Day 4	0.05 ± 0.01	0.04 ± 0.01	0.05 ± 0.01	0.07 ± 0.03	0.03 ± 0.00	0.04 ± 0.00
Day 22	0.04 ± 0.01	0.04 ± 0.00	0.03 ± 0.00	0.04 ± 0.01	0.05 ± 0.01	0.04 ± 0.00
Methemoglobin (g/dL)						
Day 4	0.17 ± 0.04	0.34 ± 0.15	0.20 ± 0.04	0.20 ± 0.05[b]	0.27 ± 0.04	0.22 ± 0.04
Day 22	0.20 ± 0.03	0.27 ± 0.02	0.20 ± 0.03	0.18 ± 0.03	0.17 ± 0.03	0.21 ± 0.06

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Week Drinking Water Study of Sodium Chlorate

	0 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Male (continued)						
Clinical Chemistry						
Day 4	10	10	10	10	9	10
Day 22	10	10	10	10	10	10
Urea nitrogen (mg/dL)						
Day 4	10.0 ± 0.9	11.2 ± 0.7	9.5 ± 0.5	9.1 ± 0.7	10.3 ± 0.8	10.8 ± 0.5
Day 22	10.7 ± 0.4	10.4 ± 0.4	10.7 ± 0.5	10.9 ± 0.4	10.1 ± 0.4	10.3 ± 0.5
Creatinine (mg/dL)						
Day 4	0.39 ± 0.01	0.38 ± 0.02	0.34 ± 0.02	0.38 ± 0.02	0.40 ± 0.02	0.38 ± 0.01
Day 22	0.41 ± 0.01	0.42 ± 0.01	0.42 ± 0.02	0.41 ± 0.01	0.40 ± 0.02	0.44 ± 0.02
Total protein (g/dL)						
Day 4	5.4 ± 0.1	5.5 ± 0.1	5.4 ± 0.1	5.4 ± 0.1	5.5 ± 0.2	5.6 ± 0.1
Day 22	5.8 ± 0.1	5.9 ± 0.1	5.8 ± 0.1	5.8 ± 0.1	5.8 ± 0.1	5.8 ± 0.1
Albumin (g/dL)						
Day 4	4.0 ± 0.1	4.0 ± 0.1	3.9 ± 0.1[b]	3.9 ± 0.1	4.0 ± 0.1	4.1 ± 0.1
Day 22	4.3 ± 0.1	4.5 ± 0.0	4.3 ± 0.0	4.3 ± 0.0	4.3 ± 0.0	4.4 ± 0.0
Alanine aminotransferase (IU/L)						
Day 4	69 ± 2	66 ± 1	64 ± 1	69 ± 2	62 ± 2	64 ± 2
Day 22	52 ± 1	54 ± 2	52 ± 1	54 ± 1	54 ± 1	51 ± 1
Alkaline phosphatase (IU/L)						
Day 4	740 ± 21	720 ± 34	682 ± 17	730 ± 31	733 ± 26	706 ± 16
Day 22	536 ± 8	548 ± 8	531 ± 6	541 ± 7	544 ± 9	489 ± 10*
Creatine kinase (IU/L)						
Day 4	236 ± 23	224 ± 27	238 ± 27	274 ± 26	252 ± 39	228 ± 25
Day 22	104 ± 19	78 ± 11[b]	83 ± 10	109 ± 17[c]	68 ± 7[b]	99 ± 17[c]
Sorbitol dehydrogenase (IU/L)						
Day 22	6 ± 0[d]	8 ± 0*[d]	8 ± 2[b]	8 ± 2[c]	7 ± 1[c]	6 ± 1[c]
Bile acids (μmol/L)						
Day 4	34.3 ± 5.7	28.1 ± 2.3	27.5 ± 1.9	30.4 ± 4.2	30.5 ± 2.5	26.0 ± 2.6
Day 22	32.6 ± 2.7	28.5 ± 3.0	28.0 ± 1.9	25.3 ± 1.1	26.0 ± 1.0	38.6 ± 4.3
Female						
n	10	10	10	10	10	10
Hematology						
Hematocrit (%)						
Day 4	43.4 ± 0.6	43.6 ± 0.7	43.9 ± 0.9	42.1 ± 0.9	43.1 ± 0.8	42.7 ± 0.6
Day 22	43.9 ± 0.6	43.7 ± 0.6	44.1 ± 1.1	44.4 ± 0.6	44.8 ± 0.3	43.4 ± 0.7
Hemoglobin (g/dL)						
Day 4	14.2 ± 0.2	14.2 ± 0.2	14.6 ± 0.3	13.8 ± 0.3	14.2 ± 0.3	14.0 ± 0.1
Day 22	14.8 ± 0.2	14.6 ± 0.2	14.8 ± 0.3	14.9 ± 0.2	14.9 ± 0.1	14.3 ± 0.2
Erythrocytes (10^6/μL)						
Day 4	7.60 ± 0.09	7.61 ± 0.13	7.65 ± 0.17	7.30 ± 0.15	7.51 ± 0.14	7.40 ± 0.08
Day 22	8.41 ± 0.13	8.28 ± 0.11	8.34 ± 0.24	8.47 ± 0.12	8.47 ± 0.08	8.20 ± 0.13
Reticulocytes (10^6/μL)						
Day 4	0.60 ± 0.03	0.63 ± 0.02	0.60 ± 0.02	0.66 ± 0.02	0.62 ± 0.02	0.60 ± 0.03
Day 22	0.24 ± 0.01[b]	0.24 ± 0.01	0.29 ± 0.07	0.24 ± 0.01	0.25 ± 0.01	0.26 ± 0.01
Mean cell volume (fL)						
Day 4	57.1 ± 0.3	57.4 ± 0.1	57.5 ± 0.3	57.8 ± 0.1	57.5 ± 0.3	57.7 ± 0.3
Day 22	52.3 ± 0.2	52.8 ± 0.1	53.0 ± 0.5	52.4 ± 0.2	52.8 ± 0.2	52.9 ± 0.2

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Week Drinking Water Study of Sodium Chlorate

	0 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Female (continued)						
n	10	10	10	10	10	10
Hematology (continued)						
Mean cell hemoglobin (pg)						
Day 4	18.7 ± 0.1	18.7 ± 0.1	19.0 ± 0.1	19.0 ± 0.1	18.9 ± 0.1	18.9 ± 0.1
Day 22	17.6 ± 0.1	17.6 ± 0.1	17.7 ± 0.2	17.6 ± 0.1	17.6 ± 0.1	17.5 ± 0.1
Mean cell hemoglobin concentration (g/dL)						
Day 4	32.8 ± 0.2	32.6 ± 0.2	33.1 ± 0.2	32.8 ± 0.3	32.9 ± 0.1	32.8 ± 0.3
Day 22	33.7 ± 0.2	33.4 ± 0.2	33.5 ± 0.2	33.5 ± 0.1	33.3 ± 0.1	33.0 ± 0.1*
Platelets (10^3/μL)						
Day 4	834.0 ± 19.3	846.3 ± 21.4	832.7 ± 7.6	818.1 ± 18.5	866.9 ± 24.6	843.4 ± 10.2
Day 22	846.0 ± 16.9	871.8 ± 14.2	844.3 ± 13.7	803.3 ± 17.8	842.2 ± 19.3	860.5 ± 18.8
Leukocytes (10^3/μL)						
Day 4	8.83 ± 0.41	8.57 ± 0.47	8.94 ± 0.40	8.44 ± 0.30	8.24 ± 0.51	8.53 ± 0.34
Day 22	10.14 ± 0.35	9.32 ± 0.29	9.71 ± 0.61	10.63 ± 0.39	10.28 ± 0.51	10.63 ± 0.43
Segmented neutrophils (10^3/μL)						
Day 4	1.02 ± 0.08	0.87 ± 0.08	0.82 ± 0.03*	0.67 ± 0.04**	0.58 ± 0.05**	0.46 ± 0.03**
Day 22	0.93 ± 0.05	0.63 ± 0.03**	0.66 ± 0.05**	0.61 ± 0.04**	0.57 ± 0.07**	0.46 ± 0.04**
Lymphocytes (10^3/μL)						
Day 4	7.54 ± 0.37	7.50 ± 0.42	7.84 ± 0.39	7.51 ± 0.28	7.40 ± 0.47	7.80 ± 0.31
Day 22	8.94 ± 0.31	8.45 ± 0.26	8.75 ± 0.56	9.72 ± 0.35	9.40 ± 0.46	9.88 ± 0.40
Activated lymphocytes (10^3/μL)						
Day 4	0.10 ± 0.01	0.11 ± 0.01	0.11 ± 0.01	0.11 ± 0.01	0.10 ± 0.02	0.13 ± 0.01
Day 22	0.08 ± 0.01	0.07 ± 0.01	0.09 ± 0.01	0.09 ± 0.01	0.10 ± 0.01	0.10 ± 0.01*
Monocytes (10^3/μL)						
Day 4	0.12 ± 0.02	0.11 ± 0.01	0.11 ± 0.01	0.10 ± 0.01	0.08 ± 0.01*	0.09 ± 0.01*
Day 22	0.11 ± 0.01	0.10 ± 0.01	0.13 ± 0.01	0.14 ± 0.01	0.13 ± 0.01	0.10 ± 0.01
Basophils (10^3/μL)						
Day 4	0.006 ± 0.002	0.008 ± 0.002	0.007 ± 0.002	0.008 ± 0.002	0.010 ± 0.001	0.008 ± 0.001
Day 22	0.016 ± 0.003	0.013 ± 0.003	0.017 ± 0.003	0.015 ± 0.002	0.019 ± 0.004	0.016 ± 0.003
Eosinophils (10^3/μL)						
Day 4	0.05 ± 0.01	0.03 ± 0.01	0.05 ± 0.01	0.05 ± 0.01	0.06 ± 0.01	0.05 ± 0.01
Day 22	0.06 ± 0.01	0.06 ± 0.01	0.07 ± 0.01	0.06 ± 0.01	0.06 ± 0.01	0.07 ± 0.01
Methemoglobin (g/dL)						
Day 4	0.14 ± 0.02	0.14 ± 0.03	0.19 ± 0.03	0.15 ± 0.02	0.14 ± 0.02	0.18 ± 0.02
Day 22	0.21 ± 0.03	0.20 ± 0.03	0.21 ± 0.02	0.21 ± 0.02	0.21 ± 0.03	0.19 ± 0.02
Clinical Chemistry						
Urea nitrogen (mg/dL)						
Day 4	11.1 ± 0.7	10.6 ± 7.5	11.6 ± 0.6	10.0 ± 0.6	10.3 ± 0.7	11.4 ± 0.7
Day 22	15.0 ± 0.4	14.3 ± 0.4	14.0 ± 0.6	13.8 ± 0.3	13.9 ± 0.5	12.53 ± 0.4**
Creatinine (mg/dL)						
Day 4	0.37 ± 0.02	0.37 ± 0.02	0.37 ± 0.02	0.37 ± 0.02	0.36 ± 0.02	0.38 ± 0.01
Day 22	0.51 ± 0.01	0.54 ± 0.01	0.52 ± 0.02	0.50 ± 0.02	0.53 ± 0.02	0.50 ± 0.00
Total protein (g/dL)						
Day 4	5.4 ± 0.1	5.3 ± 0.1	5.3 ± 0.1	5.3 ± 0.1	5.4 ± 0.1	5.4 ± 0.1
Day 22	6.1 ± 0.1	5.9 ± 0.1	6.1 ± 0.1	5.8 ± 0.1	6.1 ± 0.1	6.0 ± 0.1
Albumin (g/dL)						
Day 4	4.2 ± 0.1	4.2 ± 0.1	4.2 ± 0.1	4.1 ± 0.1	4.2 ± 0.1	4.2 ± 0.1
Day 22	4.7 ± 0.1	4.7 ± 0.0	4.7 ± 0.1	4.5 ± 0.0	4.7 ± 0.0	4.6 ± 0.1

TABLE F1
Hematology and Clinical Chemistry Data for Rats in the 3-Week Drinking Water Study of Sodium Chlorate

	0 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Female (continued)						
n	10	10	10	10	10	10
Clinical Chemistry (continued)						
Alanine aminotransferase (IU/L)						
Day 4	49 ± 2	51 ± 2	49 ± 2	47 ± 1	57 ± 6[b]	52 ± 2
Day 22	40 ± 2	41 ± 1	43 ± 1	42 ± 1	41 ± 1	39 ± 1
Alkaline phosphatase (IU/L)						
Day 4	557 ± 17	564 ± 12	554 ± 15	572 ± 14	551 ± 13	570 ± 20[b]
Day 22	388 ± 11	377 ± 6	367 ± 10	374 ± 7	360 ± 8	366 ± 8
Creatine kinase (IU/L)						
Day 4	294 ± 63	254 ± 30	242 ± 36	208 ± 19	298 ± 76	248 ± 30
Day 22	152 ± 15	116 ± 8	160 ± 26	120 ± 19	148 ± 18	114 ± 12
Sorbitol dehydrogenase (IU/L)						
Day 22	4 ± 1	3 ± 0	3 ± 0	4 ± 0	4 ± 0	3 ± 0
Bile acids (μmol/L)						
Day 4	30.6 ± 3.0	30.2 ± 2.2	28.9 ± 1.2	29.4 ± 2.1	30.8 ± 2.4	31.6 ± 2.2
Day 22	23.3 ± 2.6	23.1 ± 1.8	22.8 ± 1.9	20.4 ± 1.1	24.8 ± 1.9	17.9 ± 1.0

* Significantly different ($P \leq 0.05$) from the chamber control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error. Statistical tests were performed on unrounded data.
[b] n=9
[c] n=8
[d] n=7

TABLE F2
Hematology Data for Mice in the 3-Week Drinking Water Study of Sodium Chlorate[a]

	0 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
Male						
n	10	10	10	10	10	10
Hematocrit (%)	49.6 ± 1.1	48.0 ± 0.5	47.7 ± 0.5	48.9 ± 0.6	49.2 ± 0.8	49.1 ± 0.4
Hemoglobin (g/dL)	16.5 ± 0.4	16.0 ± 0.1	15.9 ± 0.2	16.3 ± 0.2	16.1 ± 0.3	15.9 ± 0.1
Erythrocytes (10^6/µL)	10.46 ± 0.25	10.16 ± 0.11	10.09 ± 0.11	10.44 ± 0.13	10.38 ± 0.17	10.21 ± 0.08
Reticulocytes (10^6/µL)	0.33 ± 0.00	0.34 ± 0.01	0.35 ± 0.01	0.34 ± 0.01	0.34 ± 0.01	0.34 ± 0.01
Mean cell volume (fL)	47.5 ± 0.2	47.2 ± 0.2	47.3 ± 0.1	46.9 ± 0.2	47.4 ± 0.2	48.1 ± 0.1
Mean cell hemoglobin (pg)	15.8 ± 0.1	15.8 ± 0.1	15.7 ± 0.1	15.6 ± 0.1	15.6 ± 0.1	15.6 ± 0.1
Mean cell hemoglobin concentration (g/dL)	33.3 ± 0.1	33.4 ± 0.1	33.2 ± 0.2	33.3 ± 0.3	32.8 ± 0.2*	32.5 ± 0.2**
Platelets (10^3/µL)	1,204.5 ± 55.6	1,182.6 ± 37.7	1,224.0 ± 39.9	1,197.4 ± 49.1	1,198.5 ± 53.0	1,273.0 ± 43.0
Leukocytes (10^3/µL)	5.38 ± 0.32	5.04 ± 0.44	5.41 ± 0.56	5.36 ± 0.59	5.12 ± 0.29	4.39 ± 0.51
Segmented neutrophils (10^3/µL)	0.61 ± 0.10	0.58 ± 0.09	0.53 ± 0.07	0.63 ± 0.14	0.44 ± 0.05	0.40 ± 0.05
Lymphocytes (10^3/µL)	4.64 ± 0.29	4.32 ± 0.35	4.74 ± 0.49	4.59 ± 0.51	4.57 ± 0.25	3.89 ± 0.45
Activated lymphocytes (10^3/µL)	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.0	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00
Monocytes (10^3/µL)	0.07 ± 0.01	0.07 ± 0.01	0.08 ± 0.01	0.08 ± 0.01	0.07 ± 0.01	0.06 ± 0.01
Basophils (10^3/µL)	0.003 ± 0.002	0.000 ± 0.000	0.004 ± 0.002	0.005 ± 0.002	0.000 ± 0.000	0.002 ± 0.001
Eosinophils (10^3/µL)	0.04 ± 0.01	0.05 ± 0.01	0.05 ± 0.01	0.05 ± 0.01	0.03 ± 0.00*	0.02 ± 0.01*
Methemoglobin (g/dL)	0.23 ± 0.02	0.19 ± 0.02	0.21 ± 0.03	0.23 ± 0.02	0.19 ± 0.03	0.26 ± 0.01
Female						
n	9	10	10	10	10	10
Hematocrit (%)	49.0 ± 0.6	48.4 ± 0.8	49.4 ± 0.4	49.1 ± 0.7	47.5 ± 0.8	48.1 ± 0.5
Hemoglobin (g/dL)	16.2 ± 0.3	15.9 ± 0.2	16.0 ± 0.1	16.0 ± 0.2	15.6 ± 0.2	15.4 ± 0.2
Erythrocytes (10^6/µL)	10.21 ± 0.17	10.14 ± 0.16	10.27 ± 0.10	10.20 ± 0.15	9.83 ± 0.17	9.86 ± 0.14
Reticulocytes (10^6/µL)	0.31 ± 0.01	0.30 ± 0.01	0.31 ± 0.01	0.31 ± 0.01	0.33 ± 0.02	0.33 ± 0.02
Mean cell volume (fL)	48.0 ± 0.3	47.7 ± 0.2	48.1 ± 0.2	48.2 ± 0.2	48.4 ± 0.2	48.8 ± 0.2*
Mean cell hemoglobin (pg)	15.8 ± 0.1	15.7 ± 0.1	15.6 ± 0.1	15.7 ± 0.1	15.9 ± 0.1	15.6 ± 0.1
Mean cell hemoglobin concentration (g/dL)	33.0 ± 0.3	33.0 ± 0.3	32.5 ± 0.2	32.7 ± 0.2	32.8 ± 0.2	32.0 ± 0.1**
Platelets (10^3/µL)	888.6 ± 34.5	970.8 ± 50.0	879.70 ± 56.5	863.7 ± 49.6	961.1 ± 56.5	948.1 ± 41.6
Leukocytes (10^3/µL)	4.61 ± 0.45	4.44 ± 0.20	4.90 ± 0.34	4.64 ± 0.44	4.76 ± 0.28	4.39 ± 0.28
Segmented neutrophils (10^3/µL)	0.43 ± 0.06	0.49 ± 0.04	0.48 ± 0.05	0.49 ± 0.05	0.46 ± 0.05	0.40 ± 0.04
Lymphocytes (10^3/µL)	4.04 ± 0.39	3.81 ± 0.19	4.28 ± 0.29	4.02 ± 0.39	4.16 ± 0.24	3.86 ± 0.26
Activated lymphocytes (10^3/µL)	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00
Monocytes (10^3/µL)	0.07 ± 0.01	0.06 ± 0.01	0.06 ± 0.01	0.07 ± 0.01	0.07 ± 0.01	0.06 ± 0.01
Basophils (10^3/µL)	0.004 ± 0.002	0.003 ± 0.002	0.006 ± 0.002	0.005 ± 0.002	0.003 ± 0.002	0.007 ± 0.002
Eosinophils (10^3/µL)	0.06 ± 0.01	0.06 ± 0.01	0.07 ± 0.01	0.05 ± 0.01	0.06 ± 0.01	0.06 ± 0.01
Methemoglobin (g/dL)	0.18 ± 0.02	0.13 ± 0.04	0.19 ± 0.04	0.19 ± 0.05	0.15 ± 0.03	0.15 ± 0.04

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

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

TABLE G1 Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 3-Week Drinking Water Study of Sodium Chlorate 230
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TABLE G1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 3-Week Drinking Water Study of Sodium Chlorate[a]

	0 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
n	10	10	10	10	10	10
Male						
Necropsy body wt	184 ± 3	183 ± 4	191 ± 4	189 ± 3	183 ± 2	177 ± 2
Heart						
Absolute	0.644 ± 0.012	0.631 ± 0.014	0.650 ± 0.018	0.669 ± 0.026	0.623 ± 0.010	0.544 ± 0.015**
Relative	3.509 ± 0.056	3.444 ± 0.036	3.411 ± 0.057	3.538 ± 0.105	3.402 ± 0.037	3.071 ± 0.067**
R. Kidney						
Absolute	0.705 ± 0.013	0.700 ± 0.017	0.733 ± 0.023	0.740 ± 0.012	0.702 ± 0.012	0.637 ± 0.020*
Relative	3.842 ± 0.064	3.822 ± 0.063	3.846 ± 0.075	3.925 ± 0.069	3.834 ± 0.043	3.593 ± 0.087
Liver						
Absolute	7.680 ± 0.191	7.920 ± 0.206	8.110 ± 0.266	8.562 ± 0.345	7.868 ± 0.169	7.501 ± 0.240[b]
Relative	41.856 ± 1.050	43.210 ± 0.592	42.514 ± 0.728	45.248 ± 1.262	42.959 ± 0.696	42.612 ± 1.349[b]
Lung						
Absolute	1.123 ± 0.081[b]	1.113 ± 0.062	1.169 ± 0.041	1.245 ± 0.095	1.172 ± 0.052	0.988 ± 0.030
Relative	6.141 ± 0.492[b]	6.078 ± 0.315	6.154 ± 0.231	6.562 ± 0.424	6.399 ± 0.270	5.584 ± 0.171
R. Testis						
Absolute	1.085 ± 0.036	1.075 ± 0.030	1.091 ± 0.023	1.100 ± 0.026	1.089 ± 0.024	1.036 ± 0.032
Relative	5.893 ± 0.131	5.863 ± 0.093	5.735 ± 0.094	5.835 ± 0.135	5.949 ± 0.113	5.850 ± 0.162
Thymus						
Absolute	0.384 ± 0.013	0.349 ± 0.028	0.385 ± 0.012	0.397 ± 0.016	0.377 ± 0.012	0.378 ± 0.012
Relative	2.089 ± 0.065	1.915 ± 0.156	2.025 ± 0.065	2.100 ± 0.068	2.058 ± 0.066	2.133 ± 0.062
Female						
Necropsy body wt	130 ± 1	132 ± 2	130 ± 1	131 ± 2	132 ± 2	131 ± 2
Heart						
Absolute	0.468 ± 0.012	0.482 ± 0.019	0.469 ± 0.008	0.482 ± 0.009	0.486 ± 0.007	0.464 ± 0.011
Relative	3.611 ± 0.078	3.649 ± 0.133	3.623 ± 0.064	3.693 ± 0.061	3.704 ± 0.086	3.541 ± 0.069
R. Kidney						
Absolute	0.531 ± 0.010	0.539 ± 0.018	0.518 ± 0.009	0.537 ± 0.010	0.553 ± 0.012	0.523 ± 0.012
Relative	4.099 ± 0.071	4.077 ± 0.106	4.003 ± 0.077	4.111 ± 0.045	4.204 ± 0.061	3.990 ± 0.070
Liver						
Absolute	5.046 ± 0.089	5.010 ± 0.126	4.963 ± 0.064	5.091 ± 0.110	5.171 ± 0.163	5.035 ± 0.177
Relative	38.941 ± 0.539	37.918 ± 0.748	38.338 ± 0.444	38.992 ± 0.691	39.284 ± 0.975	38.390 ± 1.171
Lung						
Absolute	0.821 ± 0.030	0.821 ± 0.031	0.804 ± 0.025	0.895 ± 0.034	0.807 ± 0.025	0.785 ± 0.027
Relative	6.338 ± 0.230	6.210 ± 0.197	6.207 ± 0.174	6.838 ± 0.182	6.129 ± 0.134	5.990 ± 0.192
Thymus						
Absolute	0.314 ± 0.010	0.322 ± 0.007	0.329 ± 0.008	0.333 ± 0.011	0.316 ± 0.013	0.313 ± 0.010
Relative	2.423 ± 0.081	2.440 ± 0.044	2.539 ± 0.057	2.545 ± 0.070	2.399 ± 0.090	2.388 ± 0.085

* Significantly different ($P \leq 0.05$) from the chamber control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9

TABLE G2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 3-Week Drinking Water Study of Sodium Chlorate[a]

	0 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L	2,000 mg/L
n	10	10	10	10	10	10
Male						
Necropsy body wt	29.8 ± 0.3	29.8 ± 0.3	30.0 ± 0.5	29.8 ± 0.4	29.8 ± 0.4	30.2 ± 0.4
Heart						
Absolute	0.155 ± 0.005	0.146 ± 0.004	0.150 ± 0.006	0.148 ± 0.004	0.149 ± 0.004	0.144 ± 0.004
Relative	5.209 ± 0.172	4.894 ± 0.177	4.999 ± 0.182	4.970 ± 0.107	4.996 ± 0.145	4.769 ± 0.131
R. Kidney						
Absolute	0.283 ± 0.006	0.274 ± 0.005	0.282 ± 0.010	0.285 ± 0.008	0.284 ± 0.007	0.276 ± 0.007
Relative	9.506 ± 0.176	9.182 ± 0.117	9.410 ± 0.332	9.570 ± 0.190	9.522 ± 0.216	9.151 ± 0.268
Liver						
Absolute	1.438 ± 0.058	1.399 ± 0.036	1.443 ± 0.043	1.439 ± 0.035	1.427 ± 0.041	1.369 ± 0.026
Relative	48.321 ± 1.956	46.832 ± 0.832	48.080 ± 1.172	48.327 ± 0.838	47.777 ± 1.043	45.392 ± 1.010
Lung						
Absolute	0.207 ± 0.014	0.181 ± 0.010	0.189 ± 0.014	0.196 ± 0.012	0.201 ± 0.019	0.178 ± 0.006
Relative	6.986 ± 0.549	6.066 ± 0.324	6.308 ± 0.452	6.599 ± 0.424	6.711 ± 0.589	5.881 ± 0.138
R. Testis						
Absolute	0.107 ± 0.002[b]	0.110 ± 0.002	0.111 ± 0.002	0.110 ± 0.002	0.110 ± 0.002	0.111 ± 0.002
Relative	3.610 ± 0.051[b]	3.689 ± 0.057	3.709 ± 0.046	3.700 ± 0.063	3.688 ± 0.070	3.663 ± 0.052
Thymus						
Absolute	0.046 ± 0.001	0.042 ± 0.001	0.047 ± 0.001	0.044 ± 0.003	0.043 ± 0.002	0.044 ± 0.002
Relative	1.548 ± 0.053	1.389 ± 0.039	1.562 ± 0.030	1.475 ± 0.079	1.439 ± 0.055	1.464 ± 0.069
Female						
Necropsy body wt	22.8 ± 0.4	22.8 ± 0.1	23.0 ± 0.3	22.5 ± 0.2	23.4 ± 0.5	22.6 ± 0.6
Heart						
Absolute	0.118 ± 0.003	0.118 ± 0.004	0.118 ± 0.002	0.119 ± 0.004	0.121 ± 0.004	0.117 ± 0.002
Relative	5.185 ± 0.122	5.178 ± 0.181	5.134 ± 0.110	5.292 ± 0.136	5.183 ± 0.149	5.197 ± 0.134
R. Kidney						
Absolute	0.167 ± 0.004	0.171 ± 0.004	0.170 ± 0.005	0.170 ± 0.003	0.173 ± 0.005	0.166 ± 0.005
Relative	7.332 ± 0.146	7.505 ± 0.189	7.387 ± 0.209	7.568 ± 0.157	7.407 ± 0.205	7.351 ± 0.200
Liver						
Absolute	1.048 ± 0.026	1.024 ± 0.021	1.025 ± 0.039	1.006 ± 0.024	1.020 ± 0.038	1.038 ± 0.030
Relative	46.035 ± 0.975	44.940 ± 0.893	44.446 ± 1.292	44.733 ± 0.863	43.521 ± 0.927	45.895 ± 0.562
Lung						
Absolute	0.167 ± 0.010	0.168 ± 0.006	0.175 ± 0.010	0.187 ± 0.009	0.165 ± 0.008	0.175 ± 0.010
Relative	7.400 ± 0.575	7.377 ± 0.282	7.579 ± 0.363	8.318 ± 0.372	7.082 ± 0.372	7.745 ± 0.396
Thymus						
Absolute	0.061 ± 0.001	0.056 ± 0.003	0.063 ± 0.002	0.062 ± 0.002	0.061 ± 0.001	0.061 ± 0.002
Relative	2.677 ± 0.075	2.461 ± 0.148	2.722 ± 0.072	2.773 ± 0.111	2.632 ± 0.087	2.708 ± 0.078

[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9

APPENDIX H
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

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CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

Procurement and Characterization of Sodium Chlorate

A single lot of sodium chlorate (14019PQ) was obtained from Aldrich Chemical Company, Inc. (Milwaukee, WI), by the analytical chemistry laboratory, Battelle Columbus (Columbus, OH), and provided to the study laboratory, Southern Research Institute (Birmingham, AL). Lot 14019PQ was used in the 3-week and 2-year studies. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory and the study laboratory. Reports on analyses performed in support of the sodium chlorate studies are on file at the National Institute of Environmental Health Sciences.

Lot 14019PQ, a white crystalline solid, was identified as sodium chlorate by the analytical chemistry laboratory and the study laboratory using infrared spectroscopy and by Galbraith Laboratories, Inc. (Knoxville, TN) using melting point determination. All spectra were consistent with a literature spectrum (*Aldrich*, 1985) of sodium chlorate. The infrared spectrum is presented in Figure H1. The determined melting point agreed with the range of values reported in the literature (MSDS, 1986; *Sax's*, 1996; *Hawley's*, 1997; MDL, 1997)

The moisture content of lot 14019PQ was determined by Galbraith Laboratories, Inc., using Karl Fischer titration. The purity of lot 14019PQ was determined by the analytical chemistry laboratory using argentimetric titration, by the analytical chemistry laboratory and the study laboratory using anion exchange ion chromatography (IC), and by Galbraith Laboratories, Inc., using elemental analysis. Argentimetric titration was performed by heating samples of sodium chlorate in solutions of sulfurous and nitric acids, adding solutions of 0.1 N silver nitrate and ferric ammonium sulfate indicator after cooling, and titrating to the end point with 0.1 N ammonium thiocyanate. IC was performed by the analytical chemistry laboratory using system A and by the study laboratory using system B.

A) Dionex Corp. (Sunnyvale, CA), an Ionpac AS9-SC ion exchange column (250 mm × 4 mm; and a mobile phase of A) 40 mM boric acid and 20 mM sodium hydroxide and B) 200 mM boric acid and 100 mM NaOH. Following 6 minutes of isocratic elution with 50% A:50 % B, the mobile phase was linearly changed to 30% A and 70% B in 2 minutes; and to 100% B in 2 minutes Following a 3-minute hold, the gradient was linearly changed to 50% A:50% B in 1 minute, followed by a 4-minute hold. The flow rate was 1.5 mL/minute and suppressed conductivity detection was used.

B) Alltech Associates, Inc. (Deerfield, CA), Odyssey Basic Ion Chromatograph, an Alltech Anion HC ion exchange column (150 mm × 4.6 mm, Alltech Associates), using an isocratic mobile phase of 2.8 mM sodium bicarbonate and 4.4 mM sodium carbonate in deionized organic-free water. The flow rate was 1.4 mL/minute, the column temperature was 50° C, and suppressed conductivity detection was used.

Karl Fischer titration indicated a moisture content of less than 0.05%. Elemental analysis for chlorine was in agreement with the theoretical value for sodium chlorate; however, elemental analysis for sodium was higher (108%) than the theoretical value. Argentimetric titration indicated a purity of 99.7%. IC by system A indicated one major peak with no reportable impurities. IC by system B indicated a relative purity of 101% based on major peak comparison with a frozen reference standard of the same lot. Major peak area percent indicated a purity of 100%. The overall purity of lot 14019PQ was determined to be greater than 99%.

Stability studies of the bulk chemical were performed by the analytical chemistry laboratory. IC by system A indicated that sodium chlorate was stable as a bulk chemical for 15 days when stored under a minimal headspace protected from light at temperatures up to 60° C. To ensure stability, the bulk chemical was stored at room temperature, protected from light, in amber glass containers with Teflon®-lined lids. Stability was monitored by

the study laboratory during the 2-year studies with IC by system B. No degradation of the bulk chemical was detected.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared once during the 3-week studies and every 4 weeks during the 2-year studies by mixing sodium chlorate with tap water (Table H1). Formulations were stored at room temperature in NALGENE® containers and protected from light.

Homogeneity studies of 125 and 2,000 mg/L dose formulations were performed by the study laboratory with IC by a system similar to system B. Stability studies of a 2 mg/L dose formulation were performed by the analytical chemistry laboratory with IC by a system similar to system A. Homogeneity was confirmed and stability was confirmed for at least 44 days for dose formulations stored in sealed NALGENE® containers at temperatures up to 25° C, and for at least 7 days when stored in drinking water bottles under simulated animal room conditions.

Periodic analyses of the dose formulations of sodium chlorate were conducted by the study laboratory using IC by systems similar to system B. During the 3-week studies, the dose formulations were analyzed once; all five of the dose formulations for rats and mice were within 10% of the target concentrations (Table H2). Animal room samples of these dose formulations were also analyzed; all five of the animal room samples for rats and mice were within 10% of the target concentrations.

During the 2-year studies, the dose formulations were analyzed approximately every 10 weeks (Table H3). Of the dose formulations used for rats and mice, 40 of 42 were within 10% of the target concentrations. One dose formulation for rats and one dose formulation for mice were inadvertently used at 14% and 11% of target, respectively. All 12 of the animal room samples analyzed for rats and mice were within 10% of the target concentrations.

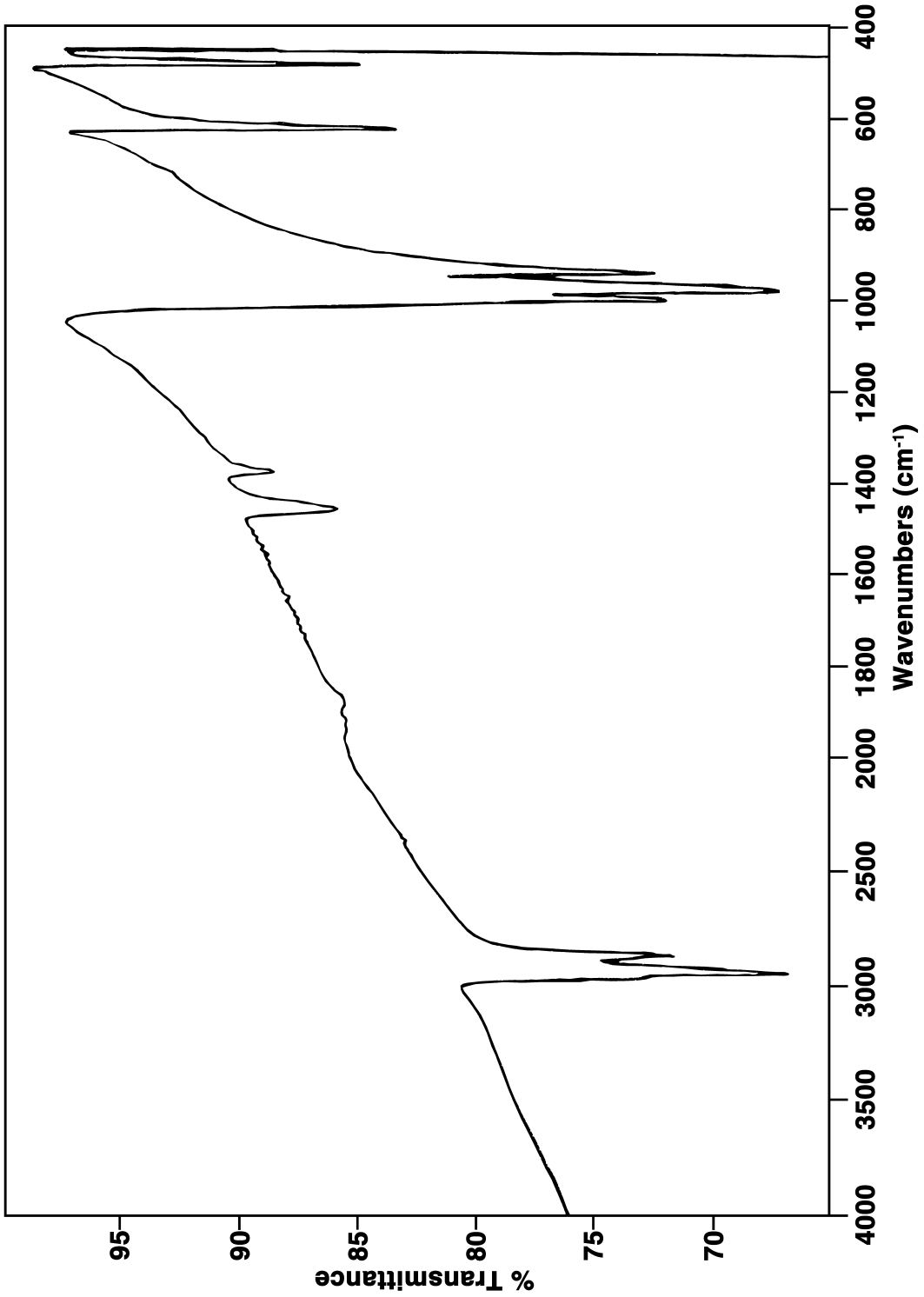

FIGURE H1
Infrared Absorption Spectrum of Sodium Chlorate

TABLE H1
Preparation and Storage of Dose Formulations in the 3-Week and 2-Year Drinking Water Studies of Sodium Chlorate

Preparation
A premix was prepared in a beaker with tap water and then thoroughly mixed with additional tap water in a NALGENE® mixing tank for approximately 15 minutes. Dose formulations were prepared once during the 3-week studies and every 4 weeks during the 2-year studies.

Chemical Lot Number
14019PQ

Maximum Storage Time
44 days

Storage Conditions
Stored in NALGENE® containers at room temperature in the dark

Study Laboratory
Southern Research Institute (Birmingham, AL)

TABLE H2
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 3-Week Drinking Water Studies of Sodium Chlorate

Date Prepared	Date Analyzed	Target Concentration (mg/L)	Determined Concentration[a] (mg/L)	Difference from Target (%)
Rats				
May 11, 1998	May 13, 1998	125	131	+5
		250	253	+1
		500	510	+2
		1,000	1,015	+2
		2,000	1,976	–1
	June 11, 1998[b]	125	133	+7
		250	260	+4
		500	522	+4
		1,000	1,027	+3
		2,000	2,022	+1
Mice				
May 11, 1998	May 13, 1998	125	131	+5
		250	253	+1
		500	510	+2
		1,000	1,015	+2
		2,000	1,976	–1
	June 12, 1998[b]	125	134	+8
		250	265	+6
		500	528	+6
		1,000	1,032	+3
		2,000	2,075	+4

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

TABLE H3
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Sodium Chlorate

Date Prepared	Date Analyzed	Target Concentration (mg/L)	Determined Concentration[a] (mg/L)	Difference from Target[b] (%)
Rats				
September 10, 1998	September 11, 1998	125	125	+1
		1,000	1,041	+4
		2,000	2,025	+1
	October 19-20, 1998[c]	125	123	–2
		1,000	990	–1
		2,000	1,963	–2
November 6, 1998	November 9, 1998	125	127	+2
		1,000	1,004	0
		1,000	995	–1
		2,000	1,976	–1
		2,000	1,976	–1
January 29, 1999	February 1, 1999	125	142	+14
		1,000	1,095	+10
		2,000	2,125	+6
March 26, 1999	March 29-31, 1999	125	128	+3
		1,000	991	–1[d]
		2,000	1,982	–1[d]
	April 30, 1999[c]	125	137	+10
		1,000	1,042	+4
		2,000	2,103	+5
April 1, 1999	April 1, 1999	1,000	993	–1[e]
		2,000	1,966	–2[e]
June 18, 1999	June 21-22, 1999	125	125	0
		1,000	973	–3
		2,000	1,963	–2
August 13, 1999	August 16-17, 1999	125	132	+5
		1,000	1,016	+2
		2,000	2,045	+2
November 5, 1999	November 8, 1999	125	125	0
		1,000	1,004	0
		2,000	1,994	0
	December 13, 1999[c]	125	129	+3
		1,000	1,037	+4
		2,000	2,045	+2
December 28, 1999	January 3, 2000	125	135	+8
		1,000	1,076	+8
		2,000	2,133	+7
March 23, 2000	March 24, 2000	125	127	+1
		1,000	1,007	+1
		2,000	1,991	0

TABLE H3
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Sodium Chlorate

Date Prepared	Date Analyzed	Target Concentration (mg/L)	Determined Concentration (mg/L)	Difference from Target (%)
Rats (continued)				
May 18, 2000	May 19, 2000	125	127	+2
		1,000	1,047	+5
		2,000	2,014	+1
	June 26, 2000[c]	125	122	–2
		1,000	1,034	+3
		2,000	2,016	+1
August 10, 2000	August 11, 2000	125	113	–10
		1,000	985	–2
		2,000	1,955	–2
Mice				
September 10, 1998	September 11, 1998	500	504	+2
		1,000	1,041	+4
		2,000	2,025	+1
	October 19-20, 1998[c]	500	493	–1
		1,000	1,013	+1
		2,000	1,971	–1
November 6, 1998	November 9, 1998	500	506	+1
		1,000	1,004	0
		1,000	995	–1
		2,000	1,976	–1
		2,000	1,976	–1
January 29, 1999	February 1, 1999	500	556	+11
		1,000	1,095	+10
		2,000	2,125	+6
March 26, 1999	March 29-31, 1999	500	537	+7
		1,000	991	–1[d]
		2,000	1,982	–1[d]
	April 30, 1999[c]	500	544	+9
		1,000	1,051	+5
		2,000	2,076	+4
April 1, 1999	April 1, 1999	1,000	993	–1[e]
		2,000	1,966	–2[e]
June 18, 1999	June 21-22, 1999	500	471	–6
		1,000	973	–3
		2,000	1,963	–2
August 13, 1999	August 16-17, 1999	500	503	+1
		1,000	1,016	+2
		2,000	2,045	+2

TABLE H3
Results of Analyses of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Sodium Chlorate

Date Prepared	Date Analyzed	Target Concentration (mg/L)	Determined Concentration (mg/L)	Difference from Target (%)
Mice (continued)				
November 5, 1999	November 8, 1999	500	509	+2
		1,000	1,004	0
		2,000	1,994	0
	December 13, 1999[c]	500	512	+2
		1,000	1,020	+2
		2,000	2,008	0
December 28, 1999	January 3, 2000	500	534	+7
		1,000	1,076	+8
		2,000	2,133	+7
March 23, 2000	March 24, 2000	500	527	+5
		1,000	1,007	+1
		2,000	1,991	0
May 18, 2000	May 19, 2000	500	527	+5
		1,000	1,047	+5
		2,000	2,014	+1
	June 26, 2000[c]	500	535	+7
		1,000	1,036	+4
		2,000	2,052	+3
August 10, 2000	August 11, 2000	500	478	–4
		1,000	985	–2
		2,000	1,955	–2

[a] Results of duplicate analyses
[b] Reported percentages are based on unrounded raw data; therefore, some percentages may not be reproducible when calculated from the rounded concentration values presented here.
[c] Animal room samples
[d] Remixed, not used in study
[e] Results of remix; not used in study

APPENDIX I
WATER AND COMPOUND CONSUMPTION IN THE 2-YEAR DRINKING WATER STUDIES OF SODIUM CHLORATE

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TABLE I1
Water and Compound Consumption by Male Rats in the 2-Year Drinking Water Study of Sodium Chlorate

Week	0 mg/L		125 mg/L			1,000 mg/L			2,000 mg/L		
	Water (g)[a]	Body Weight (g)	Water (g)	Body Weight (g)	Dose (mg/kg)[b]	Water (g)	Body Weight (g)	Dose (mg/kg)	Water (g)	Body Weight (g)	Dose (mg/kg)
4	15.9	187	16.8	187	11.3	16.2	185	87.5	17.1	186	183.5
8	16.4	261	16.3	263	7.8	17.2	266	64.7	17.5	270	129.3
12	16.0	312	15.9	315	6.3	16.5	319	51.7	16.6	322	103.2
16	15.6	348	14.6	351	5.2	15.5	357	43.5	15.3	358	85.6
20	15.3	373	15.5	374	5.2	15.6	379	41.2	15.8	382	83.0
24	14.8	393	14.7	396	4.6	15.3	402	38.1	15.8	403	78.4
28	15.3	420	15.6	423	4.6	16.3	429	37.9	17.4	428	81.3
32	14.1	437	14.2	439	4.1	14.3	445	32.2	14.7	446	66.2
36	13.5	442	13.4	445	3.8	13.2	452	29.3	14.1	451	62.5
40	14.3	459	14.8	461	4.0	14.4	466	30.9	14.6	468	62.4
44	13.2	467	14.4	474	3.8	14.4	477	30.3	14.6	478	61.2
48	13.3	475	13.7	479	3.6	13.8	482	28.7	13.8	486	56.7
52	13.4	487	13.8	491	3.5	13.5	493	27.4	13.8	494	55.7
56	14.2	489	14.7	493	3.7	14.7	497	29.6	15.1	498	60.8
60	15.0	495	15.2	499	3.8	15.4	501	30.7	15.6	501	62.1
64	15.2	499	15.1	503	3.8	15.2	505	30.1	15.7	505	62.1
68	14.8	500	15.0	503	3.7	15.1	504	30.0	15.5	505	61.2
72	14.7	497	15.4	502	3.8	15.8	506	31.3	15.5	504	61.5
76	15.4	508	15.6	506	3.9	16.1	508	31.7	16.1	509	63.3
80	14.6	508	14.4	506	3.6	14.8	507	29.1	15.6	508	61.4
84	15.2	512	15.6	508	3.8	16.1	513	31.4	16.7	510	65.6
88	15.7	509	15.7	501	3.9	15.8	516	30.6	17.2	510	67.5
92	14.8	514	15.8	501	3.9	15.1	514	29.4	16.2	508	63.9
96	14.9	507	14.9	500	3.7	15.2	505	30.1	15.7	498	63.0
100	14.1	497	14.7	486	3.8	15.5	504	30.7	16.4	488	67.2
104	15.0	490	16.5	497	4.2	15.7	500	31.4	17.2	496	69.3
Mean for weeks											
1-13	16.1	254	16.4	255	8.5	16.6	257	68.0	17.1	259	138.7
14-52	14.3	430	14.5	433	4.2	14.6	438	34.0	15.0	439	69.3
53-104	14.9	502	15.3	500	3.8	15.4	506	30.5	16.0	503	63.8

[a] Grams of water consumed per animal per day
[b] Milligrams of sodium chlorate consumed per kilogram body weight per day

TABLE I2
Water and Compound Consumption by Female Rats in the 2-Year Drinking Water Study of Sodium Chlorate

Week	0 mg/L		125 mg/L			1,000 mg/L			2,000 mg/L		
	Water (g)[a]	Body Weight (g)	Water (g)	Body Weight (g)	Dose (mg/kg)[b]	Water (g)	Body Weight (g)	Dose (mg/kg)	Water (g)	Body Weight (g)	Dose (mg/kg)
4	12.7	140	12.9	141	11.5	12.8	140	91.8	12.6	138	182.8
8	12.2	169	12.5	171	9.1	12.6	170	74.2	12.8	169	151.6
12	11.5	186	12.0	187	8.0	11.8	188	62.6	11.6	186	124.8
16	11.1	197	11.3	200	7.1	11.1	199	55.6	10.6	196	107.7
20	10.6	205	11.3	208	6.8	10.9	208	52.6	10.9	204	106.6
24	10.8	213	11.1	215	6.4	10.8	216	50.3	11.3	212	106.3
28	11.5	228	11.7	230	6.3	11.7	232	50.5	11.9	226	105.6
32	10.5	232	11.1	236	5.9	10.9	237	45.9	11.0	231	94.8
36	10.1	235	10.4	239	5.5	9.7	240	40.5	10.1	236	86.0
40	10.7	246	10.9	250	5.4	10.8	248	43.4	10.9	244	89.4
44	10.1	259	10.9	268	5.1	10.5	265	39.8	11.0	259	84.6
48	10.4	260	10.6	266	5.0	10.3	263	39.3	10.4	259	80.4
52	10.5	271	11.3	277	5.1	10.3	276	37.2	10.5	267	79.1
56	11.1	278	11.5	283	5.1	11.9	284	41.8	11.7	276	85.0
60	11.3	285	12.0	287	5.2	12.6	293	43.1	12.8	283	90.3
64	11.9	294	12.3	301	5.1	12.5	304	41.2	12.7	291	87.2
68	11.8	304	12.1	310	4.9	12.0	309	38.9	12.4	298	83.3
72	12.1	308	12.4	313	4.9	12.8	316	40.5	12.7	305	83.2
76	12.8	322	13.2	325	5.1	12.8	328	39.1	13.3	317	83.8
80	12.4	327	11.8	331	4.5	12.0	332	36.1	12.4	323	76.6
84	12.9	331	13.1	337	4.8	13.2	337	39.1	13.7	330	83.0
88	13.4	337	13.6	338	5.0	13.7	341	40.1	13.7	331	83.2
92	13.2	340	12.4	342	4.5	13.4	345	38.9	13.5	339	79.5
96	13.8	340	14.0	343	5.1	13.5	352	38.5	14.2	332	85.5
100	13.5	342	13.4	350	4.8	13.9	351	39.5	14.5	337	86.0
104	13.4	339	13.1	351	4.7	14.7	359	41.0	14.1	341	82.5
Mean for weeks											
1-13	12.1	165	12.5	166	9.5	12.4	166	76.2	12.3	164	153.1
14-52	10.6	235	11.1	239	5.9	10.7	238	45.5	10.9	234	94.1
53-104	12.6	319	12.7	324	4.9	13.0	327	39.8	13.2	316	83.8

[a] Grams of water consumed per animal per day
[b] Milligrams of sodium chlorate consumed per kilogram body weight per day

TABLE I3
Water and Compound Consumption by Male Mice in the 2-Year Drinking Water Study of Sodium Chlorate

Week	0 mg/L		500 mg/L			1,000 mg/L			2,000 mg/L		
	Water (g)[a]	Body Weight (g)	Water (g)	Body Weight (g)	Dose (mg/kg)[b]	Water (g)	Body Weight (g)	Dose (mg/kg)	Water (g)	Body Weight (g)	Dose (mg/kg)
4	3.6	28.1	4.0	27.7	72	3.8	28.2	136	3.9	28.2	274
8	3.3	33.9	3.6	33.3	54	3.3	33.5	100	3.3	33.8	197
12	3.1	38.7	3.3	38.2	43	3.0	38.4	78	3.3	38.6	171
16	3.2	43.6	3.2	43.0	37	3.1	43.5	71	2.9	43.6	134
20	2.8	47.1	2.9	46.5	31	2.9	47.4	61	2.8	47.0	120
24	3.0	49.5	3.0	48.8	31	3.0	49.1	61	3.1	49.6	125
28	3.4	50.5	3.3	49.8	33	3.3	49.9	67	3.4	50.2	135
32	3.3	50.7	3.3	49.7	33	3.3	49.8	67	3.4	50.4	137
36	3.5	51.3	3.6	50.7	35	3.6	50.6	72	3.6	51.2	141
40	3.8	51.8	3.7	51.1	37	4.0	51.4	79	3.8	51.8	145
44	3.7	52.2	3.7	50.9	36	3.6	51.3	71	3.7	52.1	140
48	3.9	53.0	3.7	51.8	36	3.8	51.7	73	3.8	52.8	142
52	3.8	52.6	3.6	51.8	34	3.7	52.1	71	3.7	52.9	140
56	4.1	52.7	3.9	52.1	38	4.0	52.2	76	4.0	52.5	151
60	4.1	53.0	4.1	52.2	39	4.3	52.6	81	4.0	53.0	152
64	4.2	53.4	4.2	53.2	39	4.5	52.7	85	4.2	53.4	157
68	4.2	53.2	4.3	53.5	40	4.3	53.2	81	4.2	54.5	153
72	3.8	54.1	4.0	53.4	37	4.0	52.8	75	3.9	54.2	144
76	3.9	53.6	4.0	53.0	38	4.1	52.2	79	4.0	54.0	149
80	4.2	52.5	4.0	52.4	39	4.4	51.8	84	4.1	52.9	155
84	4.1	53.0	4.2	52.4	40	4.1	53.0	77	4.1	51.7	157
88	4.1	51.7	3.9	51.4	38	3.9	52.3	74	3.9	50.6	156
92	4.9	50.9	4.3	50.6	43	4.3	51.4	83	4.2	49.6	169
96	4.8	50.7	4.3	49.7	43	4.0	50.3	80	4.1	49.6	164
100	4.3	48.6	4.0	47.1	43	3.8	48.1	79	3.9	48.1	161
104	4.2	46.6	4.2	45.1	46	4.1	46.5	89	4.0	48.5	166
Mean for weeks											
1-13	3.4	33.6	3.6	33.1	57	3.4	33.3	105	3.5	33.5	214
14-52	3.5	50.2	3.4	49.4	34	3.4	49.7	69	3.4	50.2	136
53-104	4.2	51.8	4.1	51.2	40	4.1	51.5	80	4.0	51.7	156

[a] Grams of water consumed per animal per day
[b] Milligrams of sodium chlorate consumed per kilogram body weight per day

TABLE I4
Water and Compound Consumption by Female Mice in the 2-Year Drinking Water Study of Sodium Chlorate

Week	0 mg/L		500 mg/L			1,000 mg/L			2,000 mg/L		
	Water (g)[a]	Body Weight (g)	Water (g)	Body Weight (g)	Dose (mg/kg)[b]	Water (g)	Body Weight (g)	Dose (mg/kg)	Water (g)	Body Weight (g)	Dose (mg/kg)
4	3.5	22.3	3.4	22.2	78	3.4	22.4	151	3.9	22.0	356
8	2.9	27.3	3.1	26.6	58	3.2	27.1	117	3.5	26.3	266
12	3.1	32.0	3.2	31.4	51	3.1	31.6	98	3.5	30.2	234
16	3.0	36.5	3.1	35.9	43	3.6	36.0	100	3.1	35.0	175
20	2.4	42.3	2.4	41.9	29	2.4	42.3	57	2.5	41.2	123
24	2.5	46.9	2.3	46.5	25	2.3	46.8	50	2.4	45.1	106
28	2.4	49.9	2.7	49.7	27	2.3	50.3	46	2.9	48.6	118
32	2.5	52.5	2.4	51.9	23	2.4	52.7	45	2.4	51.4	93
36	2.3	54.4	2.5	54.2	23	2.3	54.3	43	2.5	53.0	94
40	2.3	57.8	2.3	58.0	20	2.2	57.4	39	2.4	56.1	87
44	2.5	58.4	2.7	58.5	23	2.4	57.2	42	2.8	56.6	99
48	2.3	60.2	2.4	59.6	20	2.4	58.6	41	2.7	59.0	90
52	2.4	61.0	2.4	60.8	19	2.4	59.9	40	2.5	60.5	82
56	2.5	61.2	2.5	61.0	20	2.5	60.1	42	2.6	61.4	83
60	2.6	62.2	2.6	61.1	22	2.8	60.9	46	2.8	62.1	89
64	2.8	62.8	2.7	62.4	22	2.7	62.7	43	3.2	62.0	103
68	2.6	63.4	2.7	62.3	21	2.8	62.9	44	2.5	63.7	80
72	2.4	64.2	2.8	61.8	23	2.5	63.1	40	2.7	64.5	84
76	2.7	65.0	2.8	63.9	22	2.9	64.3	44	2.8	64.6	86
80	2.9	66.5	2.8	64.7	22	3.0	65.0	46	2.9	65.2	89
84	2.8	65.7	2.8	64.9	22	3.1	64.3	49	2.8	65.1	87
88	2.6	65.9	3.0	62.9	24	3.3	61.7	54	2.7	63.7	86
92	3.1	64.9	3.8	60.2	32	3.7	62.3	60	3.0	61.9	96
96	3.2	64.3	3.5	57.8	30	4.0	60.1	67	3.2	58.5	110
100	3.4	63.3	4.2	56.3	37	4.5	57.3	79	3.4	58.6	116
104	3.6	61.0	3.7	53.7	35	5.1	55.0	93	4.1	54.6	150
Mean for weeks											
1-13	3.2	27.2	3.2	26.7	62	3.2	27.0	122	3.6	26.2	285
14-52	2.5	52.0	2.5	51.7	25	2.5	51.6	50	2.6	50.7	107
53-104	2.9	63.9	3.1	61.0	25	3.3	61.5	54	3.0	62.0	97

[a] Grams of water consumed per animal per day
[b] Milligrams of sodium consumed per kilogram body weight per day

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

TABLE J1	Ingredients of NTP-2000 Rat and Mouse Ration	250
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TABLE J1
Ingredients of NTP-2000 Rat and Mouse Ration

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

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

TABLE J2
Vitamins and Minerals in NTP-2000 Rat and Mouse Ration[a]

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

[a] Per kg of finished product

TABLE J3
Nutrient Composition of NTP-2000 Rat and Mouse Ration

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	13.5 ± 0.44	12.7 – 14.5	25
Crude fat (% by weight)	8.1 ± 0.26	7.6 – 8.6	25
Crude fiber (% by weight)	9.2 ± 0.66	7.9 – 10.5	25
Ash (% by weight)	4.9 ± 0.19	4.7 – 5.4	25
Amino Acids (% of total diet)			
Arginine	0.748 ± 0.053	0.670 – 0.850	12
Cystine	0.223 ± 0.027	0.150 – 0.250	12
Glycine	0.702 ± 0.043	0.620 – 0.750	12
Histidine	0.343 ± 0.023	0.310 – 0.390	12
Isoleucine	0.534 ± 0.041	0.430 – 0.590	12
Leucine	1.078 ± 0.059	0.960 – 1.140	12
Lysine	0.729 ± 0.065	0.620 – 0.830	12
Methionine	0.396 ± 0.053	0.260 – 0.460	12
Phenylalanine	0.611 ± 0.038	0.540 – 0.660	12
Threonine	0.492 ± 0.045	0.430 – 0.590	12
Tryptophan	0.129 ± 0.016	0.110 – 0.160	12
Tyrosine	0.378 ± 0.054	0.280 – 0.460	12
Valine	0.658 ± 0.049	0.550 – 0.710	12
Essential Fatty Acids (% of total diet)			
Linoleic	3.89 ± 0.278	3.49 – 4.54	12
Linolenic	0.30 ± 0.038	0.21 – 0.35	12
Vitamins			
Vitamin A (IU/kg)	5,694 ± 1,010	3,700 – 7,790	25
Vitamin D (IU/kg)	1,000[a]		
α-Tocopherol (ppm)	84.3 ± 17.06	52.0 – 110.0	12
Thiamine (ppm)[b]	7.9 ± 0.83	6.3 – 9.3	25
Riboflavin (ppm)	6.4 ± 2.11	4.20 – 11.20	12
Niacin (ppm)	78.6 ± 10.86	66.4 – 98.2	12
Pantothenic acid (ppm)	23.1 ± 3.61	17.4 – 29.1	12
Pyridoxine (ppm)[b]	8.88 ± 2.05	6.4 – 12.4	12
Folic acid (ppm)	1.84 ± 0.56	1.26 – 3.27	12
Biotin (ppm)	0.337 ± 0.13	0.225 – 0.704	12
Vitamin B_{12} (ppb)	64.8 ± 50.9	18.3 – 174.0	12
Choline (ppm)[b]	3,094 ± 292	2,700 – 3,790	12
Minerals			
Calcium (%)	0.998 ± 0.045	0.903 – 1.090	25
Phosphorus (%)	0.564 ± 0.028	0.505 – 0.618	25
Potassium (%)	0.668 ± 0.023	0.627 – 0.694	12
Chloride (%)	0.368 ± 0.033	0.300 – 0.423	12
Sodium (%)	0.189 ± 0.016	0.160 – 0.212	12
Magnesium (%)	0.200 ± 0.009	0.185 – 0.217	12
Sulfur (%)	0.176 ± 0.026	0.116 – 0.209	12
Iron (ppm)	177 ± 46.2	135 – 311	12
Manganese (ppm)	53.4 ± 6.42	42.1 – 63.1	12
Zinc (ppm)	52.5 ± 6.95	43.3 – 66.0	12
Copper (ppm)	6.64 ± 1.283	5.08 – 9.92	12
Iodine (ppm)	0.535 ± 0.242	0.233 – 0.972	12
Chromium (ppm)	0.545 ± 0.125	0.330 – 0.751	12
Cobalt (ppm)	0.23 ± 0.041	0.20 – 0.30	12

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

TABLE J4
Contaminant Levels in NTP-2000 Rat and Mouse Ration[a]

Nutrient	Mean ± Standard Deviation[b]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.16 ± 0.070	0.10 – 0.33	25
Cadmium (ppm)	0.04 ± 0.006	0.04 – 0.07	25
Lead (ppm)	0.11 ± 0.104	0.05 – 0.54	25
Mercury (ppm)	<0.02		25
Selenium (ppm)	0.19 ± 0.033	0.14 – 0.28	25
Aflatoxins (ppb)	<5.00		25
Nitrate nitrogen (ppm)[c]	10.8 ± 2.98	9.04 – 21.1	25
Nitrite nitrogen (ppm)[c]	<0.61		25
BHA (ppm)[d]	<1.0		25
BHT (ppm)[d]	<1.0		25
Aerobic plate count (CFU/g)	10 ± 2	10 – 20	25
Coliform (MPN/g)	0.4 ± 1.2	0.0 – 3.6	25
Escherichia coli (MPN/g)	<10		25
Salmonella (MPN/g)	Negative		25
Total nitrosoamines (ppb)[e]	4.6 ± 1.64	2.1 – 8.8	25
N-Nitrosodimethylamine (ppb)[e]	1.8 ± 0.86	1.0 – 5.1	25
N-Nitrosopyrrolidine (ppb)[e]	2.8 ± 1.10	1.0 – 5.6	25
Pesticides (ppm)			
α-BHC	<0.01		25
β-BHC	<0.02		25
γ-BHC	<0.01		25
δ-BHC	<0.01		25
Heptachlor	<0.01		25
Aldrin	<0.01		25
Heptachlor epoxide	<0.01		25
DDE	<0.01		25
DDD	<0.01		25
DDT	<0.01		25
HCB	<0.01		25
Mirex	<0.01		25
Methoxychlor	<0.05		25
Dieldrin	<0.01		25
Endrin	<0.01		25
Telodrin	<0.01		25
Chlordane	<0.05		25
Toxaphene	<0.10		25
Estimated PCBs	<0.20		25
Ronnel	<0.01		25
Ethion	<0.02		25
Trithion	<0.05		25
Diazinon	<0.10		25
Methyl chlorpyrifos	0.145 ± 0.124	0.023 – 0.499	25
Methyl parathion	<0.02		25
Ethyl parathion	<0.02		25
Malathion	0.217 ± 0.188	0.020 – 0.826	25
Endosulfan I	<0.01		25
Endosulfan II	<0.01		25
Endosulfan sulfate	<0.03		25

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

APPENDIX K
SENTINEL ANIMAL PROGRAM

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SENTINEL ANIMAL PROGRAM

METHODS

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

During the 2-year studies, serum samples were collected from randomly selected sentinel rats and mice at 6, 12, and 18 months and 2,000 mg/L rats and mice at study termination. Blood from each animal was collected and allowed to clot, and the serum was separated. Samples were processed appropriately and sent to BioReliance Corporation, Rockville, MD, for determination of antibody titers. The laboratory serology methods and viral agents for which testing was performed are tabulated below; the times at which blood was collected during the studies are also listed.

Method and Test	Time of Analysis
RATS	
ELISA	
Mycoplasma arthritidis	6 months, study termination
Mycoplasma pulmonis	6 months, study termination
PVM (pneumonia virus of mice)	6, 12, and 18 months, study termination
RCV/SDA (rat coronavirus/sialodacryoadentis virus)	6, 12, and 18 months, study termination
Sendai	6, 12, and 18 months, study termination
Immunofluorescence Assay	
Parvovirus	6, 12, and 18 months, study termination

Method and Test	Time of Analysis
MICE	
ELISA	
Ectromelia virus	6, 12, and 18 months, study termination
EDIM (epizootic diarrhea of infant mice)	6, 12, and 18 months, study termination
GDVII (mouse encephalomyelitis virus)	6, 12, and 18 months, study termination
LCM (lymphocytic choriomeningitis virus)	6, 12, and 18 months, study termination
Mouse adenoma virus-FL	6, 12, and 18 months, study termination
MHV (mouse hepatitis virus)	6, 12, and 18 months, study termination
M. arthritidis	6 months, study termination
M. pulmonis	6 months, study termination
PVM	6, 12, and 18 months, study termination
Reovirus 3	6, 12, and 18 months, study termination
Sendai	6, 12, and 18 months, study termination
Immunofluorescence Assay	
Ectromelia virus	18 months
EDIM	18 months
GDVII	18 months
LCM	18 months
Mouse adenoma virus-FL	12 and 18 months
MCMV (mouse cytomegalovirus)	6 months, study termination
MHV	18 months
M. arthritidis	6 months, study termination
Parvovirus	6, 12, and 18 months, study termination
PVM	18 months
Reovirus 3	18 months

RESULTS

For the 2-year studies in rats and mice, all serology tests were negative.