NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 432

TOXICOLOGY AND CARCINOGENESIS STUDIES OF BARIUM CHLORIDE DIHYDRATE

(CAS NO. 10326-27-9)

IN F344/N RATS AND B6C3F$_1$ MICE

(DRINKING WATER STUDIES)

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

FOREWORD

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

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

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

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology and carcinogenesis studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection *per se* is not an indicator of a chemical's carcinogenic potential.

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NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

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NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
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ABSTRACT

$BaCl_2 \cdot 2H_2O$

BARIUM CHLORIDE DIHYDRATE

CAS No. 10326-27-9

Chemical Formula: $BaCl_2 \cdot 2H_2O$ Molecular Weight: 244.28

Barium chloride dihydrate, a white crystalline granule or powder, is used in pigments, aluminum refining, leather tanning and coloring, the manufacture of magnesium metal, ceramics, glass, and paper products, as a pesticide, and in medicine as a cardiac stimulant. Toxicology and carcinogenicity studies were conducted by administering barium chloride dihydrate (99% pure) in drinking water to F344/N rats and B6C3F$_1$ mice for 15 days, 13 weeks, and 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, and mouse lymphoma cells.

15-DAY STUDY IN RATS

Groups of five males and five females received barium chloride dihydrate in the drinking water at concentrations of 0, 125, 250, 500, 1,000, or 2,000 ppm for 15 days, corresponding to average daily doses of 10, 15, 35, 60, or 110 mg barium/kg body weight to males and females. No chemical-related deaths, differences in final mean body weights, or clinical findings of toxicity were observed. Water consumption by male and female rats exposed to 2,000 ppm was slightly less (≤16%) than controls during week 2. There were no significant differences in absolute or relative organ weights between exposed and control rats. No biologically significant differences in hematology, clinical chemistry, or neurobehavioral parameters occurred in rats.

15-DAY STUDY IN MICE

Groups of five males and five females received barium chloride dihydrate in the drinking water at concentrations of 0, 40, 80, 173, 346, or 692 ppm for 15 days, corresponding to average daily doses of 5, 10, 20, 40, or 70 mg barium/kg body weight to males and 5, 10, 15, 40, or 85 mg barium/kg body weight to females. No chemical-related deaths, differences in mean body weights or in water consumption, or clinical findings of toxicity were observed in mice. The relative liver weight of males receiving 692 ppm was significantly greater than that of the controls. The absolute and relative liver weights of females that received 692 ppm were significantly greater than those of the controls. No histopathologic evidence of toxicity was observed in mice.

13-WEEK STUDY IN RATS

Groups of 10 males and 10 females received barium chloride dihydrate in the drinking water at concentrations of 0, 125, 500, 1,000, 2,000, or 4,000 ppm for 13 weeks, corresponding to average daily doses of 10, 30, 65, 110, or 200 mg barium/kg body weight to males and 10, 35, 65, 115, or 180 mg barium/kg body weight to females. Three males and one female in the 4,000 ppm groups died during the last week of the study. The final mean body weights of male and female rats receiving 4,000 ppm were significantly lower (13% and 8%) than those of the controls.

Water consumption by male and female rats in the 4,000 ppm groups was approximately 30% lower than that by the controls. No clearly chemical-related clinical findings of toxicity or neurobehavioral or cardiovascular effects were noted. Serum phosphorus levels in 2,000 and 4,000 ppm male and female rats were significantly higher than those in controls, but there were no biologically significant differences in hematology parameters or in serum sodium, potassium, or calcium levels. Renal tubule dilatation in the outer stripe of the outer medulla and cortex occurred in male and female rats receiving 4,000 ppm.

13-Week Study in Mice

Groups of 10 males and 10 females received barium chloride dihydrate in the drinking water at concentrations of 0, 125, 500, 1,000, 2,000, or 4,000 ppm for 13 weeks, corresponding to average daily doses of 15, 55, 100, 205, or 450 mg barium/kg body weight to males and 15, 60, 110, 200, or 495 mg barium/kg body weight to females. Six males and seven females that received 4,000 ppm and one male that received 125 ppm died during the study. Final mean body weights of male and female mice receiving 4,000 ppm were significantly lower (>30%) than those of controls. Water consumption by male mice in the 4,000 ppm group was 18% lower than that by the controls; water consumption by other exposed groups of male and female mice was similar to that by the controls. Clinical findings of toxicity were limited to debilitation in the surviving male and female mice receiving 4,000 ppm. The absolute and/or relative liver weights of mice receiving 1,000, 2,000, and 4,000 ppm were significantly lower than those of the controls. Multifocal to diffuse nephropathy characterized by tubule dilatation, regeneration, and atrophy occurred in 4,000 ppm male and female mice.

2-Year Study in Rats

Groups of 60 males and 60 females received barium chloride dihydrate in the drinking water at concentrations of 0, 500, 1,250, or 2,500 ppm for 104 (males) or 105 weeks (females), corresponding to average daily doses of 15, 30, or 60 mg barium/kg body weight for males and 15, 45, or 75 mg barium/kg body weight for females. The high dose of 2,500 ppm was selected based on decreased final mean body weights, mortality, decreased water consumption, and chemical-related kidney lesions observed in the 4,000 ppm groups in the 13-week study.

Survival, Body Weights, Water Consumption, and Clinical Findings

Two-year survival of exposed male and female rats was similar to that of the controls. The final mean body weights of male and female rats that received 2,500 ppm were (5% and 11%) lower than those of controls. Beginning as early as week 5, water consumption by male and female rats receiving 2,500 ppm was substantially lower than that by controls (male: 11% to 30%; female: 19% to 33%). There were no chemical-related clinical findings.

Hematology and Clinical Chemistry

There were no chemical-related differences in hematology or clinical chemistry parameters in male or female rats.

Special Studies

At the 15-month interim evaluation, the plasma barium concentrations (mg/mL) were significantly increased in males receiving 1,250 and 2,500 ppm and in all exposed groups of females (male: 0 ppm, 0.98; 500 ppm, 1.00; 1,250 ppm, 1.23; 2,500 ppm, 1.68; female: 0 ppm, 0.74; 500 ppm, 0.99; 1,250 ppm, 0.97; 2,500 ppm, 1.43). Barium levels in bone in rats from the 2,500 ppm groups were about 400 times greater than those in the controls.

Pathology Findings

At the end of 2 years, there were no increased incidences of neoplasms or nonneoplastic lesions that could be attributed to barium chloride dihydrate. However, there were dose-related decreased incidences of adrenal medulla pheochromocytomas and mononuclear cell leukemia in male rats.

2-Year Study in Mice

Groups of 60 males and 60 females received barium chloride dihydrate in the drinking water at concentrations of 0, 500, 1,250, or 2,500 ppm for 103 (males) or 104 weeks (females), corresponding to average daily doses of 30, 75, or 160 mg barium/kg body weight for males and 40, 90, or 200 mg barium/kg body weight for females. The high dose of 2,500 ppm was selected based on decreased final mean body weights, mortality, decreased water consumption, and chemical-related kidney lesions observed in the 4,000 ppm groups in the 13-week study.

Survival, Body Weights, Water Consumption, and Clinical Findings

Two-year survival of male and female mice receiving 2,500 ppm was significantly lower than that of the controls due to renal toxicity. Final mean body weights of 2,500 ppm males and females were 9% and 12% lower than those of controls. Water consumption by male and female mice receiving barium chloride was similar to that by the controls. There were no chemical-related clinical findings.

Hematology and Clinical Chemistry

There were no differences in hematology or clinical chemistry parameters measured at the 15-month interim evaluation.

Special Studies

At the 15-month interim evaluation, plasma barium concentrations (mg/mL) were significantly increased in all exposed groups of mice (male: 0 ppm, 0.62; 500 ppm, 0.77; 1,250 ppm, 0.89; 2,500 ppm, 1.49; female: 0 ppm, 0.52; 500 ppm, 0.74; 1,250 ppm, 1.01; 2,500 ppm, 1.35).

Pathology Findings

At the end of the 2-year study, there were increased incidences of nephropathy in male and female mice (male: 1/50, 0/50, 2/48, 19/50; female: 0/50, 2/53, 1/50, 37/54).

There were no chemical-related increased incidences of neoplasms in male or female mice. The incidence of hepatocellular adenoma was significantly decreased in male mice receiving 2,500 ppm.

GENETIC TOXICOLOGY

Barium chloride dihydrate was not mutagenic in *Salmonella typhimurium* strains TA97, TA98, TA100, TA1535, or TA1537, with or without exogenous metabolic activation (S9). It was mutagenic in L5178Y mouse lymphoma cells in the presence of S9, but it did not induce sister chromatid exchanges or chromosomal aberrations in cultured Chinese hamster ovary cells, with or without S9.

CONCLUSIONS

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity** of barium chloride dihydrate in male or female F344/N rats that received 500, 1,250, or 2,500 ppm. There was *no evidence of carcinogenic activity* of barium chloride dihydrate in male or female B6C3F_1 mice that received 500, 1,250, or 2,500 ppm.

There were chemical-related increased incidences of nephropathy in male and female mice.

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

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of Barium Chloride Dihydrate

Variable	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Doses	0, 500, 1,250, or 2,500 ppm in water (approximately 15, 30, or 60 mg barium/kg body weight)	0, 500, 1,250, or 2,500 ppm in water (approximately 15, 45, or 75 mg barium/kg body weight)	0, 500, 1,250, or 2,500 ppm in water (approximately 30, 75, or 160 mg barium/kg body weight)	0, 500, 1,250, or 2,500 ppm in water (approximately 40, 90, or 200 mg barium/kg body weight)
Body weights	High-dose group lower than controls	High-dose group lower than controls	High-dose group lower than controls	High-dose group lower than controls
2-Year survival rates	22/50, 31/50, 29/50, 33/50	31/50, 36/50, 39/50, 32/50	45/50, 43/50, 39/50, 32/50	38/50, 37/50, 36/50, 13/50
Nonneoplastic effects	None	None	Kidney: nephropathy (1/50, 0/50, 2/48, 19/50)	Kidney: nephropathy (0/50, 2/53, 1/50, 37/54)
Decreased incidences	Hematopoietic system: mononuclear cell leukemia (35/50, 25/50, 26/50, 15/50); Adrenal gland: benign or malignant pheochromocytomas (13/49, 11/50, 12/49, 6/50)	None	Liver: hepatocellular adenoma (24/51, 20/50, 15/48, 8/50)	None
Level of evidence of carcinogenic activity	No evidence	No evidence	No evidence	No evidence
Genetic toxicology				
Salmonella typhimurium gene mutation	Negative with and without S9 in strains TA97, TA98, TA100, TA1535, and TA1537			
L5178Y mouse lymphoma mutation	Positive with S9; negative without S9			
Sister chromatid exchanges				
Chinese hamster ovary cells *in vitro*:	Negative with and without S9			
Chromosomal aberrations				
Chinese hamster ovary cells *in vitro*:	Negative with and without S9			

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

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

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

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

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

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

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS
TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the draft NTP Technical Report on barium chloride dihydrate on June 22, 1993, 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 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 June 22, 1993, the draft Technical Report on the toxicology and carcinogenesis studies of barium chloride dihydrate received public review by the National Toxicology Program 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. K.M. Abdo, NIEHS, introduced the toxicology and carcinogenesis studies of barium chloride dihydrate by discussing the uses of the chemical, describing the experimental design, reporting on survival and body weight effects, and commenting on chemical-related nonneoplastic lesions in male and female mice. The proposed conclusions were *no evidence of carcinogenic activity** of barium chloride dihydrate in male or female F344/N rats or in male or female B6C3F$_1$ mice.

Dr. Davis, a principal reviewer, agreed with the proposed conclusions. He suggested that plasma concentrations are a better measure of exposure than dose per unit surface area or body weight, noting that compounds excreted by the kidney and having the ability to cause nephropathy may have their plasma concentrations significantly raised, thereby skewing the relationship between administered dose and actual exposure. Dr. Abdo agreed that measurements of area under the plasma concentration curve would have been the best way to determine actual exposure. Dr. Davis thought that the decrease in water consumption by male rats was sufficient justification for the dose being high enough. Dr. Abdo said he would add a sentence to the discussion about the decrease in water consumption being a consideration in dose setting for the 2-year study in rats.

Dr. Bailey, the second principal reviewer, agreed with the proposed conclusions. He asked why plasma barium levels were measured in the 2-year studies while serum levels were determined in the subchronic studies. Dr. Abdo said that the use of plasma was for convenience because the volume available for analysis was greater.

Mr. Beliczky, the third principal reviewer, also agreed with the proposed conclusions. He commented that for future industrial chemical studies, when available, Material Safety Data Sheets should be provided to reviewers. As another example of useful information, he provided a full review of barium and its soluble compounds prepared by the American Council of Governmental Industrial Hygienists. Dr. D.B. Walters, NIEHS, reported that the NTP Laboratory Health and Safety Office requires contractors to request and obtain Material Safety Data Sheets whenever they order a chemical, and additionally, they are required to search the hazardous substances data base or equivalent for information about the material.

Dr. Brown inquired about the rationale for the study. Dr. Abdo responded that the International Agency for Research on Cancer had found there was sufficient evidence that barium chromate was a human carcinogen. Because there was sufficient evidence that all the hexavalent chromium compounds were carcinogenic, it was hoped the current study would shed light on the potential carcinogenicity of barium itself. There was some discussion as to the chemical forms available in the body, whether elemental barium or the chloride dihydrate.

Dr. Davis moved that the Technical Report on barium chloride dihydrate be accepted with the revisions discussed and with the conclusions as written for male and female rats and mice, *no evidence of carcinogenic activity*. Dr. Bailey seconded the motion, which was accepted unanimously with ten votes.

INTRODUCTION

$BaCl_2 \cdot 2H_2O$

BARIUM CHLORIDE DIHYDRATE

CAS No. 10326-27-9

Chemical Formula: $BaCl_2 \cdot 2H_2O$ Molecular Weight: 244.28

CHEMICAL AND PHYSICAL PROPERTIES

Barium chloride does not occur naturally, but barium is the 16th most abundant element in the earth's crust (Mason, 1958). Barium is an alkaline earth metal having an atomic mass of 137.34 and an atomic number of 56. It is found in the minerals barite (barium sulfate) and witherite (barium carbonate) (Browning, 1969). Naturally occurring barium is a mixture of seven stable isotopes, of which ^{138}Ba is the most abundant (Weast, 1984). Barium chloride dihydrate is a white crystalline granule or powder with a bitter salty taste. It has a density of 3.86 and a melting point of 963° C. It is very soluble in water, soluble in methanol, but almost insoluble in ethanol, acetone, and ethyl acetate (*Merck Index*, 1983).

PRODUCTION, USE, AND HUMAN EXPOSURE

Barium chloride dihydrate is prepared by reacting aqueous barium sulfide with hydrochloric acid. The reaction mixture is purified and then evaporated to yield crystalline barium chloride dihydrate (EHC, 1990).

The United States' consumption of barite in 1989 was 1,407 short tons (1.28 million kg). About 5% of the barite is used in the production of major barium chemicals such as barium carbonate, barium chloride, and barium hydroxide (EHC, 1990). The majority of barite is used as a weighing agent for oil- and gas-well drilling muds to counteract high pressures within the substrata. Ninety percent of the barite produced in 1976 was consumed by the oil- and gas-well drilling industries (U.S. Bureau of Mines, 1976).

Barium chloride is used in the manufacture of pigments such as barium lithol red and color lakes such as barium salt of red lake C. Barium chloride is also used in the manufacture of glass and ceramics. It serves as a mordant for acid dyes, as a flux in the manufacture of magnesium metal, as a pesticide, and as a lubricating oil additive. In addition, barium chloride is used in aluminum refining, leather tanning and finishing, photographic paper, and boiler compounds for softening water. It is also used as a cardiac stimulant and as a radioactive compound in experimental bone scanning. Barium chloride was formerly employed as a purgative in horses and a ruminatoric in cattle (*Merck Index*, 1983). Anhydrous barium chloride serves as an ingredient in case-hardening and heat-treating baths used in the metal industry (EHC, 1990).

Although no specific information regarding exposure to barium chloride was found, barium is present in and around all living things, with concentrations in the earth's crust of 400 to 500 mg/kg (Davis, 1972). Therefore, human exposure to this element is quite extensive. Ocean and sea water concentrations for barium range from 5.2 to 25.2 mg/L for the eastern Pacific Ocean, from 10.6 to 12.7 mg/L for the Mediterranean Sea (Wolgemuth and Brocker, 1970), from 0.8 to 37.0 mg/L for the equatorial region of the

Atlantic Ocean, and from 0.04 to 22.8 mg/L for the North Atlantic Ocean (Andersen and Hume, 1968).

Fresh water barium concentrations in the United States range from 9 to 150 mg/L in river water (Durum, 1960) and from 10 to 12,000 mg/L in surface water (Bradford, 1971). In some drinking water supplies, barium levels may exceed 20 ppm (McCauley and Washington, 1983). In a study of the water supplies of the 100 largest cities in the U.S., a median value of 43 mg/L was reported; 94% of the values reported were less than 100 mg/L (Durfor and Becker, 1964).

Barium is present in all food products. Tea and coffee have the highest concentrations (2.7 and 1.2 mg/100 g) among plant products. Bran flakes, which have the highest concentration for cereal products, contain 0.39 mg/100 g. The highest concentration of barium in the fruit group is found in unpeeled apples (0.075 mg/100 g). Beets have the highest concentration among vegetables (0.26 mg/100 g) and pecans have the highest concentration within the nut group. Eggs contain 0.76 mg/100 g while meats contain 0.04 mg/100 mg (IPCS, 1990).

Barium concentrations in air samples from 18 cities and four suburban areas in the U.S. ranged from less than 0.005 to 1.5 mg/m^3 (Tabor and Warren, 1958). Dustfall and house dust, measured using standard methods, in three communities in New York, NY, were found to contain an average of 137 mg barium/g and 20 mg barium/g, respectively (USEPA, 1974; Creason *et al.*, 1975).

Durfor and Becker (1964) have estimated that in the U.S., drinking water contains an average of less than 100 mg/L barium and that the average intake of barium from drinking water is less than 200 mg/day. Dietary intake of barium from foods consumed in hospitals and from self-selected diets by adults was estimated to range from 300 to 1,770 mg/day (Tipton *et al.*, 1969; Gormican, 1970). Barium intake via the lungs was estimated at 0.04 mg/day for newborn babies, 1.6 mg/day for adults engaging in light activities, and 3.1 mg/day for adults engaging in strenuous activities (ICRP, 1975). It is clear from these data that the most important route of human exposure is by ingestion of barium through drinking water or food.

REGULATORY STATUS

The current Occupational Safety and Health Administration permissible exposure limit (PEL) is 0.5 mg of soluble barium compounds per cubic meter of air (mg/m^3) averaged over an 8-hour workday (RTECS, 1985). The threshold limit value/time-weighted average (TLV-TWA) for soluble barium compounds adopted by the American Conference of Governmental Industrial Hygienists is 0.5 mg Ba/m^3 (ACGIH, 1990). The U.S. Public Health Service (USPHS, 1962) and the U.S. Environmental Protection Agency (USEPA, 1975) have set the safe limit of barium in drinking water at 1 ppm.

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Experimental Animals

Weanling male rats receiving a single oral dose of $^{133}BaCl_2$ (1, 5, 25, or 125 mg/kg) rapidly absorbed ^{133}Ba from the gastrointestinal (GI) tract with peak concentrations in the blood and soft tissues occurring 30 minutes after administration. The absorption was influenced by the presence of food in the intestine, the sulfate content in the food, and the age of the animal. Total absorption of ^{133}Ba increased as the dose level increased while relative absorption decreased with increasing dose. Taylor *et al.* (1962) investigated the influence of food deprivation (18 hours) and the age of animals on absorption of barium in the form of $^{140}BaCl_2$. In this study, brown hooded female rats (14 days to 70 weeks old) received a single intragastric dose of 10 mCi $^{140}BaCl_2$ (in 0.2 to 0.5 mL of 0.01 N HCl). Absorption was calculated as the percentage of dose remaining in the carcass and in the urine 7 hours after dosing, less that in the GI tract. Barium absorption was less in older rats. Rats 14 to 18 days old absorbed 84.6% of the dose while 60- to 70-week-old rats absorbed only 7.5% of the same dose.

Groups of brown hooded female rats 6 to 8 weeks or 13 to 15 months of age received injections into a lateral tail vein of 20 to 80 mCi of $^{140}BaCl_2$ (in 0.2 to 0.5 mL of 0.01 N HCl) and were evaluated 8 minutes to 80 days after dosing. The highest concentration of ^{140}Ba was found in bone; the radioactivity reached a peak in approximately 3.5 hours. The uptake of radioactivity into bone decreased with age. The distal ends of bone had the highest concentration of labeled

barium suggesting that the highest uptake occurs in growing areas of the bone. Barium concentrations in the muscle, liver, lungs, and the submaxillary gland were 2 to 15 times lower than that observed in bone. The highest concentrations of ^{140}Ba in soft tissues were noted in the lung and submaxillary gland. The peak concentration in tissues other than bone was observed 10 minutes after ^{140}Ba injection (Bligh and Taylor, 1963). McCauley and Washington (1983) determined the concentration of labeled barium in six tissues excised from male Sprague-Dawley rats (weight: 250 to 300 g) 24 hours after intragastric administration of 5 mg $^{131}BaCl_2$. The highest concentration was found in the heart followed by the eye, skeletal muscle, kidney, liver, and blood. Labeled barium was found in the submaxillary gland, adrenal gland, kidney, gastric mucosa, and blood vessels of weanling male rats receiving a single oral dose of 1 to 125 mg $^{133}BaCl_2$/kg (Clary and Tardiff, 1974). Peak concentrations were observed 30 minutes after administration; deposition of label in bone was observed 2 hours after administration. In a drinking water study, male and female Charles River rats received 10, 50, or 250 mg $BaCl_2$/L for 4, 8, or 13 weeks. The concentration of barium in the liver, skeletal muscle, heart, and bone was dependent on dose but not on sex or duration of exposure (Tardiff *et al.*, 1980). The highest concentration was found in bone.

Blood barium levels were determined in male Sprague-Dawley rats (weight: 250 to 300 g) that were fed or fasted for 24 hours prior to the administration of a single gavage dose of 5 mg $^{131}BaCl$ in 0.5 mL water/100 g body weight. Rats were evaluated 2 to 480 minutes after dosing. The highest blood barium levels were observed in fasted rats (about 3-fold higher than in nonfasted rats) with levels reaching a peak 15 minutes after dosing. The peak in nonfasted rats was reached 60 minutes after dosing (McCauley and Washington, 1983). In a similar experiment, the bioavailability of barium in the form of sulfate, carbonate, and chloride salts was compared. Blood levels of ^{131}Ba from barium sulfate or carbonate salt were 85% and 45% of the levels from the chloride salt.

In rats receiving a single intraperitoneal dose of 15 mg $^{133}BaCl_2$/kg, ^{133}Ba was excreted in both the urine and the feces, with the majority of label appearing in the feces (Clary and Tardiff, 1974). The biological half-life for barium in bone was estimated to be 100 days for mice (Dencker *et al.*, 1976) and 90 to 120 days for rats (Clary and Tardiff, 1974). Over 65% of an initial injection of barium chloride was eliminated by rats within 16 days (Domanski *et al.*, 1964).

Humans

The barium content of a 70-kg man was estimated at 1.54 g (Tipton *et al.*, 1963). An estimated 91% of the element is present in bone and the remainder in soft tissues (Schroeder, 1970). Average barium concentrations (mg/kg wet weight) were 0.15 in the large intestine, muscle, and lung; 0.1 in the liver and kidney (Tipton and Cook, 1963; Tipton *et al.*, 1965; Schroeder, 1970); 4.2 in the enamel of men under 20 years; and 22 in the enamel of men over 20 years of age (Losee *et al.*, 1974). Barium concentrations in human hair ranged from 1 to 2 mg/kg (Creason *et al.*, 1975, 1976).

In humans, barium is eliminated in the feces, urine, and sweat, with 91% of elimination occurring via the feces (Schroeder *et al.*, 1972). In a 60 year-old man, 20% of an intravenous injection of $^{133}BaCl_2$ was eliminated in the urine and feces within 24 hours, 70% within 3 days, 85% within 10 days, and 89.5% within 15 days. After 8 days the ratio of cumulative fecal to urinary barium excretion was 9 to 1 (Harrison *et al.*, 1966).

TOXICITY

Experimental Animals

The reported LD_{50} values of barium chloride administered to rats and mice by various routes are presented in Table 1. It is clear that barium chloride is least toxic when given subcutaneously and most toxic when injected intravenously. Rats appear to be more sensitive to oral exposure than mice. The acute toxicity of barium salts is a function of their water solubilities (Syed and Hosain, 1972; Borzelleca *et al.*, 1988). Barium sulfate is water insoluble; this nontoxic salt is used in radiology as a radiopaque material (Nielsen, 1986). In contrast, soluble barium salts such as carbonate, chloride, and acetate produce a variety of effects in the body, the most important of which is the intense stimulation of smooth, striated, and cardiac muscle (Brenniman *et al.*, 1981). Barium chloride (0.5 to 2.0 μmole/kg per minute) administered intravenously to anesthetized dogs over a 10- to 100-minute period caused ectopic ventricular contraction, respiratory paralysis, and ventricular fibrillation

TABLE 1
LD_{50} Values for Barium Chloride in Rats and Mice

Species	Route of Administration	Dose (mg/kg)	Reference
Rat	Oral	118	RTECS (1985)
Rat	Subcutaneous	178	RTECS (1985)
Mouse	Oral	430	Woodward and Calvery (unpublished)
Mouse	Intravenous	19.2	Syed and Hosain (1972)
Mouse	Intraperitoneal	54	RTECS (1985)

(Roza and Berman, 1971). These effects were due to hypokalemia that resulted from the accumulation of potassium in the intracellular compartment rather than from potassium loss in the urine or feces.

Barium chloride (300 mg/kg) administered by gavage once daily for 10 days to Sprague-Dawley rats caused a decrease in survival, a decrease in the ovary/brain weight ratio in females, and decreases in blood urea nitrogen levels in both males and females (Borzelleca *et al.*, 1988). Because of the lack of an effect of barium chloride (4,000 ppm in drinking water given for 60 days) on reproductive indices of female F344 rats (Dietz *et al.*, 1992), the decrease in relative ovary weight was not considered biologically significant. The decrease in blood urea nitrogen suggests that barium chloride may be nephrotoxic to rats. No effects were seen in rats receiving lower doses (100, 145, or 209 mg/kg). Tardiff *et al.* (1980) conducted a 13-week study with barium chloride administered to Charles River rats in the drinking water at concentrations of 0, 10, 50, or 250 mg barium/L. Except for a decrease in the relative weight of the adrenal gland of males receiving 50 or 250 mg barium/L and females receiving 10, 50, or 250 mg/L, no chemical-related adverse effects were observed. The decrease in the relative weight of the adrenal gland was observed at week 8 but not at week 13 in males, and at week 13 in females. No chemical-related adverse effects or histopathologic lesions were observed in male Sprague-Dawley rats receiving 1 to 250 mg barium/L (as barium chloride) for 36 weeks or female rats receiving the same doses for 46 weeks. However, rats that received 1,000 mg/L for 16 weeks had basement membrane thickening, epithelial foot process fusion, and myelin figures in the kidney glomeruli (McCauley *et al.*, 1985).

Female weanling Long-Evans rats administered 10 or 100 mg barium/L (as barium chloride) in their drinking water for 16 months developed hypertension; those receiving 1 mg/L did not (Perry *et al.*, 1983, 1985). At the 100 mg/L level, there was a decrease in contractility and excitability of cardiac muscle fiber. Metabolic disturbances included decreases in cardiac ATP, phosphocreatine levels, and phosphorylation potential, and increases in ADP levels. Rats receiving 100 mg/L also displayed hypersensitivity as measured by cardiologic responses to phenobarbital anesthesia (Kopp *et al.*, 1985).

Humans

The lowest reported lethal dose of barium chloride in humans was 11.4 mg/kg (RTECS, 1985). Paralysis, parathesia, and cardiac symptoms were observed in residents of the district of Kiating in China accidentally poisoned by consuming table salt containing up to 26% barium chloride (Allen, 1943). Accidental scalding with barium chloride solution caused cardiac dysfunction in one victim, and death due to cardiac arrest in another (Wang *et al.*, 1989). Acute renal failure was observed in a 52-year-old man who ingested 13 g of barium chloride (Wetherill *et al.*, 1981). Toxic signs exhibited by this patient included diarrhea, abdominal pain, weakness in the lower extremities, and paralysis. Blood potassium levels and blood urea nitrogen levels were depressed and the urine sediment contained renal tubule cells and granular casts. The patient recovered after treatment with intravenous magnesium sulfate and saline diuresis for 9 hours followed by intravenous potassium administration over a 16-hour period. This report suggests that barium chloride nephrotoxicity was related to electrolyte, particularly potassium, imbalance. In two cases of suicidal

poisoning with barium chloride, gastroenteritis, loss of consciousness, disturbance of heart rhythm, and hypokalemia were observed (Zajac-Nedza, 1978). Volunteers (27 to 61 years old) received 1.5 liters of water containing 5 mg barium from barium chloride per day for 3 to 6 weeks followed by 10 mg barium/L water for 7 to 10 weeks. Slight but not statistically or clinically significant increases in the number of premature arterial contractions were observed (Wones *et al.*, 1990). No changes were observed in electrocardiograms, blood pressure, or the levels of serum total cholesterol, triglycerides, high- or low-density lipoproteins, serum potassium, or glucose levels.

Results of epidemiologic studies regarding the association between barium levels in drinking water and mortalities from cardiovascular disease were inconclusive. A questionable negative correlation was reported by Schroeder and Kraemer (1974). In a retrospective study, Brenniman *et al.* (1979) found a high correlation between age-adjusted death rates from cardiovascular disease and areas with high barium levels in the drinking water. Although the results were adjusted for age, sex, number of persons per household, ethnic characteristics, income, and education, the results of this study were clouded by the fact that no corrections were made for the population dynamics in the areas studied or the use of water softeners in the homes of people surveyed. In a follow-up study, no differences were found in blood pressure, heart disease, or kidney disease between populations consuming high and low levels of barium in their drinking water (Brenniman *et al.*, 1981). Corrections were made for home water softener use, the duration of exposure, and the use of high blood pressure medications.

Exposure to finely ground barium salts has been known to cause baritosis in barium miners (Pendergrass and Greening, 1953). Baritosis or benign pneumoconiosis is characterized by the presence of radiopaque spots, nodular lesions, and massive fibrosis in the lung (Seaton *et al.*, 1986). Higher incidences of musculoskeletal symptoms, gastrointestinal surgery, skin problems, and respiratory disorders were observed in metal alloy workers than in nonworkers (NIOSH, 1979).

Reproductive and Developmental Toxicity

Experimental Animals

No adverse anatomical changes were observed in the offspring of Fischer 344 rats and $B6C3F_1$ mice administered barium chloride in drinking water (rat: 0 to 4,000 ppm; mice: 0 to 2,000 ppm) for 60 days prior to mating (Dietz *et al.*, 1992). Rats receiving 4,000 ppm had marginal reductions in litter sizes and pup weights. Reproductive indices in both rats and mice were unaffected. Barium chloride (20 mg) injected in the yolk sac on day 8 of development was teratogenic to developing chick embryos and resulted in the development of curled toes (Ridgeway and Karnofsky, 1952).

Humans

No information on the potential reproductive or developmental toxicity of barium in humans was found in the literature.

Carcinogenicity

Experimental Animals

No increase in neoplasm incidence was observed in male Sprague-Dawley rats that received 10, 100, or 250 mg barium/L (as barium chloride) in their drinking water for 68 weeks (McCauley *et al.*, 1985). The adequacy of this study for assessing the carcinogenic potential of barium chloride is questionable because the duration of the study was short and the doses used appear to be lower than the minimum toxic dose.

Humans

No epidemiologic studies or case reports implicating barium chloride as a human carcinogen were found in the literature. However, barium in contraceptive devices had a precancerous effect on uterine cells. Barium chloride at a concentration of 1.25×10^{-3} M *in vitro* resulted in the transformation of cervical epithelial cells into bizarre, multinucleated cells with profound alteration of the nuclear chromatin characteristic of severe premalignant dysplasia. Two to 3 weeks after direct application of barium chloride to cervical cells of one subject, the dysplastic cells had been exfoliated with complete regression to normal.

This experiment was repeated five times on this subject with the same results each time (Ayre and LeGuerrier, 1967).

Barium chromate is the only barium compound for which there is sufficient evidence that it is a human carcinogen (IARC, 1980). Because the International Agency for Research on Cancer found sufficient evidence for the carcinogenicity of all hexavalent chromium compounds in humans and animals (IARC, 1987), it is not possible to determine whether barium contributed to the carcinogenicity of barium chromate.

GENETIC TOXICITY

The test data for the barium ion, administered in the form of barium chloride dihydrate or barium chloride, indicate that this metal is not genotoxic. Neither barium chloride (Shimizu *et al.*, 1985) nor its dihydrate (Zeiger *et al.*, 1988) induced gene mutations in *Salmonella typhimurium*, with or without S9 metabolic activation. In addition, barium chloride was negative in DNA damage assays in *Bacillus subtilis* (Nishioka, 1975; Kanematsu *et al.*, 1980) and gene mutation assays in *Escherichia coli* (Shimizu *et al.*, 1985; Rossman and Molina, 1986). The effect of barium chloride on meiosis in *Saccharomyces cerevisiae* was investigated and no clear indication of barium-induced modification of the meiotic process was observed, except for a slightly increased frequency of recombination which the authors considered difficult to interpret (Sora *et al.*, 1986). There are no reported studies on the genetic effects of barium in cultured mammalian cells or whole animals. No induction of unscheduled DNA synthesis was observed in mature *Petunia* pollen treated for 2 hours with barium chloride (2 mM), although unscheduled DNA synthesis was observed in pollen cells treated with several other metal chloride salts (Jackson and Linskens, 1982). The only positive result reported for barium chloride was an increase in the number of rice plants exhibiting chlorophyll mutations after seeds were soaked in an aqueous solution of 10^{-4} M barium chloride for 24 hours (Reddy and Vaidyanath, 1978). Whether this was the result of a genetic alteration or some other barium-induced toxic effect is unclear.

STUDY RATIONALE

Barium chloride dihydrate was nominated by the National Cancer Institute for toxicity and carcinogenicity studies because of widespread human exposure to barium, and because barium chloride was reported to cause rapid transformation of cervical cells into bizarre multinucleated cells. Drinking water was selected as the route of administration because of the high water solubility of barium chloride dihydrate and because human exposure to this chemical is primarily by ingestion.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF BARIUM CHLORIDE DIHYDRATE

Barium chloride dihydrate was obtained from J.T. Baker Chemical Company (Phillipsburg, NJ) in two lots (123120 and 423103). Lot 123120 was used throughout the 15-day and 13-week studies and lot 423103 was used throughout the 2-year studies. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO). Reports on analyses performed in support of the barium chloride dihydrate studies are on file at the National Institute of Environmental Health Sciences (NIEHS).

Both lots of the chemical, a white, crystalline solid, were characterized by elemental analyses, weight loss on drying, complexometric titration, precipitation titration, spark source mass spectrometry, and by American Chemical Society tests for oxidizing substances, heavy metals, and iron. Elemental analyses of both lots for barium, chlorine, and hydrogen, as well as results of weight loss on drying were in good agreement with the theoretical values for barium chloride dihydrate, confirming the identity of the chemical. Titrametric analyses indicated purities ranging from 99% to 100%. The overall purity was found to be greater than 99% for both lots. Accelerated bulk chemical stability studies were not performed because the physical and chemical properties of barium chloride dihydrate are such that the chemical should be stable over a wide range of temperatures. The purity and water content of the bulk chemical were reanalyzed every 4 months during the 2-year studies at the study laboratory by complexometric titration and weight loss on drying. The results indicated that the purity and moisture content of the barium chloride dihydrate did not change during the 2-year studies.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared by mixing barium chloride dihydrate and water in a volumetric flask and stirring mechanically for 1 minute (Table J1). Dose formulations were prepared once during the 15-day studies and weekly during the 13-week and 2-year studies. Stability studies of the 500 ppm dosed water solutions were performed using ultraviolet spectroscopy by the analytical chemistry laboratory. Stability of the dose formulations was confirmed for at least 3 weeks when stored in the dark at 25° C and for at least 3 days when stored exposed to air and light. No special handling was required during dosing.

Periodic analyses of the dose formulations of barium chloride dihydrate were conducted at the study laboratory and the analytical chemistry laboratory using complexometric titration. The dose formulations were analyzed at the beginning of the 15-day studies (Table J2). During the 13-week studies, the dose formulations were analyzed at the initiation and midpoint of the studies (Table J3). During the 2-year studies, the dose formulations were analyzed at least once every 8 weeks (Table J4). All the dose formulations were within 10% of the target concentrations. Results of periodic referee analyses performed by the analytical chemistry laboratory were in good agreement with the results obtained by the study laboratory (Table J5).

15-DAY STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Simonsen Laboratories, Inc. (Gilroy, CA). At receipt the rats were 56 days old and mice were 63 days old. The animals were quarantined for 14 days before exposure began. During this time two males and females of each species were randomly selected and evaluated for evidence of disease.

Groups of five male and five female rats received 0, 125, 250, 500, 1,000, or 2,000 ppm of barium chloride dihydrate in distilled drinking water for 15 days; groups of five male and five female mice received 0, 40, 80, 173, 346, or 692 ppm of barium chloride dihydrate in distilled drinking water for 15 days. Animals were housed five per cage; water and feed

were available *ad libitum*. Water consumption was measured twice weekly, and clinical findings were recorded once daily. Animals were weighed at study initiation, twice a week, and at the end of the studies. Details of study design and animal maintenance are summarized in Table 2.

Neurobehavioral studies were conducted with barium chloride dihydrate as part of an NTP initiative for evaluating the reproducibility and the predictive ability of various neurobehavioral assays. Behavioral assessments were performed on each rat before and after 14 days of exposure to dosed drinking water. The behavioral tests consisted of spontaneous motor activity, forelimb and hindlimb grip strengths, thermal sensitivity, startle response to acoustic and air-puff stimuli, and hindlimb foot splay (Appendix G).

At the end of the 15-day studies, blood was collected from all rats by cardiac puncture for clinical pathology analyses. The clinical pathology parameters measured are listed in Table 2. A necropsy was performed on all rats and mice. The heart, liver, right kidney, lung, right testis, and thymus of rats and mice were weighed. Tissues for microscopic examination were embedded in paraffin, sectioned to a thickness of 4 to 6 μm, and stained with hematoxylin and eosin. Histopathologic examinations were conducted on all rats receiving 2,000 ppm and all mice receiving 692 ppm. The tissues examined microscopically are listed in Table 2. The livers of all control animals and rats that received 125, 250, 500, or 1,000 ppm were examined microscopically.

13-Week Studies

The 13-week studies were conducted to evaluate the cumulative toxic effects of repeated exposure to barium chloride dihydrate and to determine the appropriate exposure levels to be used in the 2-year studies.

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Simonsen Laboratories, Inc. (Gilroy, CA); all rats and mice were 32 days old upon receipt. The animals were quarantined for 11 days before exposure began. At this time, five males and five females of each species were randomly selected and evaluated for evidence of disease.

Groups of 10 male and 10 female rats and mice received barium chloride dihydrate in distilled drinking water at doses of 0, 125, 500, 1,000, 2,000, or 4,000 ppm 7 days per week for 13 weeks. Animals were housed five per cage; water and feed were available *ad libitum*. Water consumption was measured once weekly, and clinical findings were recorded once weekly. The animals were weighed at study initiation, once weekly, and at the end of the studies. Further details of study design and animal maintenance are summarized in Table 2.

Behavioral assessments were performed on rats and mice before exposure and after 45 and 90 days of exposure to dosed drinking water. The behavioral studies measured spontaneous motor activity, forelimb and hindlimb grip strengths, thermal sensitivity, startle response to acoustic and air-puff stimuli, and hindlimb foot splay (Appendix G). Cardiovascular studies were performed on each rat before exposure and after 45 and 91 days of exposure to dosed drinking water. The studies included electrocardiogram recordings and analysis and blood pressure measurements (Appendix G).

At the end of the 13-week studies, blood was collected from all rats by cardiac puncture for hematology and clinical chemistry analyses. The parameters measured are listed in Table 2. A necropsy was performed on all animals. The adrenal gland, brain, heart, right kidney, liver, lung, right testis, and thymus of rats and mice were weighed. Tissues for microscopic examination were embedded in paraffin, sectioned to a thickness of 4 to 6 μm, and stained with hematoxylin and eosin. A complete histopathologic examination was performed on all control animals, all mice receiving 2,000 ppm, and all animals receiving 4,000 ppm. Table 2 lists the tissues and organs routinely examined microscopically. The kidney, liver, spleen, and thymus of rats that received 2,000 ppm; the kidney of male mice that received 1,000 ppm; and the adrenal gland, heart, and salivary gland of female rats that received 2,000 ppm were examined microscopically.

2-Year Studies

Study Design

Groups of 60 male and 60 female rats and mice received 0, 500, 1,250, or 2,500 ppm barium chloride dihydrate in distilled drinking water for 105 (female rats), 104 (male rats and female mice), or 103 weeks (male mice). Ten male and 10 female rats and six to 10 male and female mice per group were randomly

selected for interim evaluations after 15 months of chemical administration.

Source and Specification of Animals

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Facility (Frederick, MD) for use in the 2-year studies. Rats were quarantined for 12 (males) or 14 (females) days, and mice were quarantined for 15 (males) or 16 (females) days before the beginning of the studies. Five rats and five mice of each sex were randomly selected and evaluated for evidence of disease. Serology samples were collected for viral screening. Rats were 7 weeks old and mice were 6 weeks old at the beginning of the 2-year studies. The health of the animals was monitored during the studies according to the NTP Sentinel Animal Program (Appendix M).

Animal Maintenance

Rats were housed five per cage; mice were housed individually. Feed and water were available *ad libitum*, and water consumption was measured weekly (Appendix K). Cages were rotated every 2 weeks. Further details of animal maintenance are given in Table 2. Information on feed composition and contaminants is provided in Appendix L.

Clinical Examinations and Pathology

All animals were observed twice daily. Clinical findings and body weights were recorded initially, weekly for 13 weeks, then monthly and at the interim evaluations. Blood was collected from the jugular vein of all rats and mice at the 15-month interim evaluations for hematology and clinical chemistry. The parameters measured are listed in Table 2. The adrenal gland, brain, heart, right kidney, liver, lung, ovary, spleen, right testis, thymus, and uterus of rats and mice were weighed at the 15-month interim evaluations.

At the 15-month interim evaluations, plasma from blood collected for clinical pathology was analyzed to determine plasma barium concentrations in rats and mice. In addition, the left femur from eight male and eight female rats in the control and 2,500 ppm groups were analyzed for barium, calcium, and phosphorus concentrations, and bone density. Further details of these analyses are provided in Appendix I.

A complete necropsy was performed on all animals. At necropsy, all organs and tissues were examined for gross lesions, and all major tissues were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin for microscopic examination. Complete histopathologic examinations were performed on all rats and mice and on all tissues with grossly visible lesions. Tissues examined are listed in Table 2.

Microscopic evaluations were completed by the study laboratory pathologist, and the pathology data were entered into the Toxicology Data Management System. The microscopic slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit. The slides, individual animal data records, and pathology tables were evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, the slide and tissue counts were verified, and histotechnique was evaluated. A quality assessment pathologist reviewed the liver, spleen and miscellaneous organs of rats (to verify the incidence of mononuclear cell leukemia) and the kidney of mice for accuracy and consistency of lesion diagnosis.

The quality assessment report and slides were submitted to the NTP Pathology Working Group (PWG) chair. Representative histopathology slides containing examples of disagreements in diagnosis between the laboratory and quality assessment pathologists, or lesions of general interest were presented by the chair 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 exposure groups or previously rendered diagnoses. When the consensus opinion of the PWG differed from the laboratory pathologist, the diagnosis was changed. Thus, the final diagnoses represent a consensus of contractor pathologists 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 pathology data, the diagnosed lesions for each tissue type were evaluated separately or combined according to the guidelines of McConnell *et al.* (1986).

Statistical Methods

Survival Analyses

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

Calculation of Incidence

The incidences of neoplasms or nonneoplastic lesions as presented in Tables A1, A5, B1, B4, C1, C4, D1, and D4 are given as the number of animals bearing such lesions at a specific anatomic site and the number of animals with that site examined microscopically. For calculation of statistical significance, the incidences of most neoplasms (Tables A3, B3, C3, and D3) and all nonneoplastic lesions are given as the ratio of the number of affected animals to the number of animals with the site examined microscopically. However, when macroscopic examination was required to detect neoplasms in certain tissues (e.g., skin, intestine, harderian gland, and mammary gland) 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.

Analysis of Neoplasm Incidences

The majority of neoplasms in these studies were considered to be incidental to the cause of death or not rapidly lethal. Thus, the primary statistical method used was logistic regression analysis, which assumed that the diagnosed neoplasms were discovered as the result of death from an unrelated cause and thus did not affect the risk of death. In this approach, neoplasm prevalence was modeled as a logistic function of chemical exposure and time. Both linear and quadratic terms in time were incorporated initially, and the quadratic term was eliminated if it did not significantly enhance the fit of the model. The exposed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and Haseman (1986). When neoplasms are incidental, this comparison of the time-specific neoplasm prevalences also provides a comparison of the time-specific neoplasm incidences (McKnight and Crowley, 1984).

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

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

Analysis of Nonneoplastic Lesion Incidences

Because all nonneoplastic lesions in these studies were considered to be incidental to the cause of death or not rapidly lethal, the primary statistical analysis used was a logistic regression analysis in which lesion prevalence was modeled as a logistic function of chemical exposure and time. For lesions detected at the interim evaluation, the Fisher exact test was used, a procedure based on the overall proportion of affected animals.

Historical Control Data

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

Analysis of Continuous Variables

Two approaches were employed to assess the significance of pairwise comparisons between exposed and control groups in the analysis of continuous variables.

Organ and body weight data, which have approximately normal distributions, were analyzed using the parametric multiple comparison procedures of Dunnett (1955) and Williams (1971, 1972). Clinical chemistry, hematology, neurobehavioral, and cardiovascular data, which have typically skewed distributions, were analyzed using the nonparametric multiple comparison methods of Dunn (1964) and Shirley (1977). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of the dose-response 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-response trend (Dunnett's or Dunn's test). Average severity values were analyzed for significance using the Mann-Whitney U test (Hollander and Wolfe, 1973).

Quality Assurance Methods

The 13-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, they were audited retrospectively by an independent quality assurance contractor. Separate audits covering completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and preliminary review draft of this NTP Technical Report were conducted. Audit procedures and findings are presented in the reports and are on file at NIEHS. The audit findings were reviewed and assessed by NTP staff so that all discrepancies had been resolved or were otherwise addressed during the preparation of this Technical Report.

GENETIC TOXICOLOGY

The genetic toxicity of barium chloride dihydrate was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium* and L5178Y mouse lymphoma cells and chromosome damage in cultured Chinese hamster ovary cells. The protocols for these studies and the results are given in Appendix E.

The genetic toxicity studies of barium chloride dihydrate are part of a larger effort by the NTP to develop a database that would permit the evaluation of carcinogenicity in experimental animals from the structure of the chemical and its responses in short-term *in vitro* and *in vivo* genetic toxicity tests. These genetic toxicity tests were originally developed to study mechanisms of chemically induced DNA damage and to predict carcinogenicity in animals, based on the electrophilic theory of chemical carcinogenesis and the somatic mutation theory (Miller and Miller, 1977; Straus, 1981; Crawford, 1985).

There is a strong correlation between a chemical's potential electrophilicity (structural alert to DNA reactivity), mutagenicity in *Salmonella*, and carcinogenicity in rodents. The combination of electrophilicity and *Salmonella* mutagenicity is highly correlated with the induction of carcinogenicity in rats and mice and/or at multiple tissue sites (Ashby and Tennant, 1991). Other *in vitro* genetic toxicity tests do not correlate well with rodent carcinogenicity (Tennant *et al.*, 1987; Zeiger *et al.*, 1990), although these other tests can provide information on the types of DNA and chromosome effects that can be induced by the chemical being investigated. Data from NTP studies show that a positive response in *Salmonella* is currently the most predictive *in vitro* test for rodent carcinogenicity (89% of the *Salmonella* mutagens were rodent carcinogens), and that there is no complementarity among the *in vitro* genetic toxicity tests. That is, no battery of tests that included the *Salmonella* test improved the predictivity of the *Salmonella* test alone. The predictivity for carcinogenicity of a positive response in bone marrow chromosome aberration or micronucleus tests is not yet defined.

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of Barium Chloride Dihydrate

15-Day Studies	13-Week Studies	2-Year Studies
Study Laboratory		
SRI International (Menlo Park, CA)	SRI International (Menlo Park, CA)	EG&G Mason Research Institute (Worcester, MA)
Strain and Species		
Rats: F344/N Mice: $B6C3F_1$	Rats: F344/N Mice: $B6C3F_1$	Rats: F344/N Mice: $B6C3F_1$
Animal Source		
Simonsen Laboratories Inc. (Gilroy, CA)	Simonsen Laboratories, Inc. (Gilroy, CA)	Frederick Cancer Research Facility (Frederick, MD)
Time Held Before Studies		
14 days	11 days	Rats: 12 days (males) 14 days (females) Mice: 15 days (males) 16 days (females)
Average Age When Studies Began		
Rats: 10 weeks Mice: 11 weeks	6 weeks	Rats: 6 weeks Mice: 7 weeks
Date of First Dose		
Rats: 23-25 November 1982 Mice: 30 November - 2 December 1982	Rats: 10-14 May 1983 Mice: 3-7 May 1983	Rats: 9 September 1985 (males) 11 September 1985 (females) Mice: 9 October 1985 (males) 10 October 1985 (females)
Duration of Dosing		
15 days	95 days	Rats: 104 weeks (male) 105 weeks (female) Mice: 103 weeks (male) 104 weeks (female)
Date of Last Dose		
Rats: 7-9 December 1982 Mice: 14-16 December 1982	Rats: 9-15 August 1983 Mice: 2-8 August 1983	Rats: 31 August 1987 (males) 9 September 1987 (females) Mice: 24 September 1987 (males) 5 October 1987 (females)
Method of Sacrifice		
Anesthetized with sodium pentobarbital followed by exsanguination	Same as 15-day studies	Carbon dioxide asphyxiation

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of Barium Chloride Dihydrate (continued)

15-Day Studies	13-Week Studies	2-Year Studies
Necropsy Dates Rats: 7-9 December 1982 Mice: 14-16 December 1982	Rats: 9-15 August 1983 Mice: 2-8 August 1983	Rats: 8-14 September 1987 (males) 17-25 September 1987 (females) Mice: 2-9 October 1987 (males) 13-16 October 1987 (females)
Average Age at Necropsy Rats: 12 weeks Mice: 13 weeks	19 weeks	Rats: 111 weeks (males) 112 weeks (females) Mice: 110 weeks (males) 112 weeks (females)
Size of Study Groups 5 males and 5 females	10 males and 10 females	60 males and 60 females
Method of Distribution Distributed using a table of random numbers.	Same as 15-day studies	Same as 15-day studies
Animals per Cage 5	Same as 15-day studies	Rats: 5 Mice: 1
Method of Animal Identification Ear clip	Same as 15-day studies	Toe clip
Diet* NIH-07 open-formula pellets diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*	Same as 15-day studies	NIH-07 open stock mash diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*
Maximum Storage Time for Feed 120 days from milling date	Same as 15-day studies	Same as 15-day studies
Water Water was supplied in 12 oz water bottles (rats) and 8 oz bottles (mice) (Lab Products, Inc., Rochelle Park, NJ), available *ad libitum*	Same as 15-day studies	Water was supplied in 16 oz (rats) and 12 oz (mice) bottles (Lab Products, Inc., Garfield, NJ or Puritan Bottle Co., Worcester, MA), available *ad libitum*
Cages Polycarbonate (Lab Products, Inc., Rochelle Park, NJ), changed twice weekly	Same as 15-day studies	Same as 15-day studies

* NIH-07 diet used contained less than 20 ppm barium

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of Barium Chloride Dihydrate (continued)

15-Day Studies	13-Week Studies	2-Year Studies
Bedding		
Ab-Sorb-Dri® hardwood chips (Lab Products, Inc., Rochelle Park, NJ), changed twice weekly	Same as 15-day studies	BetaChips®, hardwood laboratory bedding (Northeastern Products, Corp., Warrensburg, NY), changed twice weekly
Cage Filters		
Polyester (Lab Products, Inc., Rochelle Park, NJ)	Polyester (Snow Filtration, Cincinnati, OH), changed once every 2 weeks	Nonwoven polyester (Snow Filtration, Cincinnati, OH), changed once every 2 weeks
Racks		
Stainless steel (Lab Products, Inc., Rochelle Park, NJ)	Stainless steel (Lab Products, Inc., Rochelle Park, NJ), changed once every 2 weeks.	Same as 13-week studies
Animal Room Environment		
Temperature: 22° ± 1° C Relative humidity: 40%-60% Fluorescent light: 12 hours/day Room air changes: 13 changes/hour	Temperature: 21°-24° C Relative humidity: 40%-62% Fluorescent light: 12 hours/day Room air changes: 13.5 changes/hour	Temperature: 21°-23° C Relative humidity: Rats – 45%-54% Mice – 46%-59% Fluorescent light: 12 hours/day Room air changes: 10/hour
Doses		
Rats: 0, 125, 250, 500, 1,000, or 2,000 ppm barium chloride dihydrate in distilled drinking water, available *ad libitum* Mice: 0, 40, 80, 173, 346, or 692 ppm barium chloride dihydrate in distilled drinking water, available *ad libitum*	0, 125, 500, 1,000, 2,000, or 4,000 ppm barium chloride dihydrate in distilled drinking water, available *ad libitum*	0, 500, 1,250, or 2,500 ppm barium chloride dihydrate in distilled drinking water, available *ad libitum*
Type and Frequency of Observation		
Clinical observations recorded daily; animals weighed at the beginning of the study, twice a week, and at the end of the studies; water consumption measured twice weekly.	Animals observed daily; clinical observations recorded once weekly; animals weighed initially, once weekly, and at the end of the studies; water consumption recorded by cage weekly.	Animals observed twice daily; clinical observations and animal weights recorded initially, weekly for 13 weeks, then monthly and at interim evaluations; water consumption measured weekly.
Necropsy		
Necropsy performed on all animals. Organ weights recorded for brain, heart, right kidney, liver, lung, right testis, and thymus.	Necropsy performed on all animals. Organ weights recorded for adrenal gland, brain, heart, right kidney, liver, lung, right testis, and thymus.	Necropsy performed on all animals. Organs weighed were adrenal gland, brain, heart, right kidney, liver, lung, ovary, right testis, spleen, thymus, and uterus.

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of Barium Chloride Dihydrate (continued)

15-Day Studies	13-Week Studies	2-Year Studies
Clinical Pathology Blood was collected from all rats by cardiac puncture. ***Hematology:*** hematocrit, hemoglobin, erythrocytes, mean erythrocyte volume, and leukocyte count and differential ***Clinical chemistry:*** barium, sodium, potassium, calcium, and phosphorus	Blood was collected from all rats by cardiac puncture. ***Hematology:*** hematocrit, hemoglobin, erythrocytes, mean erythrocyte volume, mean erythrocyte hemoglobin, mean erythrocyte hemoglobin concentration, platelets, nucleated erythrocytes, and leukocyte count and differential ***Clinical chemistry:*** barium, sodium, potassium, calcium, and phosphorus	Blood was collected from the jugular vein of all rats and mice at the 15-month interim evaluations. ***Hematology:*** hemoglobin, hematocrit, erythrocytes, mean erythrocyte volume, mean erythrocyte hemoglobin, mean erythrocyte hemoglobin concentration, platelets, reticulocytes, nucleated erythrocytes, and leukocyte count and differential ***Clinical chemistry:*** urea nitrogen, creatinine, calcium, phosphorus, alanine aminotransferase, creatine kinase, lactate dehydrogenase, sorbitol dehydrogenase (rats), and γ-glutamyltransferase
Plasma and Bone Analyses None	None	Plasma barium levels were determined in rats and mice; bone density, barium, calcium, and phosphorus levels in bone were determined in control and high-dose rats.
Histopathology Histopathology was performed on all rats receiving 2,000 ppm and all mice receiving 692 ppm. In addition to gross lesions, the tissues examined included: adrenal gland, bone and marrow, brain, epididymis, esophagus, heart, kidney, large intestine (colon), liver, lung, mammary gland, mandibular and mesenteric lymph nodes, ovary, pancreas, parathyroid gland, pituitary gland, prostate gland, salivary gland, seminal vesicle, skin, small intestine, spleen, stomach, testis, thymus, thyroid gland, trachea, urinary bladder, and uterus. In addition, the livers from all controls rats and mice, and rats that received 125, 250, 500, or 1,000 ppm were examined.	Complete histopathology was performed on all controls, all mice receiving 2,000 ppm, and all rats and mice receiving 4,000 ppm. In addition to gross lesions, the tissues examined included: adrenal gland, brain, epididymis, esophagus, heart, kidney, large intestine (cecum, colon, rectum), liver, lung, mammary gland, mandibular lymph node, mesenteric lymph node, nose, ovary, pancreas, parathyroid gland, pituitary gland, prostate gland, salivary gland, seminal vesicle, skin, small intestine, spleen, sternebrae (including marrow), stomach, testis, thyroid gland, trachea, thymus, urinary bladder, and uterus. In addition, the kidney of male mice receiving 1,000 ppm; the kidney, liver, spleen, and thymus of rats receiving 2,000 ppm; and the adrenal gland, heart, and salivary gland of female rats receiving 2,000 ppm were examined.	Complete histopathology was performed on all rats and mice. In addition to gross lesions, tissue masses, and associated lymph nodes, the tissues examined included: adrenal gland, brain, bone and marrow, clitoral gland (rats), large intestine (cecum, colon, rectum), epididymis, esophagus, gallbladder (mice), heart, kidney, liver, lung, mandibular and mesenteric lymph nodes, mammary gland, nose, ovary, pancreas, parathyroid gland, pituitary gland, preputial gland (rats), prostate gland, salivary gland, seminal vesicle, skin, small intestine (duodenum, jejunum, ileum), spleen, stomach (forestomach and glandular), testis, thymus, thyroid gland, trachea, urinary bladder, and uterus.

TABLE 2
Experimental Design and Materials and Methods in the Drinking Water Studies of Barium Chloride Dihydrate (continued)

15-Day Studies	13-Week Studies	2-Year Studies
Neurobehavioral Studies		
Neurobehavioral assessments were conducted on all rats before and after 14 days of exposure. The tests consisted of spontaneous motor activity, forelimb and hindlimb grip strength, thermal sensitivity, acoustic and air-puff startle response, and hindlimb foot splay.	Neurobehavioral assessments were conducted on all rats and mice at 0, 45, and 90 days. The tests conducted were the same as those in the 15-day studies.	None
Cardiovascular Studies		
None	Cardiovascular studies were performed on each rat at 0, 45, and 91 days. The studies conducted included heart rate and systolic arterial pressure measurements and analysis of electrocardiogram recordings.	None

RESULTS

RATS

15-DAY STUDY

No chemical-related deaths occurred among male or female rats. One male rat that received 2,000 ppm was accidentally killed on day 14 (Table 3). While the final mean body weights of male and female rats receiving barium chloride dihydrate were within 5% of the controls, the mean body weight gain of male rats receiving 2,000 ppm was 18% lower than that of controls. Water consumption by male and female rats that received 2,000 ppm was slightly lower than that by the controls (≤16%) during week 2. Drinking water levels of 125, 250, 500, 1,000, or 2,000 ppm barium chloride dihydrate were estimated to deliver daily doses of 10, 15, 35, 60, or 110 mg barium/kg body weight. There were no chemical-related clinical findings of toxicity or lesions noted at necropsy. Motor activity, grip strength, and thermal sensitivity were not affected in exposed rats (Table G1). No significant differences in absolute or relative organ weights were observed in rats receiving barium chloride dihydrate (Table F1). No biologically significant differences in the serum levels of potassium, phosphorus, and calcium or hematology parameters were observed in exposed rats (Table H1).

TABLE 3
Survival, Mean Body Weights, and Water Consumption of Rats in the 15-Day Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Week 1	Week 2
Male							
0	5/5	176 ± 6	215 ± 5	38 ± 2		20	19
125	5/5	182 ± 5	224 ± 6	42 ± 3	104	20	18
250	5/5	178 ± 6	223 ± 6	45 ± 6	104	22	19
500	5/5	176 ± 6	217 ± 7	41 ± 4	101	19	18
1,000	5/5	174 ± 7	216 ± 5	42 ± 3	100	20	17
2,000	4/5[d]	180 ± 6	211 ± 5	31 ± 3	98	19	16
Female							
0	5/5	132 ± 6	149 ± 3	17 ± 4		15	16
125	5/5	134 ± 3	152 ± 3	19 ± 1	102	16	19
250	5/5	132 ± 3	144 ± 3	12 ± 1	97	16	15
500	5/5	132 ± 2	151 ± 3	19 ± 2	102	15	17
1,000	5/5	135 ± 2	150 ± 3	15 ± 2	101	16	14
2,000	5/5	130 ± 4	148 ± 4	18 ± 2	100	14	12

[a] Number of animals surviving at 15 days/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study. Differences from the control group are not significant by Williams' or Dunnett's test.
[c] Water consumption is expressed as grams per animal per day.
[d] Day of death: 14

13-WEEK STUDY

Three males and one female that received 4,000 ppm died during the last week of the study (Table 4). The cause of these deaths was not apparent histologically, but the deaths were considered to be chemical-related. The final mean body weights and mean body weight gains of male and female rats receiving 4,000 ppm were significantly lower than those of the controls (final mean body weights: 13% and 8% lower; mean body weight gains: 18% and 24% lower). Water consumption by male and female rats that received 4,000 ppm was lower than that by controls; these groups consumed approximately 70% of that consumed by the controls. Drinking water containing 125, 500, 1,000, 2,000, or 4,000 ppm barium chloride dihydrate was estimated to deliver daily doses of 10, 30, 65, 110, or 200 mg barium/kg body weight to males and 10, 35, 65, 115, or 180 mg barium/kg body weight to females. No chemical-related clinical findings of toxicity were noted.

A slight but significant decrease in undifferentiated motor activity in rats that received 4,000 ppm was observed at day 90 of the study (Table G2). A marginal decrease in this parameter was observed at day 90 of the study in all other exposed groups of rats except in 1,000 ppm females.

Serum phosphorus levels in males receiving 2,000 and 4,000 ppm and in females receiving 500, 1,000, 2,000, and 4,000 ppm were significantly higher than those in controls (Table H2). Elevations in serum phosphorus levels may have been caused by renal tubule damage. However, due to the minimal to mild

TABLE 4
Survival, Mean Body Weights, and Water Consumption of Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	Survival[a]	Mean Body Weight[b] (g) Initial	Final	Change	Final Weight Relative to Controls (%)	Water Consumption[c] Week 2[d]	Week 13
Male							
0	10/10	138 ± 5	356 ± 8	217 ± 6		21	22
125	10/10	130 ± 7	359 ± 8	229 ± 7	101	21	21
500	10/10	126 ± 6	367 ± 6	240 ± 6	103	20	21
1,000	10/10	122 ± 6	349 ± 6	227 ± 7	98	19	18
2,000	10/10	128 ± 7	344 ± 6	215 ± 8	97	20	19
4,000	7/10[e]	133 ± 4	311 ± 6**	177 ± 9**	87	16	14
Female							
0	10/10	104 ± 3	194 ± 3	90 ± 4		16	15
125	10/10	110 ± 3	200 ± 4	90 ± 4	103	17	15
500	10/10	104 ± 3	195 ± 3	91 ± 4	101	15	15
1,000	10/10	104 ± 3	191 ± 3	88 ± 4	99	15	17
2,000	10/10	104 ± 3	189 ± 4	85 ± 6	97	14	11
4,000	9/10[e]	109 ± 2	178 ± 6**	68 ± 6**	92	11	10

** Significantly different ($P \leq 0.01$) from the control group by Williams' or Dunnett's test
[a] Number of animals surviving at 13 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[c] Water consumption is expressed as grams per animal per day.
[d] Week 1 values were not used because of excess water spillage.
[e] Week of death: 13

severity of this lesion, it is more likely that the elevated values were due to an artifact from hemolysis of collected blood samples. Significantly decreased sodium levels in 4,000 ppm male rats and calcium levels in 1,000 ppm males did not occur in a dose-related manner and thus were not considered to be clearly related to barium chloride dihydrate exposure.

The absolute and relative kidney weights of females that received 2,000 and 4,000 ppm and the relative kidney weight of males that received 4,000 ppm were significantly greater than those of the controls and were associated with chemical-induced renal lesions (Table F2). The differences in the absolute and/or relative weights in other organs could be attributed to the decrease in mean body weights observed in 4,000 ppm male and female rats.

Chemical-related kidney lesions occurred in three male and three female rats receiving 4,000 ppm. None were observed in the controls or in any of the remaining exposure groups. Grossly, the kidneys were pale and had roughened surfaces. Microscopically, the kidney lesions appeared as a minimal to mild, focal to multifocal dilatation of the proximal convoluted tubules in the outer medulla and the renal cortex (Plate 1). The tubule epithelial cells were usually low cuboidal cells with a decreased cytoplasmic volume, yet they contained a nucleus of typical size (Plate 2). Tubule dilatation observed in this study was different from the common spontaneous lesions observed in the kidney of rats. In this study, early lesions of nephropathy were observed in virtually all males and in small numbers of females in all treatment groups as well as the controls. Additionally, minimal to mild atrophy of the spleen and/or thymus was observed in small numbers of male and female rats that received 4,000 ppm.

Dose selection rationale: Because of mortality, lower final mean body weights, decreased water consumption, and the presence of kidney lesions in male and female rats receiving 4,000 ppm for 13 weeks, the high dose selected for the 2-year study was 2,500 ppm.

2-YEAR STUDY

Survival

Estimates of survival probabilities for male and female rats are shown in Table 5 and in the Kaplan-Meier curves in Figure 1. Survival of exposed female groups was similar to that of the controls. The marginally increased survival of exposed male groups was probably due to a decreased incidence of leukemia.

Water and Compound Consumption

Barium chloride dihydrate in drinking water caused a dose-related decrease in water consumption. Average water consumption (g/day) over the 2-year period for males was: 0 ppm, 21.2; 500 ppm, 20.2; 1,250 ppm, 18.7; 2,500 ppm, 16.5; and over the 2-year period for females was: 16.2, 15.6, 14.9, and 12.1. The greatest effect on water consumption was observed in rats receiving 2,500 ppm. Beginning as early as week 5, water consumption by these groups was substantially depressed (males: 11% to 30%; females: 19% to 33%; Tables K1 and K2). Based on the water consumption data the average daily dose of barium chloride dihydrate received by rats was 15, 30, or 60 mg barium/kg body weight for males, and 15, 45, or 75 mg barium/kg body weight for females.

Body Weights and Clinical Findings

Mean body weights of male rats receiving 2,500 ppm were slightly lower than controls from week 18 to the end of the study (Figure 2 and Table 6). Female rats that received 2,500 ppm had mean body weights 5% to 11% lower than the controls beginning at week 49 (Figure 2 and Table 7). The final mean body weights of males receiving 500 and 1,250 ppm and females receiving 500 ppm were similar to those of the controls. The final mean body weight of males that received 2,500 ppm was 5% lower than that of the controls. The final mean body weights of females receiving 1,250 and 2,500 ppm were 6% and 11% lower than the controls, respectively. There were no chemical-related clinical findings noted in male or female rats.

TABLE 5
Survival of Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	0	500	1,250	2,500
Male				
Animals initially in study	60	60	60	60
15-month interim evaluation[a]	10	10	10	10
Natural deaths	9	5	3	3
Moribund kills	19	14	18	14
Animals surviving to study termination	22[e]	31	29	33
Percent probability of survival at end of study[b]	44	62	58	67
Mean survival (days)[c]	646	651	655	644
Survival analysis[d]	P=0.153N	P=0.193N	P=0.236N	P=0.111N
Female				
Animals initially in study	60	60	60	60
15-month interim evaluation[a]	10	10	10	10
Natural deaths	5	3	2	2
Moribund kills	14	11	9	16
Animals surviving to study termination	31[e]	36	39	32
Percent probability of survival at end of study	62	72	79	64
Mean survival (days)	645	669	655	662
Survival analysis	P=0.969N	P=0.231N	P=0.155N	P=0.789N

[a] Censored from survival analyses
[b] Kaplan-Meier determinations based on the number of animals alive on the first day of terminal sacrifice
[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 dosed columns. A negative trend or a lower mortality in a dose group is indicated by N.
[e] Includes one animal that died during the last week of the study.

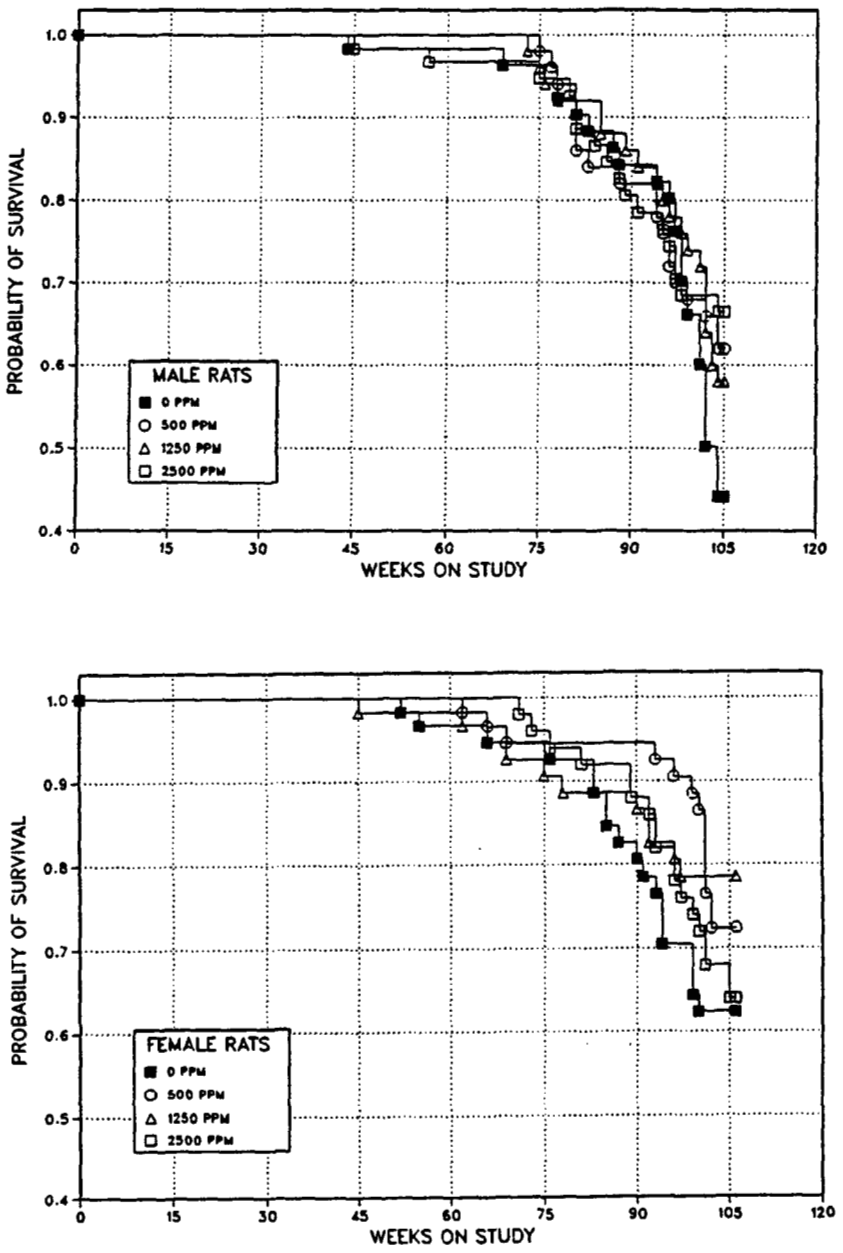

FIGURE 1
Kaplan-Meier Survival Curves for Male and Female Rats Administered Barium Chloride Dihydrate in Drinking Water for 2 Years

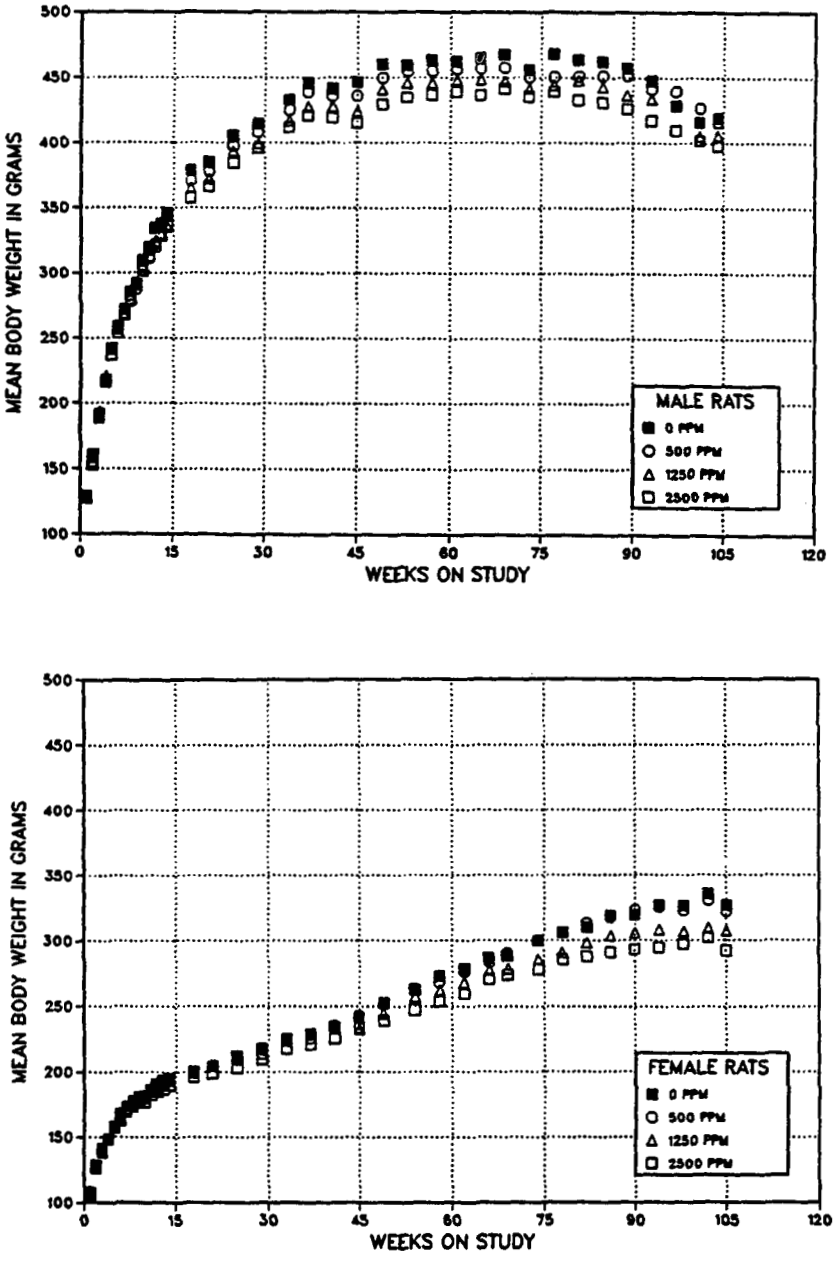

FIGURE 2
Growth Curves for Male and Female Rats Administered Barium Chloride Dihydrate in Drinking Water for 2 Years

TABLE 6
Mean Body Weights and Survival of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Weeks on Study	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	129	60	128	99	60	128	99	60	127	99	60
2	161	60	159	99	60	155	97	60	153	95	60
3	192	60	190	99	60	193	101	60	189	98	60
4	218	60	217	100	60	221	102	60	216	99	60
5	242	60	237	98	60	241	100	60	237	98	60
6	259	60	257	99	60	258	100	60	255	98	60
7	272	60	269	99	60	268	99	60	268	98	60
8	286	60	278	97	60	283	99	60	280	98	60
9	292	60	288	99	60	293	101	60	291	100	60
10	310	60	304	98	60	306	99	60	302	98	60
11	320	60	311	97	60	318	99	60	313	98	60
12	335	60	323	96	60	325	97	60	320	96	60
13	338	60	330	98	60	329	98	60	328	97	60
14	346	60	337	98	60	335	97	60	336	97	60
18	379	60	371	98	60	365	96	60	358	94	60
21	385	60	378	98	60	372	97	60	367	95	60
25	406	60	398	98	60	394	97	60	385	95	60
29	415	60	408	99	60	399	96	60	396	96	60
34	433	60	425	98	60	417	96	60	412	95	60
37	446	60	439	98	60	428	96	60	421	94	60
41	441	60	436	99	60	428	97	60	419	95	60
45	446	59	436	98	60	424	95	60	415	93	60
49	460	59	450	98	60	441	96	60	430	93	59
53	459	59	455	99	60	446	97	60	435	95	59
57	463	59	455	98	60	446	96	60	437	94	59
61	462	59	457	99	60	448	97	60	439	95	58
65[a]	465	59	457	98	60	449	97	60	437	94	58
69	468	49	458	98	50	447	96	50	442	94	48
73	456	48	450	99	50	442	97	49	436	96	48
77	468	48	450	96	49	444	95	47	439	94	47
81	464	46	451	97	46	448	97	46	433	93	46
85	462	44	451	98	42	443	96	44	431	93	43
89	457	42	452	99	41	437	96	44	426	93	41
93	448	42	441	99	41	434	97	42	417	93	39
97	429	38	440	103	35	429	100	39	410	96	35
101	416	30	427	103	34	406	98	37	402	97	34
104	419	22	416	99	31	406	97	29	398	95	34
Mean for weeks											
1-13	258		253	98		255	99		252	98	
14-52	416		408	98		400	96		394	95	
53-104	453		447	99		438	97		427	94	

[a] Interim evaluation occurred.

TABLE 7
Mean Body Weights and Survival of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Weeks on Study	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	106	60	108	102	60	109	103	60	107	102	60
2	129	60	128	99	60	127	99	60	126	98	60
3	141	60	140	99	60	140	99	60	139	98	60
4	149	60	148	100	60	149	101	60	149	100	60
5	158	60	158	100	60	157	99	60	158	100	60
6	167	60	165	99	60	164	98	60	163	97	60
7	173	60	171	99	60	170	98	60	169	98	60
8	178	60	176	99	60	175	98	60	173	97	60
9	181	60	180	99	60	179	99	60	176	98	60
10	182	60	180	99	60	180	99	60	177	97	60
11	186	60	185	99	60	185	99	60	182	98	60
12	190	60	189	99	60	188	99	60	185	97	60
13	194	60	193	99	60	192	99	60	187	96	60
14	195	60	194	100	60	193	99	60	190	97	60
18	200	60	200	100	60	200	100	60	196	98	60
21	204	60	205	100	60	204	100	60	199	97	60
25	212	60	210	99	60	210	99	60	203	96	60
29	218	60	217	99	60	214	98	60	210	96	60
33	225	60	225	100	60	224	99	60	218	97	60
37	230	60	230	100	60	226	99	60	221	96	60
41	235	60	236	100	60	233	99	60	226	96	60
45	242	60	243	100	60	233	96	60	234	97	60
49	253	60	252	100	60	245	97	59	240	95	60
54	263	59	263	100	60	257	98	59	248	94	60
58	273	58	269	98	60	262	96	59	254	93	60
62	279	58	276	99	60	269	96	59	260	93	60
66[a]	287	53	284	99	57	278	97	53	271	95	53
69	288	47	290	101	47	278	97	46	274	95	50
74	300	47	300	100	47	286	95	46	278	93	48
78	306	46	307	100	47	291	95	45	286	93	47
82	310	46	313	101	47	298	96	44	288	93	46
86	319	42	318	100	47	304	95	44	291	91	46
90	319	41	323	101	47	306	96	44	293	92	44
94	327	37	326	100	46	308	94	41	295	90	41
98	326	35	323	99	45	307	94	39	297	91	38
102	336	31	331	99	38	310	92	39	302	90	34
105	327	31	323	99	36	308	94	39	292	89	34
Mean for weeks											
1-13	164		163	99		163	99		161	98	
14-52	221		221	100		218	99		214	97	
53-105	304		303	100		290	95		281	92	

[a] Interim evaluation occurred.

Hematology, Clinical Chemistry, Plasma Barium Levels, and Bone Analyses

Hematologic and clinical chemistry parameters measured at the 15-month interim evaluation were considered to be within the range of normal values (Table H3). The results of plasma barium and bone analyses are presented in Table 8 and Appendix I. Plasma barium levels were significantly increased in males receiving 2,500 ppm and all exposed groups of females (Table I1). The density of femoral bone in rats that received 2,500 ppm was similar to that of the controls (Table I3). Barium levels in all portions of femoral bone were approximately 400 times greater in males and females receiving 2,500 ppm than in controls (Table I4). Calcium levels in the upper portion of the femoral bone of male and female rats receiving 2,500 ppm were slightly but significantly lower than those of the controls. Phosphorus levels in exposed males and females were similar to those in the controls.

Pathology and Statistical Analyses of Results

This section describes the statistically significant or biologically noteworthy decreases in the incidences of mononuclear cell leukemia and neoplasms and nonneoplastic lesions of the adrenal gland and mammary gland. There were no increased incidences of neoplasms in rats receiving barium chloride dihydrate. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, the statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group, and historical control incidences for biologically significant neoplasms mentioned in this section are presented in Appendix A for male rats and Appendix B for female rats.

TABLE 8
Plasma Barium and Bone Analyses of Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

Dose (ppm)	0	500	1,250	2,500
Male				
Plasma barium (μg/mL)	0.98 ± 0.06	1.00 ± 0.07	1.23 ± 0.06*	1.68 ± 0.07**
Bone density (mg/mL)	1.64 ± 0.03			1.64 ± 0.02
Femur barium (ppm)				
Upper portion	3.7 ± 0.8			1,311.8 ± 20.4**
Middle portion	3.9 ± 1.4			1,684.5 ± 20.8**
Lower portion	3.4 ± 0.8			1,221.4 ± 15.3**
Female				
Plasma barium (μg/mL)	0.74 ± 0.05	0.99 ± 0.06**	0.97 ± 0.05**	1.43 ± 0.06**
Bone density (mg/mL)	1.69 ± 0.07			1.66 ± 0.02
Femur barium (ppm)				
Upper portion	2.1 ± 1.0			1,181.1 ± 30.8**
Middle portion	5.5 ± 2.1			1,463.5 ± 37.7**
Lower portion	2.5 ± 1.0			1,113.8 ± 29.5**

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error for plasma barium and femur barium levels; mean ± standard deviation for bone density. Bone density and femur barium levels were not measured for groups receiving 500 and 1,250 ppm.

Multiple organs: Mononuclear cell leukemia was not observed in males at 15 months (Table A1). However, at 2 years, there was a significant negative trend in the incidence of mononuclear cell leukemia in males and the incidences in exposed male groups were significantly decreased (Tables 9 and A3). The decreased incidence of this lethal neoplasm may account for the marginal increase in survival of exposed males (Figure 1). The incidences of mononuclear cell leukemia in exposed females were similar to that in the controls (0 ppm, 15/50; 500 ppm, 13/50; 1,250 ppm, 9/50; 2,500 ppm, 9/50; Table B3).

Adrenal gland: A significant negative trend in the incidence of adrenal medulla pheochromocytoma (benign or malignant) was observed in male rats (13/49, 11/50, 12/49, 6/50; Table A3). The incidence of this neoplasm in the 2,500 ppm males was significantly decreased. The incidences of adrenal medulla hyperplasia in exposed male rats were similar to that in the controls (7/49, 11/50, 5/49, 9/50; Table A5). Incidences of adrenal medulla pheochromocytoma and hyperplasia in exposed females were similar to those in controls (Tables B3 and B4).

Mammary gland: A significant negative trend in the incidence of mammary gland neoplasms (fibroadenoma, adenoma, or carcinoma) was observed in female rats (17/50, 21/50, 13/50, 11/50; Table B3).

TABLE 9
Incidences of Mononuclear Cell Leukemia in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	0	500	1,250	2,500
Mononuclear Cell Leukemia[a]				
Overall rate[b]	35/50 (70%)	25/50 (50%)	26/50 (52%)	15/50 (30%)
Adjusted rate[c]	72.8%	56.5%	60.1%	37.0%
Terminal rate[d]	9/22 (41%)	13/31 (42%)	12/29 (41%)	8/33 (24%)
First incidence (days)	305	520	590	564
Life table test[e]	P<0.001N	P=0.031N	P=0.036N	P<0.001N
Logistic regression test[e]	P<0.001N	P=0.033N	P=0.055N	P<0.001N

[a] Historical incidence for 2-year drinking water studies with untreated control groups (mean ± standard deviation): 164/281 (58.4% ± 12.8%); range 40%-70%
[b] Number of animals with neoplasm per number of rats necropsied
[c] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[d] Observed incidence in animals surviving until the end of the study
[e] In the control column are the P values associated with the trend test. In the dosed group columns are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression analysis regards these lesions as nonfatal. A negative trend or a lower incidence in a dose group is indicated by N.

MICE

15-DAY STUDY

All mice survived to the end of the study (Table 10). The final mean body weights of all exposed groups of male and female mice were similar to those of the controls. There were no chemical-related clinical findings of toxicity. Water consumption by exposed groups was similar to that by the controls. Drinking water levels of 40, 80, 173, 346, or 692 ppm barium chloride dihydrate were estimated to deliver daily doses of 5, 10, 20, 40, or 70 mg barium/kg body weight to males and 5, 10, 15, 40, or 85 mg barium/kg body weight to females. The absolute and relative liver weights of females exposed to 692 ppm and the relative liver weights of 692 ppm males were significantly greater than those of controls (Table F4). No treatment-related histopathologic lesions were found.

TABLE 10
Survival, Mean Body Weights, and Water Consumption of Mice in the 15-Day Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Week 1	Week 2
Male							
0	5/5	28.7 ± 0.8	31.3 ± 1.4	2.6 ± 0.7		5.2	7.1
40	5/5	28.3 ± 1.0	30.3 ± 0.6	2.0 ± 0.4	97	4.4	5.4
80	5/5	27.9 ± 0.7	30.2 ± 0.7	2.3 ± 0.3	96	6.3	5.8
173	5/5	27.7 ± 0.7	30.8 ± 0.8	3.1 ± 0.2	98	5.4	6.2
346	5/5	27.5 ± 0.6	29.4 ± 0.5	1.9 ± 0.5	94	6.8	5.5
692	5/5	27.4 ± 1.0	30.3 ± 1.0	2.9 ± 0.2	97	5.5	4.9
Female							
0	5/5	21.3 ± 0.4	23.1 ± 0.4	1.8 ± 0.1		4.2	4.4
40	5/5	22.5 ± 0.5	24.2 ± 0.5	1.7 ± 0.8	105	3.7	3.2
80	5/5	21.8 ± 0.4	24.8 ± 0.7	3.0 ± 0.4	108	4.5	4.7
173	5/5	21.4 ± 0.4	23.0 ± 0.6	1.7 ± 0.4	100	3.6	4.1
346	5/5	22.4 ± 0.6	23.8 ± 0.2	1.3 ± 0.6	103	5.6	3.4
692	5/5	21.8 ± 0.4	24.0 ± 0.7	2.2 ± 0.5	104	5.1	4.8

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

13-Week Study

Six males and seven females that received 4,000 ppm and one male that received 125 ppm died or were killed moribund during the study (Table 11). All but one of these deaths occurred on or after week 5 of the study. The final mean body weights of male and female mice receiving 4,000 ppm were significantly lower (>30%) than those of the controls. Water consumption by male mice in the 4,000 ppm group was 18% lower than that by the controls; water consumption by other exposed groups of male and female mice was similar to that by the controls. Drinking water levels of 125, 500, 1,000, 2,000, or 4,000 ppm barium chloride dihydrate were estimated to deliver daily doses of 15, 55, 100, 205, or 450 mg barium/kg body weight to males and 15, 60, 110, 200, or 495 mg barium/kg body weight to females. Chemical-related clinical findings of toxicity were limited to debilitation in the surviving male and female mice that received 4,000 ppm.

The forelimb grip strength of female mice receiving 4,000 ppm was significantly lower than that of the controls at 90 days, possibly due to debilitation (Table G3). There were no significant differences in the other behavioral parameters measured.

The absolute and/or relative liver weights of mice exposed to 1,000, 2,000, and 4,000 ppm and the absolute and relative thymus weights of 4,000 ppm mice were significantly lower than those of the controls (Table F5).

Chemical-related nephropathy was observed in 10 male and nine female mice receiving 4,000 ppm; none was observed in the controls or the other exposed groups of mice. Grossly, the kidneys were pale and had roughened surfaces. The nephropathy consisted of mild to moderate, multifocal to diffuse tubule dilatation, regeneration, and atrophy with sporadic birefringent crystals in the lumens of the atrophic tubules (Plate 3). In the mildly affected kidneys, tubule dilatation was most prominent in the outer stripe of the medulla and extended into the medullary rays and toward the capsular surface of the cortex. Dilated tubules had flattened epithelium (atrophy) and contained pale yellow, refractile crystals and small, pale, eosinophilic casts. The casts were finely granular with smooth or rough surfaces and varied in shape from irregularly rounded to elongated to cellular. Tubule cell regeneration was present within the foci of tubule dilatation, and many tubules were decreased in diameter and lined with closely packed epithelial cells with a scant amount of basophilic cytoplasm (Plate 4). An increased amount of fibrous connective tissue was present in the interstitium of the moderately affected kidneys, with most of the outer medulla and cortex consisting of dilated, regenerative, or atrophic tubules. Additionally, subtle evidence of renal tubule degeneration was observed in one male mouse that was exposed to 2,000 ppm. It could not be determined if this was a compound-related effect.

Atrophy of the thymus and spleen was observed in the majority of early death male and female mice receiving 4,000 ppm. Grossly, the thymuses were small or not visible and the spleens were small and mottled or discolored. The thymic lesions consisted of necrosis or moderate to marked depletion of thymic lymphocytes. In some mice, the thymus consisted of only remnants of stromal cells, while in others, the thymus was not even identifiable in the tissue section. The splenic atrophy was characterized by a diminution of the hematopoietic elements of the red pulp and depletion of lymphocytes in the periarteriolar lymphoid sheath, leaving only a thin layer of mature lymphocytes surrounding the arterioles.

Dose selection rationale: Because of mortality, lower final mean body weights, decreased water consumption, and the presence of renal, thymic, and splenic lesions observed in male and female mice receiving 4,000 ppm, the high dose selected for the 2-year study was 2,500 ppm.

TABLE 11
Survival, Mean Body Weights, and Water Consumption of Mice in the 13-Week Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)	Water Consumption[c]	
		Initial	Final	Change		Week 2[d]	Week 13
Male							
0	10/10	25.7 ± 0.3	38.7 ± 0.6	12.9 ± 0.7		5.0	4.8
125	9/10[e]	25.3 ± 0.6	38.1 ± 1.5	13.1 ± 1.5	99	5.5	5.2
500	10/10	25.5 ± 0.5	38.9 ± 1.0	13.4 ± 0.9	101	5.5	3.8
1,000	10/10	25.3 ± 0.6	37.3 ± 1.1	12.0 ± 0.9	96	5.0	4.1
2,000	10/10	25.9 ± 0.5	38.9 ± 1.3	13.1 ± 1.0	101	5.5	4.5
4,000	4/10[f]	24.9 ± 0.9	26.8 ± 2.0**	−0.1 ± 2.5**	69	4.0	4.0
Female							
0	10/10	19.2 ± 0.3	29.9 ± 0.8	10.8 ± 0.7		4.0	3.3
125	10/10	19.8 ± 0.5	29.3 ± 0.9	9.5 ± 0.6	98	4.0	3.5
500	10/10	19.3 ± 0.4	28.1 ± 1.0	8.9 ± 0.8	94	4.0	3.6
1,000	10/10	19.4 ± 0.3	29.7 ± 1.1	10.4 ± 1.0	99	4.0	3.4
2,000	10/10	19.7 ± 0.3	27.8 ± 1.1	8.1 ± 0.9*	93	4.5	2.9
4,000	3/10[g]	19.4 ± 0.3	15.4 ± 1.9**	−4.3 ± 1.6**	52	5.0	3.8[h]

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Number of animals surviving/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[c] Water consumption is expressed as grams per animal per day.
[d] Week 1 values were not used because of excess water spillage.
[e] Week of death: 8
[f] Week of death: 2, 5, 7, 7, 11, 12
[g] Week of death: 9, 10, 11, 11, 12, 12, 13
[h] Value from week 12 used

2-YEAR STUDY

Survival

Estimates of survival probabilities for male and female mice are shown in Table 12 and in the Kaplan-Meier curves in Figure 3. Survival of male and female mice receiving 2,500 ppm was significantly lower than that of the controls. The reduction in survival of female mice that received 2,500 ppm was first observed at week 15 of the study and by the end of the 2 years only 26% of the animals were alive. Survival in male mice receiving 2,500 ppm was noticeably decreased by week 65. The reduced survival of exposed mice was attributed to chemical-related renal lesions.

Water and Compound Consumption

Water consumption by exposed mice was similar to that by the controls (Tables K3 and K4). Concentrations of 500, 1,250, and 2,500 ppm barium chloride dihydrate delivered estimated daily doses of 30, 75, or 160 mg barium/kg body weight to males and 40, 90, or 200 mg barium/kg body weight to females.

Body Weights and Clinical Findings

Final mean body weights of males and females exposed to 2,500 ppm were lower than those of controls (Figure 4 and Tables 13 and 14). There were no significant clinical findings of organ-specific toxicity. Animals killed moribund or dying before the end of the study had moderate to marked weight loss.

TABLE 12
Survival of Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	0	500	1,250	2,500
Male				
Animals initially in study	60	60	59	60
15-month interim evaluation[a]	9	10	10	10
Natural deaths	1	2	4	8
Moribund kills	5	5	6	10
Animals surviving to study termination	45[e]	43	39[e]	32
Percent probability of survival at end of study[b]	89	86	81	65
Mean survival (days)[c]	666	666	657	624
Survival analysis[d]	P=0.001	P=0.977	P=0.378	P=0.009
Female				
Animals initially in study	60	60	60	60
15-month interim evaluation[a]	10	7	10	6
Natural deaths	3	5	5	6
Moribund kills	9	11	9	35
Animals surviving to study termination	38[e]	37	36	13
Percent probability of survival at end of study	76	71	73	26
Mean survival (days)	663	655	666	463
Survival analysis	P<0.001	P=0.535	P=0.911	P<0.001

[a] Censored from survival analyses
[b] Kaplan-Meier determinations based on the number of animals alive on the first day of terminal sacrifice
[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 dosed columns.
[e] Includes one animal that died during the last week of the study.

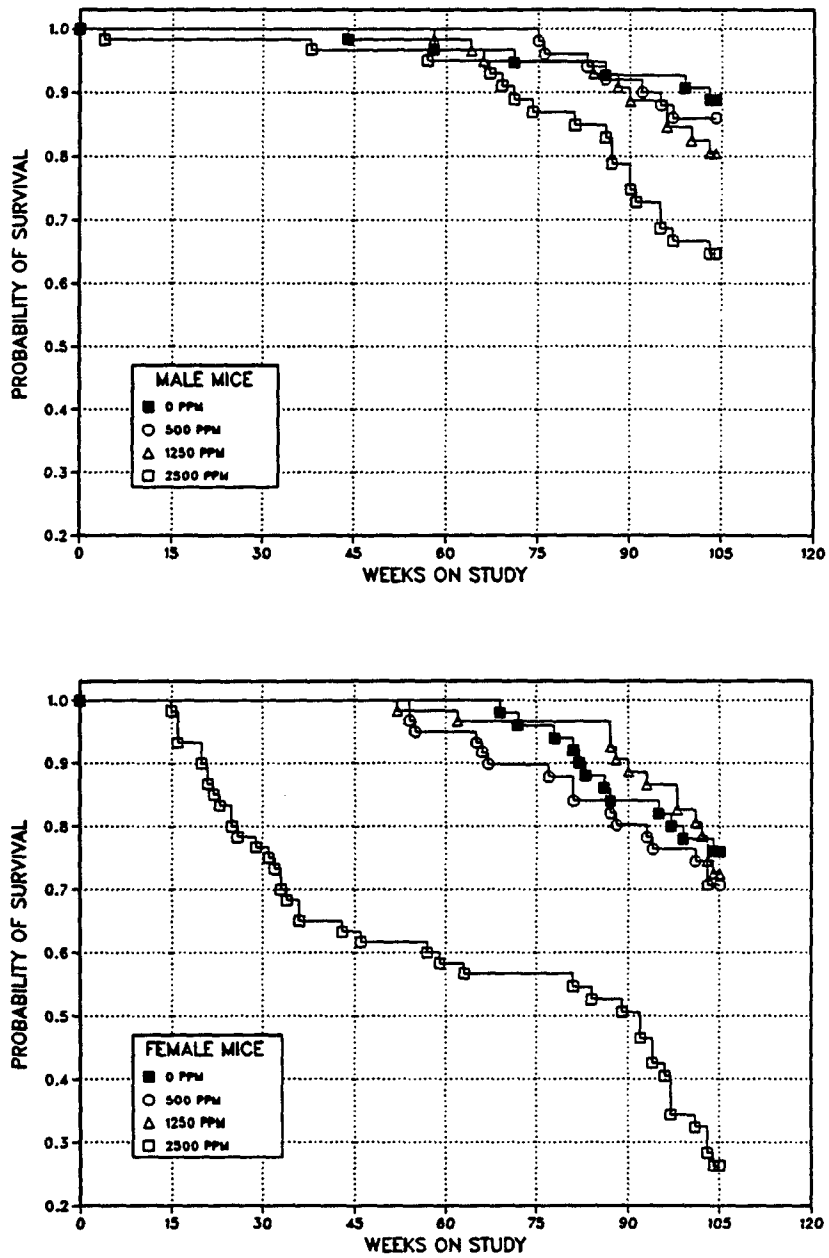

FIGURE 3
Kaplan-Meier Survival Curves for Male and Female Mice Administered Barium Chloride Dihydrate in Drinking Water for 2 Years

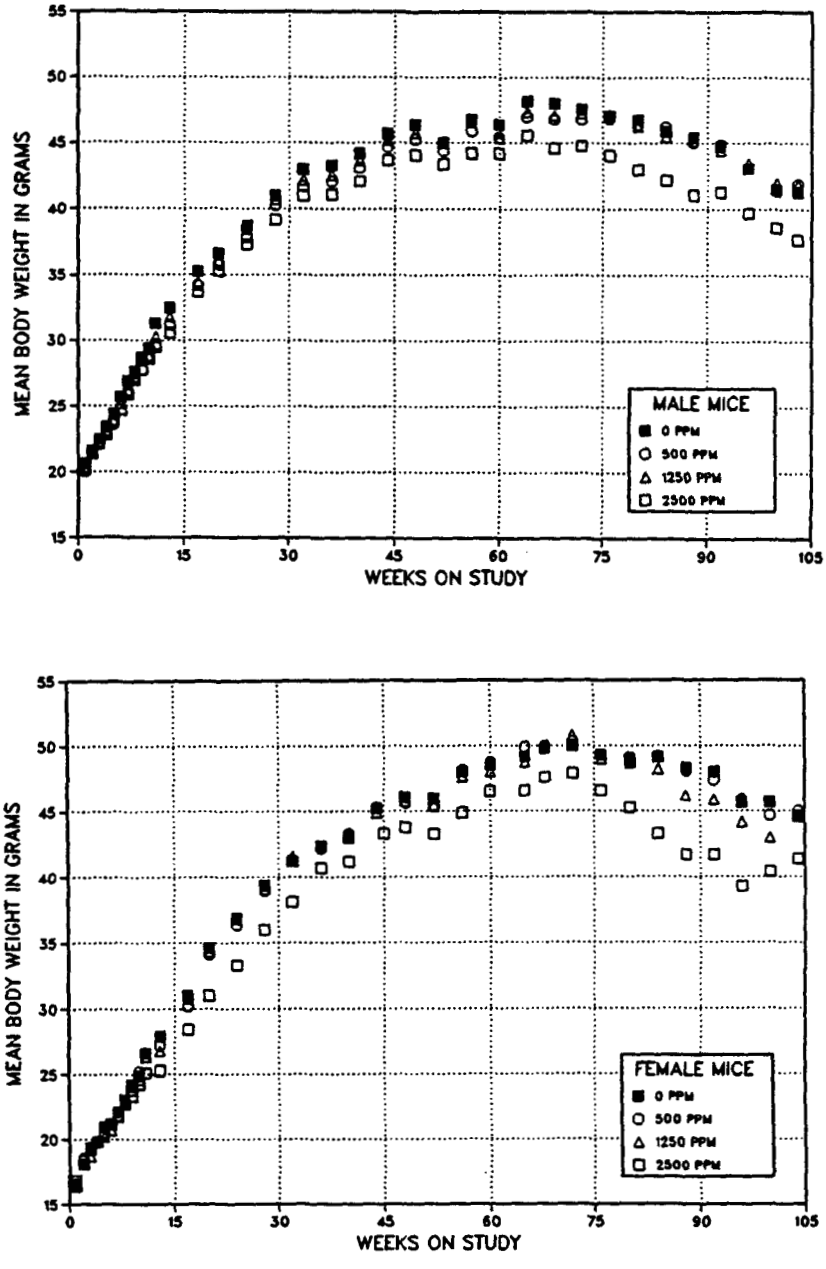

FIGURE 4
Growth Curves for Male and Female Mice Administered Barium Chloride Dihydrate in Drinking Water for 2 Years

TABLE 13
Mean Body Weights and Survival of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Weeks on Study	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	20.6	60	20.0	97	60	20.2	98	59	20.3	99	60
2	21.6	60	21.4	99	60	21.4	99	59	21.5	100	60
3	22.5	60	22.3	99	60	22.1	98	59	22.3	99	60
4	23.4	60	23.1	99	60	23.0	98	59	22.8	97	60
5	24.4	60	23.6	97	60	23.9	98	59	23.8	98	59
6	25.7	60	24.7	96	60	25.2	98	59	24.7	96	59
7	26.9	60	26.1	97	60	26.2	97	59	25.9	96	59
8	27.6	60	27.5	100	60	27.2	99	59	27.0	98	59
9	28.7	60	27.8	97	60	28.5	99	59	27.8	97	59
10	29.4	60	28.7	98	60	28.8	98	59	28.6	97	59
11	31.1	60	29.7	96	60	30.2	97	59	29.4	95	59
13	32.5	60	31.2	96	60	31.8	98	59	30.6	94	59
17	35.3	60	34.2	97	60	34.5	98	59	33.7	96	59
20	36.6	60	35.8	98	60	36.1	99	59	35.3	96	59
24	38.7	60	37.9	98	60	38.5	100	59	37.3	96	59
28	41.0	60	40.3	98	60	40.7	99	59	39.2	96	59
32	43.0	60	41.7	97	60	42.2	98	59	41.0	95	59
36	43.3	60	42.1	97	60	42.6	98	59	41.1	95	59
40	44.2	60	43.1	98	60	43.7	99	59	42.1	95	58
44	45.7	59	44.7	98	60	45.2	99	59	43.7	96	58
48	46.4	59	45.3	98	60	45.8	99	59	44.1	95	58
52	45.0	59	44.4	99	60	45.0	100	59	43.4	96	58
56	46.8	59	45.9	98	60	46.6	100	59	44.2	94	58
60	46.4	58	45.4	98	60	45.4	98	58	44.2	95	57
64	48.2	58	47.0	98	60	47.4	98	57	45.6	95	57
68[a]	48.0	49	46.8	98	50	47.1	98	46	44.6	93	46
72	47.6	48	46.8	98	50	47.3	99	46	44.8	94	44
76	47.1	48	46.9	100	49	47.2	100	46	44.1	94	43
80	46.8	48	46.4	99	48	46.3	99	46	43.0	92	43
84	45.9	48	46.2	101	47	45.5	99	46	42.2	92	42
88	45.5	47	45.1	99	46	45.2	99	44	41.1	90	39
92	44.8	47	44.9	100	46	44.5	99	43	41.3	92	36
96	43.1	47	43.1	100	44	43.5	101	42	39.7	92	34
100	41.5	46	41.4	100	43	42.0	101	40	38.6	93	33
103	41.3	46	41.9	102	43	41.9	102	40	37.7	91	33
Mean for weeks											
1-13	26.2		25.5	97		25.7	98		25.4	97	
14-52	41.9		41.0	98		41.4	99		40.1	96	
53-103	45.6		45.2	99		45.4	100		42.4	93	

[a] Interim evaluation occurred.

TABLE 14
Mean Body Weights and Survival of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Weeks on Study	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	16.4	60	16.6	101	60	16.4	100	60	16.8	102	60
2	18.1	60	18.5	102	60	18.1	100	60	18.3	101	60
3	19.3	60	19.4	101	60	18.7	97	60	19.2	100	60
4	19.8	60	19.8	100	60	19.9	101	60	19.8	100	60
5	20.9	60	20.4	98	60	20.2	97	60	20.5	98	60
6	21.1	60	21.3	101	60	20.7	98	60	21.2	101	60
7	22.1	60	21.8	99	60	22.1	100	60	21.7	98	60
8	23.0	60	23.0	100	60	22.8	99	60	22.7	99	60
9	24.2	60	23.8	98	60	24.1	100	60	23.3	96	60
10	24.9	60	25.2	101	60	24.6	99	60	24.2	97	60
11	25.9	60	25.8	100	60	25.8	100	60	24.6	95	60
13	27.9	60	27.2	98	60	26.8	96	60	25.3	91	60
17	31.0	60	30.2	97	60	30.8	99	60	28.4	92	56
20	34.6	60	34.1	99	60	34.3	99	60	31.0	90	54
24	36.9	60	36.4	99	60	36.8	100	60	33.3	90	50
28	39.4	60	39.0	99	60	39.1	99	60	36.0	91	47
32	41.2	60	41.3	100	60	41.6	101	60	38.1	93	44
36	42.4	60	42.2	100	60	42.4	100	60	40.7	96	39
40	43.0	60	43.3	101	60	43.4	101	60	41.2	96	39
44-45	45.3	60	45.3	100	60	44.4	98	60[a]	43.3	96	38
48	46.1	60	45.7	99	60	45.8	99	60	43.8	95	37
52	46.0	60	45.4	99	60	45.5	99	59	43.3	94	37
56	48.0	60	48.1	100	57	47.6	99	59	44.9	94	37
60	48.5	60	48.7	100	57	48.0	99	59	46.5	96	35
65	49.2	60	49.9	101	56	48.8	99	58	46.6	95	34
68[b]	49.8	50	50.0	100	47	50.0	100	48	47.6	96	28
72	50.0	48	50.3	101	47	50.8	102	48	47.9	96	28
76	49.3	48	49.3	100	47	49.0	99	48	46.6	95	28
80	48.9	47	49.1	100	46	48.7	100	48	45.3	93	28
84	49.1	44	49.2	100	44	48.2	98	48	43.3	88	26
88	48.3	42	48.1	100	42	46.2	96	45	41.7	86	26
92	48.0	42	47.4	99	42	45.9	96	44	41.7	87	23
96	45.7	41	45.9	100	40	44.2	97	43	39.3	86	20
100	45.7	39	44.7	98	40	43.0	94	40[a]	40.4	88	17
Mean for weeks											
1-13	22.0		21.9	100		21.7	99		21.5	98	
14-52	40.6		40.3	99		40.4	100		37.9	93	
53-100	48.4		48.4	100		47.5	98		44.3	92	

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

Hematology, Clinical Chemistry, and Plasma Barium Levels

There were no significant differences in hematology or clinical chemistry parameters between control and exposed mice (Table H4). There were dose-related significant increases in plasma barium levels in exposed groups of male and female mice (Tables 15 and I2).

Pathology and Statistical Analyses of Results

This section describes the statistically or biologically noteworthy changes in the incidences of neoplasms or nonneoplastic lesions of the kidney, hematopoietic system, and liver. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary neoplasms that occurred at an incidence of at least 5% in at least one animal group are presented in Appendix C for male mice and Appendix D for female mice. No increased incidences of neoplasms were observed in exposed mice. The incidences of many neoplasms were lower in female mice exposed to 2,500 ppm than in the controls because of the marked reduction in survival of this group.

Kidney: The incidence of nephropathy was significantly increased in male and female mice receiving 2,500 ppm (Tables 16, C4, and D4). The nephropathy was morphologically distinct from the spontaneous degenerative lesions that are commonly observed in aging B6C3F$_1$ mice. The nephropathy was characterized by extensive regeneration of cortical and medullary renal tubule epithelium, tubule dilatation, hyaline cast formation, multifocal interstitial fibrosis, and, in some kidneys, glomerulosclerosis (Plates 5, 6, 7, and 8). These lesions were accompanied by the presence of irregularly shaped aggregates of brown crystals located both within renal tubule lumens and in the interstitium. Some of the crystals appeared granular, while others had both straight and rounded edges and ranged in size from 8 to 50 μm. They were weakly anisotropic. Their location was difficult to determine because of their size and the possibility that dislocation had occurred with sectioning. However, most appeared to be located in tubule lumens of both the cortex and medulla, and in the lumen of the renal pelvis. The quantity of the crystals ranged from few to numerous in a particular kidney. While the chemical composition of the crystals is unknown, they may consist of precipitated barium or barium salts. The kidney lesions were considered to be the cause of the morbidity or death for most of the animals which did not survive to the end of the study.

TABLE 15
Plasma Barium Levels in Mice at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

Dose (ppm)	0	500	1,250	2,500
Male				
n	8	10	10	9
Barium (μg/mL)	0.62 ± 0.02	0.77 ± 0.04**	0.89 ± 0.05**	1.49 ± 0.14**
Female				
n	8	7	6	6
Barium (μg/mL)	0.52 ± 0.05	0.74 ± 0.09*	1.01 ± 0.06**	1.35 ± 0.19**

* Significantly different ($P \leq 0.05$) from the control group by Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error

TABLE 16
Incidences of Nonneoplastic Lesions of the Kidney of Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Dose (ppm)	0	500	1,250	2,500
Male				
15-Month Interim Evaluation				
Renal Tubule[a]	9	10	10	10
Crystals[b]	0	0	0	1
2-Year Study				
Renal Tubule	50	50	48	50
Crystals	0	0	1	21**(2.2)[c]
Cyst	3	1	4	2
Nephropathy	1	0	2	19**(3.6)
Female				
15-Month Interim Evaluation				
Renal Tubule	10	7	10	6
Casts	0	0	0	1
2-Year Study				
Renal Tubule	50	53	50	54
Crystals	0	0	0	36**(2.0)
Nephropathy	0	2	1	37**(3.6)

** Significantly different (P≤0.01) from the control group by life table analysis
[a] Number of mice with kidney examined microscopically
[b] Number of mice with lesion
[c] Average severity grade of lesions in affected animals: 1 = minimal, 2 = mild, 3 = moderate, 4 = marked

Hematopoietic system: At the 15-month interim evaluation the absolute and relative spleen weights of female mice exposed to 2,500 ppm were significantly lower than those of controls (Table F6). In 2,500 ppm male and/or female mice there were increased incidences of lymphoid depletion of the spleen (male: 0 ppm, 0/50; 500 ppm, 8/50; 1,250 ppm, 4/48; 2,500 ppm, 9/50; female: 2/50, 2/53, 0/50, 11/52; Tables C4 and D4), thymus (male: 0/39, 0/42, 2/44, 5/35; female: 1/43, 1/46, 0/47, 12/38), and mesenteric lymph node (male: 0/49, 1/47, 0/46, 4/39; female: 0/49, 0/49, 0/49, 10/39). Because the majority of the thymic and splenic lymphoid lesions occurred in the 2,500 ppm animals that were found dead or killed moribund relatively early in the study, it is likely that these lesions are the result of debilitation associated with nephropathy.

Liver: There was a significant negative trend in the incidence of hepatocellular adenoma in male mice and the incidence in the 2,500 ppm group was significantly lower than in the controls (24/51, 20/50, 15/48, 8/50; Table C3). The incidence of hepatocellular carcinoma in exposed males was similar to that in the controls (5/51, 7/50, 6/48, 3/50; Table C3).

GENETIC TOXICOLOGY

Barium chloride dihydrate (100 to 10,000 μg/plate) did not induce gene mutations in any of five strains (TA97, TA98, TA100, TA1535, and TA1537) of *Salmonella typhimurium* when tested in a pre-incubation protocol with and without Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9 (Table E1; Zeiger *et al.*, 1992). In contrast, barium chloride dihydrate, at concentrations of 250 μg/mL and above, induced gene mutations at the $TK^{+/-}$ locus of L5178Y mouse lymphoma cells in the presence of Aroclor 1254-induced male Fischer 344 rat liver S9; without S9, no increase in the number of mutant colonies was observed (Table E2). At the 1,000 μg/mL concentration, a precipitate of barium chloride dihydrate was observed, and results for this dose point were not considered in making the positive call. In cytogenetic tests with cultured Chinese hamster ovary cells, barium chloride dihydrate did not induce sister chromatid exchanges (Table E3) or chromosomal aberrations (Table E4), with or without Aroclor 1254-induced male Sprague-Dawley rat liver S9. No cell cycle delay was observed at any of the concentrations tested in either assay; precipitation was noted in the chromosomal aberration assay at doses of 2,000 μg/mL and above.

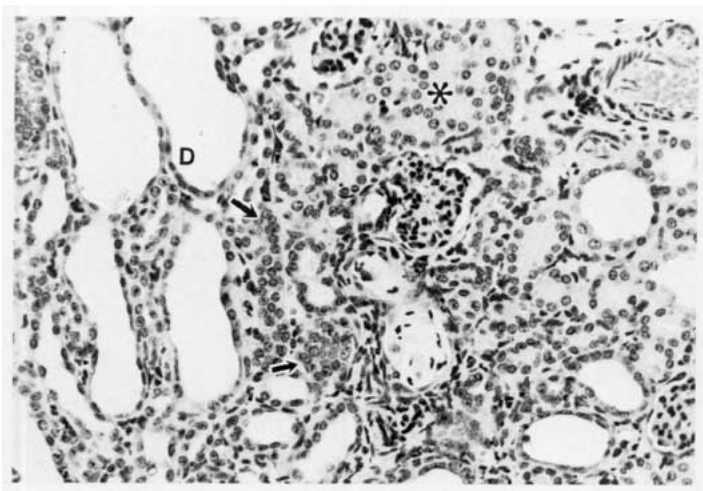

PLATE 1
Focal areas of tubule dilatation (arrows) in a female F344/N rat exposed to 4,000 ppm barium chloride dihydrate in the 13-week drinking water study. H&E, 55×

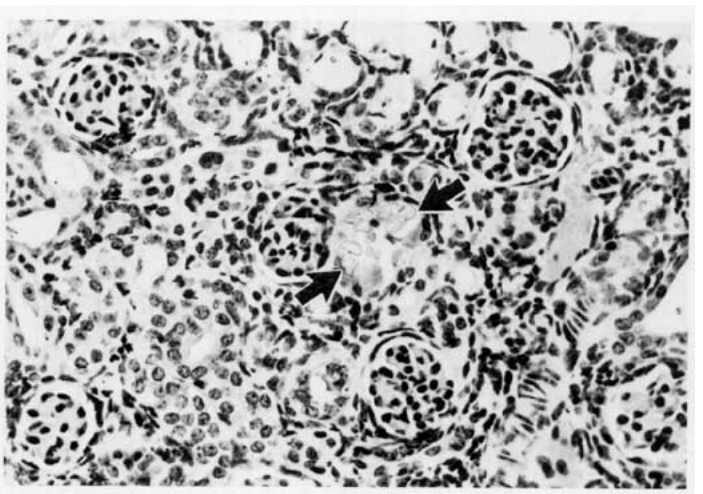

PLATE 2
Higher magnification of Plate 1. Note the scattered dilated renal tubules lined by flattened cuboidal epithelium (arrows). H&E, 280×

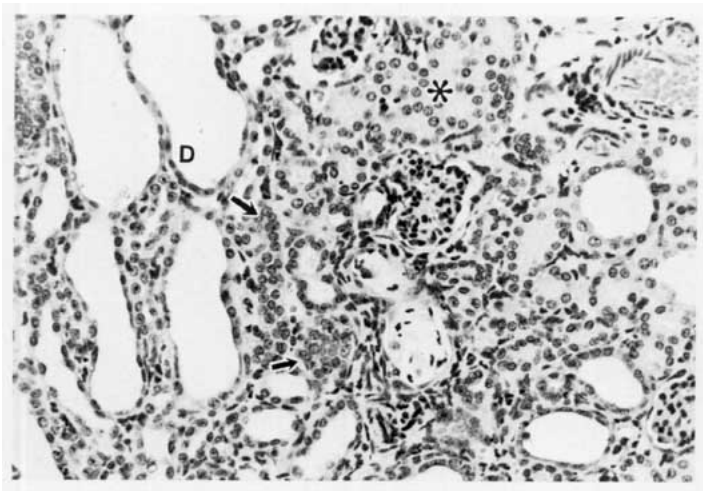

PLATE 3
Focal areas of dilated (D), regenerative (arrows) and normal (*) renal tubules in a female B6C3F$_1$ mouse exposed to 4,000 ppm barium chloride dihydrate in the 13-week drinking water study. H&E, 170×

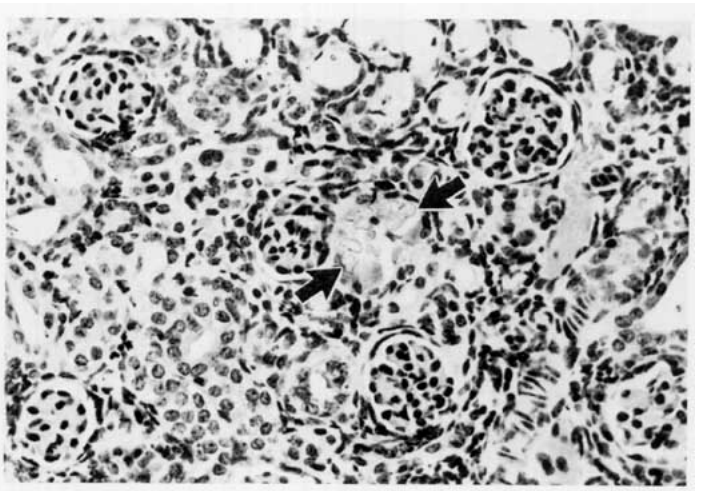

PLATE 4
Aggregates of crystals (arrows) in the tubules of the renal cortex of a female B6C3F$_1$ mouse exposed to 4,000 ppm barium chloride dihydrate in the 13-week drinking water study. H&E, 240×

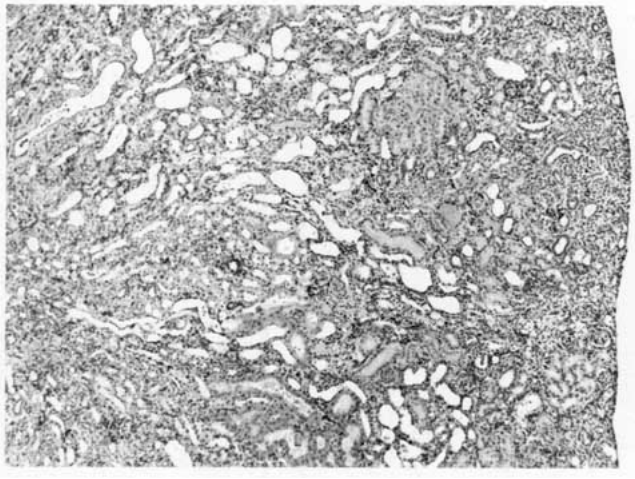

PLATE 5
Diffuse tubule dilatation of the renal medulla and cortex in the kidney of a female B6C3F$_1$ mouse exposed to 2,500 ppm barium chloride dihydrate in the 2-year drinking water study. H&E, 55×

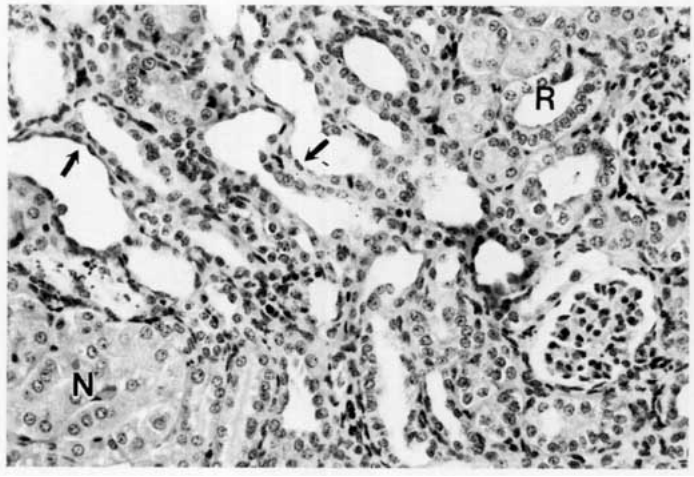

PLATE 6
Higher magnification of Plate 5. Note the dilated tubules lined by flattened epithelium (arrows), regenerative tubules (R) and normal tubules (N). H&E, 210×

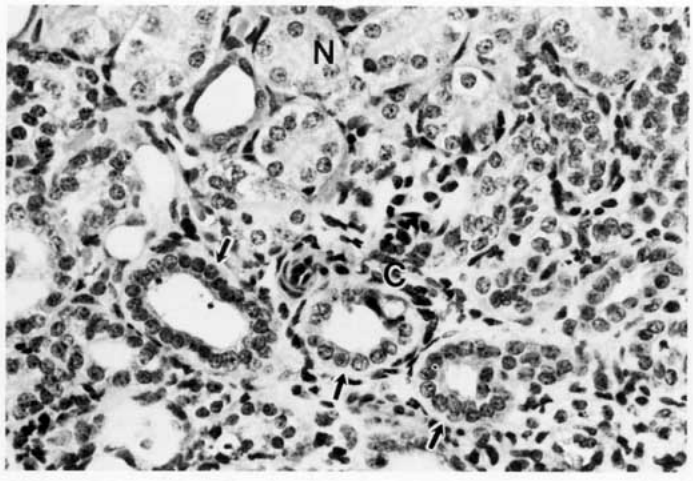

PLATE 7
Tubule cell regeneration (arrows) with an embedded crystal (C) and normal tubules (N) in the kidney of a female B6C3F$_1$ mouse exposed to 2,500 ppm barium chloride dihydrate in the 2-year drinking water study. H&E, 320×

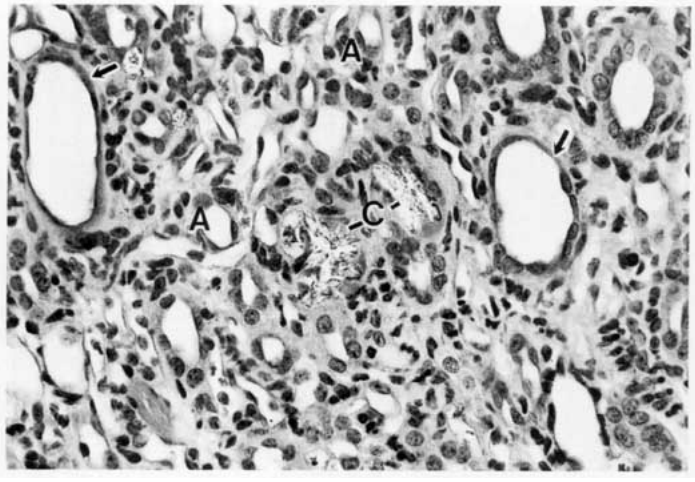

PLATE 8
Dilated (arrows) atrophic tubules (A) and embedded crystals surrounded by increased fibrous connective tissue in the interstitium of the kidney of a female B6C3F$_1$ mouse exposed to 2,500 ppm barium chloride dihydrate in the 2-year drinking water study. H&E, 320×

DISCUSSION AND CONCLUSIONS

Barium chloride dihydrate is used in pigments, aluminum refining, leather tanning and coloring, the manufacture of magnesium metal, ceramics, glass, and paper products, as a pesticide, and as a cardiac stimulant in human medicine (*Merck Index*, 1983). The chemical was nominated by the National Cancer Institute for study because of widespread human exposure and because of reported transformation of cervical cells to bizarre multinucleated cells (Ayre and LeGuerrier, 1967). Toxicology and carcinogenicity studies were conducted by administering barium chloride dihydrate (99% pure) in drinking water to F344/N rats and B6C3F$_1$ mice for 15 days, 13 weeks, and 2 years. Drinking water was selected as the route of administration because of the high water solubility of barium chloride dihydrate and because ingestion is the primary route for human exposure.

Barium chloride dihydrate produced minimal and biologically insignificant effects in rats and mice in the NTP 15-day studies. This lack of an effect was due to the low doses of barium chloride dihydrate received by the animals. Rats and mice receiving the highest concentrations of barium chloride dihydrate (2,000 ppm and 692 ppm) received estimated daily doses of 200 and 100 mg/kg, respectively. Borzelleca *et al.* (1988) reported that barium chloride at daily doses of up to 209 mg/kg administered in water by gavage for 10 days was not toxic to Sprague-Dawley rats. At a daily dose of 300 mg/kg, barium chloride produced minimal effects (decreases in ovary-weight-to-brain-weight ratio and blood urea nitrogen). Because of this lack of chemical-related toxicity, higher concentrations of barium chloride dihydrate were used in the drinking water of rats and mice in the 13-week studies.

The major toxic effects observed in the 13-week studies were limited to rats and mice receiving the highest concentration of 4,000 ppm barium chloride dihydrate. The effects included lower final mean body weights and/or mean body weight gains, decreased water consumption (rats and male mice), mortality, and renal toxicity. Based on these data, the no-observable-effect concentration for barium chloride dihydrate in drinking water for rats and mice was estimated at approximately 2,000 ppm. It was concluded that rats and mice are equally sensitive to the toxic effects of barium chloride dihydrate, although the estimated amount of chemical per unit body weight received by mice was two to three times greater than that received by rats, and mice in the 2,000 ppm group consumed as much barium chloride dihydrate as rats in the 4,000 ppm group without any detectable toxicity. This conclusion was made because the estimated doses of barium chloride dihydrate per unit surface area (a better measure of dose than per unit body weight because of its proportionality to metabolic body weight) received by rats and mice were similar.

The kidney is the primary site of toxicity for barium chloride dihydrate. Nephropathy occurred in rats and mice receiving 4,000 ppm. The lesion was less severe in rats than in mice and was characterized by tubule dilatation. In addition to renal tubule dilatation, the lesion in mice was also characterized by renal tubule atrophy and by the presence of crystals primarily in the lumen of renal tubules. Similar lesions occurred in guinea pigs administered barium chloride orally (50 mg/kg per day) for 30 days (Izrael'son, 1967). As in rats, these lesions were not accompanied by crystal formation.

Although the chemical identity of the crystals found in the kidneys of mice receiving barium chloride dihydrate was not determined, they were probably insoluble barium salts. Radiopaque particles, presumably barium sulfate, have been found in the kidneys of patients suffering from renal failure caused by accidental ingestion of barium chloride (Wetherill *et al.*, 1981). The difference between the species with regard to crystal formation may be due to the concentration of the dose administered, rapidity by which barium ions are eliminated from the kidney, and concentration of coprecipitating ions in urine (e.g., sulfate).

Although barium has been reported to affect cardiovascular parameters resulting in high blood pressure and abnormal electrocardiogram in humans and dogs

(Roza and Berman, 1971; Stokinger, 1981), these effects were not seen in exposed rats in these NTP studies. Renal vasculature responds to elevated blood pressure by the development of nephrosclerosis (hyaline thickening of the arteriole wall) (Tarazi and Gifford, 1979; Alfery, 1981) which may lead to reduced blood flow within the kidney. This sclerotic lesion was not seen in these NTP studies. Renal tubule atrophy and tubule dilatation, two lesions that are associated with reduced blood flow, were observed in these NTP studies. The kidney was the primary site of toxicity although earlier studies indicated that this organ was not the primary site for deposition or elimination of barium chloride. Barium concentrations in the kidneys of rats dosed orally with barium chloride were lower than the concentrations in the heart, eye, and skeletal muscle of these animals (McCauley and Washington, 1983). Only 7% of barium from an intraperitoneal dose of barium chloride was recovered in the urine, while 20% was recovered in the feces (Bauer *et al.*, 1956; Clary and Tardiff, 1974). However, an association between barium and cardiovascular effects in the present studies does not seem to be likely since no differences in blood pressure or electrocardiogram occurred in rats as a result of barium chloride dihydrate administration.

Lymphoid tissue depletion of the thymus, spleen, and lymph nodes was limited to rats and mice receiving 4,000 ppm barium chloride dihydrate. Because the majority of the animals with this lesion were found dead or killed moribund, the lymphoid depletion was considered to be a result of reduced body weight and stress.

Exposure levels of 0, 500, 1,250, or 2,500 ppm barium chloride dihydrate were selected for the 2-year drinking water studies in rats and mice based on lower mean body weights, mortality, and nephropathy in the 4,000 ppm groups in the 13-week studies. The concentrations used in the 2-year studies were sufficiently high to allow the assessment of the carcinogenic potential of barium chloride dihydrate; this was evidenced by the lower (5% and 11%) final mean body weights of male and female rats receiving 2,500 ppm and the significantly reduced probability of survival in male and female mice receiving 2,500 ppm.

Earlier studies reported that barium deposition occurs preferentially in the most active areas of bone growth (Bligh and Taylor, 1963), but results of later studies indicated that barium deposition occurs primarily in the periosteal, endosteal, and trabecular surfaces of the bone (Ellsasser *et al.*, 1969). Calcium levels in the upper portion of the femoral bone in male and female rats receiving 2,500 ppm were slightly but significantly lower than those in the controls. There was no difference in phosphorus content of femoral bone between control and 2,500 ppm male and female rats.

In the 2-year rat study, there were no increased neoplasm incidences that could be attributed to barium chloride dihydrate administration. Similar results were obtained in Sprague-Dawley rats that received barium chloride in drinking water at concentrations of 1, 10, or 100 mg/L for 16 months (Perry *et al.*, 1985). Barium acetate (another soluble barium salt) administered to Long-Evans rats for their lifetime at a concentration of 5 ppm in drinking water had no effect on survival or neoplasm incidence (Schroeder and Mitchener, 1975a).

Several neoplasms occurred with a dose-related decreased incidence in male rats. These included benign and malignant pheochromocytomas (combined) of the adrenal medulla (0 ppm, 13/49; 500 ppm, 11/50; 1,250 ppm, 12/49; 2,500 ppm, 6/50) and mononuclear cell leukemia (35/50, 25/50, 26/50, 15/50). Barium ions are known to substitute for calcium ions in reactions controlling hormone secretion (Douglas *et al.*, 1983). Barium induced a secretagogic effect on the output of melanocyte stimulating hormone of the mouse pituitary gland. Additionally, barium ions triggered the release of catecholamines from adrenal medullary cells (Izumi *et al.*, 1986). Based on this information, the dose-related decreased incidences of mononuclear cell leukemia and adrenal medulla pheochromocytomas observed in rats could be related to a change in the hormonal profile of these animals. However, such an association is not clear since hormonal profiles of rats in the 2-year study were not determined.

No treatment-related increased incidences of neoplasms were observed in male or female mice in the 2-year study. However, the incidence of hepatocellular adenoma was significantly decreased in 2,500 ppm males. Other marginally decreased neoplasm incidences were attributed to the reduced survival rate of 2,500 ppm mice. No reports were found in the literature that describe neoplastic or

nonneoplastic effects of barium chloride in mice. However, barium acetate administered in drinking water (5 ppm) to Swiss-Webster mice for their lifetime did not induce neoplasms or nonneoplastic lesions (Schroeder and Mitchener, 1975b).

The probability of survival in 2,500 ppm female mice was significantly reduced; 41 females died or were killed moribund. These animals were emaciated and the cause of death or morbidity was attributed to chemical-related nephropathy. The kidneys of female mice that received 2,500 ppm had a granular appearance or abnormal pigmentation; these same mice also exhibited elevated blood urea nitrogen levels. These elevated levels are indicative of renal toxicity.

The nephropathy was characterized by dilatation, regeneration, and atrophy of the renal tubule epithelium and by the presence of crystals (probably insoluble barium salt) within renal tubules in the medulla. The renal lesions were similar to those observed in exposed rats and mice in the 13-week studies. The occurrence of chemical-related kidney lesions in mice, but not in rats, in the 2-year studies may be due to the two- to fourfold increase in the amount of barium chloride dihydrate consumed by mice per unit body weight as compared to rats.

Barium chromate is the only barium compound for which there is sufficient evidence that barium is a possible human carcinogen (IARC, 1980). However, the contribution of barium to the carcinogenicity of barium chromate was not known. Since barium chloride in the NTP studies was not carcinogenic to rats or mice of either sex, it is concluded that the carcinogenicity of barium chromate was solely due to the chromate ion.

CONCLUSIONS

Under the conditions of these 2-year drinking water studies, there was *no evidence of carcinogenic activity** of barium chloride dihydrate in male or female F344/N rats that received 500, 1,250, or 2,500 ppm. There was *no evidence of carcinogenic activity* of barium chloride dihydrate in male or female B6C3F$_1$ mice that received 500, 1,250, or 2,500 ppm.

There were chemical-related increased incidences of nephropathy in male and female mice.

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

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APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF BARIUM CHLORIDE DIHYDRATE

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	19	14	18	14
Natural deaths	9	5	3	3
Survivors				
Died last week of study	1			
Terminal sacrifice	21	31	29	33
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Stomach, forestomach	(10)	(10)	(10)	(10)
Squamous cell papilloma			1 (10%)	
Cardiovascular System				
None				
Endocrine System				
Adrenal gland, medulla	(9)	(9)	(9)	(9)
Pheochromocytoma benign			1 (11%)	
Pituitary gland	(10)	(10)	(10)	(10)
Pars distalis, adenoma	2 (20%)	4 (40%)	3 (30%)	2 (20%)
Thyroid gland	(9)	(10)	(10)	(9)
C-cell, adenoma			1 (10%)	
Follicular cell, carcinoma			1 (10%)	
General Body System				
None				
Genital System				
Epididymis	(10)	(10)	(10)	(10)
Mesothelioma NOS				1 (10%)
Testes	(10)	(10)	(10)	(10)
Mesothelioma NOS				1 (10%)
Bilateral, interstitial cell, adenoma	1 (10%)	1 (10%)	1 (10%)	1 (10%)
Interstitial cell, adenoma	3 (30%)	3 (30%)	3 (30%)	6 (60%)
Hematopoietic System				
None				
Integumentary System				
None				

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
None				
Systemic Lesions				
Multiple organs[b]	(10)	(10)	(10)	(10)
Mesothelioma NOS				1 (10%)
2-Year Study				
Alimentary System				
Intestine large, cecum	(43)	(45)	(48)	(47)
Lipoma		1 (2%)		
Intestine large, colon	(45)	(45)	(49)	(48)
Intestine small, ileum	(42)	(45)	(47)	(47)
Intestine small, jejunum	(43)	(45)	(47)	(47)
Liver	(49)	(50)	(50)	(50)
Mesentery	(3)	(4)	(10)	(3)
Fibrosarcoma			1 (10%)	
Pancreas	(45)	(48)	(49)	(50)
Acinus, adenocarcinoma	1 (2%)			
Acinus, adenoma	3 (7%)	4 (8%)	1 (2%)	3 (6%)
Pharynx	(2)			
Squamous cell papilloma	1 (50%)			
Salivary glands	(50)	(49)	(50)	(50)
Osteosarcoma, metastatic			1 (2%)	
Stomach, forestomach	(49)	(50)	(50)	(49)
Squamous cell papilloma		2 (4%)		
Stomach, glandular	(47)	(48)	(50)	(48)
Tongue	(1)	(1)		
Squamous cell papilloma		1 (100%)		

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Fibroma	1 (2%)			
Endocrine System				
Adrenal gland, cortex	(49)	(50)	(50)	(50)
Adenoma	1 (2%)			1 (2%)
Adrenal gland, medulla	(49)	(50)	(49)	(50)
Pheochromocytoma malignant	2 (4%)	2 (4%)	2 (4%)	
Pheochromocytoma benign	10 (20%)	7 (14%)	8 (16%)	6 (12%)
Pheochromocytoma benign, two	1 (2%)	2 (4%)	2 (4%)	
Islets, pancreatic	(45)	(48)	(48)	(49)
Adenoma	3 (7%)	2 (4%)	5 (10%)	5 (10%)
Carcinoma	2 (4%)		2 (4%)	
Parathyroid gland	(48)	(47)	(47)	(49)
Pituitary gland	(48)	(45)	(49)	(46)
Pars distalis, adenoma	21 (44%)	20 (44%)	16 (33%)	21 (46%)
Pars distalis, adenoma, two		1 (2%)	1 (2%)	
Pars distalis, carcinoma	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Thyroid gland	(49)	(48)	(50)	(50)
Bilateral, C-cell, adenoma	1 (2%)			
C-cell, adenoma	4 (8%)	5 (10%)	7 (14%)	7 (14%)
C-cell, adenoma, two				1 (2%)
C-cell, carcinoma		1 (2%)		1 (2%)
Follicular cell, adenoma	1 (2%)			
Follicular cell, carcinoma			1 (2%)	1 (2%)
General Body System				
None				
Genital System				
Epididymis	(48)	(50)	(50)	(50)
Preputial gland	(49)	(49)	(50)	(50)
Adenoma	1 (2%)	2 (4%)	2 (4%)	
Carcinoma	1 (2%)	1 (2%)		1 (2%)
Prostate	(48)	(50)	(50)	(49)
Seminal vesicle	(49)	(49)	(49)	(50)
Testes	(49)	(50)	(50)	(50)
Bilateral, interstitial cell, adenoma	27 (55%)	32 (64%)	31 (62%)	23 (46%)
Interstitial cell, adenoma	12 (24%)	12 (24%)	15 (30%)	14 (28%)
Hematopoietic System				
Blood	(26)	(39)	(39)	(9)
Bone marrow	(45)	(49)	(50)	(49)
Lymph node	(49)	(47)	(50)	(50)
Lymph node, mandibular	(49)	(47)	(50)	(50)
Lymph node, mesenteric	(47)	(47)	(50)	(49)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Spleen	(49)	(48)	(50)	(49)
Sarcoma	1 (2%)			
Thymus	(44)	(47)	(47)	(44)
Integumentary System				
Mammary gland	(42)	(34)	(43)	(44)
Fibroadenoma	2 (5%)	3 (9%)	1 (2%)	
Skin	(50)	(50)	(49)	(48)
Basal cell carcinoma	1 (2%)			2 (4%)
Fibroma			1 (2%)	1 (2%)
Fibrosarcoma	1 (2%)		1 (2%)	1 (2%)
Hemangioma		1 (2%)		1 (2%)
Keratoacanthoma	1 (2%)	3 (6%)		
Lipoma	1 (2%)		1 (2%)	
Trichoepithelioma	1 (2%)		1 (2%)	
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma			1 (2%)	
Skeletal muscle			(1)	
Nervous System				
Brain	(50)	(50)	(50)	(50)
Astrocytoma malignant				1 (2%)
Carcinoma, metastatic, thyroid gland				1 (2%)
Peripheral nerve		(2)	(1)	(1)
Schwannoma benign		1 (50%)		
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Carcinoma, metastatic			1 (2%)	
Osteosarcoma, metastatic			1 (2%)	
Nose	(50)	(48)	(50)	(50)
Adenoma		2 (4%)		
Special Senses System				
Zymbal's gland		(2)	(1)	(2)
Carcinoma		2 (100%)	1 (100%)	2 (100%)
Urinary System				
Kidney	(47)	(47)	(49)	(49)
Urinary bladder	(42)	(45)	(47)	(48)
Leiomyoma, two	1 (2%)			
Transitional epithelium, papilloma				1 (2%)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Systemic Lesions				
Multiple organs	(50)	(50)	(50)	(50)
Leukemia mononuclear	35 (70%)	25 (50%)	26 (52%)	15 (30%)
Lymphoma malignant lymphocytic		1 (2%)		
Mesothelioma benign	1 (2%)			
Mesothelioma malignant			1 (2%)	
Mesothelioma NOS	1 (2%)		1 (2%)	
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	6	7	9	9
2-Year study	50	50	50	48
Total primary neoplasms				
15-Month interim evaluation	6	8	11	10
2-Year study	140	134	130	110
Total animals with benign neoplasms				
15-Month interim evaluation	6	7	8	8
2-Year study	46	50	48	44
Total benign neoplasms				
15-Month interim evaluation	6	8	10	9
2-Year study	94	101	92	84
Total animals with malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	39	27	34	25
Total malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	45	33	37	26
Total animals with metastatic neoplasms				
2-Year study			2	1
Total metastatic neoplasms				
2-Year study			3	1
Total animals with neoplasms uncertain-benign or malignant				
15-Month interim evaluation				1
2-Year study	1		1	
Total uncertain neoplasms				
15-Month interim evaluation				2
2-Year study	2		1	

[a] Number of animals examined microscopically at site and number of animals with lesion
[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 Barium Chloride Dihydrate: 0 ppm

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

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

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

Number of Days on Study	7 2 2	7 2 2	7 2 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	0 0 5 3	0 0 8 2	0 0 6 5	0 0 1 1	0 0 2 1	0 0 3 2	0 0 5 1	0 0 5 2	0 0 6 4	0 0 9 2	0 1 1 3	0 1 1 4	0 1 2 2	0 0 2 2	0 0 6 2	0 0 6 3	0 0 9 1	0 1 1 2	0 1 1 3	0 0 3 1	0 0 4 3	0 0 7 2	0 0 7 3	0 0 8 1	0 1 2 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesentery					+																					3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Acinus, adenocarcinoma														X												1
Acinus, adenoma											X		X											X		3
Pharynx	+							+																		2
Squamous cell papilloma								X																		1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Tongue																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma										X																1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma			X																							1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant								X																		2
Pheochromocytoma benign					X								X	X					X		X				X	10
Pheochromocytoma benign, two																X										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenoma							X																			3
Carcinoma																		X								2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma	X			X		X		X	X	X		X	X		X		X	X	X	X			X	X		21
Pars distalis, carcinoma					X																					1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bilateral, C-cell, adenoma																										1
C-cell, adenoma							X																			4
Follicular cell, adenoma														X												1

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

Number of Days on Study	3	4	5	5	5	5	6	6	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7
	0	8	4	4	6	7	0	1	5	7	7	7	8	8	8	8	9	0	0	0	0	0	0	1
	5	2	3	3	5	8	5	2	5	1	3	3	1	1	4	7	1	1	1	3	8	8	8	2
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1
	9	9	1	1	0	2	7	6	8	7	1	8	4	5	2	2	4	4	0	0	1	2	8	2
	5	3	4	5	1	4	1	1	5	4	3	4	1	4	5	4	2	4	4	2	2	3	3	3
General Body System																								
None																								
Genital System																								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	M
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Adenoma																								
Carcinoma					X																			
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	A	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Bilateral, interstitial cell, adenoma		X							X		X	X	X			X	X		X	X	X		X	
Interstitial cell, adenoma					X	X	X							X				X				X		X	
Hematopoietic System																								
Blood			+				+	+	+	+		+		+	+		+			+	+	+	+	+	
Bone marrow	+	I	+	+	+	+	I	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Lymph node, mesenteric	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Sarcoma							X																		
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	M	+
Integumentary System																								
Mammary gland	A	M	M	+	M	+	M	+	+	+	+	M	M	+	M	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																				X					
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Fibrosarcoma										X															
Keratoacanthoma																								X	
Lipoma																									
Trichoepithelioma																									
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Eye											A														

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

Number of Days on Study	7 2 2	7 2 2	7 2 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	0 0 5 3	0 0 8 2	0 0 6 5	0 0 1 1	0 0 2 1	0 0 3 2	0 0 5 1	0 0 5 2	0 0 6 4	0 0 9 2	0 1 1 3	0 1 1 4	0 1 2 2	0 0 2 2	0 0 6 2	0 0 6 3	0 0 9 1	0 1 2 2	0 1 0 3	0 1 3 1	0 0 3 3	0 0 4 2	0 0 7 3	0 0 7 3	0 0 8 1	0 1 2 1	Total Tissues/ Tumors
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma													X													1
Carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bilateral, interstitial cell, adenoma	X	X	X	X			X	X		X		X	X	X	X	X		X			X	X			X	27
Interstitial cell, adenoma					X						X						X		X					X		12
Hematopoietic System																										
Blood					+		+		+					+		+	+	+	+	+	+			+	+	26
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	45
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	I	M	+	M	+	+	44
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Fibroadenoma																		X								2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma							X																			1
Fibrosarcoma																										1
Keratoacanthoma																										1
Lipoma									X																	1
Trichoepithelioma																							X			1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye														+												1

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

Number of Days on Study	3	4	5	5	5	5	6	6	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7
	0	8	4	4	6	7	0	1	5	7	7	7	8	8	8	8	9	0	0	0	0	0	0	1
	5	2	3	3	5	8	5	2	5	1	3	3	1	1	4	7	1	1	1	3	8	8	8	2
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1
	9	9	1	1	0	2	7	6	8	7	1	8	4	5	2	2	4	4	0	0	1	2	8	2	1
	5	3	4	5	1	4	1	1	5	4	3	4	1	4	5	4	2	4	4	2	2	3	3	3	1
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
Urinary bladder	A	A	+	+	+	+	+	+	+	+	A	+	A	+	+	A	+	+	A	+	+	+	+	+	M
Leiomyoma, two															X										
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X	X	X	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Mesothelioma benign			X																						
Mesothelioma NOS			X																						

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

Number of Days on Study	7 2 2	7 2 2	7 2 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	0 0 5 3	0 0 8 2	0 0 6 5	0 0 1 1	0 0 2 1	0 0 3 2	0 0 5 1	0 0 5 2	0 0 6 4	0 0 9 2	0 1 1 3	0 1 1 4	0 1 2 2	0 0 2 2	0 0 6 2	0 0 6 3	0 0 9 1	0 1 1 2	0 1 0 3	0 0 3 1	0 0 4 3	0 0 7 2	0 0 7 3	0 0 8 1	0 1 2 1	Total Tissues/ Tumors
Urinary System																									
Kidney	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Urinary bladder	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Leiomyoma, two																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X	X	X	X		X	X	X					X		X	X		X							35
Mesothelioma benign																										1
Mesothelioma NOS																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm

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

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	
Carcass ID Number	0 1 9 3	0 1 9 4	0 2 0 1	0 2 0 2	0 2 0 3	0 2 1 1	0 2 1 2	0 2 1 3	0 2 1 4	0 2 2 2	0 2 2 3	0 2 2 4	0 2 3 1	0 2 3 2	0 2 3 3	0 2 3 4	0 2 4 2	0 2 4 3	0 2 6 1	0 2 6 2	0 2 6 3	0 2 6 4	0 2 8 1	0 2 8 2	0 2 8 3	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lipoma																										1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	45
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery																										4
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Acinus, adenoma	X								X			X														4
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																										2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Tongue																										1
Squamous cell papilloma																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																			X							2
Pheochromocytoma benign						X				X								X		X						7
Pheochromocytoma benign, two			X																							2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																							X			2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	45
Pars distalis, adenoma		X									X	X	X		X		X	X				X	X			20
Pars distalis, adenoma, two							X																			1
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C-cell, adenoma				X	X					X									X							5
C-cell, carcinoma																										1
General Body System																										
None																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	5 2 0	5 3 7	5 4 4	5 6 2	5 6 5	5 6 5	5 6 5	5 8 0	6 1 5	6 5 3	6 5 8	6 6 1	6 6 9	6 7 0	6 7 3	6 8 7	7 0 8	7 2 3	7 2 4	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2
Carcass ID Number	0 1 5 1	0 2 4 1	0 2 1 5	0 1 4 1	0 1 3 1	0 1 9 5	0 2 2 1	0 1 8 4	0 1 4 4	0 2 3 5	0 2 4 5	0 2 0 4	0 1 3 4	0 1 4 3	0 2 4 4	0 1 3 2	0 1 6 5	0 1 5 3	0 1 7 2	0 1 3 3	0 1 4 2	0 1 5 2	0 1 7 1	0 1 9 1	0 1 9 2
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma			X	X						X		X	X	X		X				X		X		X	X
Interstitial cell, adenoma	X					X	X		X		X				X		X		X			X			
Hematopoietic System																									
Blood	+	+	+			+		+				+	+	+						+	+	+	+	+	+
Bone marrow	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	A	+	+	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Spleen	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Thymus	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	+	M	M	+	M	M	+	+	+	M	+	+	M	M	+	M	+	+	+	+	+	+	+	+
Fibroadenoma																				X					
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Keratoacanthoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve																+	+								
Schwannoma benign																	X								
Spinal cord																+									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma								X																	
Trachea	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye		+																							
Zymbal's gland			+						+																
Carcinoma			X						X																
Urinary System																									
Kidney	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	A	+	+	+	+	+	A	A	+	+	+	A	+	A	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	
Carcass ID Number	0 1 9 3	0 1 9 4	0 2 0 1	0 2 0 2	0 2 0 3	0 2 1 1	0 2 1 2	0 2 1 3	0 2 1 4	0 2 2 2	0 2 2 3	0 2 2 4	0 2 3 1	0 2 3 2	0 2 3 3	0 2 3 4	0 2 4 2	0 2 4 3	0 2 6 1	0 1 6 2	0 1 6 3	0 1 6 4	0 1 8 1	0 1 8 2	0 1 8 3	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	49
Adenoma						X						X														2
Carcinoma									X																	1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X	X	X		X	X	X	X	X	X		X	X		X	X	X	X	X	X	X		X	X	X	32
Interstitial cell, adenoma				X										X												12
Hematopoietic System																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	47
Integumentary System																										
Mammary gland	+	+	+	M	M	+	+	+	+	+	+	+	M	+	+	+	M	M	+	M	M	+	+	+	+	34
Fibroadenoma	X									X						+										3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																X										1
Keratoacanthoma							X						X						X							3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										2
Schwannoma benign																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nose	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																					X					2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Special Senses System																										
Eye																										1
Zymbal's gland																										2
Carcinoma																										2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	5	5	5	5	5	5	5	5	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	
	2	3	4	6	6	6	6	8	1	5	5	6	6	7	7	8	0	2	2	3	3	3	3	3	
	0	7	4	2	5	5	5	0	5	3	8	1	9	0	3	7	8	3	4	2	2	2	2	2	
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1	2	2	1	1	1	2	1	1	2	2	2	1	1	2	1	1	1	1	1	1	1	1	1	
	5	4	1	4	3	9	2	8	4	3	4	0	3	4	4	3	6	5	7	3	4	5	7	9	
	1	1	5	1	1	5	1	4	4	5	5	4	4	3	4	2	5	3	2	3	2	2	1	1	
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear	X		X	X		X	X	X	X	X		X	X	X		X				X				X	
Lymphoma malignant lymphocytic																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 1 9 3	0 1 9 4	0 2 0 1	0 2 0 2	0 2 0 3	0 2 1 1	0 2 1 2	0 2 1 3	0 2 1 4	0 2 2 2	0 2 2 3	0 2 2 4	0 2 3 1	0 2 3 2	0 2 3 3	0 2 3 4	0 2 4 2	0 2 4 3	0 2 6 1	0 1 6 2	0 1 6 3	0 1 6 4	0 1 8 1	0 1 8 2	0 1 8 3	Total Tissues/ Tumors
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X				X				X	X	X		X	X	X				X			X				25
Lymphoma malignant lymphocytic		X																								1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm

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

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	
Carcass ID Number	0 2 7 2	0 2 7 3	0 2 7 4	0 2 8 1	0 2 9 1	0 2 9 2	0 2 9 3	0 2 9 4	0 3 0 1	0 3 0 2	0 3 0 3	0 3 1 3	0 3 2 1	0 3 2 2	0 3 2 3	0 3 3 1	0 3 3 2	0 3 3 3	0 3 3 4	0 3 4 2	0 3 4 3	0 3 6 2	0 3 6 3	0 3 1 4	0 3 6 4	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery				+									+				+									10
Fibrosarcoma																	X									1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinus, adenoma																						X				1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant									X										X							2
Pheochromocytoma benign		X									X			X	X			X		X					X	8
Pheochromocytoma benign, two																							X			2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma			X			X								X					X							5
Carcinoma														X							X					2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma									X		X					X	X				X		X			16
Pars distalis, adenoma, two														X												1
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma									X							X			X				X			7
Follicular cell, carcinoma										X																1
General Body System																										
None																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	5 0 6	5 2 0	5 2 8	5 4 3	5 9 0	5 9 1	6 2 1	6 3 6	6 5 5	6 6 1	6 6 7	6 8 3	6 8 8	7 0 4	7 0 8	7 0 9	7 0 9	7 1 1	7 1 7	7 1 9	7 2 3	7 3 1	7 3 1	7 3 1
Carcass ID Number	0 2 5 4	0 3 1 1	0 2 9 5	0 3 5 1	0 2 7 1	0 3 1 2	0 3 6 5	0 3 2 5	0 2 5 3	0 3 2 4	0 3 4 5	0 3 5 2	0 3 4 1	0 2 8 4	0 3 5 3	0 2 8 2	0 2 8 3	0 3 5 4	0 3 4 4	0 3 6 1	0 3 3 5	0 2 5 1	0 2 5 2	0 2 6 1	0 2 6 2
Genital System																								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma				X							X	X	X		X	X	X		X	X	X	X		X	X
Interstitial cell, adenoma					X		X	X	X	X				X				X					X		
Hematopoietic System																								
Blood	+	+		+		+	+	+	+	+	+			+		+	+		+			+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																								
Mammary gland	+	+	M	+	M	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Fibroadenoma																									
Skin	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
Fibrosarcoma								X																	
Lipoma																									
Trichoepithelioma														X											
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma						X																			
Skeletal muscle																		+							
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve						+																			
Spinal cord						+																			
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic		X																							
Osteosarcoma, metastatic						X																			
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	
Carcass ID Number	0 2 7 2	0 2 7 3	0 2 7 4	0 2 8 1	0 2 9 1	0 2 9 2	0 2 9 3	0 2 9 4	0 3 0 1	0 3 0 2	0 3 0 3	0 3 1 3	0 3 2 1	0 3 2 2	0 3 2 3	0 3 3 1	0 3 3 2	0 3 3 3	0 3 3 4	0 3 4 2	0 3 4 3	0 3 6 2	0 3 6 3	0 3 1 4	0 3 6 4	Total Tissues/ Tumors
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																	X	X									2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X	X	X	X	X		X		X		X		X	X	X	X		X		X		X	X	X	X		31
Interstitial cell, adenoma						X		X		X		X					X		X		X						15
Hematopoietic System																											
Blood	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+		+		+	+	+	+	+	+	+	39
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	M	47
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	43
Fibroadenoma																						X					1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibroma									X																		1
Fibrosarcoma																											1
Lipoma														X													1
Trichoepithelioma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																											1
Skeletal muscle																											1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																											1
Spinal cord																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic																											1
Osteosarcoma, metastatic																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	5	5	5	5	5	5	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7
	0	2	2	4	9	9	2	3	5	6	6	8	8	0	0	0	0	1	1	1	2	3	3	3	3
	6	0	8	3	0	1	1	6	5	1	7	3	8	4	8	9	9	1	7	9	3	1	1	1	1
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	3	2	3	2	3	3	3	2	3	3	3	3	2	3	2	2	3	3	3	3	2	2	2	2
	5	1	9	5	7	1	6	2	5	2	4	5	4	8	5	8	8	5	4	6	3	5	5	6	6
	4	1	5	1	1	2	5	5	3	4	5	2	1	4	3	2	3	4	4	1	5	1	2	1	2
Special Senses System																									
Eye												+													
Zymbal's gland		+																							
Carcinoma		X																							
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	A	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X		X		X	X	X	X	X	X	X	X	X		X	X	X		X	X	X
Mesothelioma malignant																		X							
Mesothelioma NOS																		X							

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	
Carcass ID Number	0 2 7 2	0 2 7 3	0 2 7 4	0 2 8 1	0 2 9 1	0 2 9 2	0 2 9 3	0 2 9 4	0 3 0 1	0 3 0 2	0 3 0 3	0 3 1 3	0 3 2 1	0 3 2 2	0 3 2 3	0 3 3 1	0 3 3 2	0 3 3 3	0 3 3 4	0 3 4 2	0 3 4 3	0 3 6 2	0 3 6 3	0 3 1 4	0 3 6 4	Total Tissues/ Tumors
Special Senses System																										
Eye										+				+												3
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear						X		X		X		X			X	X	X	X			X					26
Mesothelioma malignant																										1
Mesothelioma NOS																										1

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

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

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 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 3 9 3	0 3 9 4	0 4 0 1	0 4 1 2	0 4 1 3	0 4 2 2	0 4 2 3	0 4 2 4	0 4 3 2	0 4 3 3	0 4 4 1	0 4 4 2	0 4 4 3	0 4 4 4	0 4 4 5	0 4 5 4	0 4 5 5	0 4 6 1	0 4 6 2	0 4 6 3	0 4 7 2	0 4 7 3	0 4 7 4	0 4 8 1	0 4 8 2	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery										+								+								3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinus, adenoma												X												X	X	3
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	48
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																						X				1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign								X									X						X		X	6
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma													X	X	X											5
Parathyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Pars distalis, adenoma	X	X			X					X	X		X			X	X			X		X				21
Pars distalis, carcinoma																										2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma		X		X				X								X			X					X		7
C-cell, adenoma, two																					X					1
C-cell, carcinoma																										1
Follicular cell, carcinoma				X																						1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																	X									1
Prostate	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	3 1 2	3 9 7	5 2 0	5 5 9	5 6 4	5 6 4	5 8 2	6 0 1	6 1 5	6 2 0	6 3 3	6 5 9	6 6 9	6 7 4	6 7 5	6 8 1	7 2 6	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 4 2 1	0 4 2 5	0 4 3 4	0 3 7 2	0 4 0 3	0 4 5 2	0 4 1 1	0 4 5 1	0 4 8 4	0 4 0 2	0 4 8 3	0 3 8 4	0 4 1 4	0 4 6 4	0 4 7 1	0 4 3 1	0 3 9 5	0 3 7 1	0 3 7 3	0 3 7 4	0 3 8 1	0 3 8 2	0 3 8 3	0 3 9 1	0 3 9 2
Genital System (continued)																								
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma													X	X					X			X	X	X
Interstitial cell, adenoma					X	X		X			X						X	X			X			
Hematopoietic System																								
Blood					+	+	+	+			+	+		+	+	+								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	M	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Integumentary System																								
Mammary gland	+	+	M	M	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																								
Fibroma																	X							
Fibrosarcoma					X																			
Hemangioma																								
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant																								
Carcinoma, metastatic, thyroid gland																								
Peripheral nerve															+									
Spinal cord															+									
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Eye															+									
Zymbal's gland							+		+															
Carcinoma							X		X															
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+
Transitional epithelium, papilloma																								
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X					X	X	X	X	X	X				X		X	X	

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 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 3 9 3	0 3 9 4	0 4 0 1	0 4 1 2	0 4 1 3	0 4 2 2	0 4 2 3	0 4 2 4	0 4 3 2	0 4 3 3	0 4 4 1	0 4 4 2	0 4 4 3	0 4 4 4	0 4 4 5	0 4 5 4	0 4 5 5	0 4 6 1	0 4 6 2	0 4 6 3	0 4 7 2	0 4 7 3	0 4 7 4	0 4 8 1	0 4 8 2	Total Tissues/ Tumors
Genital System (continued)																										
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma		X			X	X	X	X	X	X			X	X		X	X	X		X		X	X	X		23
Interstitial cell, adenoma	X		X	X							X	X									X				X	14
Hematopoietic System																										
Blood																										9
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	M	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	44
Integumentary System																										
Mammary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	44
Skin	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	48
Basal cell carcinoma			X			X																				2
Fibroma																										1
Fibrosarcoma																										1
Hemangioma		X																								1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant								X																		1
Carcinoma, metastatic, thyroid gland				X																						1
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye						+																+				3
Zymbal's gland																										2
Carcinoma																										2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Transitional epithelium, papilloma																			X							1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear					X				X						X						X	X				15

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	11/49 (22%)	9/50 (18%)	10/49 (20%)	6/50 (12%)
Adjusted rate[b]	40.2%	27.0%	32.9%	18.2%
Terminal rate[c]	7/22 (32%)	7/31 (23%)	9/29 (31%)	6/33 (18%)
First incidence (days)	691	673	704	730 (T)
Life table test[d]	P=0.040N	P=0.180N	P=0.256N	P=0.033N
Logistic regression test[d]	P=0.085N	P=0.321N	P=0.377N	P=0.086N
Cochran-Armitage test[d]	P=0.129N			
Fisher exact test[d]		P=0.382N	P=0.500N	P=0.133N
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rate	13/49 (27%)	11/50 (22%)	12/49 (24%)	6/50 (12%)
Adjusted rate	45.5%	31.8%	39.6%	18.2%
Terminal rate	8/22 (36%)	8/31 (26%)	11/29 (38%)	6/33 (18%)
First incidence (days)	605	653	704	730 (T)
Life table test	P=0.012N	P=0.181N	P=0.237N	P=0.011N
Logistic regression test	P=0.038N	P=0.353N	P=0.407N	P=0.044N
Cochran-Armitage test	P=0.055N			
Fisher exact test		P=0.385N	P=0.500N	P=0.056N
Mammary Gland: Fibroadenoma				
Overall rate	2/50 (4%)	3/50 (6%)	1/50 (2%)	0/50 (0%)
Adjusted rate	7.6%	9.7%	3.4%	0.0%
Terminal rate	1/22 (5%)	3/31 (10%)	1/29 (3%)	0/33 (0%)
First incidence (days)	703	730 (T)	730 (T)	–[e]
Life table test	P=0.059N	P=0.632	P=0.416N	P=0.187N
Logistic regression test	P=0.076N	P=0.553	P=0.465N	P=0.228N
Cochran-Armitage test	P=0.093N			
Fisher exact test		P=0.500	P=0.500N	P=0.247N
Pancreas: Adenoma				
Overall rate	3/45 (7%)	4/48 (8%)	1/49 (2%)	3/50 (6%)
Adjusted rate	13.6%	12.9%	3.4%	9.1%
Terminal rate	3/22 (14%)	4/31 (13%)	1/29 (3%)	3/33 (9%)
First incidence (days)	730 (T)	730 (T)	730 (T)	730 (T)
Life table test	P=0.312N	P=0.630N	P=0.210N	P=0.465N
Logistic regression test	P=0.312N	P=0.630N	P=0.210N	P=0.465N
Cochran-Armitage test	P=0.413N			
Fisher exact test		P=0.536	P=0.277N	P=0.610N
Pancreas: Adenoma or Carcinoma				
Overall rate	4/45 (9%)	4/48 (8%)	1/49 (2%)	3/50 (6%)
Adjusted rate	18.2%	12.9%	3.4%	9.1%
Terminal rate	4/22 (18%)	4/31 (13%)	1/29 (3%)	3/33 (9%)
First incidence (days)	730 (T)	730 (T)	730 (T)	730 (T)
Life table test	P=0.199N	P=0.445N	P=0.103N	P=0.283N
Logistic regression test	P=0.199N	P=0.445N	P=0.103N	P=0.283N
Cochran-Armitage test	P=0.288N			
Fisher exact test		P=0.606N	P=0.155N	P=0.441N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Pancreatic Islets: Adenoma				
Overall rate	3/45 (7%)	2/48 (4%)	5/48 (10%)	5/49 (10%)
Adjusted rate	10.9%	5.9%	15.7%	14.0%
Terminal rate	1/22 (5%)	1/31 (3%)	4/29 (14%)	3/33 (9%)
First incidence (days)	708	673	591	633
Life table test	P=0.281	P=0.429N	P=0.478	P=0.517
Logistic regression test	P=0.202	P=0.474N	P=0.397	P=0.393
Cochran-Armitage test	P=0.210			
Fisher exact test		P=0.469N	P=0.394	P=0.406
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	21/48 (44%)	21/45 (47%)	17/49 (35%)	21/46 (46%)
Adjusted rate	70.6%	53.6%	46.3%	52.3%
Terminal rate	14/22 (64%)	12/29 (41%)	10/29 (34%)	14/32 (44%)
First incidence (days)	543	537	506	520
Life table test	P=0.202N	P=0.299N	P=0.079N	P=0.188N
Logistic regression test	P=0.507N	P=0.501	P=0.195N	P=0.526
Cochran-Armitage test	P=0.519N			
Fisher exact test		P=0.470	P=0.240N	P=0.509
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rate	22/48 (46%)	22/45 (49%)	18/49 (37%)	23/46 (50%)
Adjusted rate	74.2%	55.0%	47.4%	56.1%
Terminal rate	15/22 (68%)	12/29 (41%)	10/29 (34%)	15/32 (47%)
First incidence (days)	543	537	506	520
Life table test	P=0.256N	P=0.282N	P=0.079N	P=0.226N
Logistic regression test	P=0.476	P=0.500	P=0.203N	P=0.439
Cochran-Armitage test	P=0.468			
Fisher exact test		P=0.465	P=0.241N	P=0.422
Preputial Gland: Adenoma or Carcinoma				
Overall rate	2/49 (4%)	3/49 (6%)	2/50 (4%)	1/50 (2%)
Adjusted rate	6.6%	10.0%	6.9%	3.0%
Terminal rate	1/22 (5%)	3/30 (10%)	2/29 (7%)	1/33 (3%)
First incidence (days)	565	730 (T)	730 (T)	730 (T)
Life table test	P=0.207N	P=0.612	P=0.618N	P=0.412N
Logistic regression test	P=0.285N	P=0.504	P=0.689N	P=0.492N
Cochran-Armitage test	P=0.291N			
Fisher exact test		P=0.500	P=0.684N	P=0.492N
Skin: Keratoacanthoma				
Overall rate	1/50 (2%)	3/50 (6%)	0/50 (0%)	0/50 (0%)
Adjusted rate	3.8%	9.7%	0.0%	0.0%
Terminal rate	0/22 (0%)	3/31 (10%)	0/29 (0%)	0/33 (0%)
First incidence (days)	712	730 (T)	-	-
Life table test	P=0.090N	P=0.424	P=0.459N	P=0.446N
Logistic regression test	P=0.109N	P=0.350	P=0.490N	P=0.496N
Cochran-Armitage test	P=0.127N			
Fisher exact test		P=0.309	P=0.500N	P=0.500N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Skin: Keratoacanthoma, Trichoepithelioma, or Basal Cell Carcinoma				
Overall rate	3/50 (6%)	3/50 (6%)	1/50 (2%)	2/50 (4%)
Adjusted rate	12.6%	9.7%	2.7%	6.1%
Terminal rate	2/22 (9%)	3/31 (10%)	0/29 (0%)	2/33 (6%)
First incidence (days)	712	730 (T)	704	730 (T)
Life table test	P=0.232N	P=0.506N	P=0.226N	P=0.332N
Logistic regression test	P=0.293N	P=0.583N	P=0.274N	P=0.423N
Cochran-Armitage test	P=0.334N			
Fisher exact test		P=0.661N	P=0.309N	P=0.500N
Testes: Adenoma				
Overall rate	39/49 (80%)	44/50 (88%)	46/50 (92%)	37/50 (74%)
Adjusted rate	90.4%	95.6%	100.0%	92.4%
Terminal rate	18/22 (82%)	29/31 (94%)	29/29 (100%)	30/33 (91%)
First incidence (days)	482	520	543	564
Life table test	P=0.021N	P=0.340N	P=0.467N	P=0.026N
Logistic regression test	P=0.175N	P=0.221	P=0.082	P=0.346N
Cochran-Armitage test	P=0.174N			
Fisher exact test		P=0.194	P=0.068	P=0.337N
Thyroid Gland (C-cell): Adenoma				
Overall rate	5/49 (10%)	5/48 (10%)	7/50 (14%)	8/50 (16%)
Adjusted rate	13.3%	16.1%	20.6%	24.2%
Terminal rate	1/22 (5%)	5/31 (16%)	4/29 (14%)	8/33 (24%)
First incidence (days)	565	730 (T)	506	730 (T)
Life table test	P=0.319	P=0.514N	P=0.492	P=0.460
Logistic regression test	P=0.192	P=0.620	P=0.369	P=0.290
Cochran-Armitage test	P=0.195			
Fisher exact test		P=0.617	P=0.394	P=0.290
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rate	5/49 (10%)	6/48 (13%)	7/50 (14%)	9/50 (18%)
Adjusted rate	13.3%	18.7%	20.6%	25.9%
Terminal rate	1/22 (5%)	5/31 (16%)	4/29 (14%)	8/33 (24%)
First incidence (days)	565	723	506	564
Life table test	P=0.268	P=0.615N	P=0.492	P=0.352
Logistic regression test	P=0.151	P=0.491	P=0.369	P=0.204
Cochran-Armitage test	P=0.154			
Fisher exact test		P=0.485	P=0.394	P=0.205
All Organs: Mononuclear Cell Leukemia				
Overall rate	35/50 (70%)	25/50 (50%)	26/50 (52%)	15/50 (30%)
Adjusted rate	72.8%	56.5%	60.1%	37.0%
Terminal rate	9/22 (41%)	13/31 (42%)	12/29 (41%)	8/33 (24%)
First incidence (days)	305	520	590	564
Life table test	P<0.001N	P=0.031N	P=0.036N	P<0.001N
Logistic regression test	P<0.001N	P=0.033N	P=0.055N	P<0.001N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.033N	P=0.050N	P<0.001N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
All Organs: Benign Neoplasms				
Overall rate	47/50 (94%)	50/50 (100%)	49/50 (98%)	45/50 (90%)
Adjusted rate	97.9%	100.0%	100.0%	100.0%
Terminal rate	21/22 (95%)	31/31 (100%)	29/29 (100%)	33/33 (100%)
First incidence (days)	305	520	506	520
Life table test	P=0.023N	P=0.198N	P=0.185N	P=0.022N
Logistic regression test	P=0.128N	P=0.138	P=0.391	P=0.387N
Cochran-Armitage test	P=0.098N			
Fisher exact test		P=0.121	P=0.309	P=0.357N
All Organs: Malignant Neoplasms				
Overall rate	39/50 (78%)	27/50 (54%)	34/50 (68%)	25/50 (50%)
Adjusted rate	78.0%	60.2%	70.8%	56.4%
Terminal rate	11/22 (50%)	14/31 (45%)	15/29 (52%)	14/33 (42%)
First incidence (days)	305	520	520	564
Life table test	P=0.016N	P=0.015N	P=0.101N	P=0.005N
Logistic regression test	P=0.016N	P=0.010N	P=0.226N	P=0.003N
Cochran-Armitage test	P=0.017N			
Fisher exact test		P=0.010N	P=0.184N	P=0.003N
All Organs: Benign or Malignant Neoplasms				
Overall rate	50/50 (100%)	50/50 (100%)	50/50 (100%)	48/50 (96%)
Adjusted rate	100.0%	100.0%	100.0%	100.0%
Terminal rate	22/22 (100%)	31/31 (100%)	29/29 (100%)	33/33 (100%)
First incidence (days)	305	520	506	520
Life table test	P=0.037N	P=0.096N	P=0.118N	P=0.027N
Logistic regression test	P=0.053N	-[f]	-	P=0.193N
Cochran-Armitage test	P=0.045N			
Fisher exact test		P=1.000N	P=1.000N	P=0.247N

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

TABLE A4
Historical Incidence of Leukemia in Untreated Male F344 Rats[a]

	Incidence in Controls[b]
Overall Historical Incidence	
Total	164/281 (58.4%)
Standard deviation	12.8%
Range	40%–70%

[a] Data as of 20 August 1992
[b] Includes data for lymphocytic, monocytic, mononuclear cell, and undifferentiated leukemia

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

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	19	14	18	14
Natural deaths	9	5	3	3
Survivors				
Died last week of study	1			
Terminal sacrifice	21	31	29	33
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Intestine large, cecum	(10)	(10)	(10)	(10)
Hemorrhage			1 (10%)	
Parasite metazoan				1 (10%)
Intestine large, colon	(10)	(9)	(10)	(10)
Parasite metazoan	2 (20%)	1 (11%)	2 (20%)	1 (10%)
Intestine large, rectum	(10)	(10)	(10)	(10)
Parasite metazoan	6 (60%)	2 (20%)	5 (50%)	1 (10%)
Liver	(10)	(10)	(10)	(10)
Clear cell focus		1 (10%)		
Congestion	1 (10%)	1 (10%)		
Cytoplasmic alteration, focal	1 (10%)			1 (10%)
Fatty change	5 (50%)	4 (40%)	4 (40%)	5 (50%)
Granuloma				1 (10%)
Bile duct, hyperplasia	7 (70%)	7 (70%)	9 (90%)	6 (60%)
Mesentery	(2)	(2)		(1)
Accessory spleen	1 (50%)			
Hemorrhage		1 (50%)		
Fat, necrosis	1 (50%)	1 (50%)		1 (100%)
Pancreas	(10)	(10)	(10)	(10)
Acinus, atrophy, focal	4 (40%)	3 (30%)	3 (30%)	2 (20%)
Stomach, forestomach	(10)	(10)	(10)	(10)
Hyperkeratosis, focal		1 (10%)		
Stomach, glandular	(10)	(10)	(10)	(10)
Inflammation, chronic, focal	2 (20%)			
Cardiovascular System				
Heart	(10)	(10)	(10)	(10)
Cardiomyopathy	4 (40%)	7 (70%)	7 (70%)	6 (60%)
Endocrine System				
Adrenal gland, cortex	(10)	(10)	(9)	(10)
Congestion, focal				1 (10%)
Cytoplasmic alteration, focal			1 (11%)	

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Endocrine System (continued)				
Pituitary gland	(10)	(10)	(10)	(10)
Pars distalis, cyst	2 (20%)	1 (10%)		
Pars distalis, hyperplasia, focal	4 (40%)	1 (10%)	2 (20%)	4 (40%)
Thyroid gland	(9)	(10)	(10)	(9)
Ultimobranchial cyst		1 (10%)		
C-cell, hyperplasia	1 (11%)			
General Body System				
None				
Genital System				
Preputial gland	(10)	(10)	(10)	(10)
Cyst				1 (10%)
Inflammation, acute, focal		2 (20%)	1 (10%)	1 (10%)
Inflammation, chronic, focal	1 (10%)	2 (20%)	1 (10%)	1 (10%)
Prostate	(10)	(10)	(10)	(10)
Hyperplasia				1 (10%)
Seminal vesicle	(10)	(10)	(10)	(10)
Fibrosis				1 (10%)
Hemorrhage		1 (10%)		
Testes	(10)	(10)	(10)	(10)
Bilateral, interstitial cell, hyperplasia	2 (20%)	2 (20%)	3 (30%)	3 (30%)
Bilateral, seminiferous tubule, atrophy, focal		1 (10%)		
Interstitial cell, hyperplasia	1 (10%)	2 (20%)		2 (20%)
Hematopoietic System				
Lymph node	(10)	(10)	(10)	(10)
Mediastinal, congestion		2 (20%)	3 (30%)	
Pancreatic, congestion		1 (10%)	1 (10%)	
Lymph node, mandibular	(10)	(8)	(9)	(10)
Congestion	4 (40%)	2 (25%)	3 (33%)	4 (40%)
Pigmentation		1 (13%)		
Lymph node, mesenteric	(10)	(10)	(10)	(10)
Lymphatic, angiectasis		1 (10%)	1 (10%)	
Spleen	(10)	(10)	(10)	(10)
Congestion		2 (20%)		
Hematopoietic cell proliferation			1 (10%)	4 (40%)
Pigmentation, hemosiderin				1 (10%)
Integumentary System				
Mammary gland	(9)	(7)	(9)	(10)
Lactation	2 (22%)	1 (14%)		2 (20%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Integumentary System (continued)				
Skin	(10)	(10)	(9)	(10)
Abscess		1 (10%)		
Cyst epithelial inclusion	1 (10%)			
Inflammation, granulomatous, chronic		1 (10%)		
Musculoskeletal System				
Bone	(10)	(10)	(10)	(10)
Fibrosis				1 (10%)
Nervous System				
None.				
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Congestion		1 (10%)		1 (10%)
Alveolar epithelium, hyperplasia, adenomatous				1 (10%)
Nose	(10)	(10)	(10)	(10)
Fungus	1 (10%)			
Inflammation, acute	1 (10%)			
Inflammation, chronic, focal	8 (80%)	10 (100%)	9 (90%)	8 (80%)
Metaplasia, squamous		1 (10%)	1 (10%)	
Special Senses System				
Eye			(1)	(2)
Cataract				2 (100%)
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Nephropathy	7 (70%)	10 (100%)	9 (90%)	9 (90%)
Urinary bladder	(10)	(10)	(10)	(10)
Hemorrhage, focal				1 (10%)
Inflammation, chronic, focal	1 (10%)			
2-Year Study				
Alimentary System				
Intestine large, cecum	(43)	(45)	(48)	(47)
Parasite metazoan	2 (5%)	1 (2%)	2 (4%)	2 (4%)
Intestine large, colon	(45)	(45)	(49)	(48)
Parasite metazoan	3 (7%)	2 (4%)	7 (14%)	11 (23%)
Intestine large, rectum	(44)	(46)	(49)	(48)
Parasite metazoan	3 (7%)	4 (9%)	7 (14%)	7 (15%)
Ulcer				1 (2%)
Intestine small, ileum	(42)	(45)	(47)	(47)
Hyperplasia, lymphoid			1 (2%)	

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Liver	(49)	(50)	(50)	(50)
Basophilic focus	3 (6%)	4 (8%)	6 (12%)	4 (8%)
Clear cell focus	3 (6%)	8 (16%)	8 (16%)	4 (8%)
Clear cell focus, multiple	1 (2%)			
Congestion				1 (2%)
Cyst			1 (2%)	
Developmental malformation	3 (6%)		1 (2%)	1 (2%)
Fatty change	12 (24%)	10 (20%)	15 (30%)	12 (24%)
Granuloma	3 (6%)	4 (8%)	2 (4%)	2 (4%)
Hemorrhage, focal		1 (2%)		
Hepatodiaphragmatic nodule	2 (4%)	4 (8%)	3 (6%)	4 (8%)
Hepatodiaphragmatic nodule, two				1 (2%)
Necrosis, focal	1 (2%)		1 (2%)	3 (6%)
Artery, inflammation, chronic			1 (2%)	
Bile duct, hyperplasia	43 (88%)	48 (96%)	45 (90%)	45 (90%)
Hepatocyte, hyperplasia, focal	2 (4%)	4 (8%)	6 (12%)	3 (6%)
Lymphatic, angiectasis			1 (2%)	
Serosa, fibrosis	1 (2%)			
Mesentery	(3)	(4)	(10)	(3)
Accessory spleen			1 (10%)	
Mineralization, focal		1 (25%)		
Fat, necrosis	2 (67%)	4 (100%)	6 (60%)	3 (100%)
Pancreas	(45)	(48)	(49)	(50)
Congestion				1 (2%)
Cyst			1 (2%)	
Inflammation, chronic			1 (2%)	
Acinus, atrophy	19 (42%)	16 (33%)	18 (37%)	20 (40%)
Artery, fibrosis		1 (2%)		
Artery, inflammation, chronic				3 (6%)
Pharynx	(2)			
Hyperplasia, focal	1 (50%)			
Stomach, forestomach	(49)	(50)	(50)	(49)
Acanthosis	1 (2%)	2 (4%)		1 (2%)
Hyperkeratosis		1 (2%)		
Hyperplasia, basal cell		1 (2%)		
Ulcer	4 (8%)	2 (4%)		2 (4%)
Stomach, glandular	(47)	(48)	(50)	(48)
Edema			1 (2%)	
Mineralization	1 (2%)			1 (2%)
Tongue	(1)	(1)		
Hyperkeratosis	1 (100%)			
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	38 (76%)	38 (76%)	37 (74%)	35 (70%)
Dilatation	2 (4%)			
Atrium, dilatation			1 (2%)	
Atrium, thrombosis		1 (2%)		

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Endocrine System				
Adrenal gland, cortex	(49)	(50)	(50)	(50)
Congestion	1 (2%)			
Cytoplasmic alteration, focal	3 (6%)		4 (8%)	1 (2%)
Hyperplasia, focal	1 (2%)			
Vacuolization cytoplasmic, focal	1 (2%)			1 (2%)
Adrenal gland, medulla	(49)	(50)	(49)	(50)
Hyperplasia, focal	7 (14%)	11 (22%)	5 (10%)	9 (18%)
Hyperplasia, focal, two	1 (2%)			
Islets, pancreatic	(45)	(48)	(48)	(49)
Hyperplasia	4 (9%)	1 (2%)	2 (4%)	
Parathyroid gland	(48)	(47)	(47)	(49)
Hyperplasia	1 (2%)			
Pituitary gland	(48)	(45)	(49)	(46)
Infarct			1 (2%)	
Pars distalis, angiectasis		1 (2%)		1 (2%)
Pars distalis, cyst	1 (2%)	4 (9%)	4 (8%)	3 (7%)
Pars distalis, degeneration, focal			1 (2%)	
Pars distalis, hemorrhage	1 (2%)			
Pars distalis, hyperplasia, focal	4 (8%)	1 (2%)	7 (14%)	4 (9%)
Thyroid gland	(49)	(48)	(50)	(50)
Cyst	1 (2%)			
Cyst multilocular		1 (2%)		
C-cell, hyperplasia	6 (12%)	4 (8%)	8 (16%)	4 (8%)
Follicle, cyst			1 (2%)	
General Body System				
None				
Genital System				
Epididymis	(48)	(50)	(50)	(50)
Fibrosis		1 (2%)		
Spermatocele		1 (2%)		
Preputial gland	(49)	(49)	(50)	(50)
Abscess			2 (4%)	1 (2%)
Congestion				1 (2%)
Cyst	1 (2%)	3 (6%)		
Inflammation, acute			1 (2%)	2 (4%)
Inflammation, chronic	10 (20%)	11 (22%)	11 (22%)	11 (22%)
Duct, ectasia				1 (2%)
Prostate	(48)	(50)	(50)	(49)
Abscess	1 (2%)			
Atrophy				1 (2%)
Hyperplasia, focal	2 (4%)	6 (12%)	4 (8%)	1 (2%)
Inflammation, acute	1 (2%)	1 (2%)	2 (4%)	
Inflammation, chronic	1 (2%)	1 (2%)	1 (2%)	

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year study (continued)				
Genital System (continued)				
Seminal vesicle	(49)	(49)	(49)	(50)
Atrophy	26 (53%)	29 (59%)	27 (55%)	26 (52%)
Dilatation			1 (2%)	1 (2%)
Inflammation, acute	2 (4%)			
Testes	(49)	(50)	(50)	(50)
Artery, inflammation, chronic	2 (4%)			
Bilateral, interstitial cell, hyperplasia			1 (2%)	
Interstitial cell, hyperplasia	1 (2%)			
Seminiferous tubule, atrophy	10 (20%)	9 (18%)	7 (14%)	8 (16%)
Hematopoietic System				
Bone marrow	(45)	(49)	(50)	(49)
Atrophy		1 (2%)	1 (2%)	
Hyperplasia	11 (24%)	9 (18%)	14 (28%)	8 (16%)
Myelofibrosis	1 (2%)		1 (2%)	
Lymph node	(49)	(47)	(50)	(50)
Deep cervical, lymphatic, angiectasis				1 (2%)
Mediastinal, congestion		3 (6%)	3 (6%)	1 (2%)
Mediastinal, lymphatic, angiectasis		1 (2%)		1 (2%)
Pancreatic, hemorrhage				1 (2%)
Pancreatic, lymphatic, angiectasis			1 (2%)	
Lymph node, mandibular	(49)	(47)	(50)	(50)
Angiectasis				2 (4%)
Congestion				1 (2%)
Infarct			1 (2%)	
Infiltration cellular, plasma cell	2 (4%)	2 (4%)		2 (4%)
Lymphatic, angiectasis	2 (4%)	2 (4%)	3 (6%)	1 (2%)
Lymph node, mesenteric	(47)	(47)	(50)	(49)
Congestion			1 (2%)	
Hyperplasia				1 (2%)
Lymphatic, angiectasis	2 (4%)	2 (4%)		2 (4%)
Spleen	(49)	(48)	(50)	(49)
Congestion			1 (2%)	3 (6%)
Cyst	1 (2%)			1 (2%)
Developmental malformation			1 (2%)	
Fibrosis	9 (18%)	3 (6%)	8 (16%)	13 (27%)
Hematopoietic cell proliferation			1 (2%)	2 (4%)
Infarct	4 (8%)		1 (2%)	1 (2%)
Necrosis, focal			1 (2%)	
Pigmentation, hemosiderin			1 (2%)	2 (4%)
Capsule, fibrosis				1 (2%)
Thymus	(44)	(47)	(47)	(44)
Congestion				1 (2%)
Cyst	1 (2%)	1 (2%)		

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Integumentary System				
Mammary gland	(42)	(34)	(43)	(44)
Galactocele	1 (2%)	1 (3%)		1 (2%)
Lactation				2 (5%)
Skin	(50)	(50)	(49)	(48)
Abscess				1 (2%)
Acanthosis			1 (2%)	
Cyst epithelial inclusion				1 (2%)
Fibrosis	1 (2%)			
Hyperkeratosis	2 (4%)			1 (2%)
Thrombosis	1 (2%)			
Ulcer	1 (2%)		1 (2%)	1 (2%)
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hyperostosis			2 (4%)	1 (2%)
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression		2 (4%)	2 (4%)	2 (4%)
Congestion			1 (2%)	
Hemorrhage, focal	5 (10%)	3 (6%)	7 (14%)	3 (6%)
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion		1 (2%)		2 (4%)
Fungus	1 (2%)			1 (2%)
Hemorrhage, focal		2 (4%)	1 (2%)	
Alveolar epithelium, metaplasia	4 (8%)	2 (4%)	2 (4%)	1 (2%)
Nose	(50)	(48)	(50)	(50)
Congestion				1 (2%)
Cyst	1 (2%)			
Fungus	8 (16%)	7 (15%)	7 (14%)	4 (8%)
Inflammation, acute	11 (22%)	12 (25%)	8 (16%)	7 (14%)
Inflammation, chronic	37 (74%)	37 (77%)	41 (82%)	41 (82%)
Trachea	(50)	(48)	(50)	(50)
Fungus	1 (2%)			
Special Senses System				
Eye	(1)	(1)	(3)	(3)
Cataract	1 (100%)	1 (100%)	3 (100%)	1 (33%)
Hemorrhage				1 (33%)
Retina, degeneration			1 (33%)	3 (100%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Urinary System				
Kidney	(47)	(47)	(49)	(49)
Congestion				3 (6%)
Cyst	1 (2%)		2 (4%)	1 (2%)
Fibrosis			1 (2%)	
Infarct			2 (4%)	
Mineralization	1 (2%)		1 (2%)	1 (2%)
Nephropathy	46 (98%)	47 (100%)	48 (98%)	47 (96%)
Pigmentation, bile		1 (2%)	1 (2%)	
Artery, fibrosis		1 (2%)		
Urinary bladder	(42)	(45)	(47)	(48)
Calculus microscopic observation only	1 (2%)			
Cyst				1 (2%)
Ectasia	1 (2%)			
Inflammation, acute	1 (2%)			
Inflammation, chronic		1 (2%)		
Transitional epithelium, hyperplasia	1 (2%)			

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

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF BARIUM CHLORIDE DIHYDRATE

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	14	11	9	16
Natural deaths	5	3	2	2
Survivors				
Died last week of study	1			
Terminal sacrifice	30	36	39	32
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
None				
Cardiovascular System				
None				
Endocrine System				
Pituitary gland	(10)	(10)	(9)	(10)
Pars distalis, adenoma	1 (10%)		3 (33%)	2 (20%)
Thyroid gland	(10)	(10)	(9)	(10)
C-cell, adenoma	1 (10%)		1 (11%)	1 (10%)
General Body System				
None				
Genital System				
Uterus	(10)	(10)	(10)	(10)
Polyp stromal	2 (20%)		1 (10%)	2 (20%)
Hematopoietic System				
None				
Integumentary System				
None				
Musculoskeletal System				
None				

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Nervous System				
Brain	(10)	(10)	(10)	(10)
Glioma malignant			1 (10%)	1 (10%)
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Intestine large, cecum	(47)	(48)	(49)	(50)
Intestine large, colon	(47)	(47)	(50)	(49)
Adenocarcinoma	1 (2%)			
Intestine large, rectum	(47)	(48)	(50)	(50)
Schwannoma malignant		1 (2%)		
Intestine small, duodenum	(47)	(48)	(50)	(50)
Schwannoma malignant		1 (2%)		
Liver	(50)	(50)	(50)	(50)
Adenoma				1 (2%)
Fibrosarcoma, metastatic			1 (2%)	
Hepatocellular adenoma		1 (2%)		
Osteosarcoma, metastatic		1 (2%)		
Mesentery	(3)	(1)	(3)	
Schwannoma malignant		1 (100%)		
Pancreas	(49)	(47)	(49)	(50)
Schwannoma malignant		1 (2%)		
Acinus, adenoma	1 (2%)		1 (2%)	
Salivary glands	(49)	(50)	(50)	(50)
Stomach, forestomach	(50)	(50)	(50)	(50)
Squamous cell papilloma	1 (2%)		2 (4%)	
Tongue			(1)	
Squamous cell papilloma			1 (100%)	
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Endocrine System				
Adrenal gland, cortex	(50)	(49)	(49)	(50)
Adenoma	1 (2%)	3 (6%)	1 (2%)	
Osteosarcoma, metastatic		1 (2%)		
Adrenal gland, medulla	(50)	(49)	(49)	(50)
Osteosarcoma, metastatic		1 (2%)		
Pheochromocytoma malignant				1 (2%)
Pheochromocytoma complex		1 (2%)		
Pheochromocytoma benign	1 (2%)	3 (6%)	2 (4%)	1 (2%)
Pheochromocytoma benign, two	1 (2%)	1 (2%)		
Islets, pancreatic	(49)	(48)	(49)	(49)
Adenoma		1 (2%)	1 (2%)	1 (2%)
Carcinoma		2 (4%)		
Pituitary gland	(48)	(48)	(49)	(50)
Pars distalis, adenoma	27 (56%)	26 (54%)	25 (51%)	22 (44%)
Pars distalis, adenoma, two	2 (4%)		2 (4%)	2 (4%)
Pars distalis, carcinoma	4 (8%)	6 (13%)	4 (8%)	5 (10%)
Thyroid gland	(49)	(50)	(50)	(50)
C-cell, adenoma	5 (10%)	8 (16%)	8 (16%)	8 (16%)
C-cell, adenoma, two			1 (2%)	1 (2%)
C-cell, carcinoma	1 (2%)			
Follicular cell, adenoma	1 (2%)	1 (2%)		
General Body System				
None				
Genital System				
Clitoral gland	(50)	(49)	(50)	(47)
Adenoma		1 (2%)		2 (4%)
Carcinoma	1 (2%)	3 (6%)		1 (2%)
Carcinoma, two	2 (4%)			
Ovary	(49)	(50)	(50)	(50)
Granulosa cell tumor benign				1 (2%)
Osteosarcoma, metastatic		1 (2%)		
Schwannoma malignant		1 (2%)		
Uterus	(50)	(50)	(50)	(50)
Polyp stromal	12 (24%)	8 (16%)	10 (20%)	11 (22%)
Polyp stromal, two	1 (2%)			3 (6%)
Sarcoma stromal		2 (4%)	1 (2%)	
Hematopoietic System				
Blood	(36)	(37)	(43)	(32)
Lymph node	(50)	(50)	(50)	(50)
Mediastinal, schwannoma malignant		1 (2%)		
Lymph node, mandibular	(49)	(48)	(49)	(50)
Sarcoma, metastatic		1 (2%)		
Lymph node, mesenteric	(50)	(49)	(50)	(50)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Spleen	(50)	(50)	(50)	(50)
Osteosarcoma, metastatic		1 (2%)		
Schwannoma malignant		1 (2%)		
Thymus	(44)	(47)	(46)	(47)
Thymoma benign				1 (2%)
Integumentary System				
Mammary gland	(43)	(46)	(46)	(50)
Adenocarcinoma	1 (2%)		1 (2%)	
Adenoma	1 (2%)	2 (4%)		
Fibroadenoma	15 (35%)	15 (33%)	11 (24%)	8 (16%)
Fibroadenoma, multiple		4 (9%)	1 (2%)	3 (6%)
Lipoma	1 (2%)			
Sarcoma				1 (2%)
Skin	(48)	(50)	(49)	(49)
Fibroma	4 (8%)	1 (2%)		1 (2%)
Fibrosarcoma	1 (2%)		1 (2%)	
Keratoacanthoma		1 (2%)	1 (2%)	
Lipoma		1 (2%)		1 (2%)
Squamous cell carcinoma	1 (2%)			1 (2%)
Squamous cell papilloma	1 (2%)			
Subcutaneous tissue, sarcoma	1 (2%)			
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Osteosarcoma		1 (2%)		
Skeletal muscle	(1)		(2)	(1)
Lipoma	1 (100%)			
Nervous System				
Brain	(50)	(50)	(50)	(50)
Astrocytoma malignant	1 (2%)			
Carcinoma, metastatic	3 (6%)	2 (4%)	1 (2%)	2 (4%)
Ependymoma malignant			1 (2%)	
Glioma malignant	1 (2%)			
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	1 (2%)	1 (2%)	
Alveolar/bronchiolar carcinoma		1 (2%)		1 (2%)
Carcinoma adenosquamous		1 (2%)		
Fibrosarcoma, metastatic			1 (2%)	
Osteosarcoma, metastatic		1 (2%)		
Sarcoma, metastatic		1 (2%)		
Nose	(50)	(50)	(50)	(50)
Sarcoma, metastatic		1 (2%)		

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Special Senses System				
Eye	(5)	(8)	(3)	(1)
Sarcoma		1 (13%)		
Zymbal's gland	(2)			(1)
Carcinoma	1 (50%)			1 (100%)
Urinary System				
Kidney	(48)	(48)	(50)	(50)
Urinary bladder	(45)	(47)	(49)	(48)
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(50)	(50)
Leukemia mononuclear	15 (30%)	13 (26%)	9 (18%)	9 (18%)
Lymphoma malignant lymphocytic				1 (2%)
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	3		4	5
2-Year study	48	44	44	45
Total primary neoplasms				
15-Month interim evaluation	4		6	6
2-Year study	108	116	85	88
Total animals with benign neoplasms				
15-Month interim evaluation	3		4	5
2-Year study	43	39	39	38
Total benign neoplasms				
15-Month interim evaluation	4		5	5
2-Year study	77	78	68	67
Total animals with malignant neoplasms				
15-Month interim evaluation			1	1
2-Year study	27	27	15	21
Total malignant neoplasms				
15-Month interim evaluation			1	1
2-Year study	31	38	17	21
Total animals with metastatic neoplasms				
2-Year study	3	4	2	2
Total metastatic neoplasms				
2-Year study	3	11	3	2

[a] Number of animals examined microscopically at site and number of animals with lesion
[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 Barium Chloride Dihydrate: 0 ppm

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

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

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

Number of Days on Study	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	0 5 6 1	0 5 6 2	0 5 6 3	0 5 6 4	0 5 6 5	0 5 6 7 2	0 5 7 3	0 5 7 8 1	0 5 8 2	0 5 8 3	0 5 9 1	0 5 9 2	0 5 9 3	0 5 9 4	0 6 0 1	0 6 0 2	0 6 1 2	0 6 2 2	0 6 2 3	0 6 3 1	0 6 3 2	0 6 4 1	0 6 4 2	0 6 4 3	0 6 4 4	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenocarcinoma																										1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery																										3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinus, adenoma																			X							1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign			X																							1
Pheochromocytoma benign, two																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid gland	M	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	43
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma	X		X	X		X		X	X				X	X	X	X	X	X				X			X	27
Pars distalis, adenoma, two												X								X						2
Pars distalis, carcinoma					X					X									X							4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell, adenoma									X					X												5
C-cell, carcinoma									X																	1
Follicular cell, adenoma																										1
General Body System																										
None																										

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

Number of Days on Study	3 5 9	3 8 0	4 6 2	5 2 6	5 7 5	5 7 5	5 8 9	5 9 1	6 0 6	6 2 5	6 3 4	6 4 5	6 5 2	6 5 3	6 5 8	6 8 7	6 8 7	6 9 2	6 9 8	7 3 9	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5
Carcass ID Number	0 5 9 5	0 6 3 5	0 5 7 4	0 5 5 3	0 6 2 4	0 6 4 5	0 6 1 1	0 5 8 4	0 6 0 3	0 6 3 3	0 5 4 3	0 6 1 4	0 6 5 3	0 6 5 2	0 6 5 4	0 5 5 1	0 5 5 1	0 6 1 3	0 5 7 1	0 6 2 1	0 5 4 1	0 5 4 2	0 5 4 5	0 5 5 2	0 5 5 5
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Carcinoma, two																								X	
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal			X			X				X				X		X							X	X	
Polyp stromal, two																									
Vagina	+		+																						
Hematopoietic System																									
Blood				+	+		+		+	+	+	+			+	+	+	+	+		+	+		+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	M	+	+	+	+	I	+	+	+	+	+	+	+	+	M	M	+	+	+	+
Integumentary System																									
Mammary gland	M	+	M	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+
Adenocarcinoma																						X			
Adenoma							X																		
Fibroadenoma															X		X			X	X				X
Lipoma																			X						
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Fibroma																					X				
Fibrosarcoma																X									
Squamous cell carcinoma												X													
Squamous cell papilloma																									
Subcutaneous tissue, sarcoma		X																							
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle				+																					
Lipoma				X																					
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant														X											
Carcinoma, metastatic																						X			
Glioma malignant													X												
Peripheral nerve									+																
Spinal cord									+																

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

Number of Days on Study	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	0 5 6 1	0 5 6 2	0 5 6 3	0 5 6 4	0 5 6 5	0 5 7 2	0 5 7 3	0 5 8 1	0 5 8 2	0 5 8 3	0 5 9 1	0 5 9 2	0 5 9 3	0 5 9 4	0 6 0 1	0 6 0 2	0 6 1 2	0 6 2 2	0 6 2 3	0 6 3 1	0 6 3 2	0 6 4 1	0 6 4 2	0 6 4 3	0 6 4 4	Total Tissues/ Tumors
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma						X																				1
Carcinoma, two																				X						2
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal		X						X										X			X			X		12
Polyp stromal, two										X																1
Vagina																										2
Hematopoietic System																										
Blood	+	+	+		+	+	+	+	+	+		+	+		+	+	+	+	+	+	+		+		+	36
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	44
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	43
Adenocarcinoma																										1
Adenoma																										1
Fibroadenoma						X	X			X					X		X		X	X	X			X	X	15
Lipoma																										1
Skin	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibroma									X			X					X									4
Fibrosarcoma																										1
Squamous cell carcinoma																										1
Squamous cell papilloma												X														1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Lipoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant																										1
Carcinoma, metastatic					X														X							3
Glioma malignant																										1
Peripheral nerve																										1
Spinal cord																										1

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

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

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

Number of Days on Study	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	0 5 6 1	0 5 6 2	0 5 6 3	0 5 6 4	0 5 6 5	0 5 7 2	0 5 7 3	0 5 8 1	0 5 8 2	0 5 8 3	0 5 9 1	0 5 9 2	0 5 9 3	0 5 9 4	0 6 0 1	0 6 0 2	0 6 1 2	0 6 2 2	0 6 2 3	0 6 3 1	0 6 3 2	0 6 4 1	0 6 4 2	0 6 4 3	0 6 4 4	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye														+											+	5
Zymbal's gland																						+				2
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear								X					X				X	X	X							15

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 5	7 5 5	7 5 5	7 5 5	7 5 5	7 5 5	7 5 5	7 5 5	7 5 5	
Carcass ID Number	0 7 2 2	0 7 2 3	0 7 3 1	0 7 3 2	0 7 3 3	0 7 4 1	0 7 4 2	0 7 4 3	0 7 4 4	0 7 4 5	0 7 5 2	0 7 6 1	0 7 7 1	0 7 7 2	0 7 7 3	0 6 6 1	0 6 6 2	0 6 6 3	0 6 9 1	0 6 9 2	0 6 9 3	0 6 9 4	0 6 9 5	0 7 0 1	0 7 0 2	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Schwannoma malignant																										1
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Schwannoma malignant																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																										1
Osteosarcoma, metastatic																										1
Mesentery																										1
Schwannoma malignant																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Schwannoma malignant																										1
Pharynx																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																					X				X	3
Osteosarcoma, metastatic																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Osteosarcoma, metastatic																										1
Pheochromocytoma complex																	X									1
Pheochromocytoma benign			X																	X						3
Pheochromocytoma benign, two								X																		1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																					X					1
Carcinoma																									X	2
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma	X	X		X	X	X			X	X			X			X		X	X	X		X				26
Pars distalis, carcinoma							X								X				X		X				X	6
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma							X			X					X							X			8
Follicular cell, adenoma											X															1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	4 2 8	4 5 7	4 7 7	6 4 7	6 6 6	6 8 9	6 9 5	7 0 6	7 0 6	7 0 6	7 0 7	7 0 7	7 0 7	7 1 3	7 1 3	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4
Carcass ID Number	0 7 5 5	0 6 8 5	0 7 0 4	0 7 5 3	0 7 3 4	0 6 6 4	0 7 6 4	0 6 8 4	0 7 6 2	0 7 6 3	0 7 0 3	0 7 5 1	0 6 7 3	0 7 2 4	0 6 7 1	0 6 7 2	0 6 8 1	0 6 8 2	0 6 8 3	0 7 1 1	0 7 1 2	0 7 1 3	0 7 1 4	0 7 1 5	0 7 2 1
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma				X					X																
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic															X										
Schwannoma malignant			X																						
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal											X										X			X	
Sarcoma stromal																									
Hematopoietic System																									
Blood			+	+					+		+	+	+	+	+	+	+	+	+	+		+		+	+
Bone marrow	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, schwannoma malignant			X																						
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic							X																		
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic															X										
Schwannoma malignant			X																						
Thymus	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	M	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma														X											
Fibroadenoma				X													X	X			X			X	
Fibroadenoma, multiple												X	X		X										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
Keratoacanthoma																									
Lipoma					X																				
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma															X										
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	7 4 5	
Carcass ID Number	0 7 2 2	0 7 2 3	0 7 3 1	0 7 3 2	0 7 3 3	0 7 4 1	0 7 4 2	0 7 4 3	0 7 4 4	0 7 4 5	0 7 5 2	0 7 6 1	0 7 7 1	0 7 7 2	0 7 7 3	0 7 6 1	0 6 6 2	0 6 6 3	0 6 9 1	0 6 9 2	0 6 9 3	0 6 9 4	0 6 9 5	0 7 0 1	0 7 0 2	Total Tissues/ Tumors
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma										X																1
Carcinoma							X																			3
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic																										1
Schwannoma malignant																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal											X		X	X					X				X			8
Sarcoma stromal								X													X					2
Hematopoietic System																										
Blood	+		+	I		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	37
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, schwannoma malignant																										1
Lymph node, mandibular	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic																										1
Schwannoma malignant																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma																							X			2
Fibroadenoma				X		X	X			X				X	X			X		X		X			X	15
Fibroadenoma, multiple													X													4
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma											X															1
Keratoacanthoma	X																									1
Lipoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic							X								X											2

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	
Carcass ID Number	0 7 8 3	0 8 2 2	0 8 2 3	0 8 4 1	0 8 4 2	0 8 4 3	0 8 4 4	0 8 5 1	0 8 5 2	0 8 5 3	0 8 5 4	0 8 5 5	0 8 6 1	0 8 8 1	0 8 8 2	0 8 8 3	0 8 8 4	0 8 9 3	0 8 9 4	0 8 7 1	0 8 7 2	0 8 7 3	0 8 7 4	0 8 9 1	0 8 9 2	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic					X																				1
Mesentery																						+			3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinus, adenoma																					X				1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																									2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue																								+	1
Squamous cell papilloma																								X	1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Adenoma																									1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign															X										2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																									1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	49
Pars distalis, adenoma	X		X		X	X			X	X		X	X	X	X			X	X		X			X	X	25
Pars distalis, adenoma, two							X				X															2
Pars distalis, carcinoma																		X		X						4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma	X										X						X					X				8
C-cell, adenoma, two												X														1
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	3 1 0	4 3 0	4 6 2	4 8 3	5 2 0	5 4 1	6 2 7	6 4 3	6 4 3	6 6 8	6 7 3	7 4 1	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 3	7 4 3
Carcass ID Number	0 8 3 5	0 8 1 5	0 8 0 4	0 8 3 4	0 7 8 4	0 8 1 2	0 8 4 5	0 8 6 2	0 8 8 5	0 8 9 5	0 8 2 1	0 7 9 4	0 7 9 1	0 7 9 2	0 7 9 3	0 8 0 1	0 8 0 2	0 8 0 3	0 8 1 3	0 8 2 4	0 8 3 1	0 8 3 2	0 8 3 3	0 7 8 1	0 7 8 2
Genital System (continued)																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal									X							X			X						
Sarcoma stromal							X																		
Hematopoietic System																									
Blood			+		+	+	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	I	+	+	+	+	M	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Adenocarcinoma										X															
Fibroadenoma					X									X	X				X		X			X	
Fibroadenoma, multiple												X													
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Fibrosarcoma																									
Keratoacanthoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle												+											+		
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic																									
Ependymoma malignant								X																	
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									X
Fibrosarcoma, metastatic																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye		+	+																						
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X	X						X	X														X

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 3	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	7 4 4	
Carcass ID Number	0 7 8 3	0 8 2 2	0 8 2 3	0 8 4 1	0 8 4 2	0 8 4 3	0 8 4 4	0 8 5 1	0 8 5 2	0 8 5 3	0 8 5 4	0 8 5 5	0 8 5 5	0 8 6 1	0 8 8 1	0 8 8 2	0 8 8 3	0 8 8 4	0 8 9 3	0 9 9 4	0 7 7 1	0 8 7 2	0 8 7 3	0 8 7 4	0 8 9 1	0 8 9 2	Total Tissues/ Tumors
Genital System (continued)																										
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal			X			X				X		X			X			X							X	10
Sarcoma stromal																										1
Hematopoietic System																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+		+	+	+	+	43
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	46
Integumentary System																										
Mammary gland	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenocarcinoma																										1
Fibroadenoma		X	X															X	X						X	11
Fibroadenoma, multiple																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrosarcoma					X																					1
Keratoacanthoma														X												1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										2
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic																				X						1
Ependymoma malignant																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Fibrosarcoma, metastatic					X																					1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye		+																								3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X											X					X					X			9

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

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

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 9 0 2	0 9 0 3	0 9 0 4	0 9 3 3	0 9 3 4	0 9 4 1	0 9 4 2	0 9 4 3	0 9 4 4	0 9 5 1	0 9 6 1	0 9 6 2	0 9 6 4	0 9 9 4	0 9 9 3	0 9 9 4	0 9 9 5	0 0 0 1	0 0 1 2	0 0 1 3	0 0 9 7	0 9 7 2	0 9 8 1	0 9 9 1	0 9 9 2	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma								X																		1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pharynx								+																		1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant			X																							1
Pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Adenoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X	X			X	X		X	X		X			X					X		X			22
Pars distalis, adenoma, two																										2
Pars distalis, carcinoma																	X								X	5
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma										X	X		X	X					X	X						8
C-cell, adenoma, two																										1
General Body System																										
None																										
Genital System																										
Clitoral gland	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma														X												2
Carcinoma																					X					1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granulosa cell tumor benign			X																							1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	4	5	5	5	6	6	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7
	9	1	2	6	1	2	4	4	5	6	6	7	9	9	0	0	3	3	3	3	3	3	3	4
	3	0	7	3	7	1	4	7	0	9	9	9	2	9	7	7	0	0	7	7	7	7	8	1
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9	9	9	0	9	9	9	9	9	9	0	9	9	9	9	9	9	9	9	9	9	9	9	9
	7	5	8	0	6	7	9	5	8	0	0	2	2	4	3	8	2	5	1	1	1	2	3	9	0
	4	4	4	1	3	3	5	3	3	5	2	4	3	5	1	2	2	2	1	2	3	1	2	3	1
Genital System (continued)																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal						X			X							X						X			X
Polyp stromal, two																	X								
Hematopoietic System																									
Blood	+		+						+	+	+		+		+	+							+		+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																				X					
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																X	X		X	X					X
Fibroadenoma, multiple																									
Sarcoma																X									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Fibroma															X										
Lipoma									X																
Squamous cell carcinoma									X																
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle											+														
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic											X														
Peripheral nerve	+																								
Spinal cord	+																								
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																									
Zymbal's gland							+																		
Carcinoma							X																		
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 9 0 2	0 9 0 3	0 9 0 4	0 9 3 3	0 9 3 4	0 9 4 1	0 9 4 2	0 9 4 3	0 9 4 4	0 9 5 1	0 9 6 1	0 9 6 2	0 9 6 4	0 9 9 4	0 9 9 4	0 9 9 3	0 9 9 4	0 9 9 5	0 9 9 6	0 9 9 7	0 9 9 8	0 9 9 9	0 9 9 10	0 9 9 11	0 9 9 12	0 9 9 13	0 9 9 14	Total Tissues/ Tumors
Genital System (continued)																											
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal				X		X		X						X	X											X	11
Polyp stromal, two							X											X									3
Hematopoietic System																											
Blood	+	+	+	+	+			+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	32
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thymoma benign																											1
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroadenoma	X													X							X						8
Fibroadenoma, multiple		X																				X		X			3
Sarcoma																											1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibroma																											1
Lipoma																											1
Squamous cell carcinoma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																											1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic																										X	2
Peripheral nerve																											1
Spinal cord																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma																				X							1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																											
Eye						+																					1
Zymbal's gland																											1
Carcinoma																											1
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	4	5	5	5	6	6	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7
	9	1	2	6	1	2	4	4	5	6	6	7	9	9	0	0	3	3	3	3	3	3	3	3	4
	3	0	7	3	7	1	4	7	0	9	9	9	2	9	7	7	0	0	7	7	7	7	7	8	1
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9	9	9	0	9	9	9	9	9	9	0	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	7	5	8	0	6	7	9	5	8	0	0	2	2	4	3	8	2	5	1	1	1	2	3	9	0
	4	4	4	1	3	3	5	3	3	5	2	4	3	5	1	2	2	2	1	2	3	1	2	3	1
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X											X					X	X	X						
Lymphoma malignant lymphocytic						X																			

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 9 0 2	0 9 0 3	0 9 0 4	0 9 3 3	0 9 3 4	0 9 4 1	0 9 4 2	0 9 4 3	0 9 4 4	0 9 5 1	0 9 6 1	0 9 6 2	0 9 6 4	0 9 9 4	0 9 9 3	0 0 0 4	0 0 0 5	0 0 1 1	0 0 1 2	0 0 1 3	0 9 7 1	0 9 7 2	0 9 8 1	0 9 9 1	0 9 9 2	Total Tissues/ Tumors
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear							X		X			X			X											9
Lymphoma malignant lymphocytic																										1

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Adrenal Cortex: Adenoma				
Overall rate[a]	1/50 (2%)	3/49 (6%)	1/49 (2%)	0/50 (0%)
Adjusted rate[b]	3.2%	8.3%	2.6%	0.0%
Terminal rate[c]	1/31 (3%)	3/36 (8%)	1/38 (3%)	0/32 (0%)
First incidence (days)	737 (T)	737 (T)	737 (T)	–[e]
Life table test[d]	P=0.168N	P=0.359	P=0.716N	P=0.494N
Logistic regression test[d]	P=0.168N	P=0.359	P=0.716N	P=0.494N
Cochran-Armitage test[d]	P=0.175N			
Fisher exact test[d]		P=0.301	P=0.747	P=0.500N
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate	2/50 (4%)	4/49 (8%)	2/49 (4%)	1/50 (2%)
Adjusted rate	6.5%	10.3%	5.3%	2.4%
Terminal rate	2/31 (6%)	3/36 (8%)	2/38 (5%)	0/32 (0%)
First incidence (days)	737 (T)	647	737 (T)	669
Life table test	P=0.233N	P=0.413	P=0.620N	P=0.474N
Logistic regression test	P=0.229N	P=0.387	P=0.620N	P=0.478N
Cochran-Armitage test	P=0.240N			
Fisher exact test		P=0.329	P=0.684	P=0.500N
Adrenal Medulla: Benign, Complex, or Malignant Pheochromocytoma				
Overall rate	2/50 (4%)	5/49 (10%)	2/49 (4%)	2/50 (4%)
Adjusted rate	6.5%	13.0%	5.3%	5.5%
Terminal rate	2/31 (6%)	4/36 (11%)	2/38 (5%)	1/32 (3%)
First incidence (days)	737 (T)	647	737 (T)	669
Life table test	P=0.355N	P=0.285	P=0.620N	P=0.671N
Logistic regression test	P=0.345N	P=0.267	P=0.620N	P=0.668N
Cochran-Armitage test	P=0.361N			
Fisher exact test		P=0.210	P=0.684	P=0.691N
Clitoral Gland: Carcinoma				
Overall rate	3/50 (6%)	3/49 (6%)	0/50 (0%)	1/47 (2%)
Adjusted rate	9.7%	7.1%	0.0%	3.3%
Terminal rate	3/31 (10%)	1/36 (3%)	0/39 (0%)	1/30 (3%)
First incidence (days)	737 (T)	647	–	737 (T)
Life table test	P=0.124N	P=0.572N	P=0.084N	P=0.316N
Logistic regression test	P=0.127N	P=0.629N	P=0.084N	P=0.316N
Cochran-Armitage test	P=0.135N			
Fisher exact test		P=0.651	P=0.121N	P=0.332N
Clitoral Gland: Adenoma or Carcinoma				
Overall rate	3/50 (6%)	4/49 (8%)	0/50 (0%)	3/47 (6%)
Adjusted rate	9.7%	9.7%	0.0%	10.0%
Terminal rate	3/31 (10%)	2/36 (6%)	0/39 (0%)	3/30 (10%)
First incidence (days)	737 (T)	647	–	737 (T)
Life table test	P=0.448N	P=0.598	P=0.084N	P=0.650
Logistic regression test	P=0.444N	P=0.552	P=0.084N	P=0.650
Cochran-Armitage test	P=0.457N			
Fisher exact test		P=0.489	P=0.121N	P=0.631

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Mammary Gland: Fibroadenoma				
Overall rate	15/50 (30%)	19/50 (38%)	12/50 (24%)	11/50 (22%)
Adjusted rate	45.2%	48.4%	29.8%	32.2%
Terminal rate	13/31 (42%)	16/36 (44%)	11/39 (28%)	9/32 (28%)
First incidence (days)	658	647	520	707
Life table test	P=0.080N	P=0.478	P=0.132N	P=0.203N
Logistic regression test	P=0.067N	P=0.511	P=0.224N	P=0.150N
Cochran-Armitage test	P=0.093N			
Fisher exact test		P=0.263	P=0.326N	P=0.247N
Mammary Gland: Adenoma or Fibroadenoma				
Overall rate	16/50 (32%)	21/50 (42%)	12/50 (24%)	11/50 (22%)
Adjusted rate	46.4%	52.3%	29.8%	32.2%
Terminal rate	13/31 (42%)	17/36 (47%)	11/39 (28%)	9/32 (28%)
First incidence (days)	589	647	520	707
Life table test	P=0.041N	P=0.415	P=0.094N	P=0.149N
Logistic regression test	P=0.033N	P=0.394	P=0.182N	P=0.111N
Cochran-Armitage test	P=0.049N			
Fisher exact test		P=0.204	P=0.252N	P=0.184N
Mammary Gland: Adenoma, Fibroadenoma, or Carcinoma				
Overall rate	17/50 (34%)	21/50 (42%)	13/50 (26%)	11/50 (22%)
Adjusted rate	49.4%	52.3%	31.5%	32.2%
Terminal rate	14/31 (45%)	17/36 (47%)	11/39 (28%)	9/32 (28%)
First incidence (days)	589	647	520	707
Life table test	P=0.031N	P=0.502	P=0.094N	P=0.104N
Logistic regression test	P=0.025N	P=0.491	P=0.187N	P=0.072N
Cochran-Armitage test	P=0.037N			
Fisher exact test		P=0.268	P=0.257N	P=0.133N
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	0/49 (0%)	3/48 (6%)	1/49 (2%)	1/49 (2%)
Adjusted rate	0.0%	8.3%	2.6%	2.8%
Terminal rate	0/31 (0%)	3/36 (8%)	1/39 (3%)	0/31 (0%)
First incidence (days)	–	737 (T)	737 (T)	707
Life table test	P=0.613N	P=0.148	P=0.546	P=0.530
Logistic regression test	P=0.601N	P=0.148	P=0.546	P=0.505
Cochran-Armitage test	P=0.604N			
Fisher exact test		P=0.117	P=0.500	P=0.500
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	29/48 (60%)	26/48 (54%)	27/49 (55%)	24/50 (48%)
Adjusted rate	71.9%	61.5%	64.0%	57.4%
Terminal rate	20/31 (65%)	20/36 (56%)	23/38 (61%)	15/32 (47%)
First incidence (days)	526	647	430	563
Life table test	P=0.219N	P=0.123N	P=0.139N	P=0.175N
Logistic regression test	P=0.134N	P=0.243N	P=0.354N	P=0.131N
Cochran-Armitage test	P=0.147N			
Fisher exact test		P=0.340N	P=0.373N	P=0.151N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Pituitary Gland (Pars Distalis): Carcinoma				
Overall rate	4/48 (8%)	6/48 (13%)	4/49 (8%)	5/50 (10%)
Adjusted rate	12.9%	15.6%	10.5%	14.0%
Terminal rate	4/31 (13%)	5/36 (14%)	4/38 (11%)	3/32 (9%)
First incidence (days)	737 (T)	428	737 (T)	669
Life table test	P=0.538	P=0.459	P=0.528N	P=0.538
Logistic regression test	P=0.561N	P=0.379	P=0.528N	P=0.559
Cochran-Armitage test	P=0.562			
Fisher exact test		P=0.370	P=0.631N	P=0.526
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rate	33/48 (69%)	31/48 (65%)	30/49 (61%)	29/50 (58%)
Adjusted rate	82.1%	71.7%	71.2%	66.7%
Terminal rate	24/31 (77%)	24/36 (67%)	26/38 (68%)	18/32 (56%)
First incidence (days)	526	428	430	563
Life table test	P=0.245N	P=0.131N	P=0.071N	P=0.211N
Logistic regression test	P=0.138N	P=0.311N	P=0.259N	P=0.146N
Cochran-Armitage test	P=0.154N			
Fisher exact test		P=0.414N	P=0.287N	P=0.186N
Skin: Fibroma				
Overall rate	4/50 (8%)	1/50 (2%)	0/50 (0%)	1/50 (2%)
Adjusted rate	12.9%	2.8%	0.0%	2.8%
Terminal rate	4/31 (13%)	1/36 (3%)	0/39 (0%)	0/32 (0%)
First incidence (days)	737 (T)	737 (T)	-	707
Life table test	P=0.103N	P=0.136N	P=0.038N	P=0.165N
Logistic regression test	P=0.101N	P=0.136N	P=0.038N	P=0.149N
Cochran-Armitage test	P=0.113N			
Fisher exact test		P=0.181N	P=0.059N	P=0.181N
Thyroid Gland (C-cell): Adenoma				
Overall rate	5/49 (10%)	8/50 (16%)	9/50 (18%)	9/50 (18%)
Adjusted rate	15.0%	19.2%	22.3%	25.6%
Terminal rate	4/31 (13%)	4/36 (11%)	8/39 (21%)	7/32 (22%)
First incidence (days)	606	647	541	493
Life table test	P=0.200	P=0.400	P=0.320	P=0.222
Logistic regression test	P=0.212	P=0.325	P=0.230	P=0.228
Cochran-Armitage test	P=0.202			
Fisher exact test		P=0.290	P=0.205	P=0.205
Uterus: Stromal Polyp				
Overall rate	13/50 (26%)	8/50 (16%)	10/50 (20%)	14/50 (28%)
Adjusted rate	34.5%	21.5%	24.9%	38.1%
Terminal rate	8/31 (26%)	7/36 (19%)	9/39 (23%)	10/32 (31%)
First incidence (days)	462	707	643	621
Life table test	P=0.301	P=0.093N	P=0.172N	P=0.555
Logistic regression test	P=0.312	P=0.143N	P=0.293N	P=0.538
Cochran-Armitage test	P=0.291			
Fisher exact test		P=0.163N	P=0.318N	P=0.500

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rate	13/50 (26%)	10/50 (20%)	11/50 (22%)	14/50 (28%)
Adjusted rate	34.5%	26.9%	26.6%	38.1%
Terminal rate	8/31 (26%)	9/36 (25%)	9/39 (23%)	10/32 (31%)
First incidence (days)	462	707	627	621
Life table test	P=0.367	P=0.196N	P=0.239N	P=0.555
Logistic regression test	P=0.378	P=0.276N	P=0.388N	P=0.538
Cochran-Armitage test	P=0.354			
Fisher exact test		P=0.318N	P=0.408N	P=0.500
All Organs: Mononuclear Cell Leukemia				
Overall rate	15/50 (30%)	13/50 (26%)	9/50 (18%)	9/50 (18%)
Adjusted rate	36.7%	30.9%	20.5%	24.2%
Terminal rate	7/31 (23%)	8/36 (22%)	5/39 (13%)	5/32 (16%)
First incidence (days)	359	666	462	493
Life table test	P=0.080N	P=0.246N	P=0.074N	P=0.111N
Logistic regression test	P=0.085N	P=0.463N	P=0.137N	P=0.155N
Cochran-Armitage test	P=0.077N			
Fisher exact test		P=0.412N	P=0.121N	P=0.121N
All Organs: Benign Neoplasms				
Overall rate	44/50 (88%)	39/50 (78%)	40/50 (80%)	38/50 (76%)
Adjusted rate	93.6%	88.6%	86.8%	82.4%
Terminal rate	28/31 (90%)	31/36 (86%)	33/39 (85%)	24/32 (75%)
First incidence (days)	380	647	310	493
Life table test	P=0.184N	P=0.028N	P=0.027N	P=0.124N
Logistic regression test	P=0.095N	P=0.049N	P=0.180N	P=0.064N
Cochran-Armitage test	P=0.130N			
Fisher exact test		P=0.143N	P=0.207N	P=0.096N
All Organs: Malignant Neoplasms				
Overall rate	27/50 (54%)	27/50 (54%)	15/50 (30%)	22/50 (44%)
Adjusted rate	59.3%	58.0%	33.1%	51.6%
Terminal rate	13/31 (42%)	17/36 (47%)	9/39 (23%)	12/32 (38%)
First incidence (days)	359	428	462	493
Life table test	P=0.115N	P=0.295N	P=0.008N	P=0.190N
Logistic regression test	P=0.105N	P=0.431	P=0.016N	P=0.268N
Cochran-Armitage test	P=0.092N			
Fisher exact test		P=0.579N	P=0.013N	P=0.212N
All Organs: Benign or Malignant Neoplasms				
Overall rate	48/50 (96%)	44/50 (88%)	44/50 (88%)	45/50 (90%)
Adjusted rate	96.0%	89.8%	88.0%	93.7%
Terminal rate	29/31 (94%)	31/36 (86%)	33/39 (85%)	29/32 (91%)
First incidence (days)	359	428	310	493
Life table test	P=0.349N	P=0.047N	P=0.037N	P=0.237N
Logistic regression test	P=0.289N	P=0.138N	P=0.217N	P=0.189N
Cochran-Armitage test	P=0.288N			
Fisher exact test		P=0.134N	P=0.134N	P=0.218N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

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

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

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	10
Early deaths				
Moribund	14	11	9	16
Natural deaths	5	3	2	2
Survivors				
Died last week of study	1			
Terminal sacrifice	30	36	39	32
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Intestine large, cecum	(10)	(10)	(10)	(10)
Parasite metazoan			1 (10%)	2 (20%)
Intestine large, colon	(10)	(10)	(10)	(10)
Parasite metazoan	2 (20%)		1 (10%)	1 (10%)
Intestine large, rectum	(10)	(9)	(10)	(9)
Parasite metazoan	3 (30%)	2 (22%)		
Liver	(10)	(10)	(10)	(10)
Angiectasis			2 (20%)	
Basophilic focus		5 (50%)		
Clear cell focus			1 (10%)	
Cytoplasmic alteration, focal				1 (10%)
Developmental malformation		1 (10%)	2 (20%)	
Fatty change	1 (10%)			
Granuloma		2 (20%)		
Hemorrhage, focal	1 (10%)			
Hepatodiaphragmatic nodule	1 (10%)		1 (10%)	1 (10%)
Hepatodiaphragmatic nodule, two	1 (10%)			
Bile duct, hyperplasia		1 (10%)	1 (10%)	3 (30%)
Perivascular, inflammation, chronic	3 (30%)			5 (50%)
Mesentery	(1)			
Fat, necrosis	1 (100%)			
Pancreas	(10)	(10)	(10)	(10)
Acinus, atrophy, focal	2 (20%)	1 (10%)	2 (20%)	2 (20%)
Stomach, glandular	(10)	(10)	(10)	(10)
Inflammation, chronic, focal				2 (20%)
Tooth	(1)			
Inflammation, acute	1 (100%)			
Cardiovascular System				
Heart	(10)	(10)	(10)	(10)
Cardiomyopathy		6 (60%)	6 (60%)	3 (30%)
Endocrine System				
Adrenal gland, cortex	(10)	(10)	(9)	(10)
Cytoplasmic alteration		1 (10%)		

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Endocrine System (continued)				
Pituitary gland	(10)	(10)	(9)	(10)
Pars distalis, cyst	1 (10%)	2 (20%)	1 (11%)	4 (40%)
Pars distalis, hyperplasia, focal	5 (50%)	3 (30%)		
Thyroid gland	(10)	(10)	(9)	(10)
C-cell, hyperplasia	1 (10%)	2 (20%)		3 (30%)
General Body System				
None				
Genital System				
Clitoral gland	(10)	(10)	(10)	(10)
Cyst	1 (10%)		1 (10%)	1 (10%)
Inflammation, acute		1 (10%)		
Inflammation, chronic, focal	1 (10%)	1 (10%)	1 (10%)	2 (20%)
Ovary	(10)	(10)	(10)	(10)
Cyst	1 (10%)			1 (10%)
Uterus	(10)	(10)	(10)	(10)
Dilatation	1 (10%)			
Hematopoietic System				
Lymph node	(10)	(10)	(10)	(10)
Mediastinal, congestion	1 (10%)	2 (20%)	2 (20%)	1 (10%)
Mediastinal, pigmentation			1 (10%)	5 (50%)
Pancreatic, congestion		2 (20%)		
Pancreatic, pigmentation			1 (10%)	
Lymph node, mandibular	(10)	(10)	(9)	(9)
Congestion	5 (50%)	6 (60%)	3 (33%)	5 (56%)
Pigmentation			1 (11%)	
Lymph node, mesenteric	(10)	(10)	(9)	(10)
Congestion	2 (20%)	4 (40%)	1 (11%)	1 (10%)
Lymphatic, angiectasis				1 (10%)
Spleen	(10)	(10)	(10)	(10)
Hematopoietic cell proliferation	2 (20%)			
Pigmentation, hemosiderin	8 (80%)	6 (60%)	8 (80%)	10 (100%)
Integumentary System				
Mammary gland	(9)	(6)	(9)	(9)
Lactation	3 (33%)		1 (11%)	
Musculoskeletal System				
None				
Nervous System				
None				

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Respiratory System				
Lung	(10)	(10)	(10)	(10)
Congestion	2 (20%)		1 (10%)	1 (10%)
Alveolus, metaplasia			1 (10%)	
Nose	(10)	(10)	(10)	(10)
Fungus			1 (10%)	
Inflammation, acute			1 (10%)	
Inflammation, chronic, focal	4 (40%)	7 (70%)	8 (80%)	6 (60%)
Metaplasia, squamous	2 (20%)			1 (10%)
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Cyst	1 (10%)			
Hypertrophy	1 (10%)			
Nephropathy	5 (50%)	4 (40%)	7 (70%)	4 (40%)
Renal tubule, pigmentation				1 (10%)
Urinary bladder	(10)	(10)	(10)	(10)
Inflammation, focal		1 (10%)		
2-Year Study				
Alimentary System				
Intestine large, cecum	(47)	(48)	(49)	(50)
Edema				1 (2%)
Infiltration cellular, lymphocyte				1 (2%)
Parasite metazoan	1 (2%)	1 (2%)	3 (6%)	1 (2%)
Muscularis, hypertrophy			1 (2%)	1 (2%)
Intestine large, colon	(47)	(47)	(50)	(49)
Parasite metazoan	3 (6%)	3 (6%)	7 (14%)	4 (8%)
Intestine large, rectum	(47)	(48)	(50)	(50)
Parasite metazoan	5 (11%)	11 (23%)	11 (22%)	8 (16%)
Intestine small, duodenum	(47)	(48)	(50)	(50)
Parasite metazoan			1 (2%)	
Artery, inflammation, acute			1 (2%)	
Intestine small, ileum	(47)	(47)	(49)	(50)
Autolysis				1 (2%)
Intestine small, jejunum	(46)	(47)	(49)	(50)
Parasite metazoan	1 (2%)			
Liver	(50)	(50)	(50)	(50)
Angiectasis	1 (2%)			2 (4%)
Basophilic focus	39 (78%)	38 (76%)	41 (82%)	40 (80%)
Clear cell focus	6 (12%)	4 (8%)	7 (14%)	11 (22%)
Congestion	1 (2%)		1 (2%)	
Developmental malformation	2 (4%)	4 (8%)	3 (6%)	2 (4%)
Fatty change	12 (24%)	10 (20%)	8 (16%)	10 (20%)
Granuloma	17 (34%)	19 (38%)	17 (34%)	14 (28%)

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Liver (continued)	(50)	(50)	(50)	(50)
Hematopoietic cell proliferation				1 (2%)
Hemorrhage	1 (2%)	1 (2%)		
Hepatodiaphragmatic nodule	6 (12%)	3 (6%)	2 (4%)	5 (10%)
Hepatodiaphragmatic nodule, two	1 (2%)			
Inflammation, acute, focal				1 (2%)
Inflammation, chronic, focal		1 (2%)		
Necrosis, focal				1 (2%)
Bile duct, hyperplasia	6 (12%)	6 (12%)	8 (16%)	6 (12%)
Hepatocyte, hyperplasia, focal	5 (10%)			1 (2%)
Serosa, fibrosis	1 (2%)			
Mesentery	(3)	(1)	(3)	
Accessory spleen			1 (33%)	
Artery, inflammation, chronic			1 (33%)	
Fat, necrosis	3 (100%)		1 (33%)	
Pancreas	(49)	(47)	(49)	(50)
Autolysis	1 (2%)			
Necrosis				1 (2%)
Acinus, atrophy	10 (20%)	6 (13%)	9 (18%)	14 (28%)
Artery, inflammation, acute			1 (2%)	
Pharynx		(1)		(1)
Hyperplasia, basal cell		1 (100%)		
Stomach, forestomach	(50)	(50)	(50)	(50)
Acanthosis				2 (4%)
Bulla				1 (2%)
Edema				1 (2%)
Erosion	1 (2%)			
Fibrosis	1 (2%)			
Hyperkeratosis		2 (4%)		
Hyperplasia, basal cell		1 (2%)		
Ulcer	2 (4%)			1 (2%)
Stomach, glandular	(49)	(50)	(50)	(50)
Cyst epithelial inclusion	1 (2%)			
Erosion	1 (2%)			
Inflammation, chronic	2 (4%)	1 (2%)		
Mineralization				1 (2%)
Ulcer		1 (2%)		
Artery, inflammation, chronic			1 (2%)	
Cardiovascular System				
Heart	(50)	(50)	(50)	(50)
Cardiomyopathy	23 (46%)	22 (44%)	21 (42%)	24 (48%)
Mineralization				2 (4%)
Artery, inflammation, chronic			1 (2%)	
Atrium, thrombosis	1 (2%)			

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Endocrine System				
Adrenal gland, cortex	(50)	(49)	(49)	(50)
Congestion	1 (2%)		1 (2%)	
Cytoplasmic alteration, focal	1 (2%)	1 (2%)	4 (8%)	4 (8%)
Hematopoietic cell proliferation				1 (2%)
Hypertrophy			1 (2%)	
Infarct	1 (2%)			
Adrenal gland, medulla	(50)	(49)	(49)	(50)
Hyperplasia, focal	6 (12%)	1 (2%)	2 (4%)	1 (2%)
Islets, pancreatic	(49)	(48)	(49)	(49)
Ectopic tissue				2 (4%)
Hyperplasia	1 (2%)	1 (2%)		1 (2%)
Parathyroid gland	(43)	(47)	(50)	(46)
Hyperplasia				2 (4%)
Pituitary gland	(48)	(48)	(49)	(50)
Pars distalis, angiectasis			3 (6%)	
Pars distalis, cyst	7 (15%)	6 (13%)	3 (6%)	5 (10%)
Pars distalis, hyperplasia, focal	2 (4%)	1 (2%)	4 (8%)	3 (6%)
Thyroid gland	(49)	(50)	(50)	(50)
Ultimobranchial cyst		1 (2%)		1 (2%)
C-cell, hyperplasia	4 (8%)	12 (24%)	5 (10%)	5 (10%)
Follicle, cyst		1 (2%)		
General Body System				
None				
Genital System				
Clitoral gland	(50)	(49)	(50)	(47)
Abscess		6 (12%)	2 (4%)	
Abscess, two		1 (2%)	1 (2%)	
Cyst	11 (22%)	4 (8%)	2 (4%)	4 (9%)
Cyst, two	1 (2%)			1 (2%)
Inflammation, acute		1 (2%)	1 (2%)	2 (4%)
Inflammation, chronic			1 (2%)	1 (2%)
Ovary	(49)	(50)	(50)	(50)
Congestion		3 (6%)	1 (2%)	1 (2%)
Cyst	2 (4%)	3 (6%)	2 (4%)	4 (8%)
Granuloma				1 (2%)
Uterus	(50)	(50)	(50)	(50)
Abscess				1 (2%)
Congestion	1 (2%)			
Cyst	2 (4%)		1 (2%)	1 (2%)
Dilatation	2 (4%)			1 (2%)
Hemorrhage		1 (2%)		
Prolapse				1 (2%)
Thrombosis	1 (2%)			
Endometrium, cyst		1 (2%)	1 (2%)	3 (6%)
Endometrium, necrosis				1 (2%)
Vagina	(2)			
Inflammation, acute	1 (50%)			

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Hematopoietic System				
Bone marrow	(50)	(49)	(50)	(49)
Atrophy			1 (2%)	
Hyperplasia	13 (26%)	11 (22%)	9 (18%)	10 (20%)
Lymph node	(50)	(50)	(50)	(50)
Mediastinal, congestion	1 (2%)	2 (4%)		5 (10%)
Mediastinal, pigmentation, hemosiderin		1 (2%)		1 (2%)
Pancreatic, lymphatic, angiectasis	1 (2%)			
Renal, pigmentation, hemosiderin	1 (2%)			
Lymph node, mandibular	(49)	(48)	(49)	(50)
Infiltration cellular, plasma cell		1 (2%)	1 (2%)	
Lymphatic, angiectasis		2 (4%)		1 (2%)
Lymph node, mesenteric	(50)	(49)	(50)	(50)
Autolysis		1 (2%)		
Congestion	1 (2%)	2 (4%)		2 (4%)
Depletion lymphoid				1 (2%)
Lymphatic, angiectasis				2 (4%)
Spleen	(50)	(50)	(50)	(50)
Congestion, focal			1 (2%)	
Fibrosis	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Granuloma		1 (2%)		
Hematopoietic cell proliferation	3 (6%)	4 (8%)	1 (2%)	1 (2%)
Hemorrhage, focal			1 (2%)	1 (2%)
Hyperplasia, histiocytic, lymphoid	1 (2%)	3 (6%)		
Infarct	1 (2%)	1 (2%)		
Necrosis, focal	1 (2%)			
Pigmentation, hemosiderin		3 (6%)	2 (4%)	2 (4%)
Capsule, fibrosis		1 (2%)		
Thymus	(44)	(47)	(46)	(47)
Congestion	1 (2%)		1 (2%)	
Integumentary System				
Mammary gland	(43)	(46)	(46)	(50)
Galactocele	7 (16%)	9 (20%)	8 (17%)	5 (10%)
Galactocele, multiple		2 (4%)	1 (2%)	
Lactation	2 (5%)	2 (4%)	3 (7%)	
Skin	(48)	(50)	(49)	(49)
Hyperkeratosis			1 (2%)	
Hyperplasia, basal cell			1 (2%)	
Pigmentation, melanin		1 (2%)		
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Hyperostosis	8 (16%)	11 (22%)	10 (20%)	11 (22%)
Skeletal muscle	(1)		(2)	(1)
Degeneration			1 (50%)	
Fibrosis			1 (50%)	

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Nervous System				
Brain	(50)	(50)	(50)	(50)
Compression	5 (10%)	8 (16%)	4 (8%)	8 (16%)
Hemorrhage, focal	1 (2%)		1 (2%)	1 (2%)
Hydrocephalus			1 (2%)	
Spinal cord	(1)			(1)
Hemorrhage, focal	1 (100%)			
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Congestion	2 (4%)	1 (2%)		2 (4%)
Hemorrhage, focal			1 (2%)	
Metaplasia, osseous		1 (2%)		
Alveolar epithelium, metaplasia		1 (2%)	2 (4%)	2 (4%)
Bronchus, metaplasia, squamous				1 (2%)
Nose	(50)	(50)	(50)	(50)
Fungus	3 (6%)	5 (10%)	2 (4%)	2 (4%)
Inflammation, acute	3 (6%)	5 (10%)	3 (6%)	2 (4%)
Inflammation, chronic	38 (76%)	41 (82%)	42 (84%)	45 (90%)
Metaplasia, squamous			1 (2%)	
Special Senses System				
Eye	(5)	(8)	(3)	(1)
Cataract	1 (20%)	6 (75%)	2 (67%)	1 (100%)
Degeneration	1 (20%)			
Hemorrhage		1 (13%)		
Synechia	1 (20%)			
Cornea, inflammation, acute	1 (20%)			
Retina, degeneration		2 (25%)		
Urinary System				
Kidney	(48)	(48)	(50)	(50)
Autolysis		1 (2%)	2 (4%)	
Fibrosis, focal	2 (4%)		2 (4%)	
Mineralization		1 (2%)		3 (6%)
Nephropathy	43 (90%)	44 (92%)	46 (92%)	48 (96%)
Pigmentation, bile	1 (2%)	1 (2%)		
Papilla, fibrosis, focal			1 (2%)	
Papilla, necrosis				1 (2%)
Urinary bladder	(45)	(47)	(49)	(48)
Hemorrhage, focal			1 (2%)	

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

APPENDIX C
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR DRINKING STUDY OF BARIUM CHLORIDE DIHYDRATE

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	59	60
15-Month interim evaluation	9	10	10	10
Early deaths				
Moribund	5	5	6	10
Natural deaths	1	2	4	8
Survivors				
Died last week of study	1		1	
Terminal sacrifice	44	43	38	32
Animals examined microscopically	60	60	59	60
15-Month Interim Evaluation				
Alimentary System				
Intestine small, duodenum	(9)	(10)	(10)	(10)
Polyp adenomatous		1 (10%)		
Liver	(9)	(10)	(10)	(10)
Hepatocellular carcinoma			1 (10%)	
Hepatocellular adenoma	1 (11%)	1 (10%)	2 (20%)	2 (20%)
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
None				
Integumentary System				
None				
Musculoskeletal System				
None				

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Nervous System				
None				
Respiratory System				
Lung	(9)	(10)	(10)	(10)
Alveolar/bronchiolar adenoma	1 (11%)	1 (10%)		1 (10%)
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Gallbladder	(44)	(47)	(46)	(41)
Intestine large, cecum	(48)	(49)	(47)	(46)
Intestine small, duodenum	(48)	(48)	(45)	(45)
Intestine small, jejunum	(49)	(48)	(46)	(44)
Adenocarcinoma	1 (2%)			1 (2%)
Intestine small, ileum	(49)	(44)	(46)	(44)
Liver	(51)	(50)	(48)	(50)
Carcinoma, metastatic	1 (2%)			
Hemangiosarcoma	2 (4%)	1 (2%)		1 (2%)
Hepatoblastoma			1 (2%)	
Hepatocellular carcinoma	5 (10%)	7 (14%)	6 (13%)	3 (6%)
Hepatocellular adenoma	12 (24%)	14 (28%)	10 (21%)	8 (16%)
Hepatocellular adenoma, multiple	12 (24%)	6 (12%)	5 (10%)	
Sarcoma			1 (2%)	
Sarcoma, metastatic			1 (2%)	
Pancreas	(50)	(50)	(48)	(50)
Hepatocellular carcinoma, metastatic			1 (2%)	
Sarcoma, metastatic			1 (2%)	
Acinus, adenoma	1 (2%)			
Pharynx	(1)	(1)		
Squamous cell carcinoma		1 (100%)		
Salivary glands	(51)	(50)	(49)	(50)
Stomach, forestomach	(50)	(50)	(48)	(48)
Sarcoma, metastatic			1 (2%)	
Squamous cell carcinoma		1 (2%)		
Squamous cell papilloma				1 (2%)
Cardiovascular System				
Heart	(51)	(50)	(49)	(50)
Hemangioma			1 (2%)	1 (2%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Endocrine System				
Adrenal cortex	(49)	(50)	(48)	(49)
Adenoma			1 (2%)	
Capsule, adenoma			3 (6%)	
Islets, pancreatic	(50)	(50)	(46)	(50)
Adenoma	3 (6%)		2 (4%)	1 (2%)
Carcinoma		1 (2%)		
Pituitary gland	(47)	(49)	(45)	(43)
Pars distalis, adenoma	1 (2%)	1 (2%)	2 (4%)	
Thyroid gland	(51)	(48)	(48)	(49)
Follicular cell, adenoma	1 (2%)	1 (2%)		
General Body System				
Tissue NOS	(1)			(2)
Hemangiosarcoma, metastatic				1 (50%)
Genital System				
Epididymis	(51)	(49)	(49)	(50)
Sarcoma				1 (2%)
Prostate	(50)	(47)	(48)	(49)
Seminal vesicle	(50)	(50)	(49)	(50)
Testes	(51)	(50)	(49)	(50)
Interstitial cell, adenoma			1 (2%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(48)	(48)
Lymph node	(2)		(4)	
Lymph node, mandibular	(36)	(46)	(43)	(36)
Lymph node, mesenteric	(49)	(47)	(46)	(39)
Hepatocellular carcinoma, metastatic			1 (2%)	
Sarcoma, metastatic			1 (2%)	
Spleen	(50)	(50)	(48)	(50)
Hemangioma				1 (2%)
Hemangiosarcoma	1 (2%)		2 (4%)	2 (4%)
Thymus	(39)	(42)	(44)	(35)
Integumentary System				
Skin	(51)	(50)	(49)	(49)
Fibroma	1 (2%)			1 (2%)
Fibrosarcoma				1 (2%)
Hemangioma				1 (2%)
Musculoskeletal System				
Bone	(51)	(50)	(49)	(50)
Sarcoma, metastatic			1 (2%)	

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Nervous System				
None				
Respiratory System				
Lung	(51)	(50)	(49)	(50)
Alveolar/bronchiolar adenoma	13 (25%)	9 (18%)	7 (14%)	5 (10%)
Alveolar/bronchiolar adenoma, multiple		1 (2%)		
Alveolar/bronchiolar adenoma, two	1 (2%)		1 (2%)	1 (2%)
Alveolar/bronchiolar carcinoma	1 (2%)			3 (6%)
Carcinoma, metastatic	2 (4%)			
Hepatocellular carcinoma, metastatic			1 (2%)	2 (4%)
Sarcoma, metastatic			2 (4%)	
Special Senses System				
Harderian gland	(6)	(2)	(2)	(2)
Adenoma	5 (83%)	2 (100%)	1 (50%)	2 (100%)
Carcinoma	1 (17%)			
Urinary System				
Kidney	(50)	(50)	(48)	(50)
Urinary bladder	(49)	(49)	(45)	(45)
Hemangioma			1 (2%)	
Systemic Lesions				
Multiple organs[b]	(51)	(50)	(49)	(50)
Lymphoma malignant	1 (2%)			
Lymphoma malignant histiocytic	2 (4%)			
Lymphoma malignant lymphocytic		1 (2%)	2 (4%)	1 (2%)
Lymphoma malignant mixed	5 (10%)	2 (4%)	8 (16%)	2 (4%)
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	2	3	2	3
2-Year study	45	33	32	26
Total primary neoplasms				
15-Month interim evaluation	2	3	3	3
2-Year study	69	48	55	37
Total animals with benign neoplasms				
15-Month interim evaluation	2	3	2	3
2-Year study	36	28	25	18
Total benign neoplasms				
15-Month interim evaluation	2	3	2	3
2-Year study	50	34	35	22

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Neoplasm Summary (continued)				
Total animals with malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	16	13	16	13
Total malignant neoplasms				
15-Month interim evaluation			1	
2-Year study	19	14	20	15
Total animals with metastatic neoplasms				
2-Year study	3		2	3
Total metastatic neoplasms				
2-Year study	3		10	3

[a] Number of animals examined microscopically at site and number of animals with lesion
[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 Barium Chloride Dihydrate: 0 ppm

Number of Days on Study	3 0 3	4 0 6	4 9 2	5 9 6	6 9 3	7 1 7	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1
Carcass ID Number	0 2 2 1	0 2 7 1	0 0 3 1	0 1 0 1	0 3 9 1	0 5 0 1	0 4 1 1	0 4 2 1	0 4 3 1	0 4 6 1	0 4 8 1	0 5 2 1	0 5 3 1	0 5 4 1	0 5 6 1	0 5 7 1	0 5 8 1	0 5 9 1	0 0 2 1	0 1 8 1	0 1 1 1	0 1 2 1	0 1 3 1	0 1 4 1	0 1 5 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	A	+	+	M	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	+	+	+	+	+	+	+	A	M	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic																			X						
Hemangiosarcoma													X												
Hepatocellular carcinoma					X													X				X			
Hepatocellular adenoma					X					X						X		X					X	X	
Hepatocellular adenoma, multiple						X			X					X	X										X
Mesentery		+														+									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma			X																						
Pharynx																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Tongue						+																+			
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	+	+	+	I	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma														X				X							
Parathyroid gland	M	M	+	+	+	+	+	+	M	M	M	+	+	M	+	+	M	M	+	+	+	+	M	+	M
Pituitary gland	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
Tissue NOS																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland			+	+			+	+	+			+		+					+				+	+	+

+: 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 Barium Chloride Dihydrate: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 1 6 1	0 1 7 1	0 1 9 1	0 2 0 1	0 2 1 1	0 2 3 1	0 2 4 1	0 2 5 1	0 2 8 1	0 3 0 1	0 3 1 1	0 3 2 1	0 3 3 1	0 3 4 1	0 3 5 1	0 3 7 1	0 4 0 1	0 4 4 1	0 4 5 1	0 4 7 1	0 5 5 1	0 5 4 1	0 5 5 1	0 6 1 1	0 7 1 1	0 7 9 1	Total Tissues/ Tumors
Alimentary System																												
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	50	
Gallbladder	+	+	+	M	I	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	44	
Intestine large, colon	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46	
Intestine large, rectum	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47	
Intestine large, cecum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48	
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48	
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Adenocarcinoma		X																									1	
Intestine small, ileum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51	
Carcinoma, metastatic																											1	
Hemangiosarcoma										X																	2	
Hepatocellular carcinoma								X								X											5	
Hepatocellular adenoma	X		X										X						X		X				X		12	
Hepatocellular adenoma, multiple				X	X	X			X		X				X		X										12	
Mesentery		+																									3	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Acinus, adenoma																											1	
Pharynx								+																			1	
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51	
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Tongue																											2	
Cardiovascular System																												
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51	
Endocrine System																												
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Adenoma																								X			3	
Parathyroid gland	+	M	M	M	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	M	+	+	+	+	+	35	
Pituitary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	47	
Pars distalis, adenoma																											1	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51	
Follicular cell, adenoma		X																									1	
General Body System																												
Tissue NOS																					+						1	
Genital System																												
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51	
Preputial gland	+	+	+	+	+	+	+	+				+	+	+		+	+	+		+	+	+	+	+	+	+	32	

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 0 ppm (continued)

Number of Days on Study	3	4	4	5	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	0	0	9	9	9	1	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	3	6	2	6	3	7	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2	2	0	1	3	5	4	4	4	4	4	5	5	5	5	5	5	5	0	0	1	1	1	1	1
	2	7	3	0	9	0	1	2	3	6	8	2	3	4	6	7	8	9	2	8	1	2	3	4	5
	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
Genital System (continued)																									
Prostate	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Blood		+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node													+						+						
Lymph node, mandibular	M	+	+	+	+	M	+	+	M	M	+	+	A	M	M	+	M	+	I	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Thymus	+	M	+	M	M	I	+	M	M	+	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma		X				X				X								X							X
Alveolar/bronchiolar adenoma, two											X														
Alveolar/bronchiolar carcinoma																				X					
Carcinoma, metastatic												X						X							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Harderian gland							+					+									+		+		
Adenoma							X														X		X		
Carcinoma												X													
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant													X												
Lymphoma malignant histiocytic																	X								
Lymphoma malignant mixed																		X	X						

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 0 ppm (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 2	7 3 2	7 3 2	7 3 2	
Carcass ID Number	0 1 6 1	0 1 7 1	0 1 9 1	0 2 0 1	0 2 1 1	0 2 3 1	0 2 4 1	0 2 5 1	0 2 8 1	0 3 0 1	0 3 1 1	0 3 2 1	0 3 3 1	0 3 4 1	0 3 5 1	0 3 7 1	0 4 0 1	0 4 4 1	0 4 5 1	0 4 7 1	0 5 5 1	0 0 4 1	0 0 5 1	0 0 6 1	0 0 7 1	0 0 9 1	Total Tissues/ Tumors
Genital System (continued)																											
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hematopoietic System																											
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node																											2
Lymph node, mandibular	+	M	+	+	+	+	+	M	+	+	M	+	+	M	M	+	+	+	+	M	+	+	+	+	+	+	36
Lymph node, mesenteric	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																						X					1
Thymus	+	I	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	39
Integumentary System																											
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Fibroma							X																				1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Alveolar/bronchiolar adenoma	X		X									X	X		X				X	X	X						13
Alveolar/bronchiolar adenoma, two																											1
Alveolar/bronchiolar carcinoma																											1
Carcinoma, metastatic																											2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																											
Harderian gland																									+	+	6
Adenoma																									X	X	5
Carcinoma																											1
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymphoma malignant																											1
Lymphoma malignant histiocytic								X																			2
Lymphoma malignant mixed									X								X							X			5

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	0 9 1 1	0 9 3 1	0 9 4 1	0 9 6 1	0 9 8 1	1 0 0 1	1 0 1 1	1 0 2 1	1 0 4 1	1 0 5 1	1 0 6 1	1 1 0 1	1 1 1 1	1 1 2 1	1 1 3 1	1 1 5 1	1 1 6 1	1 1 8 1	1 1 9 1	1 2 0 1	1 7 5 1	0 8 0 1	0 8 1 1	0 8 6 1	0 8 8 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	47
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	48
Intestine small, ileum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Hepatocellular carcinoma											X										X	X	X	X		7
Hepatocellular adenoma	X										X						X		X		X			X		14
Hepatocellular adenoma, multiple			X											X		X										6
Mesentery									+																	1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pharynx		+																								1
Squamous cell carcinoma		X																								1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma													X													1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue																				+						1
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Parathyroid gland	+	+	M	+	M	+	M	M	M	+	M	M	M	+	M	+	+	M	+	+	M	+	+	+	+	34
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	48
Follicular cell, adenoma																										1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland	+	+			+	+			+		+	+	+	+	+	+	+	+	+			+	+	+	+	33
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	47
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	5 2 0	5 2 9	5 7 8	6 0 2	6 4 1	6 6 1	6 7 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 6 2 1	0 7 1 1	0 9 5 1	0 6 5 1	1 1 7 1	0 6 1 1	1 1 4 1	0 6 3 1	0 6 4 1	0 6 6 1	0 6 7 1	0 6 8 1	0 6 9 1	0 7 0 1	0 7 2 1	0 7 3 1	0 7 4 1	0 7 6 1	0 7 7 1	0 8 2 1	0 8 3 1	0 8 4 1	0 8 5 1	0 8 9 1	0 9 0 1
Hematopoietic System																										
Blood											+															
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	M	+	M	+	M	M	M	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma			X			X				X					X							X				
Alveolar/bronchiolar adenoma, multiple																									X	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	
Special Senses System																										
Harderian gland													+				+									
Adenoma													X				X									
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																										
Lymphoma malignant mixed									X																	

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	
Carcass ID Number	0 9 1 1	0 9 3 1	0 9 4 1	0 9 6 1	0 9 8 1	1 0 0 1	1 0 1 1	1 0 2 1	1 0 4 1	1 0 5 1	1 0 6 1	1 1 0 1	1 1 1 1	1 1 2 1	1 1 3 1	1 1 5 1	1 1 6 1	1 1 8 1	1 1 9 1	1 2 0 1	7 5 1	8 0 1	8 1 1	8 6 1	8 8 1	Total Tissues/ Tumors
Hematopoietic System																										
Blood																										1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	46
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	42
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X										X	X									X				9
Alveolar/bronchiolar adenoma, multiple																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	48
Special Senses System																										
Harderian gland																										2
Adenoma																										2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic	X																									1
Lymphoma malignant mixed															X											2

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm

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

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	1 4 5 1	1 4 7 1	1 4 9 1	1 5 2 1	1 5 4 1	1 5 6 1	1 5 8 1	1 5 9 1	1 6 3 1	1 6 4 1	1 6 5 1	1 6 6 1	1 6 7 1	1 6 8 1	1 7 0 1	1 7 1 1	1 7 2 1	1 7 4 1	1 7 9 1	1 8 0 1	1 2 1 1	1 2 3 1	1 2 4 1	1 2 5 1	Total Tissues/ Tumors
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hepatoblastoma																									1
Hepatocellular carcinoma												X									X				6
Hepatocellular adenoma			X				X							X	X						X				10
Hepatocellular adenoma, multiple					X																				5
Sarcoma																									1
Sarcoma, metastatic																									1
Mesentery																									1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hepatocellular carcinoma, metastatic																									1
Sarcoma, metastatic																									1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic																									1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangioma																									1
Endocrine System																									
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma					X																				1
Capsule, adenoma						X																			3
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	47
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma																X									2
Parathyroid gland	+	M	M	+	+	+	M	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	38
Pituitary gland	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Pars distalis, adenoma							X																		2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland		+		+	+	+	+	+		+	+	+	+	+	+	+	+	+	+						26
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	4 0 3	4 4 2	4 5 7	5 8 8	6 1 3	6 2 9	6 6 6	6 6 9	6 9 5	7 2 0	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8
Carcass ID Number	1 6 9 1	1 2 2 1	1 4 3 1	1 3 7 1	1 7 3 1	1 3 8 1	1 3 5 1	1 4 2 1	1 5 0 1	1 6 2 1	1 5 5 1	1 7 5 1	1 7 6 1	1 7 7 1	1 7 8 1	2 2 6 1	2 2 7 1	2 2 8 1	2 3 9 1	3 3 0 1	3 3 1 1	3 3 4 1	3 3 6 1	3 3 9 1	4 4 0 1
Genital System (continued)																								
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell, adenoma																	X							
Hematopoietic System																								
Blood				+	+	+		+				+	+	+		+		+	+	+	+		+	+
Bone marrow	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node				+				+																
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	M	+	+
Lymph node, mesenteric	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic									X															
Sarcoma, metastatic					X																			
Spleen	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma						X																		
Thymus	+	+	M	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																								
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic					X																			
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma													X							X		X		
Alveolar/bronchiolar adenoma, two																								
Hepatocellular carcinoma, metastatic									X															
Sarcoma, metastatic					X				X															
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Eye		+																						
Harderian gland		+																						
Adenoma																								
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	A	+	+	+	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																								
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic								X			X													
Lymphoma malignant mixed				X				X									X							

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	1 4 5 1	1 4 7 1	1 4 9 1	1 5 2 1	1 5 4 1	1 5 6 1	1 5 8 1	1 5 9 1	1 6 3 1	1 6 4 1	1 6 5 1	1 6 6 1	1 6 7 1	1 6 8 1	1 7 0 1	1 7 1 1	1 7 2 1	1 7 4 1	1 7 9 1	1 8 0 1	1 2 1 1	1 2 3 1	1 2 4 1	1 2 5 1	Total Tissues/ Tumors
Genital System (continued)																										
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Interstitial cell, adenoma																										1
Hematopoietic System																										
Blood	+	+	+	+			+	+	+	+			+	+	+			+								27
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node					+																			+		4
Lymph node, mandibular	+	+	+	+	+	I	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	43
Lymph node, mesenteric	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Hepatocellular carcinoma, metastatic																										1
Sarcoma, metastatic																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hemangiosarcoma																				X						2
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+		44
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sarcoma, metastatic																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma					X								X						X						X	7
Alveolar/bronchiolar adenoma, two		X																								1
Hepatocellular carcinoma, metastatic																										1
Sarcoma, metastatic																										2
Nose	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Special Senses System																										
Eye																										1
Harderian gland								+																		2
Adenoma								X																		1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Hemangioma																					X					1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										2
Lymphoma malignant mixed		X			X													X			X		X			8

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm

Number of Days on Study	0 2 3 4 4 4 5 5 6 6 6 6 6 6 6 6 7 7 7 7 7 7 7 7 2 6 9 6 8 9 1 6 0 0 0 2 2 3 5 6 7 2 2 2 2 2 2 2 2 3 1 9 9 3 4 8 7 2 5 5 6 7 1 9 4 5 0 5 5 5 5 5 5 5
Carcass ID Number	2 2 2 2 1 2 2 1 2 2 2 2 1 2 1 1 2 1 1 1 1 1 1 1 1 2 3 0 3 8 0 3 9 2 1 3 3 9 3 8 9 2 8 8 8 8 8 9 9 9 1 0 3 2 9 0 7 0 9 4 4 3 1 6 8 4 6 6 1 4 5 7 2 3 5 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
Alimentary System	
Esophagus	+ + + + + + + + + + + + + + + + + + M + + + + + +
Gallbladder	M A + + + + A + + + + + A + + + A A + + + + + + + +
Intestine large, colon	+ + + + + + + A + + + + A + + + A A + + + + + + + +
Intestine large, rectum	+ + M + + + + + + + + + A + + + A + + + + + + + +
Intestine large, cecum	+ + + + + + A + + + + + A + + + A A + + + + + + + +
Intestine small, duodenum	+ + + + + + A A + + + + A + + + A A + + + + + + + +
Intestine small, jejunum	+ + + + + + A A + + + + A + + + A A + + + + + + + M
Adenocarcinoma	
Intestine small, ileum	+ + + + + + A A + + + + A + + + A A + + + + + + M +
Liver	+ +
Hemangiosarcoma	
Hepatocellular carcinoma	X
Hepatocellular adenoma	X X X X
Mesentery	
Pancreas	+ +
Salivary glands	+ +
Stomach, forestomach	+ + + + + + + + + + M + + + + A + + + + + + + + +
Squamous cell papilloma	
Stomach, glandular	+ + + + + + + A + + + + + + + A A + + + + + + + +
Cardiovascular System	
Heart	+ +
Hemangioma	
Endocrine System	
Adrenal cortex	+ M + +
Adrenal medulla	+ M + +
Islets, pancreatic	+ +
Adenoma	X
Parathyroid gland	+ + + M M + + + + M + M M + I I + + + + + + + M +
Pituitary gland	M + M + + + M + M + + + + + + + + + + + + + + + +
Thyroid gland	+ + + M +
General Body System	
Tissue NOS	+
Hemangiosarcoma, metastatic	
Genital System	
Epididymis	+ +
Sarcoma	
Penis	+
Preputial gland	+ +
Prostate	+ + M +
Seminal vesicle	+ +
Testes	+ +

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	
Carcass ID Number	1 9 6 1	1 9 7 1	1 9 8 1	1 9 9 1	2 0 1 1	2 0 2 1	2 0 4 1	2 0 5 1	2 0 7 1	2 1 0 1	2 1 1 1	2 1 2 1	2 1 5 1	2 1 6 1	2 1 8 1	2 1 9 1	2 2 3 1	2 2 4 1	2 2 7 1	2 2 8 1	2 3 1 1	2 3 5 1	2 3 8 1	2 3 9 1	2 4 0 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Gallbladder	+	+	M	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Adenocarcinoma													X													1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma							X																			1
Hepatocellular carcinoma	X													X												3
Hepatocellular adenoma										X										X		X	X			8
Mesentery																					+					1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Squamous cell papilloma								X																		1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																								X		1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	48
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Parathyroid gland	+	+	+	M	+	+	M	M	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	36
Pituitary gland	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	43
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
Tissue NOS																	+									2
Hemangiosarcoma, metastatic																	X									1
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma																						X				1
Penis																										1
Preputial gland	+		+	+	+	+	+		+	+	+	+	+		+		+		+	+	+	+		+		30
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	0 2 3 4 4 4 5 5 6 6 6 6 6 6 6 6 7 7 7 7 7 7 7
	2 6 9 6 8 9 1 6 0 0 0 2 2 3 5 6 7 2 2 2 2 2 2 2
	3 1 9 9 3 4 8 7 2 5 5 6 7 1 9 4 5 0 5 5 5 5 5 5
Carcass ID Number	2 2 2 2 1 2 2 1 2 2 2 2 1 2 1 1 2 1 1 1 1 1 1 1
	2 3 0 3 8 0 3 9 2 1 3 3 9 3 8 9 2 8 8 8 8 8 9 9
	1 0 3 2 9 0 7 0 9 4 4 3 1 6 8 4 6 6 1 4 5 7 2 3
	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Hematopoietic System	
Blood	+ + + + + + +
Bone marrow	+ + + + + + + + + + + + + + A + + + + + + + +
Lymph node, mandibular	+ + + M + + + M M M + + + M M M M M + + M + + +
Lymph node, mesenteric	+ M + + + M M M + + + + M + + M M + + + + M + + +
Spleen	+ +
Hemangioma	X
Hemangiosarcoma	
Thymus	+ M I + + M M + + M + M M M M M M + + + + + + + +
Integumentary System	
Mammary gland	M M M M M M M M M M M M M M M M M M M M M M M M
Skin	+ A +
Fibroma	X
Fibrosarcoma	
Hemangioma	
Musculoskeletal System	
Bone	+ +
Nervous System	
Brain	+ +
Respiratory System	
Lung	+ +
Alveolar/bronchiolar adenoma	X
Alveolar/bronchiolar adenoma, two	X
Alveolar/bronchiolar carcinoma	X
Hepatocellular carcinoma, metastatic	X
Nose	+ +
Trachea	+ +
Special Senses System	
Harderian gland	+ A
Adenoma	X
Urinary System	
Kidney	+ +
Urinary bladder	+ + + + + + A A + + + A + + + A A + + + + + + +
Systemic Lesions	
Multiple organs	+ +
Lymphoma malignant lymphocytic	
Lymphoma malignant mixed	X

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	7 2 5	
Carcass ID Number	1 9 6 1	1 9 7 1	1 9 8 1	1 9 9 1	2 0 1 1	2 0 2 1	2 0 4 1	2 0 5 1	2 0 7 1	2 1 0 1	2 1 1 1	2 1 2 1	2 1 5 1	2 1 6 1	2 1 8 1	2 1 9 1	2 2 3 1	2 2 4 1	2 2 7 1	2 2 8 1	2 3 1 1	2 3 5 1	2 3 8 1	2 3 9 1	2 4 0 1	Total Tissues/ Tumors
Hematopoietic System																										
Blood	+	+		+			+	+	+				+		+						+		+	+	+	22
Bone marrow	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mandibular	+	+	M	+	M	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	36
Lymph node, mesenteric	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	39
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Hemangiosarcoma															X		X									2
Thymus	M	+	+	+	+	+	+	+	+	I	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	35
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibroma																										1
Fibrosarcoma										X																1
Hemangioma																	X									1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma				X									X			X						X				5
Alveolar/bronchiolar adenoma, two																										1
Alveolar/bronchiolar carcinoma																	X	X								3
Hepatocellular carcinoma, metastatic														X												2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland																						+				2
Adenoma																						X				2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic			X																							1
Lymphoma malignant mixed														X												2

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Adrenal Cortex: Adenoma				
Overall rates[a]	0/51 (0%)	0/50 (0%)	3/49 (6%)	0/50 (0%)
Adjusted rates[b]	0.0%	0.0%	7.7%	0.0%
Terminal rates[c]	0/45 (0%)	0/43 (0%)	3/39 (8%)	0/32 (0%)
First incidence (days)	–[e]	–	725 (T)	–
Life table tests[d]	P=0.426	–	P=0.097	–
Logistic regression tests[d]	P=0.426	–	P=0.097	–
Cochran-Armitage test[d]	P=0.511			
Fisher exact test[d]		–	P=0.114	–
Harderian Gland: Adenoma				
Overall rates	5/51 (10%)	2/50 (4%)	1/49 (2%)	2/50 (4%)
Adjusted rates	11.1%	4.7%	2.6%	5.6%
Terminal rates	5/45 (11%)	2/43 (5%)	1/39 (3%)	1/32 (3%)
First incidence (days)	725 (T)	725 (T)	725 (T)	626
Life table tests	P=0.280N	P=0.235N	P=0.139N	P=0.362N
Logistic regression tests	P=0.228N	P=0.235N	P=0.139N	P=0.285N
Cochran-Armitage test	P=0.178N			
Fisher exact test		P=0.226N	P=0.112N	P=0.226N
Harderian Gland: Adenoma or Carcinoma				
Overall rates	6/51 (12%)	2/50 (4%)	1/49 (2%)	2/50 (4%)
Adjusted rates	13.3%	4.7%	2.6%	5.6%
Terminal rates	6/45 (13%)	2/43 (5%)	1/39 (3%)	1/32 (3%)
First incidence (days)	725 (T)	725 (T)	725 (T)	626
Life table tests	P=0.189N	P=0.149N	P=0.084N	P=0.261N
Logistic regression tests	P=0.149N	P=0.149N	P=0.084N	P=0.194N
Cochran-Armitage test	P=0.109N			
Fisher exact test		P=0.141N	P=0.062N	P=0.141N
Liver: Hepatocellular Adenoma				
Overall rates	24/51 (47%)	20/50 (40%)	15/48 (31%)	8/50 (16%)
Adjusted rates	51.1%	44.4%	37.2%	23.5%
Terminal rates	22/45 (49%)	18/43 (42%)	14/39 (36%)	6/32 (19%)
First incidence (days)	693	641	403	675
Life table tests	P=0.010N	P=0.350N	P=0.139N	P=0.019N
Logistic regression tests	P=0.002N	P=0.318N	P=0.093N	P=0.008N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.304N	P=0.080N	P<0.001N
Liver: Hepatocellular Carcinoma				
Overall rates	5/51 (10%)	7/50 (14%)	6/48 (13%)	3/50 (6%)
Adjusted rates	10.8%	15.2%	13.7%	8.5%
Terminal rates	4/45 (9%)	5/43 (12%)	3/39 (8%)	2/32 (6%)
First incidence (days)	693	529	403	605
Life table tests	P=0.394N	P=0.355	P=0.419	P=0.537N
Logistic regression tests	P=0.191N	P=0.352	P=0.466	P=0.431N
Cochran-Armitage test	P=0.230N			
Fisher exact test		P=0.366	P=0.457	P=0.369N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rates	27/51 (53%)	24/50 (48%)	18/48 (38%)	11/50 (22%)
Adjusted rates	57.4%	51.0%	42.5%	31.1%
Terminal rates	25/45 (56%)	20/43 (47%)	15/39 (38%)	8/32 (25%)
First incidence (days)	693	529	403	605
Life table tests	P=0.019N	P=0.435N	P=0.168N	P=0.036N
Logistic regression tests	P=0.002N	P=0.370N	P=0.102N	P=0.010N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.383N	P=0.090N	P=0.001N
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	14/51 (27%)	10/50 (20%)	8/49 (16%)	6/50 (12%)
Adjusted rates	29.7%	22.1%	20.5%	18.8%
Terminal rates	12/45 (27%)	8/43 (19%)	8/39 (21%)	6/32 (19%)
First incidence (days)	406	578	725 (T)	725 (T)
Life table tests	P=0.138N	P=0.287N	P=0.202N	P=0.170N
Logistic regression tests	P=0.062N	P=0.262N	P=0.142N	P=0.078N
Cochran-Armitage test	P=0.035N			
Fisher exact test		P=0.260N	P=0.135N	P=0.044N
Lung: Alveolar/bronchiolar Carcinoma				
Overall rates	1/51 (2%)	0/50 (0%)	0/49 (0%)	3/50 (6%)
Adjusted rates	2.2%	0.0%	0.0%	8.2%
Terminal rates	1/45 (2%)	0/43 (0%)	0/39 (0%)	2/32 (6%)
First incidence (days)	725 (T)	–	–	399
Life table tests	P=0.050	P=0.509N	P=0.529N	P=0.218
Logistic regression tests	P=0.107	P=0.509N	P=0.529N	P=0.336
Cochran-Armitage test	P=0.078			
Fisher exact test		P=0.505N	P=0.510N	P=0.301
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rates	15/51 (29%)	10/50 (20%)	8/49 (16%)	9/50 (18%)
Adjusted rates	31.8%	22.1%	20.5%	26.6%
Terminal rates	13/45 (29%)	8/43 (19%)	8/39 (21%)	8/32 (25%)
First incidence (days)	406	578	725 (T)	399
Life table tests	P=0.362N	P=0.220N	P=0.148N	P=0.385N
Logistic regression tests	P=0.172N	P=0.195N	P=0.100N	P=0.175N
Cochran-Armitage test	P=0.126N			
Fisher exact test		P=0.194N	P=0.094N	P=0.133N
Pancreatic Islets: Adenoma				
Overall rates	3/50 (6%)	0/50 (0%)	2/46 (4%)	1/50 (2%)
Adjusted rates	6.8%	0.0%	5.3%	2.6%
Terminal rates	3/44 (7%)	0/43 (0%)	2/38 (5%)	0/32 (0%)
First incidence (days)	725 (T)	–	725 (T)	626
Life table tests	P=0.479N	P=0.125N	P=0.567N	P=0.412N
Logistic regression tests	P=0.414N	P=0.125N	P=0.567N	P=0.333N
Cochran-Armitage test	P=0.376N			
Fisher exact test		P=0.121N	P=0.540N	P=0.309N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Pancreatic Islets: Adenoma or Carcinoma				
Overall rates	3/50 (6%)	1/50 (2%)	2/46 (4%)	1/50 (2%)
Adjusted rates	6.8%	2.1%	5.3%	2.6%
Terminal rates	3/44 (7%)	0/43 (0%)	2/38 (5%)	0/32 (0%)
First incidence (days)	725 (T)	602	725 (T)	626
Life table tests	P=0.395N	P=0.313N	P=0.567N	P=0.412N
Logistic regression tests	P=0.303N	P=0.311N	P=0.567N	P=0.333N
Cochran-Armitage test	P=0.301N			
Fisher exact test		P=0.309N	P=0.540N	P=0.309N
All Organs: Hemangioma				
Overall rates	0/51 (0%)	0/50 (0%)	2/49 (4%)	3/50(6%)
Adjusted rates	0.0%	0.0%	5.1%	8.5%
Terminal rates	0/45 (0%)	0/43 (0%)	2/39 (5%)	2/32 (6%)
First incidence (days)	–	–	725 (T)	605
Life table tests	P=0.012	–	P=0.208	P=0.079
Logistic regression tests	P=0.019	–	P=0.208	P=0.109
Cochran-Armitage test	P=0.025			
Fisher exact test		–	P=0.238	P=0.118
All Organs: Hemangiosarcoma				
Overall rates	3/51 (6%)	1/50 (2%)	2/49 (4%)	3/50 (6%)
Adjusted rates	6.7%	2.1%	4.8%	9.4%
Terminal rates	3/45 (7%)	0/43 (0%)	1/39 (3%)	3/32 (9%)
First incidence (days)	725 (T)	578	629	725 (T)
Life table tests	P=0.318	P=0.319N	P=0.558N	P=0.498
Logistic regression tests	P=0.426	P=0.323N	P=0.521N	P=0.498
Cochran-Armitage test	P=0.447			
Fisher exact test		P=0.316N	P=0.519N	P=0.652
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	3/51 (6%)	1/50 (2%)	4/49 (8%)	5/50 (10%)
Adjusted rates	6.7%	2.1%	9.8%	14.6%
Terminal rates	3/45 (7%)	0/43 (0%)	3/39 (8%)	4/32 (13%)
First incidence (days)	725 (T)	578	629	605
Life table tests	P=0.062	P=0.319N	P=0.429	P=0.202
Logistic regression tests	P=0.118	P=0.323N	P=0.469	P=0.268
Cochran-Armitage test	P=0.134			
Fisher exact test		P=0.316N	P=0.477	P=0.346
All Organs: Malignant Lymphoma (Histiocytic, Lymphocytic, or Mixed)				
Overall rates	8/51 (16%)	3/50 (6%)	9/49 (18%)	3/50 (6%)
Adjusted rates	17.8%	7.0%	21.6%	9.4%
Terminal rates	8/45 (18%)	3/43 (7%)	7/39 (18%)	3/32 (9%)
First incidence (days)	725 (T)	725 (T)	588	725 (T)
Life table tests	P=0.409N	P=0.115N	P=0.381	P=0.241N
Logistic regression tests	P=0.318N	P=0.115N	P=0.445	P=0.241N
Cochran-Armitage test	P=0.211N			
Fisher exact test		P=0.106N	P=0.464	P=0.106N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
All Organs: Benign Neoplasms				
Overall rates	36/51 (71%)	28/50 (56%)	25/49 (51%)	19/50 (38%)
Adjusted rates	73.4%	59.6%	62.3%	52.5%
Terminal rates	32/45 (71%)	24/43 (56%)	24/39 (62%)	15/32 (47%)
First incidence (days)	406	578	403	605
Life table tests	P=0.078N	P=0.148N	P=0.117N	P=0.079N
Logistic regression tests	P=0.006N	P=0.086N	P=0.039N	P=0.005N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.094N	P=0.036N	P<0.001N
All Organs: Malignant Neoplasms				
Overall rates	16/51 (31%)	13/50 (26%)	17/49 (35%)	13/50 (26%)
Adjusted rates	34.8%	28.0%	37.4%	37.3%
Terminal rates	15/45 (33%)	10/43 (23%)	11/39 (28%)	11/32 (34%)
First incidence (days)	693	529	403	399
Life table tests	P=0.300	P=0.383N	P=0.336	P=0.442
Logistic regression tests	P=0.447N	P=0.350N	P=0.442	P=0.511N
Cochran-Armitage test	P=0.406N			
Fisher exact test		P=0.353N	P=0.444	P=0.353N
All Organs: Benign or Malignant Neoplasms				
Overall rates	45/51 (88%)	33/50 (66%)	32/49 (65%)	26/50 (52%)
Adjusted rates	91.8%	67.3%	70.9%	69.9%
Terminal rates	41/45 (91%)	27/43 (63%)	26/39 (67%)	21/32 (66%)
First incidence (days)	406	529	403	399
Life table tests	P=0.133N	P=0.033N	P=0.080N	P=0.073N
Logistic regression tests	P=0.002N	P=0.006N	P=0.007N	P<0.001N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.007N	P=0.006N	P<0.001N

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

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

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	59	60
15-Month interim evaluation	9	10	10	10
Early deaths				
Moribund	5	5	6	10
Natural deaths	1	2	4	8
Survivors				
Died last week of study	1		1	
Terminal sacrifice	44	43	38	32
Animals examined microscopically	60	60	59	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(9)	(10)	(10)	(10)
Fatty change	7 (78%)	6 (60%)	9 (90%)	8 (80%)
Necrosis, focal	1 (11%)		1 (10%)	1 (10%)
Mesentery				(1)
Fat, necrosis				1 (100%)
Pancreas	(9)	(10)	(10)	(10)
Necrosis, focal			1 (10%)	
Salivary glands	(9)	(10)	(10)	(10)
Inflammation, chronic, focal	2 (22%)	2 (20%)	3 (30%)	1 (10%)
Stomach, glandular	(9)	(10)	(10)	(10)
Inflammation, chronic, focal			1 (10%)	
Cardiovascular System				
Heart	(9)	(10)	(10)	(10)
Perivascular, inflammation, chronic	1 (11%)			
Endocrine System				
Adrenal cortex	(9)	(10)	(9)	(9)
Atrophy				1 (11%)
Cytoplasmic alteration, focal		1 (10%)		
Islets, pancreatic	(9)	(10)	(10)	(10)
Hyperplasia	5 (56%)	5 (50%)	4 (40%)	5 (50%)
General Body System				
None				
Genital System				
Epididymis	(9)	(10)	(10)	(10)
Fibrosis, focal		1 (10%)		

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Genital System (continued)				
Preputial gland	(2)	(8)	(4)	(7)
Cyst	1 (50%)	6 (75%)	3 (75%)	5 (71%)
Cyst, two		1 (13%)		
Ectasia			2 (50%)	2 (29%)
Inflammation, acute, focal	1 (50%)	1 (13%)		
Inflammation, chronic, focal		1 (13%)		
Prostate	(9)	(10)	(9)	(10)
Hemorrhage, focal				1 (10%)
Inflammation, chronic, focal	1 (11%)		2 (22%)	1 (10%)
Seminal vesicle	(9)	(10)	(10)	(10)
Congestion			1 (10%)	
Dilatation		1 (10%)		
Inflammation, chronic, focal			1 (10%)	
Hematopoietic System				
Lymph node, mesenteric	(9)	(10)	(10)	(10)
Congestion		1 (10%)		
Spleen	(9)	(10)	(10)	(10)
Congestion		1 (10%)		
Depletion lymphoid				1 (10%)
Hematopoietic cell proliferation	1 (11%)	3 (30%)	3 (30%)	1 (10%)
Integumentary System				
Skin	(9)	(10)	(10)	(10)
Subcutaneous tissue, necrosis				1 (10%)
Musculoskeletal System				
None				
Nervous System				
Brain	(9)	(10)	(9)	(10)
Mineralization, focal	1 (11%)	7 (70%)	7 (78%)	4 (40%)
Respiratory System				
Nose	(9)	(10)	(10)	(10)
Inflammation, acute, focal				1 (10%)
Inflammation, chronic, focal	6 (67%)	4 (40%)	10 (100%)	9 (90%)
Special Senses System				
None				

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Urinary System				
Kidney	(9)	(10)	(10)	(10)
Crystals				1 (10%)
Cyst	1 (11%)			
Inflammation, chronic, focal		1 (10%)	2 (20%)	
Mineralization, focal	1 (11%)	1 (10%)	4 (40%)	2 (20%)
Renal tubule, regeneration	8 (89%)	10 (100%)	9 (90%)	9 (90%)
Urinary bladder	(9)	(10)	(10)	(10)
Inflammation, chronic, focal	2 (22%)		1 (10%)	1 (10%)
2-Year Study				
Alimentary System				
Gallbladder	(44)	(47)	(46)	(41)
Degeneration, hyaline			1 (2%)	
Dilatation	3 (7%)		1 (2%)	1 (2%)
Intestine large, colon	(46)	(48)	(47)	(46)
Parasite metazoan				1 (2%)
Intestine large, rectum	(47)	(50)	(46)	(47)
Parasite metazoan				1 (2%)
Intestine large, cecum	(48)	(49)	(47)	(46)
Hyperplasia, lymphoid	29 (60%)	34 (69%)	39 (83%)	9 (20%)
Serosa, fibrosis	1 (2%)			
Intestine small, jejunum	(49)	(48)	(46)	(44)
Hyperplasia, lymphoid				1 (2%)
Intestine small, ileum	(49)	(44)	(46)	(44)
Hyperplasia, lymphoid			1 (2%)	1 (2%)
Liver	(51)	(50)	(48)	(50)
Angiectasis		3 (6%)		
Basophilic focus	2 (4%)	1 (2%)		
Clear cell focus	8 (16%)	13 (26%)	5 (10%)	2 (4%)
Clear cell focus, multiple		1 (2%)		
Congestion			1 (2%)	
Eosinophilic focus	9 (18%)	9 (18%)	3 (6%)	5 (10%)
Fatty change	2 (4%)	3 (6%)	4 (8%)	3 (6%)
Fibrosis		1 (2%)		
Hematopoietic cell proliferation	1 (2%)	1 (2%)		
Hemorrhage				2 (4%)
Infarct			1 (2%)	
Mixed cell focus		1 (2%)		
Necrosis, focal	3 (6%)	2 (4%)	2 (4%)	
Nuclear alteration	1 (2%)			1 (2%)
Thrombosis	1 (2%)			
Artery, fibrosis			1 (2%)	
Artery, thrombosis			1 (2%)	
Bile duct, hyperplasia			1 (2%)	
Mesentery	(3)	(1)	(1)	(1)
Fibrosis		1 (100%)		
Inflammation, chronic	1 (33%)			
Inflammation, granulomatous			1 (100%)	1 (100%)
Fat, necrosis	1 (33%)	1 (100%)		

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Pancreas	(50)	(50)	(48)	(50)
Congestion			1 (2%)	
Inflammation, granulomatous			1 (2%)	
Serosa, necrosis	1 (2%)			
Pharynx	(1)	(1)		
Developmental malformation	1 (100%)			
Stomach, forestomach	(50)	(50)	(48)	(48)
Acanthosis	1 (2%)		3 (6%)	1 (2%)
Diverticulum	1 (2%)			
Hyperkeratosis	1 (2%)	3 (6%)		
Hyperplasia, squamous				1 (2%)
Inflammation, granulomatous			1 (2%)	
Ulcer	2 (4%)			1 (2%)
Stomach, glandular	(50)	(50)	(47)	(47)
Cyst epithelial inclusion	1 (2%)			
Diverticulum			1 (2%)	
Erosion		1 (2%)		
Hyperplasia, focal	1 (2%)			
Inflammation, chronic		1 (2%)	1 (2%)	
Inflammation, granulomatous			1 (2%)	
Metaplasia, squamous	1 (2%)			
Mineralization				1 (2%)
Necrosis, focal			1 (2%)	
Ulcer			1 (2%)	
Tongue	(2)	(1)		
Depletion cellular	1 (50%)			
Hemorrhage, focal		1 (100%)		
Pigmentation	1 (50%)			
Tooth		(1)		
Hypertrophy		1 (100%)		
Cardiovascular System				
Heart	(51)	(50)	(49)	(50)
Cardiomyopathy				1 (2%)
Dilatation	3 (6%)			1 (2%)
Mineralization	1 (2%)			
Valve, pigmentation				1 (2%)
Endocrine System				
Adrenal cortex	(49)	(50)	(48)	(49)
Accessory adrenal cortical nodule			1 (2%)	
Congestion			1 (2%)	1 (2%)
Cyst				1 (2%)
Hyperplasia	2 (4%)	2 (4%)	2 (4%)	3 (6%)
Hyperplasia, focal	15 (31%)	17 (34%)	14 (29%)	5 (10%)
Hypertrophy, focal		1 (2%)	3 (6%)	1 (2%)
Capsule, hyperplasia			2 (4%)	

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Endocrine System (continued)				
Adrenal medulla	(48)	(50)	(47)	(48)
Hemorrhage				1 (2%)
Islets, pancreatic	(50)	(50)	(46)	(50)
Atrophy			1 (2%)	
Hyperplasia	22 (44%)	24 (48%)	21 (46%)	16 (32%)
Hypoplasia				1 (2%)
Pituitary gland	(47)	(49)	(45)	(43)
Congestion	1 (2%)		1 (2%)	1 (2%)
Pars distalis, cyst		2 (4%)	1 (2%)	
Pars distalis, hyperplasia, focal		1 (2%)		
Thyroid gland	(51)	(48)	(48)	(49)
Follicle, cyst	1 (2%)			1 (2%)
Follicular cell, hyperplasia, focal	1 (2%)	2 (4%)		
General Body System				
None				
Genital System				
Epididymis	(51)	(49)	(49)	(50)
Inflammation, chronic			1 (2%)	
Inflammation, granulomatous		1 (2%)	1 (2%)	1 (2%)
Penis				(1)
Inflammation, acute				1 (100%)
Preputial gland	(32)	(33)	(26)	(30)
Abscess	1 (3%)			
Cyst	16 (50%)	17 (52%)	19 (73%)	15 (50%)
Cyst, multiple	1 (3%)			
Cyst, two	3 (9%)		1 (4%)	8 (27%)
Ectasia	21 (66%)	21 (64%)	10 (38%)	14 (47%)
Inflammation, chronic	1 (3%)			
Prostate	(50)	(47)	(48)	(49)
Cyst				1 (2%)
Dilatation		1 (2%)		
Inflammation, chronic	2 (4%)			
Inflammation, granulomatous			1 (2%)	
Artery, inflammation, chronic	1 (2%)			
Seminal vesicle	(50)	(50)	(49)	(50)
Atrophy			1 (2%)	
Dilatation	11 (22%)	10 (20%)	10 (20%)	2 (4%)
Fibrosis				1 (2%)
Inflammation, granulomatous			1 (2%)	
Testes	(51)	(50)	(49)	(50)
Interstitial cell, hyperplasia			2 (4%)	
Hematopoietic System				
Blood	(49)	(1)	(27)	(22)
Neutrophilia				2 (9%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Bone marrow	(50)	(50)	(48)	(48)
Hyperplasia		1 (2%)		
Hyperplasia, neutrophil	1 (2%)		2 (4%)	4 (8%)
Myelofibrosis			1 (2%)	1 (2%)
Lymph node, mandibular	(36)	(46)	(43)	(36)
Lymphatic, angiectasis	1 (3%)	2 (4%)		
Lymph node, mesenteric	(49)	(47)	(46)	(39)
Congestion	3 (6%)		1 (2%)	2 (5%)
Depletion lymphoid		1 (2%)		4 (10%)
Hyperplasia, lymphoid	4 (8%)			
Infiltration cellular, plasma cell	1 (2%)			
Infiltration cellular, histiocyte		1 (2%)		
Inflammation, granulomatous			1 (2%)	1 (3%)
Necrosis, focal	1 (2%)		2 (4%)	1 (3%)
Lymphatic, angiectasis		1 (2%)		
Spleen	(50)	(50)	(48)	(50)
Angiectasis				1 (2%)
Congestion			4 (8%)	
Depletion lymphoid		8 (16%)	4 (8%)	9 (18%)
Developmental malformation			1 (2%)	
Fibrosis			1 (2%)	
Hematopoietic cell proliferation	6 (12%)	8 (16%)	8 (17%)	5 (10%)
Necrosis, focal			2 (4%)	
Thymus	(39)	(42)	(44)	(35)
Cyst	1 (3%)			
Depletion lymphoid			2 (5%)	5 (14%)
Necrosis, focal			1 (2%)	1 (3%)
Integumentary System				
Skin	(51)	(50)	(49)	(49)
Congestion			1 (2%)	
Edema				1 (2%)
Hyperkeratosis			1 (2%)	
Inflammation, chronic active				1 (2%)
Inflammation, granulomatous			1 (2%)	
Pigmentation				1 (2%)
Ulcer			1 (2%)	
Musculoskeletal System				
None				
Nervous System				
Brain	(51)	(50)	(49)	(50)
Mineralization	25 (49%)	25 (50%)	22 (45%)	35 (70%)

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Respiratory System				
Lung	(51)	(50)	(49)	(50)
Congestion	1 (2%)		1 (2%)	
Hemorrhage			1 (2%)	
Inflammation, chronic, focal				1 (2%)
Inflammation, granulomatous			1 (2%)	1 (2%)
Pigmentation		1 (2%)		
Alveolar epithelium, metaplasia	2 (4%)	3 (6%)	2 (4%)	4 (8%)
Nose	(51)	(50)	(48)	(50)
Inflammation, chronic	42 (82%)	43 (86%)	31 (65%)	42 (84%)
Metaplasia, squamous		1 (2%)	1 (2%)	
Special Senses System				
None				
Urinary System				
Kidney	(50)	(50)	(48)	(50)
Atrophy, focal		4 (8%)	4 (8%)	
Autolysis			1 (2%)	
Casts		1 (2%)		
Congestion			1 (2%)	
Crystals			1 (2%)	21 (42%)
Cyst	3 (6%)	1 (2%)	4 (8%)	2 (4%)
Glomerulosclerosis			1 (2%)	
Inflammation, acute, focal			1 (2%)	
Inflammation, chronic				1 (2%)
Mineralization	28 (56%)	33 (66%)	32 (67%)	36 (72%)
Nephropathy	1 (2%)		2 (4%)	19 (38%)
Cortex, cyst	1 (2%)			
Renal tubule, cyst		1 (2%)		
Renal tubule, degeneration		1 (2%)	1 (2%)	
Renal tubule, dilatation		1 (2%)	2 (4%)	
Renal tubule, mineralization	1 (2%)			
Renal tubule, regeneration	25 (50%)	23 (46%)	28 (58%)	21 (42%)
Urinary bladder	(49)	(49)	(45)	(45)
Inflammation, granulomatous			1 (2%)	

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

APPENDIX D
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF BARIUM CHLORIDE DIHYDRATE

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	7	10	6
Early deaths				
Moribund	9	11	9	35
Natural deaths	3	5	5	6
Survivors				
Died last week of study	1			
Terminal sacrifice	37	37	36	13
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(7)	(10)	(6)
Hepatocellular adenoma		1 (14%)	1 (10%)	
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
None				
Integumentary System				
None				
Musculoskeletal System				
None				
Nervous System				
None				

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Respiratory System				
Lung	(10)	(7)	(10)	(6)
Alveolar/bronchiolar adenoma	1 (10%)			1 (17%)
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Gallbladder	(45)	(49)	(46)	(48)
Intestine large, colon	(48)	(51)	(48)	(52)
Intestine large, rectum	(49)	(52)	(50)	(54)
Intestine large, cecum	(48)	(51)	(47)	(49)
Leiomyoma		2 (4%)		
Intestine small, duodenum	(47)	(50)	(48)	(48)
Intestine small, jejunum	(47)	(50)	(46)	(48)
Adenocarcinoma				1 (2%)
Intestine small, ileum	(49)	(48)	(46)	(47)
Liver	(50)	(53)	(50)	(54)
Hemangioma				1 (2%)
Hemangiosarcoma	1 (2%)	2 (4%)		
Hepatocellular carcinoma	4 (8%)	2 (4%)	6 (12%)	1 (2%)
Hepatocellular adenoma	10 (20%)	11 (21%)	10 (20%)	4 (7%)
Hepatocellular adenoma, multiple	3 (6%)	2 (4%)	4 (8%)	1 (2%)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Mesentery	(2)	(6)	(4)	(4)
Fibrosarcoma		1 (17%)		
Fibrosarcoma, metastatic		1 (17%)		
Pancreas	(50)	(52)	(50)	(54)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Salivary glands	(50)	(52)	(50)	(53)
Stomach, forestomach	(50)	(52)	(50)	(53)
Squamous cell papilloma	1 (2%)		1 (2%)	
Stomach, glandular	(49)	(52)	(49)	(53)
Cardiovascular System				
Heart	(50)	(53)	(50)	(54)
Alveolar/bronchiolar carcinoma, metastatic, lung		1 (2%)		
Hemangiosarcoma		1 (2%)		1 (2%)

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Endocrine System				
Adrenal cortex	(50)	(53)	(50)	(52)
Adenoma	1 (2%)			1 (2%)
Adenoma, two	1 (2%)			
Capsule, adenoma		1 (2%)		
Adrenal medulla	(49)	(52)	(49)	(50)
Pheochromocytoma malignant	1 (2%)			
Pheochromocytoma complex				1 (2%)
Pheochromocytoma benign			1 (2%)	
Islets, pancreatic	(50)	(52)	(50)	(54)
Adenoma			3 (6%)	
Carcinoma		1 (2%)	1 (2%)	
Pituitary gland	(48)	(51)	(47)	(47)
Pars distalis, adenoma	9 (19%)	6 (12%)	5 (11%)	2 (4%)
Pars distalis, carcinoma			2 (4%)	
Pars intermedia, adenoma			1 (2%)	
Thyroid gland	(50)	(53)	(50)	(53)
Adenoma			1 (2%)	
C-cell, adenoma	1 (2%)			
Follicular cell, adenoma		1 (2%)		2 (4%)
General Body System				
None				
Genital System				
Clitoral gland	(1)			(2)
Ovary	(49)	(52)	(49)	(53)
Cystadenoma			3 (6%)	
Granulosa cell tumor benign	1 (2%)			
Hemangioma			1 (2%)	
Uterus	(50)	(53)	(50)	(54)
Hemangiosarcoma			1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Polyp stromal	3 (6%)	1 (2%)	4 (8%)	
Sarcoma stromal		1 (2%)		
Hematopoietic System				
Bone marrow	(49)	(53)	(50)	(52)
Lymph node	(6)	(5)	(8)	(2)
Lymph node, mandibular	(49)	(52)	(49)	(42)
Lymph node, mesenteric	(49)	(49)	(49)	(39)
Hemangiosarcoma		1 (2%)		
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Spleen	(50)	(53)	(50)	(52)
Hemangiosarcoma		2 (4%)	2 (4%)	1 (2%)
Thymus	(43)	(46)	(47)	(38)

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Integumentary System				
Skin	(50)	(52)	(50)	(54)
Fibrosarcoma	3 (6%)	1 (2%)	1 (2%)	3 (6%)
Hemangiosarcoma				1 (2%)
Squamous cell carcinoma		1 (2%)		
Musculoskeletal System				
Bone	(50)	(53)	(50)	(54)
Fibrosarcoma, metastatic		1 (2%)		
Osteosarcoma	1 (2%)			
Skeletal muscle	(1)	(1)		
Fibrosarcoma, metastatic		1 (100%)		
Nervous System				
Brain	(50)	(53)	(50)	(54)
Carcinoma, metastatic, pituitary gland			2 (4%)	
Respiratory System				
Lung	(50)	(53)	(50)	(54)
Alveolar/bronchiolar adenoma	3 (6%)	2 (4%)	3 (6%)	1 (2%)
Alveolar/bronchiolar carcinoma		1 (2%)	2 (4%)	
Carcinoma, metastatic	1 (2%)			
Fibrosarcoma, metastatic		1 (2%)	1 (2%)	1 (2%)
Hepatocellular carcinoma, metastatic	1 (2%)	1 (2%)	2 (4%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Nose	(49)	(53)	(49)	(54)
Special Senses System				
Harderian gland	(1)	(1)		
Carcinoma	1 (100%)	1 (100%)		
Urinary System				
Kidney	(50)	(53)	(50)	(54)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Renal tubule, adenoma			1 (2%)	
Urinary bladder	(47)	(46)	(46)	(48)
Systemic Lesions				
Multiple organs[b]	(50)	(53)	(50)	(54)
Lymphoma malignant histiocytic	1 (2%)			1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)	4 (8%)	1 (2%)
Lymphoma malignant mixed	13 (26%)	9 (17%)	9 (18%)	4 (7%)

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	1	1	1	1
2-Year study	34	32	39	17
Total primary neoplasms				
15-Month interim evaluation	1	1	1	1
2-Year study	59	51	66	27
Total animals with benign neoplasms				
15-Month interim evaluation	1	1	1	1
2-Year study	25	20	27	10
Total benign neoplasms				
15-Month interim evaluation	1	1	1	1
2-Year study	33	26	38	12
Total animals with malignant neoplasms				
2-Year study	21	20	26	11
Total malignant neoplasms				
2-Year study	26	25	28	15
Total animals with metastatic neoplasms				
2-Year study	3	3	5	1
Total metastatic neoplasms				
2-Year study	8	6	5	1

[a] Number of animals examined microscopically at site and number of animals with lesion
[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 Barium Chloride Dihydrate: 0 ppm

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

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 0 ppm (continued)

Number of Days on Study	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	3 0 3 1	3 0 5 1	3 0 6 1	2 5 6 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 2 1	2 6 3 1	2 6 5 1	2 6 6 1	2 6 8 1	2 6 9 1	2 7 1 1	2 7 2 1	2 7 3 1	2 7 4 1	2 8 2 1	2 8 8 1	2 9 6 1	3 0 1 1	3 0 2 1	3 0 7 1	3 1 3 1	3 1 4 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	45
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma												X														1
Hepatocellular carcinoma								X					X						X							4
Hepatocellular adenoma		X			X				X									X	X					X		10
Hepatocellular adenoma, multiple											X															3
Histiocytic sarcoma, metastatic, liver																										1
Mesentery																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma, metastatic, liver																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Adenoma, two																										1
Adrenal medulla	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	M	+	+	M	+	+	M	+	+	+	+	+	M	M	+	M	M	+	+	M	M	M	M	+	+	29
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma								X							X			X		X				X	9
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma	X																									1
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 0 ppm (continued)

Number of Days on Study	4 7 8	4 9 8	5 4 1	5 6 1	5 7 3	5 8 0	6 0 2	6 0 5	6 6 5	6 7 5	6 9 2	7 2 2	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7
Carcass ID Number	3 0 9 1	3 0 0 1	2 8 5 1	2 9 9 1	3 0 8 1	3 1 2 1	3 1 5 1	2 7 0 1	2 7 7 1	2 7 8 1	2 6 7 1	2 6 4 1	2 7 5 1	2 7 6 1	2 7 9 1	2 8 0 1	2 8 3 1	2 8 4 1	2 8 6 1	2 8 7 1	2 8 9 1	2 9 0 1	2 9 3 1	2 9 5 1	2 9 7 1
Genital System																								
Clitoral gland																	+							
Ovary	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor benign																								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver												X												
Polyp stromal						X																		
Hematopoietic System																								
Blood		+	+	+			+	+		+			+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node					+					+							+							+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver												X												
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	M	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																								
Mammary gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma				X				X																
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma			X																					
Skeletal muscle	+																							
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																								X
Carcinoma, metastatic																				X				
Hepatocellular carcinoma, metastatic																								
Histiocytic sarcoma, metastatic, liver												X												
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Ear		+																						
Harderian gland																				+				
Carcinoma																				X				

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 0 ppm (continued)

Number of Days on Study	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	3 0 3 1	3 0 5 1	3 0 6 1	2 5 6 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 2 1	2 6 3 1	2 6 5 1	2 6 6 1	2 6 8 1	2 6 9 1	2 7 1 1	2 7 2 1	2 7 3 1	2 7 4 1	2 8 2 1	2 8 8 1	2 9 6 1	3 0 1 1	3 0 2 1	3 0 7 1	3 1 3 1	3 1 4 1	Total Tissues/ Tumors
Genital System																										
Clitoral gland																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Granulosa cell tumor benign														X												1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma, metastatic, liver																										1
Polyp stromal								X										X								3
Hematopoietic System																										
Blood	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
Lymph node																						+		+		6
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	49
Histiocytic sarcoma, metastatic, liver																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	M	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	43
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma		X																								3
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma				X																			X			3
Carcinoma, metastatic																										1
Hepatocellular carcinoma, metastatic								X																		1
Histiocytic sarcoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Harderian gland																										1
Carcinoma																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 0 ppm (continued)

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

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 0 ppm (continued)

Number of Days on Study	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	3 0 3 1	3 0 5 1	3 0 6 1	2 5 6 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 2 1	2 6 3 1	2 6 5 1	2 6 6 1	2 6 8 1	2 6 9 1	2 7 1 1	2 7 2 1	2 7 3 1	2 7 4 1	2 8 2 1	2 8 8 1	2 9 6 1	3 0 1 1	3 0 2 1	3 0 7 1	1 3 1	1 4 1	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma, metastatic, liver																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+		47
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed		X							X				X				X	X				X				13

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm

Number of Days on Study	3 7 3	3 7 7	3 8 0	4 5 5	4 6 2	4 6 7	5 3 5	5 6 1	5 6 4	6 0 7	6 1 6	6 4 5	6 5 5	7 0 3	7 1 9	7 2 1	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
Carcass ID Number	3 6 8 1	3 7 1 1	3 2 0 1	3 4 3 1	3 6 1 1	3 1 6 1	3 4 4 1	3 7 5 1	3 3 2 1	3 6 9 1	3 2 5 1	3 4 5 1	3 4 5 1	3 5 8 1	3 7 4 1	3 1 7 1	3 3 8 1	3 3 9 1	3 4 6 1	3 4 7 1	3 4 9 1	3 5 0 1	3 5 1 1	3 5 2 1	3 5 4 1	3 5 5 1	3 5 6 1
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	A	A	+	+	+	+	A	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																											
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	A	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	A	+	+	M	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	M
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma															X	X											
Hepatocellular carcinoma										X																	
Hepatocellular adenoma								X										X		X							
Hepatocellular adenoma, multiple																							X				
Mesentery														+							+				+		
Fibrosarcoma														X													
Fibrosarcoma, metastatic																										X	
Pancreas	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																											
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic, lung		X																									
Hemangiosarcoma																X											
Endocrine System																											
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																											
Adrenal medulla	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma															X												
Parathyroid gland	+	+	M	+	+	+	M	+	+	M	+	+	M	+	+	+	+	M	M	+	+	+	M	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma													X								X	X	X			X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																											
General Body System																											
None																											
Genital System																											
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal																								X			
Sarcoma stromal																											

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	3 5 8 1	3 5 9 1	3 6 0 1	3 6 2 1	3 6 3 1	3 6 4 1	3 6 5 1	3 6 7 1	3 7 0 1	3 7 2 1	3 1 9 1	3 2 1 1	3 2 2 1	3 2 3 1	3 2 4 1	3 2 6 1	3 2 7 1	3 2 8 1	3 2 9 1	3 3 1 1	3 3 3 1	3 3 4 1	3 3 5 1	3 4 6 1	4 0 1	4 2 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Leiomyoma							X																		X	2
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Hemangiosarcoma																										2
Hepatocellular carcinoma																								X		2
Hepatocellular adenoma				X					X		X		X					X	X				X	X		11
Hepatocellular adenoma, multiple																				X						2
Mesentery				+												+				+						6
Fibrosarcoma																										1
Fibrosarcoma, metastatic																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Tongue	+										+															2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Alveolar/bronchiolar carcinoma, metastatic, lung																										1
Hemangiosarcoma																										1
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Capsule, adenoma													X													1
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	52
Carcinoma																										1
Parathyroid gland	+	+	M	+	+	+	M	+	+	+	+	+	+	+	M	+	M	+	+	+	M	+	+	+	+	41
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	51
Pars distalis, adenoma																		X								6
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Follicular cell, adenoma																					X					1
General Body System																										
None																										
Genital System																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Polyp stromal																										1
Sarcoma stromal																			X							1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	3 7 3	3 7 7	3 8 0	4 5 5	4 6 2	4 6 7	5 3 5	5 6 1	5 6 4	6 0 7	6 1 6	6 4 5	6 5 5	7 0 3	7 1 9	7 2 1	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
Carcass ID Number	3 6 8 1	3 7 1 1	3 2 0 1	3 4 3 1	3 6 1 1	3 1 6 1	3 4 4 1	3 7 5 1	3 3 2 1	3 6 9 1	3 2 5 1	3 4 5 1	3 4 5 1	3 5 8 1	3 7 7 1	3 7 4 1	3 3 7 1	3 3 8 1	3 4 9 1	3 4 6 1	3 4 7 1	3 5 9 1	3 5 0 1	3 5 1 1	3 5 2 1	3 5 4 1	3 5 5 1	3 5 6 1
Hematopoietic System																											
Blood	+																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node																		+									
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																X											
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																X											
Thymus	M	M	+	+	+	+	+	+	M	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																											
Mammary gland	M	+	+	M	+	M	+	M	+	+	+	M	+	+	M	+	+	+	M	+	+	+	+	M	M	+	M
Skin	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																										X	
Squamous cell carcinoma							X																				
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic																										X	
Skeletal muscle																										+	
Fibrosarcoma, metastatic																										X	
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal cord						+																					
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																											
Alveolar/bronchiolar carcinoma		X																									
Fibrosarcoma, metastatic																										X	
Hepatocellular carcinoma, metastatic										X																	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																											
Harderian gland																			+								
Carcinoma																			X								
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	M	M	A	A	A	+	+	+	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic								X																			
Lymphoma malignant mixed																		X						X			

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 500 ppm (continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	
Carcass ID Number	3 5 8 1	3 5 9 1	3 6 0 1	3 6 2 1	3 6 3 1	3 6 4 1	3 6 5 1	3 6 7 1	3 6 0 1	3 7 2 1	3 7 9 1	3 1 1 1	3 2 1 1	3 2 2 1	3 2 3 1	3 2 4 1	3 2 6 1	3 2 7 1	3 2 8 1	3 2 9 1	3 3 1 1	3 3 3 1	3 3 4 1	3 3 5 1	3 3 6 1	4 4 0 1	4 4 2 1	Total Tissues/ Tumors
Hematopoietic System																											
Blood																											1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Lymph node							+								+				+				+				5
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	49
Hemangiosarcoma																											1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Hemangiosarcoma													X														2
Thymus	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Integumentary System																											
Mammary gland	+	M	+	M	+	+	M	M	+	+	+	+	M	+	M	+	M	+	+	+	+	M	M	+	+	+	34
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Fibrosarcoma																											1
Squamous cell carcinoma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Fibrosarcoma, metastatic																											1
Skeletal muscle																											1
Fibrosarcoma, metastatic																											1
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Spinal cord																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Alveolar/bronchiolar adenoma																X			X								2
Alveolar/bronchiolar carcinoma																											1
Fibrosarcoma, metastatic																											1
Hepatocellular carcinoma, metastatic																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Special Senses System																											
Harderian gland																											1
Carcinoma																											1
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Lymphoma malignant lymphocytic																											1
Lymphoma malignant mixed		X					X	X											X				X	X	X		9

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm

Number of Days on Study	3 6 0	4 2 9	6 0 5	6 0 9	6 1 6	6 2 7	6 4 5	6 8 0	6 8 5	7 0 7	7 1 4	7 2 0	7 2 1	7 2 3	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	3 9 8 1	3 7 6 1	3 9 3 1	4 0 6 1	3 9 1 1	4 0 7 1	3 8 4 1	4 1 9 1	3 8 2 1	3 8 5 1	4 1 2 1	4 0 3 1	4 1 1 1	4 0 8 1	4 1 3 1	4 1 4 1	4 1 6 1	4 1 7 1	4 1 8 1	4 2 0 1	4 2 2 1	4 2 4 1	4 2 5 1	4 2 6 1	4 2 7 1
Alimentary System																								
Esophagus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	A	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	A	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	A	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	A	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma											X		X											
Hepatocellular adenoma					X		X												X					
Hepatocellular adenoma, multiple																						X		
Mesentery					+																			
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																								
Stomach, glandular	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																								
Cardiovascular System																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																								
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal medulla	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																								
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																						X		
Carcinoma												X												
Parathyroid gland	+	M	+	+	M	M	M	M	+	M	M	+	M	+	+	+	+	M	+	+	M	+	+	+
Pituitary gland	+	+	+	M	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																	X					X		
Pars distalis, carcinoma																								
Pars intermedia, adenoma																								
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
General Body System																								
None																								
Genital System																								
Ovary	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma														X										
Hemangioma																		X						
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																								
Polyp stromal															X									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	4 2 8 1	4 2 9 1	4 3 0 1	4 3 1 1	4 3 2 1	4 3 4 1	3 7 7 1	3 7 8 1	3 7 9 1	3 8 1 1	3 8 3 1	3 8 7 1	3 8 8 1	3 8 9 1	3 9 0 1	3 9 2 1	3 9 6 1	3 9 7 1	3 9 9 1	4 0 0 1	4 0 1 1	4 0 2 1	4 0 4 1	4 0 9 1	4 0 3 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma			X		X			X									X									6
Hepatocellular adenoma	X				X		X				X									X			X			10
Hepatocellular adenoma, multiple						X							X			X										4
Mesentery			+				+										+									4
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma										X																1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue			+							+																2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign		X																								1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																						X			X	3
Carcinoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	M	+	+	M	M	+	35
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma													X		X					X						5
Pars distalis, carcinoma			X			X																				2
Pars intermedia, adenoma	X																									1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma		X																								1
General Body System																										
None																										
Genital System																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cystadenoma												X							X							3
Hemangioma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																		X								1
Polyp stromal				X																				X	X	4

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	3 6 0	4 2 9	6 0 5	6 0 9	6 1 6	6 2 7	6 4 5	6 8 0	6 8 5	7 0 7	7 1 4	7 2 0	7 2 1	7 2 3	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	3 9 8 1	3 7 6 1	3 9 3 1	4 0 6 1	3 9 1 1	4 0 7 1	3 8 4 1	4 1 9 1	3 8 2 1	3 8 5 1	4 1 2 1	4 0 3 1	4 0 1 1	4 0 8 1	4 1 3 1	4 1 4 1	4 1 6 1	4 1 7 1	4 1 8 1	4 2 0 1	4 2 2 1	4 2 4 1	4 2 5 1	4 2 6 1	4 2 7 1
Hematopoietic System																								
Blood	+		+	+		+									+	+	+	+	+	+		+		+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+					+	+																+		
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma														X											
Thymus	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma										X															
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma							X	X																	
Fibrosarcoma, metastatic										X															
Hepatocellular carcinoma, metastatic													X												
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																									
Urinary bladder	+	A	+	+	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic				X																					
Lymphoma malignant mixed	X								X														X		

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 1,250 ppm (continued)

Number of Days on Study	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	
Carcass ID Number	4 2 8 1	4 2 9 1	4 3 0 1	4 3 1 1	4 3 2 1	4 3 4 1	3 7 7 1	3 7 8 1	3 7 9 1	3 8 1 1	3 8 3 1	3 8 7 1	3 8 8 1	3 8 9 1	3 9 0 1	3 9 2 1	3 9 6 1	3 9 7 1	3 9 9 1	4 0 0 1	4 0 1 1	4 0 2 1	4 0 4 1	4 0 9 1	4 3 3 1	Total Tissues/ Tumors
Hematopoietic System																									
Blood	+	+	+	+	+												+	+		+	+	+	+	+	25
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node		+					+						+										+		8
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma										X															2
Thymus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma																									1
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pituitary gland			X			X																			2
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma															X		X			X					3
Alveolar/bronchiolar carcinoma																									2
Fibrosarcoma, metastatic																									1
Hepatocellular carcinoma, metastatic								X																	2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenoma							X																		1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic							X									X		X							4
Lymphoma malignant mixed				X							X	X	X							X		X			9

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm

Number of Days on Study	1 0 4	1 0 6	1 0 8	1 1 2	1 3 5	1 3 5	1 4 2	1 4 2	1 5 0	1 5 7	1 7 1	1 7 3	1 7 7	2 0 3	2 1 3	2 2 1	2 2 5	2 3 0	2 3 4	2 4 8	2 4 8	2 9 8	3 1 7	3 9 5	4 1 2	4 3 6	5 6 1
Carcass ID Number	4 6 5 1	4 5 8 1	4 6 4 1	4 6 0 1	4 5 3 1	4 8 4 1	4 3 8 1	4 4 9 1	4 8 8 1	4 5 5 1	4 6 3 1	4 5 9 1	4 5 7 1	4 4 2 1	4 4 0 1	4 7 2 1	4 5 2 1	4 4 1 1	4 6 1 1	4 6 9 1	4 9 4 1	4 6 6 1	4 5 4 1	4 3 9 1	4 8 9 1	4 9 5 1	4 7 7 1
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+
Gallbladder	+	I	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	A	+
Intestine large, colon	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	A	A	+	A	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	M	+	+	M	+	+	M	M	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	A	+	A	+	+	+	M	+
Adenocarcinoma																											
Intestine small, ileum	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	+	A	A	A	+	A	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																											
Hepatocellular carcinoma																											
Hepatocellular adenoma																											
Hepatocellular adenoma, multiple																											
Mesentery																									+		
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																											
Endocrine System																											
Adrenal cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																											
Adrenal medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	I	+	+	+	+	+
Pheochromocytoma complex																											
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	+	M	+	+	+	+	+	M	+	+	+	+	M	+	+	+	I	M	+	+	M	M	+
Pituitary gland	I	+	+	M	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																											
Thyroid gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																											
General Body System																											
None																											
Genital System																											
Clitoral gland												+													+		
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	5 8 5	6 1 7	6 4 3	6 4 3	6 5 8	6 5 8	6 6 6	6 7 3	7 7 4	7 7 9	7 0 7	7 1 8	7 2 0	7 2 3	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	4 7 1 1	4 6 7 1	4 4 3 1	4 8 3 1	4 5 1 1	4 7 9 1	4 8 6 1	4 7 3 1	4 6 2 1	4 9 3 1	4 9 2 1	4 7 6 1	4 8 2 1	4 8 0 1	4 3 6 1	4 3 7 1	4 4 5 1	4 4 7 1	4 5 0 1	4 5 6 1	4 6 8 1	4 7 0 1	4 7 4 1	4 7 8 1	4 8 1 1	4 9 0 1	4 9 1 1	Total Tissues/ Tumors
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma																						X					1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Hemangioma								X																			1
Hepatocellular carcinoma													X														1
Hepatocellular adenoma							X					X										X				X	4
Hepatocellular adenoma, multiple																								X			1
Mesentery											+								+		+						4
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Hemangiosarcoma																								X			1
Endocrine System																											
Adrenal cortex	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenoma				X																							1
Adrenal medulla	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma complex													X														1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Parathyroid gland	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	M	+	+	M	+	M	+	M	M	38
Pituitary gland	+	+	I	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma																			X					X			2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Follicular cell, adenoma																								X		X	2
General Body System																											
None																											
Genital System																											
Clitoral gland																											2
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	1 0 4	1 0 6	1 0 8	1 1 2	1 3 5	1 3 5	1 4 2	1 4 2	1 5 0	1 5 7	1 7 1	1 7 3	1 7 7	2 0 3	2 1 3	2 2 1	2 2 5	2 3 0	2 3 4	2 4 8	2 4 8	2 9 8	3 1 7	3 9 5	4 1 2	4 3 6	5 6 1
Carcass ID Number	4 6 5 1	4 5 8 1	4 6 4 1	4 6 0 1	4 5 3 1	4 8 4 1	4 3 8 1	4 4 9 1	4 8 8 1	4 5 5 1	4 6 3 1	4 5 9 1	4 5 7 1	4 4 2 1	4 4 0 1	4 7 2 1	4 5 2 1	4 4 1 1	4 6 1 1	4 6 9 1	4 9 4 1	4 6 6 1	4 5 4 1	4 3 9 1	4 8 9 1	4 9 9 1	4 7 5 1	4 7 7 1
Hematopoietic System																											
Blood																							+	+		+	
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	I	+	+	+
Lymph node																											
Lymph node, mandibular	M	+	+	+	M	M	+	+	M	+	I	M	+	M	M	+	+	M	+	+	M	+	+	+	+	+	+
Lymph node, mesenteric	M	M	M	M	+	M	M	+	+	+	+	M	+	M	M	M	+	M	+	+	M	+	+	+	+	+	M
Spleen	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																											
Thymus	+	M	M	M	+	+	+	+	+	M	M	+	+	+	M	+	+	M	+	M	M	+	+	+	+	M	+
Integumentary System																											
Mammary gland	+	+	+	+	M	+	M	M	M	M	+	M	+	+	M	+	M	+	M	M	M	+	M	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																											X
Hemangiosarcoma																											
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																											
Fibrosarcoma, metastatic																											
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	A	A	+	A	+	+	+	A	+
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																											
Lymphoma malignant lymphocytic																											
Lymphoma malignant mixed																											

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate: 2,500 ppm (continued)

Number of Days on Study	5 8 5	6 1 7	6 4 3	6 4 3	6 5 8	6 5 8	6 6 6	6 7 3	6 7 4	6 7 9	7 0 7	7 1 8	7 2 0	7 2 3	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	4 7 1 1	4 6 7 1	4 4 3 1	4 8 3 1	4 5 1 1	4 7 9 1	4 8 6 1	4 7 3 1	4 6 2 1	4 9 3 1	4 9 2 1	4 7 6 1	4 8 2 1	4 8 3 1	4 3 6 1	4 3 7 1	4 4 5 1	4 4 7 1	4 5 0 1	4 5 6 1	4 6 8 1	4 7 0 1	4 7 4 1	4 7 8 1	4 8 1 1	4 9 0 1	4 9 1 1	Total Tissues/ Tumors
Hematopoietic System																											
Blood		+	+	+			+												+	+		+	+	+		+		13
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node												+													+			2
Lymph node, mandibular	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Lymph node, mesenteric	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	39
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hemangiosarcoma																									X			1
Thymus	M	+	M	+	+	+	I	+	+	M	+	+	M	I	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Fibrosarcoma										X	X																	3
Hemangiosarcoma																									X			1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Alveolar/bronchiolar adenoma																				X								1
Fibrosarcoma, metastatic										X																		1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Lymphoma malignant histiocytic						X																						1
Lymphoma malignant lymphocytic																	X											1
Lymphoma malignant mixed												X												X	X	X		4

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Liver: Hepatocellular Adenoma				
Overall rates[a]	13/50 (26%)	13/53 (25%)	14/50 (28%)	5/54 (9%)
Adjusted rates[b]	32.1%	33.9%	36.3%	31.3%
Terminal rates[c]	11/38 (29%)	12/37 (32%)	12/36 (33%)	3/13 (23%)
First incidence (days)	561	561	616	666
Life table tests[d]	P=0.478	P=0.562	P=0.457	P=0.604
Logistic regression tests[d]	P=0.300N	P=0.591N	P=0.515	P=0.319N
Cochran-Armitage test[d]	P=0.020N			
Fisher exact test[d]		P=0.521N	P=0.500	P=0.022N
Liver: Hepatocellular Carcinoma				
Overall rates	4/50 (8%)	2/53 (4%)	6/50 (12%)	1/54 (2%)
Adjusted rates	9.9%	4.9%	15.6%	6.7%
Terminal rates	3/38 (8%)	1/37 (3%)	4/36 (11%)	0/13 (0%)
First incidence (days)	580	607	714	720
Life table tests	P=0.508	P=0.346N	P=0.353	P=0.533N
Logistic regression tests	P=0.493N	P=0.305N	P=0.377	P=0.370N
Cochran-Armitage test	P=0.230N			
Fisher exact test		P=0.312N	P=0.370	P=0.158N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rates	16/50 (32%)	14/53 (26%)	19/50 (38%)	6/54 (11%)
Adjusted rates	38.5%	35.4%	47.1%	35.9%
Terminal rates	13/38 (34%)	12/37 (32%)	15/36 (42%)	3/13 (23%)
First incidence (days)	561	561	616	666
Life table tests	P=0.390	P=0.443N	P=0.301	P=0.583N
Logistic regression tests	P=0.319N	P=0.398N	P=0.351	P=0.233N
Cochran-Armitage test	P=0.015N			
Fisher exact test		P=0.342N	P=0.338	P=0.009N
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	3/50 (6%)	2/53 (4%)	3/50 (6%)	1/54 (2%)
Adjusted rates	7.9%	5.4%	8.3%	7.7%
Terminal rates	3/38 (8%)	2/37 (5%)	3/36 (8%)	1/13 (8%)
First incidence (days)	735 (T)	735 (T)	735 (T)	735 (T)
Life table tests	P=0.561	P=0.512N	P=0.639	P=0.715N
Logistic regression tests	P=0.561	P=0.512N	P=0.639	P=0.715N
Cochran-Armitage test	P=0.252N			
Fisher exact test		P=0.472N	P=0.661N	P=0.280N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rates	3/50 (6%)	3/53 (6%)	5/50 (10%)	1/54 (2%)
Adjusted rates	7.9%	7.2%	12.5%	7.7%
Terminal rates	3/38 (8%)	2/37 (5%)	3/36 (8%)	1/13 (8%)
First incidence (days)	735 (T)	377	645	735 (T)
Life table tests	P=0.494	P=0.655	P=0.344	P=0.715N
Logistic regression tests	P=0.450N	P=0.615N	P=0.363	P=0.715N
Cochran-Armitage test	P=0.254N			
Fisher exact test		P=0.633N	P=0.357	P=0.280N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Ovary: Cystadenoma				
Overall rates	0/49 (0%)	0/52 (0%)	3/49 (6%)	0/53 (0%)
Adjusted rates	0.0%	0.0%	8.1%	0.0%
Terminal rates	0/38 (0%)	0/36 (0%)	2/36 (6%)	0/13 (0%)
First incidence (days)	–[e]	–	723	–
Life table tests	P=0.279	–	P=0.115	–
Logistic regression tests	P=0.326	–	P=0.124	–
Cochran-Armitage test	P=0.530			
Fisher exact test		–	P=0.121	–
Pancreatic Islets: Adenoma				
Overall rates	0/50 (0%)	0/52 (0%)	3/50 (6%)	0/54 (0%)
Adjusted rates	0.0%	0.0%	8.3%	0.0%
Terminal rates	0/38 (0%)	0/36 (0%)	3/36 (8%)	0/13 (0%)
First incidence (days)	–	–	735 (T)	–
Life table tests	P=0.273	–	P=0.111	–
Logistic regression tests	P=0.273	–	P=0.111	–
Cochran-Armitage test	P=0.532			
Fisher exact test		–	P=0.121	–
Pancreatic Islets: Adenoma or Carcinoma				
Overall rates	0/50 (0%)	1/52 (2%)	4/50 (8%)	0/54 (0%)
Adjusted rates	0.0%	2.6%	10.7%	0.0%
Terminal rates	0/38 (0%)	0/36 (0%)	3/36 (8%)	0/13 (0%)
First incidence (days)	–	719	720	–
Life table tests	P=0.292	P=0.500	P=0.060	–
Logistic regression tests	P=0.361	P=0.495	P=0.065	–
Cochran-Armitage test	P=0.603			
Fisher exact test		P=0.510	P=0.059	–
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	9/48 (19%)	6/51 (12%)	5/47 (11%)	2/47 (4%)
Adjusted rates	23.4%	16.4%	13.9%	15.4%
Terminal rates	8/37 (22%)	5/35 (14%)	5/36 (14%)	2/13 (15%)
First incidence (days)	605	655	735 (T)	735 (T)
Life table tests	P=0.218N	P=0.323N	P=0.201N	P=0.361N
Logistic regression tests	P=0.125N	P=0.291N	P=0.172N	P=0.210N
Cochran-Armitage test	P=0.025N			
Fisher exact test		P=0.246N	P=0.205N	P=0.027N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rates	9/48 (19%)	6/51 (12%)	7/47 (15%)	2/47 (4%)
Adjusted rates	23.4%	16.4%	19.4%	15.4%
Terminal rates	8/37 (22%)	5/35 (14%)	7/36 (19%)	2/13 (15%)
First incidence (days)	605	655	735 (T)	735 (T)
Life table tests	P=0.313N	P=0.323N	P=0.407N	P=0.361N
Logistic regression tests	P=0.187N	P=0.291N	P=0.359N	P=0.210N
Cochran-Armitage test	P=0.036N			
Fisher exact test		P=0.246N	P=0.410N	P=0.027N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Skin: Fibrosarcoma				
Overall rates	3/50 (6%)	1/53 (2%)	1/50 (2%)	3/54 (6%)
Adjusted rates	6.9%	2.7%	2.4%	14.3%
Terminal rates	1/38 (3%)	1/37 (3%)	0/36 (0%)	0/13 (0%)
First incidence (days)	561	735 (T)	707	561
Life table tests	P=0.209	P=0.313N	P=0.297N	P=0.329
Logistic regression tests	P=0.412	P=0.245N	P=0.297N	P=0.558
Cochran-Armitage test	P=0.505			
Fisher exact test		P=0.287N	P=0.309N	P=0.623N
Uterus: Stromal Polyp				
Overall rates	3/50 (6%)	1/53 (2%)	4/50 (8%)	0/54 (0%)
Adjusted rates	7.4%	2.7%	11.1%	0.0%
Terminal rates	2/38 (5%)	1/37 (3%)	4/36 (11%)	0/13 (0%)
First incidence (days)	580	735 (T)	735 (T)	–
Life table tests	P=0.462N	P=0.316N	P=0.480	P=0.311N
Logistic regression tests	P=0.339N	P=0.288N	P=0.505	P=0.197N
Cochran-Armitage test	P=0.168N			
Fisher exact test		P=0.287N	P=0.500	P=0.108N
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rates	3/50 (6%)	2/53 (4%)	4/50 (8%)	0/54 (0%)
Adjusted rates	7.4%	5.4%	11.1%	0.0%
Terminal rates	2/38 (5%)	2/37 (5%)	4/36 (11%)	0/13 (0%)
First incidence (days)	580	735 (T)	735 (T)	–
Life table tests	P=0.416N	P=0.512N	P=0.480	P=0.311N
Logistic regression tests	P=0.297N	P=0.488N	P=0.505	P=0.197N
Cochran-Armitage test	P=0.132N			
Fisher exact test		P=0.472N	P=0.500	P=0.108N
All Organs: Hemangiosarcoma				
Overall rates	1/50 (2%)	3/53 (6%)	3/50 (6%)	1/54 (2%)
Adjusted rates	2.6%	7.7%	8.1%	7.7%
Terminal rates	1/38 (3%)	1/37 (3%)	2/36 (6%)	1/13 (8%)
First incidence (days)	735 (T)	719	723	735 (T)
Life table tests	P=0.342	P=0.301	P=0.290	P=0.506
Logistic regression tests	P=0.429	P=0.301	P=0.310	P=0.506
Cochran-Armitage test	P=0.457N			
Fisher exact test		P=0.331	P=0.309	P=0.733N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	1/50 (2%)	3/53 (6%)	4/50 (8%)	2/54 (4%)
Adjusted rates	2.6%	7.7%	10.8%	12.3%
Terminal rates	1/38 (3%)	1/37 (3%)	3/36 (8%)	1/13 (8%)
First incidence (days)	735 (T)	719	723	673
Life table tests	P=0.108	P=0.301	P=0.167	P=0.195
Logistic regression tests	P=0.184	P=0.301	P=0.182	P=0.282
Cochran-Armitage test	P=0.493			
Fisher exact test		P=0.331	P=0.181	P=0.529

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
All Organs: Malignant Lymphoma (Histiocytic, Lymphocytic, or Mixed)				
Overall rates	15/50 (30%)	10/53 (19%)	13/50 (26%)	6/54 (11%)
Adjusted rates	35.1%	26.0%	32.4%	37.9%
Terminal rates	11/38 (29%)	9/37 (24%)	10/36 (28%)	4/13 (31%)
First incidence (days)	541	561	360	658
Life table tests	P=0.458	P=0.205N	P=0.448N	P=0.583
Logistic regression tests	P=0.255N	P=0.163N	P=0.418N	P=0.268N
Cochran-Armitage test	P=0.027N			
Fisher exact test		P=0.138N	P=0.412N	P=0.015N
All Organs: Malignant Lymphoma or Histiocytic Sarcoma				
Overall rates	15/50 (30%)	10/53 (19%)	13/50 (26%)	6/54 (11%)
Adjusted rates	35.1%	26.0%	32.4%	37.9%
Terminal rates	11/38 (29%)	9/37 (24%)	10/36 (28%)	4/13 (31%)
First incidence (days)	541	561	360	658
Life table tests	P=0.458	P=0.205N	P=0.448N	P=0.583
Logistic regression tests	P=0.255N	P=0.163N	P=0.418N	P=0.268N
Cochran-Armitage test	P=0.027N			
Fisher exact test		P=0.138N	P=0.412N	P=0.015N
All Organs: Benign Neoplasms				
Overall rates	26/50 (52%)	21/53 (40%)	27/50 (54%)	11/54 (20%)
Adjusted rates	63.1%	53.6%	69.0%	57.1%
Terminal rates	23/38 (61%)	19/37 (51%)	24/36 (67%)	6/13 (46%)
First incidence (days)	561	561	616	142
Life table tests	P=0.233	P=0.242N	P=0.409	P=0.469
Logistic regression tests	P=0.281N	P=0.211N	P=0.552	P=0.144N
Cochran-Armitage test	P=0.002N			
Fisher exact test		P=0.144N	P=0.500	P<0.001N
All Organs: Malignant Neoplasms				
Overall rates	22/50 (44%)	20/53 (38%)	26/50 (52%)	11/54 (20%)
Adjusted rates	48.5%	44.9%	56.4%	55.9%
Terminal rates	15/38 (39%)	13/37 (35%)	16/36 (44%)	5/13 (38%)
First incidence (days)	541	377	360	561
Life table tests	P=0.173	P=0.461N	P=0.274	P=0.321
Logistic regression tests	P=0.335N	P=0.331N	P=0.269	P=0.340N
Cochran-Armitage test	P=0.013N			
Fisher exact test		P=0.328N	P=0.274	P=0.009N
All Organs: Benign or Malignant Neoplasms				
Overall rates	36/50 (72%)	32/53 (60%)	39/50 (78%)	18/54 (33%)
Adjusted rates	79.8%	70.9%	82.9%	76.5%
Terminal rates	29/38 (76%)	24/37 (65%)	28/36 (78%)	8/13 (62%)
First incidence (days)	541	377	360	142
Life table tests	P=0.073	P=0.345N	P=0.282	P=0.180
Logistic regression tests	P=0.258N	P=0.227N	P=0.334	P=0.180N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.150N	P=0.322	P<0.001N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

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

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

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	7	10	6
Early deaths				
Moribund	9	11	9	35
Natural deaths	3	5	5	6
Survivors				
Died last week of study	1			
Terminal sacrifice	37	37	36	13
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Gallbladder	(9)	(6)	(10)	(6)
Inflammation, chronic, focal	1 (11%)			
Intestine large, rectum	(9)	(7)	(9)	(6)
Ulcer				1 (17%)
Liver	(10)	(7)	(10)	(6)
Eosinophilic focus			1 (10%)	
Fatty change	4 (40%)	2 (29%)	4 (40%)	2 (33%)
Granuloma	1 (10%)			
Inflammation, chronic, focal	1 (10%)		1 (10%)	
Necrosis, focal		1 (14%)		
Mesentery	(1)	(1)		
Fat, necrosis	1 (100%)	1 (100%)		
Pancreas	(10)	(7)	(10)	(6)
Inflammation, chronic, focal	4 (40%)		2 (20%)	1 (17%)
Salivary glands	(10)	(7)	(10)	(6)
Inflammation, chronic, focal	8 (80%)	3 (43%)	7 (70%)	3 (50%)
Stomach, glandular	(10)	(6)	(9)	(6)
Inflammation, chronic, focal		1 (17%)		
Cardiovascular System				
Heart	(10)	(7)	(10)	(6)
Inflammation, chronic, focal			1 (10%)	
Endocrine System				
Islets, pancreatic	(10)	(7)	(10)	(6)
Hyperplasia	1 (10%)		2 (20%)	4 (67%)
Pituitary gland	(10)	(6)	(10)	(6)
Pars distalis, hyperplasia, focal	1 (10%)			
Thyroid gland	(10)	(7)	(9)	(6)
C-cell, hyperplasia		1 (14%)		
General Body System				
None				

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
15-Month Interim Evaluation (continued)				
Genital System				
Ovary	(10)	(7)	(10)	(6)
Cyst	1 (10%)	1 (14%)	1 (10%)	
Uterus	(10)	(7)	(10)	(6)
Dilatation	3 (30%)		2 (20%)	
Endometrium, hyperplasia, cystic	8 (80%)	7 (100%)	8 (80%)	6 (100%)
Hematopoietic System				
Spleen	(10)	(7)	(8)	(6)
Hematopoietic cell proliferation	4 (40%)		3 (38%)	2 (33%)
Integumentary System				
None				
Musculoskeletal System				
None				
Nervous System				
Brain	(10)	(7)	(10)	(6)
Mineralization, focal	4 (40%)	4 (57%)	3 (30%)	2 (33%)
Respiratory System				
Nose	(10)	(7)	(10)	(6)
Degeneration, hyaline	1 (10%)	1 (14%)	2 (20%)	1 (17%)
Inflammation, chronic, focal	10 (100%)	3 (43%)	9 (90%)	6 (100%)
Special Senses System				
None				
Urinary System				
Kidney	(10)	(7)	(10)	(6)
Casts				1 (17%)
Renal tubule, regeneration	1 (10%)			
Urinary bladder	(10)	(7)	(10)	(6)
Inflammation, chronic, focal	4 (40%)	2 (29%)	4 (40%)	1 (17%)
2-Year Study				
Alimentary System				
Gallbladder	(45)	(49)	(46)	(48)
Autolysis			1 (2%)	
Dilatation		2 (4%)	1 (2%)	

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Intestine large, colon	(48)	(51)	(48)	(52)
Hyperplasia, lymphoid			1 (2%)	
Intestine large, cecum	(48)	(51)	(47)	(49)
Edema	1 (2%)			
Hyperplasia, lymphoid	39 (81%)	30 (59%)	35 (74%)	23 (47%)
Intestine small, duodenum	(47)	(50)	(48)	(48)
Fibrosis			1 (2%)	
Hyperplasia, lymphoid	1 (2%)			
Inflammation, acute		1 (2%)		
Intestine small, jejunum	(47)	(50)	(46)	(48)
Hyperplasia, lymphoid	2 (4%)	1 (2%)		
Inflammation, acute		1 (2%)		
Intestine small, ileum	(49)	(48)	(46)	(47)
Hyperplasia, lymphoid	2 (4%)		3 (7%)	
Ulcer		1 (2%)		
Liver	(50)	(53)	(50)	(54)
Amyloid deposition		1 (2%)		
Angiectasis	1 (2%)	2 (4%)	1 (2%)	
Angiectasis, focal			1 (2%)	
Basophilic focus	3 (6%)		2 (4%)	1 (2%)
Clear cell focus	1 (2%)	4 (8%)	2 (4%)	2 (4%)
Congestion		1 (2%)		1 (2%)
Eosinophilic focus	4 (8%)	4 (8%)	8 (16%)	2 (4%)
Fatty change	4 (8%)	10 (19%)	6 (12%)	5 (9%)
Hematopoietic cell proliferation	1 (2%)	1 (2%)	1 (2%)	
Hemorrhage, focal	1 (2%)		1 (2%)	1 (2%)
Infarct			1 (2%)	
Inflammation, chronic, focal			1 (2%)	
Mineralization, focal	1 (2%)			
Mixed cell focus		1 (2%)	2 (4%)	1 (2%)
Necrosis, focal	5 (10%)	5 (9%)	1 (2%)	4 (7%)
Mesentery	(2)	(6)	(4)	(4)
Fibrosis			1 (25%)	
Fat, necrosis	2 (100%)	4 (67%)	4 (100%)	4 (100%)
Pancreas	(50)	(52)	(50)	(54)
Congestion	1 (2%)			
Cyst			1 (2%)	
Inflammation, chronic		1 (2%)		
Inflammation, chronic, focal		1 (2%)		
Acinus, atrophy	2 (4%)			
Duct, ectasia		1 (2%)		
Salivary glands	(50)	(52)	(50)	(53)
Congestion				1 (2%)
Inflammation, chronic, focal				1 (2%)
Stomach, forestomach	(50)	(52)	(50)	(53)
Abscess	2 (4%)			1 (2%)
Acanthosis		2 (4%)		5 (9%)
Bulla	1 (2%)			
Cyst epithelial inclusion	1 (2%)			

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Alimentary System (continued)				
Stomach, forestomach (continued)	(50)	(52)	(50)	(53)
Diverticulum	1 (2%)		1 (2%)	2 (4%)
Edema		1 (2%)		
Hyperkeratosis		1 (2%)	2 (4%)	1 (2%)
Ulcer	2 (4%)	1 (2%)	1 (2%)	4 (8%)
Stomach, glandular	(49)	(52)	(49)	(53)
Diverticulum	1 (2%)			
Erosion	3 (6%)		1 (2%)	1 (2%)
Inflammation, acute		1 (2%)		
Mineralization	1 (2%)		2 (4%)	
Necrosis, focal			1 (2%)	
Ulcer	1 (2%)	1 (2%)		
Mucosa, hyperplasia	1 (2%)			
Tongue	(1)	(2)	(2)	
Angiectasis			2 (100%)	
Hyperkeratosis		2 (100%)		
Necrosis, focal	1 (100%)			
Cardiovascular System				
Heart	(50)	(53)	(50)	(54)
Cardiomyopathy		2 (4%)	2 (4%)	1 (2%)
Dilatation	1 (2%)			
Edema			1 (2%)	
Pericardium, fibrosis		1 (2%)		
Valve, pigmentation			2 (4%)	
Ventricle, hypertrophy	1 (2%)			
Endocrine System				
Adrenal cortex	(50)	(53)	(50)	(52)
Angiectasis			1 (2%)	
Congestion		1 (2%)		
Hematopoietic cell proliferation	1 (2%)			
Hyperplasia, focal	1 (2%)	1 (2%)	2 (4%)	
Capsule, hyperplasia		1 (2%)		
Zona reticularis, degeneration, fatty				1 (2%)
Zona reticularis, hemorrhage			3 (6%)	
Zona reticularis, hyperplasia			1 (2%)	
Islets, pancreatic	(50)	(52)	(50)	(54)
Hyperplasia	13 (26%)	14 (27%)	11 (22%)	5 (9%)
Parathyroid gland	(29)	(41)	(35)	(38)
Hyperplasia			1 (3%)	
Pituitary gland	(48)	(51)	(47)	(47)
Congestion		2 (4%)		1 (2%)
Pars distalis, angiectasis	1 (2%)			
Pars distalis, hyperplasia, focal	10 (21%)	7 (14%)	6 (13%)	6 (13%)
Rathke's cleft, hemorrhage		1 (2%)		

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Endocrine System (continued)				
Thyroid gland	(50)	(53)	(50)	(53)
Atrophy	1 (2%)			
Cyst			1 (2%)	
Inflammation, acute, focal		1 (2%)		
C-cell, hyperplasia		1 (2%)		
Follicle, cyst	1 (2%)	1 (2%)		1 (2%)
Follicular cell, hyperplasia	4 (8%)	6 (11%)	2 (4%)	3 (6%)
General Body System				
None				
Genital System				
Clitoral gland	(1)			(2)
Cyst				1 (50%)
Ovary	(49)	(52)	(49)	(53)
Angiectasis			1 (2%)	
Atrophy				1 (2%)
Congestion	1 (2%)			1 (2%)
Cyst	17 (35%)	9 (17%)	12 (24%)	10 (19%)
Hemorrhage	1 (2%)			3 (6%)
Thrombosis			1 (2%)	
Follicle, hemorrhage		2 (4%)	1 (2%)	
Uterus	(50)	(53)	(50)	(54)
Angiectasis	3 (6%)	2 (4%)	3 (6%)	
Atrophy		4 (8%)	4 (8%)	20 (37%)
Cyst		1 (2%)		
Dilatation	14 (28%)	14 (26%)	13 (26%)	6 (11%)
Hemorrhage	2 (4%)		1 (2%)	1 (2%)
Mineralization	1 (2%)			
Necrosis	1 (2%)			
Thrombosis	1 (2%)	1 (2%)		
Endometrium, cyst				2 (4%)
Endometrium, hyperplasia, cystic	40 (80%)	36 (68%)	34 (68%)	20 (37%)
Endometrium, metaplasia, squamous			1 (2%)	
Lumen, hemorrhage		1 (2%)		
Myometrium, inflammation, chronic, focal	1 (2%)			
Hematopoietic System				
Blood	(43)	(1)	(25)	(13)
Neutrophilia	1 (2%)		1 (4%)	
Bone marrow	(49)	(53)	(50)	(52)
Atrophy		1 (2%)		
Hyperplasia	1 (2%)			
Hyperplasia, megakaryocyte				1 (2%)
Hyperplasia, neutrophil	3 (6%)	4 (8%)	2 (4%)	3 (6%)
Myelofibrosis	37 (76%)	35 (66%)	33 (66%)	18 (35%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Hematopoietic System (continued)				
Lymph node	(6)	(5)	(8)	(2)
Lumbar, infiltration cellular, plasma cell			2 (25%)	
Lumbar, inflammation, acute			1 (13%)	
Lumbar, lymphatic, angiectasis			2 (25%)	
Mediastinal, congestion	1 (17%)			
Mediastinal, hyperplasia, lymphoid		1 (20%)		
Mediastinal, infiltration cellular, plasma cell			1 (13%)	
Lymph node, mandibular	(49)	(52)	(49)	(42)
Depletion lymphoid				2 (5%)
Infiltration cellular, plasma cell		1 (2%)		
Lymphatic, angiectasis		2 (4%)		
Lymph node, mesenteric	(49)	(49)	(49)	(39)
Angiectasis				1 (3%)
Congestion		2 (4%)		1 (3%)
Depletion lymphoid				10 (26%)
Hyperplasia, lymphoid	2 (4%)			
Necrosis, focal		1 (2%)		
Lymphatic, angiectasis		2 (4%)		
Spleen	(50)	(53)	(50)	(52)
Amyloid deposition		2 (4%)		
Congestion		3 (6%)	2 (4%)	2 (4%)
Depletion lymphoid	2 (4%)	2 (4%)		11 (21%)
Fibrosis			1 (2%)	3 (6%)
Hematopoietic cell proliferation	8 (16%)	11 (21%)	10 (20%)	8 (15%)
Hyperplasia, lymphoid		1 (2%)	2 (4%)	
Infarct			1 (2%)	
Necrosis, focal		2 (4%)	1 (2%)	
Pigmentation, hemosiderin	1 (2%)	1 (2%)		2 (4%)
Thymus	(43)	(46)	(47)	(38)
Depletion lymphoid	1 (2%)	1 (2%)		12 (32%)
Hyperplasia, lymphoid	2 (5%)			
Necrosis, focal		1 (2%)	1 (2%)	
Integumentary System				
Mammary gland	(48)	(34)	(49)	(42)
Ectasia	1 (2%)			
Skin	(50)	(52)	(50)	(54)
Congestion			1 (2%)	
Edema	1 (2%)			
Musculoskeletal System				
Skeletal muscle	(1)	(1)		
Necrosis	1 (100%)			

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
2-Year Study (continued)				
Nervous System				
Brain	(50)	(53)	(50)	(54)
Compression	1 (2%)			
Mineralization	27 (54%)	30 (57%)	30 (60%)	24 (44%)
Respiratory System				
Lung	(50)	(53)	(50)	(54)
Congestion		2 (4%)	1 (2%)	2 (4%)
Hemorrhage	1 (2%)	1 (2%)		2 (4%)
Hyperplasia, lymphoid			1 (2%)	
Alveolar epithelium, metaplasia		1 (2%)		3 (6%)
Peribronchial, inflammation, chronic		1 (2%)		
Nose	(49)	(53)	(49)	(54)
Inflammation, acute		1 (2%)		1 (2%)
Inflammation, chronic	45 (92%)	44 (83%)	41 (84%)	36 (67%)
Metaplasia, squamous			4 (8%)	4 (7%)
Special Senses System				
Ear	(1)			
Artery, internal ear, inflammation, chronic	1 (100%)			
Urinary System				
Kidney	(50)	(53)	(50)	(54)
Amyloid deposition		2 (4%)		
Atrophy, focal	2 (4%)	2 (4%)	4 (8%)	1 (2%)
Casts			1 (2%)	
Congestion		1 (2%)	1 (2%)	
Crystals				36 (67%)
Glomerulosclerosis	1 (2%)	1 (2%)		
Hyperplasia, lymphoid			1 (2%)	
Inflammation, focal			1 (2%)	
Metaplasia, osseous			1 (2%)	
Mineralization	3 (6%)		1 (2%)	2 (4%)
Nephropathy		2 (4%)	1 (2%)	37 (69%)
Papilla, necrosis		1 (2%)		
Renal tubule, degeneration		2 (4%)		
Renal tubule, dilatation		2 (4%)	1 (2%)	2 (4%)
Renal tubule, pigmentation, hemosiderin		1 (2%)		
Renal tubule, regeneration	5 (10%)	6 (11%)	9 (18%)	2 (4%)
Urinary bladder	(47)	(46)	(46)	(48)
Hyperplasia, lymphoid			1 (2%)	
Inflammation, chronic, focal				2 (4%)

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

APPENDIX E
GENETIC TOXICOLOGY

GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST PROTOCOL

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

Each trial consisted of triplicate plates of concurrent positive and negative controls, and of at least five doses of barium chloride dihydrate. The high dose was limited to 10,000 μg/plate.

In this test, a positive response was defined as a reproducible, dose-related increase in histidine-independent (revertant) colonies in any one strain/activation combination. An equivocal response was defined as an increase in revertants that was not dose related, not reproducible, nor was of sufficient magnitude to support a determination of mutagenicity. A negative response was obtained when no increase in revertant colonies was observed following chemical treatment. There was no minimum percentage or fold increase required for a chemical to be judged positive or weakly positive.

MOUSE LYMPHOMA MUTAGENICITY TEST PROTOCOL

The experimental protocol is presented in detail by Myhr *et al.* (1985). Barium chloride dihydrate was supplied as a coded aliquot by Radian Corporation. The high dose of barium chloride dihydrate was determined by solubility and did not exceed 1,000 μg/mL. L5178Y mouse lymphoma cells were maintained at 37° C as suspension cultures in Fischer's medium supplemented with *l*-glutamine, sodium pyruvate, pluronic F68, antibiotics, and heat-inactivated horse serum; normal cycling time was approximately 10 hours. To reduce the number of spontaneously occurring trifluorothymidine-resistant cells, subcultures were exposed once to medium containing THMG (thymidine, hypoxanthine, methotrexate, glycine) for 1 day, to THG for 1 day, and to normal medium for 3 to 5 days. For cloning, the horse serum content was increased and Noble agar was added.

All treatment levels within an experiment, including concurrent positive and solvent controls, were replicated. Treated cultures contained 6×10^6 cells in 10 mL medium. This volume included the S9 fraction in those experiments performed with metabolic activation. Incubation with barium chloride dihydrate continued for 4 hours, at which time the medium plus barium chloride dihydrate was removed and the cells were resuspended in fresh medium and incubated for an additional 48 hours to express the mutant phenotype. Cell density was monitored so that log phase growth was maintained. After the 48-hour expression period, 3×10^6 cells were plated in medium and soft agar supplemented with trifluorothymidine (TFT) for selection of TFT-resistant ($TK^{-/-}$) cells; 600 cells were plated in nonselective medium and soft agar to determine cloning efficiency. Plates were incubated at 37° C in 5% CO_2 for 10 to 12 days. The test was initially performed without S9. If a clearly positive response was not obtained, the test was repeated using freshly prepared S9 from the livers of Aroclor 1254-induced male Fischer 344 rats.

Minimum criteria for accepting an experiment as valid and a detailed description of the statistical analysis and data evaluation are presented in Caspary *et al.* (1988). All data were evaluated statistically for trend and peak responses. Both responses had to be significant ($P \leq 0.05$) for a chemical to be considered

positive, i.e., capable of inducing TFT resistance. A single significant response led to a "questionable" conclusion, and the absence of both a trend and peak response resulted in a "negative" call.

CHINESE HAMSTER OVARY CELL CYTOGENETICS PROTOCOLS

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

Sister Chromatid Exchange Test: In the SCE test without S9, CHO cells were incubated for 26 hours with barium chloride dihydrate in McCoy's 5A medium supplemented with fetal bovine serum, *l*-glutamine, and antibiotics. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 26 hours, the medium containing barium chloride dihydrate was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 3 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with barium chloride dihydrate, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing serum and BrdU and no barium chloride dihydrate and incubation proceeded for an additional 26 to 27 hours, with Colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9. All slides were scored blind and those from a single test were read by the same person. Fifty second-division metaphase cells were scored for frequency of SCEs/cell from each dose level.

Statistical analyses were conducted on the slopes of the dose-response curves and the individual dose points (Galloway *et al.*, 1987). An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001. An increase of 20% or greater at any single dose was considered weak evidence of activity; increases at two or more doses resulted in a determination that the trial was positive. A statistically significant trend ($P \leq 0.05$) in the absence of any responses reaching 20% above background led to a call of equivocal.

Chromosomal Aberrations Test: In the Abs test without S9, cells were incubated in McCoy's 5A medium with barium chloride dihydrate for 10 hours; Colcemid was added and incubation continued for 2 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the Abs test with S9, cells were treated with barium chloride dihydrate and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 10 to 11 hours in fresh medium, with Colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9.

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

Chromosomal aberration data are presented as percentage of cells with aberrations. To arrive at a statistical call for a trial, analyses were conducted on both the dose response curve and individual dose points. For a single trial, a statistically significant ($P \leq 0.05$) difference for one dose point and a significant trend ($P \leq 0.015$) are considered weak evidence for a positive response; significant differences for two or

more doses indicate the trial is positive. A positive trend test in the absence of a statistically significant increase at any one dose results in an equivocal call (Galloway *et al.*, 1987). Ultimately the trial calls were based on a consideration of the statistical analyses as well as the biological information available to the reviewers.

RESULTS

Barium chloride dihydrate (100 to 10,000 μg/plate) did not induce gene mutations in any of five strains (TA100, TA1535, TA1537, TA97, and TA98) of *S. typhimurium* when tested in a preincubation protocol with and without Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9 (Table E1; Zeiger *et al.*, 1992). In contrast, barium chloride dihydrate, at concentrations of 250 μg/mL and above, induced gene mutations at the $TK^{+/-}$ locus of L5178Y mouse lymphoma cells in the presence of Aroclor 1254-induced male Fischer 344 rat liver S9; without S9, no increase in the number of mutant colonies was observed (Table E2). At the 1,000 μg/mL concentration, a precipitate of barium chloride dihydrate was observed, and results for this dose point were not considered in making the positive call. In cytogenetic tests with cultured Chinese hamster ovary cells, barium chloride dihydrate did not induce sister chromatid exchanges (Table E3) or chromosomal aberrations (Table E4), with or without Aroclor 1254-induced male Sprague-Dawley rat liver S9. No cell cycle delay was observed at any of the concentrations tested in either assay; precipitation was noted in the chromosomal aberration assay at doses of 2,000 μg/mL and above.

TABLE E1
Mutagenicity of Barium Chloride Dihydrate in *Salmonella typhimurium*[a]

Strain	Dose (μg/plate)	Revertants/plate[b] -S9 Trial 1	-S9 Trial 2	+hamster S9 10%	+hamster S9 30%	+rat S9 10%	+rat S9 30%
TA100	0	126 ± 11.5	98 ± 1.0	80 ± 4.7	166 ± 11.7	90 ± 3.8	167 ± 17.5
	100	129 ± 8.6	89 ± 2.5	84 ± 2.3	157 ± 8.1	95 ± 0.3	161 ± 2.1
	333	123 ± 8.7	103 ± 4.3[c]	75 ± 4.4	167 ± 9.2	98 ± 4.5	168 ± 7.4
	1,000	112 ± 4.4	90 ± 2.4[c]	82 ± 2.9	164 ± 10.4	96 ± 12.3	184 ± 14.5
	3,333	108 ± 4.7	106 ± 5.4[c]	67 ± 2.9	123 ± 6.7	95 ± 6.2	169 ± 1.9
	10,000	96 ± 1.7[c]	87 ± 1.5	88 ± 9.2[c]	126 ± 6.9[c]	102 ± 10.1[c]	165 ± 7.4[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control[d]		368 ± 6.9	338 ± 18.6	505 ± 19.0	594 ± 9.0	723 ± 15.6	803 ± 30.3
TA1535	0	18 ± 0.7	24 ± 1.9	9 ± 2.5	11 ± 2.7	10 ± 1.2	5 ± 1.9
	100	21 ± 5.0	27 ± 3.5	12 ± 0.9	13 ± 3.5	10 ± 2.3	10 ± 0.3
	333	18 ± 2.2	23 ± 0.9[c]	11 ± 3.2	8 ± 0.3	12 ± 3.1	10 ± 1.5
	1,000	13 ± 2.1	24 ± 3.3[c]	11 ± 3.1	9 ± 1.7	12 ± 2.3	10 ± 1.0
	3,333	14 ± 2.1	22 ± 2.6[c]	11 ± 0.0	14 ± 3.3	8 ± 2.1	10 ± 1.5
	10,000	18 ± 1.8[c]	20 ± 1.3	10 ± 0.7[c]	9 ± 2.6	9 ± 1.9[c]	10 ± 0.3
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		212 ± 8.4	258 ± 4.3	61 ± 8.1	75 ± 6.5	165 ± 6.7	134 ± 13.5

		Revertants/plate -S9	+S9 30% hamster	+S9 30% rat
TA1537	0	9 ± 2.1	6 ± 1.7	8 ± 2.2
	100	9 ± 1.5	7 ± 2.0	7 ± 1.0
	333	7 ± 1.7	5 ± 0.3	11 ± 2.6
	1,000	8 ± 1.3	6 ± 0.6	12 ± 1.0
	3,333	8 ± 2.0	8 ± 1.8	6 ± 1.8
	10,000	6 ± 1.3[c]	4 ± 0.3	6 ± 1.8
Trial summary		Negative	Negative	Negative
Positive control		70 ± 7.3	181 ± 9.8	61 ± 5.1

TABLE E1
Mutagenicity of Barium Chloride Dihydrate in *Salmonella typhimurium* (continued)

Strain	Dose (μg/plate)	Revertants/plate -S9 Trial 1	-S9 Trial 2	+ hamster S9 10%	+ hamster S9 30%	+ rat S9 10%	+ rat S9 30%
TA97	0	79 ± 6.6	79 ± 5.8	98 ± 3.0	150 ± 13.2	113 ± 1.8	178 ± 22.3
	100	74 ± 6.2	72 ± 7.0	93 ± 9.4	134 ± 15.9	115 ± 4.9	148 ± 14.0
	333	90 ± 3.3	73 ± 5.2[c]	101 ± 2.1	141 ± 8.5	111 ± 8.5	200 ± 1.0
	1,000	60 ± 1.5	71 ± 8.5[c]	81 ± 20.6	146 ± 8.0	127 ± 2.2	199 ± 7.8
	3,333	72 ± 6.1	68 ± 2.2[c]	98 ± 9.5	122 ± 17.5	115 ± 6.4	138 ± 7.0
	10,000	46 ± 4.6[c]	60 ± 3.2	94 ± 6.0[c]	145 ± 2.0	118 ± 3.2[c]	195 ± 6.2
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		227 ± 12.6	182 ± 11.0	725 ± 121.9	1,062 ± 20.9	1,274 ± 55.3	482 ± 14.7
TA98	0	14 ± 0.9	17 ± 2.2	28 ± 3.0	22 ± 3.8	31 ± 1.5	23 ± 0.6
	100	14 ± 3.3	11 ± 1.3	33 ± 2.7	30 ± 3.1	22 ± 1.3	28 ± 2.7
	333	14 ± 3.3	17 ± 1.8[c]	27 ± 0.6	19 ± 3.4	25 ± 3.1	25 ± 1.2
	1,000	16 ± 1.7	14 ± 1.9[c]	32 ± 5.5	16 ± 3.0	26 ± 0.0	23 ± 2.8
	3,333	12 ± 1.5[c]	17 ± 0.9[c]	25 ± 1.0[c]	23 ± 1.7	27 ± 2.3[c]	22 ± 3.3
	10,000	10 ± 2.6[c]	14 ± 2.0	22 ± 1.5[c]	28 ± 4.0[c]	23 ± 5.3[c]	23 ± 0.9[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		122 ± 10.9	222 ± 15.6	235 ± 12.0	83 ± 3.3	249 ± 2.6	173 ± 6.4

[a] Study performed at Microbiological Associates, Inc. The detailed protocol is presented in Zeiger *et al.* (1992).
[b] Revertants are presented as mean ± the standard error from three plates.
[c] Slight toxicity
[d] 2-Aminoanthracene was used on all strains in the presence of S9. The positive controls in the absence of metabolic activation were sodium azide (TA1535 and TA100), 9-aminoacridine (TA97 and TA1537), 4-nitro-*o*-phenylenediamine (TA98).

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Barium Chloride Dihydrate[a]

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction[b]	Average Mutant Fraction[c]
-S9						
Trial 1						
Distilled water						
		81	93	81	33	
		87	94	58	22	
		102	112	77	25	
		92	101	58	21	25
Methyl methanesulfonate						
	5	51	29	510	333	
		74	49	479	215	
		52	30	499	317	288*
Barium chloride dihydrate						
	62.5	82	93	61	25	
		79	84	85	36	
		70	62	66	32	31
	125	89	89	82	31	
		80	92	76	32	
		82	68	101	41	35
	250	92	118	79	29	
		82	75	74	30	
		87	87	61	23	27
	500	100	88	76	25	
		82	70	97	40	
		74	70	69	31	32
	750	86	59	70	27	
		100	73	76	25	
		93	63	72	26	26
	1,000	90	35	64	24	
		89	59	53	20	
		84	49	83	33	26

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Barium Chloride Dihydrate (continued)

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
-S9 (continued)						
Trial 2						
Distilled water						
		96	113	111	39	
		63	87	83	44	41
Methyl methanesulfonate						
	5	61	62	504	277	
		85	74	506	198	
		95	100	478	167	214*
Barium chloride dihydrate						
	62.5	81	94	98	40	
		63	54	85	45	43
	125	80	63	87	36	
		84	95	103	41	
		100	128	74	25	34
	250	110	114	90	27	
	500	98	114	76	26	
		118	124	65	18	22
	750	102	87	73	24	
		114	108	103	30	27
	1,000	67	34	84	42	
		99	61	76	26	34

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Barium Chloride Dihydrate (continued)

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
+S9						
Trial 1						
Distilled water						
		107	103	59	18	
		104	101	34	11	
		82	96	56	23	
		94	101	88	31	21
Methylcholanthrene						
	2.5	69	29	508	245	
		89	39	335	125	
		61	30	519	283	218[c]
Barium chloride dihydrate						
	62.5	83	104	46	18	
		76	105	52	23	21
	125	97	81	73	25	
		101	108	71	23	
		97	119	79	27	25
	250	60	65	75	41	
		91	101	95	35	
		112	101	107	32	36[c]
	500	107	87	118	37	
		91	81	99	36	
		94	72	66	23	32[c]
	750	78	63	85	36	
		92	78	101	37	
		84	55	95	38	37[c]
	1,000[d]	87	28	106	41	
		75	37	75	33	
		96	38	123	43	39[c]

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by Barium Chloride Dihydrate (continued)

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
+S9 (continued)						
Trial 2						
Distilled water						
		53	84	62	39	
		86	102	71	28	
		94	113	84	30	32
Methylcholanthrene						
	2.5	80	51	866	359	
		95	59	656	231	
		86	68	637	246	279*
Barium chloride dihydrate						
	62.5	45	56	50	37	
		67	64	74	37	
		52	68	35	22	32
	125	63	34	82	44	
		60	59	64	36	
		86	69	55	21	33
	250	66	53	67	34	
		57	49	60	35	
		64	52	33	17	29
	500	45	21	63	47	
		58	17	91	52	
		86	27	125	49	49*
	750	59	11	124	70	
		71	18	82	39	
		71	11	113	53	54*
	1,000[d]	70	11	147	70	
		88	8	128	49	59*

* Significant positive response ($P \leq 0.05$)
[a] Study performed at Litton Bionetics, Inc. The experimental protocol is presented in detail by Myhr *et al.* (1985).
[b] Mean ± standard error from three replicate plates of approximately 1/3 (3×10^6) cells each.
[c] Mutant fraction (frequency) is a ratio of the mutant count to the cloning efficiency, divided by 3 (to arrive at MF/1 $\times 10^6$ cells treated); MF = mutant fraction.
[d] Precipitate formed at this concentration

TABLE E3
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Barium Chloride Dihydrate[a]

Compound	Dose (μg/mL)	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hrs in BrdU	Relative SCEs/ Chromosome (%)[b]
-S9								
Trial 1								
Summary: Negative								
Distilled water		50	1,028	365	0.35	7.3	27.0	
Mitomycin-C	0.003	50	1,030	1,024	0.99	20.5	27.0	180.01
	0.005	50	1,039	1,461	1.40	29.2	27.0	296.04
Barium chloride dihydrate	50	50	1,031	365	0.35	7.3	27.0	-0.29
	160	50	1,027	399	0.38	8.0	27.0	9.42
	500	50	1,040	388	0.37	7.8	27.0	5.08
	1,600	50	1,019	407	0.39	8.1	27.0	12.49
								P=0.037[c]
Trial 2								
Summary: Negative								
Distilled water		50	1,045	357	0.34	7.1	27.0	
Mitomycin-C	0.005	50	1,039	1,188	1.14	23.8	27.0	234.70
Barium chloride dihydrate	100	50	1,038	353	0.34	7.1	27.0	-0.45
	250	50	1,038	405	0.39	8.1	27.0	14.21
	500	50	1,030	407	0.39	8.1	27.0	15.67
	1,000	50	1,040	358	0.34	7.2	27.0	0.76
								P=0.125

TABLE E3
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by Barium Chloride Dihydrate (continued)

Compound	Dose (μg/mL)	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hrs in BrdU	Relative SCEs/ Chromosome[b] (%)
+S9								
Trial 1								
Summary: Negative								
Distilled water								
		50	1,030	384	0.37	7.7	27.0	
Cyclophosphamide								
	2	50	1,034	1,338	1.29	26.8	27.0	247.09
Barium chloride dihydrate								
	50	50	1,031	358	0.34	7.2	27.0	-6.86
	160	50	1,042	406	0.38	8.1	27.0	4.51
	500	50	1,042	393	0.37	7.9	27.0	1.16
	1,600	50	1,029	397	0.38	7.9	27.0	3.49
								P=0.176
Trial 2								
Summary: Negative								
Distilled water								
		50	1,041	378	0.36	7.6	26.0	
Cyclophosphamide								
	2	50	1,035	1,686	1.62	33.7	26.0	348.62
Barium chloride dihydrate								
	500	50	1,033	363	0.35	7.3	26.0	-3.23
	750	50	1,029	363	0.35	7.3	26.0	-2.85
	1,600	50	1,040	359	0.34	7.2	26.0	-4.94
	3,000	50	1,035	377	0.36	7.5	26.0	0.31
								P=0.519

[a] Study performed at Environmental Health Research & Testing, Inc. The protocol is presented in detail by Galloway *et al.* (1987). SCE = sister chromatid exchange; BrdU = bromodeoxyuridine.
[b] SCEs/chromosome of culture exposed to barium chloride dihydrate relative to those of culture exposed to solvent.
[c] Significance of relative SCEs/chromosome tested by the linear regression trend test vs. log of the dose.

TABLE E4
Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by Barium Chloride Dihydrate[a]

-S9					+S9				
Dose (μg/mL)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells w/Abs	Dose (μg/mL)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells w/Abs
Trial 1 - Harvest time: 12.0 hours Summary: Negative					**Trial 1** - Harvest time: 12.5 hours Summary: Negative				
Distilled Water					Distilled Water				
	100	0	0.00	0.0		100	0	0.00	0.0
Mitomycin-C					Cyclophosphamide				
0.25	100	40	0.40	24.0	50	100	38	0.38	26.0
Barium chloride dihydrate					Barium chloride dihydrate[b]				
50	100	2	0.02	2.0	50	100	0	0.00	0.0
160	100	1	0.01	1.0	160	100	0	0.00	0.0
500	100	2	0.02	2.0	500	100	0	0.00	0.0
1,600	100	2	0.02	2.0	1,600	100	2	0.02	2.0
					5,000	100	0	0.03	0.0
				P=0.141[c]					P=0.106
Trial 2 - Harvest time: 12.0 hours Summary: Negative					**Trial 2** - Harvest time: 12.0 hours Summary: Negative				
Distilled water					Distilled water				
	100	1	0.01	1.0		100	2	0.02	2.0
Mitomycin-C					Cyclophosphamide				
0.25	100	21	0.21	20.0	50	100	49	0.49	34.0
Barium chloride dihydrate[b]					Barium chloride dihydrate[b]				
100	100	0	0.00	0.0	500	100	2	0.02	2.0
250	100	0	0.00	0.0	1,600	100	1	0.01	1.0
500	100	4	0.04	3.0	3,000	100	0	0.00	0.0
1,000	100	1	0.01	1.0	4,000	100	0	0.00	0.0
1,500	100	3	0.03	3.0	5,000	100	0	0.00	0.0
2,000	100	0	0.00	0.0					
				P=0.178					P=0.991

[a] Study performed at Environmental Health Research, Inc. Abs= aberrations. A detailed presentation of the technique for detecting chromosomal aberrations is found in Galloway *et al.* (1987).
[b] Precipitate formed at doses of 2,000 μg/mL and greater.
[c] Significance of percent cells with aberrations tested by the linear regression trend test vs. log of the dose.

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

TABLE F1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 15-Day Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	125 ppm	250 ppm	500 ppm	1,000 ppm	2,000 ppm
n	5	5	5	5	5	5
Male						
Necropsy body wt	210 ± 5	218 ± 6	220 ± 6	215 ± 7	214 ± 5	211 ± 6
Brain						
Absolute	1.852 ± 0.039	1.886 ± 0.033	1.886 ± 0.011	1.854 ± 0.010	1.882 ± 0.024	1.858 ± 0.032
Relative	8.83 ± 0.19	8.65 ± 0.14	8.62 ± 0.28	8.68 ± 0.28	8.83 ± 0.21	8.85 ± 0.28
Heart						
Absolute	0.750 ± 0.017	0.802 ± 0.040	0.778 ± 0.032	0.754 ± 0.043	0.748 ± 0.009	0.758 ± 0.025
Relative	3.57 ± 0.07	3.67 ± 0.14	3.54 ± 0.10	3.51 ± 0.11	3.51 ± 0.09	3.61 ± 0.17
R. Kidney						
Absolute	0.818 ± 0.027	0.872 ± 0.052	0.846 ± 0.024	0.832 ± 0.056	0.818 ± 0.049	0.814 ± 0.015
Relative	3.89 ± 0.08	3.98 ± 0.17	3.85 ± 0.06	3.86 ± 0.17	3.82 ± 0.18	3.87 ± 0.08
Liver						
Absolute	8.782 ± 0.372	9.384 ± 0.467	9.306 ± 0.329	8.948 ± 0.484	9.066 ± 0.339	8.858 ± 0.361
Relative	41.73 ± 0.82	42.87 ± 1.08	42.39 ± 1.03	41.61 ± 1.07	42.42 ± 1.18	42.04 ± 1.16
Lungs						
Absolute	1.046 ± 0.044	1.092 ± 0.058	1.072 ± 0.061	1.124 ± 0.084	1.050 ± 0.091	1.106 ± 0.079
Relative	4.99 ± 0.20	5.00 ± 0.22	4.88 ± 0.21	5.28 ± 0.47	4.93 ± 0.45	5.27 ± 0.41
R. Testis						
Absolute	1.270 ± 0.037	1.273 ± 0.018	1.264 ± 0.036	1.267 ± 0.032	1.249 ± 0.033	1.246 ± 0.041
Relative	6.05 ± 0.15	5.84 ± 0.08	5.76 ± 0.14	5.91 ± 0.07	5.84 ± 0.07	5.91 ± 0.05
Thymus						
Absolute	0.337 ± 0.024	0.389 ± 0.043	0.431 ± 0.031	0.403 ± 0.043	0.387 ± 0.033	0.365 ± 0.029
Relative	1.61 ± 0.12	1.78 ± 0.18	1.97 ± 0.17	1.88 ± 0.19	1.82 ± 0.15	1.74 ± 0.13
Female						
Necropsy body wt	144 ± 4	149 ± 4	142 ± 3	150 ± 3	149 ± 3	147 ± 5
Brain						
Absolute	1.734 ± 0.029	1.738 ± 0.037	1.762 ± 0.039	1.788 ± 0.043	1.816 ± 0.024	1.748 ± 0.036
Relative	12.07 ± 0.33	11.70 ± 0.48	12.41 ± 0.15	11.93 ± 0.10	12.24 ± 0.31	11.90 ± 0.38
Heart						
Absolute	0.546 ± 0.013	0.556 ± 0.019	0.566 ± 0.020	0.586 ± 0.031	0.528 ± 0.012	0.526 ± 0.023
Relative	3.80 ± 0.15	3.73 ± 0.11	3.98 ± 0.08	3.90 ± 0.15	3.56 ± 0.11	3.58 ± 0.16
R. Kidney						
Absolute	0.582 ± 0.016	0.540 ± 0.022	0.566 ± 0.007	0.580 ± 0.027	0.594 ± 0.022	0.618 ± 0.021
Relative	4.05 ± 0.16	3.63 ± 0.16	3.99 ± 0.07	3.87 ± 0.16	4.00 ± 0.14	4.20 ± 0.07
Liver						
Absolute	5.600 ± 0.186	5.854 ± 0.169	5.334 ± 0.198	5.854 ± 0.230	5.934 ± 0.206	5.840 ± 0.284
Relative	38.93 ± 1.21	39.30 ± 1.02	37.51 ± 0.56	39.01 ± 0.85	39.90 ± 0.88	39.58 ± 1.08
Lungs						
Absolute	0.770 ± 0.043	0.836 ± 0.040	0.810 ± 0.046	0.912 ± 0.096	0.836 ± 0.034	0.868 ± 0.085
Relative	5.34 ± 0.20	5.61 ± 0.25	5.70 ± 0.26	6.06 ± 0.54	5.62 ± 0.14	5.86 ± 0.43
Thymus						
Absolute	0.304 ± 0.018	0.317 ± 0.029	0.304 ± 0.012	0.340 ± 0.019	0.344 ± 0.023	0.355 ± 0.022
Relative	2.11 ± 0.12	2.13 ± 0.20	2.14 ± 0.08	2.27 ± 0.13	2.31 ± 0.13	2.41 ± 0.13

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

TABLE F2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Male						
n	10	10	10	10	10	7
Necropsy body wt	348 ± 8	352 ± 8	360 ± 6	342 ± 5	340 ± 6	307 ± 5**
Adrenal Gland						
Absolute	0.052 ± 0.002	0.050 ± 0.001	0.049 ± 0.001	0.049 ± 0.002	0.047 ± 0.002*	0.045 ± 0.002**
Relative	0.15 ± 0.00	0.14 ± 0.00	0.14 ± 0.00	0.14 ± 0.00	0.14 ± 0.00	0.15 ± 0.01
Brain						
Absolute	2.097 ± 0.035	2.095 ± 0.030	2.095 ± 0.022	2.075 ± 0.014	2.051 ± 0.021	2.049 ± 0.021
Relative	6.05 ± 0.13	5.96 ± 0.10	5.84 ± 0.12	6.07 ± 0.09	6.04 ± 0.07	6.68 ± 0.12**
Heart						
Absolute	1.025 ± 0.030	1.037 ± 0.027	1.073 ± 0.027	1.010 ± 0.027	0.953 ± 0.019	0.901 ± 0.019**
Relative	2.95 ± 0.06	2.94 ± 0.05	2.99 ± 0.09	2.95 ± 0.06	2.81 ± 0.05	2.94 ± 0.07
R. Kidney						
Absolute	1.061 ± 0.035	1.044 ± 0.031	1.097 ± 0.022	1.092 ± 0.022	1.064 ± 0.025	1.050 ± 0.037
Relative	3.05 ± 0.05	2.96 ± 0.04	3.05 ± 0.05	3.19 ± 0.03	3.13 ± 0.05	3.42 ± 0.10**
Liver						
Absolute	11.956 ± 0.439	12.033 ± 0.462	12.839 ± 0.252	12.572 ± 0.493	11.549 ± 0.324	10.099 ± 0.296**
Relative	34.31 ± 0.65	34.05 ± 0.72	35.71 ± 0.36	36.70 ± 1.17	33.94 ± 0.48	32.86 ± 0.62
Lungs						
Absolute	1.729 ± 0.063	1.725 ± 0.048	1.777 ± 0.034	1.728 ± 0.063	1.663 ± 0.052	1.701 ± 0.074
Relative	4.98 ± 0.18	4.91 ± 0.13	4.96 ± 0.14	5.04 ± 0.15	4.90 ± 0.15	5.53 ± 0.20
R. Testis						
Absolute	1.451 ± 0.016	1.442 ± 0.018[b]	1.516 ± 0.026	1.509 ± 0.014	1.250 ± 0.135	1.489 ± 0.056
Relative	4.19 ± 0.09	4.14 ± 0.07[b]	4.22 ± 0.07	4.42 ± 0.06	3.72 ± 0.41	4.85 ± 0.14*
Thymus						
Absolute	0.309 ± 0.013[b]	0.402 ± 0.038	0.342 ± 0.021	0.324 ± 0.020	0.287 ± 0.015	0.255 ± 0.016[c]
Relative	0.89 ± 0.03[b]	1.13 ± 0.09	0.95 ± 0.05	0.95 ± 0.06	0.85 ± 0.05	0.84 ± 0.06[c]

TABLE F2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Female						
n	10	10	10	10	10	9
Necropsy body wt	190 ± 3	197 ± 4	191 ± 3	187 ± 3	186 ± 4	173 ± 5**
Adrenal Gland						
Absolute	0.051 ± 0.002	0.055 ± 0.003	0.054 ± 0.002	0.052 ± 0.002	0.053 ± 0.001	0.048 ± 0.002
Relative	0.27 ± 0.01	0.28 ± 0.01	0.29 ± 0.01	0.28 ± 0.01	0.29 ± 0.00	0.28 ± 0.01
Brain						
Absolute	1.892 ± 0.025	1.961 ± 0.031	1.921 ± 0.025	1.974 ± 0.035	1.913 ± 0.032	1.871 ± 0.038
Relative	9.99 ± 0.14	9.98 ± 0.21	10.09 ± 0.16	10.58 ± 0.22	10.33 ± 0.22	10.83 ± 0.22**
Heart						
Absolute	0.627 ± 0.013	0.645 ± 0.013	0.628 ± 0.016	0.630 ± 0.008	0.619 ± 0.013	0.609 ± 0.020
Relative	3.31 ± 0.05	3.28 ± 0.05	3.30 ± 0.07	3.38 ± 0.09	3.34 ± 0.05	3.53 ± 0.14
R. Kidney						
Absolute	0.570 ± 0.011	0.609 ± 0.022	0.591 ± 0.009	0.602 ± 0.013	0.635 ± 0.014**	0.620 ± 0.018*
Relative	3.01 ± 0.04	3.09 ± 0.09	3.10 ± 0.04	3.22 ± 0.04*	3.42 ± 0.05**	3.59 ± 0.09**
Liver						
Absolute	5.944 ± 0.156	6.439 ± 0.143	6.083 ± 0.098	5.899 ± 0.192	5.858 ± 0.137	5.024 ± 0.173**
Relative	31.32 ± 0.58	32.68 ± 0.40	31.93 ± 0.44	31.52 ± 0.68	31.57 ± 0.47	29.00 ± 0.59**
Lungs						
Absolute	1.207 ± 0.050	1.297 ± 0.056	1.287 ± 0.046	1.358 ± 0.046	1.259 ± 0.046[b]	1.216 ± 0.060
Relative	6.36 ± 0.23	6.58 ± 0.24	6.75 ± 0.22	7.26 ± 0.21*	6.86 ± 0.23[b]	7.01 ± 0.27
Thymus						
Absolute	0.237 ± 0.010	0.234 ± 0.008	0.254 ± 0.012	0.253 ± 0.014	0.229 ± 0.020	0.185 ± 0.019*
Relative	1.25 ± 0.05	1.19 ± 0.04	1.34 ± 0.07	1.35 ± 0.07	1.24 ± 0.11	1.05 ± 0.10

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9
[c] n=6

TABLE F3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Male				
n	10	10	10	10
Necropsy body wt	460 ± 12	452 ± 9	439 ± 8	418 ± 7**
Adrenal Gland				
Absolute	0.049 ± 0.003	0.050 ± 0.003	0.048 ± 0.003	0.050 ± 0.002
Relative	0.11 ± 0.01	0.11 ± 0.01	0.11 ± 0.01	0.12 ± 0.01
Brain				
Absolute	2.082 ± 0.014	2.028 ± 0.026	2.050 ± 0.021	2.030 ± 0.018
Relative	4.55 ± 0.10	4.51 ± 0.12	4.69 ± 0.10	4.86 ± 0.09*
Heart				
Absolute	1.224 ± 0.038	1.201 ± 0.029	1.125 ± 0.012*	1.064 ± 0.027**
Relative	2.66 ± 0.05	2.66 ± 0.03	2.57 ± 0.05	2.54 ± 0.04
R. Kidney				
Absolute	1.449 ± 0.039	1.449 ± 0.045	1.347 ± 0.017*	1.322 ± 0.028*
Relative	3.15 ± 0.04	3.20 ± 0.05	3.08 ± 0.05	3.16 ± 0.05
Liver				
Absolute	16.270 ± 0.777	15.077 ± 0.529	14.914 ± 0.336	14.465 ± 0.293*
Relative	35.19 ± 0.90	33.31 ± 0.70	33.99 ± 0.42	34.61 ± 0.71
Lungs				
Absolute	2.036 ± 0.091	2.012 ± 0.111	1.945 ± 0.039	1.828 ± 0.044
Relative	4.42 ± 0.17	4.45 ± 0.22	4.45 ± 0.13	4.37 ± 0.09
Spleen				
Absolute	0.955 ± 0.035	0.912 ± 0.025	0.886 ± 0.028	0.907 ± 0.030
Relative	2.07 ± 0.04	2.02 ± 0.05	2.02 ± 0.07	2.17 ± 0.06
R. Testis				
Absolute	1.526 ± 0.057	1.616 ± 0.039[b]	1.564 ± 0.019	1.656 ± 0.090
Relative	3.31 ± 0.09	3.56 ± 0.07[b]	3.57 ± 0.06	3.97 ± 0.24**
Thymus				
Absolute	0.169 ± 0.013	0.165 ± 0.013	0.153 ± 0.015	0.149 ± 0.015
Relative	0.37 ± 0.03	0.37 ± 0.03	0.35 ± 0.03	0.36 ± 0.03

TABLE F3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Female				
n	10	10	10	10
Necropsy body wt	279 ± 5	264 ± 6	271 ± 7	254 ± 6**
Adrenal Gland				
Absolute	0.059 ± 0.003	0.054 ± 0.002	0.055 ± 0.001	0.054 ± 0.001
Relative	0.21 ± 0.01	0.20 ± 0.01	0.20 ± 0.00	0.21 ± 0.00
Brain				
Absolute	1.897 ± 0.015	1.843 ± 0.034	1.903 ± 0.014	1.895 ± 0.016
Relative	6.81 ± 0.11	6.99 ± 0.14	7.05 ± 0.16	7.51 ± 0.18**
Heart				
Absolute	0.786 ± 0.021[b]	0.761 ± 0.020	0.778 ± 0.016	0.755 ± 0.014
Relative	2.80 ± 0.08[b]	2.88 ± 0.05	2.88 ± 0.07	2.98 ± 0.04
R. Kidney				
Absolute	0.827 ± 0.021[b]	0.787 ± 0.023	0.848 ± 0.019	0.858 ± 0.022
Relative	2.95 ± 0.04[b]	2.98 ± 0.05	3.13 ± 0.05*	3.39 ± 0.05**
Liver				
Absolute	8.647 ± 0.253	7.571 ± 0.225*	8.088 ± 0.256*	7.699 ± 0.192**
Relative	30.99 ± 0.88	28.62 ± 0.49*	29.81 ± 0.51	30.39 ± 0.49
Lungs				
Absolute	1.312 ± 0.064	1.317 ± 0.057	1.280 ± 0.047	1.351 ± 0.137
Relative	4.69 ± 0.19	4.98 ± 0.18	4.71 ± 0.10	5.35 ± 0.55
Ovary				
Absolute	0.092 ± 0.005	0.088 ± 0.005	0.086 ± 0.005	0.138 ± 0.049
Relative	0.33 ± 0.02	0.33 ± 0.01	0.32 ± 0.02	0.54 ± 0.18
Spleen				
Absolute	0.548 ± 0.023	0.532 ± 0.040	0.509 ± 0.009	0.502 ± 0.009
Relative	1.97 ± 0.09	2.01 ± 0.13	1.88 ± 0.05	1.99 ± 0.03
Thymus				
Absolute	0.123 ± 0.010	0.137 ± 0.015	0.154 ± 0.015	0.117 ± 0.012
Relative	0.44 ± 0.04	0.51 ± 0.05	0.58 ± 0.06	0.46 ± 0.04
Uterus				
Absolute	0.637 ± 0.058	0.686 ± 0.041	0.670 ± 0.048	0.757 ± 0.052
Relative	2.30 ± 0.23	2.61 ± 0.17	2.51 ± 0.22	3.03 ± 0.27*

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

TABLE F4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 15-Day Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	40 ppm	80 ppm	173 ppm	346 ppm	692 ppm
n	5	5	5	5	5	5
Male						
Necropsy body wt	29.8 ± 1.3	28.9 ± 0.6	28.6 ± 0.7	29.4 ± 0.8	28.7 ± 0.6	30.0 ± 1.0
Brain						
Absolute	0.498 ± 0.016	0.490 ± 0.014	0.502 ± 0.012	0.462 ± 0.032	0.496 ± 0.015	0.498 ± 0.017
Relative	16.75 ± 0.57	16.96 ± 0.58	17.63 ± 0.87	15.75 ± 1.21	17.26 ± 0.38	16.69 ± 0.79
Heart						
Absolute	0.180 ± 0.003	0.168 ± 0.005	0.156 ± 0.008	0.162 ± 0.009	0.166 ± 0.005	0.162 ± 0.017
Relative	6.09 ± 0.33	5.81 ± 0.16	5.47 ± 0.35	5.50 ± 0.25	5.79 ± 0.27	5.38 ± 0.45
R. Kidney						
Absolute	0.278 ± 0.022	0.240 ± 0.010	0.272 ± 0.004	0.244 ± 0.012	0.244 ± 0.005	0.260 ± 0.018
Relative	9.27 ± 0.43	8.30 ± 0.36	9.52 ± 0.20	8.27 ± 0.24	8.51 ± 0.30	8.63 ± 0.33
Liver						
Absolute	1.700 ± 0.124	1.560 ± 0.027	1.800 ± 0.048	1.790 ± 0.100	1.580 ± 0.039	1.970 ± 0.072
Relative	56.73 ± 1.76	54.00 ± 1.44	63.04 ± 2.30	60.66 ± 2.08	55.06 ± 1.72	65.79 ± 1.78**
Lungs						
Absolute	0.262 ± 0.049	0.238 ± 0.019	0.268 ± 0.019	0.208 ± 0.015	0.182 ± 0.006	0.300 ± 0.016
Relative	8.76 ± 1.65	8.22 ± 0.62	9.44 ± 0.87	7.04 ± 0.37	6.35 ± 0.29	10.03 ± 0.57
R. Testis						
Absolute	0.115 ± 0.008	0.117 ± 0.002	0.120 ± 0.004	0.114 ± 0.002	0.107 ± 0.002	0.125 ± 0.006
Relative	3.85 ± 0.22	4.04 ± 0.06	4.20 ± 0.19	3.87 ± 0.05	3.73 ± 0.15	4.21 ± 0.31
Thymus						
Absolute	0.060 ± 0.008	0.059 ± 0.006	0.072 ± 0.008	0.057 ± 0.003	0.056 ± 0.003	0.071 ± 0.013
Relative	2.00 ± 0.18	2.05 ± 0.22	2.56 ± 0.33	1.92 ± 0.10	1.95 ± 0.12	2.36 ± 0.37
Female						
Necropsy body wt	21.7 ± 0.4	23.4 ± 0.5	23.6 ± 0.7	22.2 ± 0.5	23.0 ± 0.3	23.4 ± 0.6
Brain						
Absolute	0.482 ± 0.015	0.528 ± 0.013	0.508 ± 0.014	0.506 ± 0.012	0.520 ± 0.019	0.522 ± 0.013
Relative	22.22 ± 0.78	22.61 ± 0.66	21.59 ± 0.81	22.87 ± 0.68	22.60 ± 0.86	22.33 ± 0.25
Heart						
Absolute	0.128 ± 0.009	0.134 ± 0.006	0.142 ± 0.005	0.128 ± 0.004	0.126 ± 0.005	0.134 ± 0.010
Relative	5.89 ± 0.37	5.73 ± 0.24	6.04 ± 0.30	5.78 ± 0.15	5.48 ± 0.23	5.71 ± 0.34
R. Kidney						
Absolute	0.178 ± 0.007	0.188 ± 0.013	0.192 ± 0.011	0.180 ± 0.007	0.192 ± 0.017	0.190 ± 0.011
Relative	8.19 ± 0.28	8.04 ± 0.53	8.16 ± 0.52	8.13 ± 0.30	8.34 ± 0.75	8.13 ± 0.48
Liver						
Absolute	1.210 ± 0.033	1.440 ± 0.039	1.534 ± 0.072**	1.352 ± 0.055	1.502 ± 0.076*	1.542 ± 0.101**
Relative	55.72 ± 1.22	61.58 ± 0.95	65.19 ± 3.52	61.16 ± 2.92	65.16 ± 2.77	65.74 ± 2.98*
Lungs						
Absolute	0.188 ± 0.015	0.264 ± 0.026	0.230 ± 0.016	0.216 ± 0.017	0.266 ± 0.031	0.250 ± 0.037
Relative	8.71 ± 0.82	11.36 ± 1.29	9.77 ± 0.72	9.77 ± 0.79	11.55 ± 1.36	10.63 ± 1.42
Thymus						
Absolute	0.057 ± 0.002	0.084 ± 0.004**	0.068 ± 0.005	0.075 ± 0.006	0.087 ± 0.008**	0.076 ± 0.006
Relative	2.63 ± 0.09	3.59 ± 0.16*	2.88 ± 0.22	3.42 ± 0.29	3.79 ± 0.35*	3.26 ± 0.25

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

TABLE F5
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Male						
n	10	9	10	10	10	4
Necropsy body wt	38.1 ± 0.6	37.8 ± 1.5	38.2 ± 1.0	36.1 ± 1.1	37.9 ± 1.0	26.8 ± 2.5**
Adrenal Gland						
Absolute	0.010 ± 0.001[b]	0.009 ± 0.001[c]	0.008 ± 0.001[c]	0.009 ± 0.001	0.008 ± 0.000	0.007 ± 0.001*
Relative	0.27 ± 0.03[b]	0.24 ± 0.03[c]	0.22 ± 0.02[c]	0.25 ± 0.02	0.21 ± 0.02	0.25 ± 0.03
Brain						
Absolute	0.507 ± 0.007	0.501 ± 0.005	0.493 ± 0.004	0.482 ± 0.004	0.482 ± 0.006	0.513 ± 0.026
Relative	13.35 ± 0.26	13.44 ± 0.57	12.98 ± 0.36	13.45 ± 0.37	12.81 ± 0.36	19.63 ± 2.04**
Heart						
Absolute	0.193 ± 0.010	0.187 ± 0.006	0.181 ± 0.008	0.182 ± 0.007	0.193 ± 0.009	0.118 ± 0.008**
Relative	5.07 ± 0.25	4.99 ± 0.22	4.73 ± 0.15	5.06 ± 0.16	5.11 ± 0.21	4.46 ± 0.37
R. Kidney						
Absolute	0.306 ± 0.008	0.301 ± 0.012	0.302 ± 0.010	0.286 ± 0.010	0.291 ± 0.009	0.235 ± 0.013**
Relative	8.04 ± 0.15	8.06 ± 0.44	7.95 ± 0.34	7.94 ± 0.22	7.71 ± 0.25	8.98 ± 0.89
Liver						
Absolute	2.062 ± 0.120	2.011 ± 0.077	1.892 ± 0.037	1.716 ± 0.064**	1.714 ± 0.053**	1.088 ± 0.036**
Relative	54.19 ± 3.10	53.85 ± 2.81	49.71 ± 1.10	47.73 ± 1.69*	45.33 ± 0.94**	40.77 ± 0.93**
Lungs						
Absolute	0.289 ± 0.021	0.267 ± 0.011	0.247 ± 0.009	0.247 ± 0.009	0.265 ± 0.008	0.230 ± 0.007
Relative	7.58 ± 0.50	7.12 ± 0.33	6.53 ± 0.36	6.89 ± 0.30	7.06 ± 0.32	8.89 ± 1.13
R. Testis						
Absolute	0.135 ± 0.008	0.112 ± 0.004*[c]	0.113 ± 0.006*	0.120 ± 0.004	0.125 ± 0.002	0.115 ± 0.004
Relative	3.53 ± 0.18	2.97 ± 0.13[c]	2.96 ± 0.15	3.34 ± 0.09	3.31 ± 0.10	4.38 ± 0.28**
Thymus						
Absolute	0.044 ± 0.003	0.051 ± 0.005	0.047 ± 0.004	0.040 ± 0.004	0.042 ± 0.004	0.022 ± 0.007**
Relative	1.16 ± 0.08	1.33 ± 0.11	1.22 ± 0.10	1.11 ± 0.09	1.09 ± 0.09	0.75 ± 0.22*

TABLE F5
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Female						
n	10	10	10	10	10	3
Necropsy body wt	29.5 ± 0.8	28.5 ± 0.8	27.8 ± 1.1	29.1 ± 1.0	27.6 ± 1.0	16.4 ± 2.0**
Adrenal Gland						
Absolute	0.011 ± 0.001[b]	0.010 ± 0.000	0.011 ± 0.001	0.012 ± 0.001	0.011 ± 0.001	0.008 ± 0.002
Relative	0.38 ± 0.03[b]	0.36 ± 0.01	0.40 ± 0.03	0.40 ± 0.03	0.41 ± 0.03	0.49 ± 0.07
Brain						
Absolute	0.502 ± 0.009	0.527 ± 0.010	0.516 ± 0.009	0.516 ± 0.007	0.511 ± 0.010	0.477 ± 0.027
Relative	17.12 ± 0.56	18.59 ± 0.50	18.76 ± 0.64	17.87 ± 0.49	18.71 ± 0.72	29.55 ± 1.78**
Heart						
Absolute	0.136 ± 0.006	0.141 ± 0.005	0.139 ± 0.006	0.134 ± 0.007	0.137 ± 0.006	0.093 ± 0.012**
Relative	4.63 ± 0.22	4.96 ± 0.15	5.01 ± 0.18	4.63 ± 0.22	5.04 ± 0.31	5.71 ± 0.42
R. Kidney						
Absolute	0.181 ± 0.004	0.183 ± 0.007	0.180 ± 0.006	0.188 ± 0.006	0.182 ± 0.008	0.143 ± 0.028
Relative	6.15 ± 0.14	6.42 ± 0.18	6.51 ± 0.20	6.49 ± 0.21	6.61 ± 0.22	8.61 ± 0.65**
Liver						
Absolute	1.502 ± 0.052	1.446 ± 0.069	1.375 ± 0.074	1.334 ± 0.053	1.196 ± 0.037**	0.753 ± 0.126**
Relative	50.86 ± 1.09	50.55 ± 1.40	49.33 ± 1.43	45.84 ± 0.91**	43.47 ± 0.91**	45.53 ± 2.30**
Lungs						
Absolute	0.250 ± 0.013	0.244 ± 0.009	0.251 ± 0.014	0.240 ± 0.011	0.238 ± 0.013	0.203 ± 0.023
Relative	8.47 ± 0.37	8.59 ± 0.30	9.16 ± 0.61	8.23 ± 0.19	8.66 ± 0.47	12.46 ± 0.43**
Thymus						
Absolute	0.057 ± 0.004	0.051 ± 0.003	0.047 ± 0.003	0.052 ± 0.003	0.047 ± 0.002*	0.008 ± 0.005**
Relative	1.94 ± 0.11	1.80 ± 0.11	1.68 ± 0.09	1.79 ± 0.08	1.72 ± 0.07	0.46 ± 0.25**

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9
[c] n=8

TABLE F6
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Male				
n	9	9	10	10
Necropsy body wt	45.4 ± 0.8	44.7 ± 1.5	45.8 ± 1.3	43.1 ± 1.0
Adrenal Gland				
Absolute	0.007 ± 0.001	0.005 ± 0.000	0.005 ± 0.000	0.006 ± 0.001[b]
Relative	0.15 ± 0.02	0.12 ± 0.02	0.12 ± 0.01	0.14 ± 0.02[b]
Brain				
Absolute	0.465 ± 0.004	0.441 ± 0.007	0.454 ± 0.006	0.440 ± 0.008*
Relative	10.26 ± 0.13	9.97 ± 0.40	9.96 ± 0.23	10.24 ± 0.17
Heart				
Absolute	0.189 ± 0.006	0.201 ± 0.010	0.192 ± 0.007	0.183 ± 0.005
Relative	4.16 ± 0.09	4.49 ± 0.15	4.20 ± 0.14	4.26 ± 0.13
R. Kidney				
Absolute	0.346 ± 0.011	0.348 ± 0.015	0.363 ± 0.016	0.325 ± 0.008
Relative	7.62 ± 0.12	7.79 ± 0.21	7.91 ± 0.21	7.55 ± 0.14
Liver				
Absolute	1.869 ± 0.092	1.779 ± 0.092	2.005 ± 0.151	1.773 ± 0.104
Relative	41.07 ± 1.53	39.65 ± 1.05	43.67 ± 3.14	41.53 ± 3.18
Lungs				
Absolute	0.236 ± 0.010	0.226 ± 0.013	0.248 ± 0.012	0.235 ± 0.010
Relative	5.21 ± 0.23	5.05 ± 0.21	5.42 ± 0.19	5.47 ± 0.24
Spleen				
Absolute	0.066 ± 0.004	0.067 ± 0.004	0.073 ± 0.003	0.060 ± 0.004
Relative	1.46 ± 0.08	1.48 ± 0.06	1.60 ± 0.07	1.41 ± 0.10
R. Testis				
Absolute	0.113 ± 0.003	0.114 ± 0.002[c]	0.116 ± 0.003	0.107 ± 0.003
Relative	2.50 ± 0.04	2.56 ± 0.07[c]	2.54 ± 0.06	2.49 ± 0.06
Thymus				
Absolute	0.059 ± 0.007	0.024 ± 0.002**	0.048 ± 0.006	0.034 ± 0.005*
Relative	1.28 ± 0.15	0.54 ± 0.04**	1.05 ± 0.13	0.79 ± 0.11*

TABLE F6
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Female				
n	10	8	10	6
Necropsy body wt	47.6 ± 2.3	50.3 ± 2.7	44.5 ± 1.7	46.6 ± 2.0
Adrenal Gland				
Absolute	0.011 ± 0.001	0.011 ± 0.001	0.010 ± 0.001	0.010 ± 0.002
Relative	0.24 ± 0.02	0.22 ± 0.03	0.24 ± 0.03	0.23 ± 0.04
Brain				
Absolute	0.474 ± 0.006	0.468 ± 0.008	0.464 ± 0.006	0.468 ± 0.005
Relative	10.13 ± 0.39	9.49 ± 0.48	10.54 ± 0.38	10.14 ± 0.48
Heart				
Absolute	0.146 ± 0.003	0.158 ± 0.013	0.144 ± 0.004	0.144 ± 0.009
Relative	3.10 ± 0.09	3.14 ± 0.13	3.25 ± 0.10	3.09 ± 0.10
R. Kidney				
Absolute	0.222 ± 0.006	0.231 ± 0.008	0.213 ± 0.006	0.210 ± 0.009
Relative	4.70 ± 0.12	4.63 ± 0.11	4.81 ± 0.15	4.51 ± 0.09
Lungs				
Absolute	0.226 ± 0.010	0.235 ± 0.013	0.224 ± 0.010[b]	0.207 ± 0.012
Relative	4.79 ± 0.15	4.68 ± 0.08	5.15 ± 0.16[b]	4.45 ± 0.14
Ovary				
Absolute	0.023 ± 0.002	0.028 ± 0.005	0.030 ± 0.005	0.018 ± 0.002
Relative	0.49 ± 0.03	0.56 ± 0.10	0.69 ± 0.12	0.38 ± 0.03
Spleen				
Absolute	0.094 ± 0.005	0.089 ± 0.007	0.082 ± 0.005	0.071 ± 0.002**
Relative	2.01 ± 0.14	1.80 ± 0.17	1.86 ± 0.12	1.53 ± 0.07*
Thymus				
Absolute	0.030 ± 0.003	0.031 ± 0.005	0.029 ± 0.004[b]	0.021 ± 0.003
Relative	0.63 ± 0.06	0.64 ± 0.12	0.65 ± 0.06[b]	0.46 ± 0.05
Uterus				
Absolute	0.299 ± 0.034[d]	0.374 ± 0.057	0.321 ± 0.036	0.276 ± 0.051
Relative	6.38 ± 0.97[d]	7.40 ± 0.90	7.18 ± 0.71	5.97 ± 1.06

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9
[c] n=8
[d] n=7

APPENDIX G
NEUROBEHAVIORAL AND CARDIOVASCULAR ANALYSES

NEUROBEHAVIORAL AND CARDIOVASCULAR ANALYSES

MATERIALS AND METHODS

15-Day Studies

Approximately one day before exposure began and again on day 14 of the studies, all rats and mice were tested for spontaneous motor activity, forelimb and hindlimb grip strength, tail flick latency, startle response, and hindlimb foot splay.

Spontaneous motor activity was measured using five Automex activity monitors (Columbus Instruments, Columbus, OH). Darkened, sound-insulating chambers were used to house individual acrylic test cages. The flat aluminum top of each cage had ventilation holes and was grounded to the monitor. The cage and its occupant were centered above the low-intensity radiofrequency field of the activity monitor. Activity counts from each activity monitor were routed to a 6-channel printer (Columbus Instruments, Columbus, OH) located outside the chamber. Activity was monitored for 30 minutes.

Grip strength was measured using a device and procedure similar to that described by Meyer *et al.* (1979). Each animal was allowed to grip a circular ring with its forepaws and was pulled back along a platform until its grip was broken. As the backward motion continued, its hindpaws reached a T-shaped rear-limb grip bar which it was allowed to grasp and then was forced to release by continued pulling. Push-pull strain gauges (Chatillon, Model DPP) were used to record the maximum strain required to break the animal's grip in each case. The average of three valid measurements was taken as the animal's score for either forelimb or hindlimb grip strength.

Tail flick latency was measured by placing each animal in a horizontally positioned cylinder with a slot running half the length of the bottom of the cylinder to allow the tail to hang freely. The test was started after the animal had acclimated to the cylinder. The tip of the tail (5 cm) was immersed in a 250-mL beaker of water taken from a nearby water bath maintained at 55° C. The time the animal took to raise its tail out of the hot water was measured to the nearest 0.1 second with a stopwatch. Each rat was given one trial.

Startle responses were measured by placing each animal on a acrylic platform mounted on a Model UC3 universal transducer (Statham Instruments, Co., Oxnard, CA) attached to a 1-pound load assembly. Output from the transducer went to a solid-state electronic instrument to measure the amplitude of the startle response. Each animal was acclimated to the platform for at least 10 seconds. Then, when the animal was not moving, an acoustic stimulus was presented, followed no sooner than 20 seconds later by an air-puff stimulus. The acoustic stimulus was a 110-dB burst of white noise having a duration of 100 msec. Background noise in the room was 35 dB. The air-puff was delivered from a compressed air tank for 100 msec by routing the air through a solenoid valve (the opening of which was controlled by a Grass S4 stimulus generator) before it was delivered to three 18-gauge needles mounted in the center of each of the three walls and 4.0 cm (rats) or 2.0 cm (mice) above the platform. Each animal generally received only one trial. If there was no measurable response in the first trial, one or two additional trials were performed.

For the hindlimb foot splay test, the hind paws of the animals were marked by placing them firmly on a pad impregnated with India ink. Each animal was dropped from a height of 32 cm onto a white blotter. The distance between the fourth digits of the hind paws shown on the inked impression was measured in millimeters. The average measurement of three trials was taken as the estimate of hindlimb foot splay.

13-Week Studies

During the 13-week studies, each rat and mouse was tested for spontaneous motor activity, forelimb and hindlimb grip strength, tail flick latency, startle response, and hindlimb foot splay on the day before exposure began and again at days 45 and 90 of exposure. Measurements were made following the same procedures described in the 15-day studies.

Cardiovascular testing was performed on all rats before exposure began and on days 45 and 91 of exposure to determine heart rate and blood pressure. For electrocardiogram (ECG) recordings, the conscious rats were restrained in the prone position in a tubular plastic holder and subcutaneous pin electrodes were positioned over the right scapula and lumbar vertebrae. The amplified signal was displayed on a Tektronix 502A oscilloscope and photographed with a C-12 oscilloscope camera. To decrease noise and facilitate the accurate measurement of ECG intervals, segments, and voltages, repetitive ECGs were collected, averaged, and analyzed via on-line biosignal processing with a laboratory computer (PDP MINC-11, Digital Equipment Corp.). Changes in ECG intervals were assessed for individual rats in terms of changes (in milliseconds) from pretreatment values. The *t*-test was used to compare pretreatment and post-treatment values.

Blood pressure was measured using a photoelectric sensor (IITC Inc., Landing, NJ) for end-point detection. As with other tail-cuff methods, the endpoint for determining systolic pressure was the resumption of blood flow to the tail during cuff deflation. The sensor consisted of a miniature focused light on top and a photoresistive cell on the bottom, both of which were mounted amidst a 50-mm-long, inflatable rubber cuff. Pulse signals from the photocell were fed into an amplifier (Model 59, IITC, Inc.) for regulation of gain, offset, and intensity of the light source. A sphygmomanometer was connected to the rubber cuff to keep the inflation-deflation rates constant and to register pressure changes with a transducer. Signals from the photocell amplifier and cuff pressure transducer were recorded continuously on separate channels of a Cross Model 7, ink-writing recorder. Attempts to accurately measure changes in mean and diastolic arterial pressure using this system were generally unsuccessful. Systolic arterial pressure was determined from an average of three trials per rat. The *t*-test was employed to establish the significance of the mean changes between pretreatment and posttreatment values.

TABLE G1
Neurobehavioral Data for Rats in the 15-Day Drinking Water Study of Barium Chloride Dihydrate[a]

Parameter/Day	0 ppm	125 ppm	250 ppm	500 ppm	1,000 ppm	2,000 ppm
Male						
n	5	5	5	5	5	5
Hindlimb foot splay test (mm)						
0	81.88 ± 3.25	81.32 ± 3.03	80.54 ± 3.62	87.14 ± 4.51	85.54 ± 2.81	81.94 ± 3.59
14	94.40 ± 7.46	81.60 ± 3.17	85.60 ± 3.37	90.20 ± 5.60	93.00 ± 3.63	95.60 ± 2.14
Tail flick latency test (s)						
0	2.64 ± 0.34	2.50 ± 0.32	2.80 ± 0.13	2.50 ± 0.19	2.12 ± 0.12*	2.60 ± 0.18
14	3.24 ± 0.21	3.54 ± 0.19	3.34 ± 0.20	2.94 ± 0.18	2.86 ± 0.25	2.66 ± 0.38
Startle response latency (ms)						
0	358.6 ± 88.2	272.2 ± 33.5	277.2 ± 26.3	287.2 ± 57.3	280.0 ± 25.7[b]	281.8 ± 28.4[b]
14	258.6 ± 17.1	277.8 ± 15.5	244.8 ± 28.2	259.2 ± 33.8	247.0 ± 17.4	262.4 ± 33.6
Forelimb grip strength (g)						
0	487.3 ± 55.6	477.3 ± 12.7	494.0 ± 26.9	435.3 ± 51.5	387.3 ± 12.9*	416.0 ± 43.2
14	676.0 ± 45.2	761.6 ± 67.9	774.6 ± 33.5	727.2 ± 51.8	802.2 ± 17.6	779.4 ± 28.1
Hindlimb grip strength (g)						
0	190.0 ± 7.5	187.3 ± 4.9	185.3 ± 12.2	195.4 ± 8.5	204.0 ± 7.3	198.7 ± 16.7
14	276.8 ± 12.1	286.6 ± 8.9	267.2 ± 15.4	261.2 ± 14.1	276.6 ± 20.1	290.0 ± 14.5
Undifferentiated motor activity (square root of count/30 min)						
0	18.98 ± 2.97	16.38 ± 2.06[b]	21.76 ± 3.60	17.40 ± 3.24	16.98 ± 0.75	24.08 ± 1.82[b]
14	17.20 ± 1.28	21.40 ± 2.18	22.40 ± 1.12*	19.00 ± 1.95	19.40 ± 1.96	23.00 ± 1.58*
Startle magnitude-acoustic stimulus (g)						
0	227.2 ± 58.8	334.2 ± 70.8	241.4 ± 76.6	271.6 ± 18.2	204.8 ± 69.4	301.2 ± 50.7
14	335.4 ± 78.7	286.4 ± 53.3	418.4 ± 104	412.4 ± 93.0	457.0 ± 44.8	435.2 ± 81.9
Startle duration-acoustic stimulus (ms)						
0	204.4 ± 52.5	220.2 ± 26.9	151.2 ± 43.4	149.2 ± 54.6	169.6 ± 46.4	192.4 ± 47.0
14	218.2 ± 12.9	179.2 ± 22.9	213.6 ± 52.5	194.6 ± 38.9	188.0 ± 43.6	227.6 ± 29.4
Startle magnitude-air puff stimulus (g)						
0	120.00 ± 60.70	94.40 ± 30.78	123.60 ± 38.25	199.20 ± 59.05	75.20 ± 40.13	144.40 ± 71.53
14	403.8 ± 109.0	247.0 ± 64.5	333.0 ± 48.5	276.2 ± 82.6	235.2 ± 104.0	292.4 ± 77.3
Startle duration-air puff stimulus (ms)						
0	90.20 ± 39.49	59.40 ± 20.24	78.00 ± 26.22	160.20 ± 35.83	64.80 ± 26.17	120.60 ± 56.40
14	276.6 ± 61.4	150.8 ± 34.4	257.0 ± 60.4	154.6 ± 25.5	190.8 ± 45.8	221.8 ± 35.2

TABLE G1
Neurobehavioral Data for Rats in the 15-Day Drinking Water Study of Barium Chloride Dihydrate
(continued)

Parameter/Day	0 ppm	125 ppm	250 ppm	500 ppm	1,000 ppm	2,000 ppm
Female						
n	5	5	5	5	5	5
Hindlimb foot splay test (mm)						
0	75.60 ± 5.55	73.62 ± 0.61	74.18 ± 4.71	76.54 ± 3.06	73.46 ± 2.22	72.72 ± 2.86
14	80.40 ± 2.40	70.00 ± 3.30	76.60 ± 4.87	72.20 ± 3.48	76.40 ± 5.68	71.60 ± 5.16
Tail flick latency test (s)						
0	2.72 ± 0.21	2.84 ± 0.09	2.60 ± 0.17	2.72 ± 0.31	2.64 ± 0.14	2.56 ± 0.32
14	2.52 ± 0.19	2.78 ± 0.21	2.92 ± 0.30	3.28 ± 0.31	3.20 ± 0.32	3.26 ± 0.29
Startle response latency (ms)						
0	286.6 ± 27.9	226.8 ± 50.9	254.6 ± 22.0	289.4 ± 33.8	299.5 ± 41.0[b]	282.8 ± 49.5
14	273.4 ± 10.2	308.2 ± 36.0	306.2 ± 24.3	308.0 ± 26.3	277.0 ± 20.2	258.4 ± 20.1
Forelimb grip strength (g)						
0	480.0 ± 44.2	417.7 ± 11.4	408.0 ± 33.7	464.0 ± 34.0	454.7 ± 51.3	402.7 ± 31.0
14	624.0 ± 54.4	591.2 ± 31.3	632.0 ± 33.0	668.8 ± 32.6	627.8 ± 42.8	674.6 ± 47.0
Hindlimb grip strength (g)						
0	162.0 ± 9.0	160.7 ± 5.3	178.7 ± 17.8	164.7 ± 11.5	172.7 ± 11.5	178.0 ± 11.8
14	255.4 ± 20.6	242.8 ± 12.2	237.4 ± 14.7	212.0 ± 13.6	219.8 ± 18.3	216.8 ± 14.2
Undifferentiated motor activity (square root of count/30min)						
0	22.86 ± 3.11	17.90 ± 2.60[b]	20.86 ± 2.64	17.52 ± 1.45	23.66 ± 3.43	24.67 ± 2.08[c]
14	22.00 ± 2.14	23.40 ± 2.94	21.00 ± 2.12	22.00 ± 1.92	24.40 ± 2.84	24.60 ± 2.25
Startle magnitude-acoustic stimulus (g)						
0	198.0 ± 24.1	118.4 ± 14.6	220.0 ± 29.4	244.8 ± 57.5	127.3 ± 43.1[b]	152.6 ± 59.5
14	218.2 ± 60.7	145.8 ± 40.4	230.8 ± 56.9	248.0 ± 88.4	261.6 ± 52.5	239.6 ± 69.3
Startle duration-acoustic stimulus (ms)						
0	157.4 ± 34.5	118.8 ± 41.2	204.0 ± 7.9	172.8 ± 31.8	110.0 ± 32.6[b]	118.4 ± 38.5
14	155.4 ± 21.4	173.0 ± 40.3	145.0 ± 32.3	192.0 ± 36.6	154.6 ± 36.4	138.4 ± 44.1
Startle magnitude-air puff stimulus (g)						
0	135.00 ± 31.12[b]	46.60 ± 18.30	104.60 ± 39.45	119.40 ± 50.19	61.25 ± 14.92[b]	98.40 ± 29.58
14	134.2 ± 30.1	181.4 ± 75.4	158.6 ± 39.8	308.2 ± 96.5	263.0 ± 73.9	148.8 ± 24.9
Startle duration-air puff stimulus (ms)						
0	98.75 ± 28.08[b]	36.00 ± 10.45[b]	64.60 ± 31.47	129.80 ± 32.43	45.75 ± 2.87[b]	98.60 ± 24.22
14	168.4 ± 49.4	164.6 ± 51.6	144.4 ± 43.4	265.0 ± 62.4	212.8 ± 57.5	151.0 ± 49.2

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
[a] Mean ± standard error
[b] n=4
[c] n=3

TABLE G2
Neurobehavioral and Cardiovascular Data for Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate[a]

Parameter/Day	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Male						
n	10	10	10	10	10	10
Neurobehavioral Data						
Hindlimb foot splay test (mm)						
0	70.90 ± 2.01	67.60 ± 2.15	69.70 ± 2.00	64.20 ± 1.74*	65.30 ± 2.10	66.10 ± 2.19
45	79.76 ± 4.62	80.03 ± 2.83	86.59 ± 2.50	79.27 ± 1.91	76.88 ± 2.15	86.17 ± 2.17
90	85.60 ± 3.29	87.42 ± 2.66	87.57 ± 2.73	75.57 ± 2.45*	76.86 ± 2.31*	82.54 ± 3.57[b]
Tail flick latency test (s)						
0	1.81 ± 0.09	2.13 ± 0.10*	2.25 ± 0.19	2.02 ± 0.17	2.17 ± 0.15*	2.35 ± 0.16*
45	3.09 ± 0.15	3.30 ± 0.23	3.46 ± 0.19	3.29 ± 0.22	3.56 ± 0.17	3.68 ± 0.13*
90	2.80 ± 0.14	2.78 ± 0.17	2.81 ± 0.17	2.41 ± 0.11	2.50 ± 0.18	2.66 ± 0.22[b]
Startle response latency (ms)						
0	271.8 ± 13.9	261.5 ± 31.3	259.7 ± 17.5	287.1 ± 26.0	265.5 ± 18.8	295.2 ± 28.6
45	230.2 ± 16.4	234.6 ± 11.8	252.5 ± 26.2	243.3 ± 26.4	227.6 ± 26.0[c]	215.4 ± 5.8
90	269.7 ± 15.5	233.2 ± 6.0	264.1 ± 13.3	235.4 ± 6.5	238.9 ± 11.0	247.7 ± 19.2[b]
Forelimb grip strength (g)						
0	420.0 ± 33.8	430.7 ± 23.5	431.9 ± 23.5	434.3 ± 21.1	444.9 ± 21.4	467.9 ± 20.6
45	726.5 ± 51.7	829.5 ± 62.3	694.9 ± 23.1	752.3 ± 48.7	708.7 ± 47.6	668.0 ± 31.5
90	803.1 ± 51.7	826.9 ± 40.6	805.4 ± 26.2	759.4 ± 39.9	800.8 ± 47.7	740.0 ± 54.8[b]
Hindlimb grip strength (g)						
0	200.3 ± 23.0	187.7 ± 20.1	158.6 ± 11.7	158.4 ± 12.5	194.9 ± 16.8	219.1 ± 20.4
45	378.4 ± 16.5	394.8 ± 24.4	389.3 ± 21.2	368.0 ± 18.6	382.7 ± 12.5	380.4 ± 19.1
90	456.4 ± 9.9	438.0 ± 20.3	493.3 ± 26.7	456.5 ± 22.6	455.3 ± 17.1	448.1 ± 25.8[b]
Undifferentiated motor activity (square root of count/30 min)						
0	14.30 ± 1.26	11.99 ± 0.59	13.14 ± 0.60	11.13 ± 1.02	12.52 ± 0.89	11.90 ± 0.71
45	20.46 ± 0.86	18.60 ± 0.95	20.04 ± 0.91	20.34 ± 1.34	23.13 ± 1.66	19.99 ± 1.22
90	21.08 ± 0.90	18.25 ± 1.00*	18.77 ± 0.51*	19.47 ± 0.37*	18.78 ± 0.78*	17.13 ± 1.21**[b]
Startle magnitude-acoustic stimulus (g)						
0	2.53 ± 0.05	2.57 ± 0.02	2.35 ± 0.09	2.37 ± 0.08	2.37 ± 0.11	2.49 ± 0.04
45	2.76 ± 0.01	2.66 ± 0.05	2.69 ± 0.06	2.71 ± 0.03	2.71 ± 0.05	2.75 ± 0.02
90	2.55 ± 0.06	2.62 ± 0.03	2.55 ± 0.05	2.65 ± 0.03	2.58 ± 0.06	2.69 ± 0.02*[b]
Startle duration-acoustic stimulus (ms)						
0	230.6 ± 18.6	282.3 ± 26.0	206.7 ± 42.3	172.3 ± 28.1	229.1 ± 29.4	250.9 ± 14.7
45	291.6 ± 19.9	258.8 ± 25.2	254.0 ± 24.0	285.0 ± 17.8	291.3 ± 33.0	243.1 ± 25.4
90	231.6 ± 21.8	270.4 ± 31.9	236.2 ± 20.8	256.6 ± 7.2	268.2 ± 14.7	249.6 ± 19.8[b]
Startle magnitude-air puff stimulus (g)						
0	2.20 ± 0.11	2.39 ± 0.08	2.22 ± 0.09	2.26 ± 0.07	2.35 ± 0.06	2.33 ± 0.08
45	2.58 ± 0.06	2.67 ± 0.04	2.65 ± 0.06	2.65 ± 0.06	2.55 ± 0.08	2.67 ± 0.06
90	2.52 ± 0.10	2.65 ± 0.04	2.53 ± 0.07	2.66 ± 0.04	2.65 ± 0.04	2.66 ± 0.02[b]
Startle duration-air puff stimulus (ms)						
0	162.8 ± 30.0	232.8 ± 33.2	152.2 ± 25.8	224.6 ± 43.1	185.9 ± 30.9	179.9 ± 36.7
45	299.7 ± 26.8	302.5 ± 21.3	299.3 ± 19.2	256.8 ± 24.3	283.0 ± 30.1	292.3 ± 25.6
90	252.0 ± 29.5	293.4 ± 20.6	265.9 ± 23.4	282.1 ± 21.0	291.8 ± 23.2	262.9 ± 17.2[b]

TABLE G2
Neurobehavioral and Cardiovascular Data for Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate (continued)

Parameter/Day	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Male (continued)						
n	10	10	10	10	10	10
Cardiovascular Data						
Heart rate (beats/min)						
0	545.0 ± 9.6	533.0 ± 12.5	547.0 ± 12.7	549.0 ± 9.2	543.0 ± 5.8	537.0 ± 10.8
45	508.0 ± 8.4	511.0 ± 6.9	507.0 ± 8.2	493.0 ± 10.2	503.0 ± 5.4	496.0 ± 11.4
91	475.0 ± 8.6	464.0 ± 10.0	453.0 ± 15.1	468.0 ± 11.6	430.0 ± 8.3**	468.3 ± 12.2[c]
Systolic arterial pressure (mm Hg)						
0	130.9 ± 4.2	125.7 ± 5.0	124.5 ± 3.7	130.2 ± 4.3	131.0 ± 2.8	131.2 ± 3.3
45	140.6 ± 5.3	138.5 ± 6.2	128.1 ± 4.0*	143.4 ± 6.0	126.7 ± 3.8*	131.0 ± 3.3*
91	136.1 ± 3.2	126.4 ± 3.5	131.6 ± 2.7	129.4 ± 4.4	126.3 ± 5.4	135.4 ± 7.7[b]
Electrocardiogram-QαT interval (ms)						
0	28.35 ± 0.32	27.60 ± 0.57	29.82 ± 0.75	29.47 ± 0.93	30.66 ± 1.26	29.21 ± 1.18
45	31.14 ± 1.02	31.87 ± 1.80	33.05 ± 1.50	30.20 ± 0.66	31.86 ± 1.01	32.58 ± 0.83
91	33.39 ± 0.99	31.43 ± 0.82	33.39 ± 0.64	32.37 ± 1.14	33.87 ± 1.22	32.37 ± 1.68[b]
Electrocardiogram-QRS complex (ms)						
0	9.82 ± 0.25	10.18 ± 0.22	10.82 ± 0.40	10.16 ± 0.26	10.01 ± 0.34	9.96 ± 0.25
45	9.91 ± 0.42	10.41 ± 0.18	11.47 ± 0.75	10.48 ± 0.30	10.47 ± 0.39	10.84 ± 0.26
91	11.77 ± 0.46	10.74 ± 0.14	12.33 ± 0.83	11.08 ± 0.40	11.91 ± 0.57	14.41 ± 1.68[b]
Female						
Neurobehavioral Data						
Hindlimb foot splay test (mm)						
0	64.60 ± 1.84	61.00 ± 1.98	63.10 ± 2.47	61.50 ± 3.02	59.80 ± 2.99	60.90 ± 1.82
45	72.51 ± 3.79	69.62 ± 2.52	66.93 ± 2.65	76.24 ± 3.66	70.09 ± 3.57	70.25 ± 2.82
90	72.67 ± 3.39	65.70 ± 2.40	69.79 ± 3.01	70.82 ± 3.63	69.52 ± 4.07	65.28 ± 1.75[d]
Tail flick latency test (s)						
0	2.15 ± 0.13	2.16 ± 0.14	2.21 ± 0.09	1.93 ± 0.09	1.96 ± 0.09	2.18 ± 0.12
45	3.27 ± 0.22	3.41 ± 0.26	3.18 ± 0.18	3.49 ± 0.19	3.24 ± 0.16	3.29 ± 0.19
90	2.64 ± 0.19	2.69 ± 0.24	2.70 ± 0.22	2.56 ± 0.14	2.65 ± 0.20	2.39 ± 0.18[d]
Startle response latency (ms)						
0	260.5 ± 23.9	294.8 ± 23.4	249.5 ± 12.4	237.2 ± 10.4	257.2 ± 15.1	254.7 ± 26.9
45	263.4 ± 13.8	235.7 ± 8.7	283.6 ± 35.7	250.8 ± 30.1	261.1 ± 18.0	256.9 ± 12.1
90	243.4 ± 12.4	262.9 ± 15.4	255.1 ± 13.5	237.4 ± 9.1	272.2 ± 19.9	243.6 ± 12.2[d]
Forelimb grip strength (g)						
0	398.4 ± 25.9	407.7 ± 21.7	433.7 ± 32.1	404.3 ± 23.0	409.6 ± 19.8	396.0 ± 24.9
45	638.9 ± 25.3	612.6 ± 30.0	677.4 ± 32.1	612.3 ± 25.0	624.6 ± 23.9	655.1 ± 43.8
90	691.0 ± 33.5	655.3 ± 31.4	679.2 ± 36.9	637.8 ± 22.9	677.3 ± 30.8	618.9 ± 39.7[d]
Hindlimb grip strength (g)						
0	145.7 ± 11.0	154.6 ± 16.3	149.0 ± 14.2	184.6 ± 24.4	153.1 ± 11.6	165.8 ± 17.6
45	277.2 ± 14.4	264.6 ± 16.4	294.6 ± 15.4	298.3 ± 16.9	297.7 ± 11.2	285.0 ± 15.3
90	324.7 ± 14.9	319.3 ± 15.8	327.8 ± 15.0	339.8 ± 20.7	320.3 ± 19.3	319.8 ± 13.5[d]
Undifferentiated motor activity (square root of count/30 min)						
0	14.13 ± 0.76	13.38 ± 1.08	12.09 ± 0.80	12.19 ± 0.81	12.74 ± 0.72	10.78 ± 0.95*
45	25.66 ± 1.33	22.36 ± 1.26	23.40 ± 1.49	22.30 ± 1.06	22.81 ± 1.41	21.69 ± 1.55
90	24.44 ± 1.16	20.42 ± 1.03*	20.87 ± 0.88*	22.79 ± 1.42	19.84 ± 1.08*	16.88 ± 2.10**[d]

TABLE G2
Neurobehavioral and Cardiovascular Data for Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate (continued)

Parameter/Day	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Female (continued)						
n	10	10	10	10	10	10
Neurobehavioral Data (continued)						
Startle magnitude-acoustic stimulus (g)						
0	2.38 ± 0.04	2.24 ± 0.07	2.41 ± 0.11	2.32 ± 0.05	2.32 ± 0.10	2.22 ± 0.11
45	2.52 ± 0.10	2.38 ± 0.13	2.49 ± 0.06	2.45 ± 0.11	2.53 ± 0.08	2.47 ± 0.08
90	2.47 ± 0.07	2.40 ± 0.11	2.38 ± 0.10	2.51 ± 0.08	2.31 ± 0.11	2.47 ± 0.06[d]
Startle duration-acoustic stimulus (ms)						
0	249.3 ± 12.2	205.5 ± 24.1	199.6 ± 22.0	206.1 ± 22.1	188.0 ± 23.4	156.0 ± 26.1**
45	216.9 ± 28.5	180.4 ± 33.7	229.9 ± 21.1	190.7 ± 35.4	214.5 ± 27.2	207.6 ± 21.5
90	191.0 ± 28.2	201.2 ± 29.3	188.3 ± 28.9	228.8 ± 26.3	165.2 ± 24.7	244.7 ± 12.4[d]
Startle magnitude-air puff stimulus (g)						
0	2.24 ± 0.05	2.15 ± 0.08	2.18 ± 0.09	2.15 ± 0.09	2.25 ± 0.10	2.13 ± 0.08
45	2.42 ± 0.10	2.41 ± 0.11	2.41 ± 0.13	2.43 ± 0.08	2.41 ± 0.10	2.41 ± 0.09
90	2.38 ± 0.08	2.28 ± 0.09	2.19 ± 0.12	2.21 ± 0.06	2.27 ± 0.10	2.15 ± 0.11[d]
Startle duration-air puff stimulus (ms)						
0	183.6 ± 40.4	203.4 ± 35.3	147.7 ± 31.4	134.1 ± 35.8	167.2 ± 41.1	152.1 ± 34.6
45	248.5 ± 37.5	286.5 ± 37.1	231.9 ± 30.9	246.3 ± 35.1	234.3 ± 29.5	216.9 ± 25.5
90	247.8 ± 38.3	240.7 ± 36.8	190.6 ± 38.3	209.9 ± 25.8	183.6 ± 34.1[d]	180.2 ± 31.6[d]
Cardiovascular Data						
Heart rate (beats/min)						
0	554.0 ± 11.4	547.0 ± 7.3	548.0 ± 8.9	549.0 ± 6.4	550.0 ± 10.7	551.0 ± 5.5
45	498.0 ± 8.0	498.0 ± 8.5	492.0 ± 9.0	496.0 ± 6.9	493.0 ± 7.9	494.0 ± 5.4
91	485.0 ± 9.7	475.0 ± 12.1	494.0 ± 8.2	488.0 ± 9.9	490.0 ± 6.7	481.3 ± 6.1[e]
Systolic arterial pressure (mm Hg)						
0	127.8 ± 6.9	120.3 ± 4.7	126.9 ± 2.6	129.4 ± 6.3	125.4 ± 4.4	106.8 ± 4.9*
45	116.2 ± 4.5	119.7 ± 2.6	123.3 ± 4.6	117.7 ± 3.6	111.6 ± 3.7	121.1 ± 4.5
91	116.8 ± 2.9	118.0 ± 3.7	118.2 ± 5.1	113.6 ± 3.7	116.9 ± 4.1	121.6 ± 6.0[d]
Electrocardiogram-QαT (ms)						
0	27.55 ± 0.34	28.88 ± 0.60	29.00 ± 0.57	29.53 ± 0.61*	30.60 ± 0.64**	29.92 ± 0.73**
45	31.30 ± 0.42	32.70 ± 0.88	33.12 ± 0.86	32.23 ± 0.72	33.83 ± 1.18	35.00 ± 0.98**
91	31.77 ± 0.50	31.27 ± 0.42	33.70 ± 1.26*	33.44 ± 0.91	34.81 ± 1.24*	36.72 ± 3.65[d]
Electrogram-QRS complex (ms)						
0	9.82 ± 0.22	9.62 ± 0.25	10.87 ± 0.32	10.07 ± 0.27	10.20 ± 0.33	10.77 ± 0.97
45	10.30 ± 0.55	10.35 ± 0.40	11.17 ± 0.41	10.13 ± 0.36	10.96 ± 0.79	10.71 ± 0.29
91	10.89 ± 0.60	10.41 ± 0.19	11.33 ± 0.27	10.45 ± 0.25	11.16 ± 0.46	12.87 ± 0.99[d]

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error
[b] n=7
[c] n=6
[d] n=9
[e] n=8

TABLE G3
Neurobehavioral Data for Mice in the 15-Day Drinking Water Study of Barium Chloride Dihydrate[a]

Parameter/Day	0 ppm	40 ppm	80 ppm	173 ppm	346 ppm	692 ppm
Male						
n	5	5	5	5	5	5
Hindlimb foot splay test (mm)						
0	46.88 ± 1.60	49.26 ± 3.11	50.60 ± 1.52	46.38 ± 1.68	45.32 ± 1.68	45.34 ± 1.34
14	51.80 ± 1.16	51.80 ± 3.20	50.40 ± 2.14	50.40 ± 2.04	52.40 ± 1.25	52.00 ± 2.17
Tail flick latency test (s)						
0	0.640 ± 0.081	0.680 ± 0.058	0.620 ± 0.058	0.700 ± 0.055	0.680 ± 0.049	0.600 ± 0.071
14	0.680 ± 0.086	0.580 ± 0.086	0.680 ± 0.058	0.600 ± 0.063	0.660 ± 0.051	0.540 ± 0.068
Startle response latency (ms)						
0	202.8 ± 14.5	191.4 ± 2.2	198.6 ± 9.4	175.8 ± 22.0	180.2 ± 10.9	190.2 ± 27.2
14	184.4 ± 5.0	192.6 ± 13.6	180.8 ± 7.4[b]	188.8 ± 6.9	180.4 ± 6.0	197.0 ± 8.5
Forelimb grip strength (g)						
0	90.00 ± 4.34	78.00 ± 12.84	88.66 ± 8.34	86.68 ± 2.78	88.00 ± 11.76	97.34 ± 6.45
14	97.40 ± 9.83	91.60 ± 7.15	92.00 ± 7.54	95.40 ± 5.02	94.80 ± 11.58	104.00 ± 7.47
Hindlimb grip strength (g)						
0	58.68 ± 2.27	50.64 ± 2.66	53.32 ± 2.78	58.66 ± 1.70	59.30 ± 2.45	62.00 ± 4.77
14	60.60 ± 6.49	67.20 ± 9.05	62.60 ± 3.83	56.60 ± 4.06	65.40 ± 4.70	55.20 ± 3.47
Undifferentiated motor activity (square root of count/30 min)						
0	11.84 ± 2.65	14.56 ± 3.35	15.06 ± 3.52	10.32 ± 1.95	13.56 ± 3.27	14.70 ± 2.97
14	9.00 ± 1.30	10.20 ± 0.66	10.60 ± 1.17	9.80 ± 1.69	10.40 ± 0.93	11.40 ± 1.21
Startle magnitude-acoustic stimulus (g)						
0	22.80 ± 8.74	26.00 ± 6.54	29.40 ± 9.31	32.60 ± 6.74	48.40 ± 11.83	28.40 ± 9.55
14	39.80 ± 14.16	52.80 ± 21.55	53.00 ± 6.76[b]	43.00 ± 10.79	47.00 ± 15.02	24.80 ± 8.36
Startle duration-acoustic stimulus (ms)						
0	36.20 ± 5.21	39.00 ± 8.56	41.20 ± 9.61	47.00 ± 4.59	45.40 ± 10.60	31.20 ± 8.45
14	44.80 ± 10.16	51.80 ± 10.11	81.25 ± 28.06[b]	63.80 ± 19.93	55.40 ± 8.78	40.80 ± 4.62
Startle magnitude-air puff stimulus (g)						
0	34.00 ± 16.68[b]	19.80 ± 10.28	41.50 ± 20.75[b]	30.00 ± 14.01[b]	18.25 ± 10.14[b]	53.75 ± 15.61[b]
14	46.40 ± 12.82	42.80 ± 10.25	20.25 ± 2.95[b]	38.20 ± 9.46	53.75 ± 13.41[b]	31.00 ± 12.73[b]
Startle duration-air puff stimulus (ms)						
0	36.25 ± 13.20[b]	47.60 ± 7.67	43.00 ± 14.30[b]	41.50 ± 13.50[b]	43.00 ± 10.26[b]	59.00 ± 13.10[b]
14	49.60 ± 7.43	60.20 ± 8.23	53.00 ± 12.42[b]	66.80 ± 14.87	63.50 ± 8.37[b]	37.50 ± 5.20[b]

TABLE G3
Neurobehavioral Data for Mice in the 15-Day Drinking Water Study of Barium Chloride Dihydrate
(continued)

Parameter/Day	0 ppm	40 ppm	80 ppm	173 ppm	346 ppm	692 ppm
Female						
n	5	5	5	5	5	5
Hindlimb foot splay test (mm)						
0	43.06 ± 1.74	46.10 ± 2.52	49.60 ± 3.21	43.42 ± 2.44	44.06 ± 1.69	46.74 ± 1.49
14	51.00 ± 2.66	49.80 ± 2.92	53.00 ± 1.05	51.80 ± 2.22	56.00 ± 3.36	49.00 ± 1.67
Tail flick latency test (s)						
0	0.640 ± 0.098	0.660 ± 0.140	0.680 ± 0.092	0.660 ± 0.093	0.660 ± 0.068	0.580 ± 0.066
14	0.660 ± 0.169	0.580 ± 0.086	0.560 ± 0.051	0.500 ± 0.045	0.580 ± 0.086	0.500 ± 0.032
Startle response latency (ms)						
0	192.8 ± 10.1[b]	175.0 ± 8.9[b]	196.3 ± 9.7[b]	191.5 ± 10.9[b]	189.5 ± 5.4[b]	197.7 ± 9.4[c]
14	192.0 ± 5.1	181.3 ± 8.5[b]	197.4 ± 18.3	196.2 ± 4.8	197.3 ± 7.4[b]	210.6 ± 14.5
Forelimb grip strength (g)						
0	87.34 ± 10.08	81.34 ± 3.10	91.32 ± 7.21	82.64 ± 7.10	90.66 ± 6.80	70.66 ± 8.33
14	85.20 ± 5.00	93.40 ± 8.09	92.60 ± 6.21	78.60 ± 7.54	88.80 ± 8.57	93.20 ± 5.51
Hindlimb grip strength (g)						
0	48.68 ± 3.43	56.66 ± 3.15	54.66 ± 1.70	46.66 ± 1.50	60.68 ± 4.51	47.34 ± 1.25
14	57.80 ± 2.67	54.00 ± 4.34	63.20 ± 7.70	54.00 ± 6.69	57.20 ± 4.88	48.80 ± 3.25
Undifferentiated motor activity (square root of count/30 min)						
0	15.84 ± 3.00	14.00 ± 3.19	15.24 ± 2.74	12.56 ± 3.19	15.02 ± 3.16	14.80 ± 2.25
14	11.80 ± 1.77	11.60 ± 0.87	12.80 ± 1.24	10.80 ± 0.58	12.40 ± 0.75	13.40 ± 1.33
Startle magnitude-acoustic stimulus (g)						
0	26.00 ± 8.28[b]	31.25 ± 10.83[b]	18.50 ± 10.88[b]	29.50 ± 13.00[b]	35.25 ± 9.53[b]	22.33 ± 13.22[c]
14	28.40 ± 8.71	31.25 ± 7.75[b]	44.20 ± 15.53	23.80 ± 3.09	32.25 ± 7.12[b]	32.00 ± 5.86
Startle duration-acoustic stimulus (ms)						
0	33.50 ± 9.95[b]	43.50 ± 10.69[b]	36.50 ± 13.36[b]	39.00 ± 12.21[b]	48.25 ± 7.25[b]	32.33 ± 14.25[c]
14	38.40 ± 6.35	50.75 ± 4.82[b]	58.80 ± 5.88	45.80 ± 3.02	38.50 ± 6.66[b]	40.25 ± 5.44[b]
Startle magnitude-air puff stimulus (g)						
0	21.67 ± 11.17[c]	12.00 ± 3.00[d]	18.00 ± 2.52[c]	13.25 ± 3.50[b]	9.00[e]	4.00[e]
14	68.00 ± 12.00[d]	24.25 ± 7.30[b]	25.50 ± 10.19*[b]	27.67 ± 10.17[c]	41.00 ± 6.00[d]	24.00 ± 8.00[d]
Startle duration-air puff stimulus (ms)						
0	38.50 ± 17.50[d]	33.67 ± 3.53[c]	45.33 ± 5.17[c]	25.75 ± 8.94[b]	24.00[e]	9.00[e]
14	62.00 ± 3.00[d]	45.50 ± 8.51[b]	44.75 ± 6.01[b]	51.67 ± 11.67[c]	58.50 ± 7.50[d]	52.67 ± 9.33[c]

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
[a] Mean ± standard error
[b] n=4
[c] n=3
[d] n=2
[e] n=1; no standard error calculated

TABLE G4
Neurobehavioral Data for Mice in the 13-Week Drinking Water Study of Barium Chloride Dihydrate[a]

Parameter/Day	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Male						
n	10	10	10	10	10	10
Hindlimb foot splay test (mm)						
0	54.40 ± 1.76	52.40 ± 1.92	53.80 ± 1.32	51.10 ± 1.20	52.30 ± 0.91	51.90 ± 1.68
45	54.37 ± 1.36	53.47 ± 1.03	54.09 ± 1.27	52.68 ± 1.04	54.54 ± 0.99	52.91 ± 1.79[b]
90	54.90 ± 1.29	57.26 ± 1.31[c]	54.06 ± 0.99	52.96 ± 0.78	53.02 ± 1.42	57.60 ± 2.17[d]
Tail flick latency test (s)						
0	0.600 ± 0.033	0.650 ± 0.017	0.640 ± 0.031	0.670 ± 0.042	0.630 ± 0.045	0.660 ± 0.043
45	0.590 ± 0.038	0.590 ± 0.041	0.590 ± 0.050	0.540 ± 0.034	0.610 ± 0.041	0.500 ± 0.033[b]
90	0.480 ± 0.042	0.511 ± 0.026[c]	0.480 ± 0.039	0.430 ± 0.021	0.510 ± 0.023	0.550 ± 0.087[d]
Startle response latency (ms)						
0	168.3 ± 12.5[e]	147.8 ± 15.0[c]	163.0 ± 10.8	170.2 ± 9.3[c]	159.2 ± 11.9[c]	172.2 ± 7.9[c]
45	168.9 ± 9.1	187.3 ± 4.1[b]	181.6 ± 8.2[f]	178.4 ± 8.3[b]	174.7 ± 9.6[c]	188.2 ± 12.7[g]
90	189.8 ± 3.7	207.4 ± 8.6[e]	199.1 ± 4.5[c]	198.4 ± 2.1[e]	191.1 ± 3.3[b]	189.0[h]
Forelimb grip strength (g)						
0	73.30 ± 5.94	73.20 ± 3.68	68.00 ± 3.55	79.00 ± 4.73	68.60 ± 5.46	69.90 ± 3.24
45	94.50 ± 6.68	100.30 ± 5.33	96.70 ± 4.09	99.10 ± 4.47	103.10 ± 7.74	76.50 ± 8.65[b]
90	109.30 ± 5.90	112.78 ± 7.03[c]	104.60 ± 6.46	99.50 ± 6.92	101.30 ± 3.33	85.75 ± 14.93[d]
Hindlimb grip strength (g)						
0	46.00 ± 3.63	51.00 ± 5.05	46.00 ± 3.78	51.00 ± 6.55	47.10 ± 2.58	41.90 ± 2.25
45	55.10 ± 5.31	51.70 ± 3.76	45.10 ± 1.29	51.50 ± 3.99	58.30 ± 5.59	45.25 ± 4.35[b]
90	73.50 ± 5.86	81.89 ± 6.51[c]	69.30 ± 4.95	70.40 ± 4.85	77.90 ± 3.93	63.50 ± 8.35[d]
Undifferentiated motor activity (square root of count/30 min)						
0	10.07 ± 0.87	9.17 ± 1.18	7.46 ± 1.34	8.96 ± 1.23	9.19 ± 1.00	8.18 ± 0.72
45	9.21 ± 0.96	6.46 ± 0.81*	7.27 ± 0.70	6.91 ± 0.44	6.67 ± 0.53	6.31 ± 0.81*[b]
90	8.83 ± 0.60	6.56 ± 0.66[c]	8.67 ± 0.74	5.83 ± 0.60*	7.78 ± 0.89	9.85 ± 1.15[d]
Startle magnitude-acoustic stimulus (g)						
0	1.64 ± 0.08[e]	1.76 ± 0.08[c]	1.71 ± 0.09	1.54 ± 0.05[c]	1.67 ± 0.07[c]	1.76 ± 0.08[c]
45	1.62 ± 0.09	1.56 ± 0.06[b]	1.60 ± 0.14[g]	1.66 ± 0.08[b]	1.62 ± 0.08[c]	1.60 ± 0.06[g]
90	1.75 ± 0.07	1.73 ± 0.12[e]	1.60 ± 0.05[c]	1.77 ± 0.14[e]	1.80 ± 0.07[b]	1.68 ± 0.26[i]
Startle duration-acoustic stimulus (ms)						
0	61.14 ± 8.06[e]	72.00 ± 10.41[c]	55.40 ± 7.92	47.11 ± 6.43[c]	39.33 ± 7.93[c]	56.56 ± 9.37[c]
45	47.30 ± 4.14	43.38 ± 3.29[b]	44.00 ± 5.40[g]	43.63 ± 3.79[b]	42.11 ± 4.74[c]	36.67 ± 7.43[g]
90	53.40 ± 3.72	46.86 ± 5.49[e]	48.89 ± 3.77[c]	54.00 ± 7.01[e]	51.50 ± 2.63[b]	60.67 ± 3.18[i]
Startle magnitude-air puff stimulus (g)						
0	1.80 ± 0.09[e]	1.64 ± 0.09[b]	1.61 ± 0.10	1.58 ± 0.04[f]	1.83 ± 0.10[c]	1.68 ± 0.10[e]
45	1.55 ± 0.10[f]	1.52 ± 0.13[f]	1.40 ± 0.08[f]	1.53 ± 0.07[e]	1.55 ± 0.09[e]	1.51 ± 0.08[f]
90	1.80 ± 0.09[c]	1.72 ± 0.09[b]	1.81 ± 0.10	1.92 ± 0.11[b]	1.95 ± 0.07[c]	1.58 ± 0.17[i]
Startle duration-air puff stimulus (ms)						
0	72.00 ± 10.78[e]	62.38 ± 13.36[b]	58.10 ± 6.40	49.71 ± 5.34[e]	67.67 ± 7.09[c]	67.00 ± 12.59[e]
45	44.20 ± 3.93[f]	46.40 ± 8.59[f]	45.20 ± 8.92[f]	55.71 ± 5.01[e]	39.14 ± 3.64[e]	39.40 ± 10.02[f]
90	83.44 ± 18.71[c]	58.25 ± 9.70[b]	69.00 ± 9.38	84.38 ± 9.41[b]	70.78 ± 7.70[c]	65.00 ± 2.65[i]

TABLE G4
Neurobehavioral Data for Mice in the 13-Week Drinking Water Study of Barium Chloride Dihydrate
(continued)

Parameter/Day	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Female						
n	10	10	10	10	10	10
Hindlimb foot splay test (mm)						
0	50.80 ± 1.68	53.10 ± 1.54	52.10 ± 1.42	50.40 ± 1.42	53.50 ± 1.28	52.00 ± 1.45
45	51.33 ± 1.39	53.41 ± 1.45	50.20 ± 1.17	55.50 ± 1.44	49.80 ± 1.13	53.00 ± 0.99
90	52.32 ± 1.61	53.81 ± 1.32	51.67 ± 1.81	55.25 ± 1.20	54.58 ± 1.20	51.38 ± 2.93[d]
Tail flick latency test (s)						
0	0.630 ± 0.033	0.600 ± 0.026	0.560 ± 0.037	0.550 ± 0.027	0.530 ± 0.015*	0.560 ± 0.037
45	0.520 ± 0.039	0.510 ± 0.028	0.500 ± 0.015	0.520 ± 0.033	0.480 ± 0.025	0.480 ± 0.013
90	0.410 ± 0.031	0.460 ± 0.022	0.430 ± 0.015	0.420 ± 0.025	0.450 ± 0.027	0.550 ± 0.065[d]
Startle response latency (ms)						
0	158.1 ± 13.8	179.9 ± 4.6[b]	165.1 ± 11.5[c]	171.6 ± 9.5[c]	168.9 ± 9.0[b]	163.6 ± 9.2[c]
45	152.4 ± 19.9[f]	195.0 ± 4.1[d]	175.4 ± 21.9[f]	144.5 ± 18.2[d]	157.0 ± 33.6[i]	172.5 ± 11.7[g]
90	197.4 ± 5.7[b]	189.2 ± 3.2[f]	195.2 ± 5.4[g]	199.3 ± 1.8[b]	191.0 ± 2.9[f]	216.0[h]
Forelimb grip strength (g)						
0	61.60 ± 3.13	59.40 ± 4.61	60.60 ± 4.63	54.50 ± 3.08	59.40 ± 3.89	58.40 ± 4.82
45	98.00 ± 5.04	88.00 ± 6.39	78.20 ± 4.29*	91.60 ± 3.42	87.80 ± 5.98	89.10 ± 4.55
90	99.30 ± 3.67	108.20 ± 5.48	97.90 ± 3.63	96.40 ± 6.22	101.60 ± 6.49	53.00 ± 8.90**[d]
Hindlimb grip strength (g)						
0	41.40 ± 2.77	38.90 ± 2.66	37.50 ± 2.09	38.90 ± 3.42	42.50 ± 2.92	36.10 ± 1.84
45	43.00 ± 3.18	48.90 ± 2.71	42.90 ± 2.14	47.40 ± 4.28	49.10 ± 4.90	45.80 ± 2.14
90	61.90 ± 3.36	73.90 ± 7.89	70.40 ± 4.26	65.90 ± 4.67	69.90 ± 6.20	32.50 ± 7.60[d]
Undifferentiated motor activity (square root of count/30 min)						
0	9.00 ± 0.84	12.20 ± 0.98	10.57 ± 1.11	8.60 ± 1.29	8.10 ± 1.12	7.97 ± 1.13
45	11.27 ± 0.69	14.54 ± 1.70	12.49 ± 0.96	10.73 ± 0.79	12.80 ± 1.06	9.12 ± 0.70
90	11.91 ± 1.19	12.66 ± 1.28	11.91 ± 0.99	11.61 ± 0.88	13.88 ± 1.28	6.28 ± 3.27[d]
Startle magnitude-acoustic stimulus (g)						
0	1.52 ± 0.05	1.55 ± 0.03[c]	1.57 ± 0.05[c]	1.65 ± 0.06[c]	1.60 ± 0.07[b]	1.59 ± 0.06[c]
45	1.49 ± 0.03[f]	1.46 ± 0.06[d]	1.48 ± 0.03[f]	1.57 ± 0.05[d]	1.55 ± 0.22[i]	1.41 ± 0.04[g]
90	1.60 ± 0.06[b]	1.88 ± 0.06[f]	1.62 ± 0.05[g]	1.57 ± 0.04[b]	1.66 ± 0.09[e]	1.54[h]
Startle duration-acoustic stimulus (ms)						
0	49.00 ± 8.53	49.56 ± 13.24[c]	44.67 ± 6.48[c]	57.78 ± 11.88[c]	56.50 ± 6.42[b]	42.44 ± 4.32[c]
45	27.20 ± 3.53[f]	36.50 ± 8.54[d]	33.20 ± 3.31[f]	38.25 ± 7.22[d]	39.33 ± 10.17[i]	35.17 ± 3.79[g]
90	49.75 ± 5.28[b]	54.20 ± 3.61[f]	51.83 ± 4.89[g]	42.38 ± 2.63[b]	52.86 ± 2.58[e]	44.00[h]
Startle magnitude-air puff stimulus (g)						
0	1.60 ± 0.06[b]	1.51 ± 0.07[b]	1.51 ± 0.06[b]	1.62 ± 0.07[e]	1.59 ± 0.09[f]	1.54 ± 0.03[b]
45	1.37 ± 0.06[d]	1.43 ± 0.13[j]	1.51 ± 0.07[i]	1.47 ± 0.05[i]	1.62 ± 0.27[j]	1.43 ± 0.09[i]
90	1.63 ± 0.06[g]	1.70 ± 0.07[e]	1.41 ± 0.05[g]	1.59 ± 0.07[g]	1.77 ± 0.15[f]	1.77[h]
Startle duration-air puff stimulus (ms)						
0	49.13 ± 8.42[b]	62.25 ± 11.58[b]	43.00 ± 7.98[b]	62.57 ± 16.75[e]	48.00 ± 8.99[f]	59.00 ± 3.13[b]
45	34.75 ± 4.85[d]	36.00 ± 3.00[j]	35.00 ± 4.36[i]	50.00 ± 6.24[i]	47.00 ± 22.00[j]	38.67 ± 6.39[i]
90	53.00 ± 5.12[g]	65.14 ± 5.20[e]	49.00 ± 4.84[g]	53.33 ± 6.25[g]	68.60 ± 12.46[f]	48.00 ± 0.00[h]

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error
[b] n=8 [c] n=9
[d] n=4 [e] n=7
[f] n=5 [g] n=6
[h] n=1; no standard error was calculated due to high mortality in this group
[i] n=3 [j] n=2

APPENDIX H
HEMATOLOGY AND CLINICAL CHEMISTRY RESULTS

TABLE H1
Hematology and Clinical Chemistry Data for Rats in the 15-Day Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	125 ppm	250 ppm	500 ppm	1,000 ppm	2,000 ppm
Male						
n	5	4	5	5	5	5
Hematology						
Hematocrit (%)	39.2 ± 1.0	38.2 ± 0.6	38.1 ± 0.9	38.3 ± 0.7	36.0 ± 1.5	41.4 ± 4.4
Hemoglobin (g/dL)	14.4 ± 0.4	14.4 ± 0.2	14.2 ± 0.4	14.3 ± 0.3	13.4 ± 0.6	15.6 ± 1.6
Erythrocytes ($10^6/\mu L$)	7.19 ± 0.18	7.18 ± 0.11	7.09 ± 0.15	7.18 ± 0.14	6.67 ± 0.29	7.66 ± 0.76
Mean cell volume (fL)	54.6 ± 0.4	53.5 ± 0.3	54.0 ± 0.5	53.6 ± 0.2	54.2 ± 0.4	54.2 ± 0.2
Mean cell hemoglobin (pg)	20.0 ± 0.0	20.0 ± 0.0	20.2 ± 0.2	20.0 ± 0.3	20.2 ± 0.2	20.6 ± 0.2*
Mean cell hemoglobin concentration (g/dL)	36.8 ± 0.2	37.5 ± 0.5	37.4 ± 0.5	37.2 ± 0.2	37.4 ± 0.2	37.8 ± 0.5
Platelets ($10^3/\mu L$)	565.4 ± 26.6	616.3 ± 40.6	654.8 ± 37.8	630.0 ± 35.9	627.6 ± 45.8	548.6 ± 50.9
Leukocytes ($10^3/\mu L$)	4.83 ± 0.69[b]	6.10 ± 0.81	5.30 ± 0.32	4.82 ± 0.38	4.55 ± 0.28[b]	6.94 ± 0.95
Segmented neutrophils ($10^3/\mu L$)	0.32 ± 0.05[b]	0.61 ± 0.16	0.44 ± 0.03	0.34 ± 0.05	0.56 ± 0.13[b]	0.62 ± 0.24[b]
Lymphocytes ($10^3/\mu L$)	4.32 ± 0.64[b]	5.33 ± 0.74	4.74 ± 0.28	4.32 ± 0.32	3.83 ± 0.20[b]	5.78 ± 0.75[b]
Atypical lymphocytes ($10^3/\mu L$)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00[b]	0.00 ± 0.00[b]
Monocytes ($10^3/\mu L$)	0.14 ± 0.06[b]	0.09 ± 0.03	0.07 ± 0.03	0.10 ± 0.02	0.09 ± 0.06[b]	0.18 ± 0.13[b]
Eosinophils ($10^3/\mu L$)	0.01 ± 0.01[b]	0.03 ± 0.01	0.04 ± 0.01	0.03 ± 0.01	0.06 ± 0.05[b]	0.09 ± 0.04*[b]
Nucleated erythrocytes ($10^3/\mu L$)	0.01 ± 0.01[b]	0.00 ± 0.00	0.02 ± 0.01	0.02 ± 0.01	0.02 ± 0.01[b]	0.04 ± 0.02[b]
n	5	5	5	5	5	4
Clinical Chemistry						
Barium (mg/dL)	0.11 ± 0.03[b]	0.32 ± 0.14	0.24 ± 0.02[b]	0.20 ± 0.03	0.24 ± 0.08[b]	0.42 ± 0.04**
Sodium (mEq/L)	143 ± 1	144 ± 1	145 ± 1	146 ± 1	147 ± 1	143 ± 1
Potassium (mEq/L)	5.4 ± 0.5	5.1 ± 0.4	4.8 ± 0.2	4.8 ± 0.2	5.2 ± 0.2	4.3 ± 0.1**
Calcium (mg/dL)	10.64 ± 0.19	10.68 ± 0.19	10.70 ± 0.09	10.42 ± 0.15	10.48 ± 0.06	10.33 ± 0.11
Phosphorus (mg/dL)	7.9 ± 0.5	7.9 ± 0.3	7.5 ± 0.3	6.7 ± 0.4	7.0 ± 0.2	6.9 ± 0.3

TABLE H1
Hematology and Clinical Chemistry Data for Rats in the 15-Day Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	125 ppm	250 ppm	500 ppm	1,000 ppm	2,000 ppm
Female						
n	5	5	5	5	5	4
Hematology						
Hematocrit (%)	40.5 ± 0.8	39.5 ± 0.9	37.6 ± 1.3	36.6 ± 1.0*	37.8 ± 1.4*	38.6 ± 1.2
Hemoglobin (g/dL)	14.8 ± 0.3	14.6 ± 0.3	14.1 ± 0.5	13.5 ± 0.4*	13.8 ± 0.6	14.3 ± 0.4
Erythrocytes ($10^6/\mu L$)	7.19 ± 0.21	7.13 ± 0.19	6.80 ± 0.24	6.57 ± 0.16	6.60 ± 0.26	6.90 ± 0.28
Mean cell volume (fL)	56.4 ± 0.7	55.6 ± 0.4	55.4 ± 0.2	55.8 ± 0.2	57.4 ± 0.4	57.0 ± 0.6
Mean cell hemoglobin (pg)	20.6 ± 0.2	20.6 ± 0.2	20.6 ± 0.2	20.4 ± 0.2	20.8 ± 0.2	20.5 ± 0.3
Mean cell hemoglobin concentration (g/dL)	36.6 ± 0.2	37.2 ± 0.2	37.4 ± 0.2	36.8 ± 0.2	36.4 ± 0.4	37.0 ± 0.4
Platelets ($10^3/\mu L$)	496.2 ± 33.1	626.8 ± 32.0	514.4 ± 79.1	409.6 ± 96.0	512.2 ± 42.9	559.3 ± 54.3
Leukocytes ($10^3/\mu L$)	5.42 ± 0.98	5.64 ± 0.49	6.33 ± 0.50[b]	4.68 ± 0.69	6.97 ± 1.44[c]	5.05 ± 0.57
Segmented neutrophils ($10^3/\mu L$)	0.33 ± 0.08	0.38 ± 0.05	0.34 ± 0.04[b]	0.43 ± 0.21	0.56 ± 0.13[c]	0.25 ± 0.03
Lymphocytes ($10^3/\mu L$)	4.86 ± 0.81	5.19 ± 0.45	5.87 ± 0.46[b]	4.12 ± 0.48	6.22 ± 1.29[c]	4.68 ± 0.59
Atypical lymphocytes ($10^3/\mu L$)	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00[b]	0.00 ± 0.00	0.00 ± 0.00[c]	0.00 ± 0.00
Monocytes ($10^3/\mu L$)	0.16 ± 0.10	0.06 ± 0.02	0.09 ± 0.03[b]	0.09 ± 0.02	0.06 ± 0.02[c]	0.07 ± 0.01
Eosinophils ($10^3/\mu L$)	0.06 ± 0.05	0.01 ± 0.01	0.03 ± 0.02[b]	0.04 ± 0.03	0.05 ± 0.04[c]	0.04 ± 0.01
Nucleated erythrocytes ($10^3/\mu L$)	0.01 ± 0.01	0.01 ± 0.01	0.03 ± 0.03[b]	0.03 ± 0.02	0.03 ± 0.02[c]	0.02 ± 0.01
n	5	5	5	5	5	5
Clinical Chemistry						
Barium (mg/dL)	0.18 ± 0.07[c]	0.14 ± 0.05[b]	0.27 ± 0.07[c]	0.19 ± 0.06[b]	0.10 ± 0.03[c]	0.40 ± 0.08
Sodium (mEq/L)	143 ± 1	143 ± 1	144 ± 1	148 ± 2	144 ± 1	142 ± 1
Potassium (mEq/L)	5.1 ± 0.4	4.7 ± 0.1	5.1 ± 0.1	4.7 ± 0.3	4.7 ± 0.2	4.7 ± 0.4
Calcium (mg/dL)	10.38 ± 0.13	10.22 ± 0.27	10.54 ± 0.11	10.44 ± 0.14	10.14 ± 0.09	9.80 ± 0.43
Phosphorus (mg/dL)	6.7 ± 0.3	6.6 ± 0.4	7.1 ± 0.4	6.8 ± 0.6	6.0 ± 0.5	5.7 ± 0.3

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error
[b] n=4
[c] n=3

TABLE H2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Male						
n	10	10	9	10	8	7
Hematology						
Hematocrit (%)	41.3 ± 0.4	42.4 ± 0.4	42.4 ± 0.3	41.6 ± 0.3	41.7 ± 0.6	40.8 ± 1.8
Hemoglobin (g/dL)	15.2 ± 0.1	15.6 ± 0.2	15.3 ± 0.2	15.4 ± 0.1	15.3 ± 0.1	14.6 ± 0.7
Erythrocytes ($10^6/\mu L$)	8.33 ± 0.09	8.51 ± 0.10	8.51 ± 0.09	8.46 ± 0.07	8.27 ± 0.16	8.06 ± 0.36
Mean cell volume (fL)	49.0 ± 0.2	49.2 ± 0.3	49.2 ± 0.5	48.6 ± 0.3	49.0 ± 0.3	50.0 ± 0.5
Mean cell hemoglobin (pg)	18.0 ± 0.0	18.4 ± 0.2	17.9 ± 0.3	18.1 ± 0.1	18.4 ± 0.4	18.0 ± 0.2
Mean cell hemoglobin concentration (g/dL)	36.9 ± 0.2	36.7 ± 0.3	36.0 ± 0.5	37.0 ± 0.3	36.8 ± 0.3	35.4 ± 0.5
Platelets ($10^3/\mu L$)	498.2 ± 26.1	543.2 ± 22.4	510.6 ± 19.2	548.1 ± 16.2[b]	514.4 ± 26.6	503.1 ± 24.6
Leukocytes ($10^3/\mu L$)	5.68 ± 0.48	5.39 ± 0.18[c]	6.76 ± 0.28[c]	6.33 ± 0.30	6.53 ± 0.56	6.99 ± 0.81
Segmented neutrophils ($10^3/\mu L$)	0.43 ± 0.06	0.48 ± 0.05[c]	0.65 ± 0.05[d]	0.53 ± 0.06	0.51 ± 0.07	0.53 ± 0.09[e]
Bands ($10^3/\mu L$)	0.01 ± 0.01	0.00 ± 0.00[c]	0.01 ± 0.01[c]	0.00 ± 0.00	0.01 ± 0.01	0.01 ± 0.01
Lymphocytes ($10^3/\mu L$)	5.12 ± 0.44	4.77 ± 0.15[c]	6.04 ± 0.28[c]	5.70 ± 0.30	5.86 ± 0.50	6.13 ± 0.65
Monocytes ($10^3/\mu L$)	0.08 ± 0.01	0.09 ± 0.01[c]	0.07 ± 0.02[c]	0.07 ± 0.02	0.11 ± 0.02	0.13 ± 0.03
Eosinophils ($10^3/\mu L$)	0.03 ± 0.01[c]	0.04 ± 0.01[c]	0.05 ± 0.01[c]	0.03 ± 0.01	0.04 ± 0.01	0.05 ± 0.02
Nucleated erythrocytes/ 100 leukocytes	0.25 ± 0.08	0.15 ± 0.08	0.17 ± 0.08	0.10 ± 0.10	0.06 ± 0.06	0.07 ± 0.07
n	10	10	10	10	10	7
Clinical Chemistry						
Barium (mg/dL)	0.45 ± 0.05	0.36 ± 0.05[b]	0.51 ± 0.04	0.29 ± 0.05*	0.26 ± 0.02*[c]	0.38 ± 0.09[f]
Sodium (mEq/L)	146.2 ± 1.0	143.6 ± 0.5*	145.8 ± 1.3[b]	144.2 ± 0.9	145.3 ± 1.1	142.0 ± 0.4**[e]
Potassium (mEq/L)	4.9 ± 0.1	5.3 ± 0.3	4.8 ± 0.1[b]	5.1 ± 0.4	5.4 ± 0.2	4.8 ± 0.5[e]
Calcium (mg/dL)	10.59 ± 0.13	10.67 ± 0.08	10.92 ± 0.10	9.68 ± 0.08**	10.28 ± 0.14	10.73 ± 0.21
Phosphorus (mg/dL)	5.5 ± 0.2	5.6 ± 0.3	6.0 ± 0.1	6.2 ± 0.4	6.3 ± 0.2**	6.3 ± 0.2**

TABLE H2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	125 ppm	500 ppm	1,000 ppm	2,000 ppm	4,000 ppm
Female						
n	10	9	9	10	8	8
Hematology						
Hematocrit (%)	40.4 ± 0.3	40.7 ± 0.7	41.1 ± 0.5	39.4 ± 1.1	40.2 ± 0.6	40.5 ± 0.6
Hemoglobin (g/dL)	14.6 ± 0.2	14.9 ± 0.3	15.1 ± 0.2	14.5 ± 0.4	14.7 ± 0.1	14.9 ± 0.3
Erythrocytes ($10^6/\mu L$)	7.57 ± 0.05	7.64 ± 0.15	7.77 ± 0.10	7.45 ± 0.23	7.48 ± 0.13	7.58 ± 0.14
Mean cell volume (fL)	52.9 ± 0.3	52.7 ± 0.3	52.1 ± 0.1	52.6 ± 0.3	53.3 ± 0.6	52.9 ± 0.5
Mean cell hemoglobin (pg)	19.1 ± 0.2	19.4 ± 0.2	19.3 ± 0.2	19.2 ± 0.2	19.6 ± 0.4	19.5 ± 0.2
Mean cell hemoglobin concentration (g/dL)	36.2 ± 0.4	36.8 ± 0.2	36.9 ± 0.3	36.7 ± 0.3	36.5 ± 0.4	36.8 ± 0.4
Platelets ($10^3/\mu L$)	553.4 ± 38.8	544.9 ± 45.1	519.8 ± 31.1	516.0 ± 44.4[c]	456.1 ± 69.9	447.4 ± 78.8[d]
Leukocytes ($10^3/\mu L$)	4.47 ± 0.28	5.20 ± 0.49	5.30 ± 0.64	4.54 ± 0.50[c]	4.98 ± 0.55	4.56 ± 0.29
Segmented neutrophils ($10^3/\mu L$)	0.41 ± 0.05	0.48 ± 0.07	0.45 ± 0.10	0.45 ± 0.07[c]	0.44 ± 0.08	0.38 ± 0.05
Bands ($10^3/\mu L$)	0.00 ± 0.00	0.01 ± 0.01	0.02 ± 0.01	0.00 ± 0.00[c]	0.00 ± 0.00	0.01 ± 0.01[d]
Lymphocytes ($10^3/\mu L$)	3.96 ± 0.26	4.58 ± 0.42	4.71 ± 0.57	3.98 ± 0.43[c]	4.42 ± 0.46	4.05 ± 0.29
Monocytes ($10^3/\mu L$)	0.07 ± 0.01	0.07 ± 0.02	0.08 ± 0.02	0.07 ± 0.02[c]	0.07 ± 0.03	0.08 ± 0.02
Eosinophils ($10^3/\mu L$)	0.02 ± 0.01	0.06 ± 0.01	0.04 ± 0.01	0.04 ± 0.01[c]	0.03 ± 0.02	0.04 ± 0.01
Nucleated erythrocytes/ 100 leukocytes	0.00 ± 0.00	0.00 ± 0.00	0.06 ± 0.06	0.10 ± 0.07	0.06 ± 0.06	0.13 ± 0.08
n	10	10	10	9	10	8
Clinical Chemistry						
Barium (mg/dL)	0.25 ± 0.07[e]	0.22 ± 0.01	0.64 ± 0.06**	0.22 ± 0.02[e]	1.09 ± 0.15**[b]	0.59 ± 0.06**
Sodium (mEq/L)	146 ± 1	144 ± 1	146 ± 1	144 ± 1	145 ± 1[b]	146 ± 3
Potassium (mEq/L)	4.6 ± 0.2	4.6 ± 0.3	5.2 ± 0.2	5.5 ± 0.4*	5.8 ± 0.4*[b]	5.2 ± 0.5
Calcium (mg/dL)	10.51 ± 0.25	10.88 ± 0.12	10.62 ± 0.19	9.69 ± 0.13*	9.98 ± 0.37	10.11 ± 0.47
Phosphorus (mg/dL)	3.5 ± 0.2	4.1 ± 0.3	6.0 ± 0.2**	5.7 ± 0.3**	6.0 ± 0.3**	5.2 ± 0.1**

* Significantly different ($P \le 0.05$) from the control group by Dunn's or Shirley's test
** $P \le 0.01$
[a] Mean ± standard error
[b] n=9
[c] n=8
[d] n=7
[e] n=6
[f] n=5

TABLE H3
Hematology and Clinical Chemistry Data for Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Male				
n	10	9	8	10
Hematology				
Hematocrit (%)	45.7 ± 0.5	45.0 ± 0.4	44.9 ± 0.8	45.8 ± 0.4
Hemoglobin (g/dL)	16.4 ± 0.2	16.3 ± 0.1	16.4 ± 0.2	16.4 ± 0.2
Erythrocytes (10^6/μL)	9.25 ± 0.10	9.05 ± 0.07	9.12 ± 0.11	9.19 ± 0.11
Mean cell volume (fL)	49.6 ± 0.3	49.9 ± 0.7	49.3 ± 0.6	49.7 ± 0.3
Mean cell hemoglobin (pg)	17.7 ± 0.1	18.0 ± 0.2	18.0 ± 0.2	17.9 ± 0.1
Mean cell hemoglobin concentration (g/dL)	35.9 ± 0.2	36.1 ± 0.3	36.6 ± 0.6	35.9 ± 0.2
Platelets (10^3/μL)	530.1 ± 17.5	478.4 ± 13.0	509.9 ± 26.9	507.4 ± 22.5
Reticulocytes (10^6/μL)	0.13 ± 0.01	0.13 ± 0.01	0.15 ± 0.02	0.13 ± 0.02
Leukocytes (10^3/μL)	7.59 ± 0.41	8.26 ± 0.28	9.20 ± 0.80	8.11 ± 0.77
Segmented neutrophils (10^3/μL)	2.36 ± 0.27	2.74 ± 0.21	2.74 ± 0.33	2.98 ± 0.57
Lymphocytes (10^3/μL)	4.66 ± 0.22	4.75 ± 0.19	5.44 ± 0.51	4.35 ± 0.25
Monocytes (10^3/μL)	0.45 ± 0.10	0.55 ± 0.08	0.78 ± 0.16	0.63 ± 0.11
Eosinophils (10^3/μL)	0.08 ± 0.03	0.13 ± 0.06	0.13 ± 0.03	0.14 ± 0.04
Nucleated erythrocytes (10^3/μL)	0.02 ± 0.01	0.04 ± 0.02	0.01 ± 0.01	0.05 ± 0.03
n	10	10	10	10
Clinical Chemistry				
Urea nitrogen (mg/dL)	21.9 ± 1.0	19.1 ± 0.7	19.9 ± 1.1	22.0 ± 0.7
Creatinine (mg/dL)	0.62 ± 0.05	0.54 ± 0.03	0.53 ± 0.02	0.59 ± 0.03
Calcium (mg/dL)	10.37 ± 0.24	10.45 ± 0.22	10.62 ± 0.27	10.48 ± 0.17
Phosphorus (mg/dL)	4.3 ± 0.2	4.3 ± 0.1	4.3 ± 0.2	4.3 ± 0.2
Alanine aminotransferase (IU/L)	109 ± 6	99 ± 8	103 ± 11	98 ± 6
Creatine kinase (IU/L)	442 ± 59	471 ± 101	499 ± 60	480 ± 57
Lactate dehydrogenase (IU/L)	763 ± 82	798 ± 119	869 ± 87	772 ± 82
Sorbitol dehydrogenase (IU/L)	16 ± 2	15 ± 1	13 ± 1	11 ± 2*
γ-Glutamyltransferase (IU/L)	3.7 ± 0.9	3.2 ± 0.8	3.1 ± 0.7	3.4 ± 0.7

TABLE H3
Hematology and Clinical Chemistry Data for Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Female				
n	8	7	7	10
Hematology				
Hematocrit (%)	44.5 ± 0.8	43.6 ± 0.4	44.0 ± 0.4	43.4 ± 0.6
Hemoglobin (g/dL)	16.0 ± 0.1	15.9 ± 0.2	16.0 ± 0.1	15.8 ± 0.1
Erythrocytes ($10^6/\mu L$)	8.14 ± 0.14	8.00 ± 0.07	8.07 ± 0.08	7.98 ± 0.10
Mean cell volume (fL)	54.8 ± 0.3	54.7 ± 0.2	54.6 ± 0.4	54.3 ± 0.3
Mean cell hemoglobin (pg)	19.6 ± 0.3	19.8 ± 0.1	19.8 ± 0.1	19.8 ± 0.2
Mean cell hemoglobin concentration (g/dL)	35.9 ± 0.6	36.3 ± 0.2	36.3 ± 0.3	36.4 ± 0.4
Platelets ($10^3/\mu L$)	470.0 ± 44.4	453.0 ± 21.0	494.0 ± 23.0	442.4 ± 24.4
Reticulocytes ($10^6/\mu L$)	0.09 ± 0.01	0.07 ± 0.01	0.09 ± 0.02	0.08 ± 0.01
Leukocytes ($10^3/\mu L$)	4.01 ± 0.11	4.16 ± 0.30	4.33 ± 0.18	4.09 ± 0.18
Segmented neutrophils ($10^3/\mu L$)	1.04 ± 0.13	1.04 ± 0.10	1.00 ± 0.12	1.09 ± 0.12
Lymphocytes ($10^3/\mu L$)	2.54 ± 0.05	2.70 ± 0.23	2.89 ± 0.14	2.63 ± 0.10
Monocytes ($10^3/\mu L$)	0.35 ± 0.02	0.35 ± 0.05	0.34 ± 0.05	0.29 ± 0.03
Eosinophils ($10^3/\mu L$)	0.05 ± 0.02	0.05 ± 0.02	0.08 ± 0.02	0.02 ± 0.01
Nucleated erythrocytes ($10^3/\mu L$)	0.06 ± 0.03	0.03 ± 0.02	0.02 ± 0.01	0.04 ± 0.02
n	10	10	10	10
Clinical Chemistry				
Urea nitrogen (mg/dL)	17.3 ± 1.2	17.0 ± 0.9	15.7 ± 0.9	18.0 ± 0.9
Creatinine (mg/dL)	0.5 ± 0.0	0.4 ± 0.0	0.5 ± 0.1	0.5 ± 0.0
Calcium (mg/dL)	10.57 ± 0.13	10.43 ± 0.14	10.41 ± 0.15	10.49 ± 0.15
Phosphorus (mg/dL)	3.3 ± 0.2	2.9 ± 0.2	3.2 ± 0.3	3.2 ± 0.2
Alanine aminotransferase (IU/L)	49 ± 2	54 ± 3	55 ± 3	49 ± 3
Creatine kinase (IU/L)	310 ± 46	252 ± 27	294 ± 52	289 ± 64
Lactate dehydrogenase (IU/L)	377 ± 69	323 ± 42	346 ± 51	266 ± 32
Sorbitol dehydrogenase (IU/L)	7 ± 1	8 ± 1	7 ± 1	8 ± 1
γ-Glutamyltransferase (IU/L)	2.6 ± 0.9	2.7 ± 0.8	2.2 ± 0.6	1.8 ± 0.8

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
[a] Mean ± standard error

TABLE H4
Hematology and Clinical Chemistry Data for Mice at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Male				
n	9	8	10	10
Hematology				
Hematocrit (%)	45.6 ± 0.6	46.4 ± 0.4	45.8 ± 0.6	45.1 ± 0.4
Hemoglobin (g/dL)	15.6 ± 0.1	15.8 ± 0.1	15.8 ± 0.2	15.5 ± 0.1
Erythrocytes (10^6/μL)	9.36 ± 0.10	9.59 ± 0.07	9.40 ± 0.08	9.34 ± 0.11
Mean cell volume (fL)	48.8 ± 0.4	48.6 ± 0.2	48.6 ± 0.5	48.3 ± 0.6
Mean cell hemoglobin (pg)	16.7 ± 0.1	16.4 ± 0.1	16.7 ± 0.1	16.6 ± 0.2
Mean cell hemoglobin concentration (g/dL)	34.3 ± 0.2	34.0 ± 0.2	34.5 ± 0.5	34.5 ± 0.3
Platelets (10^3/μL)	865.3 ± 41.6	822.4 ± 26.4[b]	828.9 ± 10.8	824.8 ± 19.8
Reticulocytes (10^6/μL)	0.22 ± 0.02	0.22 ± 0.02[b]	0.20 ± 0.02	0.21 ± 0.02
Leukocytes (10^3/μL)	6.89 ± 0.26	7.90 ± 0.82	7.20 ± 0.47	6.83 ± 0.39
Segmented neutrophils (10^3/μL)	1.23 ± 0.11	1.17 ± 0.16	1.17 ± 0.10	1.11 ± 0.11
Lymphocytes (10^3/μL)	5.27 ± 0.22	6.04 ± 0.73	5.66 ± 0.40	5.43 ± 0.27
Monocytes (10^3/μL)	0.27 ± 0.05	0.54 ± 0.14	0.28 ± 0.08	0.22 ± 0.05
Eosinophils (10^3/μL)	0.10 ± 0.03	0.19 ± 0.02	0.06 ± 0.03	0.06 ± 0.02
Nucleated erythrocytes (10^3/μL)	0.00 ± 0.00	0.02 ± 0.02	0.01 ± 0.01	0.02 ± 0.02
n	9	10	10	10
Clinical Chemistry				
Urea nitrogen (mg/dL)	25.8 ± 2.6[c]	27.1 ± 2.1	22.8 ± 1.4	60.1 ± 26.2
Creatinine (mg/dL)	0.40 ± 0.08	0.36 ± 0.04	0.35 ± 0.02	0.51 ± 0.15
Calcium (mg/dL)	9.27 ± 0.15	9.30 ± 0.12	9.14 ± 0.21	9.14 ± 0.41
Phosphorus (mg/dL)	10.2 ± 0.7	8.9 ± 0.7	9.6 ± 0.4	8.4 ± 0.6
Alanine aminotransferase (IU/L)	143 ± 54[c]	98 ± 24[d]	180 ± 89	945 ± 832[c]
Creatine kinase (IU/L)	118 ± 22	109 ± 12[d]	111 ± 22	258 ± 115
Lactate dehydrogenase (IU/L)	746 ± 107	607 ± 112[d]	729 ± 186	597 ± 89[c]
γ-Glutamyltransferase (IU/L)	3.0 ± 1.2[c]	2.3 ± 0.5	1.7 ± 0.5	2.6 ± 1.5[c]

TABLE H4
Hematology and Clinical Chemistry Data for Mice at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate (continued)

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Female				
n	10	8	10	6
Hematology				
Hematocrit (%)	46.1 ± 0.2	46.8 ± 0.2	45.8 ± 0.4	47.1 ± 0.7
Hemoglobin (g/dL)	15.8 ± 0.1	16.2 ± 0.2	16.0 ± 0.2	16.1 ± 0.1
Erythrocytes ($10^6/\mu L$)	9.58 ± 0.07	9.82 ± 0.06	9.42 ± 0.11	9.77 ± 0.06
Mean cell volume (fL)	48.2 ± 0.3	47.6 ± 0.4	48.5 ± 0.4	48.5 ± 0.4
Mean cell hemoglobin (pg)	16.5 ± 0.1	16.5 ± 0.1	17.1 ± 0.4	16.5 ± 0.1
Mean cell hemoglobin concentration (g/dL)	34.3 ± 0.1	34.7 ± 0.4	35.1 ± 0.6	34.2 ± 0.4
Platelets ($10^3/\mu L$)	675.9 ± 14.0	665.0 ± 13.6	687.3 ± 19.5[d]	690.5 ± 28.2
Reticulocytes ($10^6/\mu L$)	0.20 ± 0.02	0.18 ± 0.02	0.23 ± 0.03[c]	0.19 ± 0.04[e]
Leukocytes ($10^3/\mu L$)	5.45 ± 0.42	5.81 ± 0.40	5.19 ± 0.77	4.87 ± 0.28
Segmented neutrophils ($10^3/\mu L$)	1.12 ± 0.11	0.99 ± 0.14	0.86 ± 0.12	0.85 ± 0.08
Lymphocytes ($10^3/\mu L$)	3.96 ± 0.37	4.47 ± 0.29	3.99 ± 0.71	3.61 ± 0.26
Monocytes ($10^3/\mu L$)	0.25 ± 0.04	0.22 ± 0.05	0.20 ± 0.05	0.24 ± 0.08
Eosinophils ($10^3/\mu L$)	0.11 ± 0.04	0.12 ± 0.06	0.13 ± 0.03	0.17 ± 0.03
Nucleated erythrocytes ($10^3/\mu L$)	0.00 ± 0.00	0.00 ± 0.00	0.01 ± 0.01	0.00 ± 0.00
n	10	7	10	6
Clinical Chemistry				
Urea nitrogen (mg/dL)	27.5 ± 2.9	57.4 ± 23.9	50.4 ± 13.4	45.8 ± 7.8
Creatinine (mg/dL)	0.35 ± 0.03	0.40 ± 0.03	0.37 ± 0.03	0.42 ± 0.03
Calcium (mg/dL)	10.26 ± 0.14	10.17 ± 0.28	10.08 ± 0.18	10.28 ± 0.23
Phosphorus (mg/dL)	9.3 ± 0.4	9.4 ± 0.6	8.8 ± 0.3	9.1 ± 0.5
Alanine aminotransferase (IU/L)	101 ± 24[d]	231 ± 103	217 ± 77	141 ± 56
Creatine kinase (IU/L)	192 ± 40	230 ± 40	180 ± 47	353 ± 119
Lactate dehydrogenase (IU/L)	930 ± 249	1,305 ± 330	1,477 ± 354	1,253 ± 301
γ-Glutamyltransferase (IU/L)	2.3 ± 1.1	5.3 ± 2.2	1.7 ± 1.0	2.5 ± 1.3

[a] Mean ± standard error
[b] n=7
[c] n=8
[d] n=9
[e] n=5

APPENDIX I
PLASMA BARIUM LEVELS AND BONE ANALYSES

PLASMA BARIUM LEVELS AND BONE ANALYSES

MATERIALS AND METHODS

At the 15-month interim evaluations in the 2-year studies of F344 rats and B6C3F$_1$ mice, plasma from blood collected for hematology and clinical chemistry determinations was sent to Midwest Research Institute (MRI; Kansas City, MO) for analysis of barium concentrations. In addition, the right and left femurs from eight male rats and eight female rats in the control and 2,500 ppm groups were removed to determine bone density, then the left femurs were sent to MRI for analysis of barium, calcium, and phosphorus levels.

Both plasma and femur samples were analyzed by inductively coupled plasma-atomic emission spectrometry (ICP) after preparation using an acid digestion procedure. For plasma samples, 0.100 to 0.200 mL of plasma was transferred to a 10 mL culture tube containing 1 mL of nitric acid and 1 mL of scandium internal standard. The samples were then placed in a 90° C oven for approximately 1 hour and then diluted to approximately 5 mL with water. The femurs were broken into three segments: upper, middle, and lower. Each fragment was weighed and then placed in culture tubes containing 2 mL nitric acid and 1 mL scandium internal standard. The femur samples were placed in a 90° C oven for approximately 1 hour and then diluted to approximately 10 mL with water. A Perkin Elmer Plasma II inductively coupled plasma-atomic emission spectrometer with an argon flow of 1.00 L/min was used. The following wavelengths were used for barium, calcium, and phosphorus quantitation:

Barium — 455.403 nm
Calcium — 317.933 nm
Phosphorus — 214.914 nm

To determine bone density, both femurs were removed as the last step in the necropsy procedure. After the connective tissue was removed, the femurs were placed in vials containing 0.85% saline at 25° ± 4° C for at least 1 hour. Each bone was then rinsed in distilled water and suspended from a fine stainless steel wire. While suspended, the bones were weighed to the nearest milligram both in air and in distilled water using a torsion balance (Roller Smith). Bone density was calculated using a standard temperature and pressure method, where the density of the bone (g/mL) equals the weight of the bone in air divided by the difference between the weight of the bone in air and the weight of the bone in water.

RESULTS

The mean detection limit (MDL) for barium in femur samples was estimated at 0.05 μg/10 mL of digested sample. The MDL for barium in serum samples was estimated at 0.02 μg/5 mL of digested sample. No MDLs were determined for calcium or phosphorus because they were found at significant levels in the femur samples.

TABLE I1
Plasma Barium Levels in Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Male				
n	10	10	10	10
Barium (μg/mL)	0.98 ± 0.06	1.00 ± 0.07	1.23 ± 0.06*	1.68 ± 0.07**
Female				
n	10	9	11	10
Barium (μg/mL)	0.74 ± 0.05	0.99 ± 0.06**	0.97 ± 0.05**	1.43 ± 0.06**

* Significantly different (P≤0.05) from the control group by Shirley's test
** P≤0.01
[a] Mean ± standard error

TABLE I2
Plasma Barium Levels in Mice at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	0 ppm	500 ppm	1,250 ppm	2,500 ppm
Male				
n	8	10	10	9
Barium (μg/mL)	0.62 ± 0.02	0.77 ± 0.04**	0.89 ± 0.05**	1.49 ± 0.14**
Female				
n	8	7	6	6
Barium (μg/mL)	0.52 ± 0.05	0.74 ± 0.09*	1.01 ± 0.06**	1.35 ± 0.19**

* Significantly different (P≤0.05) from the control group by Shirley's test
** P≤0.01
[a] Mean ± standard error

TABLE I3
Bone Density in Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	Males		Females	
	0 ppm	2,500 ppm	0 ppm	2,500 ppm
n	8	8	8	8
Bone density (g/mL)	1.64 ± 0.03	1.64 ± 0.02	1.69 ± 0.07	1.66 ± 0.02

[a] Mean ± standard deviation

TABLE I4
Barium, Calcium, and Phosphorus Levels in the Femur of Rats at the 15-Month Interim Evaluation in the 2-Year Drinking Water Study of Barium Chloride Dihydrate[a]

	Males		Females	
	0 ppm	2,500 ppm	0 ppm	2,500 ppm
n	8	8	8	8
Barium (ppm)				
Upper	3.7 ± 0.8	1,311.8 ± 20.4**	2.1 ± 1.0	1,181.1 ± 30.8**
Middle	3.9 ± 1.4[b]	1,684.5 ± 20.8**	5.5 ± 2.1	1,463.5 ± 37.7**
Lower	3.4 ± 0.8	1,221.4 ± 15.3**	2.5 ± 1.0	1,113.8 ± 29.5**
Calcium (%)				
Upper	19.6 ± 0.4	18.4 ± 0.4*	19.3 ± 0.4	18.3 ± 0.4*
Middle	22.9 ± 1.3	23.8 ± 1.1	23.7 ± 0.5	23.0 ± 0.6
Lower	16.7 ± 0.4	16.0 ± 0.3	16.7 ± 0.6	15.5 ± 0.4
Phosphorus (%)				
Upper	9.0 ± 0.1	9.0 ± 0.2	8.7 ± 0.1	8.5 ± 0.1
Middle	10.5 ± 0.5	11.4 ± 0.3	11.4 ± 0.2	11.4 ± 0.2
Lower	7.7 ± 0.1	7.8 ± 0.2	7.6 ± 0.2	7.3 ± 0.1

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error
[b] n=7

APPENDIX J
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

PROCUREMENT AND CHARACTERIZATION OF BARIUM CHLORIDE DIHYDRATE

Barium chloride dihydrate was obtained as a white crystalline powder from J.T. Baker Chemical Company (Phillipsburg, NJ) in two lots (123120 and 423103). Lot 123120 was used throughout the 15-day and 13-week studies in rats and mice and lot 423103 was used throughout the 2-year studies in rats and mice. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO). The reports on analyses performed in support of the barium chloride dihydrate studies are on file at the National Institute of Environmental Health Sciences.

Both lots of the chemical, a white, crystalline solid, were characterized by elemental analyses, weight loss on drying, complexometric titration, precipitation titration, spark source mass spectrometry, and by American Chemical Society (ACS) tests for oxidizing substances, heavy metals, and iron. Complexometric titration was performed by dissolving the sample in deionized water and titrating with 0.1 N ethylenediaminetetraacetic acid (EDTA) to the metalphthalein endpoint. Precipitation titration was performed by dissolving the sample in deionized water and titrating with 0.1 N sodium sulfate, using Sulfonazo III as the indicator.

Elemental analyses of both lots for barium, chlorine, and hydrogen were in good agreement with the theoretical values for barium chloride dihydrate. Weight loss on drying indicated 14.9% and 14.0% water in lots 123120 and 423103, respectively, which agreed with the theoretical value of 14.75% water for barium chloride dihydrate. For lots 123120 and 423103, complexometric titration indicated purities of 99.4% and 100%, respectively. For lots 123120 and 423103, precipitation titration indicated purities of 99.1% and 99%, respectively. For lot 123120, spark source mass spectrometry indicated only three elements at concentrations greater than 0.01%: 0.019% copper, 0.021% silicon, and 0.017% aluminum. For lot 423103, spark source mass spectrometry indicated only two elements at concentrations greater than 0.01%: 0.014% silicon and 0.014% strontium. Further tests indicated that both lots of barium chloride dihydrate met ACS specifications for oxidizing substances, heavy metals, and iron. The overall purity of both lots was determined to be greater than 99%.

Bulk chemical stability studies were not performed because the physical and chemical properties of barium chloride dihydrate are such that the chemical should be stable over a wide range of temperatures. The purity and water content of the bulk chemical were reanalyzed approximately every 4 months during the 2-year studies at the study laboratory by complexometric titration and weight loss on drying. The results indicated that the purity and moisture content of the bulk chemical did not change during the 2-year studies.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared by mixing barium chloride dihydrate and glass distilled water in a volumetric flask and stirring mechanically for 1 minute (Table J1). Dose formulations were prepared once during the 15-day studies and weekly during the 13-week and 2-year studies.

Studies to determine the stability of the 500 ppm dosed water solutions were conducted by the analytical chemistry laboratory. Aliquots (200 μL) were mixed with 10 mL of 4-(2-pyridylazo)resorcinol (2.5×10^{-4} M) reagent and 10 mL of zinc-EDTA solution (4×10^{-4} M), and shaken for 10 seconds. The samples were analyzed by absorbance at 510 nm using ultraviolet spectroscopy. The stability of the dose formulations was confirmed for at least 3 weeks when stored in the dark at 25° C and for at least 3 days when stored exposed to air and light.

Periodic analyses of the dose formulations of barium chloride dihydrate were conducted at the study laboratory and the analytical chemistry laboratory using complexometric titration. The dose formulations were diluted with deionized water and titrated with EDTA to the metalphthalein endpoint. The dose formulations were analyzed at the beginning of the 15-day studies (Table J2). During the 13-week studies, the dose formulations were analyzed at the initiation and midpoint of the studies (Table J3). During the 2-year studies, the dose formulations were analyzed at least once every 8 weeks (Table J4). All the dose formulations were within 10% of the target concentrations. Results of periodic referee analyses performed by the analytical chemistry laboratory were in good agreement with the results obtained by the study laboratory (Table J5).

TABLE J1
Preparation and Storage of Dose Formulations in the Drinking Water Studies of Barium Chloride Dihydrate

15-Day Studies	13-Week Studies	2-Year Studies
Preparation		
Barium chloride dihydrate was mixed with glass distilled water and stirred for 1 minute.	Same as 15-day studies	Same as 15-day studies
Chemical Lot Number		
123120	123120	423103
Maximum Storage Time		
2 weeks	2 weeks	3 weeks
Storage Conditions		
Not available	Not available	Stored at 4° C in labeled polyethylene carboys.
Study Laboratory		
SRI International, Menlo Park, CA	SRI International, Menlo Park, CA	EG&G Mason Research Institute, Worcester, MA
Referee Laboratory		
Midwest Research Institute, Kansas City, MO	Midwest Research Institute, Kansas City, MO	Midwest Research Institute, Kansas City, MO

TABLE J2
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 15-Day Drinking Water Studies of Barium Chloride Dihydrate

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration[a] (ppm)	% Difference from Target
Rats				
18 November 1982	21 December 1982	125	125[b]	0
		250	254	+2
		500	511	+2
		1,000	1,010	+1
		2,000	2,010	+1
Mice				
23 November 1982	21 December 1982	40	42.0	+5
		80	79.7	0
		173	175	+1
		346	348	+1
		692	696	+1

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

TABLE J3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 13-Week Drinking Water Studies of Barium Chloride Dihydrate

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration[a] (ppm)	% Difference from Target
25 April 1983	26 April 1983	125	124	–1
		500	496	–1
		1,000	994	–1
		2,000	1,990	–1
		4,000	4,020	+1
	10 May 1983[b]	125	124	–1
		500	494	–1
		1,000	1,000	0
		2,000	1,980	–1
		4,000	4,040	+1
9 June 1983	10 June 1983	125	122[c]	–2
		500	508	+2
		1,000	1,018	+2
		2,000	1,991	0
		4,000	4,046	+1
	16 June 1983[b]	125	124	–1
		500	487	–3
		1,000	952	–5
		2,000	1,873	–6
		4,000	3,820	–5

[a] Results of duplicate analyses
[b] Results of animal room samples
[c] Result of a single analysis

TABLE J4
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Barium Chloride Dihydrate

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration[a] (ppm)	% Difference from Target
3 September 1985	6 September 1985	500	490	−2
		1,250	1,240	−1
		2,500	2,480	−1
	17 September 1985[b]	500	510	+2
		1,250	1,250	0
		2,500	2,480	−1
30 October 1985	1 November 1985	500	510	+2
		1,250	1,250	0
		2,500	2,490	0
11 December 1985	13 December 1985	500	510	+2
		1,250	1,260	+1
		2,500	2,520	+1
17 February 1986	20 February 1986	500	500	0
		1,250	1,270	+2
		2,500	2,550	+2
	28 February 1986[b]	500	500	0
		1,250	1,250	0
		2,500	2,520	+1
16 April 1986	17 April 1986	500	490	−2
		1,250	1,260	+1
		2,500	2,540	+2
11 June 1986	12 June 1986	500	500	0
		1,250	1,260	+1
		2,500	2,530	+1
6 August 1986	7 August 1986	500	520	+4
		1,250	1,280	+2
		2,500	2,510	0
	25 August 1986[b]	500	520	+4
		1,250	1,280	+2
		2,500	2,540	+2
30 September 1986	1 October 1986	500	510	+2
		1,250	1,270	+2
		2,500	2,540	+2
19 November 1986	20 November 1986	500	500	0
		1,250	1,240	−1
		2,500	2,470	−1
21 January 1987	21 January 1987	500	500	0
		1,250	1,240	−1
		2,500	2,480	−1

TABLE J4
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Drinking Water Studies of Barium Chloride Dihydrate (continued)

Date Prepared	Date Analyzed	Target Concentration (ppm)	Determined Concentration (ppm)	% Difference from Target
	3 February 1987[b]	500	500	0
		1,250	1,230	–2
		2,500	2,470	–1
18 March 1987	18 March 1987	500	500	0
		1,250	1,240	–1
		2,500	2,480	–1
13 May 1987	14 May 1987	500	510	+2
		1,250	1,270	+2
		2,500	2,570	+3
8 July 1987	8 July 1987	500	510	+2
		1,250	1,260	+1
		2,500	2,510	0
	20 July 1987[b]	500	510	+2
		1,250	1,250	0
		2,500	2,500	0
9 September 1987	11 September 1987	500	490	–2
		1,250	1,250	0
		2,500	2,520	+1

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

TABLE J5
Results of Referee Analysis of Dose Formulations Administered to Rats and Mice in the 13-Week and 2-Year Drinking Water Studies of Barium Chloride Dihydrate

Date Prepared	Target Concentration (ppm)	Determined Concentration (ppm)	
		Study Laboratory[a]	Referee Laboratory[b]
13 Weeks			
25 April 1983	125	124	129 ± 0
2 Years			
3 September 1985	1,250	1,240	1,240 ± 0
16 April 1986	500	490	500 ± 0
30 September 1986	2,500	2,540	2,520 ± 10
18 March 1987	1,250	1,240	1,250 ± 0
9 September 1987	500	490	500 ± 0

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

APPENDIX K
WATER AND COMPOUND CONSUMPTION

TABLE K1
Water and Compound Consumption by Male Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Week	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
1	20.3	129	21.4	128	84	19.3	128	188	17.4	127	341
2	19.0	161	19.1	159	60	18.9	155	152	16.2	153	265
3	22.1	192	19.9	190	52	20.3	193	131	17.9	189	237
4	19.7	218	21.4	217	49	20.4	221	115	19.0	216	220
5	23.0	242	23.7	237	50	20.7	241	107	18.3	237	193
6	23.0	259	24.5	257	48	21.7	258	105	19.2	255	188
7	22.4	272	23.3	269	43	20.2	268	94	18.8	268	175
8	22.4	286	24.9	278	45	21.1	283	93	19.3	280	173
9	22.0	292	22.1	288	38	19.9	293	85	17.6	291	151
10	20.9	310	21.6	304	35	18.5	306	76	18.5	302	153
11	19.9	320	22.1	311	36	19.3	318	76	17.3	313	139
12	21.7	335	20.2	323	31	18.9	325	73	16.0	320	125
13	20.0	338	19.6	330	30	18.7	329	71	15.6	328	119
14	20.1	346	19.2	337	29	18.6	335	69	15.8	336	117
18	19.9	379	20.6	371	28	20.3	365	69	17.6	358	123
21	20.8	385	18.9	378	25	18.2	372	61	16.7	367	114
25	18.4	406	17.7	398	22	17.2	394	55	14.9	385	97
29	19.9	415	18.6	408	23	17.7	399	55	16.1	396	102
34	19.9	433	18.9	425	22	17.4	417	52	15.1	412	92
37	19.4	446	18.6	439	21	17.0	428	50	15.9	421	95
41	19.2	441	17.9	436	21	16.9	428	49	14.4	419	86
45	21.3	446	20.0	436	23	20.9	424	62	18.5	415	111
49	19.8	460	18.7	450	21	18.4	441	52	15.0	430	87
53	19.9	459	19.0	455	21	18.0	446	50	15.2	435	88
57	21.0	463	19.5	455	21	17.9	446	50	15.5	437	88
61	19.7	462	18.9	457	21	17.2	448	48	14.8	439	84
65	23.3	465	21.1	457	23	18.6	449	52	17.3	437	99
69	22.3	468	22.3	458	24	19.8	447	55	16.5	442	93
73	21.4	456	20.6	450	23	18.6	442	53	17.3	436	99
77	21.9	468	21.0	450	23	18.7	444	53	17.3	439	98
81	20.7	464	18.7	451	21	17.4	448	48	15.6	433	90
85	20.9	462	19.4	451	22	17.2	443	49	15.2	431	88
89	21.5	457	20.2	452	22	17.2	437	49	15.8	426	93
93	23.5	448	21.5	441	24	19.6	434	56	16.5	417	99
97	22.1	429	22.5	440	26	20.4	429	59	16.0	410	97
101	24.6	416	24.0	427	28	20.8	406	64	18.6	402	116
104	28.0	419	22.8	416	27	19.8	406	61	19.7	398	124
Mean for weeks											
1-13	21.3	258	21.8	253	46	19.8	255	105	17.8	252	191
14-52	19.9	416	18.9	408	23	18.3	400	57	16.0	394	102
53-104	22.2	453	20.8	447	23	18.7	438	53	16.5	427	97

[a] Grams of water consumed per animal per day
[b] Milligrams of barium chloride dihydrate consumed per kilogram body weight per day

TABLE K2
Water and Compound Consumption by Female Rats in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Week	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
1	15.9	106	16.4	108	76	17.1	109	197	15.7	107	365
2	16.0	129	15.9	128	62	16.9	127	166	14.0	126	277
3	16.9	141	15.2	140	54	16.3	140	146	14.7	139	265
4	17.8	149	16.2	148	55	19.2	149	161	15.1	149	255
5	17.6	158	15.8	158	50	18.1	157	144	12.9	158	205
6	17.3	167	15.7	165	47	17.8	164	136	13.2	163	202
7	18.1	173	16.6	171	48	18.3	170	134	13.2	169	195
8	17.2	178	15.4	176	44	17.5	175	125	12.1	173	175
9	16.9	181	14.9	180	42	16.0	179	112	13.3	176	189
10	18.4	182	15.0	180	42	17.9	180	124	13.5	177	190
11	15.9	186	14.7	185	40	16.9	185	115	11.5	182	158
12	15.6	190	14.3	189	38	13.5	188	90	11.7	185	159
13	15.3	194	14.4	193	37	13.5	192	88	10.7	187	144
14	15.2	195	14.2	194	37	13.9	193	90	11.2	190	147
18	14.0	200	13.4	200	33	12.1	200	76	10.6	196	135
21	14.3	204	13.8	205	34	13.1	204	80	11.2	199	141
25	14.1	212	13.4	210	32	11.8	210	70	10.1	203	124
29	14.7	218	14.0	217	32	13.1	214	77	11.4	210	136
33	13.4	225	13.7	225	30	12.5	224	70	10.8	218	123
37	13.8	230	13.2	230	29	12.0	226	66	9.9	221	112
41	14.5	235	14.3	236	30	12.8	233	69	10.5	226	117
45	14.6	242	14.2	243	29	13.5	233	73	11.0	234	118
49	14.0	253	13.6	252	27	12.6	245	64	10.6	240	110
54	14.2	263	14.0	263	27	12.7	257	62	10.6	248	106
58	14.1	273	13.7	269	26	12.8	262	61	10.7	254	106
62	15.5	279	14.3	276	26	14.0	269	65	11.4	260	110
66	16.4	287	15.6	284	27	14.5	278	65	12.8	271	119
69	16.1	288	16.0	290	28	16.1	278	72	12.4	274	113
74	17.5	300	17.7	300	30	16.8	286	73	13.1	278	118
78	17.8	306	18.1	307	29	16.9	291	73	13.4	286	117
82	18.5	310	17.9	313	29	16.8	298	70	13.4	288	116
86	19.5	319	19.2	318	30	18.3	304	75	14.5	291	125
90	19.1	319	17.9	323	28	16.3	306	66	12.8	293	109
94	18.6	327	17.8	326	27	17.3	308	70	14.4	295	122
98	18.7	326	17.0	323	26	17.2	307	70	12.6	297	106
102	19.0	336	18.2	331	28	17.5	310	71	14.2	302	117
105	18.9	327	17.6	323	27	18.1	308	74	13.5	292	115
Mean for weeks											
1-13	16.8	164	15.4	163	49	16.9	163	134	13.2	161	214
14-52	14.3	222	13.8	221	31	12.7	218	73	10.7	214	126
53-105	17.4	304	16.8	303	28	16.1	290	69	12.8	281	114

[a] Grams of water consumed per animal per day
[b] Milligrams of barium chloride dihydrate consumed per kilogram body weight per day

TABLE K3
Water and Compound Consumption by Male Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Week	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
2	4.6	21.6	4.8	21.4	112	4.6	21.4	267	4.6	21.5	537
3	5.1	22.5	5.5	22.3	123	6.0	22.1	340	6.2	22.3	693
4	4.9	23.4	5.3	23.1	114	5.0	23.0	274	5.2	22.8	571
5	4.4	24.4	5.2	23.6	111	5.1	23.9	268	4.8	23.8	501
6	4.7	25.7	4.7	24.7	96	4.8	25.2	240	4.6	24.7	464
7	5.3	26.9	7.2	26.1	138	7.0	26.2	335	5.7	25.9	553
8	4.4	27.6	4.7	27.5	86	4.8	27.2	219	4.5	27.0	416
9	4.7	28.7	5.3	27.8	95	5.0	28.5	218	5.0	27.8	446
10	4.6	29.4	5.3	28.7	92	5.5	28.8	240	4.5	28.6	390
11	4.6	31.1	5.0	29.7	85	5.7	30.2	236	4.6	29.4	393
13	4.4	32.5	4.9	31.2	79	5.0	31.8	197	4.6	30.6	378
17	4.4	35.3	4.7	34.2	68	5.0	34.5	182	4.4	33.7	326
20	3.8	36.6	3.9	35.8	55	3.7	36.1	129	3.7	35.3	263
24	4.0	38.7	3.8	37.9	50	3.8	38.5	124	3.6	37.3	242
28	3.5	41.0	3.5	40.3	43	3.2	40.7	98	3.3	39.2	212
32	3.4	43.0	3.5	41.7	42	3.3	42.2	99	3.4	41.0	208
36	3.4	43.3	3.7	42.1	44	3.5	42.6	103	3.3	41.1	199
40	3.8	44.2	4.1	43.1	48	3.8	43.7	108	3.7	42.1	217
44	3.6	45.7	3.6	44.7	41	4.3	45.2	119	3.2	43.7	184
48	3.6	46.4	2.4	45.3	27	2.5	45.8	67	2.4	44.1	134
52	2.6	45.0	2.7	44.4	31	2.6	45.0	73	2.5	43.4	144
56	4.1	46.8	4.3	45.9	46	4.0	46.6	107	3.9	44.2	220
60	4.1	46.4	4.2	45.4	46	4.2	45.4	115	4.0	44.2	223
64	3.9	48.2	4.0	47.0	43	3.8	47.4	99	3.9	45.6	214
68	4.4	48.0	4.5	46.8	48	4.1	47.1	109	4.1	44.6	229
72	4.5	47.6	4.4	46.8	47	4.2	47.3	112	4.4	44.8	246
76	4.4	47.1	4.8	46.9	51	4.3	47.2	115	4.5	44.1	253
80	5.0	46.8	4.9	46.4	53	4.7	46.3	126	4.9	43.0	288
84	4.7	45.9	4.5	46.2	49	4.5	45.5	124	4.8	42.2	286
88	5.2	45.5	4.9	45.1	54	4.8	45.2	132	5.7	41.1	344
92	5.3	44.8	5.0	44.9	55	4.7	44.5	131	5.4	41.3	324
96	5.1	43.1	5.3	43.1	61	4.7	43.5	135	4.8	39.7	300
100	5.2	41.5	5.0	41.4	60	5.0	42.0	148	4.8	38.6	312
103	6.0	41.3	5.6	41.9	67	5.5	41.9	165	6.2	37.7	413
Mean for weeks											
1-13	4.7	26.7	5.3	26.0	103	5.3	26.2	258	4.9	25.9	486
14-52	3.6	41.9	3.6	41.0	45	3.6	41.4	110	3.3	40.1	213
53-103	4.8	45.6	4.7	45.2	52	4.5	45.4	125	4.7	42.4	281

[a] Grams or water consumed per animal per day
[b] Milligrams of barium chloride dihydrate consumed per kilogram body weight per day

TABLE K4
Water and Compound Consumption by Female Mice in the 2-Year Drinking Water Study of Barium Chloride Dihydrate

Week	0 ppm		500 ppm			1,250 ppm			2,500 ppm		
	Water (g/day)[a]	Body Weight (g)	Water (g/day)	Body Weight (g)	Dose/ Day[b] (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)	Water (g/day)	Body Weight (g)	Dose/ Day (mg/kg/day)
2	5.5	18.1	5.9	18.5	160	5.5	18.1	382	5.8	18.3	791
3	5.6	19.3	6.8	19.4	175	5.8	18.7	390	6.4	19.2	833
4	6.5	19.8	7.3	19.8	185	7.2	19.9	455	8.2	19.8	1,038
5	5.5	20.9	6.2	20.4	151	5.7	20.2	354	6.9	20.5	842
6	5.2	21.1	6.1	21.3	144	5.9	20.7	357	7.0	21.2	831
7	5.4	22.1	6.4	21.8	147	6.7	22.1	380	7.4	21.7	848
8	5.9	23.0	7.6	23.0	165	6.6	22.8	363	7.0	22.7	775
9	6.3	24.2	6.4	23.8	135	6.8	24.1	351	7.0	23.3	756
10	7.0	24.9	7.6	25.2	151	8.0	24.6	407	7.6	24.2	785
11	6.9	25.9	7.8	25.8	152	7.2	25.8	347	8.2	24.6	833
13	6.1	27.9	6.9	27.2	127	6.3	26.8	295	7.0	25.3	693
17	5.2	31.0	6.5	30.2	107	5.5	30.8	223	7.1	28.4	625
20	4.9	34.6	5.3	34.1	78	4.9	34.3	178	5.4	31.0	432
24	4.6	36.9	5.0	36.4	68	4.5	36.8	152	5.3	33.3	396
28	3.9	39.4	4.3	39.0	55	4.0	39.1	128	4.3	36.0	297
32	3.8	41.2	3.9	41.3	48	3.8	41.6	114	4.3	38.1	285
36	3.8	42.4	4.0	42.2	47	3.9	42.4	114	3.5	40.7	213
40	4.5	43.0	4.5	43.3	52	3.9	43.4	113	4.3	41.2	258
44	3.7	45.3	3.6	45.3	40	3.6	44.4	101			
48	3.7	46.1	3.9	45.7	42	4.5	45.8	121	4.0	43.8	231
52	4.1	46.0	4.2	45.4	47	4.1	45.5	113	4.5	43.3	261
56	3.9	48.0	3.8	48.1	39	3.9	47.6	103	3.9	44.9	219
60	4.3	48.5	3.9	48.7	40	4.1	48.0	106	4.7	46.5	250
65	4.0	49.2	4.9	49.9	49	4.4	48.8	113	4.7	46.6	253
68	3.9	49.8	3.8	50.0	38	3.7	50.0	93	4.7	47.6	249
72	4.0	50.0	4.0	50.3	39	4.1	50.8	100	4.0	47.9	209
76	4.1	49.3	4.2	49.3	43	4.2	49.0	107	4.3	46.6	232
80	4.0	48.9	4.5	49.1	46	4.2	48.7	108	5.0	45.3	273
84	4.4	49.1	4.6	49.2	46	4.6	48.2	121	4.8	43.3	279
88	5.1	48.3	5.1	48.1	53	5.5	46.2	149	5.1	41.7	306
92	4.3	48.0	4.5	47.4	47	4.8	45.9	131	5.0	41.7	297
96	5.1	45.7	4.8	45.9	53	5.3	44.2	151	4.7	39.3	300
100	4.6	45.7	4.7	44.7	52	5.4	43.0	156	5.1	40.4	316
104	5.5	44.7	5.0	45.0	56	5.8	44.6	163	5.0	41.4	303
Mean for weeks											
1-13	6.0	22.5	6.8	22.4	154	6.5	22.2	371	7.1	21.9	820
14-52	4.2	40.6	4.5	40.3	58	4.3	40.4	136	4.7	37.3	333
53-104	4.4	48.1	4.4	48.1	46	4.6	47.3	123	4.7	44.1	268

[a] Grams of water consumed per animal per day
[b] Milligrams of barium chloride dihydrate consumed per kilogram body weight per day

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

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

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

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

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

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

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

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

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	22.40 ± 0.63	21.6 – 23.0	24
Crude Fat (% by weight)	5.49 ± 0.26	4.7 – 6.0	24
Crude Fiber (% by weight)	3.38 ± 0.25	2.7 – 4.0	24
Ash (% by weight)	6.55 ± 0.31	6.1 – 7.1	24
Amino Acids (% of total diet)			
Arginine	1.308 ± 0.606	1.210 – 1.390	8
Cystine	0.306 ± 0.084	0.181 – 0.400	8
Glycine	1.150 ± 0.047	1.060 – 1.210	8
Histidine	0.576 ± 0.024	0.531 – 0.607	8
Isoleucine	0.917 ± 0.029	0.881 – 0.944	8
Leucine	1.946 ± 0.055	1.850 – 2.040	8
Lysine	1.270 ± 0.058	1.200 – 1.370	8
Methionine	0.448 ± 0.128	0.306 – 0.699	8
Phenylalanine	0.987 ± 0.140	0.665 – 1.110	8
Threonine	0.877 ± 0.042	0.824 – 0.940	8
Tryptophan	0.236 ± 0.176	0.107 – 0.671	8
Tyrosine	0.676 ± 0.105	0.564 – 0.794	8
Valine	1.103 ± 0.040	1.050 – 1.170	8
Essential Fatty Acids (% of total diet)			
Linoleic	2.393 ± 0.258	1.830 – 2.570	7
Linolenic	0.280 ± 0.040	0.210 – 0.320	7
Vitamins			
Vitamin A (IU/kg)	7,514 ± 2,372	4,700 – 13,000	24
Vitamin D (IU/kg)	4,450 ± 1,382	3,000 – 6,300	4
α-Tocopherol (ppm)	37.95 ± 9.406	22.5 – 48.9	8
Thiamine (ppm)	20.25 ± 2.51	15.0 – 26.0	24
Riboflavin (ppm)	7.92 ± 0.87	6.10 – 9.00	8
Niacin (ppm)	103.4 ± 26.59	65.0 – 150.0	8
Pantothenic acid (ppm)	29.54 ± 3.60	23.0 – 34.0	8
Pyridoxine (ppm)	9.55 ± 3.48	5.60 – 14.0	8
Folic acid (ppm)	2.25 ± 0.73	1.80 – 3.70	8
Biotin (ppm)	0.254 ± 0.042	0.19 – 0.32	8
Vitamin B_{12} (ppb)	38.45 ± 22.01	10.6 – 65.0	8
Choline (ppm)	3,089 ± 328.69	2,400 – 3,430	8
Minerals			
Calcium (%)	1.19 ± 0.11	1.00 – 1.40	24
Phosphorus (%)	0.92 ± 0.06	0.73 – 1.00	24
Potassium (%)	0.883 ± 0.078	0.772 – 0.971	6
Chloride (%)	0.526 ± 0.092	0.380 – 0.635	8
Sodium (%)	0.313 ± 0.390	0.258 – 0.371	8
Magnesium (%)	0.168 ± 0.010	0.151 – 0.181	8
Sulfur (%)	0.280 ± 0.064	0.208 – 0.420	8
Iron (ppm)	360.5 ± 100	255.0 – 523.0	8
Manganese (ppm)	92.0 ± 6.01	81.70 – 99.40	8
Zinc (ppm)	54.72 ± 5.67	46.10 – 64.50	8
Copper (ppm)	11.06 ± 2.50	8.090 – 15.39	8
Iodine (ppm)	3.37 ± 0.92	1.52 – 4.13	6
Chromium (ppm)	1.79 ± 0.36	1.04 – 2.09	8
Cobalt (ppm)	0.681 ± 0.14	0.490 – 0.780	4

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

	Mean ± Standard Deviation[a]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.59 ± 0.30	0.14 – 1.07	24
Cadmium (ppm)	0.10 ± 0.02	0.10 – 0.20	24
Lead (ppm)	0.37 ± 0.25	0.05 – 0.96	24
Mercury (ppm)	<0.05 ± 0.01		24
Selenium (ppm)	0.39 ± 0.06	0.30 – 0.58	24
Aflatoxins (ppb)	<5.0		24
Nitrate nitrogen(ppm)[b]	22.17 ± 9.24	12.0 – 41.0	24
Nitrite nitrogen(ppm)[b]	0.45 ± 0.73	<0.10 – 2.60	24
BHA(ppm)[c]	2.58 ± 1.06	<2.00 – 5.00	24
BHT(ppm)[c]	1.33 ± 0.82	<1.00 – 4.00	24
Aerobic plate count (CFU/g)[d]	30,283 ± 30,188	3,100 – 11,000	24
Coliform (MPN/g)[e]	4.41 ± 4.30	<3.00 – 23	24
E. coli (MPN/g)	3.00		24
Total nitrosoamines (ppb)[f]	7.99 ± 2.90	2.80 – 12.00	24
N-Nitrosodimethylamine (ppb)[f]	6.64 ± 2.60	2.80 – 12.00	24
N-Nitrosopyrrolidine (ppb)[f]	1.34 ± 0.88	1.00 – 4.50	24
Pesticides			
α-BHC[g]	<0.01		24
β-BHC	<0.02		24
γ-BHC	<0.01		24
δ-BHC	<0.01		24
Heptachlor	<0.01		24
Aldrin	<0.01		24
Heptachlor epoxide	<0.01		24
DDE	<0.01		24
DDD	<0.01		24
DDT	<0.01		24
HCB	<0.01		24
Mirex	<0.01		24
Methoxychlor	<0.05		24
Dieldrin	<0.01		24
Endrin	<0.01		24
Telodrin	<0.01		24
Chlordane	<0.05		24
Toxaphene	<0.1		24
Estimated PCBs	<0.2		24
Ronnel	<0.01		24
Ethion	<0.02		24
Trithion	<0.05		24
Diazinon	<0.1		24
Methyl parathion	<0.02		24
Ethyl parathion	<0.02		24
Malathion[h]	0.15 ± 0.16	0.05 – 0.60	24
Endosulfan I	<0.01		24
Endosulfan II	<0.01		24
Endosulfan sulfate	<0.03		24

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

[a] For values less than the limit of detection, the detection limit is given for the mean.
[b] Sources of contamination: alfalfa, grains, and fish meal
[c] Sources of contamination: soy oil and fish meal
[d] CFU = colony forming unit
[e] MPN = most probable number
[f] All values were correct for % recovery.
[g] BHC = hexachlorocyclohexane or benzene hexachloride
[h] One lot contained more than 0.05 ppm.

APPENDIX M
SENTINEL ANIMAL PROGRAM

SENTINEL ANIMAL PROGRAM

METHODS

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

Rats

During the 2-year study, 15 male and 15 female F344/N rats were maintained with the study animals to serve as sentinel animals. At 6, 12, and 18 months, five male and five female rats were bled from the external jugular vein. Additional blood was collected from the tail artery of these or other animals at 5, 7, 8 and 19 months to better evaluate the virological burden of this study. Samples for viral screening at 24 months were collected from five control male and female rats. Blood collected from each animal was allowed to clot and the sera were separated, cooled on ice, and shipped to Microbiological Associates, Inc. (Bethesda, MD) for determination of antibody titers. The following tests were performed:

Method of Analysis	Time of Analysis
ELISA	
Mycoplasma arthritidis	5, 6, 7, 8, and 24 months
Mycoplasma pulmonis	5, 6, 7, 8, and 24 months
PVM (pneumonia virus of mice)	5, 6, 7, 8, 12, 18, 19, and 24 months
RCV/SDA (rat coronavirus/sialodacryoadenitis virus)	5, 6, 7, 8, 12, 18, 19, and 24 months
Sendai	5, 6, 7, 8, 12, 18, 19, and 24 months
Hemagglutination Inhibition	
H-1 (Toolan's H-1 virus)	5, 6, 7, 8, 12, 18, 19, and 24 months
KRV (Kilham rat virus)	5, 6, 7, 8, 12, 18, 19, and 24 months
Immunofluorescence Assay	
Sendai	5 months

Mice

Fifteen male and 15 female B6C3F$_1$ mice were randomly selected to serve as sentinel animals during the 2-year study. Five male and five female mice were bled from the external jugular vein at 6, 12, and 20 months. Additional blood was collected from the tail artery of some animals at 6 and 7 months to better evaluate the virological burden of this study. Samples for viral screening at 24 months were collected from five control male and female mice. Blood collected from each animal was allowed to clot and the sera were separated, cooled on ice, and shipped to Microbiological Associates, Inc. (Bethesda, MD) for determination of the virus antibody titers. The following tests were performed:

Method of Analysis	Time of Analysis
Complement Fixation	
LCM (lymphocytic choriomeningitis virus)	6, 7, and 12 months
ELISA	
CARB (cilia-associated respiratory bacillus)	24 months
Ectromelia virus	6, 7, 12, 20, and 24 months
GDV II (mouse encephalomyelitis virus)	6, 7, 12, 20, and 24 months
LCM	20 and 24 months
M. arthritidis	6, 7, and 24 months
M. pulmonis	6, 7, and 24 months
MHV (mouse hepatitis virus)	6, 7, 12, 20, and 24 months
Mouse adenoma virus	6, 7, 12, 20, and 24 months
MVM (minute virus of mice)	20 months
PVM	6, 7, 12, 20, and 24 months
Reovirus 3	6, 7, 12, 20, and 24 months
Sendai	6, 7, 12, 20, and 24 months
Hemagglutination Inhibition	
K (papovavirus)	6, 7, 12, 20, and 24 months
MVM	6, 7, and 12 months
Polyoma virus	6, 7, 12, 20, and 24 months
Immunofluorescence Assay	
EDIM (Epizootic diarrhea of infant mice)	6, 7, 12, 20, and 24 months
Reovirus 3	7 months

All test results were negative.

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TR No.	CHEMICAL
201	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Dermal)
206	1,2-Dibromo-3-chloropropane
207	Cytembena
208	FD & C Yellow No. 6
209	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Gavage)
210	1,2-Dibromoethane
211	C.I. Acid Orange 10
212	Di(2-ethylhexyl)adipate
213	Butyl Benzyl Phthalate
214	Caprolactam
215	Bisphenol A
216	11-Aminoundecanoic Acid
217	Di(2-Ethylhexyl)phthalate
219	2,6-Dichloro-p-phenylenediamine
220	C.I. Acid Red 14
221	Locust Bean Gum
222	C.I. Disperse Yellow 3
223	Eugenol
224	Tara Gum
225	D & C Red No. 9
226	C.I. Solvent Yellow 14
227	Gum Arabic
228	Vinylidene Chloride
229	Guar Gum
230	Agar
231	Stannous Chloride
232	Pentachloroethane
233	2-Biphenylamine Hydrochloride
234	Allyl Isothiocyanate
235	Zearalenone
236	*D*-Mannitol
237	1,1,1,2-Tetrachloroethane
238	Ziram
239	Bis(2-chloro-1-Methylethyl)ether
240	Propyl Gallate
242	Diallyl Phthalate (Mice)
243	Trichlorethylene (Rats and Mice)
244	Polybrominated Biphenyl Mixture
245	Melamine
246	Chrysotile Asbestos (Hamsters)
247	L-Ascorbic Acid
248	4,4′-Methylenedianiline Dihydrochloride
249	Amosite Asbestos (Hamsters)
250	Benzyl Acetate
251	2,4- & 2,6-Toluene Diisocyanate
252	Geranyl Acetate
253	Allyl Isovalerate
254	Dichloromethane (Methylene Chloride)
255	1,2-Dichlorobenzene
257	Diglycidyl Resorcinol Ether
259	Ethyl Acrylate
261	Chlorobenzene
263	1,2-Dichloropropane
266	Monuron
267	1,2-Propylene Oxide
269	Telone II® (1,3-Dichloropropene)
271	HC Blue No. 1
272	Propylene
273	Trichloroethylene (Four Rat Strains)
274	Tris(2-ethylhexyl)phosphate
275	2-Chloroethanol
276	8-Hydroxyquinoline
277	Tremolite
278	2,6-Xylidine
279	Amosite Asbestos
280	Crocidolite Asbestos
281	HC Red No. 3
282	Chlorodibromomethane
284	Diallylphthalate (Rats)
285	C.I. Basic Red 9 Monohydrochloride
287	Dimethyl Hydrogen Phosphite
288	1,3-Butadiene
289	Benzene
291	Isophorone
293	HC Blue No. 2
294	Chlorinated Trisodium Phosphate
295	Chrysotile Asbestos (Rats)
296	Tetrakis(hydroxymethyl) phosphonium Sulfate & Tetrakis(hydroxymethyl) phosponium Chloride
298	Dimethyl Morpholinophosphoramidate
299	C.I. Disperse Blue 1
300	3-Chloro-2-methylpropene
301	*o*-Phenylphenol
303	4-Vinylcyclohexene
304	Chlorendic Acid
305	Chlorinated Paraffins (C_{23}, 43% chlorine)
306	Dichloromethane (Methylene Chloride)
307	Ephedrine Sulfate
308	Chlorinated Pariffins (C_{12}, 60% chlorine)
309	Decabromodiphenyl Oxide
310	Marine Diesel Fuel and JP-5 Navy Fuel
311	Tetrachloroethylene (Inhalation)
312	*n*-Butyl Chloride
313	Mirex
314	Methyl Methacrylate
315	Oxytetracycline Hydrochloride
316	1-Chloro-2-methylpropene
317	Chlorpheniramine Maleate
318	Ampicillin Trihydrate
319	1,4-Dichlorobenzene
320	Rotenone
321	Bromodichloromethane
322	Phenylephrine Hydrochloride
323	Dimethyl Methylphosphonate
324	Boric Acid
325	Pentachloronitrobenzene
326	Ethylene Oxide
327	Xylenes (Mixed)
328	Methyl Carbamate
329	1,2-Epoxybutane
330	4-Hexylresorcinol
331	Malonaldehyde, Sodium Salt
332	2-Mercaptobenzothiazole
333	*N*-Phenyl-2-naphthylamine
334	2-Amino-5-nitrophenol
335	C.I. Acid Orange 3

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TR No.	CHEMICAL
336	Penicillin VK
337	Nitrofurazone
338	Erythromycin Stearate
339	2-Amino-4-nitrophenol
340	Iodinated Glycerol
341	Nitrofurantoin
342	Dichlorvos
343	Benzyl Alcohol
344	Tetracycline Hydrochloride
345	Roxarsone
346	Chloroethane
347	D-Limonene
348	α-Methyldopa Sesquihydrate
349	Pentachlorophenol
350	Tribromomethane
351	*p*-Chloroaniline Hydrochloride
352	N-Methylolacrylamide
353	2,4-Dichlorophenol
354	Dimethoxane
355	Diphenhydramine Hydrochloride
356	Furosemide
357	Hydrochlorothiazide
358	Ochratoxin A
359	8-Methoxypsoralen
360	N,N-Dimethylaniline
361	Hexachloroethane
362	4-Vinyl-1-Cyclohexene Diepoxide
363	Bromoethane (Ethyl Bromide)
364	Rhodamine 6G (C.I. Basic Red 1)
365	Pentaerythritol Tetranitrate
366	Hydroquinone
367	Phenylbutazone
368	Nalidixic Acid
369	Alpha-Methylbenzyl Alcohol
370	Benzofuran
371	Toluene
372	3,3-Dimethoxybenzidine Dihydrochloride
373	Succinic Anhydride
374	Glycidol
375	Vinyl Toluene
376	Allyl Glycidyl Ether
377	*o*-Chlorobenzalmalononitrile
378	Benzaldehyde
379	2-Chloroacetophenone
380	Epinephrine Hydrochloride
381	*d*-Carvone
382	Furfural

TR No.	CHEMICAL
384	1,2,3-Trichloropropane
385	Methyl Bromide
386	Tetranitromethane
387	Amphetamine Sulfate
388	Ethylene Thiourea
389	Sodium Azide
390	3,3′-Dimethylbenzidine Dihydrochloride
391	Tris(2-chloroethyl) Phosphate
392	Chlorinated Water and Chloraminated Water
393	Sodium Fluoride
394	Acetaminophen
395	Probenecid
396	Monochloroacetic Acid
397	C.I. Direct Blue 15
398	Polybrominated Biphenyls
399	Titanocene Dichloride
400	2,3-Dibromo-1-propanol
401	2,4-Diaminophenol Dihydrochloride
402	Furan
403	Resorcinol
404	5,5-Diphenylhydantoin
405	C.I. Acid Red 114
406	γ-Butyrolactone
407	C.I. Pigment Red 3
408	Mercuric Chloride
409	Quercetin
410	Naphthalene
411	C.I. Pigment Red 23
412	4,4-Diamino-2,2-stilbenedisulfonic Acid
413	Ethylene Glycol
414	Pentachloroanisole
415	Polysorbate 80
416	*o*-Nitroanisole
417	*p*-Nitrophenol
418	*p*-Nitroaniline
419	HC Hellow 4
420	Triamterene
421	Talc
422	Coumarin
423	Dihydrocoumarin
424	*o*-Benzyl-*p*-chlorophenol
425	Promethazine Hydrochloride
428	Manganese (II) Sulfate Monohydrate
427	Turmeric Oleoresin
431	Benzyl Acetate
434	1,3-Butadiene
443	Oxazepam

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