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TOXICOLOGY AND CARCINOGENESIS STUDIES OF BROMOETHANE

(ETHYL BROMIDE)

(CAS NO. 74-96-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES OF BROMOETHANE

(ETHYL BROMIDE)

(CAS NO. 74-96-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
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APPENDIXES

CH_3CH_2Br

BROMOETHANE

(ETHYL BROMIDE)

CAS No. 74-96-4

C_2H_5Br Molecular weight 109.0

Synonyms: monobromoethane; bromic ether; hydrobromic ether

ABSTRACT

Bromoethane is an alkylating agent used primarily as a chemical intermediate in various organic syntheses. In toxicology and carcinogenesis studies, groups of F344/N rats and $B6C3F_1$ mice of each sex received whole-body exposure to bromoethane (greater than 98% pure) once for 4 hours or for 6 hours per day, 5 days per week, for 14 days, 14 weeks, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium* and Chinese hamster ovary (CHO) cells.

Single-Exposure, Fourteen-Day, and Fourteen-Week Studies: Single-exposure inhalation studies were conducted in rats and mice at target concentrations of 625, 1,250, 2,500, 5,000, or 10,000 ppm bromoethane. All rats exposed to 10,000 ppm bromoethane and 3/5 female rats exposed to 5,000 ppm died before the end of the single-exposure studies. All mice exposed to 5,000 or 10,000 ppm bromoethane and 2/5 female mice exposed to 1,250 ppm died before the end of the studies.

Fourteen-day inhalation studies were conducted in rats and mice at target concentrations of 0, 250, 500, 1,000, 2,000, or 4,000 ppm bromoethane. All rats and mice exposed to 2,000 or 4,000 ppm died before the end of the 14-day studies. Final mean body weights of exposed and control rats were similar.

Fourteen-week inhalation studies were conducted in rats and mice at target concentrations of 0, 100, 200, 400, 800, or 1,600 ppm bromoethane. Four of 10 male and 2/10 female rats exposed to 1,600 ppm died before the end of the 14-week studies. The final mean body weights of rats exposed to 1,600 ppm were lower than the initial mean body weights. Compound-related lesions observed in rats at 1,600 ppm, but not at lower concentrations, included minimal atrophy of the thigh muscle, minimal-to-moderate multifocal mineralization in the cerebellum of the brain, minimal-to-severe hemosiderosis of the spleen, marked atrophy of the testis, and minimal-to-mild atrophy of the uterus. The effects in the testis and uterus are probably due to chemical-related loss in body weight during the studies.

In mice, compound-related deaths included 3/10 male and 1/10 female mice exposed to 1,600 ppm, 1/9 males exposed to 800 ppm, and 1/10 males exposed to 400 ppm. The final mean body weights of male and female mice exposed to 1,600 ppm were about 15% lower than those of controls. Compound-related effects included atrophy of the uterus and involution of the ovary in females exposed to 1,600 ppm. Atrophy of the skeletal muscle was observed in males and females exposed to 1,600 ppm bromoethane.

Based on these results, 2-year studies were conducted by exposing groups of 49 or 50 rats or mice of each sex to bromoethane at 0, 100, 200, or 400 ppm, 6 hours per day, 5 days per week.

Body Weight and Survival in the Two-Year Studies: Mean body weights of exposed and control rats were generally similar throughout the studies. No significant differences in survival were observed

between any groups of male rats (control, 17/49; 100 ppm, 26/50; 200 ppm, 27/50; 400 ppm, 21/50); survival of the 100-ppm group of female rats was greater than that of controls (19/50; 29/50; 24/49; 23/50), and the number of control and 400-ppm male rats and control female rats surviving to the end of the studies was low.

Mean body weights of the 400-ppm group of male mice were up to 9% lower than those of controls throughout the study. Mean body weights of the 400-ppm group of female mice were generally 6%-16% lower than those of controls after week 29. No differences in survival were observed between any group of male mice (35/50; 37/50; 30/50; 34/50). The survival of the 400-ppm group of female mice was lower than that of controls at the end of the study (36/50; 37/50; 37/49; 23/49).

Nonneoplastic and Neoplastic Effects in the Two-Year Studies: The incidences of pheochromocytomas or malignant pheochromocytomas (combined) of the adrenal medulla were increased in exposed male rats (control, 8/40; 100 ppm, 23/45; 200 ppm, 18/46; 400 ppm, 21/46).

Granular cell neoplasms of the brain were seen in exposed male rats but not in controls (0/49; 3/50; 1/50; 1/50). A glioma, an astrocytoma, or an oligodendroglioma was seen in 3/50 male rats exposed to 100 ppm. Gliomas were not observed in control female rats, but they occurred in exposed female rats with a significant positive trend (0/50; 1/50; 1/48; 3/50). The historical incidence of granular cell tumors in male F344/N rat chamber controls at the study laboratory is 0/297. The incidences of gliomas in the exposed female groups were not significantly greater than that in the controls and were within the historical incidence range for glial cell neoplasms for untreated controls in NTP studies (mean: 23/1,969, 1%; range: 0/50-3/50), but they exceeded the historical incidence range for chamber controls at the study laboratory (mean: 1/297, 0.3%; range: 0/50-1/50).

Alveolar epithelial hyperplasia was increased in rats exposed to 400 ppm bromoethane (male: 3/48; 7/49; 7/48; 18/48; female: 5/50; 4/48; 5/47; 10/49). Alveolar/bronchiolar adenomas or carcinomas (combined) were seen in four male rats exposed to 200 ppm and in one exposed to 400 ppm. Alveolar/bronchiolar adenomas were observed in 3/49 female rats at 400 ppm but not at lower concentrations or in controls. The incidences in exposed male and female rats were not significantly greater than those in controls; however, the historical incidence in rat chamber controls for alveolar/bronchiolar adenomas or carcinomas (combined) at the study laboratory is 6/299 (2%) for males and 4/297 (1.3%) for females.

The incidences of epithelial hyperplasia and squamous metaplasia of the nasal cavity were increased in rats exposed to 400 ppm. The incidence of suppurative inflammation of the nasal cavity was increased in exposed male rats, and the incidences of suppurative inflammation of the larynx and metaplasia of the olfactory sensory epithelium were increased in exposed male and female rats. An adenoma of the nose was seen in one 400-ppm male rat and in one 400-ppm female mouse.

Suppurative inflammation and dilatation of the salivary gland ducts were observed at increased incidences in the 200- and 400-ppm groups of female rats. Animals were found to be positive for rat coronavirus/sialodacryoadenitis virus antibodies.

The incidence of mammary gland neoplasms was significantly lower in female rats at 400 ppm than in controls (18/50; 15/50; 10/48; 7/50).

Adenomas (0/50; 1/50; 1/47; 6/48), adenocarcinomas (0/50; 2/50; 3/47; 19/48), and squamous cell carcinomas (0/50; 1/50; 1/47; 3/48) of the uterus occurred in exposed female mice and not in control mice.

The incidence of alveolar/bronchiolar neoplasms was greater in male mice at 400 ppm than in controls (adenomas or carcinomas, combined: 7/50; 6/50; 12/50; 15/50). Acute/chronic inflammation of the lung was observed at increased incidences in female mice at 200 and 400 ppm.

Genetic Toxicology: Bromoethane, tested in the closed environment of a desiccator, was mutagenic in *S. typhimurium* strain TA100 with and without exogenous metabolic activation; it was not mutagenic in strain TA98. In cultured CHO cells, bromoethane induced sister chromatid exchanges (SCEs) but not chromosomal aberrations in both the presence and absence of exogenous metabolic activation.

Conclusions: Under the conditions of these 2-year inhalation studies, there was *some evidence of carcinogenic activity** of bromoethane for male F344/N rats, as indicated by increased incidences of pheochromocytomas of the adrenal gland; neoplasms of the brain and lung may also have been related to exposure to bromoethane. For female F344/N rats, there was *equivocal evidence of carcinogenic activity*, as indicated by marginally increased incidences of neoplasms of the brain and lung. For male $B6C3F_1$ mice, there was *equivocal evidence of carcinogenic activity*, based on marginally increased incidences of neoplasms of the lung. There was *clear evidence of carcinogenic activity* for female $B6C3F_1$ mice, as indicated by neoplasms of the uterus.

*Explanation of Levels of Evidence of Carcinogenic Activity is on page 7.
A summary of the Peer Review comments and the public discussion on this Technical Report appears on page 10.

SUMMARY OF THE TWO-YEAR INHALATION AND GENETIC TOXICOLOGY STUDIES OF BROMOETHANE

Male F344/N Rats	Female F344/N Rats	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Exposure concentrations			
0, 100, 200, or 400 ppm bromoethane, 6 h/d, 5 d/wk	0, 100, 200, or 400 ppm bromoethane, 6 h/d, 5 d/wk	0, 100, 200, or 400 ppm bromoethane, 6 h/d, 5 d/wk	0, 100, 200, or 400 ppm bromoethane, 6 h/d, 5 d/wk
Body weights in the 2-year study			
Exposed and control similar	Exposed and control generally similar	Exposed and control generally similar	400-ppm group lower than controls
Survival rates in the 2-year study			
17/49; 26/50; 27/50; 21/50	19/50; 29/50; 24/49; 23/50	35/50; 37/50; 30/50; 34/50	36/50; 37/50; 37/49; 23/49
Nonneoplastic effects			
Alveolar and nasal epithelial hyperplasia	Alveolar and nasal epithelial hyperplasia	None	None
Neoplastic effects			
Adrenal gland: pheochromocytomas (8/40; 23/45; 18/46; 21/46); brain: granular cell tumors (0/49; 3/50; 1/50; 1/50); glial cell tumors (0/49, 3/50, 0/50, 0/50); lung: alveolar/bronchiolar adenomas or carcinomas (combined) (0/48; 0/49; 4/48; 1/48)	Brain: gliomas (0/50; 1/50; 1/48; 3/50); lung: alveolar/bronchiolar adenomas (0/50; 0/48; 0/47; 3/49)	Lung: alveolar/bronchiolar adenomas or carcinomas (combined) (7/50; 6/50; 12/50; 15/50)	Uterus: adenomas, adenocarcinomas, or squamous cell carcinomas (combined) (0/50; 4/50; 5/47; 27/48)
Level of evidence of carcinogenic activity			
Some	Equivocal	Equivocal	Clear
Genetic toxicology			
Salmonella (gene mutation)	**CHO Cells in Vitro**		
	SCE	**Aberration**	
Positive with and without S9 in vapor assay	Positive with and without S9	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 because of major flaws cannot be evaluated ("Inadequate Study"). These categories of interpretative conclusions were first adopted in June 1983 and then revised in March 1986 for use in the Technical Reports series to incorporate more specifically the concept of actual weight of evidence of carcinogenic activity. For each separate experiment (male rats, female rats, male mice, female mice), one of the following quintet is selected to describe the findings. These categories refer to the strength of the experimental evidence and not to either potency or mechanism.

- **Clear Evidence of Carcinogenic Activity** is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.

- **Some Evidence of Carcinogenic Activity** is demonstrated by studies that are interpreted as showing a chemically 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 chemically related.

- **No Evidence of Carcinogenic Activity** is demonstrated by studies that are interpreted as showing no chemically 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. This should allow for incorporation of scientific experience and current understanding of long-term carcinogenesis studies in laboratory animals, especially for those evaluations that may be on the borderline between two adjacent levels. These considerations should include:

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

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Bromoethane is based on 14-week studies that began in December 1980 and ended in March 1981 and on 2-year studies that began in December 1981 and ended in December 1983 at Battelle Pacific Northwest Laboratories (Richland, WA).

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The members of the Peer Review Panel who evaluated the draft Technical Report on bromoethane on October 3, 1988, are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, Panel members have five major responsibilities: (a) to ascertain that all relevant literature data have been adequately cited and interpreted, (b) to determine if the design and conditions of the NTP studies were appropriate, (c) to ensure that the Technical Report presents the experimental results and conclusions fully and clearly, (d) to judge the significance of the experimental results by scientific criteria, and (e) to assess the evaluation of the evidence of carcinogenicity and other observed toxic responses.

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SUMMARY OF PEER REVIEW COMMENTS ON THE TOXICOLOGY AND CARCINOGENESIS STUDIES OF BROMOETHANE

On October 3, 1988, the draft Technical Report on the toxicology and carcinogenesis studies of bromoethane received public review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting was held at the National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC.

Dr. J.H. Roycroft, NIEHS, began the discussion by reviewing the experimental design, results, and proposed conclusions (equivocal evidence of carcinogenic activity for male and female rats and male mice and clear evidence of carcinogenic activity for female mice).

Dr. Mirer, a principal reviewer, agreed with the conclusions for female rats and for male and female mice. He proposed that the conclusion for male rats be changed to some evidence of carcinogenic activity, based on the increased incidence of pheochromocytomas. He thought that there should be some discussion on the significance of the nonmalignant pheochromocytomas, including whether there was evidence of progression in other studies. Dr. Roycroft commented that pheochromocytomas do progress; however, they are late appearing and not considered life threatening, and, in these studies, most of the tumors were small and not seen at necropsy. Dr. Mirer said that it appeared that rats of each sex and male mice could have been given higher doses.

Dr. Newberne, the second principal reviewer, agreed with the proposed conclusions.

Dr. Gallo suggested that the increased incidences in pheochromocytomas and of uncommon tumors of the lung and brain were supportive of some evidence of carcinogenic activity in male rats. Dr. Perera noted the increased incidence in brain neoplasms in female rats and commented on similar increases in female rats in a companion study of chloroethane, asking why the analogous findings would not lend support to a conclusion of some evidence of carcinogenic activity in female rats. Dr. Roycroft responded that in both studies, the increases were not statistically significant, either from pairwise comparisons or from a trend test. Additionally, there were no supporting increases in hyperplasia. However, these are uncommon neoplasms.

Dr. Mirer moved that the conclusion for male rats be changed from equivocal evidence of carcinogenic activity to some evidence of carcinogenic activity, based on increased incidences of pheochromocytomas of the adrenal gland. Dr. Gallo seconded the motion, which was approved by six affirmative votes (Drs. Gallo, Gold, Klaassen, McKnight, Mirer, and Newberne) to two negative votes (Drs. Garman and Popp). Dr. Mirer moved that the conclusion for female rats be accepted as written, equivocal evidence of carcinogenic activity. Dr. Gold seconded the motion, which was approved unanimously by the Panel. Dr. Mirer moved that the conclusion for male mice be accepted as written, equivocal evidence of carcinogenic activity. Dr. Gallo seconded the motion, which was approved unanimously by the Panel. Dr. Mirer moved that the conclusion for female mice be accepted as written, clear evidence of carcinogenic activity. Dr. Gold seconded the motion, which was approved unanimously by the Panel.

I. INTRODUCTION

Properties
Use and Production
Human Exposure and Occurrence
Animal Toxicity
Genetic Toxicology
Study Rationale

I. INTRODUCTION

CH_3CH_2Br

BROMOETHANE

(ETHYL BROMIDE)

CAS No. 74-96-4

C_2H_5Br Molecular weight 109.0

Synonyms: monobromoethane; bromic ether; hydrobromic ether

Properties

Bromoethane is a colorless, volatile, flammable liquid. When exposed to air and light, it turns yellow. It has an ethereal odor and somewhat burning taste. Bromoethane has a specific gravity of 1.4505 between 4° and 25° C, a boiling point of 38.4° C, a melting point of −119° C, and a vapor pressure of 475 mm mercury at 25° C. It is 0.91% (w/w) soluble in water at 20° C and is miscible with ethanol, ethyl ether, chloroform, and other organic solvents. It has a flash point of −20° C (closed cup). The autoignition temperature is 511° C. The flammable limits in air are between 6.75% and 11.25%. Although bromoethane is relatively stable, when heated to decomposition it emits highly toxic fumes of bromine and hydrobromide; it can react with oxidizing materials (ITII, 1979; Sittig, 1979; Torkelson and Rowe, 1981; Merck, 1983; Sax, 1984).

Use and Production

Bromoethane is produced by the reaction of either hydrogen or potassium bromide with cold ethanol or with ethylene and sulfuric acid (Hawley, 1977; Sittig, 1979; Merck, 1983). It is commercially available at greater than 99% purity. Production from two U.S. manufacturers was estimated at 163.5 million pounds in 1986 (USITC, 1987); no recent import and export information was available in the literature.

Bromoethane is an alkylating agent primarily used as a chemical intermediate in organic synthesis, in the manufacture of pharmaceuticals, and for the ethylation of gasoline. To a lesser extent, it has been used as a fruit and grain fumigant, refrigerant, and solvent. Although proposed occasionally as a general anesthetic in the earlier part of this century, it has not been used to any extent for this purpose (Sayers et al., 1929; Abreu et al., 1939; ITII, 1979; Sittig, 1979; Torkelson and Rowe, 1981; Merck, 1983).

Human Exposure and Occurrence

Since the major use of bromoethane is in organic synthesis as an ethylating agent, the predominant occupational exposure would be associated with the initial production of bromoethane and its subsequent use in the synthesis of various organic chemicals. Data in the literature on actual workplace exposure to bromoethane are limited. In 1974, the National Institute for Occupational Safety and Health (NIOSH) estimated that approximately 5,000 people were exposed occupationally to bromoethane (Fed. Regist., 1974). However, a National Occupational Hazard Survey conducted by NIOSH from 1972 to 1974 estimated that 196 workers were potentially exposed to bromoethane in the workplace (NIOSH, 1976). This estimate was derived only from observation of the actual use of bromoethane. There are no health effects data in the literature associated with workplace exposure to bromoethane. The major industrial hazards appear to be due to fire. The Occupational Safety and Health Administration and American Conference of Governmental Industrial Hygienists recommended a threshold limit value (TLV) of 200 ppm (890 mg/m^3) (Fed. Regist., 1974; ACGIH, 1986).

A number of references describe typical human health effects associated with short-term exposure to bromoethane (ITII, 1979; Sittig, 1979; Torkelson and Rowe, 1981; Sax, 1984).

Consistent with its anesthetic and narcotic properties, bromoethane causes central nervous system depression, headaches, salivation, nausea, dizziness, muscular incoordination, and unconsciousness. In addition, it is irritating to the eyes, skin, and respiratory tract. Acute respiratory congestion and edema as well as liver and kidney damage (jaundice, hematuria, albuminuria, and fatty degeneration of liver and renal tissue) have been reported. Because of its irritant action on the respiratory tract and its tendency to cause liver and kidney damage, its use as a general anesthetic has been considered inadvisable. In addition, several deaths have been attributed to its use as a general anesthetic. Although epidemiologic studies have not been reported, skin irritation is reported to be associated with long-term exposure to bromoethane.

Animal Toxicity

Very few studies of bromoethane in animals are reported in the literature. All were reported over 15 years ago, and most were conducted in Russia. Because of inadequate reporting of the experimental design, the Russian papers will not be discussed.

Sayers et al. (1929) exposed guinea pigs to bromoethane at various concentrations ranging from 0.17% to 18% for periods of 5 minutes to 13.5 hours. Continuous exposure to bromoethane at 18% resulted in the deaths of 3/3 guinea pigs within 30 minutes, whereas a 30-minute exposure at 2.4% resulted in general unsteadiness and death of 3/6 by 18 hours. Animals dying before 18 hours had congested and hemorrhagic lungs; the livers were congested and moderately degenerated. Animals surviving for 18 hours were similar to controls. One of six animals exposed to 0.17% bromoethane for 13.5 hours died. Necropsy findings were similar to those reported previously, except that there was moderate degeneration in the spleen, pancreas, and kidney. The five animals surviving to day 8 exhibited similar findings upon necropsy. However, when guinea pigs were exposed to 0.32% bromoethane for 9 hours, 5/6 died before day 5. Necropsy findings similar to those reported for the animals exposed to 0.17% bromoethane for 13.5 hours were observed, except that heart muscle was also degenerated. In general, animals exposed to bromoethane at concentrations greater than 1.2% displayed clinical signs ranging from unsteadiness to unconsciousness.

Williams (1959) reported that 73%-89% of the bromoethane injected into rats was eliminated unchanged in the expired air. When bromoethane was given orally in oil at doses of 0.25-1.0 g/kg, 67%-76% was eliminated unchanged in the expired air and 34%-38% was converted to inorganic bromide. Ivanetich et al. (1978) demonstrated that bromoethane, when incubated with hepatic microsomes from phenobarbital-induced male Wistar rats, bound to cytochrome P450 and reduced its activity by 27%. Incubation with bromoethane had no effect on cytochrome c reductase or cytochrome b_5.

Male and female strain A/HE mice, when administered bromoethane by intraperitoneal injection three times per week for 24 weeks at total doses of 0, 11.0, 27.5, or 55.0 mmol/kg, did not develop lung adenomas, whereas lung tumors developed in 100% of mice exposed to urethane (Poirier et al., 1975). Dipple et al. (1981) investigated the carcinogenicity of a number of alkylating and aralkylating bromides. Six-week-old female CB hooded rats, when given a single subcutaneous injection of bromoethane at concentrations of 0, 1.25, 4.2, or 12.5 mmol/kg and observed for 90 weeks, did not develop sarcomas at the injection site. Likewise, isopropyl bromide, benzyl bromide, and triphenylmethyl bromide did not cause sarcomas at the injection site, whereas 7-bromomethyl-12-methyl- and 7-bromomethylbenz[*a*]anthracene did.

Genetic Toxicology

Bromoethane was mutagenic in *Salmonella typhimurium* within the closed environment of a desiccator (Simmon, 1981; Barber et al., 1981, 1983; see Table 24); results of Salmonella studies using a preincubation protocol and no control for volatility were negative (Haworth et al., 1983). When tested by the National Toxicology Program (NTP) for cytogenetic effects in Chinese hamster ovary (CHO) cells, bromoethane induced sister chromatid exchanges (SCEs) (see Table 25), but not chromosomal aberrations, (see Table 26) in both the presence and absence of S9 (Loveday et al., 1989). The only reported in vivo

test for genetic toxicity of bromoethane was a sex-linked recessive lethal assay in Drosophila in which no increase in mutation frequency was observed in flies fed an 8.2 mM solution of bromoethane (Vogel and Chandler, 1974).

A structural analog of bromoethane, chloroethane, was tested by the NTP within the closed environment of a desiccator for induction of gene mutations in *S. typhimurium* strains TA100, TA1535, and TA98 in both the presence and absence of Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver S9 (NTP, 1989). A positive response was observed in strain TA1535 with and without S9 and in strain TA100 only in the presence of rat liver S9; no mutagenic activity was observed in strain TA98 with or without S9. The structural analogs, iodoethane (Simmon, 1981; Barber et al., 1981), 1-bromopropane (Barber et al., 1981), and 1,1-dibromoethane (Brem et al., 1974) were also mutagenic in Salmonella when exposure occurred in a closed environment. Another structural analog, 1,2-dibromoethane, was positive in a standard Salmonella assay with and without S9 metabolic activation (Dunkel et al., 1985). 1,2-Dibromoethane has been tested by the NTP in several short-term mutagenicity tests, and it produced positive responses with and without S9 in tests for induction of trifluorothymidine resistance in mouse lymphoma cells, SCEs and chromosomal aberrations in CHO cells, and sex-linked recessive lethal mutations and reciprocal translocations in adult *Drosophila melanogaster* (Myhr and Caspary, 1989; Mitchell et al., 1989; NTP unpublished results). Another structural analog, 1,2-dibromopropane, was positive in the Drosophila sex-linked recessive lethal assay reported by Vogel and Chandler (1974).

Although these haloalkanes are positive in the Salmonella gene mutation assay and some have been demonstrated to induce mutation and chromosomal effects in Drosophila, no positive responses have been demonstrated in the limited in vivo mammalian assays conducted to date. Both chloroethane (NTP, 1989) and 1,2-dibromoethane (NTP unpublished results) were evaluated for induction of micronucleated peripheral blood erythrocytes, and the results were negative. Neither 1-bromopropane nor 1,2-dibromoethane induced dominant lethal mutations in male rats (Saito-Suzuki et al., 1982; Bishop et al., 1987).

Study Rationale

Bromoethane was studied for long-term toxicity and carcinogenicity in rodents because of the lack of carcinogenicity data and for structure-activity comparisons with concurrent studies with chloroethane (NTP, 1989). Bromoethane was administered by the inhalation route to mimic that of human exposure.

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF BROMOETHANE

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

- Vapor Generation System
- Vapor Concentration Monitoring
- Vapor Concentration Uniformity in Chamber

SINGLE-EXPOSURE STUDIES

FOURTEEN-DAY STUDIES

FOURTEEN-WEEK STUDIES

TWO-YEAR STUDIES

- Study Design
- Source and Specifications of Animals
- Animal Maintenance
- Clinical Examinations and Pathology
- Statistical Methods

GENETIC TOXICOLOGY

PROCUREMENT AND CHARACTERIZATION OF BROMOETHANE

Bromoethane was obtained from Dow Chemical Company (Midland, MI) in two lots (Table 1). Purity and identity analyses were conducted at Midwest Research Institute (MRI) (Kansas City, MO). MRI reports on the analyses performed in support of the bromoethane studies are on file at the National Institute of Environmental Health Sciences. The identity of the lots was confirmed by spectroscopic analyses. The infrared (Figures 1 and 3) and nuclear magnetic resonance (Figures 2 and 4) spectra agreed with the literature spectra (Sadtler Standard Spectra; Varian, 1963). The ultraviolet/visible spectrum was consistent with that expected for the structure of bromoethane.

The purity of each lot was determined by elemental analysis, water analysis, titration of the acidic components with 0.01 N sodium hydroxide in ethanol solution to the phenolphthalein endpoint, and gas chromatography. Gas chromatographic analysis was performed with flame ionization detection and with a 20% SP2100/0.1% Carbowax 1500 column (system 1) or a 10% Carbowax 20M-TPA column (system 2).

Analysis of the cumulative data for lot no. MM02169 determined that the purity was greater than 98%. Results of elemental analysis for carbon, hydrogen, and bromine were in agreement with theoretical values. Karl Fischer analysis indicated less than 0.01% water. Titration of the acidic components indicated 6.9 ppm acid as hydrogen bromide. Three impurities, one before and two after the major peak with areas totaling 1.58% that of the major peak, were detected by gas chromatographic analysis with system 1. System 2 indicated two impurities after the major peak with relative areas of 0.52% and 1.03%, respectively, and three impurities, two before and one after the major peak, with a combined relative area of 0.23%. Supplemental gas chromatographic (system 2)/mass spectrometric analysis of this lot of study material identified the major impurity as toluene, which was quantitated against standards and found to be present at 0.48% (v/v).

Analysis of the cumulative data for lot no. MM810615 determined that the purity was greater than 99%. Results of elemental analysis for carbon, hydrogen, and bromine were in agreement with theoretical values. Karl Fischer analysis indicated 0.008% water. Titration of the acidic components with sodium hydroxide indicated 26.9 ppm acid as hydrogen bromide. Four impurities, two before and two after the major peak with areas totaling 0.66% that of the major peak, were detected by gas chromatographic analysis with system 1. System 2 indicated the major peak and three impurities, one before and two after the major peak. The major impurity, with a relative area of 0.50%, was identified by spiking with a standard solution of toluene. Quantitation with this standard solution indicated a concentration of 0.22% (v/v). The other two impurities observed with system 2 had a combined area of 0.39% relative to that of the major peak.

TABLE 1. IDENTITY AND SOURCE OF BROMOETHANE USED IN THE INHALATION STUDIES

Single-Exposure Studies	Fourteen-Day Studies	Fourteen-Week Studies	Two-Year Studies
Lot Number			
MM02169	MM02169	MM02169	MM810615
Date of Initial Use			
4/16/80	7/23/80	12/5/80	12/30/81
Supplier			
Dow Chemical Company (Midland, MI)	Dow Chemical Company (Midland, MI)	Dow Chemical Company (Midland, MI)	Dow Chemical Company (Midland, MI)

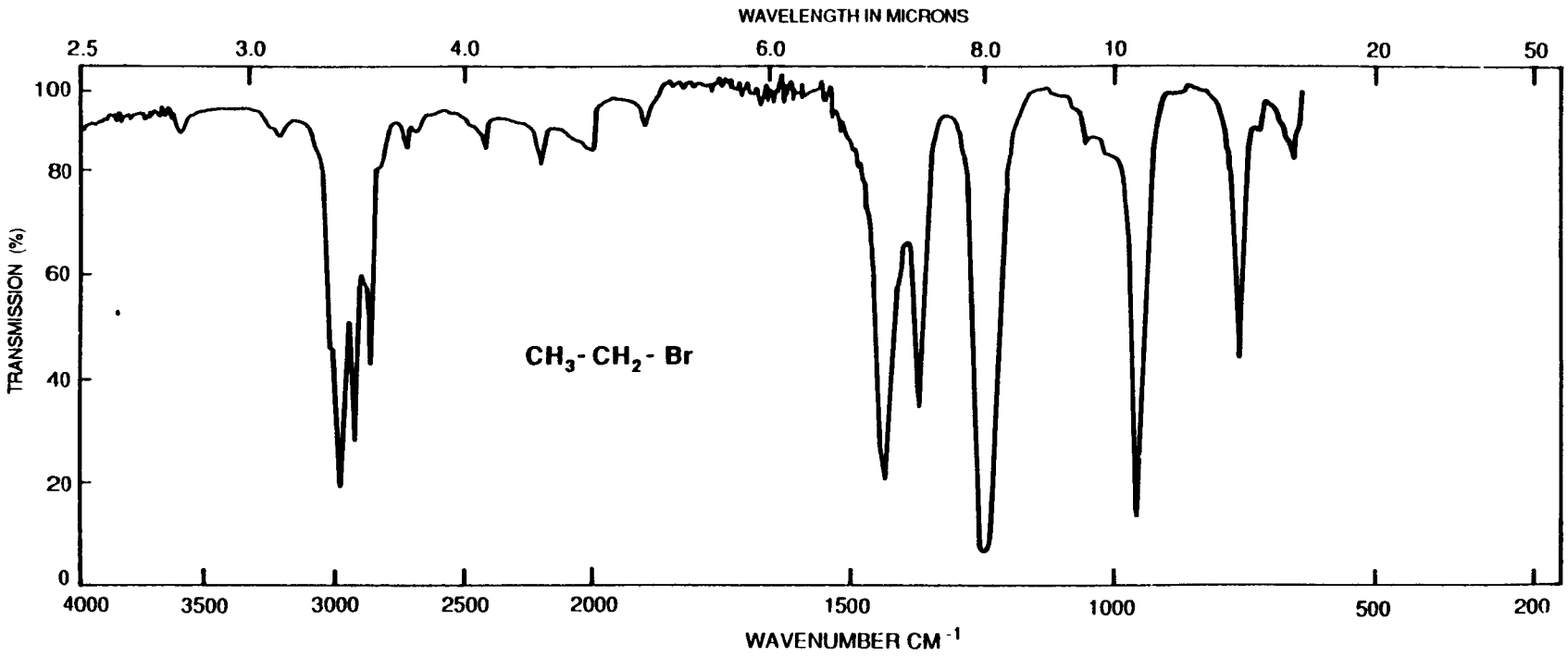

FIGURE 1. INFRARED ABSORPTION SPECTRUM OF BROMOETHANE (LOT NO. 02169)

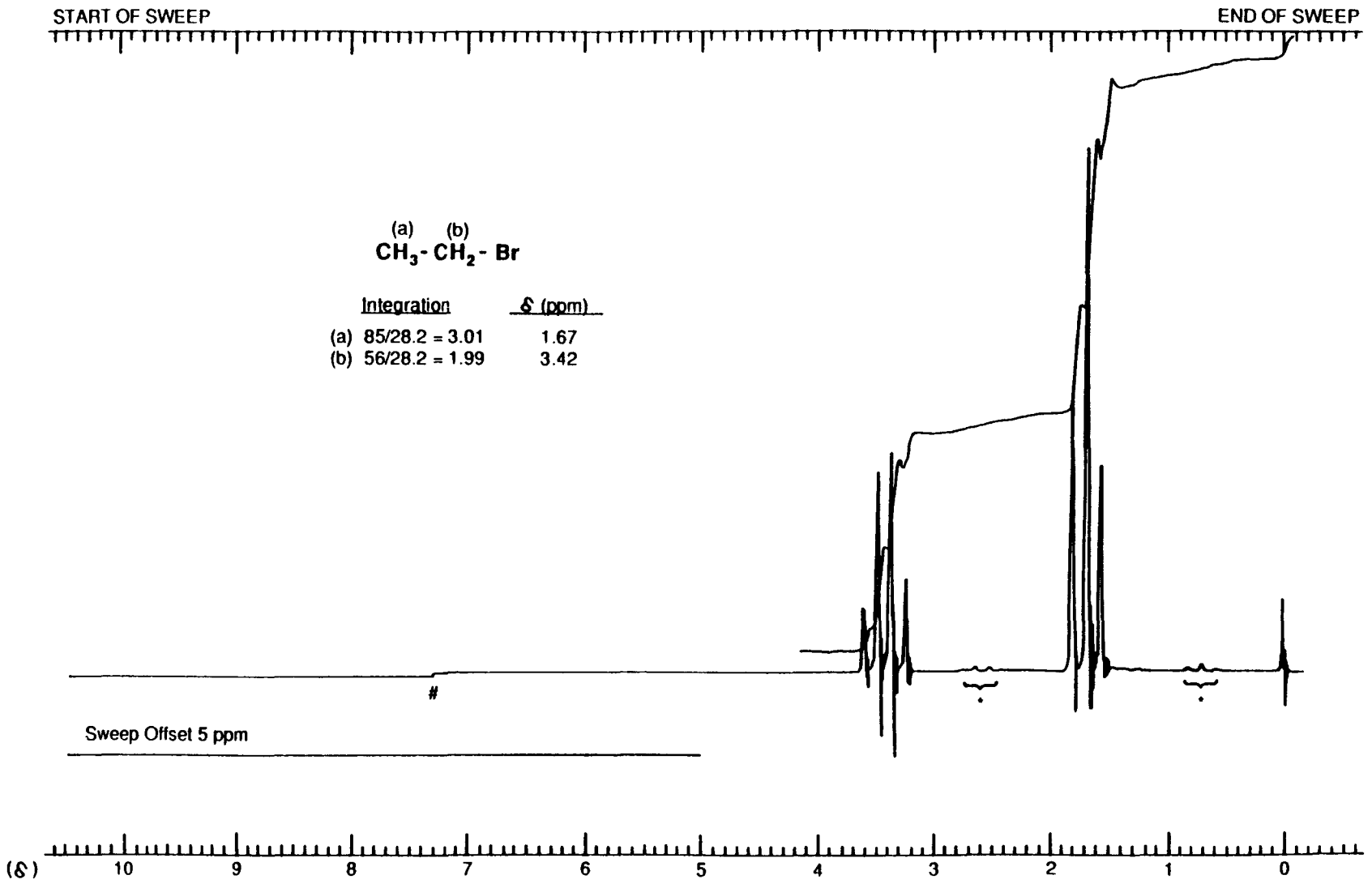

FIGURE 2. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF BROMOETHANE (LOT NO. 02169)

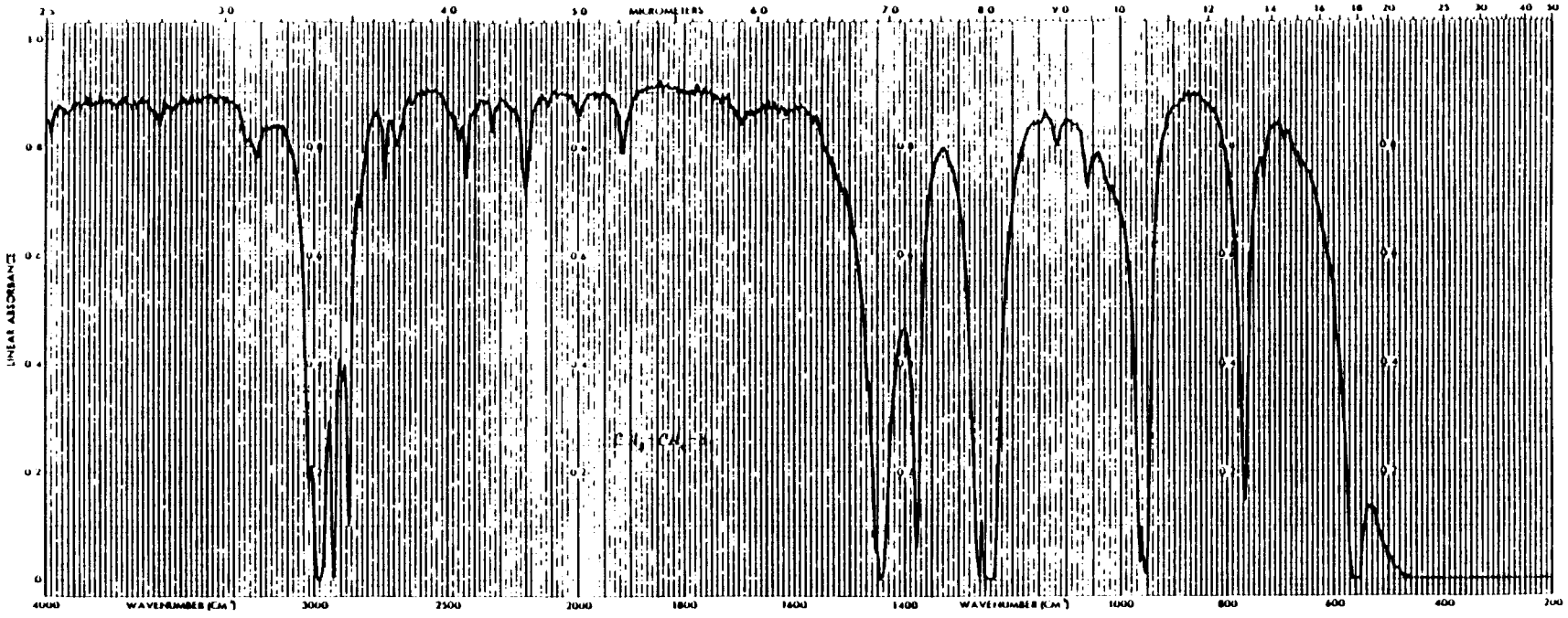

FIGURE 3. INFRARED ABSORPTION SPECTRUM OF BROMOETHANE (LOT NO. MM810615)

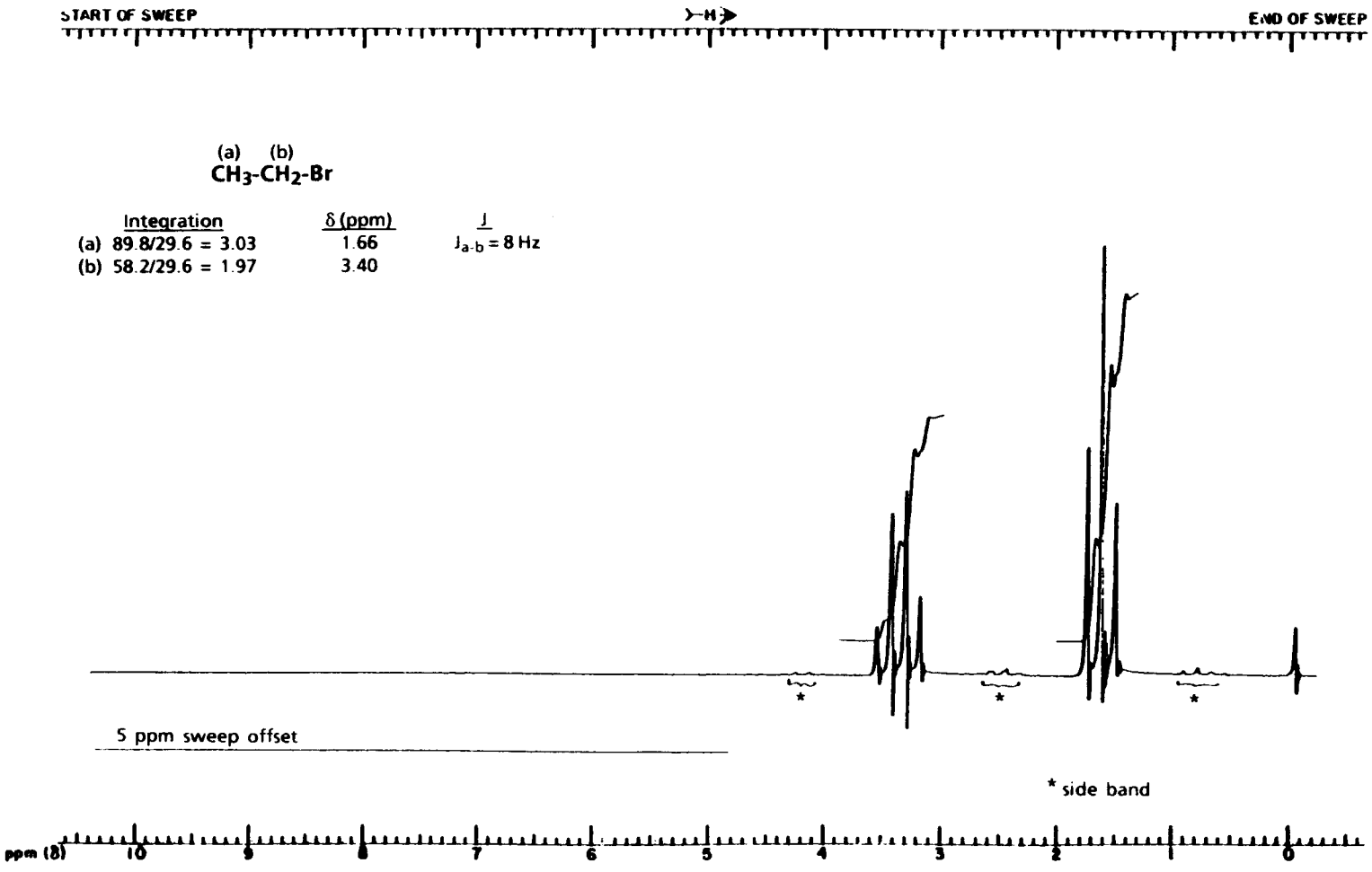

FIGURE 4. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF BROMOETHANE (LOT NO. MM810615)

Studies performed by gas chromatography with the same column as previously described for system 1, but with hexane as an internal standard, indicated that bromoethane was stable for 2 weeks when stored under nitrogen and protected from light at temperatures up to 60° C. The bulk study material was reanalyzed every 4 months over the course of the studies by gas chromatographic analysis with a Porapak PS column. No deterioration of the study material was seen by the study laboratory over the course of the studies. Therefore it is concluded that the bromoethane study material remained stable during the studies.

The potential degradation of bromoethane in the generation reservoir was investigated at the study laboratory. A sample of the study material was removed from the generation reservoir after generation of study atmospheres and was analyzed by gas chromatography with a Porapak PS column. The results of the analysis demonstrated that there was no large change in the impurities present in the study material. It was therefore concluded that the study chemical remained stable in the generation reservoir during the generation of bromoethane study atmospheres.

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

Vapor Generation System

Liquid bromoethane was pumped from a stainless steel reservoir to a vaporizer by a stable micrometering pump with adjustable pump rates. The vaporizer was initially maintained at about 40° C by an 80-watt heater (Figure 5). After a heater failure during week 58, it was discovered that bromoethane could be vaporized easily from the generator wick without the heater. By week 64, all chamber heaters were turned off and the bromoethane was vaporized without applied heat. The vaporizer was positioned in the fresh air duct leading directly into the exposure chamber to minimize material loss due to condensation on duct walls. Vapor was diluted with air before entering the chambers.

Vapor Concentration Monitoring

The concentration of bromoethane in the chambers and in the exposure room was measured by a gas chromatograph (HP-5840) equipped with a flame ionization detector. Calibration of the monitor was confirmed and corrected as necessary by checking the calibration against periodic assays of grab samples from the chambers. The flow rate was measured by timing the progress of a small bubble of room air through a three-way valve and into the clear Teflon® tube of known volume after the three-way valve was momentarily switched to the test position from the run position (Figure 5). Weekly mean exposure concentrations for the 2-year studies are presented in Figures 6 through 11. A summary of the chamber concentrations is presented in Table 2; Table 3 summarizes the distribution of mean daily concentrations.

TABLE 2. SUMMARY OF CHAMBER CONCENTRATIONS OF BROMOETHANE IN THE TWO-YEAR INHALATION STUDIES

Target Concentration (ppm)	Total Number of Readings	Determined Concentration (a) (ppm)
Rat Chambers		
100	4,925	101.5 ± 6.2
200	4,889	200.5 ± 10.6
400	4,880	400.7 ± 18.9
Mouse Chambers		
100	4,883	101.5 ± 6.2
200	4,846	200.6 ± 10.5
400	4,838	400.7 ± 18.8

(a) Mean ± standard deviation

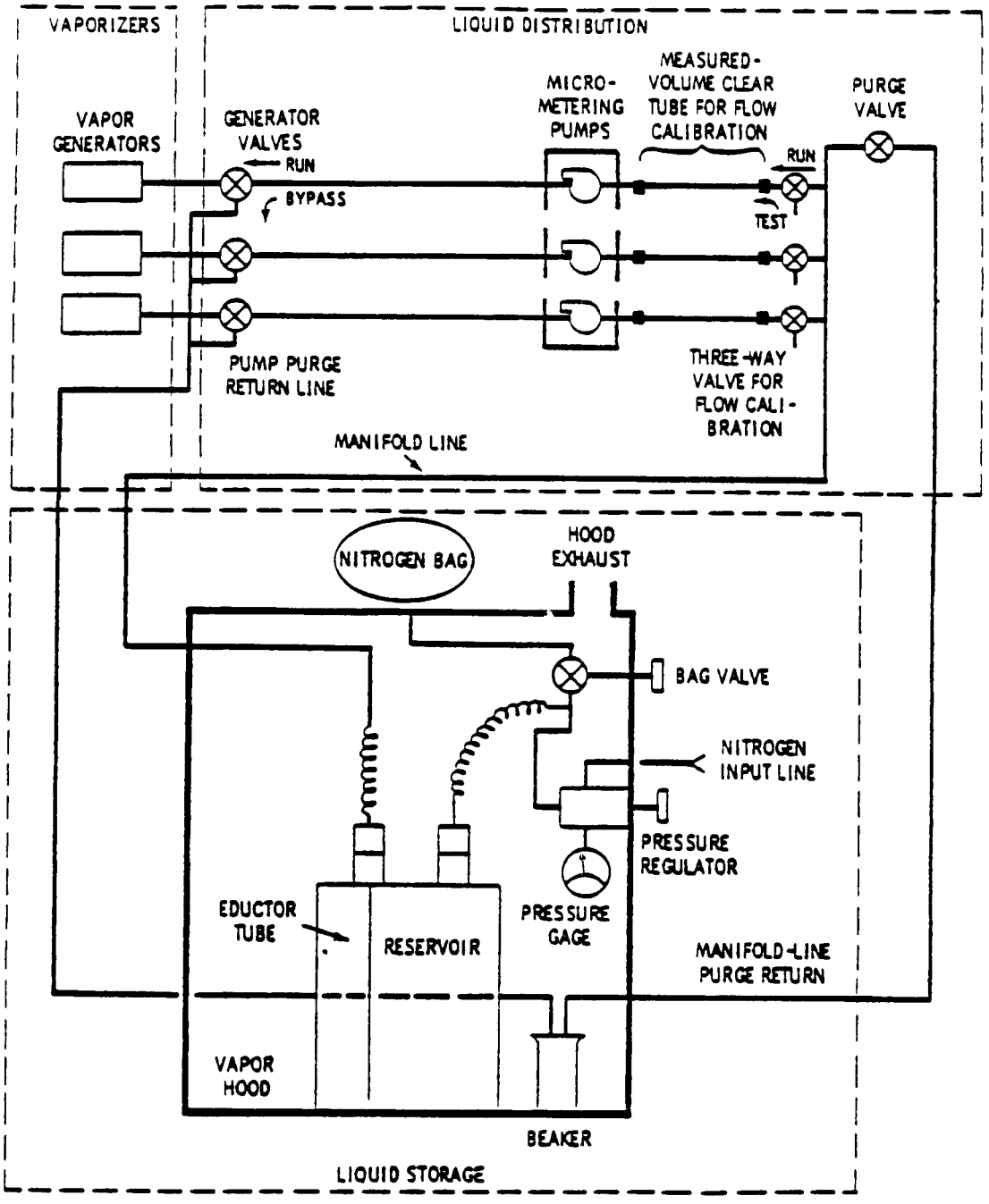

FIGURE 5. BROMOETHANE VAPOR GENERATION SYSTEM

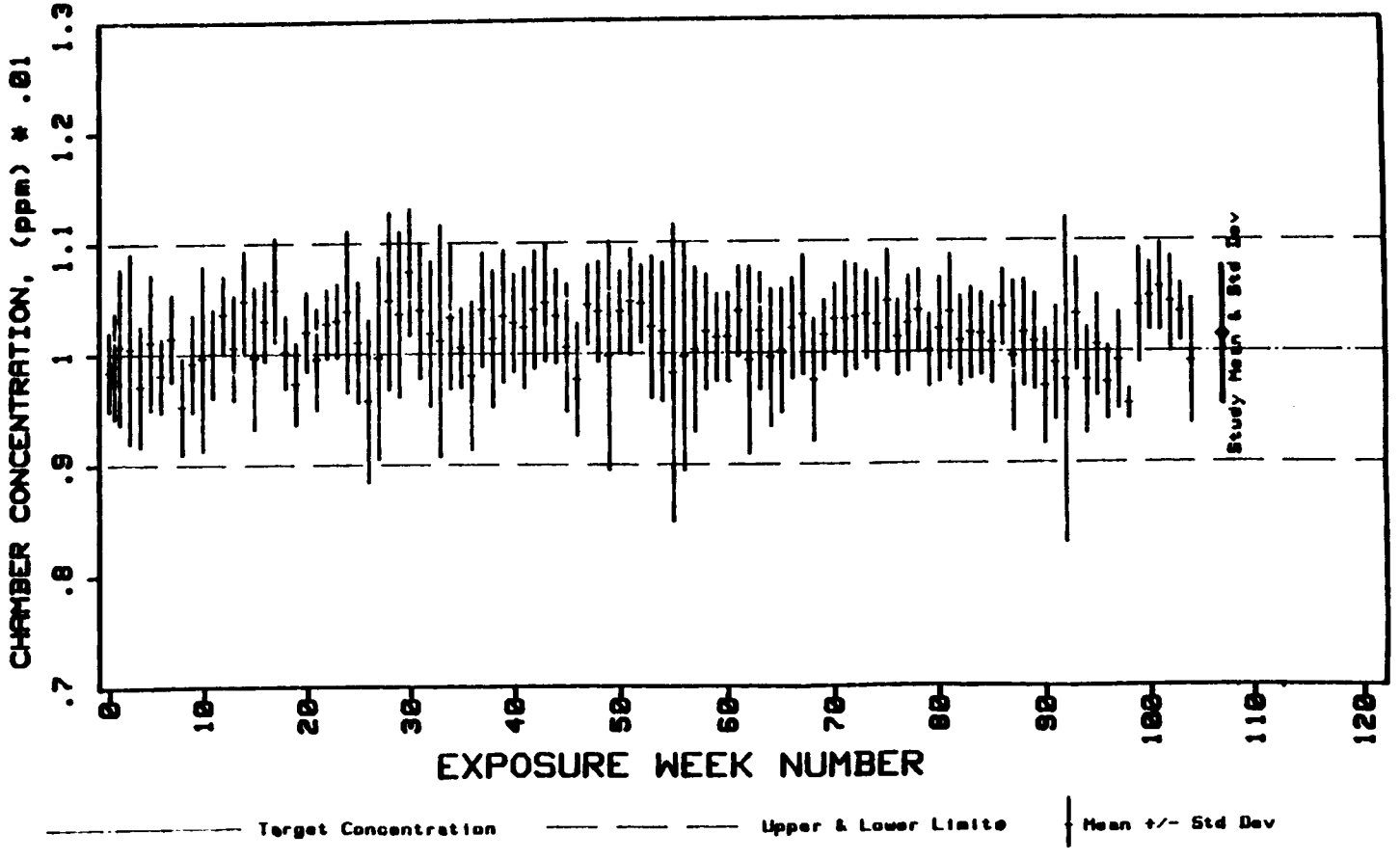

FIGURE 6. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 100-ppm BROMOETHANE RAT EXPOSURE CHAMBER FOR ENTIRE 104-WEEK STUDIES

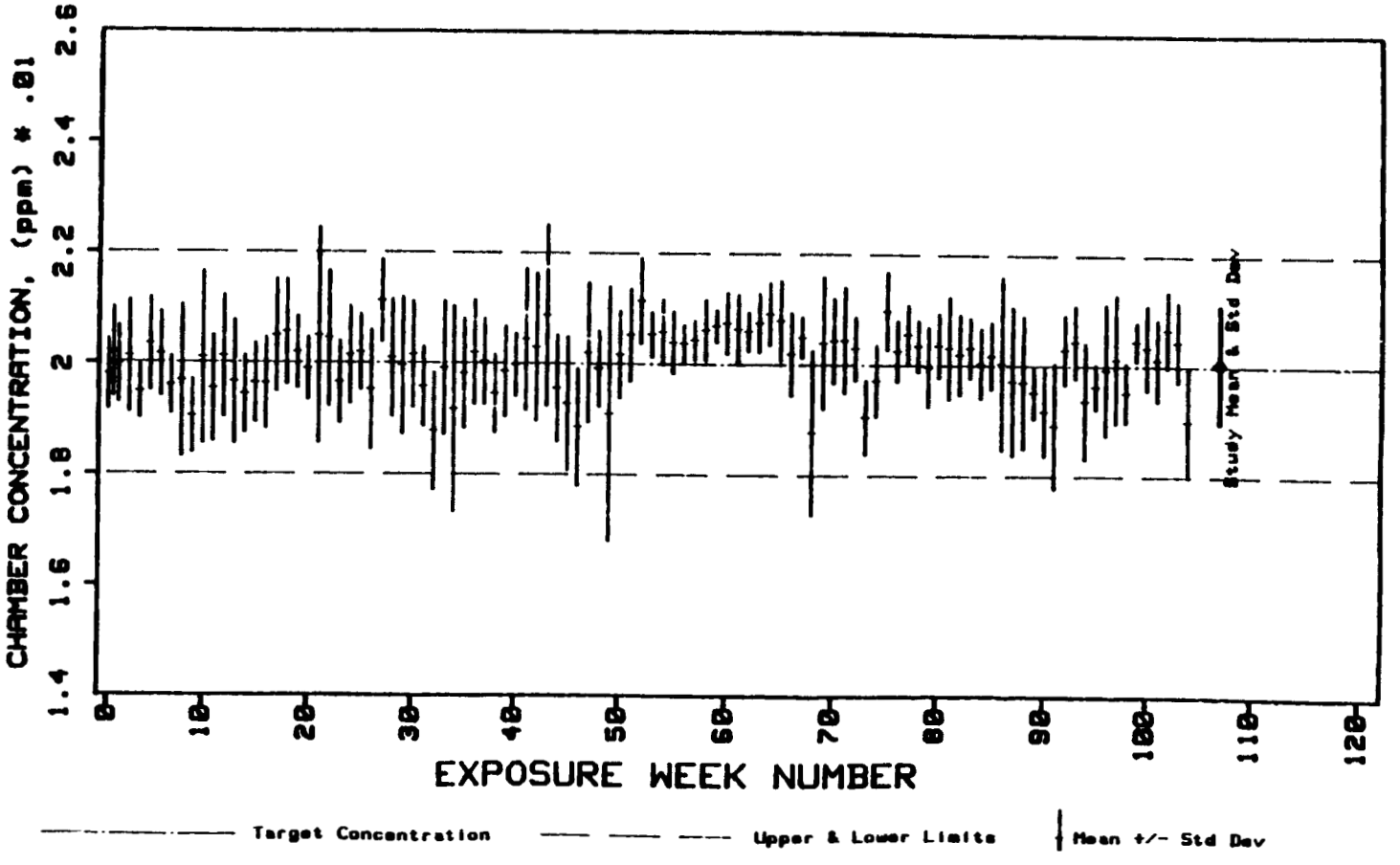

FIGURE 7. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 200-ppm BROMOETHANE RAT EXPOSURE CHAMBER FOR ENTIRE 104-WEEK STUDIES

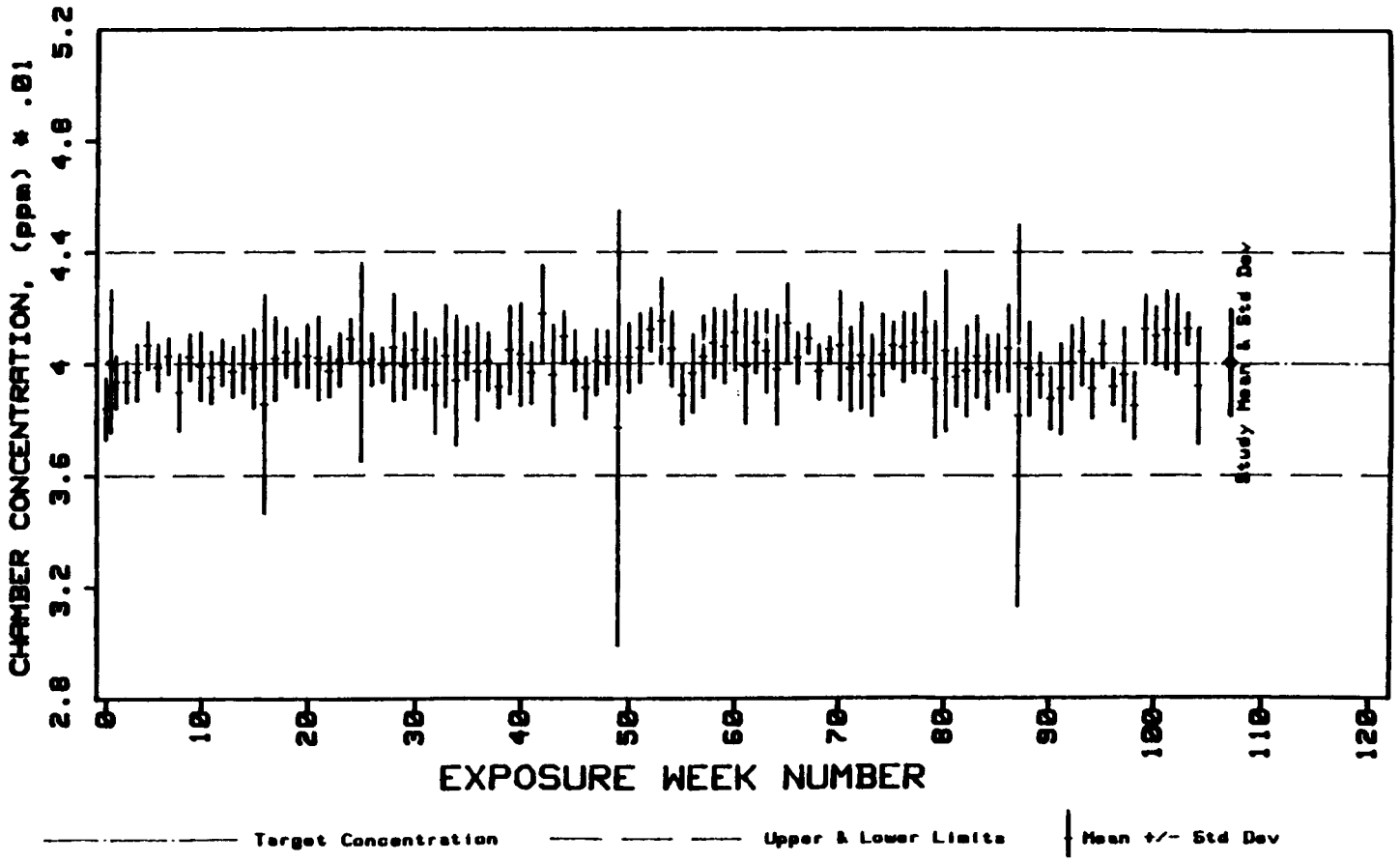

FIGURE 8. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 400-ppm BROMOETHANE RAT EXPOSURE CHAMBER FOR ENTIRE 104-WEEK STUDIES

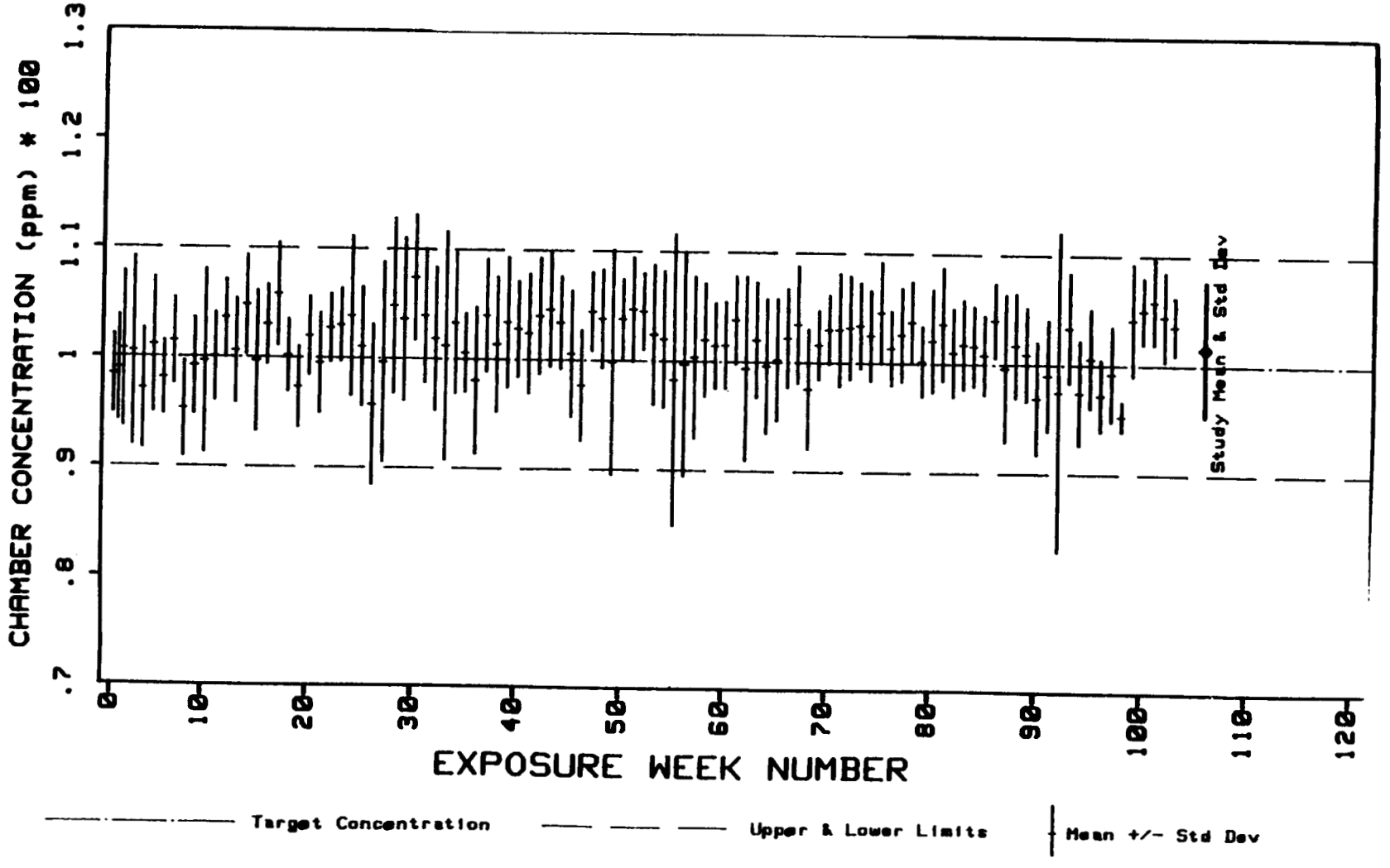

FIGURE 9. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 100-ppm BROMOETHANE MOUSE EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

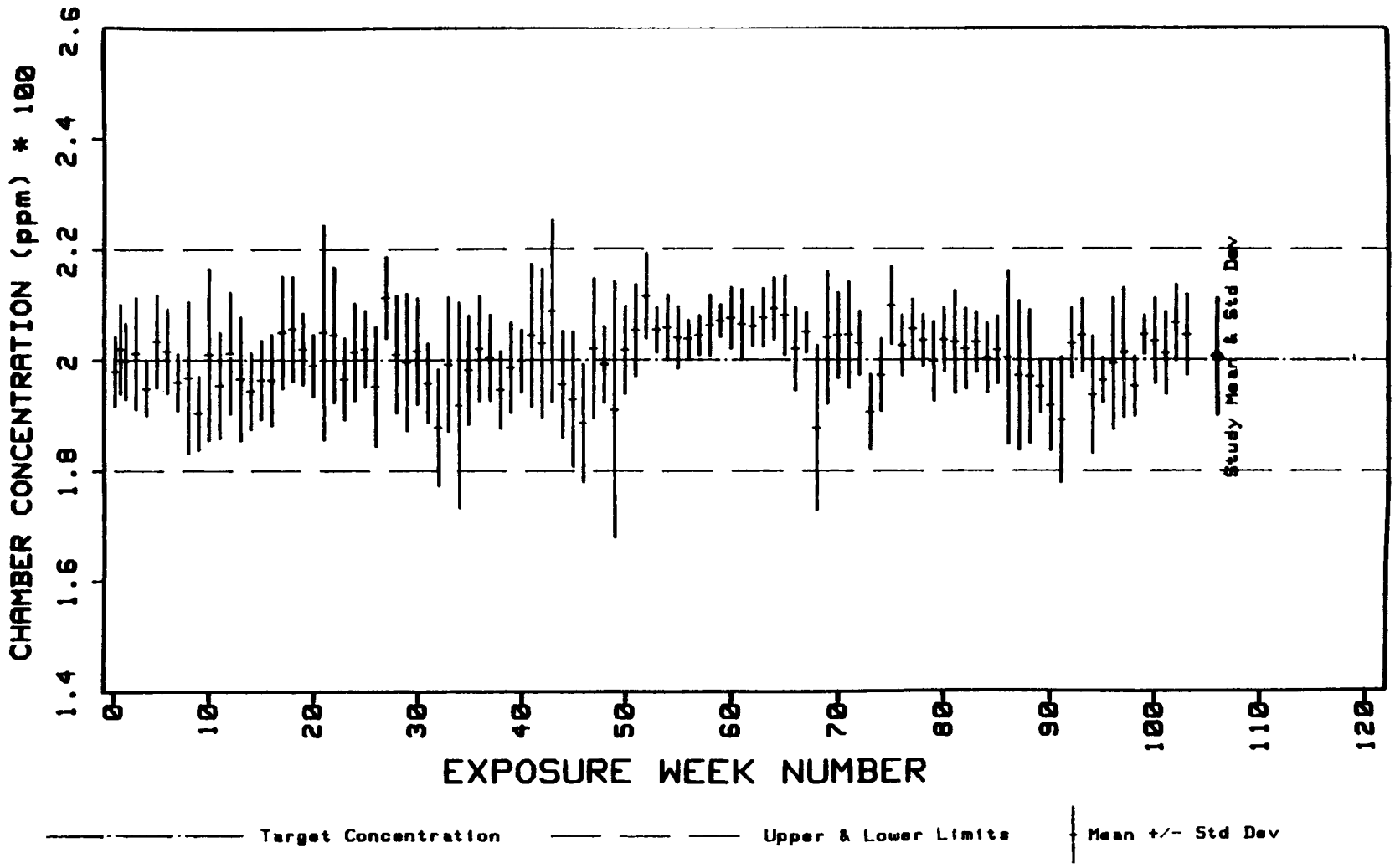

FIGURE 10. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 200-ppm BROMOETHANE MOUSE EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

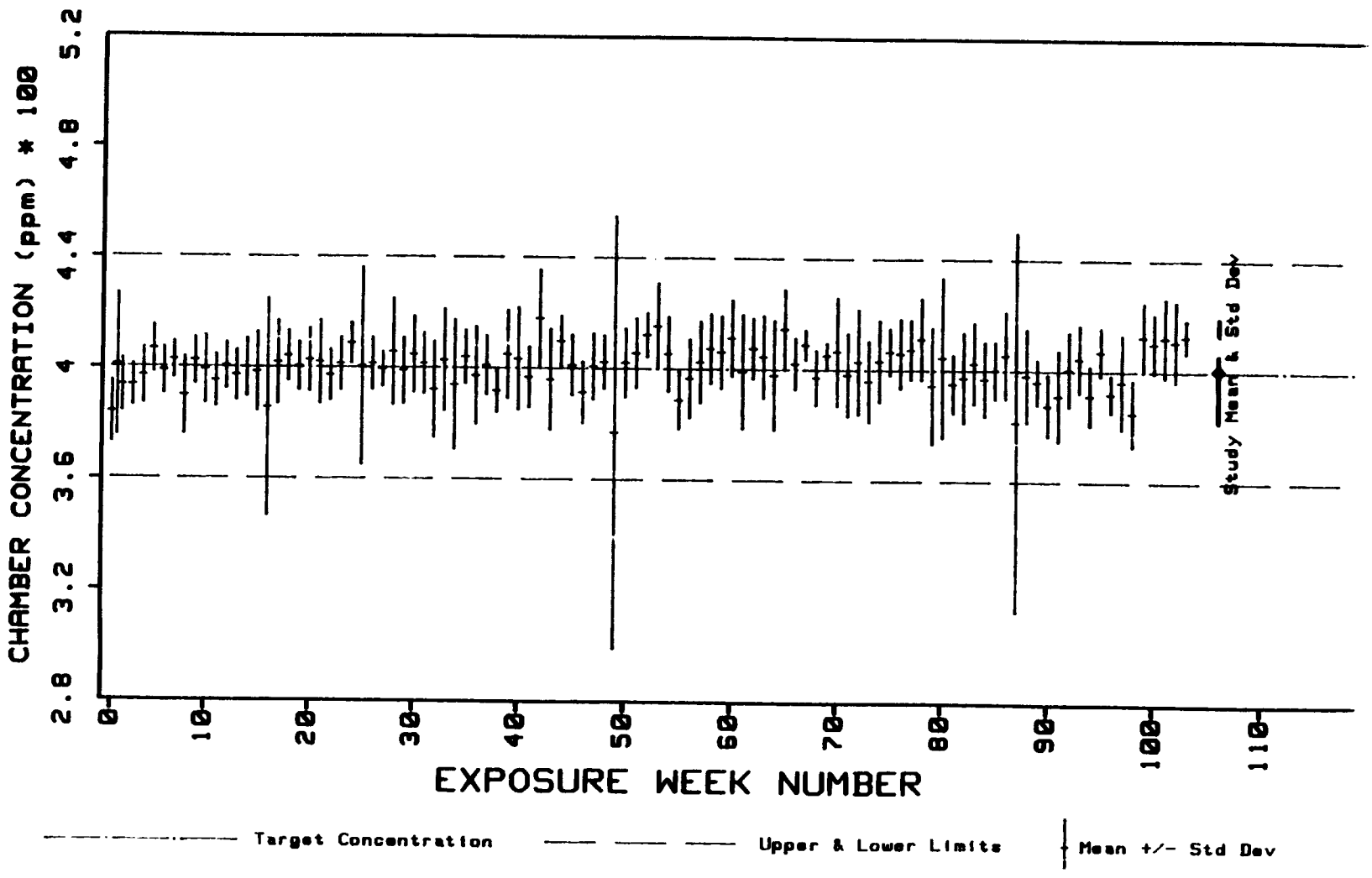

FIGURE 11. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 400-ppm BROMOETHANE MOUSE EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

TABLE 3. DISTRIBUTION OF MEAN DAILY CONCENTRATIONS OF BROMOETHANE DURING THE TWO-YEAR INHALATION STUDIES

Range of Concentration (percent of target)	Number of Days Mean Concentration Within Range		
	100 ppm	200 ppm	400 ppm
Rat Chambers			
110-120	1	0	0
100-110	341	273	267
90-100	156	223	228
80-90	0	2	1
70-80	0	0	2
Mouse Chambers			
110-120	1	0	0
100-110	339	273	266
90-100	154	219	225
80-90	0	2	1
70-80	0	0	2

SINGLE-EXPOSURE STUDIES

Groups of five rats and five mice of each sex were exposed to air containing bromoethane at concentrations of 625, 1,250, 2,500, 5,000, or 10,000 ppm for 4 hours. Rats and mice were observed continuously during exposure and three times per day for 14 days. Details of animal maintenance are presented in Table 4.

FOURTEEN-DAY STUDIES

Groups of five rats and five mice of each sex were exposed to air containing bromoethane at target concentrations of 0, 250, 500, 1,000, 2,000, or 4,000 ppm for 6 hours per day, 5 days per week for 14 days (10 exposures). Rats and mice were observed continuously during exposure and three times per day on nonexposure days; they were weighed before exposure, on day 7, and at necropsy. A necropsy was performed on all animals. Histopathologic examinations were performed on three rats and three mice exposed to bromoethane at 1,000 and 2,000 ppm. Further details are presented in Table 4.

FOURTEEN-WEEK STUDIES

Fourteen-week studies were conducted to evaluate the cumulative toxic effects of repeated exposure to bromoethane and to determine the concentrations to be used in the 2-year studies.

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Harlan Laboratories, observed for 23 days, distributed to weight classes, and assigned to study groups according to tables of random numbers. Feed was available ad libitum during nonexposure periods; water was available at all times.

Groups of 10 rats and 10 mice of each sex were exposed to air containing bromoethane at target concentrations of 0, 100, 200, 400, 800, or 1,600 ppm for 6 hours per day, 1-5 days per week for 14 weeks (65 exposures). Further experimental details are summarized in Table 4.

Animals were observed continuously during exposure and were observed three times on each nonexposure day; moribund animals were killed. Individual animal weights were recorded once per week. At the end of the 14-week studies, survivors were killed. A necropsy was performed on all animals. Further experimental details and tissues and groups examined are given in Table 4.

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF BROMOETHANE

Single-Exposure Studies	Fourteen-Day Studies	Fourteen-Week Studies	Two-Year Studies
EXPERIMENTAL DESIGN			
Size of Study Groups			
5 males and 5 females of each species	5 males and 5 females of each species	10 males and 10 females of each species	49 or 50 males and 49 or 50 females of each species
Doses			
Actual concentrations: 659, 1,249, 2,409, 5,171, or 9,883 ppm bromoethane by inhalation; target concentrations: 625, 1,250, 2,500, 5,000, or 10,000 ppm	Target concentrations: 0, 250, 500, 1,000, 2,000, or 4,000 ppm bromoethane by inhalation	Target concentrations: 0, 100, 200, 400, 800, or 1,600 ppm bromoethane by inhalation	Target concentrations: 0, 100, 200, or 400 ppm bromoethane by inhalation
Date of First Dose			
4/16/80	7/23/80	12/5/80	12/30/81
Date of Last Dose			
N/A	8/5/80	3/10/81	Rats--12/30/83; mice--12/22/83
Duration of Dosing			
4 h	6 h/d for 10 exposures over 14 d	6 h/d, 1-5 d/wk for 65 exposures over 14 wk	6 h/d, 5 d/wk for 104 wk (rats) or 103 wk (mice)
Type and Frequency of Observation			
Observed continuously during exposure and then 3 × d for 14 d	Observed continuously during exposure and then 3 × d on nonexposure days; weighed 1 × wk	Same as 14-d studies	Observed 2 × d; weighed initially, 1 × wk for 12 wk, and then 1 × mo
Necropsy, Histologic Examinations, and Supplemental Analyses			
No necropsy or histologic exams performed	Necropsy performed on all animals; histologic exams performed on 3 animals of each species from the 1,000- and 2,000-ppm groups. Tissues examined: nasal cavity, trachea, and lungs and mainstem bronchi	Necropsy performed on all animals; histologic exams performed on all controls and all animals in the 800- and 1,600-ppm groups. Tissues examined: adrenal glands, brain, colon, duodenum, epididymis/prostate/testes or ovaries/uterus, esophagus, gallbladder (mice), gross lesions and tissue masses with regional lymph nodes, harderian gland (rats), heart, ileum, jejunum, kidneys, larynx, liver, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nasal cavity and turbinates, pancreas, parathyroids, pituitary gland, preputial or clitoral gland, rectum, salivary glands, skin, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, trachea, tracheobronchial lymph nodes (rats), and urinary bladder. Liver weighed at necropsy	Necropsy and histologic exams performed on all animals; the following tissues examined histologically: adrenal glands, brain, colon, duodenum, epididymis/prostate/testes or ovaries/uterus, esophagus, gallbladder (mice), gross lesions and tissue masses with regional lymph nodes, heart, ileum, jejunum, kidneys, larynx, liver, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nasal cavity and turbinates, pancreas, parathyroids, pituitary gland, preputial or clitoral gland, rectum, salivary glands, skin, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, trachea, tracheobronchial lymph nodes, and urinary bladder

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF BROMOETHANE (Continued)

Single-Exposure Studies	Fourteen-Day Studies	Fourteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE			
Strain and Species			
F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice
Animal Source			
Charles River Breeding Laboratories (Portage, MI)	Charles River Breeding Laboratories (Portage, MI)	Harlan Industries (Indianapolis, IN)	Frederick Cancer Research Facility (Frederick, MD)
Study Laboratory			
Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories
Method of Animal Identification			
Cage numbering	Ear tags and cage numbers	Ear tags and cage numbers	Ear tags and cage numbers
Time Held Before Study			
21 d	21 d	23 d	21 d
Age When Placed on Study			
Rats--7 wk; mice--8-9 wk	Rats--7-8 wk; mice--8-9 wk	Rats--7-8 wk; mice--10-12 wk	Rats--8-10 wk; mice--9 wk
Age When Killed			
Rats--9 wk; mice--10-11 wk	Rats--9-10 wk; mice--10-11 wk	Rats--20-21 wk; mice--23-25 wk	Rats--114-116 wk; mice--114 wk
Necropsy or Kill Dates			
5/1/80	8/6/80	3/11/81-3/13/81	Rats--1/9/84-1/12/84; mice--1/3/84-1/6/84
Method of Animal Distribution			
Assigned to groups by table of random numbers	Same as single-exposure studies	Distributed to weight classes and then assigned to groups according to tables of random numbers	Same as 14-wk studies
Feed			
NIH 07 Rat and Mouse Ration (Zeigler Bros., Inc., Gardners, PA); available ad libitum during non-exposure periods	Same as single-exposure studies	Same as single-exposure studies	Same as single-exposure studies
Bedding			
None	None	None	None
Water			
Automatic watering system (Edstrom Industries, Waterford, WI); available ad libitum	Same as single-exposure studies	Same as single-exposure studies	Same as single-exposure studies
Cages			
Stainless steel wire (Harford Metal, Inc., Aberdeen, MD)	Stainless steel wire bottom cages (Hazleton System, Inc., Aberdeen, MD)	Same as 14-d studies	Same as 14-d studies
Cage Filters			
None	None	None	None

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF BROMOETHANE (Continued)

Single-Exposure Studies	Fourteen-Day Studies	Fourteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE (Continued)			
Animals per Cage			
1	1	1	1
Other Chemicals on Study in the Same Room			
None	None	None	Allyl glycidyl ether (6/21/82-12/30/83)
Chamber Environment			
Temp--72°-80° F; hum--41%-73% (exposure), 40%-60% (nonexposure); fluorescent light in room 12 h/d; 20 chamber air changes/h	Temp--71°-76° F (exposure), 60°-70° F (nonexposure); hum--46%-76%; fluorescent light in room 12 h/d; 20 chamber air changes/h during nonexposure, 10/h during exposure	Temp--72°-77° F (exposure), 72°-76° F (nonexposure); hum--37%-80% (exposure), 40%-60% (nonexposure); fluorescent light in room 12 h/d; 10 chamber air changes/h	Temp--67°-83° F; hum--33%-84%; fluorescent light in room 12 h/d; 10 chamber air changes/h

TWO-YEAR STUDIES

Study Design

Groups of 49 or 50 rats and 49 or 50 mice of each sex were exposed to air containing bromoethane at concentrations of 0 (chamber controls), 100, 200, or 400 ppm, for 6 hours per day, 5 days per week for 103 or 104 weeks. Actual concentrations are summarized in Figures 6 to 11 and Tables 2 and 3.

Source and Specifications of Animals

The male and female F344/N rats and B6C3F$_1$ (C57BL/6N, female × C3H/HeN MTV$^-$, male) mice used in these studies were produced under strict barrier conditions at Frederick Cancer Research Facility. Breeding stock for the foundation colonies at the production facility originated at the National Institutes of Health Repository. Animals shipped for study were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. Animals were shipped to the study laboratory at 5-7 weeks (rats) or 6 weeks (mice) of age. The animals were quarantined at the study laboratory for 3 weeks. Thereafter, a complete necropsy was performed on five animals of each sex and species to assess their health status. The rodents were placed on study when 8- to 10-weeks old (rats) or 9 weeks old (mice).

Animal Maintenance

Rats and mice were housed individually. Feed was available ad libitum during nonexposure periods; water was available at all times. Serologic analyses were performed as described in Appendix E. Further details of animal maintenance are summarized in Table 4.

Clinical Examinations and Pathology

All animals were observed two times per day. Body weights were recorded once per week for the first 12 weeks of the studies and once per month thereafter. Mean body weights were calculated for each group. Animals found moribund and those surviving to the end of the studies were humanely killed. A necropsy was performed on all animals, including those found dead, unless they were missexed or missing. Some tissues were excessively autolyzed or cannibalized, and thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study.

During necropsy, all organs and tissues were examined for grossly visible lesions. Tissues were preserved in 10% neutral buffered formalin,

embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Tissues examined are listed in Table 4.

When the pathology evaluation was completed by the laboratory pathologist and the pathology data entered into the Carcinogenesis Bioassay Data System, the slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit. The slides, individual animal data records, and pathology tables were sent to an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10% of the animals were evaluated by a quality assessment pathologist. The quality assessment report and slides were submitted to the Pathology Working Group (PWG) Chairperson, who reviewed all target tissues and those about which there was a disagreement between the laboratory and quality assessment pathologists.

Representative slides selected by the Chairperson were reviewed by the PWG, which included the laboratory pathologist, without knowledge of previously rendered diagnoses. When the consensus diagnosis of the PWG differed from that of the laboratory pathologist, the laboratory pathologist was asked to reconsider the original diagnosis. This procedure has been described, in part, by Maronpot and Boorman (1982) and Boorman et al. (1985). The final diagnoses represent a consensus of contractor pathologists and the NTP Pathology Working Group. For subsequent analysis of pathology data, the diagnosed lesions for each tissue type are combined according to the guidelines of McConnell et al. (1986).

Slides/tissues are generally not evaluated in a blind fashion (i.e., without knowledge of dose group) unless the lesions in question are subtle or unless there is an inconsistent diagnosis of lesions by the laboratory pathologist. Nonneoplastic lesions are not examined routinely by the quality assessment pathologist or PWG unless they are considered part of the toxic effect of the chemical.

Statistical Methods

Survival Analyses: The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals were censored from the survival analyses at the time they were found to be missing or dead from other than natural causes; animals dying from natural causes were not censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) life table test for a dose-related trend. When significant survival differences were detected, additional analyses using these procedures were carried out to determine the time point at which significant differences in the survival curves were first detected. All reported P values for the survival analysis are two-sided.

Calculation of Incidence: The incidence of neoplastic or nonneoplastic lesions is given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators include only those animals for which the site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the number of animals on which a necropsy was performed.

Analysis of Tumor Incidence: The majority of tumors in this study were considered to be incidental to the cause of death or not rapidly lethal. Thus, the primary statistical method used was an incidental tumor analysis, which assumed that the diagnosed tumors were discovered as the result of death from an unrelated cause and thus did not affect the risk of death. In this approach, the proportions of tumor-bearing animals in dosed and control groups were compared in each of five time intervals: weeks 0-52, weeks 53-78, weeks 79-92, week 93 to the week before the terminal-kill period, and the terminal-kill period. The denominators of these proportions were the number of animals actually examined

for tumors during the time interval. The individual time interval comparisons were then combined to obtain a single overall result.

In addition to incidental tumor analysis, alternative 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 tumors, and the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart et al., 1979), procedures based on the overall proportion of tumor-bearing animals.

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

Historical Control Data: Although the concurrent control group is 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 tumor incidence. Consequently, control tumor incidences from the NTP historical control data base (Haseman et al., 1984, 1985) are included for those tumors appearing to show compound-related effects. At the time of this report, the NTP historical data base for inhalation studies comprised only studies from Battelle Pacific Northwest Laboratories and no other long-term inhalation data were included.

GENETIC TOXICOLOGY

Salmonella Protocol: A modification of the technique reported by Ames et al. (1975) was used to ensure adequate exposure of the bacteria to bromoethane. The chemical was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). The minimal glucose agar plates with the *Salmonella typhimurium* tester strains TA98 and TA100 alone or with S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver) were inverted without lids on a perforated porcelain plate in glass desiccator jars. The neat study chemical was pipetted into a glass dish set below the petri plates in each jar, and the jars were sealed. The jars, containing a magnetic stirring bar on the bottom, were placed on magnetic stirrers inside a 37° C incubator. The stirrers were used to keep the vaporized bromoethane mixed with the air. The entire apparatus was incubated at 37° C for 24 hours. The plates were then removed from the desiccator and incubated at 37° C for an additional 24 hours. Each test in TA100 consisted of triplicate plates of concurrent positive and negative controls and of four to seven doses of the study chemical. The high dose was limited by toxicity. All assays in TA100 were repeated, and positive assays were repeated under the conditions that elicited the positive response. 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 which was not dose related, not reproducible, or of insufficient magnitude to support a determination of mutagenicity. A negative response was obtained when no significant increase in revertant colonies was observed after chemical treatment.

Chinese Hamster Ovary Cytogenetics Assays: Testing was performed as reported by Galloway et al. (1985, 1987) and is described briefly below. Chemicals were sent to the laboratories as coded aliquots from Radian Corporation (Austin, TX). Chemicals were tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCEs) and chromosomal aberrations 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 (BrdU)-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least three doses of the study chemical; the high dose was limited by toxicity or solubility but did not exceed 5 mg/ml.

In the SCE test without S9, CHO cells were incubated for 26 hours with the study chemical in McCoy's 5A medium supplemented with 10% fetal bovine serum, L-glutamine (2 mM), and antibiotics. BrdU was added 2 hours after culture

initiation. After 26 hours, the medium containing the study chemical was removed and replaced with fresh medium plus BrdU and colcemid, and incubation was continued for 2 more 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 the chemical, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing BrdU and no study chemical; incubation proceeded for an additional 26 hours, with colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9.

In the chromosomal aberration test without S9, cells were incubated in McCoy's 5A medium with the study chemical for 8 hours; colcemid was added, and incubation was continued for 2 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the chromosomal aberration test with S9, cells were treated with the study chemical and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 10 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.

For the SCE test, if significant chemical-induced cell cycle delay was seen, incubation time was lengthened to ensure a sufficient number of scorable cells. The harvest time for the chromosomal aberration test was based on the cell cycle information obtained in the SCE test; if cell cycle delay was anticipated, the incubation period was extended approximately 5 hours.

Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind, and those from a single test were read by the same person. For the SCE test, 50 second-division metaphase cells were usually scored for frequency of SCEs per cell from each dose; 100 first-division metaphase cells were scored at each dose for the chromosomal aberration test. 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).

Statistical analyses were conducted on both the slopes of the dose-response curves and the individual dose points. 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. Chromosomal aberration data are presented as percentage of cells with aberrations. As with SCEs, both the dose-response curve and individual dose points were statistically analyzed. A statistically significant ($P<0.003$) trend test or a significantly increased dose point ($P<0.05$) was sufficient to indicate a chemical effect.

III. RESULTS

RATS

SINGLE-EXPOSURE STUDIES

FOURTEEN-DAY STUDIES

FOURTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

MICE

SINGLE-EXPOSURE STUDIES

FOURTEEN-DAY STUDIES

FOURTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

GENETIC TOXICOLOGY

SINGLE-EXPOSURE STUDIES

All rats exposed to 10,000 ppm died on the first day, and 3/5 female rats exposed to 5,000 ppm bromoethane died before the end of the studies (Table 5). Clinical signs observed during the initial part of the exposure to 10,000 ppm included increased respiration rate, hyperactivity, and incoordination; later during the exposure, the rats were dyspneic and comatose. Compound-related clinical signs were not observed after the end of the exposure period.

FOURTEEN-DAY STUDIES

All rats exposed to 4,000 ppm died by day 2, and those to 2,000 ppm died before the end of the studies (Table 6). Final mean body weights of exposed and control rats were similar. Males exposed to 2,000 ppm were prostrate, dyspneic, lacrimating, and twitching between day 7 and day 10 (when they were found to be moribund). Hemorrhage and/or acute inflammation of the nasal turbinates, trachea, and lung were seen in one rat at 2,000 ppm, minor pulmonary congestion and hemorrhage were seen in one rat at 1,000 ppm, and minimal-to-mild pulmonary congestion was seen in two rats at 2,000 ppm.

FOURTEEN-WEEK STUDIES

Four of 10 male and 2/10 female rats exposed to 1,600 ppm died before the end of the studies (Table 7). The final mean body weights of rats exposed to 1,600 ppm were lower than the initial mean body weights. Ataxia was seen between weeks 6 and 13, and posterior paresis, dyspnea, and dacryorrhea were seen between weeks 7 and 13 in rats exposed to 1,600 ppm. Liver weight to body weight ratios for male rats at 1,600 ppm and female rats at 800 and 1,600 ppm were marginally greater than those for controls (Table 8). Positive titers to Sendai virus were seen in the sera of 10/10 rats tested at the end of the studies.

TABLE 5. SURVIVAL AND INITIAL MEAN BODY WEIGHT OF RATS IN THE SINGLE-EXPOSURE INHALATION STUDIES OF BROMOETHANE

Concentration (ppm)	Survival (a)	Initial Mean Body Weight (b) (grams)
MALE		
625	5/5	161 ± 6
1,250	5/5	150 ± 8
2,500	5/5	149 ± 8
5,000	5/5	152 ± 9
10,000	(c) 0/5	157 ± 7
FEMALE (d)		
625	5/5	121 ± 2
1,250	5/5	120 ± 2
2,500	5/5	120 ± 3
5,000	(e) 2/5	120 ± 3
10,000	(c) 0/5	119 ± 2

(a) Number surviving/number in group
(b) Initial group mean body weight ± standard error of the mean; final body weights were not recorded.
(c) Day of death: all 1
(d) LC_{50} (95% confidence interval) based on actual mean concentrations of 659, 1,249, 2,409, 5171, and 9,883 ppm by the Spearman-Karber procedure: 4,681 ppm (3,335-6,569 ppm)
(e) Day of death: 2,3,3

TABLE 6. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-DAY INHALATION STUDIES OF BROMOETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	5/5	190 ± 4	252 ± 4	+62 ± 3	
250	5/5	192 ± 6	249 ± 4	+57 ± 4	99
500	5/5	190 ± 7	255 ± 9	+65 ± 4	101
1,000	5/5	189 ± 7	247 ± 6	+58 ± 4	98
2,000	(d) 0/5	186 ± 4	(e)	(e)	(e)
4,000	(f) 0/5	188 ± 5	(e)	(e)	(e)
FEMALE					
0	5/5	124 ± 5	150 ± 5	+26 ± 6	
250	5/5	117 ± 2	148 ± 1	+31 ± 2	99
500	5/5	120 ± 4	150 ± 5	+30 ± 2	100
1,000	5/5	120 ± 4	148 ± 4	+28 ± 1	99
2,000	(g) 0/5	116 ± 3	(e)	(e)	(e)
4,000	(f) 0/5	118 ± 3	(e)	(e)	(e)

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean
(c) Mean body weight change of the group ± standard error of the mean
(d) Day of death: 9,10,10,10,10
(e) No data are reported due to the 100% mortality in this group.
(f) Day of death: all 2
(g) Day of death: all 10; killed because moribund.

TABLE 7. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-WEEK INHALATION STUDIES OF BROMOETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	146 ± 3	320 ± 6	+174 ± 8	
100	10/10	141 ± 6	338 ± 6	+197 ± 7	106
200	10/10	141 ± 3	335 ± 6	+194 ± 8	105
400	10/10	149 ± 5	326 ± 8	+177 ± 8	102
800	10/10	142 ± 4	310 ± 12	+168 ± 11	97
1,600	(d) 6/10	144 ± 3	139 ± 4	−4 ± 7	43
FEMALE					
0	10/10	110 ± 2	182 ± 3	+62 ± 3	
100	10/10	112 ± 2	193 ± 5	+81 ± 5	106
200	10/10	116 ± 3	197 ± 3	+81 ± 2	108
400	10/10	115 ± 2	189 ± 3	+74 ± 2	104
800	10/10	116 ± 3	194 ± 3	+78 ± 3	107
1,600	(e) 8/10	114 ± 2	106 ± 1	−10 ± 2	58

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean. Subsequent calculations are based on animals surviving to the end of the study.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Week of death: 6,10,10,10
(e) Week of death: 8,11

TABLE 8. LIVER WEIGHTS FOR RATS IN THE FOURTEEN-WEEK INHALATON STUDIES OF BROMOETHANE (a)

Concentration (ppm)	Number Weighed	Final Body Weight (grams)	Liver Weight (mg)	Liver Weight/ Final Body Weight (mg/g)
MALE				
0	10	320 ± 6.2	12,316 ± 545	38.5 ± 1.66
100	10	338 ± 5.8	(b) 14,196 ± 655	41.9 ± 1.44
200	10	335 ± 6.3	13,212 ± 514	39.4 ± 1.07
400	10	326 ± 8.1	13,610 ± 314	41.8 ± 0.92
800	10	310 ± 11.6	13,418 ± 490	43.6 ± 1.48
1,600	6	(c) 139 ± 4.1	(c) 6,222 ± 364	(b) 44.9 ± 2.27
FEMALE				
0	10	182 ± 3.3	6,597 ± 274	36.1 ± 1.09
100	(d) 10	193 ± 5.1	7,333 ± 199	38.6 ± 1.23
200	10	(b) 197 ± 3.0	(c) 7,525 ± 211	38.2 ± 0.81
400	10	189 ± 3.3	6,950 ± 152	36.7 ± 0.60
800	10	194 ± 2.9	(c) 8,037 ± 198	(c) 41.5 ± 0.58
1,600	8	(c) 106 ± 1.0	(c) 4,584 ± 184	(c) 43.5 ± 2.14

(a) Mean ± standard error; P values vs. the controls by Dunnett's test (Dunnett, 1955).
(b) $P<0.05$
(c) $P<0.01$
(d) One liver weight not recorded at necropsy; liver to body weight ratio based on nine animals.

Compound-related lesions were observed at 1,600 ppm, but not at lower concentrations. Minimal-to-moderate mineralization of the brain in the granular cell layer of the cerebellum was seen in 7/10 males and 7/10 females. Minimal degeneration in the lumbar spinal cord consisting of slightly increased vacuolization of the white matter and occasional axonal swelling occurred in 6/9 males and 7/10 females. Minimal-to-severe hemosiderosis was present in the spleen of all animals. Minimal-to-moderate depletion of the hematopoietic cells of the bone marrow was seen in 7/10 males and 8/9 females. Atrophy of the skeletal muscle of the thigh in 7/10 males and 6/8 females was characterized by a decrease in fiber size and staining with a relative increase in the number of muscle fiber nuclei. Severe atrophy of the testis, with almost complete absence of germinal epithelium, was seen in all males. A minimal atrophy of the uterus, characterized by a decrease in the thickness of the endometrium, occurred in all females examined. Squamous metaplasia of the excretory ducts in the submandibular salivary gland and acute inflammation were present in four male and three female rats. One additional male had acute inflammation of the Harderian gland. Although rats were serologically negative for rat coronavirus/sialodacryoadenitis virus (RCV/SDA), the lesions were typical for the SDA virus infection with respect to morphology and the tissues involved.

Dose Selection Rationale: Because of deaths observed in rats at 1,600 ppm and in mice at 800 and 1,600 ppm, exposure concentrations of bromoethane selected for rats and mice for the 2-year studies were 0, 100, 200, and 400 ppm, 6 hours per day, 5 days per week. The same concentrations were selected for rats and mice so they could occupy the same chambers in the 2-year studies.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of exposed and control male and female rats were generally similar throughout the studies (Table 9 and Figure 12). The incidence of conjunctivitis was increased for female rats at 400 ppm.

TABLE 9. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE

Weeks on Study	Chamber Control		100 ppm			200 ppm			400 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE											
0	187	49	184	98	50	184	98	50	184	98	50
1	209	49	213	102	50	213	102	50	214	102	50
2	230	49	238	103	50	236	103	50	233	101	50
3	247	49	256	104	50	257	104	50	257	104	50
4	262	49	272	104	50	266	102	50	271	103	50
5	278	49	288	104	50	281	101	50	286	103	50
6	289	49	299	103	50	294	102	50	297	103	50
7	297	49	308	104	50	305	103	50	308	104	50
8	305	49	316	104	50	312	102	50	318	104	50
9	314	49	326	104	50	322	103	50	326	104	50
10	325	49	334	103	50	330	102	50	337	104	50
11	332	49	343	103	50	338	102	50	343	103	50
12	342	49	351	103	50	348	102	50	351	103	50
17	367	49	375	102	50	371	101	50	375	102	50
21	387	49	398	103	50	387	100	50	389	101	50
25	400	49	406	102	50	398	100	50	400	100	50
29	414	49	422	102	50	414	100	50	414	100	50
33	420	49	425	101	50	420	100	50	421	100	50
38	432	49	438	101	50	430	100	50	427	99	50
42	438	49	447	102	50	441	101	50	437	100	50
46	443	49	457	103	50	444	100	50	444	100	50
51	442	49	453	102	50	443	100	50	438	99	49
55	442	48	453	102	50	445	101	50	433	98	49
60	454	47	463	102	50	455	100	50	444	98	48
64	457	47	466	102	49	457	100	50	451	99	45
67	463	46	472	102	49	461	100	50	451	97	45
72	464	46	476	103	49	466	100	50	459	99	44
77	462	44	474	103	47	465	101	50	462	100	42
81	456	41	475	104	46	464	102	47	466	102	41
84	455	38	481	106	43	467	103	44	464	102	39
89	454	34	468	103	40	459	101	43	464	102	37
93	443	31	461	104	37	455	103	37	450	102	34
98	428	25	450	105	32	453	106	32	442	103	25
102	425	20	439	103	28	438	103	30	425	100	24
FEMALE											
0	135	50	136	101	50	134	99	49	137	101	50
1	145	50	149	103	50	147	101	49	149	103	50
2	154	50	158	103	50	156	101	49	159	103	50
3	163	50	168	103	50	167	102	49	169	104	50
4	170	50	173	102	50	173	102	49	174	102	50
5	177	50	181	102	50	179	101	49	183	103	50
6	177	50	183	103	50	183	103	49	186	105	50
7	182	50	187	103	50	185	102	49	188	103	50
8	187	50	193	103	50	190	102	49	191	102	50
9	188	50	196	104	50	194	103	49	195	104	50
10	193	50	200	104	50	198	103	49	199	103	50
11	196	50	201	103	50	200	102	49	203	104	50
12	199	50	203	102	50	203	102	49	205	103	50
17	208	50	215	103	50	216	104	49	213	102	50
21	219	50	225	103	50	217	99	49	223	102	50
25	226	50	232	103	50	229	101	49	227	100	50
29	235	50	234	100	50	238	101	49	239	102	50
33	242	50	249	103	50	245	101	49	244	101	50
38	250	50	258	103	50	254	102	49	251	100	50
42	259	50	267	103	50	260	100	49	259	100	50
46	272	50	275	101	50	270	99	49	268	99	50
51	267	50	272	102	50	266	100	49	268	100	49
55	280	49	286	102	50	277	99	49	270	96	49
60	293	49	297	101	50	287	98	47	286	98	48
64	299	49	303	101	49	293	98	45	292	98	48
67	307	49	312	102	48	298	97	44	297	97	48
72	316	49	320	101	48	304	96	42	306	97	47
77	320	44	327	102	48	315	98	41	311	97	46
81	328	40	329	100	48	314	96	41	312	95	44
84	337	39	335	99	46	321	95	40	317	94	41
89	325	37	340	105	43	319	98	38	318	98	40
93	329	35	336	102	42	320	97	34	304	92	38
98	326	30	331	102	39	316	97	33	312	96	29
102	325	26	332	102	33	316	97	29	311	96	25

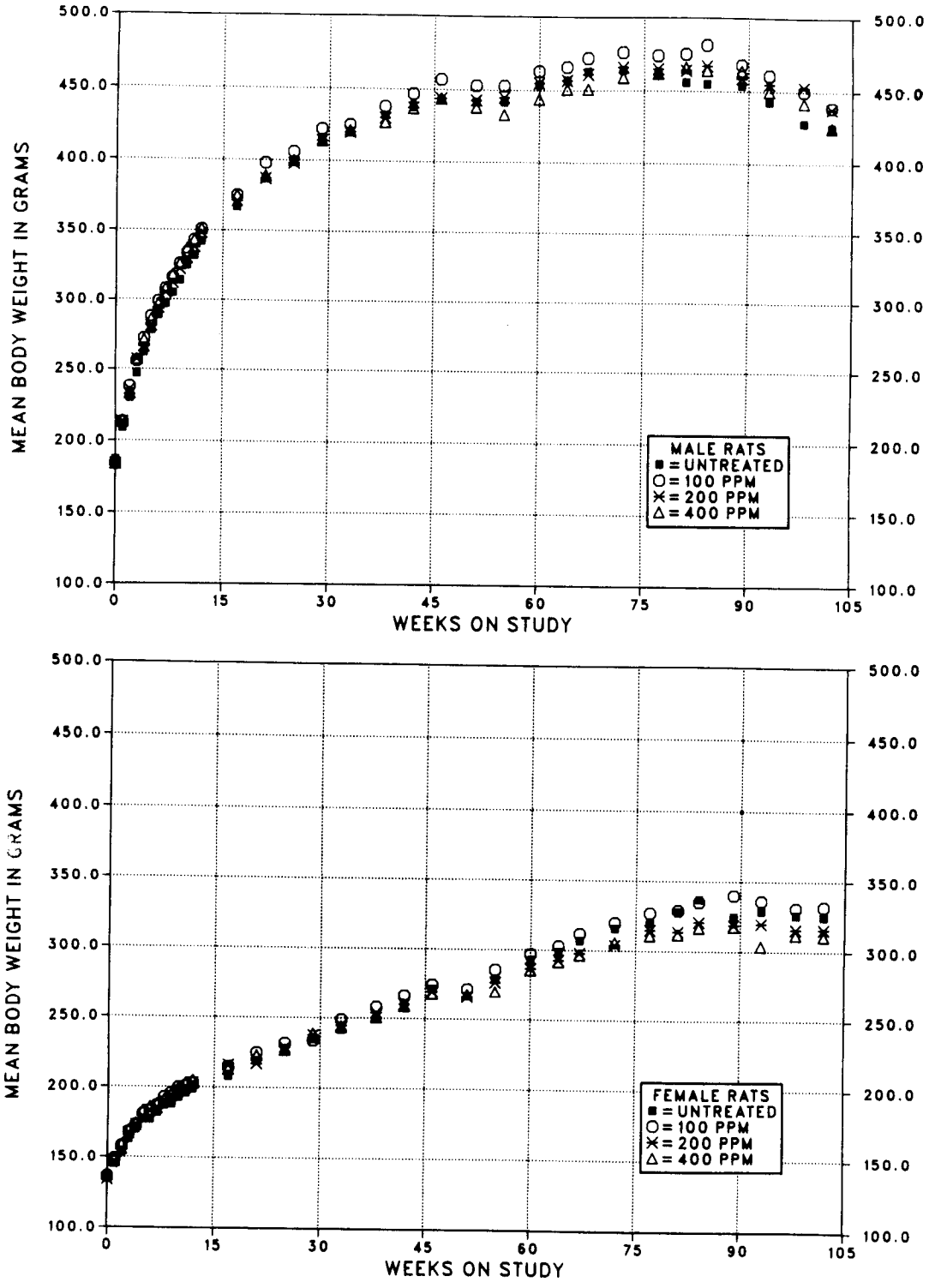

FIGURE 12. GROWTH CURVES FOR RATS EXPOSED TO BROMOETHANE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female rats exposed to bromoethane at the concentrations used in these studies and for controls are shown in Table 10 and in the Kaplan and Meier curves in Figure 13. No significant differences in survival were observed between any groups of male rats. The survival of the 100-ppm group of female rats was significantly greater than that of the controls at the end of the study.

Pathology and Statistical Analyses of Results

This section describes the statistically significant or biologically noteworthy changes in the incidences of rats with neoplastic or nonneoplastic lesions of the adrenal gland, brain, lung, nose, larynx, salivary gland, and mammary gland.

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one animal group, and historical control incidences for the neoplasms mentioned in this section are presented in Appendixes A and B for male and female rats, respectively.

TABLE 10. SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
MALE (a)				
Animals initially in study	50	50	50	50
Natural deaths	7	9	5	4
Moribund kills	25	15	19	25
Animals missexed	1	0	0	0
Animals surviving until study termination	17	26	(b) 27	21
Survival P values (c)	0.705	0.095	0.057	0.536
FEMALE (a)				
Animals initially in study	50	50	50	50
Natural deaths	2	5	5	4
Moribund kills	29	15	19	24
Accidentally killed	0	1	0	0
Animals missing	0	0	1	0
Animals missexed	0	0	1	0
Animals surviving until study termination	19	29	24	(b) 23
Survival P values (c)	1.000	0.037	0.405	0.686

(a) First week of termination period: 106
(b) One animal died or was killed in a moribund condition and was combined, for statistical purposes, with those killed at termination.
(c) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

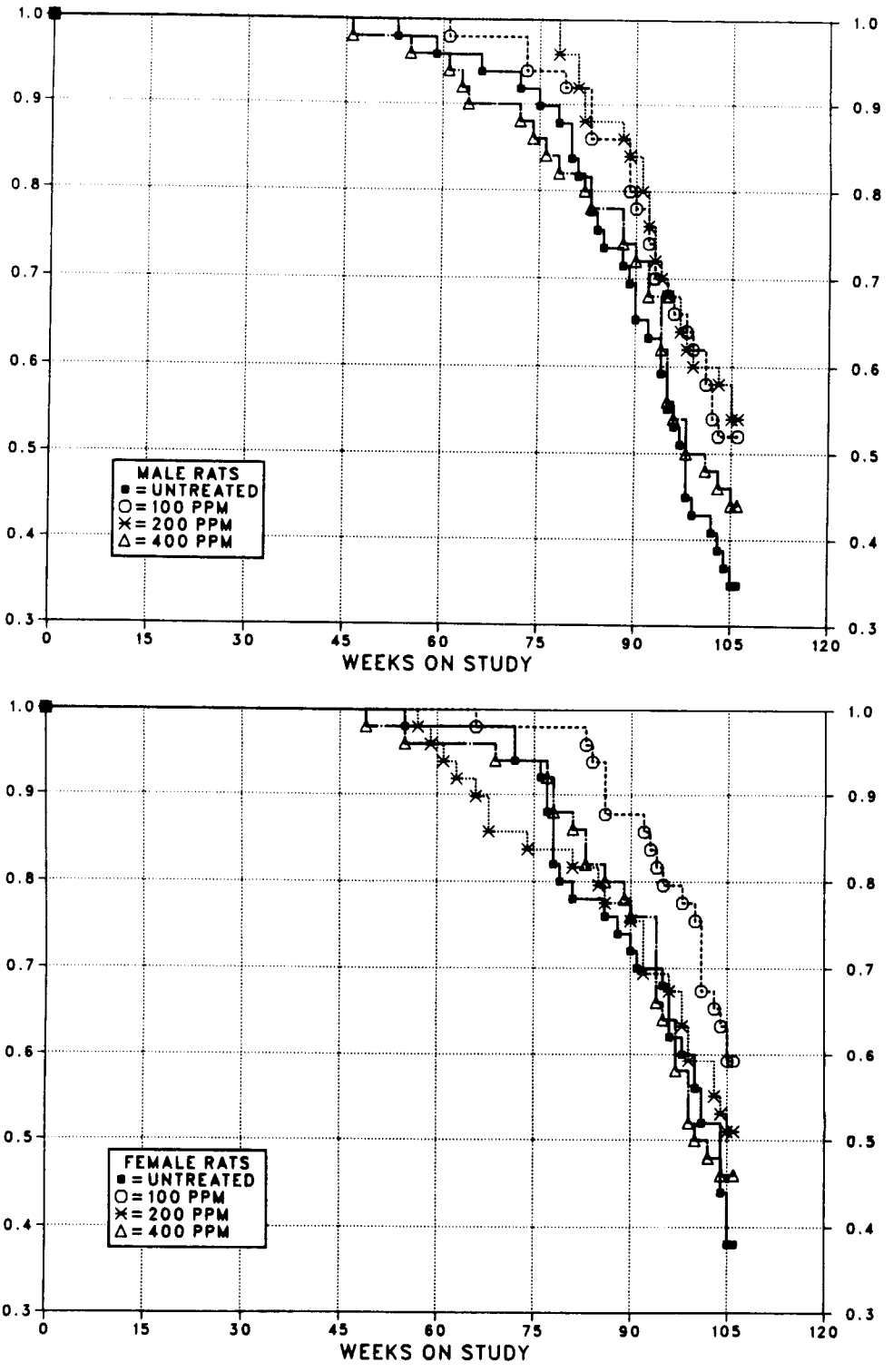

FIGURE 13. KAPLAN-MEIER SURVIVAL CURVES FOR RATS EXPOSED TO BROMOETHANE BY INHALATION FOR TWO YEARS

Adrenal Gland: Clear cell change of the cortex was observed at increased incidences in exposed male rats (control, 13/48; 100 ppm, 21/47; 200 ppm, 20/50; 400 ppm, 24/49). This lesion consisted of circumscribed foci of cortical cells filled with clear cytoplasmic vacuoles. It frequently occurred in foci of hyperplasia and may indicate a relative change in metabolism with an accumulation of lipid in the cells.

The incidences of pheochromocytomas of the adrenal medulla in the exposed groups of male rats were increased relative to that in the controls (Table 11), but the incidences of adrenal medullary hyperplasia were similar in all groups. The two malignant pheochromocytomas observed in the 200-ppm group metastasized to the lung and lymph nodes. Adrenal medullary hyperplasia and pheochromocytoma encompass a morphologic continuum, and pheochromocytoma is distinguished from hyperplasia on the basis of compression of adjacent tissue, the degree of cellular atypia, and the extent of alteration in cellular organization or growth pattern. The majority of the pheochromocytomas were microscopic and were not observed grossly.

The adrenal glands of adult rats are paired oval organs, approximately 3 mm × 2 mm; the greatest dimension of the medulla is about 1.5 mm. Because the adrenal gland is small, it is sometimes difficult to obtain sections that consistently include the medulla. In these studies, fewer adrenal medullas were sampled in the controls than in the exposed groups. Since the majority of the pheochromocytomas are microscopic and seem to occur randomly in either of the paired organs, the chance of observing a lesion is reduced if only one medulla is examined. To compensate for the unequal number of medullas examined in the different groups, additional statistical analyses were carried out using the number of animals with at least one medulla examined or using the total number of medullas examined as denominators of the incidences (Table 11). When statistics were performed using the total number of medullas examined as the denominator, the number of medullas with a neoplasm was used as the numerator rather than the number of animals with a neoplasm (some rats had bilateral pheochromocytomas). Table A3 contains the analysis based on animals with at least one adrenal gland examined, and therefore, the data in Table A3 differ from those presented in Table 11.

TABLE 11. ADRENAL MEDULLARY LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (a)

	Chamber Control	100 ppm	200 ppm	400 ppm
Hyperplasia				
Overall Rates	8/40 (20%)	14/45 (31%)	8/46 (17%)	10/46 (22%)
Pheochromocytoma or Malignant Pheochromocytoma (b,c)				
Overall Rates	8/40 (20%)	23/45 (51%)	18/46 (39%)	21/46 (46%)
Terminal Rates	4/17 (24%)	15/26 (58%)	13/26 (50%)	14/19 (74%)
Week of First Observation	98	83	92	83
Incidental Tumor Tests	P=0.021	P=0.013	P=0.112	P=0.007
Pheochromocytoma or Malignant Pheochromocytoma (d)				
Overall Rates	10/66 (15%)	29/82 (35%)	24/85 (28%)	25/86 (29%)
Incidental Tumor Tests	P=0.072	P=0.022	P=0.140	P=0.027

(a) The statistical analyses used are discussed in Section II (Statistical Methods) and Table A3 (footnotes).
(b) Historical incidence in chamber controls at study laboratory (mean ± SD): 57/296 (19% ± 16%); historical incidence in untreated controls (noninhalation) in NTP studies: 489/1,915 (26% ± 14%)
(c) Denominator is number of animals with at least one medulla examined.
(d) Numerator is number of medullas with a neoplasm; denominator is total number of medullas examined.

Brain: Three granular cell tumors occurred in the 100-ppm male rats and one each in the 200- and 400-ppm groups (Table 12). None was present in control male or female rats. Granular cell tumors arise in the meninges and consist of cells filled with PAS-positive cytoplasmic granules. The precise cell origin and the nature of the granules are unknown, but morphologic and immunochemical studies suggest that granular cell tumors are a variant of meningiomas. The historical incidence of granular cell tumors in male F344/N rat chamber controls at the study laboratory is 0/297, and the greatest observed incidence of granular cell tumors in chamber controls or untreated controls in NTP studies is 1/49.

There are three types of glial cells in the brain (astrocytes, oligodendrocytes, and microglial cells), but brain neoplasms in rats are usually derived from astrocytes or oligodendrocytes. Those glial cell neoplasms consisting of a relatively pure population of neoplastic cells are classified according to the predominant cell type as astrocytoma or oligodendroglioma. Frequently, however, glial cell neoplasms in the rat contain neoplastic cells with histologic features characteristic of both astrocytes and oligodendrocytes and are simply called gliomas.

A glioma, an astrocytoma, or an oligodendroglioma was seen in 3/50 male rats at 100 ppm. The historical incidence of glial cell tumors at

TABLE 12. BRAIN TUMORS IN RATS IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE (a)

	Chamber Control	100 ppm	200 ppm	400 ppm
MALE				
Granular Cell Tumor (a)				
Overall Rates	0/49 (0%)	3/50 (6%)	1/50 (2%)	1/50 (2%)
Terminal Rates	0/17 (0%)	3/26 (12%)	0/27 (0%)	0/22 (0%)
Week of First Observation		106	89	96
Incidental Tumor Tests	P=0.582	P=0.203	P=0.464	P=0.469
Glioma				
Overall Rates	0/49 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
Astrocytoma				
Overall Rates	0/49 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
Oligodendroglioma				
Overall Rates	0/49 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
Glioma, Astrocytoma, or Oligodendroglioma (b)				
Overall Rates	0/49 (0%)	3/50 (6%)	0/50 (0%)	0/50 (0%)
Terminal Rates	0/17 (0%)	0/26 (0%)	0/27 (0%)	0/22 (0%)
Week of First Observation		83		
Incidental Tumor Tests	P=0.394N	P=0.087	(c)	(c)
FEMALE				
Glioma (d)				
Overall Rates	0/50 (0%)	1/50 (2%)	1/48 (2%)	3/50 (6%)
Terminal Rates	0/19 (0%)	0/29 (0%)	0/24 (0%)	2/23 (9%)
Week of First Observation		62	99	78
Incidental Tumor Tests	P=0.045	P=0.205	P=0.385	P=0.107

(a) Historical incidence in chamber controls at study laboratory: 0/297; historical incidence in untreated controls (noninhalation) in NTP studies (mean ± SD): 4/1,928 (0.2% ± 0.6%)
(b) Historical incidence of glial cell tumors in chamber controls at study laboratory (mean ± SD): 3/297 (1% ± 1%); historical incidence in untreated controls (noninhalation) in NTP studies: 13/1,928 (0.7% ± 1%)
(c) No P value is reported because no tumors were observed in the control and 200- and 400-ppm groups.
(d) Historical incidence of glial cell tumors in chamber controls at study laboratory (mean ± SD): 1/297 (0.3% ± 0.8%); historical incidence in untreated controls (noninhalation) in NTP studies: 23/1,969 (1% ± 2%)

the study laboratory is 3/297 (1%), and the greatest observed incidence of glial cell tumors in chamber controls or untreated controls in NTP studies is 2/50. Gliomas occurred in one female rat in the low and mid exposure groups and in three female rats in the high exposure group. The incidences in the exposed groups were not significantly greater than that in the controls and were within the historical incidence range for untreated controls.

Lung: Alveolar epithelial hyperplasia was observed at increased incidences in 400-ppm rats (Tables 13 and 14). Many of these lesions were associated with varied number of inflammatory cells and are likely secondary to the inflammation rather than a primary proliferative process. Others were not associated with inflammation. Alveolar/bronchiolar adenomas were seen in 3/49 female rats exposed to 400 ppm. Alveolar/bronchiolar adenomas or carcinomas (combined) were seen in 0/48 control, 0/49 100-ppm, 4/48 200-ppm, and 1/48 400-ppm male rats. The incidences in the exposed groups were not significantly greater than that in the controls.

TABLE 13. LUNG LESIONS IN RATS IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
MALE				
Alveolar Epithelial Hyperplasia				
Overall Rates	3/48 (6%)	7/49 (14%)	7/48 (15%)	18/48 (38%)
Alveolar/Bronchiolar Adenoma				
Overall Rates	0/48 (0%)	0/49 (0%)	1/48 (2%)	1/48 (2%)
Alveolar/Bronchiolar Carcinoma				
Overall Rates	0/48 (0%)	0/49 (0%)	3/48 (6%)	0/48 (0%)
Alveolar/Bronchiolar Adenoma or Carcinoma (a)				
Overall Rates	0/48 (0%)	0/49 (0%)	4/48 (8%)	1/48 (2%)
Terminal Rates	0/17 (0%)	0/26 (0%)	2/27 (7%)	1/22 (5%)
Week of First Observation			93	106
Incidental Tumor Tests	P=0.250	(b)	P=0.068	P=0.551
FEMALE				
Alveolar Epithelial Hyperplasia				
Overall Rates	5/50 (10%)	4/48 (8%)	5/47 (11%)	10/49 (20%)
Alveolar/Bronchiolar Adenoma (c)				
Overall Rates	0/50 (0%)	0/48 (0%)	0/47 (0%)	3/49 (6%)
Terminal Rates	0/19 (0%)	0/29 (0%)	0/24 (0%)	3/23 (13%)
Week of First Observation				106
Incidental Tumor Tests	P=0.010	(b)	(b)	P=0.154

(a) Historical incidence in chamber controls at study laboratory (mean ± SD): 6/299 (2% ± 1%); historical incidence in untreated controls (noninhalation) in NTP studies: 43/1,933 (2% ± 2%)
(b) No P value is reported because no tumors were observed in the exposed and control groups.
(c) Historical incidence of adenomas or carcinomas (combined) in chamber controls at study laboratory (mean ± SD): 4/297 (1% ± 2%); historical incidence in untreated controls (noninhalation) in NTP studies: 22/1,974 (1% ± 1%)

TABLE 14. INCIDENCES OF RATS WITH SELECTED NONNEOPLASTIC LESIONS OF THE RESPIRATORY TRACT IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE

Site/Lesion	Chamber Control	100 ppm	200 ppm	400 ppm
MALE				
Nasal Cavity				
Suppurative inflammation	18/47	28/48	33/49	40/49
Epithelial hyperplasia	14/47	14/48	14/49	27/49
Squamous metaplasia	4/47	2/48	2/49	9/49
Olfactory epithelium, respiratory metaplasia	0/49	0/50	7/50	6/50
Larynx				
Suppurative inflammation	7/49	21/50	14/50	25/50
Epithelial hyperplasia	0/49	3/50	4/50	2/50
Lung				
Suppurative inflammation	7/48	13/49	6/48	10/48
Histiocytosis	18/48	31/49	27/48	29/48
Alveolar/epithelium hyperplasia	3/48	7/49	7/48	18/48
FEMALE				
Nasal Cavity				
Suppurative inflammation	18/49	13/47	22/47	25/48
Epithelial hyperplasia	7/49	9/47	9/47	15/48
Squamous metaplasia	2/49	2/47	2/47	9/48
Olfactory epithelium, respiratory metaplasia	0/50	3/50	0/48	5/50
Larynx				
Suppurative inflammation	12/50	17/50	22/48	20/50
Epithelial hyperplasia	1/50	2/50	2/48	3/50
Lung				
Suppurative inflammation	8/50	11/48	9/47	9/49
Histiocytosis	15/50	25/48	20/47	24/49
Alveolar/epithelium hyperplasia	5/50	4/48	5/47	10/49

Nose: Suppurative inflammation occurred at increased incidences in exposed male rats relative to controls (see Table 14). Hyperplasia and/or metaplasia of the mucosal epithelium were associated with the inflammatory lesions. Foreign material (hair and feed) were also sometimes present in these lesions. A papillary adenoma of the nose was seen in one male rat at 400 ppm. The historical incidence of nasal neoplasms in male F344/N rat chamber controls at the study laboratory is 0/300 and in untreated controls is 2/1,936 (0.1%).

Larynx: Suppurative inflammation was observed at increased incidences in exposed rats (see Table 14).

Salivary Gland: Suppurative inflammation and dilatation of the ducts were observed at increased incidences in female rats at 200 and 400 ppm (suppurative inflammation: control, 2/49; 100 ppm, 3/47; 200 ppm, 9/45; 400 ppm, 14/48; dilatation: 3/49; 3/47; 9/45; 12/48). Positive titers to rat RCV/SDA were observed in some animals with salivary gland lesions.

Mammary Gland: Mammary gland tumors in female rats occurred with significant negative trends; the incidences at 200 and 400 ppm were significantly lower than those in controls (Table 15).

TABLE 15. MAMMARY GLAND TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Adenoma				
Overall Rates	1/50 (2%)	0/50 (0%)	0/48 (0%)	0/50 (0%)
Fibroadenoma				
Overall Rates	16/50 (32%)	14/50 (28%)	8/48 (17%)	6/50 (12%)
Terminal Rates	8/19 (42%)	12/29 (41%)	5/24 (21%)	3/23 (13%)
Week of First Observation	72	86	86	83
Incidental Tumor Tests	P=0.004N	P=0.220N	P=0.042N	P=0.013N
Adenoma or Fibroadenoma				
Overall Rates	17/50 (34%)	14/50 (28%)	8/48 (17%)	6/50 (12%)
Terminal Rates	8/19 (42%)	12/29 (41%)	5/24 (21%)	3/23 (13%)
Week of First Observation	72	86	86	83
Incidental Tumor Tests	P=0.003N	P=0.168N	P=0.031N	P=0.008N
Adenocarcinoma				
Overall Rates	4/50 (8%)	2/50 (4%)	1/48 (2%)	1/50 (2%)
Adenosquamous Carcinoma				
Overall Rates	0/50 (0%)	0/50 (0%)	1/48 (2%)	0/50 (0%)
Adenoma, Fibroadenoma, Adenocarcinoma, or Adenosquamous Carcinoma (a)				
Overall Rates	18/50 (36%)	15/50 (30%)	10/48 (21%)	7/50 (14%)
Terminal Rates	8/19 (42%)	13/29 (45%)	5/24 (21%)	4/23 (17%)
Week of First Observation	72	86	66	83
Incidental Tumor Tests	P=0.004N	P=0.197N	P=0.060N	P=0.011N

(a) Historical incidence in chamber controls at study laboratory (mean ± SD): 58/299 (19% ± 8%); historical incidence in untreated controls (noninhalation) in NTP studies: 622/1,983 (31% ± 10%)

III. RESULTS: MICE

SINGLE-EXPOSURE STUDIES

All mice exposed to 5,000 or 10,000 ppm bromoethane and 2/5 female mice exposed to 1,250 ppm died before the end of the studies (Table 16). Clinical signs observed during the initial part of the exposure to 10,000 ppm included increased respiration rate, hyperactivity, and incoordination.

FOURTEEN-DAY STUDIES

All mice exposed to 4,000 ppm died by day 3, and those exposed to 2,000 ppm died before the end of the studies (Table 17). Final mean body weights were not compound related. Male mice exposed to 2,000 ppm had difficulty standing by day 3 and were dyspneic by day 7 or 8. Three mice in the 1,000- or 2,000-ppm groups were examined histologically. Minimal pulmonary congestion was seen in one mouse at 1,000 ppm, and mild pulmonary hemorrhage was seen in another mouse.

TABLE 16. SURVIVAL AND INITIAL MEAN BODY WEIGHT OF MICE IN THE SINGLE-EXPOSURE INHALATION STUDIES OF BROMOETHANE

Concentration (ppm)	Survival (a)	Initial Mean Body Weight (b) (grams)
MALE		
625	5/5	24 ± 0.8
1,250	5/5	25 ± 1.0
2,500	5/5	24 ± 0.6
5,000	(c) 0/5	24 ± 0.5
10,000	(d) 0/5	24 ± 0.7
FEMALE (e)		
625	5/5	22 ± 1.0
1,250	(f) 3/5	21 ± 0.7
2,500	5/5	21 ± 0.7
5,000	(g) 0/5	21 ± 0.7
10,000	(d) 0/5	20 ± 0.6

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean; final body weights were not recorded.
(c) Day of death: 3,4,4,4,4
(d) Day of death: all 1
(e) LC_{50} (95% confidence interval) based on actual mean concentrations of 659, 1,249, 2,409, 5171, and 9,883 ppm by the Spearman-Karber procedure: 2,723 ppm (1,995-3,718 ppm)
(f) Day of death: 7,10
(g) Day of death: 4,4,5,5,5

TABLE 17. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY INHALATION STUDIES OF BROMOETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams)			Final Weight Relative to Controls (percent)
		Initial (b)	Final	Change (c)	
MALE					
0	5/5	27.8 ± 0.7	29.0 ± 0.7	+1.2 ± 0.6	
250	5/5	26.2 ± 0.9	27.4 ± 0.7	+1.2 ± 0.4	94.5
500	5/5	28.0 ± 1.1	30.0 ± 0.8	+2.0 ± 0.6	103.4
1,000	5/5	27.0 ± 1.0	28.4 ± 1.2	+1.4 ± 0.9	97.9
2,000	(d) 0/5	27.4 ± 0.4	(e)	(e)	(e)
4,000	(f) 0/5	26.2 ± 0.7	(e)	(e)	(e)
FEMALE					
0	5/5	20.6 ± 0.2	23.6 ± 0.7	+3.0 ± 0.8	
250	5/5	19.8 ± 0.4	23.2 ± 1.1	+3.4 ± 1.0	98.3
500	5/5	21.0 ± 0.4	22.2 ± 0.2	+1.2 ± 0.4	94.1
1,000	5/5	21.6 ± 0.7	23.2 ± 1.1	+1.6 ± 0.5	98.3
2,000	(g) 0/5	22.0 ± 0.3	(e)	(e)	(e)
4,000	(h) 0/5	21.2 ± 1.1	(e)	(e)	(e)

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean
(c) Mean body weight change of the group ± standard error of the mean
(d) Day of death: 3,4,4,4,10
(e) No data are reported due to the 100% mortality in this group.
(f) Day of death: all 3
(g) Day of death: 5,6,9,10,10
(h) Day of death: 2,2,3,3,3

FOURTEEN-WEEK STUDIES

Six male and three female mice exposed to bromoethane died before the end of the studies (Table 18). The deaths of one male at 800 ppm, one female at 400 ppm, and one female at 200 ppm were accidental. The final mean body weights of mice exposed to 1,600 ppm were 15% lower than that of controls for males and 16% lower for females. Clinical signs included ataxia and tremors between weeks 11 and 13 in mice exposed to 1,600 ppm. The liver weight to body weight ratios for mice were not compound related (Table 19). Positive titers to Sendai virus were seen in the sera of all 10 mice tested at the end of the studies. A minimal-to-mild atrophy of the uterus, characterized by decreased thickness of the endometrium, was present in 3/10 female mice at 1,600 ppm. A minimal involution of the ovary was also present in 3/9 females at 800 ppm and in 7/10 females at 1,600 ppm. This functional change consisted of a decrease in the size of the ovary and the size and number of corpora lutea. Atrophy of the skeletal muscle of the thigh was present in 6/10 males and 6/6 females from the 1,600-ppm groups. This minimal change was morphologically similar to that described for the rats.

Dose Selection Rationale: Because of compound-related deaths observed at 1,600 ppm in male and female mice and deaths at 800 ppm in male mice, exposure concentrations selected for mice for the 2-year studies were 0, 100, 200, and 400 ppm, 6 hours per day, 5 days per week.

TABLE 18. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-WEEK INHALATION STUDIES OF BROMOETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	23.4 ± 0.3	29.3 ± 0.6	+5.9 ± 0.6	
100	10/10	21.7 ± 0.4	28.7 ± 0.6	+7.0 ± 0.4	98.0
200	10/10	21.5 ± 0.6	30.5 ± 1.0	+9.0 ± 0.7	104.1
400	(d) 9/10	21.6 ± 0.5	29.8 ± 0.8	+8.1 ± 0.7	101.7
800	(e) 8/10	23.5 ± 0.5	29.1 ± 0.7	+5.3 ± 0.7	99.3
1,600	(f,g) 7/10	23.5 ± 0.5	24.8 ± 0.9	+1.3 ± 0.4	84.6
FEMALE					
0	10/10	19.3 ± 0.3	27.0 ± 0.6	+7.7 ± 0.4	
100	10/10	17.9 ± 0.3	27.1 ± 0.5	+9.2 ± 0.7	100.4
200	(h) 9/10	18.2 ± 0.2	25.9 ± 0.3	+7.7 ± 0.4	95.9
400	(h) 9/10	18.4 ± 0.3	26.9 ± 0.5	+8.3 ± 0.5	99.6
800	10/10	19.3 ± 0.4	26.4 ± 0.4	+7.1 ± 0.3	97.8
1,600	(g,i) 9/10	19.0 ± 0.5	22.6 ± 0.7	+4.0 ± 0.6	83.7

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean. Subsequent calculations are based on animals surviving to the end of the study.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Week of death: 1
(e) Week of death: 6; the second death was accidental.
(f) Week of death: 1,13,13
(g) One body weight not recorded at necropsy; final weight and weight change are based on weights actually recorded.
(h) Death judged accidental
(i) Week of death: 10

TABLE 19. LIVER WEIGHTS FOR MICE IN THE FOURTEEN-WEEK INHALATION STUDIES OF BROMOETHANE (a)

Concentration (ppm)	Number Weighed	Final Body Weight (grams)	Liver Weight (mg)	Liver Weight/ Final Body Weight (mg/g)
MALE				
0	10	29.3 ± 0.63	1,645 ± 122	55.9 ± 3.64
100	10	28.7 ± 0.56	1,613 ± 37	56.3 ± 1.26
200	10	30.5 ± 0.97	1,568 ± 67	51.3 ± 1.09
400	9	29.8 ± 0.84	1,687 ± 61	56.6 ± 1.58
800	8	29.1 ± 0.71	1,506 ± 29	52.0 ± 1.56
1,600	6	(b) 24.8 ± 0.87	1,455 ± 62	58.6 ± 1.05
FEMALE				
0	10	27.0 ± 0.57	1,671 ± 32	62.1 ± 1.26
100	10	27.1 ± 0.52	1,547 ± 49	57.0 ± 1.14
200	9	25.9 ± 0.26	(b) 1,330 ± 38	(b) 51.4 ± 1.57
400	9	26.9 ± 0.51	1,531 ± 40	57.0 ± 1.40
800	10	26.4 ± 0.43	(b) 1,406 ± 40	(b) 53.4 ± 1.21
1,600	8	(b) 22.6 ± 0.73	1,486 ± 111	65.1 ± 3.24

(a) Mean ± standard error; P values vs. the controls by Dunnett's test (Dunnett, 1955).
(b) $P<0.01$

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of the 400-ppm group of male mice were 1%-9% lower than those of the controls throughout most of the study; mean body weights of the 100-ppm group of male mice were 97%-108% those of the controls throughout the study (Table 20 and Figure 14). Mean body weights of the 400-ppm group of female mice were generally 6%-16% lower than those of the controls after week 29; mean body weights of the 100-ppm group of female mice were 96%-108% those of the controls throughout the study. No compound-related clinical signs were observed.

TABLE 20. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE

Weeks on Study	Chamber Control		100 ppm			200 ppm			400 ppm		
	Av. Wt. (grams)	No. of Survivors	Av Wt grams)	Wt (percent of controls)	No of Survivors	Av Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av Wt. grams)	Wt. (percent of controls)	No of Survivors
MALE											
0	24 0	50	23 9	100	50	23 8	99	50	24 5	102	50
1	25 4	50	26 1	103	50	25 7	101	50	25 7	101	50
2	26 7	50	26 5	99	50	26 6	100	49	26 3	99	50
3	27 8	50	27 9	100	50	26 9	97	49	27 5	99	50
4	28 4	50	28 5	100	50	27 6	97	49	28 1	99	50
5	29 1	50	28 5	98	50	28 8	99	49	26 4	91	50
6	29 5	50	28 5	97	50	29 0	98	49	28 1	95	50
7	29 5	50	29 8	101	50	28 6	97	49	28 4	96	50
8	30 1	50	30 4	101	50	29 8	99	49	29 6	98	50
9	30 2	50	30 5	101	50	30 7	102	49	29 3	97	50
10	30 8	50	30 4	99	50	29 8	97	49	29 4	95	50
11	30 5	50	31 7	104	50	30 4	100	49	30 0	98	50
12	31 5	50	31 9	101	50	31 _	99	49	29 9	95	50
17	32 8	50	33 7	103	50	33 0	101	49	31 0	95	50
21	33 8	50	35 1	104	50	34 4	102	49	32 8	97	50
25	34 8	50	36 1	104	50	34 6	99	49	31 3	92	50
29	35 1	50	37 2	106	50	35 7	102	49	34 0	97	50
33	35 0	50	37 6	107	50	35 4	101	49	33 0	94	50
38	36 9	50	38 7	105	50	37 0	100	49	35 3	96	50
42	38 4	50	39 5	103	50	37 6	98	49	35 2	91	50
46	37 5	50	39 7	106	50	37 0	99	49	35 7	95	50
51	39 1	50	40 4	103	50	38 7	99	49	38 8	99	50
55	40 6	50	43 1	106	50	40 8	100	49	38 7	95	49
60	41 6	48	41 2	99	48	38 7	93	49	39 1	94	48
64	41 3	46	41 5	100	46	40 1	97	48	39 8	96	46
67	41 5	46	43 5	105	46	41 1	99	46	39 6	95	46
72	41 3	45	43 2	105	46	41 2	100	46	39 6	96	45
77	40 0	43	42 7	107	46	39 7	99	45	39 6	99	45
81	39 6	43	42 6	108	45	39 0	98	44	36 8	93	44
84	40 3	42	42 3	105	44	40 3	100	41	39 5	98	42
89	40 4	40	42 3	105	42	39 7	98	39	37 9	94	42
93	39 3	39	41 5	106	41	38 7	98	37	38 8	99	39
98	38 8	38	41 1	106	39	38 4	99	36	37 5	97	36
102	38 5	36	40 1	104	37	37 9	98	32	37 5	97	36
FEMALE											
0	17 9	50	19 0	106	50	19 3	108	50	19 6	109	49
1	20 6	50	20 8	101	50	20 8	101	50	20 5	100	49
2	21 4	50	21 6	101	50	21 8	102	50	21 4	100	49
3	22 5	50	23 4	104	50	22 6	100	50	23 6	105	49
4	22 1	50	23 6	107	50	22 9	104	50	22 8	103	49
5	23 3	50	24 1	103	50	23 8	102	50	23 8	102	49
6	23 9	50	23 5	98	50	23 3	97	50	23 8	100	49
7	24 1	50	24 8	103	50	24 2	100	50	24 0	100	49
8	25 5	50	25 3	99	50	24 5	96	50	24 4	96	49
9	24 8	50	25 8	104	50	25 4	102	50	25 1	101	49
10	25 2	50	24 7	98	50	25 7	102	50	25 1	100	49
11	25 8	50	26 8	104	50	26 1	101	50	25 1	97	49
12	25 6	50	26 2	102	50	25 1	98	50	25 2	98	49
17	27 2	50	27 6	101	50	26 9	99	50	25 9	95	49
21	29 0	50	28 4	98	49	28 5	98	50	27 6	95	49
25	28 1	50	28 5	101	49	27 5	98	50	27 1	96	49
29	29 5	50	29 0	98	49	28 6	97	50	27 8	94	49
33	29 7	50	30 4	102	49	29 1	98	50	27 0	91	49
38	30 9	50	30 8	100	49	29 1	94	49	28 2	91	49
42	31 1	50	31 5	101	49	30 2	97	49	28 3	91	48
46	31 5	50	31 7	101	49	30 6	97	49	26 6	84	48
51	33 7	50	33 3	99	48	33 3	99	49	32 2	96	48
55	35 2	50	36 8	105	48	35 3	100	49	31 5	89	48
60	35 0	50	36 1	103	48	33 6	96	49	31 8	91	48
64	36 6	50	35 2	96	48	33 4	91	47	35 4	97	48
67	35 9	50	36 5	102	48	35 2	98	46	32 1	89	46
72	36 2	49	36 3	100	48	35 1	97	45	31 4	87	46
77	35 2	49	36 5	104	46	34 7	99	45	31 5	89	46
81	35 1	49	36 3	103	45	34 6	99	45	31 5	90	46
84	35 8	49	36 7	103	43	35 4	99	45	32 7	91	43
89	34 8	47	37 6	108	43	34 9	100	45	31 6	91	40
93	33 9	42	36 1	106	41	34 7	102	44	31 5	93	35
98	34 5	38	36 4	106	40	34 4	100	40	31 3	91	28
102	34 2	36	36 6	107	37	35 1	103	39	31 5	92	25

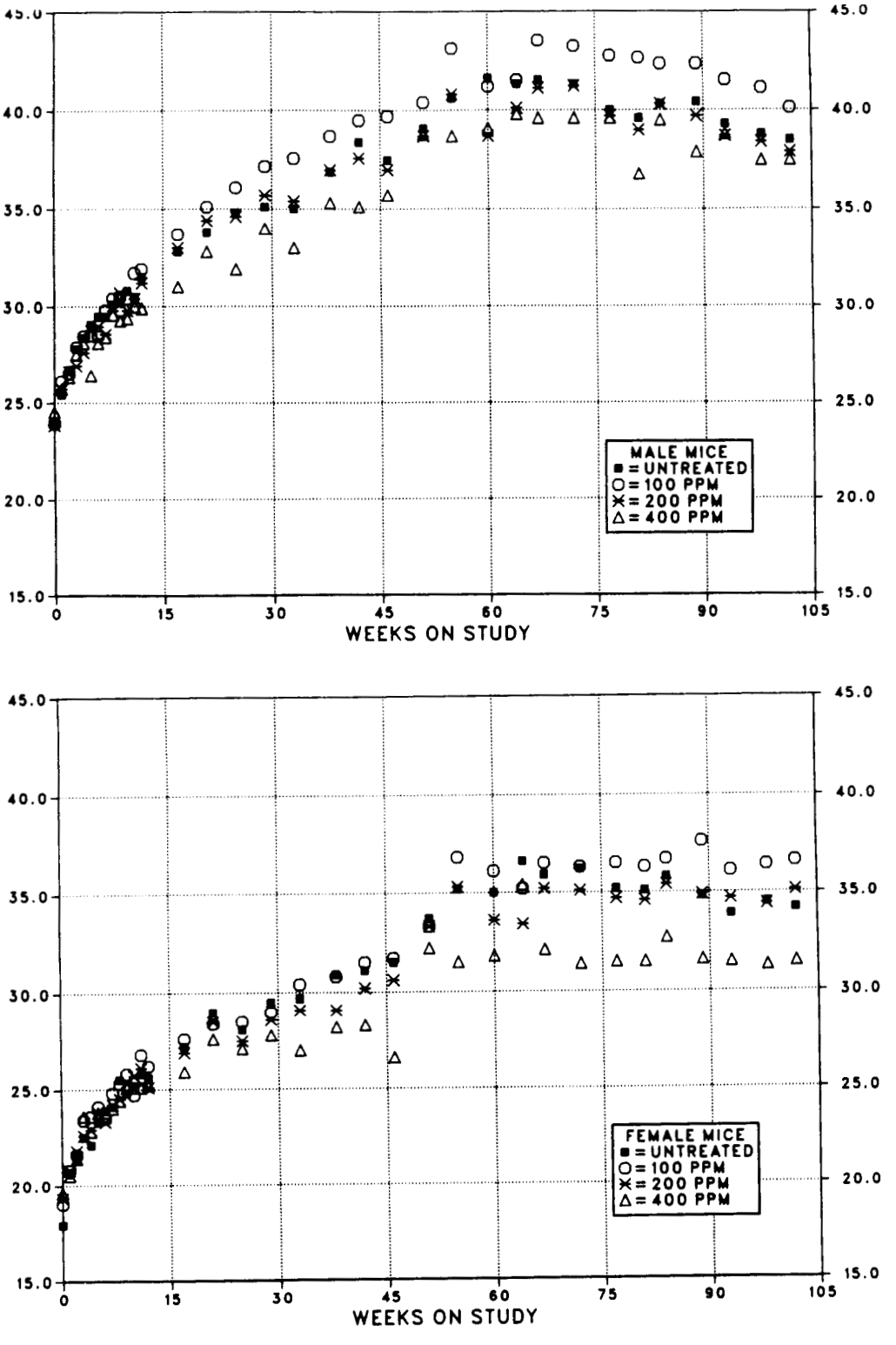

FIGURE 14. GROWTH CURVES FOR MICE EXPOSED TO BROMOETHANE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female mice exposed to bromoethane at the concentrations used in these studies and for controls are shown in Table 21 and in the Kaplan and Meier curves in Figure 15. The survival of the 400-ppm group of female mice was significantly lower than that of the controls at the end of the study. No other differences in survival were observed between any group of either sex.

Pathology and Statistical Analyses of Results

This section describes the statistically significant or biologically noteworthy changes in the incidences of mice with neoplastic or nonneoplastic lesions of the uterus, lung, nasal cavity, ovary, circulatory system, and liver.

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one animal group, and historical control incidences for the neoplasms mentioned in this section are presented in Appendixes C and D for male and female mice, respectively.

TABLE 21. SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
MALE (a)				
Animals initially in study	50	50	50	50
Natural deaths	9	10	14	8
Moribund kills	6	3	6	8
Animals surviving until study termination	35	37	30	34
Survival P values (b)	0.692	0.795	0.442	0.996
FEMALE (a)				
Animals initially in study	50	50	50	50
Natural deaths	10	8	9	12
Moribund kills	4	5	4	14
Accidentally killed	0	0	0	1
Animals missexed	0	0	1	1
Animals surviving until study termination	36	37	(c) 37	(c) 23
Survival P values (b)	0.009	0.919	0.864	0.024

(a) First week of termination period: 105
(b) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.
(c) One animal died or was killed in a moribund condition and was combined, for statistical purposes, with those killed at termination.

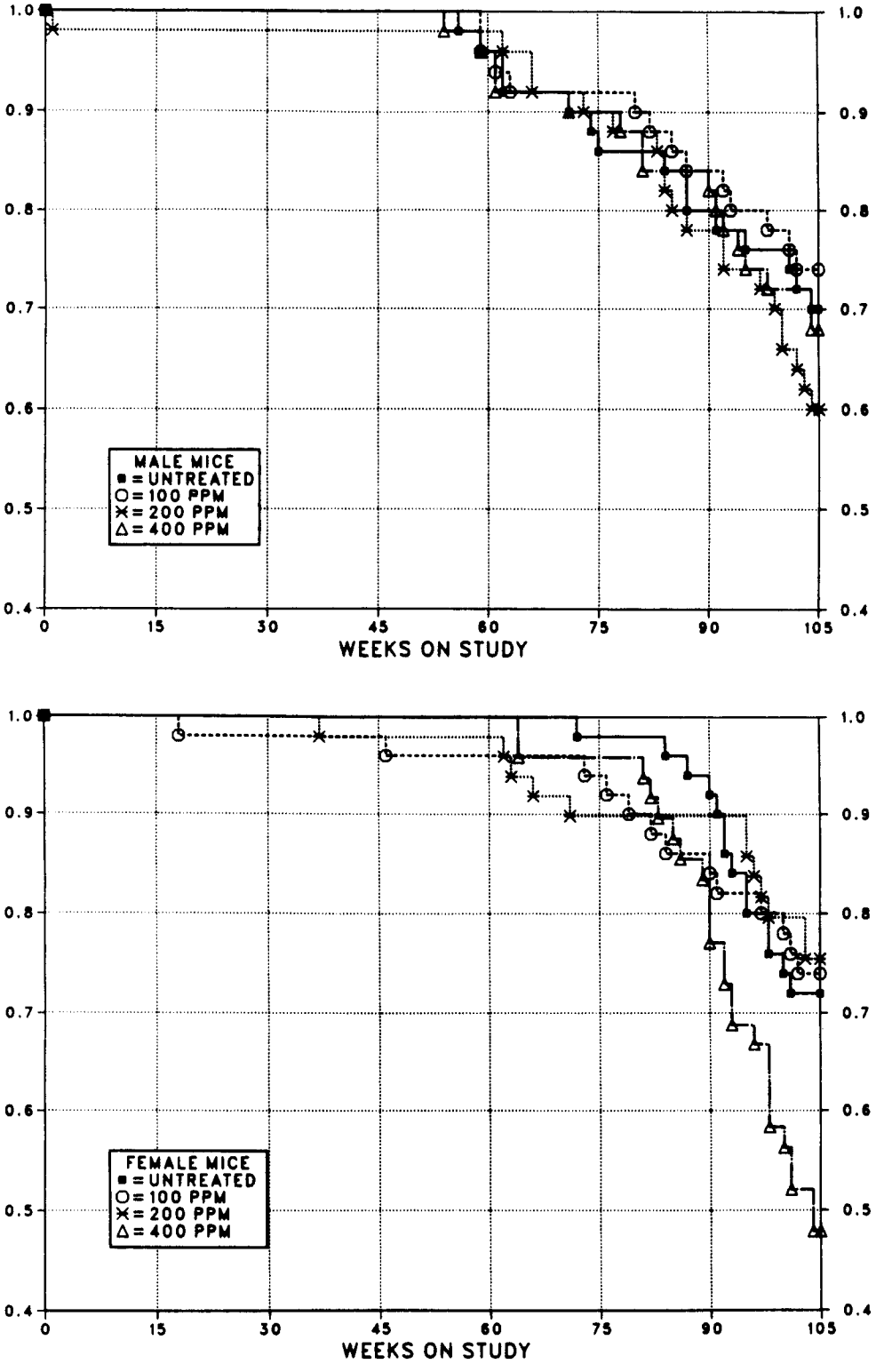

FIGURE 15. KAPLAN-MEIER SURVIVAL CURVES FOR MICE EXPOSED TO BROMOETHANE BY INHALATION FOR TWO YEARS

Uterus: Endometrial adenomas, adenocarcinomas, and squamous cell carcinomas occurred with significant positive trends. The incidences of the individual lesions (except for squamous cell carcinomas), the incidence of adenomas or adenocarcinomas (combined) in the 400-ppm group, and the incidences of adenomas, adenocarcinomas, or squamous cell carcinomas (combined) in the 200- and 400-ppm groups were significantly greater than those in the controls (Table 22). The uterine adenomas were exophytic, polyploid masses growing into the lumen of the uterus. They consisted of branching tubular glands lined by well-differentiated cuboidal to columnar epithelial cells. There was no invasion of the myometrium of the uterine wall. The adenocarcinomas were generally larger than the adenomas, often invaded the myometrium, and involved the parietal and visceral peritoneum. Some metastasized to the lung and other organs. The squamous cell carcinomas contained a predominant cellular component exhibiting squamous cell differentiation. The incidence of uterine tumors in the 400-ppm group probably contributed to the increased mortality of this group.

Lung: Acute/chronic inflammation was observed at increased incidences in female mice at 200 and 400 ppm (male: control, 2/50; 100 ppm, 1/50; 200 ppm, 1/50; 400 ppm, 1/50; female: 1/50; 1/50; 4/49; 6/49). Alveolar/bronchiolar carcinomas and adenomas or carcinomas (combined) in male mice occurred with significant positive trends; the incidence of adenomas or carcinomas (combined) in male mice at 400 ppm was significantly greater than that in the controls (Table 23).

Nasal Cavity: An adenoma was seen in one female mouse at 400 ppm.

Uterus or Ovary: Suppurative inflammation or abscesses were seen in 0/50 control, 4/50 100-ppm, 2/49 200-ppm, and 7/49 400-ppm female mice.

Circulatory System: The incidence of hemangiomas or hemangiosarcomas (combined) in the 200-ppm male mice was marginally increased relative to that in the controls (control, 1/50; 100 ppm, 3/50; 200 ppm, 6/50; 400 ppm, 0/50).

Liver: Dilatation of the hepatic sinusoid and focal cellular change were observed at increased incidences in the 200- and 400-ppm female mice (dilatation--male: control, 0/50; 100 ppm, 0/50; 200 ppm, 2/50; 400 ppm, 3/50; female: 0/50; 2/50; 13/49; 10/49; focal cellular change--male: 2/50; 2/50; 1/50; 3/50; female: 2/50; 2/50; 8/49; 7/49).

TABLE 22. UTERINE TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (a)

	Chamber Control	100 ppm	200 ppm	400 ppm
Adenoma				
Overall Rates	0/50 (0%)	1/50 (2%)	1/47 (2%)	6/48 (13%)
Adjusted Rates	0.0%	2.4%	2.7%	22.3%
Terminal Rates	0/36 (0%)	0/37 (0%)	1/37 (3%)	4/23 (17%)
Week of First Observation		97	105	85
Life Table Tests	P<0.001	P=0.505	P=0.505	P=0.005
Incidental Tumor Tests	P=0.002	P=0.388	P=0.505	P=0.011
Adenocarcinoma				
Overall Rates	0/50 (0%)	2/50 (4%)	3/47 (6%)	19/48 (40%)
Adjusted Rates	0.0%	5.3%	8.1%	57.8%
Terminal Rates	0/36 (0%)	1/37 (3%)	3/37 (8%)	10/23 (43%)
Week of First Observation		102	105	86
Life Table Tests	P<0.001	P=0.249	P=0.126	P<0.001
Incidental Tumor Tests	P<0.001	P=0.182	P=0.126	P<0.001
Adenoma or Adenocarcinoma (b)				
Overall Rates	0/50 (0%)	3/50 (6%)	4/47 (9%)	25/48 (52%)
Adjusted Rates	0.0%	7.6%	10.8%	72.5%
Terminal Rates	0/36 (0%)	1/37 (3%)	4/37 (11%)	14/23 (61%)
Week of First Observation		97	105	85
Life Table Tests	P<0.001	P=0.130	P=0.066	P<0.001
Incidental Tumor Tests	P<0.001	P=0.060	P=0.066	P<0.001
Squamous Cell Carcinoma (c)				
Overall Rates	0/50 (0%)	1/50 (2%)	1/47 (2%)	3/48 (6%)
Adjusted Rates	0.0%	2.6%	2.7%	9.8%
Terminal Rates	0/36 (0%)	0/37 (0%)	1/37 (3%)	1/23 (4%)
Week of First Observation		101	105	82
Life Table Tests	P=0.026	P=0.511	P=0.505	P=0.079
Incidental Tumor Tests	P=0.106	P=0.388	P=0.505	P=0.160
Adenoma, Adenocarcinoma, or Squamous Cell Carcinoma				
Overall Rates	0/50 (0%)	4/50 (8%)	5/47 (11%)	27/48 (56%)
Adjusted Rates	0.0%	9.9%	13.5%	74.1%
Terminal Rates	0/36 (0%)	1/37 (3%)	5/37 (14%)	14/23 (61%)
Week of First Observation		97	105	82
Life Table Tests	P<0.001	P=0.072	P=0.035	P<0.001
Incidental Tumor Tests	P<0.001	P=0.017	P=0.035	P<0.001

(a) The statistical analyses used are discussed in Section II (Statistical Methods) and Table D3 (footnotes).
(b) Historical incidence in chamber controls at study laboratory (mean ± SD): 4/335 (1% ± 2%); historical incidence in untreated controls (noninhalation) in NTP studies: 5/2,011 (0.2% ± 0.7%)
(c) Historical incidence of squamous cell neoplasms in chamber controls at study laboratory: 0/335; historical incidence in untreated controls (noninhalation) in NTP studies: 1/2,011 (<0.1%)

TABLE 23. LUNG LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Alveolar Epithelial Hyperplasia				
Overall Rates	1/50 (2%)	3/50 (6%)	1/50 (2%)	2/50 (4%)
Alveolar/Bronchiolar Adenoma				
Overall Rates	5/50 (10%)	6/50 (12%)	8/50 (16%)	9/50 (18%)
Terminal Rates	3/35 (9%)	5/37 (14%)	6/30 (20%)	7/34 (21%)
Week of First Observation	62	82	99	78
Incidental Tumor Tests	P=0.128	P=0.473	P=0.230	P=0.174
Alveolar/Bronchiolar Carcinoma				
Overall Rates	2/50 (4%)	0/50 (0%)	5/50 (10%)	6/50 (12%)
Terminal Rates	1/35 (3%)	0/37 (0%)	4/30 (13%)	4/34 (12%)
Week of First Observation	95		83	90
Incidental Tumor Tests	P=0.025	P=0.234N	P=0.236	P=0.157
Alveolar/Bronchiolar Adenoma or Carcinoma (a)				
Overall Rates	7/50 (14%)	6/50 (12%)	12/50 (24%)	15/50 (30%)
Terminal Rates	4/35 (11%)	5/37 (14%)	9/30 (30%)	11/34 (32%)
Week of First Observation	62	82	83	78
Incidental Tumor Tests	P=0.012	P=0.522N	P=0.140	P=0.049

(a) Historical incidence in chamber controls at study laboratory (mean ± SD): 75/348 (22% ± 8%); historical incidence in untreated controls (noninhalation) in NTP studies: 348/2,034 (17% ± 7%)

Bromoethane, when tested within the closed environment of a desiccator to ensure adequate exposure, was mutagenic in *Salmonella typhimurium* strain TA100 in the presence and absence of Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver S9; no mutagenic activity was observed in strain TA98 with or without S9 (Table 24). Bromoethane induced sister chromatid exchanges in Chinese hamster ovary (CHO) cells over a concentration range of 100-1,000 µg/ml in both the presence and absence of Aroclor 1254-induced male Sprague Dawley rat liver S9 (Table 25; Loveday et al., 1989). Negative results were obtained in tests for induction of chromosomal aberrations in CHO cells using 100-1,000 µg/ml bromoethane with and without S9 (Table 26; Loveday et al., 1989).

TABLE 24. MUTAGENICITY OF BROMOETHANE IN *SALMONELLA TYPHIMURIUM* (a)

Strain	Dose (µg/plate)	Revertants/Plate (b)		
		−S9	+S9 (hamster)	+S9 (rat)
TA100	0	124 ± 10.7	170 ± 4.6	178 ± 5.9
	0.01	130 ± 22.0	172 ± 22.5	175 ± 4.7
	0.025	143 ± 4.3	205 ± 7.1	193 ± 16.5
	0.05	221 ± 12.3	374 ± 10.7	329 ± 11.1
	0.075	474 ± 9.0	678 ± 37.5	668 ± 27.1
	0.1	404 ± 3.6	705 ± 15.1	647 ± 9.8
	0.15	1,140 ± 55.1	1,481 ± 36.4	1,405 ± 65.0
Trial summary		Positive	Positive	Positive
Positive control (c)		991 ± 13.9	1,639 ± 134.0	2,017 ± 60.1
TA98	0	22 ± 2.2	24 ± 2.3	26 ± 0.3
	0.01	21 ± 3.4	21 ± 1.5	24 ± 2.3
	0.05	18 ± 2.4	25 ± 0.7	28 ± 0.0
	0.1	17 ± 1.5	24 ± 4.1	29 ± 2.3
	0.5	14 ± 3.8	24 ± 1.9	33 ± 6.5
	1	17 ± 4.1	24 ± 0.7	24 ± 1.0
Trial summary		Negative	Negative	Negative
Positive control (c)		538 ± 25.2	472 ± 31.1	158 ± 13.4

(a) Study performed at SRI International. Cells and study compound or control (air) were incubated in the absence of exogenous metabolic activation (−S9) or with 30% Aroclor 1254-induced S9 from male Syrian hamster liver or male Sprague Dawley rat liver. High dose was limited by toxicity but did not exceed 0.15 µg/plate; 0 µg/plate dose is the control.
(b) Revertants are presented as mean ± standard error from three plates.
(c) Positive control; 2-aminoanthracene was used on all strains in the presence of S9. In the absence of metabolic activation, 4-nitro-*o*-phenylenediamine was used with TA98, and sodium azide was used with TA100.

TABLE 25. INDUCTION OF SISTER CHROMATID EXCHANGES IN CHINESE HAMSTER OVARY CELLS BY BROMOETHANE (a)

Compound	Dose (µg/ml)	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hours in BrdU	Relative SCEs/Cell (b) (percent)
−S9 (c)								
Trial 1--Summary: Positive								
Dimethyl sulfoxide		50	1,045	400	0.38	8.0	26.5	
Bromoethane	100	50	1,049	566	0.54	11.3	26.5	141.3
	300	50	1,048	891	0.85	17.8	26.5	222.5
	1,000	10	208	381	1.83	38.1	26.5	476.3
Mitomycin C	0.0015	50	1,051	705	0.67	14.1	26.5	176.3
	0.01	10	209	348	1.67	34.8	26.5	435.0
Trial 2--Summary: Positive								
Dimethyl sulfoxide		50	1,041	382	0.37	7.6	26.0	
Bromoethane	300	50	1,047	665	0.64	13.3	26.0	175.0
	500	50	1,052	932	0.89	18.6	26.0	244.7
	1,000	10	208	284	1.37	28.4	26.0	373.7
Mitomycin C	0.0015	50	1,045	514	0.49	10.3	26.0	135.5
	0.01	10	210	260	1.24	26.0	26.0	342.1
+S9 (d)--Summary: Positive								
Dimethyl sulfoxide		50	1,046	406	0.39	8.1	25.5	
Bromoethane	100	50	1,047	424	0.40	8.5	25.5	104.9
	300	50	1,045	503	0.48	10.1	25.5	124.7
	1,000	50	1,049	574	0.55	11.5	25.5	142.0
Cyclophosphamide	0.5	50	1,049	778	0.74	15.6	25.5	192.6
	2.5	10	210	375	1.79	37.5	25.5	463.0

(a) Study performed at Bioassay Systems Corporation. SCE = sister chromatid exchange; BrdU = bromodeoxyuridine. A detailed description of the SCE protocol is presented by Galloway et al. (1985, 1987). Briefly, Chinese hamster ovary cells were incubated with study compound or solvent (dimethyl sulfoxide) as described in (c) and (d) below and cultured for sufficient time to reach second metaphase division. Cells were then collected by mitotic shake-off, fixed, air dried, and stained.
(b) SCEs/cell in treated culture expressed as a percent of the SCEs/cell in the control culture
(c) In the absence of S9, Chinese hamster ovary cells were incubated with study compound or solvent for 2 hours at 37° C. Then BrdU was added, and incubation was continued for 24 hours. Cells were washed, fresh medium containing BrdU and colcemid was added, and incubation was continued for 2-3 hours.
(d) In the presence of S9, cells were incubated with study compound or solvent for 2 hours at 37° C. Then cells were washed, and medium containing BrdU was added. Cells were incubated for a further 26 hours, with colcemid present for the final 2-3 hours. S9 was from the liver of Aroclor 1254-induced male Sprague Dawley rats.

TABLE 26. INDUCTION OF CHROMOSOMAL ABERRATIONS IN CHINESE HAMSTER OVARY CELLS BY BROMOETHANE (a)

−S9 (b)					+S9 (c)				
Dose (µg/ml)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs	Dose (µg/ml)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs
Harvest time 10.5 h					Harvest time 12.0 h				
Dimethyl sulfoxide					Dimethyl sulfoxide				
	100	1	0.01	1.0		100	0	0	0.0
Bromoethane					Bromoethane				
100	100	4	0.04	4.0	100	100	1	0.01	1.0
300	100	2	0.02	2.0	300	100	4	0.04	3.0
1,000	100	4	0.04	4.0	1,000	100	3	0.03	1.0
Summary: Negative					Summary: Negative				
Mitomycin C					Cyclophosphamide				
5	50	36	0.72	36.0	50	50	55	1.10	54.0

(a) Study performed at Bioassay Systems Corporation. Abs = aberrations. A detailed presentation of the technique for detecting chromosomal aberrations is presented by Galloway et al. (1985, 1987). Briefly, Chinese hamster ovary cells were incubated with study compound or solvent (dimethyl sulfoxide) as indicated in (b) or (c). Cells were arrested in first metaphase by addition of colcemid and harvested by mitotic shake-off, fixed, and stained in 6% Giemsa.

(b) In the absence of S9, Chinese hamster ovary cells were incubated with study compound or solvent (dimethyl sulfoxide) for 8-10 hours at 37° C. Cells were then washed, and fresh medium containing colcemid was added for an additional 2-3 hours followed by harvest.

(c) In the presence of S9, cells were incubated with study compound or solvent (dimethyl sulfoxide) for 2 hours at 37° C. Cells were then washed, medium was added, and incubation was continued for 8-10 hours. Colcemid was added for the last 2-3 hours of incubation before harvest. S9 was from the liver of Aroclor 1254-induced male Sprague Dawley rats.

IV. DISCUSSION AND CONCLUSIONS

Short-Term Studies
Two-Year Studies in Rats
Two-Year Studies in Mice
Genetic Toxicology
Audit
Conclusions

IV. DISCUSSION AND CONCLUSIONS

Toxicology and carcinogenicity studies were conducted by administering bromoethane by inhalation to male and female F344/N rats and B6C3F$_1$ mice in single 4-hour studies and in 14-day, 14-week, and 2-year studies. The target concentrations for male and female rats and mice in the single-exposure studies were 625, 1,250, 2,500, 5,000, or 10,000 ppm. For the remaining studies, bromoethane was administered 6 hours per day, 5 days per week at the following target concentrations: 0, 250, 500, 1,000, 2,000, or 4,000 ppm for 14 days; 0, 100, 200, 400, 800, or 1,600 ppm for 14 weeks; and 0, 100, 200, or 400 ppm for 2 years. The inhalation route of exposure was chosen to mimic human exposure.

Short-Term Studies

In the single-exposure studies, deaths of male mice and female rats occurred at concentrations as low as 5,000 ppm, whereas deaths of female mice occurred at concentrations as low as 1,250 ppm. Male rats died only at 10,000 ppm bromoethane. In the 14-day studies, deaths occurred in rats and mice exposed at concentrations as low as 2,000 ppm. No compound-related effects on weight gain were observed for either rats or mice. During the first week of the studies, bromoethane caused male mice exposed to 2,000 ppm to have difficulty in breathing and standing. These effects were not observed at lower concentrations. No other clinical observations or histopathologic findings could be clearly attributed to exposure. Because of the deaths observed in all mice and rats at 2,000 ppm bromoethane and the lack of toxic effects at lower concentrations, 1,600 ppm bromoethane was selected as the highest exposure concentration for the 14-week studies.

During the 14-week studies, deaths occurred in male and female rats and female mice only at the highest concentration of bromoethane (1,600 ppm). However, deaths were observed in exposed male mice at concentrations as low as 400 ppm. Although male mice died at concentrations lower than 1,600 ppm bromoethane, mean body weights of rats and mice of each sex were markedly lower than those of controls only at 1,600 ppm. Of interest is the finding that exposure to bromoethane at 1,600 ppm reduced the rate of weight gain in mice, whereas in rats, final body weights were actually lower than the initial weights.

Bromoethane-induced clinical signs were limited to rats and mice exposed at 1,600 ppm and generally were only observed during the last few weeks of the studies and at the time of death. Rats generally had difficulty breathing and demonstrated posterior paresis, whereas mice were ataxic and showed signs of tremors. Both rats and mice had positive serologic titers to Sendai virus. Histopathologic findings were also primarily limited to animals exposed to 1,600 ppm. Minimal atrophy of the thigh muscle was observed in male and female rats and mice. The severity and morphology were similar in both species. Rats had minimal-to-moderate mineralization of the granular cell layers of the cerebellum of the brain, minimal degeneration of the lumbar spinal cord, minimal-to-severe hemosiderosis of the spleen, moderate depletion of the hematopoietic cells in the bone marrow, and a severe atrophy of the testes. In female rats and mice, a minimal-to-mild atrophy of the uterus, characterized by a decrease in endometrial thickness, was observed. In female mice, a minimal involution of the ovary was present; this functional change consisted of a decrease in the size of the ovary and the size and number of corpora lutea present. Exposure-related histopathologic findings seen primarily in animals exposed to 1,600 ppm bromoethane for 14 weeks were not observed in rats or mice exposed to bromoethane at lower concentrations for 2 years.

Because of compound-related deaths in male and female rats and mice at 1,600 ppm and male mice at 800 ppm, exposure concentrations of bromoethane selected for rats and mice for the 2-year studies were 0, 100, 200, or 400 ppm, 6 hours per day, 5 days per week. Although it appears that male and female rats and female mice could have tolerated higher exposure concentrations in the 2-year studies, 400 ppm was selected as the maximum concentration because the standard practice at the time was to house male and female rats and mice in the same chamber when possible. It was anticipated that male mice could not have tolerated a higher concentration than 400 ppm.

Two-Year Studies in Rats

In the rat studies, no significant differences in survival were observed between any groups of males; survival for females in the 100-ppm group was greater than that of controls. The number of control male and female rats surviving to the end of the studies was lower than the number of surviving exposed rats. An explanation for the rather low survival for controls could not be determined; however, 50% or more of control rats were still alive at week 98. Mean body weights of exposed and control rats were similar throughout the studies. In general, bromoethane exposure did not produce clinical signs of toxicity.

Increased incidences of pheochromocytomas or malignant pheochromocytomas (combined) of the adrenal gland were observed in exposed male rats (control, 8/40; 100 ppm, 23/45; 200 ppm, 18/46; 400 ppm, 21/46). The incidences of adrenal medullary hyperplasia were similar in all groups. The greatest incidence of adrenal gland lesions was observed in the 100-ppm group, but the incidence of pheochromocytomas in the 200-ppm group was not statistically significant. Malignant neoplasms were observed only at 100 and 200 ppm; both of these neoplasms in the 200-ppm group metastasized. The range of historical incidences for pheochromocytomas or malignant pheochromocytomas (combined) in chamber controls at this laboratory (3/48-22/49) and for untreated controls in the National Toxicology Program (NTP) studies (3/50-32/49) is variable. The historical incidence range for malignant pheochromocytomas is 0/50-2/50 for chamber controls at the study laboratory and 0/50-6/50 for untreated controls in NTP studies. The increased incidences of pheochromocytomas in exposed male rats vs. controls was attributed to bromoethane exposure. Increases in pheochromocytomas were not observed in the 2-year NTP inhalation studies of chloroethane (NTP, 1989) or 1,2-dibromoethane (NTP, 1982).

Uncommon brain neoplasms occurred in small numbers of exposed male and female rats. Granular cell tumors of the brain, although not statistically significant or concentration related, were seen in 5/150 exposed male rats. These neoplasms have not been observed in male F344/N rat chamber controls at this laboratory, and the historical incidence for untreated controls in NTP studies is 0.2%. Granular cell neoplasms were not observed in control or exposed female rats. Glial cell neoplasms (glioma, astrocytoma, or oligodendroglioma) were seen in 3/50 male rats exposed to bromoethane at 100 ppm but not in male rats exposed at higher concentrations. Gliomas were observed in exposed females with a significant positive trend; however, the incidences were not significantly greater than that in controls and were within the historical incidence range for untreated controls in NTP studies (0/50-3/50). Nonneoplastic lesions supporting an exposure-related effect were not present in exposed male or female rats. In the 2-year studies of structurally related chloroethane (NTP, 1989), glial cell neoplasms were observed in 2/50 male and 3/50 female rats exposed to 15,000 ppm. One malignant glial cell neoplasm was observed in a control male rat. In the studies of these two structurally related chemicals which were conducted at similar times, the combined incidence of brain neoplasms for both studies is 18/398 (4.5%) for exposed male and female rats, compared with 2/199 (1.0%) for control male and female rats. In contrast, inhalation exposure for 2 years to 1,2-dibromoethane in NTP studies did not result in brain neoplasms in male or female rats (NTP, 1982). Due to the small numbers of rats with brain neoplasms, the lack of a concentration response in males, and the lack of significant and supporting nonneoplastic lesions in males and females, the incidences of the two types of brain neoplasms could not be related with certainty to bromoethane exposure in male and female rats. Brain neoplasms were not observed in mice exposed to bromoethane.

Alveolar/bronchiolar adenomas and carcinomas were observed in exposed but not in control male rats; however, the incidences were not significant nor were they distributed in a concentration-related manner. The increase in hyperplasia of the alveolar epithelium in male rats was not considered supportive of a carcinogenic effect, since many of these lesions were related to an inflammatory response. Alveolar/bronchiolar adenomas were seen in 3/49 (6%) female rats exposed at 400 ppm but not at lower concentrations or in controls. These incidences can be compared with the historical incidence of 6/299

(2%) for male rat and 4/297 (1%) for female rat chamber controls at the study laboratory and 43/1,933 (2%) for male rat and 22/1,974 (1%) for female rat untreated controls in the NTP studies.

Several nonneoplastic lesions were observed at increased incidences in the nasal cavity, larynx, and lung of bromoethane-exposed rats, indicating that bromoethane irritates the respiratory tract (see Table 14).

In the concurrent bromoethane studies in mice, the incidence of alveolar/bronchiolar neoplasms was marginally increased in male mice exposed at 400 ppm bromoethane; these neoplasms were not observed in female mice. Similarly, 2-year exposure to chloroethane at 15,000 ppm resulted in a marginally increased incidence of alveolar/bronchiolar neoplasms in male mice. Alveolar/bronchiolar neoplasms have been reported for female rats exposed to 40 ppm 1,2-dibromoethane and for male and female mice exposed to 10 and 40 ppm 1,2-dibromoethane (NTP, 1982).

Although small numbers of alveolar/bronchiolar neoplasms were observed in bromoethane-exposed male and female rats (adenomas only), and although alveolar/bronchiolar neoplasms were observed in exposed male mice, the association of lung neoplasms with bromoethane exposure in rats is not clear because there is a lack of a concentration-related response in exposed males and because the overall incidence in each sex is low and, for males, is within the historical incidence range for untreated male rat controls in NTP studies.

A significant negative trend was observed for mammary gland neoplasms in female rats exposed to bromoethane (control, 18/50; 100 ppm, 15/50; 200 ppm, 10/48; 400 ppm, 7/50). The biologic significance of this finding is not known.

Two-Year Studies in Mice

Male and female mice were exposed to bromoethane at 0, 100, 200, or 400 ppm for 2 years. No significant differences in survival were observed between any groups of male mice. Survival of the 400-ppm group of female mice was significantly lower than that of controls at the end of the study. Body weights of male and female mice were highly variable throughout the studies. Mean body weights of the 400-ppm group of male mice were lower than those of controls throughout the study; the mean body weights of the 400-ppm group of female mice were generally lower than those of controls after week 29. No exposure-related clinical signs of toxicity were observed.

In the current studies, concentration-related incidences of uterine adenomas, adenocarcinomas, and squamous cell carcinomas occurred in female mice; these uterine neoplasms were not observed in control mice. A significant ($P<0.001$) incidence of uterine endometrial neoplasms was also observed in female B6C3F$_1$ mice exposed by inhalation to chloroethane at 15,000 ppm for 2 years (control, 0/49; 15,000 ppm, 43/50) (NTP, 1989). The uterine neoplasms observed in mice exposed to bromoethane at much lower concentrations than those used in the chloroethane study did not metastasize as widely as those observed in chloroethane-exposed mice. Although not statistically significant, uterine adenocarcinomas did occur in female B6C3F$_1$ mice administered 1,2-dichloroethane by gavage at time-weighted-average doses of 148 or 299 mg/kg per day for 78 weeks (NCI, 1978a). In addition, endometrial stromal sarcomas were observed in 2/49 low dose and 3/47 high dose female mice, and endometrial stromal polyps were observed in 3/49 low dose and 2/47 high dose female mice. Exposure by inhalation for 2 years to 1,2-dibromoethane at 40 ppm did not induce uterine neoplasms in B6C3F$_1$ mice (NTP, 1982). The overwhelming incidence of uterine neoplasms in female mice is clearly associated with bromoethane exposure, as was the case for chloroethane.

The incidence of alveolar/bronchiolar neoplasms was marginally greater ($P=0.049$) in male mice exposed to 400 ppm bromoethane than in controls (adenomas or carcinomas, combined: control, 7/50; 100 ppm, 6/50; 200 ppm, 12/50; 400 ppm, 15/50). The historical incidence in chamber controls at the study laboratory is 75/348 (22%), and the historical incidence in untreated controls in previous NTP noninhalation studies is 348/2,034 (17%). The 30% incidence in the 400-ppm group is greater than both mean historical incidences for these neoplasms. In these

studies, however, the association of alveolar/bronchiolar neoplasms with bromoethane exposure is not clearly established because there was no increased incidence of hyperplasia to support the incidence of neoplasms, the incidences were within the historical range, and lung neoplasms were not increased in exposed female mice.

Results from the bromoethane rat studies and from studies with structurally similar compounds suggest an effect on the lung. In the bromoethane rat studies, alveolar/bronchiolar adenomas and carcinomas were observed at low incidences in exposed male rats and adenomas were observed in female rats. In several 2-year inhalation and long-term gavage studies, lung neoplasms have been reported for structurally similar compounds. Alveolar/bronchiolar neoplasms were significant for female F344 rats exposed by inhalation to 40 ppm 1,2-dibromoethane and for male and female $B6C3F_1$ mice exposed to 10 or 40 ppm (NTP, 1982). Lung neoplasms were marginally increased in $B6C3F_1$ mice exposed by inhalation to 15,000 ppm chloroethane (NTP, 1989). Lung neoplasms were significantly increased in male $B6C3F_1$ mice dosed with 1,2-dichloroethane by gavage at 195 mg/kg per day and female $B6C3F_1$ mice dosed at 299 mg/kg per day (NCI, 1978a). Long-term gavage administration of 1,1-dichloroethane, however, did not result in alveolar/bronchiolar neoplasms (NCI, 1978b).

Genetic Toxicology

Bromoethane is mutagenic in Salmonella both in the absence and presence of exogenous metabolic activation when tested in desiccators; it was not mutagenic when tested in the standard preincubation assay. Results of these S9-independent tests are consistent with the activity of a direct alkylating agent. The above data and the chemical structure of bromoethane suggest a potential for carcinogenic activity occurring at, but not limited to, the site of initial contact. The lung, where alveolar/bronchiolar neoplasms were observed in male and female rats as well as in male mice, is an initial contact site in these inhalation studies. Although bromoethane did induce sister chromatid exchanges in cultured Chinese hamster ovary (CHO) cells, it did not induce increases in the frequency of chromosomal aberrations in cultured CHO cells.

Audit

The experimental and tabulated data for the NTP Technical Report on bromoethane were examined for accuracy, consistency, completeness, and compliance with Good Laboratory Practice regulations. As summarized in Appendix G, the audit revealed no major problems with the conduct of the studies or with collection and documentation of the experimental data. No discrepancies were found that influenced the final interpretation of the results of these studies.

Conclusions

Under the conditions of these 2-year inhalation studies, there was *some evidence of carcinogenic activity** of bromoethane for male F344/N rats, as indicated by increased incidences of pheochromocytomas of the adrenal gland; neoplasms of the brain and lung may also have been related to exposure to bromoethane. For female F344/N rats, there was *equivocal evidence of carcinogenic activity*, as indicated by marginally increased incidences of neoplasms of the brain and lung. For male $B6C3F_1$ mice, there was *equivocal evidence of carcinogenic activity*, based on marginally increased incidences of neoplasms of the lung. There was *clear evidence of carcinogenic activity* for female $B6C3F_1$ mice, as indicated by neoplasms of the uterus.

*Explanation of Levels of Evidence of Carcinogenic Activity is on page 7.
A summary of the Peer Review comments and the public discussion on this Technical Report appears on page 10.

V. REFERENCES

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APPENDIX A

SUMMARY OF LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals necropsied	49	50	50	50
Animals examined histopathologically	49	50	50	50
INTEGUMENTARY SYSTEM				
*Skin	(49)	(50)	(50)	(50)
Papilloma, NOS		1 (2%)	2 (4%)	2 (4%)
Squamous cell papilloma				1 (2%)
Squamous cell carcinoma	1 (2%)			
Basal cell tumor		2 (4%)		
Trichoepithelioma			1 (2%)	1 (2%)
Sebaceous adenoma	1 (2%)			1 (2%)
Keratoacanthoma	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Sarcoma, NOS		1 (2%)		
Fibroma	1 (2%)		3 (6%)	1 (2%)
Lipoma	1 (2%)			
Neurilemoma, malignant	1 (2%)			
RESPIRATORY SYSTEM				
#Nose	(47)	(48)	(49)	(49)
Papillary adenoma				1 (2%)
#Lung	(48)	(49)	(48)	(48)
Carcinoma, NOS, metastatic	1 (2%)			
Alveolar/bronchiolar adenoma			1 (2%)	1 (2%)
Alveolar/bronchiolar carcinoma			3 (6%)	
Adenosquamous carcinoma	1 (2%)			
Pheochromocytoma, metastatic			2 (4%)	
Chordoma, metastatic	1 (2%)			
HEMATOPOIETIC SYSTEM				
*Multiple organs	(49)	(50)	(50)	(50)
Leukemia, mononuclear cell	23 (47%)	21 (42%)	23 (46%)	20 (40%)
#Mandibular lymph node	(43)	(47)	(49)	(42)
Carcinoma, NOS, metastatic	1 (2%)			
#Bronchial lymph node	(43)	(47)	(49)	(42)
Adenosquamous carcinoma, metastatic	1 (2%)			
#Mediastinal lymph node	(43)	(47)	(49)	(42)
Pheochromocytoma, metastatic			1 (2%)	
#Mesenteric lymph node	(43)	(47)	(49)	(42)
Sarcoma, NOS				1 (2%)
CIRCULATORY SYSTEM				
#Lung	(48)	(49)	(48)	(48)
Hemangiosarcoma	1 (2%)			
#Heart	(48)	(49)	(49)	(48)
Hemangiosarcoma			1 (2%)	
*Palate	(49)	(50)	(50)	(50)
Hemangiosarcoma			1 (2%)	
DIGESTIVE SYSTEM				
#Salivary gland	(48)	(48)	(49)	(49)
Carcinoma, NOS, metastatic		1 (2%)		
#Liver	(48)	(49)	(49)	(50)
Carcinoma, NOS, metastatic	1 (2%)			
Neoplastic nodule				3 (6%)
Hepatocellular carcinoma	2 (4%)			
#Pancreas	(47)	(48)	(49)	(49)
Carcinoma, NOS				1 (2%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
DIGESTIVE SYSTEM (Continued)				
#Forestomach	(47)	(48)	(48)	(49)
Squamous cell carcinoma			1 (2%)	
#Duodenum	(46)	(48)	(48)	(47)
Neurilemoma, malignant	1 (2%)			
#Ileum	(46)	(48)	(48)	(47)
Adenomatous polyp, NOS				1 (2%)
URINARY SYSTEM				
#Kidney	(47)	(49)	(48)	(49)
Tubular cell adenoma		1 (2%)		
#Urinary bladder	(47)	(46)	(49)	(48)
Papilloma, NOS		1 (2%)		1 (2%)
ENDOCRINE SYSTEM				
#Pituitary intermedia	(45)	(49)	(48)	(48)
Adenoma, NOS	1 (2%)			
#Anterior pituitary	(45)	(49)	(48)	(48)
Carcinoma, NOS				1 (2%)
Adenoma, NOS	19 (42%)	20 (41%)	20 (42%)	20 (42%)
#Adrenal	(48)	(47)	(50)	(49)
Neoplasm, NOS			1 (2%)	
Cortical adenoma	1 (2%)		1 (2%)	
#Adrenal medulla	(48)	(47)	(50)	(49)
Pheochromocytoma	8 (17%)	23 (49%)	17 (34%)	21 (43%)
Pheochromocytoma, malignant		1 (2%)	2 (4%)	
#Thyroid	(46)	(46)	(48)	(49)
Follicular cell carcinoma		1 (2%)	1 (2%)	1 (2%)
C-cell adenoma	4 (9%)	3 (7%)	1 (2%)	2 (4%)
C-cell carcinoma			1 (2%)	2 (4%)
#Parathyroid	(29)	(34)	(39)	(34)
Adenoma, NOS			1 (3%)	
#Pancreatic islets	(47)	(48)	(49)	(49)
Islet cell adenoma	4 (9%)	2 (4%)	4 (8%)	2 (4%)
Islet cell carcinoma		3 (6%)		1 (2%)
REPRODUCTIVE SYSTEM				
*Mammary gland	(49)	(50)	(50)	(50)
Adenocarcinoma, NOS	1 (2%)			
Fibroadenoma		1 (2%)	2 (4%)	1 (2%)
*Preputial gland	(49)	(50)	(50)	(50)
Carcinoma, NOS				1 (2%)
Adenoma, NOS	5 (10%)	2 (4%)	1 (2%)	1 (2%)
#Prostate	(44)	(44)	(48)	(48)
Adenoma, NOS			1 (2%)	1 (2%)
#Testis	(48)	(50)	(50)	(49)
Interstitial cell tumor	42 (88%)	41 (82%)	47 (94%)	35 (71%)
Mesothelioma, malignant	6 (13%)	1 (2%)	1 (2%)	5 (10%)
*Epididymis	(49)	(50)	(50)	(50)
Mesothelioma, malignant	1 (2%)	1 (2%)	1 (2%)	4 (8%)
NERVOUS SYSTEM				
#Brain	(49)	(50)	(50)	(50)
Granular cell tumor, NOS		3 (6%)	1 (2%)	1 (2%)
Glioma, NOS		1 (2%)		
Astrocytoma		1 (2%)		
Oligodendroglioma		1 (2%)		

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
SPECIAL SENSE ORGANS				
*Zymbal gland	(49)	(50)	(50)	(50)
Carcinoma, NOS	1 (2%)	2 (4%)	1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM				
*Vertebra	(49)	(50)	(50)	(50)
Chordoma	1 (2%)			
*Rib	(49)	(50)	(50)	(50)
Adenosquamous carcinoma, metastatic	1 (2%)			
BODY CAVITIES				
*Pleura	(49)	(50)	(50)	(50)
Mesothelioma, malignant			1 (2%)	
*Mesentery	(49)	(50)	(50)	(50)
Mesothelioma, malignant	2 (4%)	1 (2%)	1 (2%)	3 (6%)
ALL OTHER SYSTEMS				
*Multiple organs	(49)	(50)	(50)	(50)
Mesothelioma, malignant	2 (4%)	3 (6%)	1 (2%)	1 (2%)
Diaphragm				
Adenosquamous carcinoma, metastatic	1			
Site unknown				
Adenocarcinoma, NOS			1	
ANIMAL DISPOSITION SUMMARY				
Animals initially in study	50	50	50	50
Natural death	7	9	5	4
Moribund sacrifice	25	15	19	25
Terminal sacrifice	17	26	26	21
Animal missexed	1			
TUMOR SUMMARY				
Total animals with primary tumors**	49	50	50	49
Total primary tumors	132	140	145	140
Total animals with benign tumors	46	48	50	45
Total benign tumors	88	99	103	94
Total animals with malignant tumors	32	28	31	29
Total malignant tumors	44	38	40	42
Total animals with secondary tumors##	3	1	2	
Total secondary tumors	7	1	3	
Total animals with tumors uncertain-- benign or malignant		3	2	4
Total uncertain tumors		3	2	4

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: CHAMBER CONTROL

ANIMAL NUMBER	0014	0044	0030	0012	0327	0234	0305	0040	0031	0339	0466	0220	0335	0244	0188	0288	0501	0155	0006	0411	0255	0477	0088	0299
WEEKS ON STUDY	0133	0533	0596	0662	0725	0758	0780	0800	0801	0833	0833	0844	0855	0888	0899	0900	0900	0922	0944	0944	0955	0955	0966	0977
INTEGUMENTARY SYSTEM																								
Skin	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																								
Sebaceous adenoma																								
Keratoacanthoma																								
Fibroma																								
Lipoma																								
Neurilemoma, malignant																		X						
RESPIRATORY SYSTEM																								
Lungs and bronchi	S	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic					X																			
Adenosquamous carcinoma											X													
Hemangiosarcoma																								
Chordoma, metastatic																								
Trachea	S	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	S	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
Bone marrow	S	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Spleen	S	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+
Carcinoma, NOS, metastatic					X																			
Adenosquamous carcinoma, metastatic											X													
Thymus	S	+	−	+	−	+	−	−	+	+	−	+	+	+	+	+	+	−	+	+	+	+	−	−	+
CIRCULATORY SYSTEM																								
Heart	S	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
Salivary gland	S	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	S	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic					X																			
Hepatocellular carcinoma																								
Bile duct	S	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Pancreas	S	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Esophagus	S	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	S	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Small intestine	S	−	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Neurilemoma, malignant																		X						
Large intestine	S	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
Kidney	S	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	S	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+

+: Tissue examined microscopically
−: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed

: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	0004	0022	0033	0023	0007	0002	0043	0048	0001	0003	0009	0110	0111	0113	0116	0117	0119	0121	0026	0036	0037	0038	0042	0045	0049	TOTAL:
WEEKS ON STUDY	098	098	098	099	102	103	104	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Squamous cell carcinoma																								X		1
Sebaceous adenoma																			X							1
Keratoacanthoma							X																			1
Fibroma														X												1
Lipoma													X													1
Neurilemoma, malignant																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, NOS, metastatic																										1
Adenosquamous carcinoma																										1
Hemangiosarcoma			X																							1
Chordoma, metastatic															X											1
Trachea	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph nodes	+	+	+	+	+	+	+	+	–	–	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	43
Carcinoma, NOS, metastatic																										1
Adenosquamous carcinoma, metastatic																										1
Thymus	–	+	+	+	+	–	+	–	–	–	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	34
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, NOS, metastatic																										1
Hepatocellular carcinoma									X																X	2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Neurilemoma, malignant																										1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47

* Animals necropsied

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	0014	0044	0030	0112	0332	0227	0334	0005	0400	0311	0339	0446	0220	0335	0224	0188	0228	0550	0115	0006	0441	0225	0447	0088	0029
WEEKS ON STUDY	0013	0053	0559	0666	0772	0755	0788	0800	0800	0811	0833	0833	0844	0855	0888	0899	0900	0900	0902	0944	0944	0955	0955	0966	0977
ENDOCRINE SYSTEM																									
Pituitary	S	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS			X						X	X		X		X				X		X				X	X
Adrenal	S	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma																									
Thyroid	S	+	+	+	+	–	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+
C-cell adenoma																X									
Parathyroid	S	–	–	–	+	–	+	–	+	+	–	–	+	–	–	–	+	+	+	+	–	+	–	+	–
Pancreatic islets	S	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma									X																
REPRODUCTIVE SYSTEM																									
Mammary gland	S	N	N	+	+	N	N	+	N	N	+	+	N	N	+	+	+	N	N	+	N	+	+	N	+
Adenocarcinoma, NOS																									
Testis	S	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor				X		X		X	X		X	X	X	X	X	X	X		X	X	X	X	X	X	X
Mesothelioma, malignant															X										
Prostate	S	+	+	+	+	–	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS			X					X			X														
Epididymis	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant																									
NERVOUS SYSTEM																									
Brain	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Zymbal gland	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS					X																				
MUSCULOSKELETAL SYSTEM																									
Bone	S	N	N	N	N	N	N	N	N	N	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenosquamous carcinoma, metastatic												X													
Chordoma																									
BODY CAVITIES																									
Mesentery	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant																									
Leukemia, mononuclear cell		X				X	X			X	X				X	X	X				X		X		X
Diaphragm, NOS	S																								
Adenosquamous carcinoma, metastatic												X													

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	004	022	033	023	007	002	043	048	001	003	009	010	011	013	016	017	019	021	026	036	037	038	042	045	049	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	098	098	098	099	102	103	104	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	
ENDOCRINE SYSTEM																										
Pituitary	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenoma, NOS					X		X	X	@X	X		X							X			X	X	X		19
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cortical adenoma																									X	1
Pheochromocytoma			X	X		X		X				X	X		X						X					8
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
C-cell adenoma						X	X									X										4
Parathyroid	–	–	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	–	+	+	+	–	+	29
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Islet cell adenoma								X					X			X										4
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	N	+	+	+	+	N	N	+	+	N	N	N	+	+	+	+	N	+	+	N	+	+	N	*49
Adenocarcinoma, NOS																							X			1
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Interstitial cell tumor	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	42
Mesothelioma, malignant									X	X				X								X			X	6
Prostate	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	44
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Adenoma, NOS											X				X											5
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Mesothelioma, malignant																						X				1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Carcinoma, NOS																										1
MUSCULOSKELETAL SYSTEM																										
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	*49
Adenosquamous carcinoma, metastatic																										1
Chordoma															X											1
BODY CAVITIES																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Mesothelioma, malignant														X								X				2
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Mesothelioma, malignant		X																				X				2
Leukemia, mononuclear cell	X	X		X	X	X			X		X		X	X		X					X				X	23
Diaphragm, NOS																										
Adenosquamous carcinoma, metastatic																										1

* Animals necropsied
@ Multiple occurrence of morphology

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 100 ppm

ANIMAL NUMBER	036	001	007	015	027	037	048	005	011	020	034	003	004	038	049	023	028	041	035	026	042	010	040	050	002
WEEKS ON STUDY	061	073	073	079	083	083	083	089	089	089	090	092	092	093	093	095	096	098	099	101	101	102	102	103	106
INTEGUMENTARY SYSTEM																									
Skin	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																									
Basal cell tumor																									
Keratoacanthoma																									X
Sarcoma, NOS																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Nasal cavity	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	−	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Spleen	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	−	+	−	+	+	+	+	−	+	+	−	+	+	+	+	−	+	+	+	+	−	+	−	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic															X										
Liver	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	−	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenoma																								X	
Urinary bladder	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																							X		
ENDOCRINE SYSTEM																									
Pituitary	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS			X		X			X	X		X	X	X				X		X		X		X		X
Adrenal	−	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma							X		X		X				X					X		X	X	X	X
Pheochromocytoma, malignant																									
Thyroid	−	+	−	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma																						X			
C-cell adenoma																									X
Parathyroid	−	−	−	−	+	−	−	−	+	+	−	−	+	+	+	+	−	+	+	+	+	+	+	+	+
Pancreatic islets	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma							X																		
Islet cell carcinoma													X						X						
REPRODUCTIVE SYSTEM																									
Mammary gland	N	+	N	+	+	+	+	+	N	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																								X	
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor		X		X	X	X	X	X				X		X	X	X	X	X		X		X		X	X
Mesothelioma, malignant																						X			
Prostate	+	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	+	−	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant																						X			
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granular cell tumor, NOS																									
Glioma, NOS						X																			
Astrocytoma												X													
Oligodendroglioma																	X								
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS		X													X										
BODY CAVITIES																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant																						X			
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant							X															X			
Leukemia, mononuclear cell	X			X	X		X	X		X	X			X		X	X	X	X	X	X				

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 100 ppm (Continued)

ANIMAL NUMBER	0006	0008	0009	0012	0013	0014	0016	0017	0018	0019	0021	0022	0024	0025	0029	0030	0031	0032	0033	0039	0043	0044	0045	0046	0047	TOTAL:
WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Papilloma, NOS							X																			1
Basal cell tumor							X																			2
Keratoacanthoma			X												X											2
Sarcoma, NOS								X																		1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thymus	+	+	+	+	+	+	+	+	+	−	+	+	−	−	+	+	+	+	−	+	+	+	−	−		37
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, NOS, metastatic																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tubular cell adenoma																										1
Urinary bladder	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	46
Papilloma, NOS																										1
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS			X			X	X		X		X	X				X							X			20
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pheochromocytoma			X		X		X	X	X	X	X					X	X	X	X		X		X		X	23
Pheochromocytoma, malignant								X																		1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Follicular cell carcinoma																										1
C-cell adenoma				X							X															3
Parathyroid	+	−	+	+	−	+	+	+	+	+	+	−	+	+	+	+	−	+	+	−	−	+	+	+	+	34
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Islet cell adenoma											X															2
Islet cell carcinoma								X																		3
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroadenoma																										1
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	41
Mesothelioma, malignant																										1
Prostate	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	44
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS									X									X								2
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granular cell tumor, NOS		X												X									X			3
Glioma, NOS																										1
Astrocytoma																										1
Oligodendroglioma																										1
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										2
BODY CAVITIES																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																								X		3
Leukemia, mononuclear cell				X			X	X				X	X										X		X	21

* Animals necropsied

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 200 ppm

ANIMAL NUMBER	025	047	003	020	008	044	039	021	045	049	012	018	016	019	034	004	038	050	011	015	036	007	041	001	002
WEEKS ON STUDY	078	078	081	081	082	082	088	089	091	091	092	092	093	093	094	095	097	097	098	099	103	105	105	106	106
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																		X							
Trichoepithelioma																									X
Keratoacanthoma																									
Fibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma														X									X		
Pheochromocytoma, metastatic																									
Trachea	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic																									
Thymus	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Hemangiosarcoma					X																				
DIGESTIVE SYSTEM																									
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hemangiosarcoma													X												
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Liver	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Esophagus	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Squamous cell carcinoma																								X	
Small intestine	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Large intestine	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Adenoma, NOS		X									X			X	X	X	X	X	X					X	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplasm, NOS							X																		
Cortical adenoma																									
Pheochromocytoma											X						X	X			X		X		
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Follicular cell carcinoma																									
C-cell adenoma														X											
C-cell carcinoma															X										
Parathyroid	+	+	−	+	−	−	−	+	+	−	+	+	−	+	+	+	−	+	+	+	−	−	+	+	+
Adenoma, NOS																									
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Islet cell adenoma						X										X		X							
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																			X		X				
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X
Mesothelioma, malignant										X															
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	+
Adenoma, NOS																									
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																				X					
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant										X															
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granular cell tumor, NOS								X																	
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																X									
BODY CAVITIES																									
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant										X															
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant										X															
Leukemia, mononuclear cell	X		X	X		X			X			X	X						X		X		X	X	X
Site unknown																									
Adenocarcinoma, NOS													X												

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 200 ppm (Continued)

ANIMAL NUMBER	0005	0009	0009	0110	0113	0114	0117	0222	0223	0224	0226	0227	0228	0229	0301	0311	0332	0333	0335	0337	0401	0402	0403	0406	0408	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Papilloma, NOS																	X									2
Trichoepithelioma																										1
Keratoacanthoma						X																				1
Fibroma				X							X									X						3
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Alveolar/bronchiolar adenoma					X																					1
Alveolar/bronchiolar carcinoma																					X					3
Pheochromocytoma, metastatic																				X				X		2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma, metastatic																								X		1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																										1
DIGESTIVE SYSTEM																										
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Hemangiosarcoma																										1
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	48
Squamous cell carcinoma																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma, NOS	X	X	X		X	X	X	X		X										X			X		X	20
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplasm, NOS																										1
Cortical adenoma																	X									1
Pheochromocytoma		X	X	X	X	X				X	X		X		X	X				X					X	17
Pheochromocytoma, malignant																				X				X		2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Follicular cell carcinoma																				X						1
C-cell adenoma																										1
C-cell carcinoma																										1
Parathyroid	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Adenoma, NOS																									X	1
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islet cell adenoma																X										4
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroadenoma																										2
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell tumor	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	47
Mesothelioma, malignant																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma, NOS																									X	1
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS																										1
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granular cell tumor, NOS																										1
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
BODY CAVITIES																										
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																						X				1
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																										1
Leukemia, mononuclear cell	X		X	X		X				X		X		X		X		X		X			X			23
Site unknown																										
Adenocarcinoma, NOS																										1

* Animals necropsied

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 400 ppm

ANIMAL NUMBER	0 3 9	0 1 9	0 2 2	0 2 4	0 4 1	0 4 6	0 1 0	0 3 7	0 2 1	0 4 8	0 3 0	0 1 3	0 1 8	0 4 9	0 0 5	0 3 4	0 4 2	0 4 3	0 5 0	0 0 3	0 3 1	0 4 4	0 1 6	0 1 2	0 2 0
WEEKS ON STUDY	0 4 6	0 5 5	0 6 1	0 6 3	0 6 4	0 7 2	0 7 4	0 7 6	0 7 8	0 8 2	0 8 3	0 8 8	0 8 8	0 9 0	0 9 2	0 9 2	0 9 4	0 9 4	0 9 4	0 9 5	0 9 5	0 9 5	0 9 6	0 9 8	0 9 8
INTEGUMENTARY SYSTEM																								
Skin	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																								
Squamous cell papilloma																				X				
Trichoepithelioma																								
Sebaceous adenoma																				X				
Keratoacanthoma																								
Fibroma																								
RESPIRATORY SYSTEM																								
Lungs and bronchi	−	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																								
Trachea	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary adenoma																								
HEMATOPOIETIC SYSTEM																								
Bone marrow	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	−	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Sarcoma, NOS																								
Thymus	−	+	+	−	−	−	−	+	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																								
Heart	−	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
Salivary gland	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																X				X				
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS																								
Large intestine	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
Kidney	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																								X
ENDOCRINE SYSTEM																								
Pituitary	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																					X			
Adenoma, NOS					X		X		X	X	X			X	X									X
Adrenal	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma											X			X		X		X			X		X	
Thyroid	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma																					X			
C-cell adenoma													X											
C-cell carcinoma													X									X		
Parathyroid	−	−	+	−	+	+	+	−	+	−	+	+	−	+	−	+	−	+	−	+	−	+	−	+	−
Pancreatic islets	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																								
Islet cell carcinoma																								X
REPRODUCTIVE SYSTEM																								
Mammary gland	N	N	N	+	+	+	N	+	+	+	N	+	+	+	+	+	N	+	N	N	+	N	+	+	N
Fibroadenoma																								
Testis	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor			X			X		X			X	X	X			X	X	X	X				X	X	X
Mesothelioma, malignant						X		X	X				X												
Prostate	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																								X	
Adenoma, NOS																									
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant						X			X				X												
NERVOUS SYSTEM																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granular cell tumor, NOS																						X			
SPECIAL SENSE ORGANS																								
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
BODY CAVITIES																								
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant									X				X												
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant																									
Leukemia, mononuclear cell	X	X									X			X		X	X			X	X				

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 400 ppm (Continued)

ANIMAL NUMBER	0036	0023	0047	0001	0002	0004	0006	0007	0008	0009	0011	0014	0015	0017	0025	0026	0027	0028	0029	0032	0033	0035	0038	0040	0045	TOTAL:
WEEKS ON STUDY	101	103	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	*50
Papilloma, NOS						X		X																		2
Squamous cell papilloma																										1
Trichoepithelioma																								X		1
Sebaceous adenoma																										1
Keratoacanthoma												X														1
Fibroma	X																									1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Alveolar/bronchiolar adenoma																							X			1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papillary adenoma														X												1
HEMATOPOIETIC SYSTEM																										
Bone marrow	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	−	+	+	+	+	+	+	+	+	+	+	−	−	+	+	−	+	+	+	+	+	+	+	+	+	42
Sarcoma, NOS										X																1
Thymus	+	+	−	+	+	+	+	+	+	+	+	−	+	−	−	+	+	+	+	+	+	+	−	−	−	36
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule				X																						3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS							X																			1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenomatous polyp, NOS						X																				1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Papilloma, NOS																										1
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, NOS																										1
Adenoma, NOS		X	X	X	X	X		X				X		X				X					X	X	X	20
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma		X			X	X	X		X	X				X	X		X	X		X	X	X	X	X		21
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell carcinoma																										1
C-cell adenoma										X																2
C-cell carcinoma																										2
Parathyroid	+	+	+	−	+	+	+	+	−	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	34
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islet cell adenoma					X																				X	2
Islet cell carcinoma																										1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	N	N	N	N	+	+	N	+	+	+	N	N	N	+	+	+	+	+	+	+	N	N	*50
Fibroadenoma																						X				1
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Interstitial cell tumor	X	X	X			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	35
Mesothelioma, malignant																				X						5
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	48
Adenoma, NOS	X																									1
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
Adenoma, NOS																			X							1
Epididymis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																				X						4
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granular cell tumor, NOS																										1
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS		X																								1
BODY CAVITIES																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																				X						3
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																				X						1
Leukemia, mononuclear cell	X				X	X	X	X	X	X		X								X	X	X		X		20

* Animals necropsied

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Skin: Papilloma or Squamous Cell Carcinoma				
Overall Rates (a)	1/49 (2%)	1/50 (2%)	2/50 (4%)	3/50 (6%)
Adjusted Rates (b)	5.9%	3.8%	6.5%	12.0%
Terminal Rates (c)	1/17 (6%)	1/26 (4%)	1/27 (4%)	2/22 (9%)
Week of First Observation	106	106	97	95
Life Table Tests (d)	P=0.178	P=0.665N	P=0.637	P=0.383
Incidental Tumor Tests (d)	P=0.174	P=0.665N	P=0.579	P=0.361
Cochran-Armitage Trend Test (d)	P=0.168			
Fisher Exact Test (d)		P=0.747N	P=0.508	P=0.316
Subcutaneous Tissue: Fibroma				
Overall Rates (a)	1/49 (2%)	0/50 (0%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	5.9%	0.0%	11.1%	4.0%
Terminal Rates (c)	1/17 (6%)	0/26 (0%)	3/27 (11%)	0/22 (0%)
Week of First Observation	106		106	101
Life Table Tests (d)	P=0.512	P=0.415N	P=0.481	P=0.712N
Incidental Tumor Tests (d)	P=0.499	P=0.415N	P=0.481	P=0.750N
Cochran-Armitage Trend Test (d)	P=0.475			
Fisher Exact Test (d)		P=0.495N	P=0.316	P=0.747N
Subcutaneous Tissue: Fibroma or Sarcoma				
Overall Rates (a)	1/49 (2%)	1/50 (2%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	5.9%	3.8%	11.1%	4.0%
Terminal Rates (c)	1/17 (6%)	1/26 (4%)	3/27 (11%)	0/22 (0%)
Week of First Observation	106	106	106	101
Life Table Tests (d)	P=0.607	P=0.665N	P=0.481	P=0.712N
Incidental Tumor Tests (d)	P=0.595	P=0.665N	P=0.481	P=0.750N
Cochran-Armitage Trend Test (d)	P=0.562			
Fisher Exact Test (d)		P=0.747N	P=0.316	P=0.747N
Lung: Alveolar/Bronchiolar Carcinoma				
Overall Rates (a)	0/48 (0%)	0/49 (0%)	3/48 (6%)	0/48 (0%)
Adjusted Rates (b)	0.0%	0.0%	9.5%	0.0%
Terminal Rates (c)	0/17 (0%)	0/26 (0%)	1/27 (4%)	0/22 (0%)
Week of First Observation			93	
Life Table Tests (d)	P=0.571	(e)	P=0.199	(e)
Incidental Tumor Tests (d)	P=0.529	(e)	P=0.104	(e)
Cochran-Armitage Trend Test (d)	P=0.537			
Fisher Exact Test (d)		(e)	P=0.121	(e)
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates (a)	0/48 (0%)	0/49 (0%)	4/48 (8%)	1/48 (2%)
Adjusted Rates (b)	0.0%	0.0%	13.0%	4.5%
Terminal Rates (c)	0/17 (0%)	0/26 (0%)	2/27 (7%)	1/22 (5%)
Week of First Observation			93	106
Life Table Tests (d)	P=0.270	(e)	P=0.128	P=0.551
Incidental Tumor Tests (d)	P=0.250	(e)	P=0.068	P=0.551
Cochran-Armitage Trend Test (d)	P=0.243			
Fisher Exact Test (d)		(e)	P=0.059	P=0.500
Hematopoietic System: Mononuclear Cell Leukemia				
Overall Rates (a)	23/49 (47%)	21/50 (42%)	23/50 (46%)	20/50 (40%)
Adjusted Rates (b)	65.7%	49.8%	60.1%	61.4%
Terminal Rates (c)	7/17 (41%)	7/26 (27%)	13/27 (48%)	11/22 (50%)
Week of First Observation	53	61	78	46
Life Table Tests (d)	P=0.260N	P=0.132N	P=0.143N	P=0.193N
Incidental Tumor Tests (d)	P=0.321N	P=0.517N	P=0.565N	P=0.280N
Cochran-Armitage Trend Test (d)	P=0.314N			
Fisher Exact Test (d)		P=0.385N	P=0.543N	P=0.311N

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Liver: Neoplastic Nodule				
Overall Rates (a)	0/48 (0%)	0/49 (0%)	0/49 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	0.0%	0.0%	10.2%
Terminal Rates (c)	0/17 (0%)	0/26 (0%)	0/27 (0%)	1/22 (5%)
Week of First Observation				92
Life Table Tests (d)	P=0.011	(e)	(e)	P=0.151
Incidental Tumor Tests (d)	P=0.008	(e)	(e)	P=0.102
Cochran-Armitage Trend Test (d)	P=0.013			
Fisher Exact Test (d)		(e)	(e)	P=0.129
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (a)	2/48 (4%)	0/49 (0%)	0/49 (0%)	3/50 (6%)
Adjusted Rates (b)	11.8%	0.0%	0.0%	10.2%
Terminal Rates (c)	2/17 (6%)	0/26 (0%)	0/27 (0%)	1/22 (5%)
Week of First Observation	106			92
Life Table Tests (d)	P=0.265	P=0.150N	P=0.143N	P=0.586
Incidental Tumor Tests (d)	P=0.231	P=0.150N	P=0.143N	P=0.516
Cochran-Armitage Trend Test (d)	P=0.256			
Fisher Exact Test (d)		P=0.242N	P=0.242N	P=0.519
Anterior Pituitary Gland: Adenoma				
Overall Rates (a)	19/45 (42%)	20/49 (41%)	20/48 (42%)	20/48 (42%)
Adjusted Rates (b)	63.1%	51.4%	55.5%	59.6%
Terminal Rates (c)	7/16 (44%)	9/26 (35%)	12/27 (44%)	10/22 (45%)
Week of First Observation	59	73	78	64
Life Table Tests (d)	P=0.449N	P=0.230N	P=0.177N	P=0.399N
Incidental Tumor Tests (d)	P=0.530	P=0.534N	P=0.514N	P=0.582
Cochran-Armitage Trend Test (d)	P=0.535N			
Fisher Exact Test (d)		P=0.528N	P=0.562N	P=0.562N
Anterior Pituitary Gland: Adenoma or Carcinoma				
Overall Rates (a)	19/45 (42%)	20/49 (41%)	20/48 (42%)	21/48 (44%)
Adjusted Rates (b)	63.1%	51.4%	55.5%	60.9%
Terminal Rates (c)	7/16 (44%)	9/26 (35%)	12/27 (44%)	10/22 (45%)
Week of First Observation	59	73	78	64
Life Table Tests (d)	P=0.528N	P=0.230N	P=0.177N	P=0.467N
Incidental Tumor Tests (d)	P=0.439	P=0.534N	P=0.514N	P=0.496
Cochran-Armitage Trend Test (d)	P=0.456			
Fisher Exact Test (d)		P=0.528N	P=0.562N	P=0.524
Adrenal Medulla: Pheochromocytoma				
Overall Rates (a)	8/48 (17%)	23/47 (49%)	17/50 (34%)	21/49 (43%)
Adjusted Rates (b)	37.1%	66.7%	52.4%	70.9%
Terminal Rates (c)	4/17 (24%)	15/26 (58%)	12/27 (44%)	14/22 (64%)
Week of First Observation	98	83	92	83
Life Table Tests (d)	P=0.058	P=0.037	P=0.256	P=0.023
Incidental Tumor Tests (d)	P=0.020	P=0.004	P=0.091	P=0.004
Cochran-Armitage Trend Test (d)	P=0.034			
Fisher Exact Test (d)		P<0.001	P=0.041	P=0.004
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma				
Overall Rates (a)	8/48 (17%)	23/47 (49%)	18/50 (36%)	21/49 (43%)
Adjusted Rates (b)	37.1%	66.7%	55.6%	70.9%
Terminal Rates (c)	4/17 (24%)	15/26 (58%)	13/27 (48%)	14/22 (64%)
Week of First Observation	98	83	92	83
Life Table Tests (d)	P=0.056	P=0.037	P=0.203	P=0.023
Incidental Tumor Tests (d)	P=0.019	P=0.004	P=0.065	P=0.004
Cochran-Armitage Trend Test (d)	P=0.033			
Fisher Exact Test (d)		P<0.001	P=0.026	P=0.004

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Thyroid Gland: C-Cell Adenoma				
Overall Rates (a)	4/46 (9%)	3/46 (7%)	1/48 (2%)	2/49 (4%)
Adjusted Rates (b)	17.7%	11.5%	2.6%	7.0%
Terminal Rates (c)	1/17 (6%)	3/26 (12%)	0/27 (0%)	1/22 (5%)
Week of First Observation	89	106	93	88
Life Table Tests (d)	P=0.179N	P=0.313N	P=0.100N	P=0.267N
Incidental Tumor Tests (d)	P=0.227N	P=0.424N	P=0.218N	P=0.376N
Cochran-Armitage Trend Test (d)	P=0.198N			
Fisher Exact Test (d)		P=0.500N	P=0.168N	P=0.309N
Thyroid Gland: C-Cell Adenoma or Carcinoma				
Overall Rates (a)	4/46 (9%)	3/46 (7%)	2/48 (4%)	3/49 (6%)
Adjusted Rates (b)	17.7%	11.5%	5.3%	10.3%
Terminal Rates (c)	1/17 (6%)	3/26 (12%)	0/27 (0%)	1/22 (5%)
Week of First Observation	89	106	93	88
Life Table Tests (d)	P=0.372N	P=0.313N	P=0.216N	P=0.420N
Incidental Tumor Tests (d)	P=0.442N	P=0.424N	P=0.413N	P=0.551N
Cochran-Armitage Trend Test (d)	P=0.385N			
Fisher Exact Test (d)		P=0.500N	P=0.318N	P=0.464N
Pancreatic Islets: Islet Cell Adenoma				
Overall Rates (a)	4/47 (9%)	2/48 (4%)	4/49 (8%)	2/49 (4%)
Adjusted Rates (b)	18.6%	5.9%	11.2%	9.1%
Terminal Rates (c)	2/17 (12%)	1/26 (4%)	1/27 (4%)	2/22 (9%)
Week of First Observation	80	83	82	106
Life Table Tests (d)	P=0.303N	P=0.211N	P=0.461N	P=0.248N
Incidental Tumor Tests (d)	P=0.372N	P=0.276N	P=0.633N	P=0.304N
Cochran-Armitage Trend Test (d)	P=0.324N			
Fisher Exact Test (d)		P=0.329N	P=0.619N	P=0.319N
Pancreatic Islets: Islet Cell Carcinoma				
Overall Rates (a)	0/47 (0%)	3/48 (6%)	0/49 (0%)	1/49 (2%)
Adjusted Rates (b)	0.0%	9.2%	0.0%	3.7%
Terminal Rates (c)	0/17 (0%)	1/26 (4%)	0/27 (0%)	0/22 (0%)
Week of First Observation		92		98
Life Table Tests (d)	P=0.621N	P=0.189	(e)	P=0.515
Incidental Tumor Tests (d)	P=0.597	P=0.127	(e)	P=0.469
Cochran-Armitage Trend Test (d)	P=0.622N			
Fisher Exact Test (d)		P=0.125	(e)	P=0.510
Pancreatic Islets: Islet Cell Adenoma or Carcinoma				
Overall Rates (a)	4/47 (9%)	5/48 (10%)	4/49 (8%)	3/49 (6%)
Adjusted Rates (b)	18.6%	14.8%	11.2%	12.5%
Terminal Rates (c)	2/17 (12%)	2/26 (8%)	1/27 (4%)	2/22 (9%)
Week of First Observation	80	83	82	98
Life Table Tests (d)	P=0.319N	P=0.581N	P=0.461N	P=0.400N
Incidental Tumor Tests (d)	P=0.408N	P=0.563	P=0.633N	P=0.479N
Cochran-Armitage Trend Test (d)	P=0.339N			
Fisher Exact Test (d)		P=0.514	P=0.619N	P=0.476N
Preputial Gland: Adenoma				
Overall Rates (a)	5/49 (10%)	2/50 (4%)	1/50 (2%)	1/50 (2%)
Adjusted Rates (b)	17.7%	7.7%	3.2%	4.5%
Terminal Rates (c)	2/17 (12%)	2/26 (8%)	0/27 (0%)	1/22 (5%)
Week of First Observation	59	106	99	106
Life Table Tests (d)	P=0.045N	P=0.124N	P=0.060N	P=0.081N
Incidental Tumor Tests (d)	P=0.056N	P=0.178N	P=0.129N	P=0.101N
Cochran-Armitage Trend Test (d)	P=0.057N			
Fisher Exact Test (d)		P=0.210N	P=0.098N	P=0.098N

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Preputial Gland: Adenoma or Carcinoma				
Overall Rates (a)	5/49 (10%)	2/50 (4%)	1/50 (2%)	2/50 (4%)
Adjusted Rates (b)	17.7%	7.7%	3.2%	8.1%
Terminal Rates (c)	2/17 (12%)	2/26 (8%)	0/27 (0%)	1/22 (5%)
Week of First Observation	59	106	99	98
Life Table Tests (d)	P=0.137N	P=0.124N	P=0.060N	P=0.179N
Incidental Tumor Tests (d)	P=0.160N	P=0.178N	P=0.129N	P=0.226N
Cochran-Armitage Trend Test (d)	P=0.157N			
Fisher Exact Test (d)		P=0.210N	P=0.098N	P=0.210N
Testis: Interstitial Cell Tumor				
Overall Rates (a)	42/48 (88%)	41/50 (82%)	47/50 (94%)	35/49 (71%)
Adjusted Rates (b)	100.0%	100.0%	97.9%	91.8%
Terminal Rates (c)	17/17 (100%)	26/26 (100%)	26/27 (96%)	19/22 (86%)
Week of First Observation	66	73	78	61
Life Table Tests (d)	P=0.053N	P=0.019N	P=0.094N	P=0.033N
Incidental Tumor Tests (d)	P=0.046N	P=0.088N	P=0.486	P=0.039N
Cochran-Armitage Trend Test (d)	P=0.035N			
Fisher Exact Test (d)		P=0.318N	P=0.223	P=0.044N
Brain: Granular Cell Tumor				
Overall Rates (a)	0/49 (0%)	3/50 (6%)	1/50 (2%)	1/50 (2%)
Adjusted Rates (b)	0.0%	11.5%	2.3%	3.6%
Terminal Rates (c)	0/17 (0%)	3/26 (12%)	0/27 (0%)	0/22 (0%)
Week of First Observation		106	89	96
Life Table Tests (d)	P=0.622	P=0.203	P=0.541	P=0.507
Incidental Tumor Tests (d)	P=0.582	P=0.203	P=0.464	P=0.469
Cochran-Armitage Trend Test (d)	P=0.596			
Fisher Exact Test (d)		P=0.125	P=0.505	P=0.505
Brain: Glioma, Astrocytoma, or Oligodendroglioma				
Overall Rates (a)	0/49 (0%)	3/50 (6%)	0/50 (0%)	0/50 (0%)
Adjusted Rates (b)	0.0%	7.5%	0.0%	0.0%
Terminal Rates (c)	0/17 (0%)	0/26 (0%)	0/27 (0%)	0/22 (0%)
Week of First Observation		83		
Life Table Tests (d)	P=0.306N	P=0.160	(e)	(e)
Incidental Tumor Tests (d)	P=0.394N	P=0.087	(e)	(e)
Cochran-Armitage Trend Test (d)	P=0.308N			
Fisher Exact Test (d)		P=0.125	(e)	(e)
All Sites: Malignant Mesothelioma				
Overall Rates (a)	7/49 (14%)	3/50 (6%)	2/50 (4%)	5/50 (10%)
Adjusted Rates (b)	34.1%	9.2%	6.0%	13.3%
Terminal Rates (c)	5/17 (29%)	1/26 (4%)	1/27 (4%)	1/22 (5%)
Week of First Observation	88	83	91	72
Life Table Tests (d)	P=0.338N	P=0.058N	P=0.021N	P=0.290N
Incidental Tumor Tests (d)	P=0.361N	P=0.099N	P=0.036N	P=0.310N
Cochran-Armitage Trend Test (d)	P=0.372N			
Fisher Exact Test (d)		P=0.151N	P=0.075N	P=0.366N
All Sites: Benign Tumors				
Overall Rates (a)	46/49 (94%)	48/50 (96%)	50/50 (100%)	45/50 (90%)
Adjusted Rates (b)	100.0%	100.0%	100.0%	100.0%
Terminal Rates (c)	17/17 (100%)	26/26 (100%)	27/27 (100%)	22/22 (100%)
Week of First Observation	59	73	78	61
Life Table Tests (d)	P=0.235N	P=0.057N	P=0.065N	P=0.174N
Incidental Tumor Tests (d)	P=0.516N	P=0.626N	P=0.347	P=0.596N
Cochran-Armitage Trend Test (d)	P=0.227N			
Fisher Exact Test (d)		P=0.490	P=0.117	P=0.369N

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
All Sites: Malignant Tumors				
Overall Rates (a)	32/49 (65%)	28/50 (56%)	31/50 (62%)	29/50 (58%)
Adjusted Rates (b)	84.9%	59.4%	72.5%	71.0%
Terminal Rates (c)	12/17 (71%)	8/26 (31%)	16/27 (59%)	11/22 (50%)
Week of First Observation	53	61	78	46
Life Table Tests (d)	P=0.298N	P=0.057N	P=0.065N	P=0.188N
Incidental Tumor Tests (d)	P=0.385N	P=0.369N	P=0.444N	P=0.281N
Cochran-Armitage Trend Test (d)	P=0.345N			
Fisher Exact Test (d)		P=0.229N	P=0.447N	P=0.295N
All Sites: All Tumors				
Overall Rates (a)	49/49 (100%)	50/50 (100%)	50/50 (100%)	49/50 (98%)
Adjusted Rates (b)	100.0%	100.0%	100.0%	100.0%
Terminal Rates (c)	17/17 (100%)	26/26 (100%)	27/27 (100%)	22/22 (100%)
Week of First Observation	53	61	78	46
Life Table Tests (d)	P=0.296N	P=0.047N	P=0.029N	P=0.225N
Incidental Tumor Tests (d)	P=0.295N	(f)	(f)	P=0.557N
Cochran-Armitage Trend Test (d)	P=0.200N			
Fisher Exact Test (d)		P=1.000N	P=1.000N	P=0.505N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor 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 that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the dosed and control groups.
(f) No P value is reported because tumors were observed in all animals in the dosed and control groups.

TABLE A4a. HISTORICAL INCIDENCE OF ADRENAL MEDULLARY TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Pheochromocytoma	Malignant Pheochromocytoma	Pheochromocytoma or Malignant Pheochromocytoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	3/48	0/48	3/48
Methyl methacrylate	5/49	0/49	5/49
Propylene	3/50	2/50	5/50
1,2-Epoxybutane	16/50	2/50	17/50
Dichloromethane	5/50	0/50	5/50
Tetrachloroethylene	22/49	0/49	22/49
TOTAL	54/296 (18.2%)	4/296 (1.4%)	57/296 (19.3%)
SD (b)	16.29%	2.07%	16.11%
Range (c)			
High	22/49	2/50	22/49
Low	3/50	0/50	3/48
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	459/1,915 (24.0%)	37/1,915 (1.9%)	489/1,915 (25.5%)
SD (b)	13.30%	2.70%	13.65%
Range (c)			
High	31/49	6/50	32/49
Low	2/50	0/50	3/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE A4b. HISTORICAL INCIDENCE OF BRAIN TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls	
	Granular Cell	Glial Cell
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories		
Propylene oxide	0/47	(b) 1/47
Methyl methacrylate	0/50	0/50
Propylene	0/50	(b) 1/50
1,2-Epoxybutane	0/50	0/50
Dichloromethane	0/50	(c) 1/50
TOTAL	0/297 (0.0%)	3/297 (1.0%)
SD (d)	0.00%	1.12%
Range (e)		
High	0/50	1/47
Low	0/50	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies		
TOTAL	(f) 4/1,928 (0.2%)	(g) 13/1,928 (0.7%)
SD (d)	0.62%	1.24%
Range (e)		
High	1/49	2/50
Low	0/50	0/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Glioma, NOS
(c) Astrocytoma
(d) Standard deviation
(e) Range and SD are presented for groups of 35 or more animals.
(f) Includes one benign granular cell tumor, one malignant granular cell tumor, and two granular cell tumors, NOS
(g) Includes two gliomas, NOS, nine astrocytomas, and two oligodendrogliomas

TABLE A4c. HISTORICAL INCIDENCE OF ALVEOLAR/BRONCHIOLAR TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	0/50	2/50	2/50
Methyl methacrylate	0/49	1/49	1/49
Propylene	0/50	1/50	1/50
1,2-Epoxybutane	0/50	0/50	0/50
Dichloromethane	1/50	0/50	1/50
Tetrachloroethylene	1/50	0/50	1/50
TOTAL	2/299 (0.7%)	4/299 (1.3%)	6/299 (2.0%)
SD (b)	1.03%	2.64%	1.27%
Range (c)			
High	1/50	2/50	2/50
Low	0/50	0/50	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	25/1,933 (1.3%)	20/1,933 (1.0%)	43/1,933 (2.2%)
SD (b)	1.70%	1.77%	2.20%
Range (c)			
High	3/49	3/50	4/50
Low	0/50	0/50	0/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE A4d. HISTORICAL INCIDENCE OF NASAL CAVITY TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

	Incidence in Controls
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories	
TOTAL	0/300
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	(b) 2/1,936 (0.1%)

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Includes one squamous cell papilloma and one squamous cell carcinoma

TABLE A4e. HISTORICAL INCIDENCE OF LIVER TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Neoplastic Nodule	Hepatocellular Carcinoma	Neoplastic Nodule or Hepatocellular Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	0/50	1/50	1/50
Methyl methacrylate	0/50	0/50	0/50
Propylene	0/50	0/50	0/50
1,2-Epoxybutane	2/50	0/50	2/50
Dichloromethane	0/50	2/50	2/50
Tetrachloroethylene	4/50	0/50	4/50
TOTAL	6/300 (2.0%)	3/300 (1.0%)	9/300 (3.0%)
SD (b)	3.35%	1.67%	3.03%
Range (c)			
High	4/50	2/50	4/50
Low	0/50	0/50	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	80/1,928 (4.1%)	20/1,928 (1.0%)	99/1,928 (5.1%)
SD (b)	3.87%	1.45%	4.00%
Range (c)			
High	6/49	3/50	7/49
Low	0/50	0/50	0/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals necropsied	49	50	50	50
Animals examined histopathologically	49	50	50	50
INTEGUMENTARY SYSTEM				
*Skin	(49)	(50)	(50)	(50)
Epidermal inclusion cyst		2 (4%)	1 (2%)	3 (6%)
Ulcer, NOS	2 (4%)	2 (4%)	3 (6%)	3 (6%)
Inflammation, suppurative		1 (2%)	1 (2%)	2 (4%)
Fibrosis	1 (2%)			
Acanthosis	2 (4%)	3 (6%)	4 (8%)	2 (4%)
RESPIRATORY SYSTEM				
#Nose	(47)	(48)	(49)	(49)
Foreign body, NOS	8 (17%)	7 (15%)	4 (8%)	6 (12%)
Hemorrhage	2 (4%)			1 (2%)
Inflammation, suppurative	18 (38%)	28 (58%)	33 (67%)	40 (82%)
Inflammation, chronic	3 (6%)			3 (6%)
Fibrous osteodystrophy	1 (2%)	3 (6%)		3 (6%)
Hyperplasia, epithelial	14 (30%)	14 (29%)	14 (29%)	27 (55%)
Metaplasia, squamous	4 (9%)	2 (4%)	2 (4%)	9 (18%)
#Nasal gland	(47)	(48)	(49)	(49)
Hyperplasia, NOS				1 (2%)
*Larynx	(49)	(50)	(50)	(50)
Foreign body, NOS	1 (2%)	3 (6%)	3 (6%)	1 (2%)
Mineralization		1 (2%)		
Inflammation, suppurative	7 (14%)	21 (42%)	14 (28%)	25 (50%)
Inflammation, chronic		1 (2%)		2 (4%)
Hyperplasia, epithelial		3 (6%)	4 (8%)	2 (4%)
Acanthosis		4 (8%)		1 (2%)
Metaplasia, squamous				1 (2%)
#Trachea	(46)	(47)	(47)	(49)
Inflammation, suppurative	3 (7%)	1 (2%)	1 (2%)	4 (8%)
Inflammation, chronic				2 (4%)
Hyperplasia, epithelial		1 (2%)		
Metaplasia, squamous				1 (2%)
#Lung/bronchus	(48)	(49)	(48)	(48)
Hyperplasia, epithelial		1 (2%)	1 (2%)	
#Lung/bronchiole	(48)	(49)	(48)	(48)
Inflammation, suppurative	1 (2%)	1 (2%)		1 (2%)
#Lung	(48)	(49)	(48)	(48)
Foreign body, NOS				1 (2%)
Mineralization		2 (4%)		
Hemorrhage	5 (10%)	7 (14%)	4 (8%)	9 (19%)
Fibrosis	1 (2%)			1 (2%)
Hyperplasia, alveolar epithelium	3 (6%)	7 (14%)	7 (15%)	18 (38%)
Metaplasia, osseous	1 (2%)			
#Lung/alveoli	(48)	(49)	(48)	(48)
Edema, NOS	1 (2%)			
Inflammation, suppurative	6 (13%)	12 (24%)	6 (13%)	9 (19%)
Fibrosis		1 (2%)		
Histiocytosis	18 (38%)	31 (63%)	27 (56%)	29 (60%)
HEMATOPOIETIC SYSTEM				
#Bone marrow	(47)	(47)	(48)	(48)
Atrophy, NOS	5 (11%)	2 (4%)	3 (6%)	10 (21%)
Hyperplasia, hematopoietic				1 (2%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
HEMATOPOIETIC SYSTEM (Continued)				
#Spleen	(48)	(49)	(50)	(50)
Ectopia		1 (2%)	1 (2%)	2 (4%)
Fibrosis	7 (15%)	8 (16%)	9 (18%)	3 (6%)
Necrosis, NOS	1 (2%)		1 (2%)	2 (4%)
#Mandibular lymph node	(43)	(47)	(49)	(42)
Hyperplasia, lymphoid		2 (4%)	1 (2%)	2 (5%)
#Bronchial lymph node	(43)	(47)	(49)	(42)
Hemorrhage	1 (2%)			
Pigmentation, NOS	1 (2%)			
Hyperplasia, lymphoid				1 (2%)
#Mediastinal lymph node	(43)	(47)	(49)	(42)
Fibrosis				1 (2%)
Pigmentation, NOS	1 (2%)			
Hyperplasia, lymphoid		1 (2%)		
#Thymus	(34)	(37)	(49)	(36)
Cyst, NOS		1 (3%)		
CIRCULATORY SYSTEM				
*Multiple organs	(49)	(50)	(50)	(50)
Periarteritis	6 (12%)		1 (2%)	6 (12%)
#Nose	(47)	(48)	(49)	(49)
Thrombosis, NOS	1 (2%)			1 (2%)
#Lung	(48)	(49)	(48)	(48)
Thrombosis, NOS	1 (2%)			
#Heart	(48)	(49)	(49)	(48)
Mineralization		3 (6%)		3 (6%)
#Heart/atrium	(48)	(49)	(49)	(48)
Thrombosis, NOS	1 (2%)	3 (6%)	1 (2%)	1 (2%)
#Myocardium	(48)	(49)	(49)	(48)
Degeneration, NOS	26 (54%)	23 (47%)	19 (39%)	29 (60%)
*Mesentery	(49)	(50)	(50)	(50)
Periarteritis	2 (4%)			1 (2%)
DIGESTIVE SYSTEM				
#Salivary gland	(48)	(48)	(49)	(49)
Dilatation/ducts	10 (21%)	7 (15%)	7 (14%)	7 (14%)
Inflammation, suppurative	8 (17%)	4 (8%)	5 (10%)	9 (18%)
Inflammation, chronic			2 (4%)	2 (4%)
Hyperplasia, NOS				1 (2%)
#Liver	(48)	(49)	(49)	(50)
Congenital malformation, NOS		2 (4%)	2 (4%)	2 (4%)
Granuloma, NOS	2 (4%)	1 (2%)	1 (2%)	5 (10%)
Necrosis, NOS	5 (10%)	7 (14%)	5 (10%)	7 (14%)
Metamorphosis, fatty	6 (13%)	6 (12%)	4 (8%)	3 (6%)
Basophilic cyto change	16 (33%)	23 (47%)	28 (57%)	23 (46%)
Clear cell change	15 (31%)	20 (41%)	25 (51%)	16 (32%)
Hyperplasia, NOS	5 (10%)	10 (20%)	7 (14%)	9 (18%)
Angiectasis		2 (4%)	1 (2%)	1 (2%)
#Hepatic capsule	(48)	(49)	(49)	(50)
Inflammation, suppurative				1 (2%)
#Bile duct	(48)	(49)	(49)	(50)
Hyperplasia, NOS	30 (63%)	35 (71%)	34 (69%)	36 (72%)
#Pancreas	(47)	(48)	(49)	(49)
Hemorrhage		1 (2%)		
#Pancreatic acinus	(47)	(48)	(49)	(49)
Cytoplasmic change, NOS				1 (2%)
Atrophy, NOS	18 (38%)	23 (48%)	24 (49%)	18 (37%)
Hyperplasia, NOS				1 (2%)
#Esophagus	(48)	(50)	(49)	(50)
Hyperkeratosis	3 (6%)	4 (8%)	3 (6%)	3 (6%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
DIGESTIVE SYSTEM (Continued)				
#Glandular stomach	(47)	(48)	(48)	(49)
Mineralization	1 (2%)	3 (6%)	1 (2%)	3 (6%)
Inflammation, suppurative	4 (9%)		1 (2%)	5 (10%)
Erosion	3 (6%)			3 (6%)
Atrophy, NOS		1 (2%)	1 (2%)	1 (2%)
Hyperplasia, epithelial				2 (4%)
#Forestomach	(47)	(48)	(48)	(49)
Congenital malformation, NOS			1 (2%)	
Ulcer, NOS	3 (6%)	2 (4%)	4 (8%)	5 (10%)
Erosion				1 (2%)
Hyperkeratosis	4 (9%)	4 (8%)	5 (10%)	5 (10%)
Acanthosis	8 (17%)	5 (10%)	5 (10%)	8 (16%)
#Duodenum	(46)	(48)	(48)	(47)
Inflammation, suppurative	1 (2%)			
Necrosis, NOS	1 (2%)			
#Ileum	(46)	(48)	(48)	(47)
Granuloma, NOS				1 (2%)
#Colon	(47)	(47)	(48)	(47)
Parasitism	5 (11%)	11 (23%)	12 (25%)	5 (11%)
#Cecum	(47)	(47)	(48)	(47)
Hemorrhage			1 (2%)	
*Rectum	(49)	(50)	(50)	(50)
Parasitism		4 (8%)	3 (6%)	1 (2%)
*Rectal mucosa	(49)	(50)	(50)	(50)
Atrophy, NOS			1 (2%)	1 (2%)
URINARY SYSTEM				
#Kidney	(47)	(49)	(48)	(49)
Mineralization		2 (4%)	2 (4%)	2 (4%)
Cyst, NOS			1 (2%)	
Nephropathy	46 (98%)	49 (100%)	48 (100%)	49 (100%)
#Kidney/capsule	(47)	(49)	(48)	(49)
Hemorrhage	1 (2%)		1 (2%)	1 (2%)
#Kidney/interstitium	(47)	(49)	(48)	(49)
Metamorphosis, fatty	1 (2%)			
#Kidney/pelvis	(47)	(49)	(48)	(49)
Inflammation, suppurative	1 (2%)	2 (4%)	1 (2%)	5 (10%)
Hyperplasia, epithelial	1 (2%)	4 (8%)	3 (6%)	5 (10%)
#Urinary bladder	(47)	(46)	(49)	(48)
Calculus, gross observation only				1 (2%)
Hemorrhage	1 (2%)			1 (2%)
Inflammation, suppurative	2 (4%)		1 (2%)	3 (6%)
Hyperplasia, epithelial	5 (11%)	2 (4%)	3 (6%)	4 (8%)
ENDOCRINE SYSTEM				
#Pituitary	(45)	(49)	(48)	(48)
Angiectasis		1 (2%)		
#Anterior pituitary	(45)	(49)	(48)	(48)
Necrosis, NOS	3 (7%)			1 (2%)
Hyperplasia, NOS	7 (16%)	12 (24%)	10 (21%)	10 (21%)
Angiectasis	4 (9%)	5 (10%)	6 (13%)	5 (10%)
#Adrenal cortex	(48)	(47)	(50)	(49)
Hemorrhage				1 (2%)
Necrosis, NOS				1 (2%)
Cytoplasmic vacuolization	1 (2%)			
Clear cell change	13 (27%)	21 (45%)	20 (40%)	24 (49%)
Hyperplasia, NOS	4 (8%)	10 (21%)	9 (18%)	8 (16%)
Hyperplasia, focal	3 (6%)			

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
ENDOCRINE SYSTEM (Continued)				
#Adrenal medulla	(48)	(47)	(50)	(49)
Necrosis, NOS		1 (2%)		1 (2%)
Clear cell change	1 (2%)			
Hyperplasia, NOS	8 (17%)	14 (30%)	8 (16%)	10 (20%)
Angiectasis	1 (2%)	1 (2%)		
#Thyroid	(46)	(46)	(48)	(49)
Ultimobranchial cyst	2 (4%)		1 (2%)	
Hyperplasia, C-cell	5 (11%)	9 (20%)	13 (27%)	10 (20%)
Hyperplasia, follicular cell		2 (4%)		1 (2%)
#Parathyroid	(29)	(34)	(39)	(34)
Hyperplasia, NOS	4 (14%)	6 (18%)	2 (5%)	4 (12%)
#Pancreatic islets	(47)	(48)	(49)	(49)
Hyperplasia, NOS	2 (4%)	1 (2%)	1 (2%)	3 (6%)
REPRODUCTIVE SYSTEM				
*Mammary acinus	(49)	(50)	(50)	(50)
Hyperplasia, NOS				2 (4%)
*Preputial gland	(49)	(50)	(50)	(50)
Cyst, NOS	4 (8%)	6 (12%)	3 (6%)	8 (16%)
Inflammation, suppurative	8 (16%)	6 (12%)	8 (16%)	9 (18%)
Hyperplasia, NOS	1 (2%)	1 (2%)	4 (8%)	1 (2%)
Acanthosis	3 (6%)	3 (6%)	10 (20%)	4 (8%)
#Prostate	(44)	(44)	(48)	(48)
Inflammation, suppurative	12 (27%)	11 (25%)	10 (21%)	13 (27%)
Hyperplasia, epithelial	1 (2%)	3 (7%)	3 (6%)	3 (6%)
*Seminal vesicle	(49)	(50)	(50)	(50)
Inflammation, suppurative	12 (24%)	10 (20%)	12 (24%)	14 (28%)
Hyperplasia, NOS	6 (12%)	1 (2%)	6 (12%)	4 (8%)
#Testis	(48)	(50)	(50)	(49)
Necrosis, NOS	1 (2%)		1 (2%)	2 (4%)
Atrophy, NOS	43 (90%)	45 (90%)	44 (88%)	40 (82%)
Hyperplasia, interstitial cell	1 (2%)			2 (4%)
*Epididymis	(49)	(50)	(50)	(50)
Hemorrhage	1 (2%)			
Hyperplasia, epithelial		1 (2%)		
NERVOUS SYSTEM				
*Peripheral nerve	(49)	(50)	(50)	(50)
Degeneration, NOS				1 (2%)
#Brain/meninges	(49)	(50)	(50)	(50)
Hyperplasia, NOS			1 (2%)	
#Brain	(49)	(50)	(50)	(50)
Mineralization				1 (2%)
Hemorrhage	7 (14%)		1 (2%)	4 (8%)
Gliosis		1 (2%)		1 (2%)
Degeneration, NOS				2 (4%)
Necrosis, NOS	1 (2%)			
Atrophy, NOS	8 (16%)	4 (8%)	6 (12%)	8 (16%)
*Spinal cord	(49)	(50)	(50)	(50)
Hemorrhage			1 (2%)	
*Olfactory sensory epithelium	(49)	(50)	(50)	(50)
Degeneration, NOS	4 (8%)	1 (2%)	4 (8%)	9 (18%)
Metaplasia, NOS			7 (14%)	6 (12%)
*Sciatic nerve	(49)	(50)	(50)	(50)
Mineralization		1 (2%)		

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
SPECIAL SENSE ORGANS				
*Eye	(49)	(50)	(50)	(50)
Inflammation, suppurative				1 (2%)
*Eye/sclera	(49)	(50)	(50)	(50)
Mineralization		1 (2%)	1 (2%)	1 (2%)
*Eye/cornea	(49)	(50)	(50)	(50)
Mineralization		1 (2%)		
Inflammation, chronic		1 (2%)		
*Eye/retina	(49)	(50)	(50)	(50)
Degeneration, NOS				1 (2%)
*Eye/crystalline lens	(49)	(50)	(50)	(50)
Mineralization		1 (2%)		1 (2%)
Cataract		1 (2%)		1 (2%)
MUSCULOSKELETAL SYSTEM				
*Skull	(49)	(50)	(50)	(50)
Granuloma, NOS				2 (4%)
Exostosis				1 (2%)
*Sternum	(49)	(50)	(50)	(50)
Fibrous osteodystrophy	3 (6%)	2 (4%)		3 (6%)
*Skeletal muscle	(49)	(50)	(50)	(50)
Mineralization		1 (2%)		1 (2%)
BODY CAVITIES				
*Pleura	(49)	(50)	(50)	(50)
Hyperplasia, mesothelial	1 (2%)			
*Mesentery	(49)	(50)	(50)	(50)
Hemorrhage	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Necrosis, fat	1 (2%)	1 (2%)	1 (2%)	3 (6%)
ALL OTHER SYSTEMS				
None				
SPECIAL MORPHOLOGY SUMMARY				
Animal missexed/no necropsy	1			

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site

APPENDIX B

SUMMARY OF LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals missing			1	
Animals necropsied	50	50	48	50
Animals examined histopathologically	50	50	48	50
INTEGUMENTARY SYSTEM				
*Skin	(50)	(50)	(48)	(50)
Papilloma, NOS			1 (2%)	
Basal cell tumor			1 (2%)	
Fibroma		3 (6%)		1 (2%)
Lipoma			1 (2%)	
Neurilemoma, malignant		1 (2%)	2 (4%)	
RESPIRATORY SYSTEM				
#Lung	(50)	(48)	(47)	(49)
Carcinoma, NOS, metastatic	1 (2%)			
Alveolar/bronchiolar adenoma				3 (6%)
Adenosquamous carcinoma, metastatic			1 (2%)	
Granulosa cell carcinoma, metastatic			1 (2%)	
HEMATOPOIETIC SYSTEM				
*Multiple organs	(50)	(50)	(48)	(50)
Leukemia, mononuclear cell	23 (46%)	13 (26%)	16 (33%)	15 (30%)
CIRCULATORY SYSTEM				
None				
DIGESTIVE SYSTEM				
*Palate	(50)	(50)	(48)	(50)
Papilloma, NOS	1 (2%)			
*Tongue	(50)	(50)	(48)	(50)
Squamous cell carcinoma				1 (2%)
#Liver	(50)	(49)	(47)	(48)
Neoplastic nodule	1 (2%)		3 (6%)	
Hepatocellular carcinoma			1 (2%)	
#Forestomach	(48)	(49)	(47)	(47)
Papilloma, NOS				1 (2%)
#Colon	(49)	(46)	(47)	(47)
Carcinoma, NOS				1 (2%)
*Rectum	(50)	(50)	(48)	(50)
Sarcoma, NOS, metastatic		1 (2%)		
URINARY SYSTEM				
#Urinary bladder	(49)	(48)	(48)	(47)
Carcinoma, NOS, metastatic			1 (2%)	
ENDOCRINE SYSTEM				
#Anterior pituitary	(50)	(49)	(48)	(48)
Carcinoma, NOS	1 (2%)	3 (6%)		1 (2%)
Adenoma, NOS	26 (52%)	30 (61%)	28 (58%)	28 (58%)
#Adrenal	(50)	(49)	(47)	(48)
Cortical adenoma	1 (2%)	1 (2%)		1 (2%)
#Adrenal medulla	(50)	(49)	(47)	(48)
Pheochromocytoma	1 (2%)	2 (4%)	3 (6%)	4 (8%)
Pheochromocytoma, malignant	1 (2%)		1 (2%)	1 (2%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
ENDOCRINE SYSTEM (Continued)				
#Thyroid	(48)	(48)	(47)	(46)
Follicular cell adenoma	1 (2%)			1 (2%)
Follicular cell carcinoma		1 (2%)		
C-cell adenoma	5 (10%)	3 (6%)	1 (2%)	5 (11%)
C-cell carcinoma	2 (4%)	1 (2%)	1 (2%)	
REPRODUCTIVE SYSTEM				
*Mammary gland	(50)	(50)	(48)	(50)
Adenoma, NOS	1 (2%)			
Adenocarcinoma, NOS	4 (8%)	2 (4%)	1 (2%)	1 (2%)
Adenosquamous carcinoma			1 (2%)	
Fibroadenoma	16 (32%)	14 (28%)	8 (17%)	6 (12%)
*Clitoral gland	(50)	(50)	(48)	(50)
Adenoma, NOS	1 (2%)	6 (12%)	3 (6%)	2 (4%)
#Uterus	(50)	(50)	(48)	(49)
Carcinoma, NOS			1 (2%)	
Sarcoma, NOS		1 (2%)		
Leiomyoma	2 (4%)		1 (2%)	
Endometrial stromal polyp	5 (10%)	6 (12%)	4 (8%)	4 (8%)
Endometrial stromal sarcoma	1 (2%)		1 (2%)	
#Ovary	(50)	(49)	(48)	(48)
Papillary cystadenoma, NOS		1 (2%)		
Granulosa cell carcinoma			1 (2%)	
NERVOUS SYSTEM				
#Brain	(50)	(50)	(48)	(50)
Carcinoma, NOS, metastatic	2 (4%)	3 (6%)		1 (2%)
Granulosa cell carcinoma, metastatic			1 (2%)	
Glioma, NOS		1 (2%)	1 (2%)	3 (6%)
SPECIAL SENSE ORGANS				
*Zymbal gland	(50)	(50)	(48)	(50)
Carcinoma, NOS	2 (4%)			1 (2%)
MUSCULOSKELETAL SYSTEM				
None				
BODY CAVITIES				
None				
ALL OTHER SYSTEMS				
*Multiple organs	(50)	(50)	(48)	(50)
Histiocytic sarcoma			1 (2%)	
ANIMAL DISPOSITION SUMMARY				
Animals initially in study	50	50	50	50
Natural death	2	5	5	4
Moribund sacrifice	29	15	19	24
Terminal sacrifice	19	29	24	22
Accidentally killed, nda		1		
Animal missing			1	
Animal missexed			1	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
TUMOR SUMMARY				
Total animals with primary tumors**	49	46	40	44
Total primary tumors	95	89	82	80
Total animals with benign tumors	42	41	35	38
Total benign tumors	60	66	51	56
Total animals with malignant tumors	29	20	23	20
Total malignant tumors	34	23	28	24
Total animals with secondary tumors##	2	4	2	1
Total secondary tumors	3	4	4	1
Total animals with tumors uncertain -- benign or malignant	1		3	
Total uncertain tumors	1		3	

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: CHAMBER CONTROL

ANIMAL NUMBER	0049	0023	0024	0037	0111	0334	0118	0330	0447	0333	0222	0443	0110	0002	0007	0331	0114	0336	0442	0332	0003	0005	0335	0466	0220
WEEKS ON STUDY	0557	0772	0722	0766	0777	0778	0788	0788	0789	0791	0816	0866	0888	0900	0911	0955	0966	0966	0966	0989	1000	1000	1011	1011	1044
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Thymus	+	+	+	–	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papilloma, NOS																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																								X	
Adenoma, NOS	X	X	X	X		X		X		X					X			X		X	X	X	X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma													X												
Pheochromocytoma, malignant																									X
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+
Follicular cell adenoma																									
C-cell adenoma											X														X
C-cell carcinoma													X												
Parathyroid	+	+	–	+	–	–	–	+	–	+	+	+	–	–	–	+	–	–	+	–	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																					X				
Adenocarcinoma, NOS								X			X							X						
Fibroadenoma		X	X								X	X				X		X							
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																									
Endometrial stromal polyp	X				X						X								X						
Endometrial stromal sarcoma																									X
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic																								X	
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS			X																						
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell			X	X	X		X		X				X	X	X	X	X	X	X				X		

+: Tissue examined microscopically
–: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	027	039	045	001	008	044	004	006	009	012	013	015	016	017	019	021	025	026	028	029	038	040	041	048	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	104	104	104	105	105	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS, metastatic			X																							1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thymus	+	−	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Papilloma, NOS												X														1
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule									X																	1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS																										1
Adenoma, NOS		X		X		X			X		X			X				X	X	X	X		X	X	X	26
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma											X															1
Pheochromocytoma																										1
Pheochromocytoma, malignant																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	48
Follicular cell adenoma																								X		1
C-cell adenoma					X				X						X											5
C-cell carcinoma				X																						2
Parathyroid	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	−	36
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenoma, NOS																										1
Adenocarcinoma, NOS														X												4
Fibroadenoma	X	X								X			X	X						X	X	X	X	X		16
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS							X																			1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyoma							X										X									2
Endometrial stromal polyp				X																						5
Endometrial stromal sarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS, metastatic			X																							2
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS			X																							2
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell	X	X		X	X		X				X					X			X					X	X	23

* Animals necropsied

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 100 ppm

ANIMAL NUMBER	0012	0035	0022	0029	0003	0010	0048	0041	0037	0046	0036	0013	0018	0009	0021	0034	0042	0050	0033	0005	0028	0001	0002	0004	0006
WEEKS ON STUDY	062	066	083	084	086	086	088	092	093	094	095	098	100	101	101	101	101	103	104	105	105	106	106	106	106
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma		X																							
Neurilemoma, malignant								X																	
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Trachea	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Nasal cavity	−	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	−	+	+	+	A	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	−	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Large intestine	−	+	−	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Rectum	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, metastatic														X											
URINARY SYSTEM																									
Kidney	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS											X						X			X					
Adenoma, NOS			X			X	X	X		X		X	X	X	X			X				X		X	X
Adrenal	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																				X					
Pheochromocytoma																			X						
Thyroid	+	−	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma														X											
C-cell adenoma																									
C-cell carcinoma																	X								
Parathyroid	+	−	+	−	A	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Fibroadenoma						X				X												X	X		X
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS										X						X							X	X	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS														X											
Endometrial stromal polyp						X														X					
Ovary	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary cystadenoma, NOS															X										
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic											X						X			X					
Glioma, NOS	X																								
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell		X		X				X				X			X	X						X		X	

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 100 ppm (Continued)

ANIMAL NUMBER	007	008	011	014	015	016	017	019	020	023	024	025	026	027	030	031	032	038	039	040	043	044	045	047	049	TOTAL:
WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma													X													3
Neurilemoma, malignant														X												1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	43
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	49
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS, metastatic																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS																										3
Adenoma, NOS	X	X		X	X	X	X	X				X	X	X	X		X	X	X			X	X		X	30
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cortical adenoma																										1
Pheochromocytoma												X														2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Follicular cell carcinoma																										1
C-cell adenoma					X										X	X										3
C-cell carcinoma																										1
Parathyroid	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	–	+	+	+	42
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	*50
Adenocarcinoma, NOS					X				X																	2
Fibroadenoma		X	X					X	X							X					X	X		X	X	14
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS	X																		X							6
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, NOS																										1
Endometrial stromal polyp			X			X							X												X	6
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papillary cystadenoma, NOS																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS, metastatic																										3
Glioma, NOS																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell													X	X					X	X			X			13

* Animals necropsied

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 200 ppm

ANIMAL NUMBER	0161	0501	0331	0151	0371	0344	0288	0399	0068	0134	0499	0411	0455	0099	0222	0488	0422	0332	0388	0111	0144	0005	0400	0466	0355
WEEKS ON STUDY	0133	0557	0599	0661	0663	0666	0668	0668	0674	0681	0685	0686	0690	0692	0692	0692	0696	0698	0698	0699	0699	0699	1003	1013	1045
INTEGUMENTARY SYSTEM																									
Skin	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Papilloma, NOS																									
Basal cell tumor															X										
Lipoma																									
Neurilemoma, malignant																			X	X					
RESPIRATORY SYSTEM																									
Lungs and bronchi	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Adenosquamous carcinoma, metastatic						X																			
Granulosa cell carcinoma, metastatic						X																			
Trachea	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Nasal cavity	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Spleen	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Lymph nodes	S	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+
Thymus	S	+	-	-	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	S	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+
Liver	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Neoplastic nodule																									X
Hepatocellular carcinoma																		X							
Bile duct	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Small intestine	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
Large intestine	S	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic																									
ENDOCRINE SYSTEM																									
Pituitary	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS			X		X			X	X	X	X					X	X	X	X		X	X	X	X	X
Adrenal	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma															X	X			X						
Pheochromocytoma, malignant																									
Thyroid	S	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell adenoma																									
C-cell carcinoma																									
Parathyroid	S	+	-	+	-	-	+	-	-	+	-	-	-	-	+	-	+	+	-	+	+	-	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS											X														
Adenosquamous carcinoma						X																			
Fibroadenoma												X				X						X			
Preputial/clitoral gland	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																X									
Uterus	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Carcinoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp															X										X
Endometrial stromal sarcoma		X																							
Ovary	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Granulosa cell carcinoma						X																			
NERVOUS SYSTEM																									
Brain	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Granulosa cell carcinoma, metastatic						X																			
Glioma, NOS																					X				
ALL OTHER SYSTEMS																									
Multiple organs, NOS	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Histiocytic sarcoma																	X								
Leukemia, mononuclear cell		X		X	X			X				X		X	X			X	X				X	X	

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 200 ppm (Continued)

ANIMAL NUMBER	001	002	003	004	007	008	010	012	017	018	019	020	021	023	024	025	026	027	029	030	031	036	043	044	047	TOTAL:
WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	*48
Papilloma, NOS						X																				1
Basal cell tumor																										1
Lipoma												X														1
Neurilemoma, malignant																										2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Adenosquamous carcinoma, metastatic																										1
Granulosa cell carcinoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	44
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Neoplastic nodule																X				X						3
Hepatocellular carcinoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Carcinoma, NOS, metastatic				X																						1
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Adenoma, NOS		X	X	X			X					X	X		X	X			X	X	X			X	X	28
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Pheochromocytoma																										3
Pheochromocytoma, malignant																									X	1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
C-cell adenoma																							X			1
C-cell carcinoma						X																				1
Parathyroid	+	+	+	+	+	+	+	+	–	–	–	+	+	+	+	+	+	+	+	+	+	M	+	+	–	32
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	*48
Adenocarcinoma, NOS																										1
Adenosquamous carcinoma																										1
Fibroadenoma	X			X						X									X		X					8
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	M	N	N	N	*48
Adenoma, NOS										X													X			3
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Carcinoma, NOS				X																						1
Leiomyoma										X																1
Endometrial stromal polyp										X									X							4
Endometrial stromal sarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Granulosa cell carcinoma																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Granulosa cell carcinoma, metastatic																										1
Glioma, NOS																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	M	N	N	N	*48
Histiocytic sarcoma																										1
Leukemia, mononuclear cell		X	X													X	X								X	16

* Animals necropsied

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 400 ppm

ANIMAL NUMBER	0044	0040	0024	0006	0015	0025	0007	0027	0042	0043	0021	0037	0003	0004	0011	0028	0050	0017	0020	0036	0049	0022	0038	0041	0012
WEEKS ON STUDY	0499	0555	0699	0777	0788	0781	0881	0883	0883	0886	0889	0990	0994	0994	0994	0994	0994	0995	0997	0997	0997	0999	0999	0999	1000
INTEGUMENTARY SYSTEM																									
Skin	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Alveolar/bronchiolar adenoma																									
Trachea	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	A	+
Nasal cavity	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	A	+
Spleen	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	A	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Thymus	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	A	–	
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell carcinoma															X										
Salivary gland	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Liver	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Bile duct	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Pancreas	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Papilloma, NOS																					X				
Small intestine	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	A	+
Large intestine	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	A	+
Carcinoma, NOS																									
URINARY SYSTEM																									
Kidney	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Urinary bladder	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
ENDOCRINE SYSTEM																									
Pituitary	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Carcinoma, NOS				X																					
Adenoma, NOS		X			X		X			X	X		X		X				X	X	X	X	X	X	X
Adrenal	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Cortical adenoma												X													
Pheochromocytoma																	X								
Pheochromocytoma, malignant																									
Thyroid	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Follicular cell adenoma																									
C-cell adenoma														X											
Parathyroid	–	–	+	+	+	–	+	–	+	+	+	+	–	+	–	+	+	–	+	+	+	+	+	A	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Fibroadenoma								X															X		
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
Uterus	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal polyp							X										X			X				
Ovary	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, metastatic				X																					
Glioma, NOS						X																			
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS									X																
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell			X		X						X			X	X	X		X	X	X					X

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 400 ppm (Continued)

ANIMAL NUMBER	019	029	001	002	005	008	009	010	013	014	016	018	023	026	030	031	032	033	034	035	039	045	046	047	048	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	102	104	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	
INTEGUMENTARY SYSTEM																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma					X																					1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma					X				X				X													3
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	46
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph nodes	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	49
Thymus	–	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Squamous cell carcinoma																										1
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Papilloma, NOS																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Carcinoma, NOS							X																			1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, NOS																										1
Adenoma, NOS	X	X				X				X	X	X	X	X	X		X			X	X			X	X	28
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Cortical adenoma																										1
Pheochromocytoma																	X	X				X				4
Pheochromocytoma, malignant								X																		1
Thyroid	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Follicular cell adenoma										X																1
C-cell adenoma								X									X				X				X	5
Parathyroid	–	–	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	37
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS													X													1
Fibroadenoma		X												X		X								X		6
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS								X																	X	2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endometrial stromal polyp																		X								4
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS, metastatic																										1
Glioma, NOS						X	X																			3
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell	X						X					X	X										X			15

* *Animals necropsied*

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Subcutaneous Tissue: Fibroma				
Overall Rates (a)	0/50 (0%)	3/50 (6%)	0/48 (0%)	1/50 (2%)
Adjusted Rates (b)	0.0%	7.6%	0.0%	4.3%
Terminal Rates (c)	0/19 (0%)	1/29 (3%)	0/24 (0%)	1/23 (4%)
Week of First Observation		66		106
Life Table Tests (d)	P=0.629N	P=0.163	(e)	P=0.538
Incidental Tumor Tests (d)	P=0.622	P=0.064	(e)	P=0.538
Cochran-Armitage Trend Test (d)	P=0.632			
Fisher Exact Test (d)		P=0.121	(e)	P=0.500
Lung: Alveolar/Bronchiolar Adenoma				
Overall Rates (a)	0/50 (0%)	0/48 (0%)	0/47 (0%)	3/49 (6%)
Adjusted Rates (b)	0.0%	0.0%	0.0%	13.0%
Terminal Rates (c)	0/19 (0%)	0/29 (0%)	0/24 (0%)	3/23 (13%)
Week of First Observation				106
Life Table Tests (d)	P=0.010	(e)	(e)	P=0.154
Incidental Tumor Tests (d)	P=0.010	(e)	(e)	P=0.154
Cochran-Armitage Trend Test (d)	P=0.012			
Fisher Exact Test (d)		(e)	(e)	P=0.117
Hematopoietic System: Mononuclear Cell Leukemia				
Overall Rates (a)	23/50 (46%)	13/50 (26%)	16/48 (33%)	15/50 (30%)
Adjusted Rates (b)	59.6%	33.8%	41.6%	40.4%
Terminal Rates (c)	6/19 (32%)	6/29 (21%)	5/24 (21%)	4/23 (17%)
Week of First Observation	72	66	57	69
Life Table Tests (d)	P=0.183N	P=0.008N	P=0.111N	P=0.091N
Incidental Tumor Tests (d)	P=0.173N	P=0.084N	P=0.224N	P=0.125N
Cochran-Armitage Trend Test (d)	P=0.131N			
Fisher Exact Test (d)		P=0.030N	P=0.141N	P=0.075N
Liver: Neoplastic Nodule				
Overall Rates (a)	1/50 (2%)	0/49 (0%)	3/47 (6%)	0/48 (0%)
Adjusted Rates (b)	5.3%	0.0%	11.9%	0.0%
Terminal Rates (c)	1/19 (5%)	0/29 (0%)	2/24 (8%)	0/23 (0%)
Week of First Observation	106		105	
Life Table Tests (d)	P=0.493N	P=0.416N	P=0.386	P=0.462N
Incidental Tumor Tests (d)	P=0.499N	P=0.416N	P=0.315	P=0.462N
Cochran-Armitage Trend Test (d)	P=0.513N			
Fisher Exact Test (d)		P=0.505N	P=0.285	P=0.510N
Liver: Neoplastic Nodule or Hepatocellular Carcinoma				
Overall Rates (a)	1/50 (2%)	0/49 (0%)	4/47 (9%)	0/48 (0%)
Adjusted Rates (b)	5.3%	0.0%	14.5%	0.0%
Terminal Rates (c)	1/19 (5%)	0/29 (0%)	2/24 (8%)	0/23 (0%)
Week of First Observation	106		98	
Life Table Tests (d)	P=0.535N	P=0.416N	P=0.242	P=0.462N
Incidental Tumor Tests (d)	P=0.539N	P=0.416N	P=0.151	P=0.462N
Cochran-Armitage Trend Test (d)	P=0.545N			
Fisher Exact Test (d)		P=0.505N	P=0.162	P=0.510N
Anterior Pituitary Gland: Adenoma				
Overall Rates (a)	26/50 (52%)	30/49 (61%)	28/48 (58%)	28/48 (58%)
Adjusted Rates (b)	70.8%	75.9%	70.5%	70.9%
Terminal Rates (c)	10/19 (53%)	20/29 (69%)	13/24 (54%)	12/23 (52%)
Week of First Observation	55	83	59	55
Life Table Tests (d)	P=0.447	P=0.280N	P=0.515N	P=0.555
Incidental Tumor Tests (d)	P=0.368	P=0.297	P=0.270	P=0.309
Cochran-Armitage Trend Test (d)	P=0.368			
Fisher Exact Test (d)		P=0.235	P=0.335	P=0.335

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Anterior Pituitary Gland: Carcinoma				
Overall Rates (a)	1/50 (2%)	3/49 (6%)	0/48 (0%)	1/48 (2%)
Adjusted Rates (b)	3.6%	8.2%	0.0%	2.1%
Terminal Rates (c)	0/19 (0%)	0/29 (0%)	0/24 (0%)	0/23 (0%)
Week of First Observation	101	95		77
Life Table Tests (d)	P=0.446N	P=0.403	P=0.493N	P=0.750
Incidental Tumor Tests (d)	P=0.468N	P=0.226	P=0.615N	P=0.680
Cochran-Armitage Trend Test (d)	P=0.422N			
Fisher Exact Test (d)		P=0.301	P=0.510N	P=0.742
Anterior Pituitary Gland: Adenoma or Carcinoma				
Overall Rates (a)	27/50 (54%)	33/49 (67%)	28/48 (58%)	29/48 (60%)
Adjusted Rates (b)	71.9%	77.9%	70.5%	71.5%
Terminal Rates (c)	10/19 (53%)	20/29 (69%)	13/24 (54%)	12/23 (52%)
Week of First Observation	55	83	59	55
Life Table Tests (d)	P=0.492	P=0.374N	P=0.453N	P=0.551
Incidental Tumor Tests (d)	P=0.415	P=0.148	P=0.319	P=0.283
Cochran-Armitage Trend Test (d)	P=0.429			
Fisher Exact Test (d)		P=0.124	P=0.410	P=0.331
Adrenal Medulla: Pheochromocytoma				
Overall Rates (a)	1/50 (2%)	2/49 (4%)	3/47 (6%)	4/48 (8%)
Adjusted Rates (b)	2.6%	6.5%	8.3%	15.3%
Terminal Rates (c)	0/19 (0%)	1/29 (3%)	0/24 (0%)	3/23 (13%)
Week of First Observation	88	104	92	94
Life Table Tests (d)	P=0.112	P=0.586	P=0.323	P=0.227
Incidental Tumor Tests (d)	P=0.115	P=0.503	P=0.243	P=0.209
Cochran-Armitage Trend Test (d)	P=0.105			
Fisher Exact Test (d)		P=0.492	P=0.285	P=0.168
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma				
Overall Rates (a)	2/50 (4%)	2/49 (4%)	4/47 (9%)	5/48 (10%)
Adjusted Rates (b)	6.4%	6.5%	12.1%	19.6%
Terminal Rates (c)	0/19 (0%)	1/29 (3%)	1/24 (4%)	4/23 (17%)
Week of First Observation	88	104	92	94
Life Table Tests (d)	P=0.110	P=0.604N	P=0.375	P=0.269
Incidental Tumor Tests (d)	P=0.113	P=0.679	P=0.263	P=0.248
Cochran-Armitage Trend Test (d)	P=0.102			
Fisher Exact Test (d)		P=0.684	P=0.310	P=0.201
Thyroid Gland: C-Cell Adenoma				
Overall Rates (a)	5/48 (10%)	3/48 (6%)	1/47 (2%)	5/46 (11%)
Adjusted Rates (b)	20.5%	10.3%	4.2%	19.6%
Terminal Rates (c)	2/18 (11%)	3/29 (10%)	1/24 (4%)	4/23 (17%)
Week of First Observation	81	106	106	94
Life Table Tests (d)	P=0.567	P=0.174N	P=0.070N	P=0.529N
Incidental Tumor Tests (d)	P=0.556	P=0.236N	P=0.108N	P=0.564N
Cochran-Armitage Trend Test (d)	P=0.511			
Fisher Exact Test (d)		P=0.357N	P=0.107N	P=0.602
Thyroid Gland: C-Cell Adenoma or Carcinoma				
Overall Rates (a)	7/48 (15%)	4/48 (8%)	2/47 (4%)	5/46 (11%)
Adjusted Rates (b)	26.2%	12.8%	8.3%	19.6%
Terminal Rates (c)	2/18 (11%)	3/29 (10%)	2/24 (8%)	4/23 (17%)
Week of First Observation	81	101	106	94
Life Table Tests (d)	P=0.317N	P=0.111N	P=0.052N	P=0.292N
Incidental Tumor Tests (d)	P=0.328N	P=0.192N	P=0.089N	P=0.328N
Cochran-Armitage Trend Test (d)	P=0.365N			
Fisher Exact Test (d)		P=0.262N	P=0.084N	P=0.410N

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Mammary Gland: Fibroadenoma				
Overall Rates (a)	16/50 (32%)	14/50 (28%)	8/48 (17%)	6/50 (12%)
Adjusted Rates (b)	54.1%	44.1%	27.5%	21.4%
Terminal Rates (c)	8/19 (42%)	12/29 (41%)	5/24 (21%)	3/23 (13%)
Week of First Observation	72	86	86	83
Life Table Tests (d)	P=0.005N	P=0.103N	P=0.029N	P=0.012N
Incidental Tumor Tests (d)	P=0.004N	P=0.220N	P=0.042N	P=0.013N
Cochran-Armitage Trend Test (d)	P=0.006N			
Fisher Exact Test (d)		P=0.414N	P=0.062N	P=0.014N
Mammary Gland: Adenocarcinoma				
Overall Rates (a)	4/50 (8%)	2/50 (4%)	1/48 (2%)	1/50 (2%)
Adjusted Rates (b)	12.4%	6.9%	2.5%	4.3%
Terminal Rates (c)	1/19 (5%)	2/29 (7%)	0/24 (0%)	1/23 (4%)
Week of First Observation	78	106	85	106
Life Table Tests (d)	P=0.105N	P=0.223N	P=0.173N	P=0.158N
Incidental Tumor Tests (d)	P=0.113N	P=0.351N	P=0.187N	P=0.198N
Cochran-Armitage Trend Test (d)	P=0.113N			
Fisher Exact Test (d)		P=0.339N	P=0.194N	P=0.181N
Mammary Gland: Adenoma or Fibroadenoma				
Overall Rates (a)	17/50 (34%)	14/50 (28%)	8/48 (17%)	6/50 (12%)
Adjusted Rates (b)	55.6%	44.1%	27.5%	21.4%
Terminal Rates (c)	8/19 (42%)	12/29 (41%)	5/24 (21%)	3/23 (13%)
Week of First Observation	72	86	86	83
Life Table Tests (d)	P=0.003N	P=0.071N	P=0.020N	P=0.008N
Incidental Tumor Tests (d)	P=0.003N	P=0.168N	P=0.031N	P=0.008N
Cochran-Armitage Trend Test (d)	P=0.003N			
Fisher Exact Test (d)		P=0.333N	P=0.041N	P=0.008N
Mammary Gland: Adenocarcinoma or Adenosquamous Carcinoma				
Overall Rates (a)	4/50 (8%)	2/50 (4%)	2/48 (4%)	1/50 (2%)
Adjusted Rates (b)	12.4%	6.9%	4.7%	4.3%
Terminal Rates (c)	1/19 (5%)	2/29 (7%)	0/24 (0%)	1/23 (4%)
Week of First Observation	78	106	66	106
Life Table Tests (d)	P=0.133N	P=0.223N	P=0.332N	P=0.158N
Incidental Tumor Tests (d)	P=0.148N	P=0.351N	P=0.356N	P=0.198N
Cochran-Armitage Trend Test (d)	P=0.139N			
Fisher Exact Test (d)		P=0.339N	P=0.359N	P=0.181N
Mammary Gland: Adenoma, Fibroadenoma, Adenocarcinoma, or Adenosquamous Carcinoma				
Overall Rates (a)	18/50 (36%)	15/50 (30%)	10/48 (21%)	7/50 (14%)
Adjusted Rates (b)	56.6%	47.3%	30.9%	25.3%
Terminal Rates (c)	8/19 (42%)	13/29 (45%)	5/24 (21%)	4/23 (17%)
Week of First Observation	72	86	66	83
Life Table Tests (d)	P=0.005N	P=0.068N	P=0.044N	P=0.009N
Incidental Tumor Tests (d)	P=0.004N	P=0.197N	P=0.060N	P=0.011N
Cochran-Armitage Trend Test (d)	P=0.005N			
Fisher Exact Test (d)		P=0.335N	P=0.075N	P=0.010N
Clitoral Gland: Adenoma				
Overall Rates (a)	1/50 (2%)	6/50 (12%)	3/48 (6%)	2/50 (4%)
Adjusted Rates (b)	5.3%	18.2%	10.8%	8.7%
Terminal Rates (c)	1/19 (5%)	4/29 (14%)	2/24 (8%)	2/23 (9%)
Week of irst Observation	106	94	92	106
Life Table Tests (d)	P=0.486N	P=0.138	P=0.375	P=0.567
Incidental Tumor Tests (d)	P=0.483N	P=0.103	P=0.384	P=0.567
Cochran-Armitage Trend Test (d)	P=0.502N			
Fisher Exact Test (d)		P=0.056	P=0.293	P=0.500

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Uterus: Endometrial Stromal Polyp				
Overall Rates (a)	5/50 (10%)	6/50 (12%)	4/48 (8%)	4/49 (8%)
Adjusted Rates (b)	13.4%	18.4%	14.2%	11.8%
Terminal Rates (c)	0/19 (0%)	4/29 (14%)	2/24 (8%)	1/23 (4%)
Week of First Observation	55	86	92	81
Life Table Tests (d)	P=0.355N	P=0.569N	P=0.450N	P=0.468N
Incidental Tumor Tests (d)	P=0.376N	P=0.403	P=0.579N	P=0.584N
Cochran-Armitage Trend Test (d)	P=0.373N			
Fisher Exact Test (d)		P=0.500	P=0.526N	P=0.513N
Brain: Glioma				
Overall Rates (a)	0/50 (0%)	1/50 (2%)	1/48 (2%)	3/50 (6%)
Adjusted Rates (b)	0.0%	2.0%	3.2%	10.7%
Terminal Rates (c)	0/19 (0%)	0/29 (0%)	0/24 (0%)	2/23 (9%)
Week of First Observation		62	99	78
Life Table Tests (d)	P=0.052	P=0.504	P=0.507	P=0.148
Incidental Tumor Tests (d)	P=0.045	P=0.205	P=0.385	P=0.107
Cochran-Armitage Trend Test (d)	P=0.054			
Fisher Exact Test (d)		P=0.500	P=0.490	P=0.121
All Sites: Benign Tumors				
Overall Rates (a)	42/50 (84%)	41/50 (82%)	35/48 (73%)	38/50 (76%)
Adjusted Rates (b)	95.2%	95.2%	82.7%	88.1%
Terminal Rates (c)	17/19 (89%)	27/29 (93%)	17/24 (71%)	18/23 (78%)
Week of First Observation	55	66	59	55
Life Table Tests (d)	P=0.265N	P=0.025N	P=0.074N	P=0.185N
Inxcidental Tumor Tests (d)	P=0.178N	P=0.308N	P=0.145N	P=0.227N
Cochran-Armitage Trend Test (d)	P=0.157N			
Fisher Exact Test (d)		P=0.500N	P=0.138N	P=0.227N
All Sites: Malignant Tumors				
Overall Rates (a)	29/50 (58%)	20/50 (40%)	23/48 (48%)	20/50 (40%)
Adjusted Rates (b)	68.6%	47.3%	54.8%	50.1%
Terminal Rates (c)	7/19 (37%)	8/29 (28%)	7/24 (29%)	6/23 (26%)
Week of First Observation	72	62	57	69
Life Table Tests (d)	P=0.172N	P=0.015N	P=0.163N	P=0.082N
Incidental Tumor Tests (d)	P=0.132N	P=0.194N	P=0.391N	P=0.113N
Cochran-Armitage Trend Test (d)	P=0.093N			
Fisher Exact Test (d)		P=0.055N	P=0.213N	P=0.055N
All Sites: All Tumors				
Overall Rates (a)	49/50 (98%)	46/50 (92%)	40/48 (83%)	44/50 (88%)
Adjusted Rates (b)	98.0%	95.8%	86.6%	91.5%
Terminal Rates (c)	18/19 (95%)	27/29 (93%)	18/24 (75%)	19/23 (83%)
Week of First Observation	55	62	57	55
Life Table Tests (d)	P=0.266N	P=0.013N	P=0.052N	P=0.162N
Incidental Tumor Tests (d)	P=0.105N	P=0.248N	P=0.033N	P=0.137N
Cochran-Armitage Trend Test (d)	P=0.056N			
Fisher Exact Test (d)		P=0.182N	P=0.013N	P=0.056N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor 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 that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the dosed and control groups.

TABLE B4a. HISTORICAL INCIDENCE OF BRAIN GLIAL CELL TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories	
Propylene oxide	0/49
Methyl methacrylate	0/50
Propylene	0/48
1,2-Epoxybutane	0/50
Dichloromethane	0/50
Tetrachloroethylene	(b) 1/50
TOTAL	1/297 (0.3%)
SD (c)	0.82%
Range (d)	
High	1/50
Low	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	(e) 23/1,969 (1.2%)
SD (c)	1.58%
Range (d)	
High	3/50
Low	0/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Glioma, NOS
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.
(e) Includes 18 astrocytomas, 3 oligodendrogliomas, and 2 gliomas, NOS

TABLE B4b. HISTORICAL INCIDENCE OF ALVEOLAR/BRONCHIOLAR TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	0/48	0/48	0/48
Methyl methacrylate	0/50	0/50	0/50
Propylene	0/49	0/49	0/49
1,2-Epoxybutane	1/50	1/50	2/50
Dichloromethane	1/50	0/50	1/50
Tetrachloroethylene	0/50	1/50	1/50
TOTAL	2/297 (0.7%)	2/297 (0.7%)	4/297 (1.3%)
SD (b)	1.03%	1.03%	1.63%
Range (c)			
High	1/50	1/50	2/50
Low	0/50	0/50	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	16/1,974 (0.8%)	6/1,974 (0.3%)	22/1,974 (1.1%)
SD (b)	1.19%	0.76%	1.30%
Range (c)			
High	2/50	1/39	2/50
Low	0/50	0/50	0/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE B4c. HISTORICAL INCIDENCE OF MAMMARY GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Fibroadenoma	Adenocarcinoma	Fibroadenoma or Adenocarcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	7/50	1/50	8/50
Methyl methacrylate	10/50	0/50	10/50
Propylene	9/49	0/49	9/49
1,2-Epoxybutane	(b) 16/50	1/50	17/50
Dichloromethane	5/50	1/50	6/50
Tetrachloroethylene	7/50	2/50	8/50
TOTAL	54/299 (18.1%)	5/299 (1.7%)	58/299 (19.4%)
SD (c)	7.70%	1.51%	7.65%
Range (d)			
High	16/50	2/50	17/50
Low	5/50	0/50	6/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	(e) 589/1,983 (29.7%)	(f) 52/1,983 (2.6%)	(e,f) 622/1,983 (31.4%)
SD (c)	10.19%	2.09%	10.00%
Range (d)			
High	24/49	4/50	25/50
Low	5/50	0/50	6/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Includes one adenoma, NOS
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.
(e) Includes 14 adenomas, NOS, 2 cystadenomas, NOS, and 2 papillary cystadenomas, NOS
(f) Includes three papillary adenocarcinomas and two papillary cystadenocarcinomas, NOS

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals missing			1	
Animals necropsied	50	50	48	50
Animals examined histopathologically	50	50	48	50
INTEGUMENTARY SYSTEM				
*Skin	(50)	(50)	(48)	(50)
Epidermal inclusion cyst		1 (2%)		
Inflammation, suppurative		1 (2%)		2 (4%)
Acanthosis				1 (2%)
RESPIRATORY SYSTEM				
#Nose	(49)	(47)	(47)	(48)
Foreign body, NOS	1 (2%)	3 (6%)	3 (6%)	4 (8%)
Inflammation, suppurative	18 (37%)	13 (28%)	22 (47%)	25 (52%)
Hyperplasia, epithelial	7 (14%)	9 (19%)	9 (19%)	15 (31%)
Metaplasia, squamous	2 (4%)	2 (4%)	2 (4%)	9 (19%)
#Nasal gland	(49)	(47)	(47)	(48)
Hyperplasia, NOS		1 (2%)		
*Larynx	(50)	(50)	(48)	(50)
Foreign body, NOS	2 (4%)	2 (4%)	3 (6%)	2 (4%)
Inflammation, suppurative	12 (24%)	17 (34%)	22 (46%)	20 (40%)
Inflammation, chronic	1 (2%)		1 (2%)	
Necrosis, NOS			1 (2%)	1 (2%)
Hyperplasia, epithelial	1 (2%)	2 (4%)	2 (4%)	3 (6%)
Acanthosis	2 (4%)	5 (10%)	4 (8%)	4 (8%)
#Trachea	(49)	(48)	(47)	(46)
Inflammation, suppurative		1 (2%)		2 (4%)
Necrosis, NOS				1 (2%)
Hyperplasia, epithelial		1 (2%)		
#Lung/bronchus	(50)	(48)	(47)	(49)
Hyperplasia, epithelial	2 (4%)			
#Lung/bronchiole	(50)	(48)	(47)	(49)
Inflammation, suppurative		1 (2%)		
#Lung	(50)	(48)	(47)	(49)
Foreign body, NOS		1 (2%)		
Hemorrhage	2 (4%)	1 (2%)	2 (4%)	3 (6%)
Fibrosis				1 (2%)
Hyperplasia, alveolar epithelium	5 (10%)	4 (8%)	5 (11%)	10 (20%)
#Lung/alveoli	(50)	(48)	(47)	(49)
Edema, NOS		1 (2%)	1 (2%)	
Inflammation, suppurative	8 (16%)	10 (21%)	9 (19%)	9 (18%)
Histiocytosis	15 (30%)	25 (52%)	20 (43%)	24 (49%)
HEMATOPOIETIC SYSTEM				
#Brain/meninges	(50)	(50)	(48)	(50)
Hyperplasia, granulocytic				1 (2%)
#Bone marrow	(50)	(48)	(47)	(48)
Atrophy, NOS	3 (6%)			1 (2%)
#Spleen	(50)	(49)	(47)	(48)
Hemorrhage	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Fibrosis	3 (6%)	4 (8%)	3 (6%)	2 (4%)
Necrosis, NOS			1 (2%)	
Atrophy, NOS	1 (2%)			
Hyperplasia, hematopoietic			1 (2%)	
#Mandibular lymph node	(47)	(49)	(47)	(49)
Inflammation, suppurative		1 (2%)		
Hyperplasia, lymphoid	2 (4%)			

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
HEMATOPOEITIC SYSTEM (Continued)				
#Bronchial lymph node	(47)	(49)	(47)	(49)
Hemorrhage		1 (2%)	1 (2%)	1 (2%)
Granuloma, NOS	1 (2%)			
CIRCULATORY SYSTEM				
*Multiple organs	(50)	(50)	(48)	(50)
Periarteritis			1 (2%)	1 (2%)
#Heart	(50)	(50)	(47)	(50)
Mineralization		1 (2%)		
#Heart/atrium	(50)	(50)	(47)	(50)
Thrombosis, NOS	1 (2%)		1 (2%)	1 (2%)
#Myocardium	(50)	(50)	(47)	(50)
Degeneration, NOS	13 (26%)	12 (24%)	11 (23%)	6 (12%)
*Mesentery	(50)	(50)	(48)	(50)
Periarteritis			1 (2%)	
DIGESTIVE SYSTEM				
*Palate	(50)	(50)	(48)	(50)
Acanthosis			1 (2%)	
#Salivary gland	(49)	(47)	(45)	(48)
Dilatation/ducts	3 (6%)	3 (6%)	9 (20%)	12 (25%)
Inflammation, suppurative	2 (4%)	3 (6%)	9 (20%)	14 (29%)
Inflammation, chronic			1 (2%)	3 (6%)
Hyperplasia, NOS	1 (2%)	1 (2%)	2 (4%)	1 (2%)
#Liver	(50)	(49)	(47)	(48)
Congenital malformation, NOS		3 (6%)	5 (11%)	2 (4%)
Granuloma, NOS	7 (14%)	12 (24%)	9 (19%)	13 (27%)
Necrosis, NOS	7 (14%)	8 (16%)	9 (19%)	5 (10%)
Metamorphosis, fatty	7 (14%)	8 (16%)	5 (11%)	9 (19%)
Basophilic cyto change	23 (46%)	17 (35%)	17 (36%)	23 (48%)
Clear cell change	11 (22%)	11 (22%)	12 (26%)	19 (40%)
Hyperplasia, NOS	5 (10%)	2 (4%)	5 (11%)	6 (13%)
Angiectasis		1 (2%)	1 (2%)	1 (2%)
#Bile duct	(50)	(49)	(47)	(48)
Hyperplasia, NOS	14 (28%)	8 (16%)	15 (32%)	7 (15%)
#Pancreatic acinus	(50)	(49)	(47)	(48)
Atrophy, NOS	8 (16%)	2 (4%)	9 (19%)	2 (4%)
*Pharynx	(50)	(50)	(48)	(50)
Acanthosis	1 (2%)			
#Esophagus	(48)	(50)	(48)	(49)
Hyperkeratosis		1 (2%)		
#Glandular stomach	(48)	(49)	(47)	(47)
Mineralization		1 (2%)	1 (2%)	
Ulcer, NOS	1 (2%)			
Inflammation, suppurative	1 (2%)		1 (2%)	
Erosion	1 (2%)		1 (2%)	1 (2%)
Atrophy, NOS				1 (2%)
Hyperplasia, epithelial			1 (2%)	1 (2%)
#Forestomach	(48)	(49)	(47)	(47)
Ulcer, NOS	4 (8%)	1 (2%)	2 (4%)	2 (4%)
Inflammation, suppurative	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Hyperkeratosis	4 (8%)	4 (8%)	3 (6%)	10 (21%)
Acanthosis	9 (19%)	5 (10%)	5 (11%)	12 (26%)
#Ileum	(49)	(47)	(47)	(47)
Mineralization		1 (2%)		
Parasitism			1 (2%)	
#Colon	(49)	(46)	(47)	(47)
Parasitism	6 (12%)	4 (9%)	6 (13%)	3 (6%)

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
DIGESTIVE SYSTEM (Continued)				
*Rectum	(50)	(50)	(48)	(50)
Parasitism	1 (2%)	3 (6%)	2 (4%)	2 (4%)
URINARY SYSTEM				
#Kidney	(50)	(49)	(47)	(48)
Mineralization	10 (20%)	21 (43%)	20 (43%)	16 (33%)
Cyst, NOS			1 (2%)	1 (2%)
Nephropathy	48 (96%)	49 (100%)	45 (96%)	48 (100%)
#Kidney/interstitium	(50)	(49)	(47)	(48)
Metamorphosis, fatty			1 (2%)	
#Kidney/tubule	(50)	(49)	(47)	(48)
Necrosis, cortical				1 (2%)
#Kidney/pelvis	(50)	(49)	(47)	(48)
Inflammation, suppurative			1 (2%)	1 (2%)
Hyperplasia, epithelial		1 (2%)		2 (4%)
#Urinary bladder	(49)	(48)	(48)	(47)
Calculus, unknown gross or microscopic				1 (2%)
Calculus, gross observation only			1 (2%)	
Hyperplasia, epithelial			2 (4%)	2 (4%)
ENDOCRINE SYSTEM				
#Anterior pituitary	(50)	(49)	(48)	(48)
Hemorrhage			1 (2%)	
Necrosis, NOS			1 (2%)	
Hyperplasia, NOS	7 (14%)	8 (16%)	6 (13%)	7 (15%)
Angiectasis	9 (18%)	4 (8%)	8 (17%)	9 (19%)
#Adrenal cortex	(50)	(49)	(47)	(48)
Hemorrhage	1 (2%)			1 (2%)
Necrosis, NOS				1 (2%)
Clear cell change	10 (20%)	15 (31%)	13 (28%)	12 (25%)
Hyperplasia, NOS		3 (6%)	1 (2%)	2 (4%)
#Adrenal medulla	(50)	(49)	(47)	(48)
Necrosis, NOS				1 (2%)
Hyperplasia, NOS	4 (8%)	9 (18%)	6 (13%)	1 (2%)
Angiectasis				1 (2%)
#Thyroid	(48)	(48)	(47)	(46)
Hyperplasia, C-cell	8 (17%)	9 (19%)	8 (17%)	8 (17%)
#Parathyroid	(36)	(42)	(32)	(37)
Hyperplasia, NOS	1 (3%)	1 (2%)		2 (5%)
REPRODUCTIVE SYSTEM				
*Mammary gland	(50)	(50)	(48)	(50)
Inflammation, suppurative			1 (2%)	
*Mammary duct	(50)	(50)	(48)	(50)
Acanthosis			1 (2%)	
*Mammary acinus	(50)	(50)	(48)	(50)
Hyperplasia, NOS			1 (2%)	1 (2%)
*Clitoral gland	(50)	(50)	(48)	(50)
Cyst, NOS	3 (6%)	6 (12%)	5 (10%)	11 (22%)
Inflammation, suppurative		4 (8%)	4 (8%)	4 (8%)
Hyperplasia, NOS		6 (12%)	6 (13%)	3 (6%)
Hyperkeratosis				1 (2%)
Acanthosis	4 (8%)	6 (12%)	7 (15%)	8 (16%)
*Vagina	(50)	(50)	(48)	(50)
Inflammation, suppurative			1 (2%)	
Acanthosis	1 (2%)			

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
REPRODUCTIVE SYSTEM (Continued)				
#Uterus	(50)	(50)	(48)	(49)
Dilatation, NOS	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Hemorrhage			1 (2%)	
Inflammation, suppurative	1 (2%)	2 (4%)		1 (2%)
Hyperplasia, epithelial		1 (2%)		
#Cervix uteri	(50)	(50)	(48)	(49)
Hyperplasia, NOS		1 (2%)		
#Ovary	(50)	(49)	(48)	(48)
Cyst, NOS	1 (2%)	3 (6%)	3 (6%)	
Fibrosis		1 (2%)	2 (4%)	
Atrophy, NOS		3 (6%)	3 (6%)	1 (2%)
NERVOUS SYSTEM				
#Cerebral ventricle	(50)	(50)	(48)	(50)
Dilatation, NOS			1 (2%)	
#Brain	(50)	(50)	(48)	(50)
Epidermal inclusion cyst			1 (2%)	
Hemorrhage	3 (6%)	2 (4%)	6 (13%)	4 (8%)
Gliosis	1 (2%)			1 (2%)
Demyelinization				1 (2%)
Atrophy, NOS	16 (32%)	17 (34%)	19 (40%)	20 (40%)
*Spinal cord	(50)	(50)	(48)	(50)
Hemorrhage		1 (2%)		
*Olfactory sensory epithelium	(50)	(50)	(48)	(50)
Degeneration, NOS	1 (2%)	1 (2%)	1 (2%)	4 (8%)
Metaplasia, NOS		3 (6%)		5 (10%)
SPECIAL SENSE ORGANS				
*Eye	(50)	(50)	(48)	(50)
Atrophy, NOS				2 (4%)
*Eye/sclera	(50)	(50)	(48)	(50)
Mineralization		1 (2%)		1 (2%)
*Eye/cornea	(50)	(50)	(48)	(50)
Mineralization				1 (2%)
Inflammation, chronic				1 (2%)
*Eye/crystalline lens	(50)	(50)	(48)	(50)
Mineralization		1 (2%)	1 (2%)	2 (4%)
*Nasolacrimal duct	(50)	(50)	(48)	(50)
Inflammation, suppurative		1 (2%)		
MUSCULOSKELETAL SYSTEM				
*Skull	(50)	(50)	(48)	(50)
Congenital malformation, NOS		1 (2%)		
*Mandible	(50)	(50)	(48)	(50)
Hyperostosis		1 (2%)		
*Sternum	(50)	(50)	(48)	(50)
Hyperostosis		1 (2%)		
BODY CAVITIES				
*Mesentery	(50)	(50)	(48)	(50)
Necrosis, fat	2 (4%)	3 (6%)	5 (10%)	3 (6%)
ALL OTHER SYSTEMS				
None				

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
SPECIAL MORPHOLOGY SUMMARY				
Animal missexed/no necropsy			1	
Animal missing/no necropsy			1	
Auto/necropsy/histo performed		1		1

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site

APPENDIX C

SUMMARY OF LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals necropsied	50	50	50	50
Animals examined histopathologically	50	50	50	50
INTEGUMENTARY SYSTEM				
*Subcutaneous tissue	(50)	(50)	(50)	(50)
Fibrosarcoma	1 (2%)			
RESPIRATORY SYSTEM				
#Lung	(50)	(50)	(50)	(50)
Adenocarcinoma, NOS, metastatic	1 (2%)			
Hepatocellular carcinoma, metastatic	4 (8%)	2 (4%)	4 (8%)	2 (4%)
Alveolar/bronchiolar adenoma	5 (10%)	6 (12%)	8 (16%)	9 (18%)
Alveolar/bronchiolar carcinoma	2 (4%)		5 (10%)	6 (12%)
Mucinous adenocarcinoma	1 (2%)			
HEMATOPOIETIC SYSTEM				
*Multiple organs	(50)	(50)	(50)	(50)
Malignant lymphoma, NOS			1 (2%)	
Malignant lymphoma, lymphocytic type	2 (4%)			
Malignant lymphoma, histiocytic type	1 (2%)		1 (2%)	
Malignant lymphoma, mixed type	1 (2%)	3 (6%)	1 (2%)	
#Spleen	(49)	(49)	(49)	(50)
Malignant lymphoma, histiocytic type				1 (2%)
#Mesenteric lymph node	(47)	(45)	(50)	(46)
Malignant lymphoma, lymphocytic type	1 (2%)			
#Renal lymph node	(47)	(45)	(50)	(46)
Malignant lymphoma, mixed type			1 (2%)	
#Lung	(50)	(50)	(50)	(50)
Malignant lymphoma, lymphocytic type		1 (2%)		
CIRCULATORY SYSTEM				
*Multiple organs	(50)	(50)	(50)	(50)
Hemangiosarcoma, metastatic			1 (2%)	
#Mandibular lymph node	(47)	(45)	(50)	(46)
Hemangioma			1 (2%)	
#Liver	(50)	(50)	(50)	(50)
Hemangioma			1 (2%)	
Hemangiosarcoma		1 (2%)	3 (6%)	
*Mesentery	(50)	(50)	(50)	(50)
Hemangiosarcoma		1 (2%)		
#Urinary bladder	(50)	(49)	(50)	(50)
Hemangioma		1 (2%)		
#Testis	(50)	(50)	(50)	(50)
Hemangioma	1 (2%)			
#Periadrenal tissue	(50)	(49)	(48)	(50)
Hemangioma			1 (2%)	
DIGESTIVE SYSTEM				
#Liver	(50)	(50)	(50)	(50)
Hepatocellular adenoma	10 (20%)	8 (16%)	12 (24%)	11 (22%)
Hepatocellular carcinoma	11 (22%)	10 (20%)	13 (26%)	11 (22%)
*Rectum	(50)	(50)	(50)	(50)
Fibrosarcoma, metastatic	1 (2%)			

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
URINARY SYSTEM				
#Kidney	(50)	(50)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic			1 (2%)	1 (2%)
Tubular cell adenocarcinoma		1 (2%)		
ENDOCRINE SYSTEM				
#Pituitary intermedia	(49)	(49)	(48)	(47)
Adenoma, NOS	1 (2%)	1 (2%)		
#Adrenal	(50)	(49)	(48)	(50)
Pheochromocytoma, malignant		1 (2%)		
#Adrenal/capsule	(50)	(49)	(48)	(50)
Adenoma, NOS			1 (2%)	
REPRODUCTIVE SYSTEM				
*Preputial gland	(50)	(50)	(50)	(50)
Squamous cell carcinoma				1 (2%)
NERVOUS SYSTEM				
None				
SPECIAL SENSE ORGANS				
*Harderian gland	(50)	(50)	(50)	(50)
Adenoma, NOS	3 (6%)	4 (8%)		
Adenocarcinoma, NOS	2 (4%)			
MUSCULOSKELETAL SYSTEM				
*Rib	(50)	(50)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic				1 (2%)
BODY CAVITIES				
*Mediastinum	(50)	(50)	(50)	(50)
Alveolar/bronchiolar carcinoma, metastatic				1 (2%)
ALL OTHER SYSTEMS				
None				
ANIMAL DISPOSITION SUMMARY				
Animals initially in study	50	50	50	50
Natural death	9	10	14	8
Moribund sacrifice	6	3	6	8
Terminal sacrifice	35	37	30	34

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
TUMOR SUMMARY				
Total animals with primary tumors**	30	30	34	33
Total primary tumors	42	38	49	39
Total animals with benign tumors	18	17	22	19
Total benign tumors	20	20	24	20
Total animals with malignant tumors	20	18	23	16
Total malignant tumors	22	18	25	19
Total animals with secondary tumors##	6	2	5	3
Total secondary tumors	6	2	6	5

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: CHAMBER CONTROL

ANIMAL NUMBER	0311	0110	0112	0117	0422	0119	0445	0005	0022	0335	0443	0001	0221	0027	0116	0003	0004	0006	0008	0009	0111	0113	0114	0115	0118
WEEKS ON STUDY	0356	0559	0662	0662	0771	0774	0775	0884	0887	0887	0991	0995	1001	1002	1004	1005	1005	1005	1005	1005	1005	1005	1005	1005	1005
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma													X												
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic																						X			
Hepatocellular carcinoma, metastatic			X				X				X														
Alveolar/bronchiolar adenoma			X			X																			
Alveolar/bronchiolar carcinoma												X													
Mucinous adenocarcinoma																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malignant lymphoma, lymphocytic type																			X						
Thymus	−	−	−	−	+	−	−	−	+	+	+	+	+	−	+	−	+	−	+	+	+	−	−	−	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma								X	X										X			X			
Hepatocellular carcinoma			X		X	X	X			X	X			X									X		X
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	N	+	+	+	N	+	N	+	+	N	+	+	+	+	+	+	+	N	+	+	N	N	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	−	−	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Rectum	+	N	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+
Fibrosarcoma, metastatic													X												
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	+	+	+	+	+	+	+	−	−	+	−	−	−	−	+	+	+	+	+	+	−	−	+	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																	X								X
Adenocarcinoma, NOS																						X			
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, lymphocytic type																									
Malignant lymphoma, histiocytic type																				X					
Malignant lymphoma, mixed type																									

+: Tissue examined microscopically
−: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	020	021	023	024	025	026	027	028	029	030	032	033	034	036	037	038	039	040	041	044	046	047	048	049	050	TOTAL:
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS, metastatic																										1
Hepatocellular carcinoma, metastatic																		X								4
Alveolar/bronchiolar adenoma		X																X					X			5
Alveolar/bronchiolar carcinoma	X																									2
Mucinous adenocarcinoma																		X								1
Trachea	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Malignant lymphoma, lymphocytic type																										1
Thymus	+	+	–	+	+	+	+	–	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	33
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma					X					X						X	X			X					X	10
Hepatocellular carcinoma	X																	X								11
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	N	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Rectum	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma, metastatic																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS						X																				1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid	+	+	+	–	+	–	+	–	–	+	+	+	+	+	+	+	–	–	+	+	+	–	+	+	+	34
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma					X																					1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS						X																				3
Adenocarcinoma, NOS																	X									2
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, lymphocytic type																						X		X		2
Malignant lymphoma, histiocytic type																										1
Malignant lymphoma, mixed type																				X						1

* Animals necropsied

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 100 ppm

ANIMAL NUMBER	023	037	118	009	008	001	045	030	015	013	039	117	034	002	003	004	005	006	007	010	011	012	014	016	019
WEEKS ON STUDY	059	059	061	063	080	082	085	087	092	093	098	101	102	105	105	105	105	105	105	105	105	105	105	105	105
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic				X				X																	
Alveolar/bronchiolar adenoma						X																	X		
Malignant lymphoma, lymphocytic type														X											
Trachea	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	−	−	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	−	−	−	+	+	+	+	−	+	+	+	−	−	−	+	+	−	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																	X	X		X					X
Hepatocellular carcinoma				X	X	X	X	X	X				X								X				
Hemangiosarcoma															X										
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	N	N	+	+	+	N	N	N	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenocarcinoma																									
Urinary bladder	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS												X													
Adrenal	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, malignant																									
Thyroid	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	+	+	+	−	−	−	−	−	+	−	+	+	+	−	−	−	−	+	−	+	+	+	−	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																	X					X			
BODY CAVITIES																									
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hemangiosarcoma																X									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N
Malignant lymphoma, mixed type																		X							

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 100 ppm (Continued)

ANIMAL NUMBER	020	021	022	024	025	026	027	028	029	031	032	033	035	036	038	040	041	042	043	044	046	047	048	049	050	TOTAL:
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic																										2
Alveolar/bronchiolar adenoma						X	X		X											X						6
Malignant lymphoma, lymphocytic type																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma								X		X								X			X					8
Hepatocellular carcinoma			X						X																	10
Hemangiosarcoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tubular cell adenocarcinoma											X															1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangioma		X																								1
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	49
Adenoma, NOS																										1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	49
Pheochromocytoma, malignant																							X			1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid	+	−	−	−	−	+	+	−	+	+	−	+	+	+	+	+	+	+	+	−	−	−	−	+	+	26
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS		X				X																				4
BODY CAVITIES																										
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Hemangiosarcoma																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, mixed type																				X						3

* Animals necropsied

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 200 ppm

ANIMAL NUMBER	004	036	029	050	031	018	007	045	046	032	014	013	025	024	030	001	047	019	017	022	002	003	005	006	008
WEEKS ON STUDY	001	062	066	066	073	077	083	084	084	085	087	092	092	097	099	100	100	102	103	104	105	105	105	105	105
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic							X	X	X											X					
Alveolar/bronchiolar adenoma															X	X									
Alveolar/bronchiolar carcinoma							X																		
Trachea	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																					X				
Malignant lymphoma, mixed type																									
Thymus	+	+	−	+	+	−	−	−	−	−	+	−	−	−	+	−	−	−	+	+	+	+	+	−	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma					X				X		X							X			X	X			
Hepatocellular carcinoma				X			X	X	X						X	X	X	X		X		X			
Hemangioma																									
Hemangiosarcoma											X														
Bile duct	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	+	N	+	+	+	N	N	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+
Stomach	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic							X																		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	−	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+
Adenoma, NOS														X											
Hemangioma																				X					
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	+	−	−	−	−	+	−	−	+	+	+	+	+	+	−	−	+	−	+	+	+	−	+	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hemangiosarcoma, metastatic											X														
Malignant lymphoma, NOS										X															
Malignant lymphoma, histiocytic type						X																			
Malignant lymphoma, mixed type																								X	

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 200 ppm (Continued)

ANIMAL NUMBER	009	010	011	012	015	016	020	021	023	026	027	028	033	034	035	037	038	039	040	041	042	043	044	048	049	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic																										4
Alveolar/bronchiolar adenoma						X			X				X		X		X			X						8
Alveolar/bronchiolar carcinoma									X	X	X											X				5
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Malignant lymphoma, mixed type			X																							1
Thymus	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	36
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma			X				X	X		X									X				X			12
Hepatocellular carcinoma			X				X											X								13
Hemangioma																							X			1
Hemangiosarcoma																								X	X	3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metast																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma, NOS																										1
Hemangioma																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid	+	+	+	+	+	+	+	–	–	+	–	–	–	–	+	–	–	+	–	–	+	+	–	–	+	26
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Hemangiosarcoma, metastatic																										1
Malignant lymphoma, NOS																										1
Malignant lymphoma, histiocytic type																										1
Malignant lymphoma, mixed type																										1

* Animals necropsied

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 400 ppm

ANIMAL NUMBER	012	026	019	050	029	023	003	047	046	004	010	013	007	037	011	043	001	002	005	006	008	009	014	015	016
WEEKS ON STUDY	054	059	061	061	071	078	081	081	090	091	092	094	095	098	104	104	105	105	105	105	105	105	105	105	105
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic								X																	
Alveolar/bronchiolar adenoma						X					X											X			X
Alveolar/bronchiolar carcinoma									X					X					X						
Trachea	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malignant lymphoma, histiocytic type																									
Lymph nodes	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+
Thymus	–	–	+	–	+	+	–	–	+	–	–	–	+	–	+	–	+	+	+	–	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																				X			X		
Hepatocellular carcinoma					X			X		X	X	X		X	X			X						X	X
Bile duct	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	+	N	+	+	+	–	N	N	+	+	+	N	+	+	+	N	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	–	–	+	+	+	–	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic														X											
Urinary bladder	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	+	+	+	–	+	–	+	+	–	–	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell carcinoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Alveolar/bronchiolar carcinoma, metastatic														X											
BODY CAVITIES																									
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Alveolar/bronchiolar carcinoma, metastatic														X											

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 400 ppm (Continued)

ANIMAL NUMBER	017	018	020	021	022	024	025	027	028	030	031	032	033	034	035	036	038	039	040	041	042	044	045	048	049	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic							X																			2
Alveolar/bronchiolar adenoma		X			X								X										X		X	9
Alveolar/bronchiolar carcinoma			X				X												X							6
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	48
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Malignant lymphoma, histiocytic type										X																1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	46
Thymus	+	+	+	+	−	+	−	+	+	−	+	+	+	+	+	+	+	−	+	+	+	−	+	−	+	33
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma			X	X		X								X	X		X				X	X				11
Hepatocellular carcinoma							X		X															X		11
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	−	41
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metast																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	47
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid	−	+	+	+	−	−	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	38
REPRODUCTIVE SYSTEM																										
Mammary gland	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Squamous cell carcinoma										X																1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MUSCULOSKELETAL SYSTEM																										
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Alveolar/bronchiolar carcinoma, metast																										1
BODY CAVITIES																										
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Alveolar/bronchiolar carcinoma, metast																										1

* Animals necropsied

TABLE C3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Lung: Alveolar/Bronchiolar Adenoma				
Overall Rates (a)	5/50 (10%)	6/50 (12%)	8/50 (16%)	9/50 (18%)
Adjusted Rates (b)	12.5%	15.4%	24.4%	24.3%
Terminal Rates (c)	3/35 (9%)	5/37 (14%)	6/30 (20%)	7/34 (21%)
Week of First Observation	62	82	99	78
Life Table Tests (d)	P=0.115	P=0.531	P=0.212	P=0.190
Incidental Tumor Tests (d)	P=0.128	P=0.473	P=0.230	P=0.174
Cochran-Armitage Trend Test (d)	P=0.135			
Fisher Exact Test (d)		P=0.500	P=0.277	P=0.194
Lung: Alveolar/Bronchiolar Carcinoma				
Overall Rates (a)	2/50 (4%)	0/50 (0%)	5/50 (10%)	6/50 (12%)
Adjusted Rates (b)	5.3%	0.0%	15.3%	16.2%
Terminal Rates (c)	1/35 (3%)	0/37 (0%)	4/30 (13%)	4/34 (12%)
Week of First Observation	95		83	90
Life Table Tests (d)	P=0.021	P=0.231N	P=0.176	P=0.134
Incidental Tumor Tests (d)	P=0.025	P=0.234N	P=0.236	P=0.157
Cochran-Armitage Trend Test (d)	P=0.023			
Fisher Exact Test (d)		P=0.248N	P=0.218	P=0.134
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates (a)	7/50 (14%)	6/50 (12%)	12/50 (24%)	15/50 (30%)
Adjusted Rates (b)	17.4%	15.4%	35.4%	38.7%
Terminal Rates (c)	4/35 (11%)	5/37 (14%)	9/30 (30%)	11/34 (32%)
Week of First Observation	62	82	83	78
Life Table Tests (d)	P=0.010	P=0.467N	P=0.106	P=0.049
Incidental Tumor Tests (d)	P=0.012	P=0.522N	P=0.140	P=0.049
Cochran-Armitage Trend Test (d)	P=0.012			
Fisher Exact Test (d)		P=0.500N	P=0.154	P=0.045
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type				
Overall Rates (a)	3/50 (6%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
Adjusted Rates (b)	8.6%	2.7%	0.0%	0.0%
Terminal Rates (c)	3/35 (9%)	1/37 (3%)	0/30 (0%)	0/34 (0%)
Week of First Observation	105	105		
Life Table Tests (d)	P=0.050N	P=0.285N	P=0.149N	P=0.126N
Incidental Tumor Tests (d)	P=0.050N	P=0.285N	P=0.149N	P=0.126N
Cochran-Armitage Trend Test (d)	P=0.044N			
Fisher Exact Test (d)		P=0.309N	P=0.122N	P=0.122N
Hematopoietic System: Malignant Lymphoma, Mixed Type				
Overall Rates (a)	1/50 (2%)	3/50 (6%)	2/50 (4%)	0/50 (0%)
Adjusted Rates (b)	2.9%	8.1%	6.7%	0.0%
Terminal Rates (c)	1/35 (3%)	3/37 (8%)	2/30 (7%)	0/34 (0%)
Week of First Observation	105	105	105	
Life Table Tests (d)	P=0.262N	P=0.325	P=0.446	P=0.506N
Incidental Tumor Tests (d)	P=0.262N	P=0.325	P=0.446	P=0.506N
Cochran-Armitage Trend Test (d)	P=0.242N			
Fisher Exact Test (d)		P=0.309	P=0.500	P=0.500N
Hematopoietic System: Lymphoma, All Malignant				
Overall Rates (a)	5/50 (10%)	4/50 (8%)	4/50 (8%)	1/50 (2%)
Adjusted Rates (b)	14.3%	10.8%	11.0%	2.9%
Terminal Rates (c)	5/35 (14%)	4/37 (11%)	2/30 (7%)	1/34 (3%)
Week of First Observation	105	105	77	105
Life Table Tests (d)	P=0.094N	P=0.465N	P=0.573N	P=0.108N
Incidental Tumor Tests (d)	P=0.092N	P=0.465N	P=0.560N	P=0.108N
Cochran-Armitage Trend Test (d)	P=0.080N			
Fisher Exact Test (d)		P=0.500N	P=0.500N	P=0.103N

TABLE C3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Circulatory System: Hemangioma				
Overall Rates (a)	1/50 (2%)	1/50 (2%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	2.9%	2.7%	9.7%	0.0%
Terminal Rates (c)	1/35 (3%)	1/37 (3%)	2/30 (7%)	0/34 (0%)
Week of First Observation	105	105	104	
Life Table Tests (d)	P=0.429N	P=0.749N	P=0.254	P=0.506N
Incidental Tumor Tests (d)	P=0.409N	P=0.749N	P=0.312	P=0.506N
Cochran-Armitage Trend Test (d)	P=0.409N			
Fisher Exact Test (d)		P=0.752	P=0.309	P=0.500N
Circulatory System: Hemangiosarcoma				
Overall Rates (a)	0/50 (0%)	2/50 (4%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	5.4%	9.0%	0.0%
Terminal Rates (c)	0/35 (0%)	2/37 (5%)	2/30 (7%)	0/34 (0%)
Week of First Observation		105	87	
Life Table Tests (d)	P=0.549N	P=0.251	P=0.103	(e)
Incidental Tumor Tests (d)	P=0.535N	P=0.251	P=0.134	(e)
Cochran-Armitage Trend Test (d)	P=0.531N			
Fisher Exact Test (d)		P=0.247	P=0.121	(e)
Circulatory System: Hemangioma or Hemangiosarcoma				
Overall Rates (a)	1/50 (2%)	3/50 (6%)	6/50 (12%)	0/50 (0%)
Adjusted Rates (b)	2.9%	8.1%	18.2%	0.0%
Terminal Rates (c)	1/35 (3%)	3/37 (8%)	4/30 (13%)	0/34 (0%)
Week of First Observation	105	105	87	
Life Table Tests (d)	P=0.399N	P=0.325	P=0.041	P=0.506N
Incidental Tumor Tests (d)	P=0.374N	P=0.325	P=0.066	P=0.506N
Cochran-Armitage Trend Test (d)	P=0.371N			
Fisher Exact Test (d)		P=0.309	P=0.056	P=0.500N
Liver: Hepatocellular Adenoma				
Overall Rates (a)	10/50 (20%)	8/50 (16%)	12/50 (24%)	11/50 (22%)
Adjusted Rates (b)	26.4%	21.6%	33.8%	32.4%
Terminal Rates (c)	8/35 (23%)	8/37 (22%)	8/30 (27%)	11/34 (32%)
Week of First Observation	84	105	73	105
Life Table Tests (d)	P=0.292	P=0.350N	P=0.292	P=0.471
Incidental Tumor Tests (d)	P=0.316	P=0.330N	P=0.400	P=0.495
Cochran-Armitage Trend Test (d)	P=0.350			
Fisher Exact Test (d)		P=0.398N	P=0.405	P=0.500
Liver: Hepatocellular Carcinoma				
Overall Rates (a)	11/50 (22%)	10/50 (20%)	13/50 (26%)	11/50 (22%)
Adjusted Rates (b)	24.9%	21.9%	32.0%	26.0%
Terminal Rates (c)	4/35 (11%)	3/37 (8%)	4/30 (13%)	4/34 (12%)
Week of First Observation	62	63	66	71
Life Table Tests (d)	P=0.452	P=0.463N	P=0.346	P=0.577
Incidental Tumor Tests (d)	P=0.503N	P=0.544N	P=0.555	P=0.551N
Cochran-Armitage Trend Test (d)	P=0.489			
Fisher Exact Test (d)		P=0.500N	P=0.407	P=0.595
Liver: Hepatocellular Adenoma or Carcinoma				
Overall Rates (a)	21/50 (42%)	18/50 (36%)	20/50 (40%)	22/50 (44%)
Adjusted Rates (b)	46.9%	40.3%	47.6%	53.2%
Terminal Rates (c)	12/35 (34%)	11/37 (30%)	9/30 (30%)	15/34 (44%)
Week of First Observation	62	63	66	71
Life Table Tests (d)	P=0.326	P=0.304N	P=0.505	P=0.473
Incidental Tumor Tests (d)	P=0.423	P=0.307N	P=0.400N	P=0.536
Cochran-Armitage Trend Test (d)	P=0.376			
Fisher Exact Test (d)		P=0.341N	P=0.500N	P=0.500

TABLE C3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Harderian Gland: Adenoma				
Overall Rates (a)	3/50 (6%)	4/50 (8%)	0/50 (0%)	0/50 (0%)
Adjusted Rates (b)	8.6%	10.8%	0.0%	0.0%
Terminal Rates (c)	3/35 (9%)	4/37 (11%)	0/30 (0%)	0/34 (0%)
Week of First Observation	105	105		
Life Table Tests (d)	P=0.035N	P=0.531	P=0.149N	P=0.126N
Incidental Tumor Tests (d)	P=0.035N	P=0.531	P=0.149N	P=0.126N
Cochran-Armitage Trend Test (d)	P=0.030N			
Fisher Exact Test (d)		P=0.500	P=0.121N	P=0.121N
Harderian Gland: Adenoma or Adenocarcinoma				
Overall Rates (a)	5/50 (10%)	4/50 (8%)	0/50 (0%)	0/50 (0%)
Adjusted Rates (b)	14.3%	10.8%	0.0%	0.0%
Terminal Rates (c)	5/35 (14%)	4/37 (11%)	0/30 (0%)	0/34 (0%)
Week of First Observation	105	105		
Life Table Tests (d)	P=0.008N	P=0.465N	P=0.047N	P=0.035N
Incidental Tumor Tests (d)	P=0.008N	P=0.465N	P=0.047N	P=0.035N
Cochran-Armitage Trend Test (d)	P=0.007N			
Fisher Exact Test (d)		P=0.500N	P=0.028N	P=0.028N
All Sites: Benign Tumors				
Overall Rates (a)	18/50 (36%)	17/50 (34%)	22/50 (44%)	19/50 (38%)
Adjusted Rates (b)	45.2%	43.4%	57.2%	52.3%
Terminal Rates (c)	14/35 (40%)	15/37 (41%)	14/30 (47%)	17/34 (50%)
Week of First Observation	62	82	73	78
Life Table Tests (d)	P=0.301	P=0.429N	P=0.154	P=0.463
Incidental Tumor Tests (d)	P=0.354	P=0.450N	P=0.256	P=0.471
Cochran-Armitage Trend Test (d)	P=0.384			
Fisher Exact Test (d)		P=0.500N	P=0.270	P=0.500
All Sites: Malignant Tumors				
Overall Rates (a)	20/50 (40%)	18/50 (36%)	23/50 (46%)	16/50 (32%)
Adjusted Rates (b)	44.9%	40.3%	53.8%	37.4%
Terminal Rates (c)	11/35 (31%)	11/37 (30%)	11/30 (37%)	8/34 (24%)
Week of First Observation	62	63	66	71
Life Table Tests (d)	P=0.374N	P=0.370N	P=0.247	P=0.312N
Incidental Tumor Tests (d)	P=0.219N	P=0.414N	P=0.450	P=0.215N
Cochran-Armitage Trend Test (d)	P=0.286N			
Fisher Exact Test (d)		P=0.419N	P=0.343	P=0.266N
All Sites: All Tumors				
Overall Rates (a)	30/50 (60%)	30/50 (60%)	34/50 (68%)	33/50 (66%)
Adjusted Rates (b)	65.0%	66.4%	76.8%	76.5%
Terminal Rates (c)	19/35 (54%)	22/37 (59%)	20/30 (67%)	24/34 (71%)
Week of First Observation	62	63	66	71
Life Table Tests (d)	P=0.208	P=0.472N	P=0.157	P=0.332
Incidental Tumor Tests (d)	P=0.271	P=0.519N	P=0.316	P=0.375
Cochran-Armitage Trend Test (d)	P=0.251			
Fisher Exact Test (d)		P=0.581	P=0.266	P=0.339

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor 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 that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the 400-ppm and control groups.

TABLE C4. HISTORICAL INCIDENCE OF ALVEOLAR/BRONCHIOLAR TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	14/50	2/50	15/50
Methyl methacrylate	10/50	3/50	11/50
Propylene	7/50	9/50	16/50
1,2-Epoxybutane	7/49	5/49	11/49
Dichloromethane	3/50	2/50	5/50
Ethylene oxide	5/50	6/50	11/50
Tetrachloroethylene	3/49	4/49	6/49
TOTAL	49/348 (14.1%)	31/348 (8.9%)	75/348 (21.6%)
SD (b)	7.90%	5.02%	8.18%
Range (c)			
High	14/50	9/50	16/50
Low	3/50	2/50	5/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	255/2,034 (12.5%)	102/2,034 (5.0%)	348/2,034 (17.1%)
SD (b)	6.15%	3.42%	7.26%
Range (c)			
High	14/50	8/50	17/50
Low	1/50	0/50	3/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals necropsied	50	50	50	50
Animals examined histopathologically	50	50	50	50
INTEGUMENTARY SYSTEM				
*Skin	(50)	(50)	(50)	(50)
Inflammation, necrotizing				1 (2%)
Ulcer, chronic	1 (2%)			
Alopecia		4 (8%)	2 (4%)	
Hyperkeratosis	1 (2%)			
*Subcutaneous tissue	(50)	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)	1 (2%)	1 (2%)	
Abscess, NOS	1 (2%)			
RESPIRATORY SYSTEM				
#Nasal cavity	(50)	(50)	(50)	(50)
Congestion, NOS		1 (2%)		
Inflammation, serous			3 (6%)	2 (4%)
#Nasal gland	(50)	(50)	(50)	(50)
Dilatation, NOS			1 (2%)	
#Lung	(50)	(50)	(50)	(50)
Congestion, NOS		2 (4%)	1 (2%)	3 (6%)
Edema, NOS	1 (2%)			
Hemorrhage			3 (6%)	1 (2%)
Lymphocytic inflammatory infiltrate	3 (6%)	2 (4%)		
Inflammation, interstitial	2 (4%)		1 (2%)	3 (6%)
Bronchopneumonia, acute				1 (2%)
Inflammation, acute/chronic	2 (4%)	1 (2%)	1 (2%)	1 (2%)
Infarct, acute			1 (2%)	
Pigmentation, NOS			1 (2%)	
Hyperplasia, alveolar epithelium	1 (2%)	3 (6%)	1 (2%)	2 (4%)
Histiocytosis		1 (2%)		
#Lung/alveoli	(50)	(50)	(50)	(50)
Histiocytosis				1 (2%)
HEMATOPOIETIC SYSTEM				
#Bone marrow	(50)	(50)	(49)	(50)
Inflammation, suppurative			1 (2%)	
Hyperplasia, hematopoietic				2 (4%)
Hyperplasia, megakaryocytic			1 (2%)	
#Spleen	(49)	(49)	(49)	(50)
Congenital malformation, NOS				1 (2%)
Hyperplasia, hematopoietic		1 (2%)	2 (4%)	
Hyperplasia, reticulum cell	1 (2%)			
Hyperplasia, lymphoid	1 (2%)		1 (2%)	
Hematopoiesis			1 (2%)	2 (4%)
#Splenic follicles	(49)	(49)	(49)	(50)
Atrophy, NOS	2 (4%)	1 (2%)	1 (2%)	
#Mandibular lymph node	(47)	(45)	(50)	(46)
Hyperplasia, lymphoid	1 (2%)	2 (4%)	1 (2%)	1 (2%)
#Bronchial lymph node	(47)	(45)	(50)	(46)
Hyperplasia, reticulum cell			1 (2%)	
Hyperplasia, lymphoid		1 (2%)		
#Pancreatic lymph node	(47)	(45)	(50)	(46)
Angiectasis		1 (2%)		
#Mesenteric lymph node	(47)	(45)	(50)	(46)
Congestion, NOS	1 (2%)		3 (6%)	
Hemorrhage				1 (2%)
Angiectasis	1 (2%)			2 (4%)
Hyperplasia, lymphoid	1 (2%)		2 (4%)	

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
HEMATOPOIETIC SYSTEM (Continued)				
#Lung	(50)	(50)	(50)	(50)
Leukocytosis, NOS	1 (2%)			
#Ileum	(49)	(48)	(49)	(50)
Hyperplasia, lymphoid	1 (2%)			
#Thymic lymphocytes	(33)	(39)	(36)	(33)
Atrophy, NOS	1 (3%)			
CIRCULATORY SYSTEM				
#Heart	(50)	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)			
Inflammation, acute/chronic		2 (4%)	1 (2%)	
*Coronary artery	(50)	(50)	(50)	(50)
Inflammation, NOS		1 (2%)		
*Superior pancreaticoduodenal artery	(50)	(50)	(50)	(50)
Inflammation, chronic			1 (2%)	
*Mesenteric artery	(50)	(50)	(50)	(50)
Inflammation, acute/chronic	1 (2%)			
#Hepatic sinusoid	(50)	(50)	(50)	(50)
Dilatation, NOS			2 (4%)	3 (6%)
DIGESTIVE SYSTEM				
*Tooth	(50)	(50)	(50)	(50)
Congenital malformation, NOS	1 (2%)	3 (6%)		1 (2%)
Abscess, NOS	2 (4%)		1 (2%)	1 (2%)
#Salivary gland	(50)	(50)	(50)	(49)
Lymphocytic inflammatory infiltrate	1 (2%)			
Inflammation, acute/chronic	1 (2%)			
#Liver	(50)	(50)	(50)	(50)
Cyst, NOS		1 (2%)		1 (2%)
Torsion				1 (2%)
Hemorrhage				1 (2%)
Inflammation, acute/chronic	2 (4%)	2 (4%)		
Necrosis, focal	2 (4%)	1 (2%)	2 (4%)	1 (2%)
Metamorphosis, fatty		1 (2%)		
Focal cellular change	2 (4%)	2 (4%)	1 (2%)	3 (6%)
#Bile duct	(50)	(50)	(50)	(50)
Cyst, NOS			1 (2%)	
#Pancreas	(50)	(50)	(49)	(50)
Inflammation, acute/chronic	1 (2%)			
#Pancreatic acinus	(50)	(50)	(49)	(50)
Hypoplasia, NOS				1 (2%)
#Stomach	(49)	(49)	(49)	(50)
Inflammation, suppurative			1 (2%)	
#Glandular stomach	(49)	(49)	(49)	(50)
Dilatation, NOS				1 (2%)
Pigmentation, NOS			1 (2%)	
#Forestomach	(49)	(49)	(49)	(50)
Mineralization			1 (2%)	
Hyperkeratosis			1 (2%)	
#Duodenal mucosa	(49)	(48)	(49)	(50)
Mineralization	1 (2%)			
#Duodenal gland	(49)	(48)	(49)	(50)
Dilatation, NOS	1 (2%)			
#Ileum	(49)	(48)	(49)	(50)
Amyloidosis	1 (2%)	2 (4%)	1 (2%)	
*Rectum	(50)	(50)	(50)	(50)
Inflammation, chronic				1 (2%)
Ulcer, chronic	1 (2%)			

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
URINARY SYSTEM				
#Kidney	(50)	(50)	(50)	(50)
Hydronephrosis		2 (4%)	1 (2%)	
Cyst, NOS		2 (4%)	2 (4%)	
Multiple cysts	1 (2%)			
Congestion, NOS	1 (2%)		1 (2%)	
Lymphocytic inflammatory infiltrate	1 (2%)	1 (2%)		
Inflammation, suppurative	1 (2%)	1 (2%)		
Pyelonephritis, acute				2 (4%)
Inflammation, acute/chronic	1 (2%)	1 (2%)		
Glomerulonephritis, chronic		1 (2%)	2 (4%)	
Fibrosis, focal				1 (2%)
Infarct, focal			1 (2%)	
Calcification, NOS	1 (2%)			
Metaplasia, osseous	1 (2%)			
#Kidney/interstitium	(50)	(50)	(50)	(50)
Inflammation, chronic				1 (2%)
#Kidney/tubule	(50)	(50)	(50)	(50)
Cast, NOS	1 (2%)		4 (8%)	2 (4%)
Degeneration, NOS				1 (2%)
Nephrosis, NOS	2 (4%)			1 (2%)
Necrosis, NOS	1 (2%)			
#Kidney/pelvis	(50)	(50)	(50)	(50)
Inflammation, suppurative		3 (6%)	4 (8%)	1 (2%)
#Urinary bladder	(50)	(49)	(50)	(50)
Distention	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Hemorrhage			1 (2%)	
Inflammation, suppurative		3 (6%)	3 (6%)	1 (2%)
Inflammation, acute/chronic	3 (6%)	1 (2%)	2 (4%)	3 (6%)
Inflammation, chronic		1 (2%)	2 (4%)	
Hyperplasia, epithelial			2 (4%)	1 (2%)
#Urinary bladder/mucosa	(50)	(49)	(50)	(50)
Mineralization		1 (2%)		
ENDOCRINE SYSTEM				
#Adrenal	(50)	(49)	(48)	(50)
Necrosis, NOS		1 (2%)		
#Adrenal/capsule	(50)	(49)	(48)	(50)
Hyperplasia, NOS	1 (2%)			
#Adrenal cortex	(50)	(49)	(48)	(50)
Mineralization		1 (2%)		
Amyloidosis		1 (2%)		
Hyperplasia, NOS	1 (2%)	2 (4%)	2 (4%)	
#Thyroid	(49)	(49)	(50)	(50)
Lymphocytic inflammatory infiltrate			1 (2%)	
Inflammation, acute/chronic	1 (2%)			
#Pancreatic islets	(50)	(50)	(49)	(50)
Hyperplasia, NOS	1 (2%)			
REPRODUCTIVE SYSTEM				
*Penis	(50)	(50)	(50)	(50)
Ulcer, NOS	1 (2%)			
Abscess, NOS		1 (2%)		
Inflammation, chronic	1 (2%)		1 (2%)	1 (2%)
*Prepuce	(50)	(50)	(50)	(50)
Ulcer, NOS	1 (2%)	1 (2%)		1 (2%)
Inflammation, suppurative			1 (2%)	
Inflammation, necrotizing	1 (2%)	1 (2%)	3 (6%)	1 (2%)

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
REPRODUCTIVE SYSTEM (Continued)				
*Preputial gland	(50)	(50)	(50)	(50)
Dilatation/ducts	2 (4%)	1 (2%)		
Cystic ducts	6 (12%)	1 (2%)		4 (8%)
Ulcer, NOS				1 (2%)
Inflammation, suppurative	1 (2%)	2 (4%)		1 (2%)
Abscess, NOS	1 (2%)	2 (4%)	1 (2%)	3 (6%)
Inflammation, acute/chronic				1 (2%)
Hyperplasia, intraductal		2 (4%)		
#Prostate	(50)	(49)	(50)	(50)
Hemorrhage			1 (2%)	
Inflammation, suppurative	1 (2%)	3 (6%)	2 (4%)	2 (4%)
Inflammation, acute/chronic		1 (2%)		
*Seminal vesicle	(50)	(50)	(50)	(50)
Dilatation, NOS		1 (2%)		
Distention		2 (4%)		
#Testis	(50)	(50)	(50)	(50)
Mineralization				2 (4%)
Atrophy, NOS	1 (2%)			
*Epididymis	(50)	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)			
Inflammation, granulomatous		1 (2%)		
NERVOUS SYSTEM				
#Brain	(50)	(50)	(50)	(50)
Mineralization	14 (28%)	20 (40%)	12 (24%)	6 (12%)
Hemorrhage			1 (2%)	
*Spinal cord	(50)	(50)	(50)	(50)
Lymphocytic inflammatory infiltrate	1 (2%)			
*Sciatic nerve	(50)	(50)	(50)	(50)
Inflammation, suppurative				1 (2%)
Inflammation, acute/chronic				1 (2%)
SPECIAL SENSE ORGANS				
None				
MUSCULOSKELETAL SYSTEM				
*Skeletal muscle	(50)	(50)	(50)	(50)
Inflammation, suppurative	1 (2%)		1 (2%)	
Inflammation, acute/chronic	1 (2%)			
Degeneration, NOS	1 (2%)			
*Muscle hip/thigh	(50)	(50)	(50)	(50)
Mineralization			1 (2%)	
BODY CAVITIES				
*Pleura	(50)	(50)	(50)	(50)
Inflammation, chronic			1 (2%)	
*Mesentery	(50)	(50)	(50)	(50)
Necrosis, fat		1 (2%)		

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
ALL OTHER SYSTEMS				
*Multiple organs	(50)	(50)	(50)	(50)
Inflammation, acute/chronic		1 (2%)	1 (2%)	1 (2%)
Ankle				
Inflammation, necrotizing				1
SPECIAL MORPHOLOGY SUMMARY				
No lesion reported	7	2	6	2

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site

APPENDIX D

SUMMARY OF LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals necropsied	50	50	49	49
Animals examined histopathologically	50	50	49	49
INTEGUMENTARY SYSTEM				
*Skin	(50)	(50)	(49)	(49)
Sarcoma, NOS			1 (2%)	
Fibrosarcoma		1 (2%)	2 (4%)	
RESPIRATORY SYSTEM				
#Nasal cavity	(50)	(50)	(48)	(49)
Undifferentiated carcinoma, metastatic				1 (2%)
Adenoma, NOS				1 (2%)
#Lung	(50)	(50)	(49)	(49)
Undifferentiated carcinoma, metastatic				1 (2%)
Adenocarcinoma, NOS, metastatic		1 (2%)		3 (6%)
Bile duct carcinoma, metastatic			1 (2%)	
Hepatocellular carcinoma, metastic	1 (2%)	2 (4%)		1 (2%)
Alveolar/bronchiolar adenoma	3 (6%)	2 (4%)	3 (6%)	4 (8%)
Alveolar/bronchiolar carcinoma	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Osteosarcoma, metastatic			2 (4%)	
HEMATOPOIETIC SYSTEM				
*Multiple organs	(50)	(50)	(49)	(49)
Malignant lymphoma, NOS	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Malignant lymphoma, undifferentiated type	1 (2%)			1 (2%)
Malignant lymphoma, lymphocytic type	1 (2%)	2 (4%)	1 (2%)	
Malignant lymphoma, histiocytic type	3 (6%)		1 (2%)	2 (4%)
Malignant lymphoma, mixed type	4 (8%)	5 (10%)	3 (6%)	2 (4%)
#Spleen	(50)	(49)	(48)	(49)
Malignant lymphoma, histiocytic type	1 (2%)			
Malignant lymphoma, mixed type		1 (2%)		
#Bronchial lymph node	(49)	(49)	(48)	(49)
Adenocarcinoma, NOS, metastatic				1 (2%)
Osteosarcoma, metastatic			1 (2%)	
#Mediastinal lymph node	(49)	(49)	(48)	(49)
Adenocarcinoma, NOS, metastatic				1 (2%)
#Mesenteric lymph node	(49)	(49)	(48)	(49)
Adenocarcinoma, NOS, metastatic		1 (2%)		2 (4%)
Bile duct carcinoma, metastatic			1 (2%)	
#Renal lymph node	(49)	(49)	(48)	(49)
Squamous cell carcinoma, metastatic				1 (2%)
Adenocarcinoma, NOS, metastatic				1 (2%)
Bile duct carcinoma, metastatic			1 (2%)	
#Thymus	(45)	(43)	(42)	(36)
Undifferentiated carcinoma, metastatic				1 (3%)
Alveolar/bronchiolar carcinoma, metastatic	1 (2%)			
CIRCULATORY SYSTEM				
#Spleen	(50)	(49)	(48)	(49)
Hemangiosarcoma	1 (2%)			1 (2%)
#Axillary lymph node	(49)	(49)	(48)	(49)
Hemangioma	1 (2%)			
#Lung	(50)	(50)	(49)	(49)
Hemangiosarcoma, metastatic	1 (2%)			
#Heart	(50)	(50)	(49)	(49)
Undifferentiated carcinoma, metastatic				1 (2%)
Alveolar/bronchiolar carcinoma, metastatic	1 (2%)			

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
CIRCULATORY SYSTEM (Continued)				
#Liver	(50)	(50)	(49)	(49)
Hemangioma		1 (2%)		
Hemangiosarcoma				1 (2%)
#Uterus	(50)	(50)	(47)	(48)
Hemangiosarcoma	1 (2%)			
DIGESTIVE SYSTEM				
#Salivary gland	(48)	(49)	(48)	(46)
Undifferentiated carcinoma, metastatic				1 (2%)
#Liver	(50)	(50)	(49)	(49)
Bile duct carcinoma			1 (2%)	
Hepatocellular adenoma	3 (6%)	2 (4%)	4 (8%)	2 (4%)
Hepatocellular carcinoma	2 (4%)	4 (8%)	2 (4%)	1 (2%)
#Pancreas	(50)	(50)	(48)	(49)
Adenocarcinoma, NOS, metastatic		1 (2%)		
#Duodenum	(50)	(49)	(47)	(49)
Bile duct carcinoma, metastatic			1 (2%)	
URINARY SYSTEM				
#Kidney	(50)	(50)	(49)	(49)
Osteosarcoma, metastatic			1 (2%)	
#Urinary bladder	(48)	(50)	(45)	(49)
Adenocarcinoma, NOS, invasive				1 (2%)
Adenocarcinoma, NOS, metastatic				2 (4%)
ENDOCRINE SYSTEM				
#Pituitary	(48)	(50)	(46)	(49)
Adenoma, NOS	2 (4%)	4 (8%)	1 (2%)	1 (2%)
#Pituitary intermedia	(48)	(50)	(46)	(49)
Adenoma, NOS		1 (2%)		
#Adrenal	(50)	(50)	(48)	(49)
Pheochromocytoma	1 (2%)		1 (2%)	
Fibrosarcoma, metastatic			1 (2%)	
Osteosarcoma, metastatic			1 (2%)	
#Adrenal/capsule	(50)	(50)	(48)	(49)
Adenocarcinoma, NOS, metastatic				1 (2%)
#Thyroid	(49)	(50)	(48)	(45)
Follicular cell adenoma	3 (6%)			
#Pancreatic islets	(50)	(50)	(48)	(49)
Islet cell carcinoma	1 (2%)			
REPRODUCTIVE SYSTEM				
*Mammary gland	(50)	(50)	(49)	(49)
Adenocarcinoma, NOS	1 (2%)	1 (2%)	4 (8%)	1 (2%)
*Clitoral gland	(50)	(50)	(49)	(49)
Carcinoma, NOS			1 (2%)	
#Uterus	(50)	(50)	(47)	(48)
Squamous cell carcinoma		1 (2%)	1 (2%)	3 (6%)
Adenoma, NOS		1 (2%)	1 (2%)	6 (13%)
Adenocarcinoma, NOS		2 (4%)	3 (6%)	19 (40%)
Leiomyoma			1 (2%)	
Endometrial stromal polyp	2 (4%)		3 (6%)	1 (2%)
Osteosarcoma			1 (2%)	
#Ovary	(49)	(50)	(46)	(45)
Cystadenoma, NOS		1 (2%)		
Granulosa cell tumor		1 (2%)		1 (2%)
Tubular adenoma	1 (2%)			

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
NERVOUS SYSTEM				
None				
SPECIAL SENSE ORGANS				
*Eye/lacrimal gland	(50)	(50)	(49)	(49)
Undifferentiated carcinoma				1 (2%)
*Harderian gland	(50)	(50)	(49)	(49)
Adenoma, NOS	2 (4%)		1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM				
*Vertebral column	(50)	(50)	(49)	(49)
Alveolar/bronchiolar carcinoma metastatic	1 (2%)			
BODY CAVITIES				
*Mediastinum	(50)	(50)	(49)	(49)
Alveolar/bronchiolar carcinoma metastatic	1 (2%)			
*Pleural cavity	(50)	(50)	(49)	(49)
Alveolar/bronchiolar carcinoma metastatic	1 (2%)			
*Pleura	(50)	(50)	(49)	(49)
Alveolar/bronchiolar carcinoma metastatic	1 (2%)			
ALL OTHER SYSTEMS				
*Multiple organs	(50)	(50)	(49)	(49)
Fibrosarcoma				1 (2%)
Diaphragm				
Alveolar/bronchiolar carcinoma metastatic	1			
ANIMAL DISPOSITION SUMMARY				
Animals initially in study	50	50	50	50
Natural death	10	8	9	12
Moribund sacrifice	4	5	4	14
Terminal sacrifice	36	37	36	22
Accidentally killed, nda				1
Animal missexed			1	1
TUMOR SUMMARY				
Total animals with primary tumors**	27	24	27	37
Total primary tumors	38	32	39	53
Total animals with benign tumors	13	10	12	12
Total benign tumors	18	12	15	16
Total animals with malignant tumors	20	17	20	31
Total malignant tumors	20	19	24	36
Total animals with secondary tumors##	5	3	4	10
Total secondary tumors	9	5	10	19
Total animals with tumors uncertain -- benign or malignant		1		1
Total uncertain tumors		1		1

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
# Number of animals examined microscopically at this site
Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: CHAMBER CONTROL

ANIMAL NUMBER	0003	0026	0024	0001	0034	0110	0025	0038	0028	0049	0012	0047	0013	0032	0002	0004	0005	0006	0007	0008	0009	0011	0014	0015	0016
WEEKS ON STUDY	072	084	087	090	091	092	092	093	095	095	098	098	100	101	105	105	105	105	105	105	105	105	105	105	105
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic		X																							
Alveolar/bronchiolar adenoma						X				X															
Alveolar/bronchiolar carcinoma							X				X	X													
Hemangiosarcoma, metastatic			X																						
Trachea	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Malignant lymphoma, histiocytic type																									
Lymph nodes	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma															X										
Thymus	–	+	+	+	–	+	+	–	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic											X														
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma, metastatic											X														
DIGESTIVE SYSTEM																									
Salivary gland	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma															X	X									
Hepatocellular carcinoma		X																					X		
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	N	+	+	N	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS					X																				
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma																					X				
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																X							X		
Parathyroid	+	–	+	+	+	+	+	–	+	+	–	+	+	+	+	–	+	+	–	+	+	+	–	+	–
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal polyp											X														
Hemangiosarcoma			X																						
Ovary	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular adenoma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS				X																				X	
MUSCULOSKELETAL SYSTEM																									
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Alveolar/bronchiolar carcinoma, metastatic							X																		
BODY CAVITIES																									
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Alveolar/bronchiolar carcinoma, metastatic							X				X														
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Alveolar/bronchiolar carcinoma, metastatic												X													
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS				X																					
Malignant lymphoma, undifferentiated type						X																			
Malignant lymphoma, lymphocytic type									X	X				X											
Malignant lymphoma, histiocytic type																									
Malignant lymphoma, mixed type																X				X					
Diaphragm, NOS																									
Alveolar/bronchiolar carcinoma, metastatic							X																		

+: Tissue examined microscopically
–: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	017	018	019	020	021	022	023	027	029	030	031	033	035	036	037	039	040	041	042	043	044	045	046	048	050	TOTAL:
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma											X															3
Alveolar/bronchiolar carcinoma																										3
Hemangiosarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	45
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma					X																					1
Malignant lymphoma, histiocytic type																X										1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangioma																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Alveolar/bronchiolar carcinoma, metast																										1
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma, metast																										1
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma											X															3
Hepatocellular carcinoma																										2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	50
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	48
Adenoma, NOS											X															2
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma																										1
Thyroid	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell adenoma				X																						3
Parathyroid	−	+	+	−	−	+	+	−	−	−	−	+	+	−	+	+	+	−	+	+	−	−	+	−	+	31
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islet cell carcinoma			X																							1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	*50
Adenocarcinoma, NOS																						X				1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrial stromal polyp			X																							2
Hemangiosarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tubular adenoma																					X					1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS																										2
MUSCULOSKELETAL SYSTEM																										
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Alveolar/bronchiolar carcinoma, metast																										1
BODY CAVITIES																										
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Alveolar/bronchiolar carcinoma, metast																										2
Mediastinum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Alveolar/bronchiolar carcinoma, metast																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS																										1
Malig. lymphoma, undifferentiated type																										1
Malignant lymphoma, lymphocytic type																			X							1
Malignant lymphoma, histiocytic type																										3
Malignant lymphoma, mixed type														X				X								4
Diaphragm, NOS																										
Alveolar/bronchiolar carcinoma, metast																										1

* Animals necropsied

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 100 ppm

ANIMAL NUMBER	029	027	035	043	011	006	026	012	020	042	016	021	009	001	002	003	004	005	007	008	010	013	014	015	017
WEEKS ON STUDY	018	046	073	076	079	082	084	090	091	097	100	101	102	105	105	105	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma										X															
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic													X												
Hepatocellular carcinoma, metastatic					X																				
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malignant lymphoma, mixed type																									
Lymph nodes	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic													X												
Thymus	−	+	−	−	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																		X			X				
Hepatocellular carcinoma			X		X																				
Hemangioma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	N	N	+	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic													X												
Esophagus	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS										X								X				X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	+	+	−	−	−	−	−	−	+	−	−	+	+	−	−	−	−	−	−	+	+	−	−	−
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	N	+	+	+	+	N	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS						X																			
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma												X													
Adenoma, NOS										X															
Adenocarcinoma, NOS													X												
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma, NOS		X																							
Granulosa cell tumor																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS									X																
Malignant lymphoma, lymphocytic type				X																					
Malignant lymphoma, mixed type																		X					X	X	

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 100 ppm (Continued)

ANIMAL NUMBER	0118	0119	0222	0223	0224	0225	0228	0230	0231	0232	0233	0234	0236	0237	0238	0239	0240	0241	0244	0245	0246	0247	0248	0249	0250	TOTAL:
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS, metastatic																										1
Hepatocellular carcinoma, metastatic									X																	2
Alveolar/bronchiolar adenoma									X									X								2
Alveolar/bronchiolar carcinoma														X												1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Malignant lymphoma, mixed type															X											1
Lymph nodes	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	49
Adenocarcinoma, NOS, metastatic																										1
Thymus	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	43
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																										2
Hepatocellular carcinoma									X					X												4
Hemangioma							X																			1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS, metastatic																										1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma, NOS																			X		X					5
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	50
Parathyroid	+	–	+	+	+	–	–	+	+	–	+	–	+	+	–	+	+	+	+	+	+	–	–	–	–	22
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	N	+	+	N	+	+	*50
Adenocarcinoma, NOS																										1
Uterus	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Adenoma, NOS																										1
Adenocarcinoma, NOS									X																	2
Ovary	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma, NOS																										1
Granulosa cell tumor																	X									1
NERVOUS SYSTEM																										
Brain	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS																										1
Malignant lymphoma, lymphocytic type																			X							2
Malignant lymphoma, mixed type				X								X														5

* Animals necropsied

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 200 ppm

ANIMAL NUMBER	0004	0026	0024	0036	0116	0007	0030	0034	0048	0044	0047	0023	0040	0001	0002	0003	0005	0006	0008	0009	0010	0011	0012	0013	0014
WEEKS ON STUDY	037	062	063	066	071	090	095	095	096	097	098	103	103	105	105	105	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Skin	+	+	+	N	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS										X															
Fibrosarcoma									X																
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct carcinoma, metastatic													X												
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																	X								
Osteosarcoma, metastatic		X			X																				
Trachea	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	–	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct carcinoma, metastatic													@X												
Osteosarcoma, metastatic		X																							
Thymus	–	–	–	–	–	S	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct carcinoma													X												
Hepatocellular adenoma																									
Hepatocellular carcinoma				X																					
Bile duct	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	N	N	N	S	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreas	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	–	–	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct carcinoma, metastatic													X												
Large intestine	+	+	+	–	–	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic					X																				
Urinary bladder	+	+	+	–	–	S	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	–	–	S	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Adenoma, NOS																		X							
Adrenal	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma																									
Fibrosarcoma, metastatic									X																
Osteosarcoma, metastatic					X																				
Thyroid	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	–	–	–	–	–	S	+	+	–	+	+	+	–	+	+	–	–	+	+	+	+	+	–	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	+	+	N	N	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS							X						X				X								
Preputial/clitoral gland	N	N	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Uterus	+	–	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																							X		
Adenoma, NOS														X											
Adenocarcinoma, NOS																									
Leiomyoma																									
Endometrial stromal polyp																	X								
Osteosarcoma					X																				
Ovary	+	–	+	–	–	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS														X											
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS	X																								
Malignant lymphoma, lymphocytic type																									
Malignant lymphoma, histiocytic type											X														
Malignant lymphoma, mixed type												X										X			

@ Multiple occurrence of morphology

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 200 ppm (Continued)

ANIMAL NUMBER	0015	0017	0018	0019	0020	0021	0022	0025	0027	0028	0029	0031	0032	0033	0035	0037	0038	0039	0041	0042	0043	0045	0046	0049	0050	TOTAL:
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Sarcoma, NOS																										1
Fibrosarcoma				X																						2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bile duct carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma							X											X		X						3
Alveolar/bronchiolar carcinoma																X										2
Osteosarcoma, metastatic																										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	48
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Bile duct carcinoma, metastatic																										1
Osteosarcoma, metastatic																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bile duct carcinoma																										1
Hepatocellular adenoma	X									X				X							X					4
Hepatocellular carcinoma							X																			2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Bile duct carcinoma, metastatic																										1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Osteosarcoma, metastatic																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	45
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma, NOS																										1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pheochromocytoma																X										1
Fibrosarcoma, metastatic																										1
Osteosarcoma, metastatic																										1
Thyroid	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid	–	–	+	–	+	+	+	+	–	–	–	+	+	+	–	+	–	+	–	–	+	+	+	+	+	29
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Adenocarcinoma, NOS															X											4
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Carcinoma, NOS								X																		1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Squamous cell carcinoma																										1
Adenoma, NOS																										1
Adenocarcinoma, NOS	X							X							X											3
Leiomyoma																								X		1
Endometrial stromal polyp							X													X						3
Osteosarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Adenoma, NOS																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Malignant lymphoma, NOS																										1
Malignant lymphoma, lymphocytic type			X																							1
Malignant lymphoma, histiocytic type																										1
Malignant lymphoma, mixed type														X												3

* Animals necropsied

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE: 400 ppm

ANIMAL NUMBER	02 22	03 38	04 40	03 33	00 07	02 21	04 45	00 01	03 39	01 11	03 30	03 34	00 03	02 25	02 29	03 35	04 43	01 19	04 41	04 42	05 50	00 08	01 10	01 15	01 14
WEEKS ON STUDY	040	064	064	081	082	083	085	086	089	090	090	090	092	092	093	093	096	098	098	098	098	100	101	101	104
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Undifferentiated carcinoma, metastatic		X																							
Adenocarcinoma, NOS, metastatic																									
Hepatocellular carcinoma, metastatic																									
Alveolar/bronchiolar adenoma										X															
Alveolar/bronchiolar carcinoma																									
Trachea	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Undifferentiated carcinoma, metastatic		X																							
Adenoma, NOS																							X		
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma															X										
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic					X																				
Adenocarcinoma, NOS, metastatic														X					@X						
Thymus	+	+	+	–	–	+	+	–	–	–	+	+	–	+	–	+	–	–	–	+	+	+	–	+	+
Undifferentiated carcinoma, metastatic		X																							
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Undifferentiated carcinoma, metastatic		X																							
DIGESTIVE SYSTEM																									
Salivary gland	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Undifferentiated carcinoma, metastatic		X																							
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Hepatocellular carcinoma																									
Hemangiosarcoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	N	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, invasive								X																	
Adenocarcinoma, NOS, metastatic														X				X							
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic																									
Thyroid	–	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Parathyroid	+	–	+	+	+	–	–	–	+	+	–	+	+	+	+	–	–	–	+	+	+	+	–	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+
Adenocarcinoma, NOS			X																						
Uterus	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma					X																	X			
Adenoma, NOS							X																	X	
Adenocarcinoma, NOS								X				X		X	X			X	X				X		X
Endometrial stromal polyp																									
Ovary	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+
Granulosa cell tumor																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Lacrimal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Undifferentiated carcinoma		X																							
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Fibrosarcoma																								X	
Malignant lymphoma, NOS																					X				
Malignant lymphoma, undifferentiated type																									
Malignant lymphoma, histiocytic type							X																		
Malignant lymphoma, mixed type																				X					

@ Multiple occurrence of morphology

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 400 ppm (Continued)

ANIMAL NUMBER	0 2 4	0 0 2	0 0 4	0 0 5	0 0 6	0 0 9	0 1 2	0 1 3	0 1 6	0 1 7	0 1 8	0 2 0	0 2 3	0 2 6	0 2 7	0 2 8	0 3 1	0 3 2	0 3 6	0 3 7	0 4 4	0 4 6	0 4 7	0 4 8	0 4 9	TOTAL:
WEEKS ON STUDY	1 0 4	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	TISSUES TUMORS
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Undifferentiated carcinoma, metastatic																										1
Adenocarcinoma, NOS, metastatic	X											X		X												3
Hepatocellular carcinoma, metastatic								X																		1
Alveolar/bronchiolar adenoma	X									X										X						4
Alveolar/bronchiolar carcinoma						X																	X			2
Trachea	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Nasal cavity	+	+	+	+	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Undifferentiated carcinoma, metastatic																										1
Adenoma, NOS																										1
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	–	–	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																										1
Lymph nodes	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell carcinoma, metastatic																										1
Adenocarcinoma, NOS, metastatic	X							X																		4
Thymus	–	+	+	+	+	+	S	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	36
Undifferentiated carcinoma, metastatic																										1
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Undifferentiated carcinoma, metastatic																										1
DIGESTIVE SYSTEM																										
Salivary gland	+	–	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Undifferentiated carcinoma, metastatic																										1
Liver	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular adenoma	X					X																				2
Hepatocellular carcinoma								X																		1
Hemangiosarcoma																					X					1
Bile duct	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Pancreas	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	–	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	–	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, NOS, invasive																										1
Adenocarcinoma, NOS, metastatic																										2
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS										X																1
Adrenal	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, NOS, metastatic												X														1
Thyroid	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Parathyroid	+	+	+	+	+	–	S	+	–	+	+	+	–	+	+	+	+	+	–	+	–	–	–	+	+	33
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	N	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Adenocarcinoma, NOS																										1
Uterus	+	+	–	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Squamous cell carcinoma																		X								3
Adenoma, NOS				X	X					X								X								6
Adenocarcinoma, NOS	X		X					X	X			X	X	X		X	X		X				X			19
Endometrial stromal polyp																									X	1
Ovary	+	+	+	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Granulosa cell tumor												X														1
NERVOUS SYSTEM																										
Brain	+	+	–	+	+	+	S	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																										
Lacrimal gland	N	N	N	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Undifferentiated carcinoma																										1
Harderian gland	N	N	N	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Adenoma, NOS				X																						1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	S	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Fibrosarcoma																										1
Malignant lymphoma, NOS																										1
Malig. lymphoma, undifferentiated type																						X				1
Malignant lymphoma, histiocytic type	X																									2
Malignant lymphoma, mixed type																							X			2

* Animals necropsied

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Subcutaneous Tissue: Sarcoma or Fibrosarcoma				
Overall Rates (a)	0/50 (0%)	1/50 (2%)	3/49 (6%)	0/49 (0%)
Adjusted Rates (b)	0.0%	2.4%	7.3%	0.0%
Terminal Rates (c)	0/36 (0%)	0/37 (0%)	1/37 (3%)	0/23 (0%)
Week of First Observation		97	96	
Life Table Tests (d)	P=0.562	P=0.505	P=0.130	(e)
Incidental Tumor Tests (d)	P=0.483N	P=0.388	P=0.120	(e)
Cochran-Armitage Trend Test (d)	P=0.627			
Fisher Exact Test (d)		P=0.500	P=0.117	(e)
Lung: Alveolar/Bronchiolar Adenoma				
Overall Rates (a)	3/50 (6%)	2/50 (4%)	3/49 (6%)	4/49 (8%)
Adjusted Rates (b)	7.2%	5.4%	8.1%	14.5%
Terminal Rates (c)	1/36 (3%)	2/37 (5%)	3/37 (8%)	2/23 (9%)
Week of First Observation	92	105	105	90
Life Table Tests (d)	P=0.181	P=0.503N	P=0.650N	P=0.330
Incidental Tumor Tests (d)	P=0.350	P=0.558N	P=0.510	P=0.572
Cochran-Armitage Trend Test (d)	P=0.332			
Fisher Exact Test (d)		P=0.500N	P=0.651	P=0.489
Lung: Alveolar/Bronchiolar Carcinoma				
Overall Rates (a)	3/50 (6%)	1/50 (2%)	2/49 (4%)	2/49 (4%)
Adjusted Rates (b)	7.1%	2.7%	5.4%	8.7%
Terminal Rates (c)	0/36 (0%)	1/37 (3%)	2/37 (5%)	2/23 (9%)
Week of First Observation	92	105	105	105
Life Table Tests (d)	P=0.557	P=0.314N	P=0.497N	P=0.636N
Incidental Tumor Tests (d)	P=0.475N	P=0.422N	P=0.691N	P=0.429N
Cochran-Armitage Trend Test (d)	P=0.510N			
Fisher Exact Test (d)		P=0.309N	P=0.510N	P=0.510N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates (a)	6/50 (12%)	3/50 (6%)	5/49 (10%)	6/49 (12%)
Adjusted Rates (b)	13.8%	8.1%	13.5%	22.7%
Terminal Rates (c)	1/36 (3%)	3/37 (8%)	5/37 (14%)	4/23 (17%)
Week of First Observation	92	105	105	90
Life Table Tests (d)	P=0.216	P=0.255N	P=0.490N	P=0.394
Incidental Tumor Tests (d)	P=0.457	P=0.353N	P=0.512	P=0.521N
Cochran-Armitage Trend Test (d)	P=0.421			
Fisher Exact Test (d)		P=0.243N	P=0.514N	P=0.606
Hematopoietic System: Malignant Lymphoma, Histiocytic Type				
Overall Rates (a)	4/50 (8%)	0/50 (0%)	1/49 (2%)	2/49 (4%)
Adjusted Rates (b)	9.9%	0.0%	2.5%	6.2%
Terminal Rates (c)	1/36 (3%)	0/37 (0%)	0/37 (0%)	0/23 (0%)
Week of First Observation	95		98	85
Life Table Tests (d)	P=0.471N	P=0.065N	P=0.175N	P=0.476N
Incidental Tumor Tests (d)	P=0.177N	P=0.111N	P=0.159N	P=0.170N
Cochran-Armitage Trend Test (d)	P=0.381N			
Fisher Exact Test (d)		P=0.059N	P=0.188N	P=0.349N
Hematopoietic System: Malignant Lymphoma, Mixed Type				
Overall Rates (a)	4/50 (8%)	6/50 (12%)	3/49 (6%)	2/49 (4%)
Adjusted Rates (b)	11.1%	16.2%	7.8%	7.3%
Terminal Rates (c)	4/36 (11%)	6/37 (16%)	2/37 (5%)	1/23 (4%)
Week of First Observation	105	105	103	98
Life Table Tests (d)	P=0.343N	P=0.385	P=0.481N	P=0.536N
Incidental Tumor Tests (d)	P=0.265N	P=0.385	P=0.487N	P=0.472N
Cochran-Armitage Trend Test (d)	P=0.179N			
Fisher Exact Test (d)		P=0.370	P=0.512N	P=0.349N

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Hematopoietic System: Lymphoma, All Malignant				
Overall Rates (a)	11/50 (22%)	9/50 (18%)	6/49 (12%)	6/49 (12%)
Adjusted Rates (b)	26.1%	22.5%	14.5%	19.7%
Terminal Rates (c)	6/36 (17%)	7/37 (19%)	3/37 (8%)	2/23 (9%)
Week of First Observation	90	76	37	85
Life Table Tests (d)	P=0.277N	P=0.404N	P=0.148N	P=0.380N
Incidental Tumor Tests (d)	P=0.059N	P=0.459N	P=0.178N	P=0.097N
Cochran-Armitage Trend Test (d)	P=0.105N			
Fisher Exact Test (d)		P=0.402N	P=0.154N	P=0.154N
Circulatory System: Hemangioma or Hemangiosarcoma				
Overall Rates (a)	3/50 (6%)	1/50 (2%)	0/49 (0%)	2/49 (4%)
Adjusted Rates (b)	7.5%	2.7%	0.0%	7.1%
Terminal Rates (c)	2/36 (6%)	1/37 (3%)	0/37 (0%)	1/23 (4%)
Week of First Observation	87	105		93
Life Table Tests (d)	P=0.567N	P=0.309N	P=0.125N	P=0.651N
Incidental Tumor Tests (d)	P=0.441N	P=0.315N	P=0.232N	P=0.519N
Cochran-Armitage Trend Test (d)	P=0.453N			
Fisher Exact Test (d)		P=0.309N	P=0.125N	P=0.510N
Liver: Hepatocellular Adenoma				
Overall Rates (a)	3/50 (6%)	2/50 (4%)	4/49 (8%)	2/49 (4%)
Adjusted Rates (b)	8.3%	5.4%	10.8%	8.2%
Terminal Rates (c)	3/36 (8%)	2/37 (5%)	4/37 (11%)	1/23 (4%)
Week of First Observation	105	105	105	104
Life Table Tests (d)	P=0.484	P=0.487N	P=0.515	P=0.670
Incidental Tumor Tests (d)	P=0.542	P=0.487N	P=0.515	P=0.614N
Cochran-Armitage Trend Test (d)	P=0.491N			
Fisher Exact Test (d)		P=0.500N	P=0.489	P=0.510N
Liver: Hepatocellular Carcinoma				
Overall Rates (a)	2/50 (4%)	4/50 (8%)	2/49 (4%)	1/49 (2%)
Adjusted Rates (b)	4.8%	9.4%	4.8%	4.3%
Terminal Rates (c)	1/36 (3%)	2/37 (5%)	1/37 (3%)	1/23 (4%)
Week of First Observation	84	73	66	105
Life Table Tests (d)	P=0.365N	P=0.332	P=0.680	P=0.617N
Incidental Tumor Tests (d)	P=0.232N	P=0.366	P=0.651	P=0.535N
Cochran-Armitage Trend Test (d)	P=0.271N			
Fisher Exact Test (d)		P=0.339	P=0.684	P=0.508N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall Rates (a)	5/50 (10%)	6/50 (12%)	6/49 (12%)	3/49 (6%)
Adjusted Rates (b)	12.9%	14.6%	15.4%	12.3%
Terminal Rates (c)	4/36 (11%)	4/37 (11%)	5/37 (14%)	2/23 (9%)
Week of First Observation	84	73	66	104
Life Table Tests (d)	P=0.481N	P=0.502	P=0.504	P=0.584N
Incidental Tumor Tests (d)	P=0.336N	P=0.533	P=0.462	P=0.465N
Cochran-Armitage Trend Test (d)	P=0.275N			
Fisher Exact Test (d)		P=0.500	P=0.486	P=0.369N
Pituitary Gland: Adenoma				
Overall Rates (a)	2/48 (4%)	4/50 (8%)	1/46 (2%)	1/49 (2%)
Adjusted Rates (b)	5.0%	10.8%	2.8%	4.3%
Terminal Rates (c)	1/35 (3%)	4/37 (11%)	1/36 (3%)	1/23 (4%)
Week of First Observation	91	105	105	105
Life Table Tests (d)	P=0.357N	P=0.352	P=0.499N	P=0.621N
Incidental Tumor Tests (d)	P=0.309N	P=0.345	P=0.756N	P=0.529N
Cochran-Armitage Trend Test (d)	P=0.232N			
Fisher Exact Test (d)		P=0.359	P=0.516N	P=0.492N

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Thyroid Gland: Follicular Cell Adenoma				
Overall Rates (a)	3/49 (6%)	0/50 (0%)	0/48 (0%)	0/45 (0%)
Adjusted Rates (b)	8.6%	0.0%	0.0%	0.0%
Terminal Rates (c)	3/35 (9%)	0/37 (0%)	0/36 (0%)	0/23 (0%)
Week of First Observation	105			
Life Table Tests (d)	P=0.061N	P=0.111N	P=0.116N	P=0.204N
Incidental Tumor Tests (d)	P=0.061N	P=0.111N	P=0.116N	P=0.204N
Cochran-Armitage Trend Test (d)	P=0.051N			
Fisher Exact Test (d)		P=0.117N	P=0.125N	P=0.137N
Mammary Gland: Adenocarcinoma				
Overall Rates (a)	1/50 (2%)	1/50 (2%)	4/49 (8%)	1/49 (2%)
Adjusted Rates (b)	2.8%	2.2%	9.9%	2.1%
Terminal Rates (c)	1/36 (3%)	0/37 (0%)	2/37 (5%)	0/23 (0%)
Week of First Observation	105	82	95	64
Life Table Tests (d)	P=0.416	P=0.754	P=0.196	P=0.707
Incidental Tumor Tests (d)	P=0.580N	P=0.743	P=0.185	P=0.743N
Cochran-Armitage Trend Test (d)	P=0.517			
Fisher Exact Test (d)		P=0.753	P=0.175	P=0.747
Uterus: Endometrial Stromal Polyp				
Overall Rates (a)	2/50 (4%)	0/50 (0%)	3/47 (6%)	1/48 (2%)
Adjusted Rates (b)	5.2%	0.0%	8.1%	4.3%
Terminal Rates (c)	1/36 (3%)	0/37 (0%)	3/37 (8%)	1/23 (4%)
Week of First Observation	98		105	105
Life Table Tests (d)	P=0.532	P=0.237N	P=0.510	P=0.628N
Incidental Tumor Tests (d)	P=0.597	P=0.297N	P=0.510	P=0.542N
Cochran-Armitage Trend Test (d)	P=0.574N			
Fisher Exact Test (d)		P=0.247N	P=0.470	P=0.515N
Uterus: Adenoma				
Overall Rates (a)	0/50 (0%)	1/50 (2%)	1/47 (2%)	6/48 (13%)
Adjusted Rates (b)	0.0%	2.4%	2.7%	22.3%
Terminal Rates (c)	0/36 (0%)	0/37 (0%)	1/37 (3%)	4/23 (17%)
Week of First Observation		97	105	85
Life Table Tests (d)	P<0.001	P=0.505	P=0.505	P=0.005
Incidental Tumor Tests (d)	P=0.002	P=0.388	P=0.505	P=0.011
Cochran-Armitage Trend Test (d)	P=0.001			
Fisher Exact Test (d)		P=0.500	P=0.485	P=0.012
Uterus: Adenocarcinoma				
Overall Rates (a)	0/50 (0%)	2/50 (4%)	3/47 (6%)	19/48 (40%)
Adjusted Rates (b)	0.0%	5.3%	8.1%	57.8%
Terminal Rates (c)	0/36 (0%)	1/37 (3%)	3/37 (8%)	10/23 (43%)
Week of First Observation		102	105	86
Life Table Tests (d)	P<0.001	P=0.249	P=0.126	P<0.001
Incidental Tumor Tests (d)	P<0.001	P=0.182	P=0.126	P<0.001
Cochran-Armitage Trend Test (d)	P<0.001			
Fisher Exact Test (d)		P=0.247	P=0.110	P<0.001
Uterus: Squamous Cell Carcinoma				
Overall Rates (a)	0/50 (0%)	1/50 (2%)	1/47 (2%)	3/48 (6%)
Adjusted Rates (b)	0.0%	2.6%	2.7%	9.8%
Terminal Rates (c)	0/36 (0%)	0/37 (0%)	1/37 (3%)	1/23 (4%)
Week of First Observation		101	105	82
Life Table Tests (d)	P=0.026	P=0.511	P=0.505	P=0.079
Incidental Tumor Tests (d)	P=0.106	P=0.388	P=0.505	P=0.160
Cochran-Armitage Trend Test (d)	P=0.050			
Fisher Exact Test (d)		P=0.500	P=0.485	P=0.114

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
Uterus: Adenoma or Adenocarcinoma				
Overall Rates (a)	0/50 (0%)	3/50 (6%)	4/47 (9%)	25/48 (52%)
Adjusted Rates (b)	0.0%	7.6%	10.8%	72.5%
Terminal Rates (c)	0/36 (0%)	1/37 (3%)	4/37 (11%)	14/23 (61%)
Week of First Observation		97	105	85
Life Table Tests (d)	P<0.001	P=0.130	P=0.066	P<0.001
Incidental Tumor Tests (d)	P<0.001	P=0.060	P=0.066	P<0.001
Cochran-Armitage Trend Test (d)	P<0.001			
Fisher Exact Test (d)		P=0.121	P=0.051	P<0.001
Uterus: Adenocarcinoma or Squamous Cell Carcinoma				
Overall Rates (a)	0/50 (0%)	3/50 (6%)	4/47 (9%)	22/48 (46%)
Adjusted Rates (b)	0.0%	7.7%	10.8%	63.2%
Terminal Rates (c)	0/36 (0%)	1/37 (3%)	4/37 (11%)	11/23 (48%)
Week of First Observation		101	105	82
Life Table Tests (d)	P<0.001	P=0.132	P=0.066	P<0.001
Incidental Tumor Tests (d)	P<0.001	P=0.060	P=0.066	P<0.001
Cochran-Armitage Trend Test (d)	P<0.001			
Fisher Exact Test (d)		P=0.121	P=0.051	P<0.001
Uterus: Adenoma, Adenocarcinoma, or Squamous Cell Carcinoma				
Overall Rates (a)	0/50 (0%)	4/50 (8%)	5/47 (11%)	27/48 (56%)
Adjusted Rates (b)	0.0%	9.9%	13.5%	74.1%
Terminal Rates (c)	0/36 (0%)	1/37 (3%)	5/37 (14%)	14/23 (61%)
Week of First Observation		97	105	82
Life Table Tests (d)	P<0.001	P=0.072	P=0.035	P<0.001
Incidental Tumor Tests (d)	P<0.001	P=0.017	P=0.035	P<0.001
Cochran-Armitage Trend Test (d)	P<0.001			
Fisher Exact Test (d)		P=0.059	P=0.024	P<0.001
All Sites: Benign Tumors				
Overall Rates (a)	13/50 (26%)	10/50 (20%)	12/49 (24%)	12/49 (24%)
Adjusted Rates (b)	30.7%	25.1%	32.4%	41.1%
Terminal Rates (c)	8/36 (22%)	8/37 (22%)	12/37 (32%)	7/23 (30%)
Week of First Observation	90	46	105	85
Life Table Tests (d)	P=0.177	P=0.320N	P=0.479N	P=0.295
Incidental Tumor Tests (d)	P=0.443	P=0.304N	P=0.429	P=0.549N
Cochran-Armitage Trend Test (d)	P=0.530			
Fisher Exact Test (d)		P=0.318N	P=0.523N	P=0.523N
All Sites: Malignant Tumors				
Overall Rates (a)	20/50 (40%)	17/50 (34%)	20/49 (41%)	31/49 (63%)
Adjusted Rates (b)	43.0%	37.3%	43.3%	76.8%
Terminal Rates (c)	10/36 (28%)	9/37 (24%)	11/37 (30%)	14/23 (61%)
Week of First Observation	84	73	37	64
Life Table Tests (d)	P<0.001	P=0.367N	P=0.552N	P=0.002
Incidental Tumor Tests (d)	P=0.036	P=0.498N	P=0.363	P=0.049
Cochran-Armitage Trend Test (d)	P=0.004			
Fisher Exact Test (d)		P=0.340N	P=0.548	P=0.017
All Sites: All Tumors				
Overall Rates (a)	27/50 (54%)	24/50 (48%)	27/49 (55%)	37/49 (76%)
Adjusted Rates (b)	57.1%	51.8%	58.6%	90.0%
Terminal Rates (c)	16/36 (44%)	15/37 (41%)	18/37 (49%)	19/23 (83%)
Week of First Observation	84	46	37	64
Life Table Tests (d)	P<0.001	P=0.370N	P=0.539N	P=0.001
Incidental Tumor Tests (d)	P=0.026	P=0.410N	P=0.309	P=0.031
Cochran-Armitage Trend Test (d)	P=0.007			
Fisher Exact Test (d)		P=0.345N	P=0.537	P=0.021

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor 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 that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is reported because no tumors were observed in the 400-ppm and control groups.

TABLE D4a. HISTORICAL INCIDENCE OF UTERINE TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence of Adenomas or Adenocarcinomas in Controls
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories	
Propylene oxide	0/48
Methyl methacrylate	3/48
Propylene	0/47
1,2-Epoxybutane	0/50
Dichloromethane	1/50
Ethylene oxide	0/49
Tetrachloroethylene	0/43
TOTAL	(b) 4/335 (1.2%)
SD (c)	2.36%
Range (d)	
High	3/48
Low	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	(e) 5/2,011 (0.2%)
SD (c)	0.68%
Range (d)	
High	1/47
Low	0/50

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Adenocarcinomas, NOS
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.
(e) Includes one adenoma, NOS, and four adenocarcinomas, NOS; one squamous cell carcinoma was also observed.

TABLE D4b. HISTORICAL INCIDENCE OF NASAL CAVITY TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

	Incidence of Adenomas or Adenocarcinomas in Controls
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories	
TOTAL	0/348
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	0/2,040

(a) Data as of April 29, 1987, for studies of at least 104 weeks

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE

	Chamber Control	100 ppm	200 ppm	400 ppm
Animals initially in study	50	50	50	50
Animals necropsied	50	50	49	49
Animals examined histopathologically	50	50	49	49
INTEGUMENTARY SYSTEM				
*Skin	(50)	(50)	(49)	(49)
Inflammation, acute/chronic				1 (2%)
Alopecia		5 (10%)	1 (2%)	
Hyperkeratosis	1 (2%)			
*Subcutaneous tissue	(50)	(50)	(49)	(49)
Edema, NOS				1 (2%)
RESPIRATORY SYSTEM				
#Nasal cavity	(50)	(50)	(48)	(49)
Inflammation, serous	4 (8%)	1 (2%)	1 (2%)	
Inflammation, suppurative		2 (4%)		
#Maxillary sinus	(50)	(50)	(48)	(49)
Inflammation, suppurative		1 (2%)		
#Lung	(50)	(50)	(49)	(49)
Mineralization		1 (2%)		
Atelectasis				1 (2%)
Congestion, NOS		1 (2%)	2 (4%)	
Edema, NOS		1 (2%)		
Hemorrhage	2 (4%)			1 (2%)
Lymphocytic inflammatory infiltrate	3 (6%)	3 (6%)	3 (6%)	1 (2%)
Inflammation, interstitial	1 (2%)	1 (2%)		
Inflammation, acute/chronic	1 (2%)	1 (2%)	4 (8%)	6 (12%)
Hyperplasia, alveolar epithelium	1 (2%)		1 (2%)	1 (2%)
Histiocytosis		1 (2%)		
HEMATOPOIETIC SYSTEM				
*Multiple organs	(50)	(50)	(49)	(49)
Hematopoiesis				2 (4%)
#Bone marrow	(50)	(50)	(48)	(49)
Hyperplasia, granulocytic	1 (2%)	1 (2%)	1 (2%)	3 (6%)
#Spleen	(50)	(49)	(48)	(49)
Hemosiderosis	1 (2%)			1 (2%)
Angiectasis	1 (2%)			
Hyperplasia, hematopoietic	2 (4%)	4 (8%)	4 (8%)	7 (14%)
Hyperplasia, reticulum cell				1 (2%)
Hyperplasia, lymphoid	1 (2%)	2 (4%)	2 (4%)	1 (2%)
#Mandibular lymph node	(49)	(49)	(48)	(49)
Hemorrhage	1 (2%)			
Hyperplasia, reticulum cell	1 (2%)			
Hyperplasia, lymphoid		2 (4%)	5 (10%)	
#Bronchial lymph node	(49)	(49)	(48)	(49)
Hyperplasia, plasma cell				1 (2%)
Hyperplasia, lymphoid	1 (2%)		1 (2%)	2 (4%)
#Mediastinal lymph node	(49)	(49)	(48)	(49)
Inflammation, acute/chronic				1 (2%)
#Pancreatic lymph node	(49)	(49)	(48)	(49)
Mastocytosis	1 (2%)			
#Mesenteric lymph node	(49)	(49)	(48)	(49)
Inflammation, suppurative			1 (2%)	
Abscess, NOS				1 (2%)
Hyperplasia, lymphoid		1 (2%)		1 (2%)
#Renal lymph node	(49)	(49)	(48)	(49)
Hyperplasia, lymphoid			1 (2%)	

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
HEMATOPOIETIC SYSTEM (Continued)				
#Liver	(50)	(50)	(49)	(49)
Leukemoid reaction		1 (2%)		1 (2%)
Hematopoiesis		1 (2%)		3 (6%)
#Thymus	(45)	(43)	(42)	(36)
Cyst, NOS	1 (2%)			
CIRCULATORY SYSTEM				
#Mandibular lymph node	(49)	(49)	(48)	(49)
Lymphangiectasis	1 (2%)			
#Heart	(50)	(50)	(49)	(49)
Hemorrhage				1 (2%)
Inflammation, acute/chronic		2 (4%)		
Endocardiosis	1 (2%)			
#Cardiac valve	(50)	(50)	(49)	(49)
Inflammation, suppurative				1 (2%)
#Hepatic sinusoid	(50)	(50)	(49)	(49)
Dilatation, NOS		2 (4%)	13 (27%)	10 (20%)
#Uterus	(50)	(50)	(47)	(48)
Thrombosis, NOS	1 (2%)	1 (2%)	1 (2%)	
DIGESTIVE SYSTEM				
*Pulp of tooth	(50)	(50)	(49)	(49)
Inflammation, suppurative	1 (2%)			
#Salivary gland	(48)	(49)	(48)	(46)
Inflammation, acute/chronic	1 (2%)			
#Liver	(50)	(50)	(49)	(49)
Torsion				1 (2%)
Congestion, NOS	1 (2%)	2 (4%)		
Hemorrhagic cyst				1 (2%)
Inflammation, acute/chronic	1 (2%)	1 (2%)	2 (4%)	
Necrosis, focal	3 (6%)	3 (6%)		2 (4%)
Focal cellular change	2 (4%)	2 (4%)	8 (16%)	7 (14%)
#Pancreas	(50)	(50)	(48)	(49)
Cystic ducts		1 (2%)		2 (4%)
#Pancreatic duct	(50)	(50)	(48)	(49)
Inflammation, chronic	1 (2%)			
#Pancreatic acinus	(50)	(50)	(48)	(49)
Atrophy, NOS				2 (4%)
#Stomach	(50)	(49)	(48)	(49)
Pigmentation, NOS	1 (2%)			1 (2%)
#Glandular stomach	(50)	(49)	(48)	(49)
Mineralization		1 (2%)		
Dilatation, NOS	1 (2%)			
#Gastric serosa	(50)	(49)	(48)	(49)
Inflammation, suppurative		1 (2%)		
#Forestomach	(50)	(49)	(48)	(49)
Erosion				2 (4%)
Hyperkeratosis	1 (2%)	1 (2%)	3 (6%)	7 (14%)
Acanthosis				3 (6%)
#Ileum	(50)	(49)	(47)	(49)
Amyloidosis	2 (4%)	1 (2%)		
*Rectum	(50)	(50)	(49)	(49)
Inflammation, suppurative			1 (2%)	
URINARY SYSTEM				
#Kidney	(50)	(50)	(49)	(49)
Mineralization				1 (2%)
Hydronephrosis	1 (2%)	1 (2%)		3 (6%)
Cyst, NOS			1 (2%)	

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
URINARY SYSTEM				
#Kidney (Continued)	(50)	(50)	(49)	(49)
Lymphocytic inflammatory infiltrate		1 (2%)		
Inflammation, suppurative		1 (2%)		
Inflammation, acute/chronic	1 (2%)		1 (2%)	1 (2%)
Glomerulonephritis, chronic			1 (2%)	
Pyelonephritis, chronic				1 (2%)
Fibrosis, focal		1 (2%)		
Atrophy, NOS				2 (4%)
Metaplasia, osseous	1 (2%)			
#Kidney/glomerulus	(50)	(50)	(49)	(49)
Infarct, acute				1 (2%)
#Kidney/tubule	(50)	(50)	(49)	(49)
Dilatation, NOS				1 (2%)
Cast, NOS	2 (4%)	1 (2%)		4 (8%)
Cyst, NOS	1 (2%)			
Nephrosis, NOS				1 (2%)
Necrosis, NOS	1 (2%)			
Pigmentation, NOS		1 (2%)		
#Urinary bladder	(48)	(50)	(45)	(49)
Dilatation, NOS				1 (2%)
ENDOCRINE SYSTEM				
#Pituitary	(48)	(50)	(46)	(49)
Hyperplasia, NOS	4 (8%)	4 (8%)	4 (9%)	
Angiectasis				1 (2%)
#Adrenal cortex	(50)	(50)	(48)	(49)
Cyst, NOS		1 (2%)		
Hyperplasia, focal		1 (2%)		
#Thyroid	(49)	(50)	(48)	(45)
Cyst, NOS				1 (2%)
Inflammation, suppurative		1 (2%)		
Hyperplasia, C-cell	1 (2%)			
Hyperplasia, follicular cell		1 (2%)		3 (7%)
REPRODUCTIVE SYSTEM				
*Mammary gland	(50)	(50)	(49)	(49)
Fibrosis, focal				1 (2%)
*Clitoral gland	(50)	(50)	(49)	(49)
Inflammation, suppurative				1 (2%)
#Uterus	(50)	(50)	(47)	(48)
Dilatation, NOS		1 (2%)		
Inflammation, suppurative		2 (4%)	1 (2%)	5 (10%)
Angiectasis		1 (2%)		
Adenomyosis	2 (4%)		3 (6%)	5 (10%)
#Cervix uteri	(50)	(50)	(47)	(48)
Inflammation, suppurative				1 (2%)
#Uterus/endometrium	(50)	(50)	(47)	(48)
Congestion, NOS		1 (2%)		
Hemorrhage	1 (2%)		1 (2%)	
Hyperplasia, NOS	6 (12%)	4 (8%)	6 (13%)	6 (13%)
#Ovary	(49)	(50)	(46)	(45)
Mineralization		1 (2%)		
Cyst, NOS	11 (22%)	11 (22%)	3 (7%)	6 (13%)
Multiple cysts	1 (2%)			
Hemorrhagic cyst	1 (2%)		1 (2%)	
Inflammation, suppurative		2 (4%)	1 (2%)	2 (4%)
Inflammation, hemorrhagic		1 (2%)		

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
REPRODUCTIVE SYSTEM				
#Ovary (Continued)	(49)	(50)	(46)	(45)
Abscess, NOS		2 (4%)	2 (4%)	3 (7%)
Atrophy, NOS	1 (2%)			1 (2%)
Angiectasis	1 (2%)			
NERVOUS SYSTEM				
#Brain	(50)	(50)	(48)	(49)
Mineralization	10 (20%)	14 (28%)	12 (25%)	10 (20%)
Inflammation, suppurative	1 (2%)			
Inflammation, acute/chronic			1 (2%)	
Infection, bacterial				1 (2%)
Necrosis, hemorrhagic	1 (2%)			
*Spinal cord	(50)	(50)	(49)	(49)
Hematoma, NOS	1 (2%)			
Lymphocytic inflammatory infiltrate				1 (2%)
*Sciatic nerve	(50)	(50)	(49)	(49)
Lymphocytic inflammatory infiltrate	3 (6%)		1 (2%)	1 (2%)
Inflammation, acute/chronic				1 (2%)
SPECIAL SENSE ORGANS				
None				
MUSCULOSKELETAL SYSTEM				
*Joint	(50)	(50)	(49)	(49)
Healed fracture		1 (2%)		
*Muscle hip/thigh	(50)	(50)	(49)	(49)
Lymphocytic inflammatory infiltrate				1 (2%)
Fibrosis				1 (2%)
Degeneration, NOS				1 (2%)
BODY CAVITIES				
*Peritoneum	(50)	(50)	(49)	(49)
Inflammation, suppurative		2 (4%)	1 (2%)	4 (8%)
Inflammation, acute/chronic			1 (2%)	
*Peritoneal cavity	(50)	(50)	(49)	(49)
Inflammation, suppurative				1 (2%)
*Pleural cavity	(50)	(50)	(49)	(49)
Inflammation, suppurative		1 (2%)	1 (2%)	1 (2%)
*Epicardium	(50)	(50)	(49)	(49)
Inflammation, acute/chronic				1 (2%)
*Mesentery	(50)	(50)	(49)	(49)
Inflammation, granulomatous			1 (2%)	
Necrosis, fat			2 (4%)	
ALL OTHER SYSTEMS				
*Multiple organs	(50)	(50)	(49)	(49)
Congestion, NOS	1 (2%)			
Lymphocytic inflammatory infiltrate	1 (2%)			
Inflammation, acute/chronic				1 (2%)
Adipose tissue				
Inflammation, granulomatous	1			
Omentum				
Lymphocytic inflammatory infiltrate			1	

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF BROMOETHANE (Continued)

	Chamber Control	100 ppm	200 ppm	400 ppm
SPECIAL MORPHOLOGY SUMMARY				
No lesion reported	2	3	2	1
Animal missexed/no necropsy			1	1

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
# Number of animals examined microscopically at this site

APPENDIX E

RESULTS OF SEROLOGIC ANALYSIS

APPENDIX E. RESULTS OF SEROLOGIC ANALYSIS

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.

A few F344/N rats from each exposure group were bled from the tail during month 1; rats from groups exposed at 0, 100, or 200 ppm were bled from the tail during month 15, and blood was also collected from one moribund rat at months 13 and 15. Blood was obtained from 11 moribund mice between months 15 and 23. Data from animals surviving 24 months were collected from 5/50 randomly selected control animals of each sex and species. The blood from each animal was collected and clotted, and the serum was separated. The serum was cooled on ice and shipped to Microbiological Associates' Comprehensive Animal Diagnostic Service for determination of the antibody titers. The following tests were performed:

	Hemagglutination Inhibition	Complement Fixation	ELISA
Mice	PVM (pneumonia virus of mice) Reo 3 (reovirus type 3) GDVII (Theiler's encephalomyelitis virus) Poly (polyoma virus) MVM (minute virus of mice) Ectro (infectious ectromelia) Sendai	M. Ad. (mouse adenovirus) LCM (lymphocytic choriomeningitis virus)	MHV (mouse hepatitis virus)
Rats	PVM (15,24 mo) KRV (Kilham rat virus) (15,24 mo) H-1 (Toolan's H-1 virus) (15,24 mo) Sendai (1,13,15,24 mo)	RCV (15 mo)	RCV/SDA (rat coronavirus/sialodacryoadenitis virus) (24 mo) *M. pul.* (*Mycoplasma pulmonis*) (24 mo)

Results

Results are presented in Table E1.

TABLE E1. MURINE ANTIBODY DETERMINATIONS FOR RATS AND MICE IN THE TWO-YEAR INHALATION STUDIES OF BROMOETHANE (a)

Interval (months)	Number of Animals	Positive Serologic Reaction for
RATS		
1	0/16	None positive
13-15	10/10	PVM
	1/10	KRV
	6/10	RCV
24	10/10	PVM
	8/10	RCV/SDA
MICE		
15	1/1	PVM
19-21	1/5	PVM
22-23	2/5	PVM
24	9/10	PVM

(a) Blood samples were taken from control animals just before they were killed; samples were sent to Microbiological Associates (Bethesda, MD) for determination of antibody titers.

APPENDIX F

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

Pelleted Diet: November 1981 to December 1983

(Manufactured by Zeigler Bros., Inc., Gardners, PA)

TABLE F1. 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 ground to pass through a U.S. Standard Screen No. 16 before being mixed

TABLE F2. 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 F3. NUTRIENT COMPOSITION OF NIH 07 RAT AND MOUSE RATION

Nutrients	Mean ± Standard Deviation	Range	Number of Samples
Protein (percent by weight)	23.59 ± 0.94	22.2-26.3	26
Crude fat (percent by weight)	4.96 ± 0.52	3.3-5.7	26
Crude fiber (percent by weight)	3.39 ± 0.52	2.9-5.6	26
Ash (percent by weight)	6.51 ± 0.49	5.7-7.3	26
Amino Acids (percent of total diet)			
Arginine	1.32 ± 0.072	1.310-1.390	5
Cystine	0.319 ± 0.088	0.218-0.400	5
Glycine	1.146 ± 0.063	1.060-1.210	5
Histidine	0.571 ± 0.026	0.531-0.603	5
Isoleucine	0.914 ± 0.030	0.881-0.944	5
Leucine	1.946 ± 0.056	1.850-1.990	5
Lysine	1.280 ± 0.067	1.200-1.370	5
Methionine	0.436 ± 0.165	0.306-0.699	5
Phenylalanine	0.938 ± 0.158	0.665-1.05	5
Threonine	0.855 ± 0.035	0.824-0.898	5
Tryptophan	0.277 ± 0.221	0.156-0.671	5
Tyrosine	0.618 ± 0.086	0.564-0.769	5
Valine	1.108 ± 0.043	1.050-1.170	5
Essential Fatty Acids (percent of total diet)			
Linoleic	2.290 ± 0.313	1.83-2.52	5
Linolenic	0.258 ± 0.040	0.210-0.308	5
Vitamins			
Vitamin A (IU/kg)	12,084 ± 4,821	3,600-24,000	26
Vitamin D (IU/kg)	4,450 ± 1,382	3,000-6,300	4
α-Tocopherol (ppm)	43.58 ± 6.92	31.1-48.0	5
Thiamine (ppm)	16.9 ± 2.42	12.0-21.0	26
Riboflavin (ppm)	7.6 ± 0.85	6.10-8.2	5
Niacin (ppm)	97.8 ± 31.68	65.0-150.0	5
Pantothenic acid (ppm)	30.06 ± 4.31	23.0-34.0	5
Pyridoxine (ppm)	7.68 ± 1.31	5.60-8.8	5
Folic acid (ppm)	2.62 ± 0.89	1.80-3.7	5
Biotin (ppm)	0.254 ± 0.053	0.19-0.32	5
Vitamin B_{12} (ppb)	24.21 ± 12.66	10.6-38.0	5
Choline (ppm)	3,122 ± 416.8	2,400-3,430	5
Minerals			
Calcium (percent)	1.30 ± 0.13	1.11-1.63	26
Phosphorus (percent)	0.97 ± 0.05	0.88-1.10	26
Potassium (percent)	0.900 ± 0.098	0.772-0.971	3
Chloride (percent)	0.513 ± 0.114	0.380-0.635	5
Sodium (percent)	0.323 ± 0.043	0.258-0.371	5
Magnesium (percent)	0.167 ± 0.012	0.151-0.181	5
Sulfur (percent)	0.304 ± 0.064	0.268-0.420	5
Iron (ppm)	410.3 ± 94.04	262.0-523.0	5
Manganese (ppm)	90.29 ± 7.15	81.7-99.4	5
Zinc (ppm)	52.78 ± 4.94	46.1-58.2	5
Copper (ppm)	10.72 ± 2.76	8.09-15.39	5
Iodine (ppm)	2.95 ± 1.05	1.52-3.82	4
Chromium (ppm)	1.85 ± 0.25	1.44-2.09	5
Cobalt (ppm)	0.681 ± 0.14	0.490-0.780	4

TABLE F4. CONTAMINANT LEVELS IN NIH 07 RAT AND MOUSE RATION

Contaminants	Mean ± Standard Deviation	Range	Number of Samples
Arsenic (ppm)	0.52 ± 0.13	0.29-0.77	26
Cadmium (ppm) (a)	<0.10		26
Lead (ppm)	0.76 ± 0.62	0.33-3.37	26
Mercury (ppm) (a)	<0.05		26
Selenium (ppm)	0.29 ± 0.07	0.13-0.40	26
Aflatoxins (ppb) (a)	<5.0		26
Nitrate nitrogen (ppm) (b)	8.66 ± 4.47	0.10-22.0	26
Nitrite nitrogen (ppm) (b)	2.16 ± 1.97	0.10-7.20	26
BHA (ppm) (c)	4.63 ± 4.74	2.0-17.0	26
BHT (ppm) (c)	2.67 ± 2.58	0.9-12.0	26
Aerobic plate count (CFU/g) (d)	41,212 ± 34,610	4,900-130,000	26
Coliform (MPN/g) (e)	48.42 ± 123	3.0-460	26
E. coli (MPN/g) (a)	<3.0		26
Total nitrosamines (ppb) (f)	5.25 ± 5.80	1.7-30.9	26
N-Nitrosodimethylamine (ppb) (f)	4.12 ± 5.83	0.8-30.0	26
N-Nitrosopyrrolidine (ppb) (f)	1.13 ± 0.46	0.81-2.9	26
Pesticides (ppm)			
α-BHC (a,g)	<0.01		26
β-BHC (a)	<0.02		26
γ-BHC-Lindane (a)	<0.01		26
δ-BHC (a)	<0.01		26
Heptachlor (a)	<0.01		26
Aldrin (a)	<0.01		26
Heptachlor epoxide (a)	<0.01		26
DDE (a)	<0.01		26
DDD (a)	<0.01		26
DDT (a)	<0.01		26
HCB (a)	<0.01		26
Mirex (a)	<0.01		26
Methoxychlor (a)	<0.05		26
Dieldrin (a)	<0.01		26
Endrin (a)	<0.01		26
Telodrin (a)	<0.01		26
Chlordane (a)	<0.05		26
Toxaphene (a)	<0.1		26
Estimated PCBs (a)	<0.2		26
Ronnel (a)	<0.01		26
Ethion (a)	<0.02		26
Trithion (a)	<0.05		26
Diazinon (a)	<0.1		26
Methyl parathion (a)	<0.02		26
Ethyl parathion (a)	<0.02		26
Malathion (h)	0.10 ± 0.09	0.05-0.45	26
Endosulfan I (a)	<0.01		26
Endosulfan II (a)	<0.01		25
Endosulfan sulfate (a)	<0.03		26

(a) All values were less than the detection limit, given in the table as the mean.
(b) Source of contamination: alfalfa, grains, and fish meal
(c) Source of contamination: soy oil and fish meal
(d) CFU = colony-forming unit
(e) MPN = most probable number
(f) All values were corrected for percent recovery.
(g) BHC = hexachlorocyclohexane or benzene hexachloride
(h) Thirteen lots contained more than 0.05 ppm.

APPENDIX G

AUDIT SUMMARY

APPENDIX G. AUDIT SUMMARY

The pathology specimens, experimental data, study documents, and the draft NTP Technical Report No. 363 (April 1988) for the 2-year studies of bromoethane in rats and mice were audited for the National Institute of Environmental Health Sciences (NIEHS) at the National Toxicology Program (NTP) Archives by Argus Research Laboratories, Inc., and Dynamac Corporation. The audit included a review of the following:

(1) All records concerning animal receipt, quarantine, randomization, and disposition prior to study start.
(2) All inlife records, including protocol, correspondence, animal husbandry, environmental conditions, dosing, external masses, mortality, animal identification, and serology.
(3) Body weight and clinical observation data; all data were scanned before a random 10% sample of animals in each study group was reviewed in detail.
(4) All chemistry records.
(5) All post mortem records for individual animals concerning date of death, disposition codes, condition codes, tissue accountability, correlation of masses or clinical signs recorded at the last inlife observation with gross observations and microscopic diagnoses, and correlations between gross observations and microscopic diagnoses.
(6) All wet tissue bags for inventory and wet tissues from a random 20% sample of animals in each study group, plus other relevant cases, to evaluate the integrity of individual animal identity and to examine for untrimmed potential lesions.
(7) Blocks and slides of tissues from a random 20% sample of animals from each study group, plus animals with less than complete or correct identification.
(8) Necropsy record forms for data entry errors and all microscopic diagnosis updates for a random 20% sample of animals to verify their incorporation into the final pathology tables.
(9) Correlation between the data, factual information, and procedures for the 2-year studies presented in the draft of the Technical Report and the records available at the NTP Archives.

Procedures and events during the exposure phase of the studies were documented adequately by the archival records, with the exception of the disposition of extra animals before the study start. Review of data from the entire exposure phase indicated that laboratory animal care procedures were effective and consistent during the course of the studies. Records documented that animal exposures were conducted according to protocols. Recalculation of 112 group mean body weight values revealed all to be correct. Observations of clinical signs and masses for individual animals were made consistently, and records showed that they were reviewed at the time of necropsy. Of the masses noted in the inlife records, 91/98 in rats and 15/19 in mice correlated with necropsy observations. Survival records for all animals were reviewed and found to be correct, except for the date of death for two rats and one mouse which differed by 1 day in each case between the inlife and necropsy records; wet tissue examination revealed correct identification for these animals. These differences had no impact on the number of survivors reported for each study group or on the overall survival data.

Review of the pathology specimens showed that identifiers (ear tags) were saved and read correctly for all 87 rats examined and 90/92 mice examined. The review of residual wet tissues and data trails for the two mice with missing ear tags provided evidence that the integrity of individual animal identity had been preserved throughout the studies. The archival records showed that animals were inspected and occasionally found without tags during the studies; such animals were retagged with originally assigned numbers. Inspection of the residual wet tissues for 87 rats and 92 mice detected untrimmed potential lesions in different nontarget organs of 2 rats and 1 mouse. Tissue accountability was reduced for some organs, and there were 19 blocks from rats and 25 from mice that were not cut full face; however, all gross observations were correlated with microscopic diagnoses, except for three in rats and one in mice.

Full details about these and other audit findings are presented in audit reports that are on file at the NIEHS. In conclusion, the data and factual information in the preliminary draft of the Technical Report are supported by the study records at the NTP Archives.

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