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TOXICOLOGY AND CARCINOGENESIS STUDIES OF CHLOROETHANE

(ETHYL CHLORIDE)

(CAS NO. 75-00-3)

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 CHLOROETHANE

(ETHYL CHLORIDE)

(CAS NO. 75-00-3)

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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CH_3CH_2Cl

CHLOROETHANE

(ETHYL CHLORIDE)

CAS No. 75-00-3

C_2H_5Cl Molecular weight 64.5

Synonyms: Monochloroethane; chloroethyl; ether hydrochloric; ether muriatic; aethylis; aethylis chloridum; ether chloridum; ether chloratus

Trade names: Kelene; Chelen; Anodynon; Chloryl Anesthetic; Narcotile

ABSTRACT

Toxicology and carcinogenesis studies of chloroethane (99.5% pure), an alkylating agent and chemical intermediate, as well as a topical and inhalation anesthetic, were conducted by exposing groups of F344/N rats and B6C3F$_1$ mice of each sex to chloroethane by whole-body inhalation once for 4 hours or for 6 hours per day, 5 days per week for 14 days, 13 weeks, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*.

Single-Exposure, Fourteen-Day, and Thirteen-Week Studies: In the single-exposure and 14-day inhalation studies, all rats and mice exposed to 19,000 ppm chloroethane survived. The animals were not exposed at lower concentrations. No clinical signs of toxicity were seen. In the 14-day studies, final mean body weights of exposed male rats and exposed mice were higher than those of controls. Mean body weights of exposed and control female rats were similar.

In the 13-week studies, rats and mice were exposed to 0, 2,500, 5,000, 10,000, or 19,000 ppm chloroethane. No compound-related deaths occurred in rats or mice. The final mean body weight of rats exposed to 19,000 ppm was 8% lower than that of controls for males and 4% lower for females. Final mean body weights of exposed mice were generally higher than those of controls. No compound-related clinical signs or gross or microscopic pathologic effects were seen in rats or mice. The liver weight to body weight ratios for male rats and female mice exposed to 19,000 ppm were greater than those for controls. Although no chemically related toxic effects were observed in the short-term studies, concerns about potential flammability and explosion led to the selection of 0 and 15,000 ppm as the exposure concentrations for rats and mice for the 2-year studies.

Body Weight and Survival in the Two-Year Studies: Mean body weights of exposed male rats were 4%-8% lower than those of controls after week 33. Mean body weights of exposed female rats were generally 5%-13% lower than those of controls throughout the study. Although survival of male rats and exposed female rats was low at the end of the studies (male: control, 16/50; exposed, 8/50; female: 31/50; 22/50), no statistically significant differences in survival were observed between exposed and control groups of either sex. Survival at week 90 for male rats was 37/50 (control) and 31/50 (exposed) and for females, 43/50 (control) and 33/50 (exposed). The high incidence of mononuclear cell leukemia may have contributed to the high mortality.

Mean body weights of exposed male mice were up to 13% higher than those of controls throughout the study. Mean body weights of exposed and control female mice were generally similar throughout the study. The survival of the exposed groups of both male (after day 330) and female (after day 574) mice was significantly lower than that of controls (final survival--male: 28/50; 11/50; female: 32/50;

2/50). The majority of exposed female mice died as a result of uterine carcinomas. Male mice, and particularly exposed mice, died early as a result of an ascending urinary tract infection.

Nonneoplastic and Neoplastic Effects in the Two-Year Studies: Malignant astrocytomas of the brain were seen in three exposed female rats, and gliosis was observed in a fourth. The historical incidence of glial cell neoplasms in untreated control female F344/N rats is 23/1,969. The highest incidence observed in an untreated control group is 3/50.

Trichoepitheliomas (1/50), sebaceous gland adenomas (1/50), basal cell carcinomas (3/50), and squamous cell carcinomas (2/50) of the skin were observed only in exposed male rats. Keratoacanthomas occurred in four control and two exposed male rats.

Exposure of female mice to chloroethane caused a high incidence of uterine carcinomas of endometrial origin (control, 0/49; exposed, 43/50). One control female did have a uterine carcinoma, although it was not of endometrial origin. The tumors observed in 34 exposed females were highly malignant, invading the uterine myometrium and metastasizing to a wide variety of organs, primarily lung (23), ovary (22), lymph nodes (18), kidney (8), adrenal gland (8), pancreas (7), mesentery (7), urinary bladder (7), spleen (5), and heart (4), and to a lesser extent, colon, stomach, gallbladder, small intestine, ureter, and liver.

Two marginally increased incidences of other neoplasms were observed in exposed male and female mice. The incidence of hepatocellular carcinomas in exposed female mice was greater than that in controls (3/49; 7/48). One other exposed female had a hepatocellular adenoma. The incidence of alveolar/bronchiolar neoplasms of the lung in exposed male mice was greater than that in controls (adenomas or carcinomas, combined: 5/50; 10/48).

Genetic Toxicology: Chloroethane, tested within the closed environment of a desiccator, was mutagenic with and without exogenous metabolic activation in *S. typhimurium* strain TA1535; in strain TA100, a positive response was observed only with activation. No mutagenic activity was observed in *S. typhimurium* strain TA98 with or without metabolic activation.

Conclusions: Under the conditions of these 2-year inhalation studies, there was *equivocal evidence of carcinogenic activity** of chloroethane for male F344/N rats, as indicated by benign and malignant epithelial neoplasms of the skin. For female F344/N rats, there was *equivocal evidence of carcinogenic activity*, as indicated by three uncommon malignant astrocytomas of the brain in the exposed group. The study in male $B6C3F_1$ mice was considered to be an *inadequate study of carcinogenicity* because of reduced survival in the exposed group. However, there was an increased incidence of alveolar/bronchiolar neoplasms of the lung. There was *clear evidence of carcinogenic activity* for female $B6C3F_1$ mice, as indicated by carcinomas of the uterus. A marginally increased incidence of hepatocellular neoplasms was observed in the exposed group.

*Explanation of Levels of Evidence of Carcinogenic Activity is on page 6.
A summary of the Peer Review comments and the public discussion on this Technical Report appears on page 9.

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

Male F344/N Rats	Female F344/N Rats	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Exposure concentrations			
0 or 15,000 ppm chloroethane in air, 6 h/d, 5 d/wk	0 or 15,000 ppm chloroethane in air, 6 h/d, 5 d/wk	0 or 15,000 ppm chloroethane in air, 6 h/d, 5 d/wk	0 or 15,000 ppm chloroethane in air, 6 h/d, 5 d/wk
Body weights in the 2-year study			
Lower in exposed group	Lower in exposed group	Higher in exposed group	Similar in exposed and control groups
Survival rates in the 2-year study			
16/50; 8/50	31/50; 22/50	28/50; 11/50	32/50; 2/50
Nonneoplastic effects			
None	None	None	None
Neoplastic effects			
Skin trichoepitheliomas, sebaceous gland adenomas, or basal cell carcinomas (combined) (0/50; 5/50)	Astrocytomas of the brain (0/50; 3/50)	None	Endometrial uterine carcinomas (0/49; 43/50)
Level of evidence of carcinogenic activity			
Equivocal evidence	Equivocal evidence	Inadequate study	Clear evidence
Other considerations			
	Gliosis (0/50; 1/50)	Reduced survival; alveolar/bronchiolar adenomas or carcinomas (combined) (5/50; 10/48)	Hepatocellular adenomas or carcinomas (combined) (3/49; 8/48)
Genetic toxicology			
	Salmonella (gene mutation) Positive 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 Chloroethane is based on 13-week studies that began in March 1981 and ended in June 1981 and on 2-year studies that began in March 1982 and ended in March 1984 at Battelle Pacific Northwest Laboratories (Richland, WA).

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PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the draft Technical Report on chloroethane 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 CHLOROETHANE

On October 3, 1988, the draft Technical Report on the toxicology and carcinogenesis studies of chloroethane 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, Research Triangle Park, NC.

Dr. J. Roycroft, NIEHS, began the discussion by reviewing the experimental design, results, and proposed conclusions (equivocal evidence of carcinogenic activity for male and female rats, inadequate study of carcinogenic activity for male mice, clear evidence of carcinogenic activity for female mice). Although no chemical-related toxic effects were observed in the short-term studies, concerns about potential flammability and explosion led to the selection of 0 and 15,000 ppm chloroethane as the exposure concentrations for rats and mice in the 2-year studies .

Dr. Newberne, a principal reviewer, agreed with the conclusions for female rats and male and female mice. He thought that the conclusion for male rats should be changed to no evidence of carcinogenic activity.

Dr. Mirer, a second principal reviewer, agreed with the conclusions in male and female rats and female mice, although he thought that the incidence of hepatocellular neoplasms in female mice should be considered part of the evidence also and not be designated as a marginal effect. He felt that an increased incidence of lung neoplasms in male mice was observed in spite of the high mortality and should be considered supportive of some evidence of carcinogenic activity. Dr. J. Haseman, NIEHS, said that the NTP did not consider the marginal increase in lung neoplasms to be clearly chemically related; thus, because of the reduced survival in the exposed group, the study was considered to be inadequate. Dr. J. Huff, NIEHS, commented that early mortality also decreased the sensitivity of the studies for detecting tumors that develop later in life. Dr. Mirer stated that the choice of a single exposure concentration compromised the ability of the studies to observe any dose response, given the overwhelming effect in female mice. Dr. Perera suggested adding a sentence to the Abstract explaining the selection of a single exposure concentration. Dr. Roycroft said that a single exposure concentration was chosen after no toxic effects were seen in 13-week studies at up to 19,000 ppm.

Dr. Newberne moved that the conclusion for male rats be changed to no evidence of carcinogenic activity. The motion was not seconded. Dr. Newberne then moved that the conclusion for male rats be accepted as written, equivocal evidence of carcinogenic activity. Dr. Gallo seconded the motion, which was approved unanimously by the Panel. Dr. Newberne moved that the conclusion for female rats be accepted as written, equivocal evidence of carcinogenic activity. Dr. Mirer seconded the motion, which was approved unanimously. Dr. Newberne moved that the conclusion for male mice be accepted as written, inadequate study of carcinogenic activity. Dr. Gallo seconded the motion, which was approved by six votes (Drs. Gallo, Garman, Gold, Klaassen, Newberne, and Popp) to two (Drs. McKnight and Mirer). Dr. Newberne moved that the conclusion for female mice be accepted as written, clear evidence of carcinogenic activity. Dr. Popp seconded the motion. There was discussion as to whether the word "marginally" should be removed from the sentence, "A marginally increased incidence of hepatocellular neoplasms was observed in the exposed group." The motion was then approved by five votes (Drs. Gallo, Garman, Gold, Newberne, and Popp) to three (Drs. Klaassen, McKnight, and Mirer).

I. INTRODUCTION

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

I. INTRODUCTION

CH_3CH_2Cl

CHLOROETHANE

(ETHYL CHLORIDE)

CAS No. 75-00-3

C_2H_5Cl Molecular weight 64.5

Synonyms: Monochloroethane; chloroethyl; ether hydrochloric; ether muriatic; aethylis; aethylis chloridum; ether chloridum; ether chloratus

Trade names: Kelene; Chelen; Anodynon; Chloryl Anesthetic; Narcotile

Properties

Chloroethane is a colorless, flammable gas with an ethereal, somewhat pungent odor. Under increased pressure and lower temperature, it is compressed to a colorless, volatile liquid. It has a specific gravity of 0.9214 between 0° and 4° C, a boiling point of 12.3° C, a melting point of −138.7° C, and a vapor pressure of 1,199 mm mercury at 25° C. Chloroethane is 0.57% (w/v) soluble in water at 20° C, 48% soluble in ethyl alcohol at 21° C, and miscible with ethyl ether. It has a flash point of −50° C (closed cup). Explosive limits in air are between 3.8% and 14.8%. Chloroethane is stable and noncorrosive when dry but will hydrolyze in the presence of water or alkali. Thermal decomposition can yield phosgene on combustion. It can react vigorously with oxidizing materials (ITII, 1979; Sax, 1979; Canada Safety Council, 1981; Dangerous Properties of Industrial Materials Report, 1981; Torkelson and Rowe, 1981; Merck, 1983; ACGIH, 1986).

Production, Use, and Occurrence

Chloroethane is produced by the free radical chlorination of ethane, by the addition of hydrogen chloride to ethylene, or by the action of chlorine on ethylene in the presence of the chlorides of copper or iron (Fishbein, 1979; Merck, 1983). It is commercially available at greater than 99.5% purity. The production of chloroethane in the United States was estimated to be greater than 460 million pounds in 1985, of which more than 110 million pounds was manufactured by two companies for captive use only (SRI International, 1985). Exports in 1983 and 1984 were 21.4 and 20.1 million pounds, respectively (U.S. Dept. of Commerce, 1984, 1985).

Chloroethane is an alkylating agent, primarily used in the manufacture of tetraethyl lead antiknock gasoline additives. It is also used as a chemical intermediate in the manufacture of ethylcellulose plastics, dyes, and pharmaceuticals; as a solvent for phosphorus, sulfur, fats, oils, resins, and waxes; and as an industrial refrigerant (Fishbein, 1979; Canada Safety Council, 1981; Dangerous Properties of Industrial Materials Report, 1981). In the first half of this century, chloroethane was widely employed as an inhalation anesthetic for short procedures or as a preliminary anesthetic to ethyl ether (Sayers et al., 1929; Abreu et al., 1939; Lawson, 1965). However, because of cardiac depressant effects, its use as an inhalation anesthetic has been discontinued. Because it rapidly evaporates, chloroethane can be used locally to produce anesthesia by cold (−20° C). Excessive contact can cause frostbite. This ability to freeze tissue has led to its use in various medical and dental applications, including minor operative procedures such as incision of carbuncles or furuncles and removal of localized growths or skin grafts. Its usefulness is limited in these procedures because of its short duration of action and because the thawing of frozen tissue is painful. Chloroethane is also used to alleviate pain associated with burns and insect stings and as an adjunct in the treatment of tinea lesions and creeping eruption. As a counterirritant, it is used for the relief of myofascial and visceral pain syndromes. It has also been used in dentistry as a

pulp vitality tester (Adriani, 1968; Ott, 1969; Brown, 1972; Ehrmann, 1977).

Although not considered one of the priority environmental volatile organic pollutants, chloroethane has been detected in urban air as well as in the air at hazardous waste sites; in drinking water, waste water, and landfill leachates; and in sediment and biota of lakes, waste water effluents, and marine ecosystems (Kopfler et al., 1975; Himi, 1981; Gould et al., 1983; Young et al., 1983; Ferrario et al., 1985; LaRegina et al., 1986).

Human Exposure

The major use of chloroethane is in the production of tetraethyl lead gasoline additives. Therefore, the predominant occupational exposure is associated with the production and use of these materials. Data concerning workplace exposure to chloroethane are limited; however, an Occupational Safety and Health Administration (OSHA) survey of one tetraethyl lead manufacturer determined that, on the average, workers were exposed at 0.425 mg/m^3 with a maximum of 1.143 mg/m^3 (NIOSH, 1983). There are no health effects data in the literature associated with workplace exposure to chloroethane. The major industrial hazards appear to be due to fire and explosion. The OSHA and American Conference of Governmental Industrial Hygienists recommended a threshold limit value of 1,000 ppm (2,600 mg/m^3). A survey conducted between 1972 and 1974 estimated that 142,416 workers were potentially exposed to chloroethane in the workplace either through the actual use of the compound or through the use of a trade name product or generic product suspected of containing the compound (NIOSH, 1976). A second survey conducted from 1980 to 1983 indicated that 36,289 workers, including 25,797 women, were potentially exposed to chloroethane in the workplace in 1980 (NIOSH, 1984). This estimate, however, was based only on observations of the actual use of the compound. To a much lesser extent, occupational exposure occurs to those individuals associated with medical and other health services, metal product fabrication, rubber and plastics production, and the printing and publishing industry (Parker et al., 1979). Estimates of workplace exposure through these industrial uses of chloroethane were not found in the literature.

In general, specific adverse effects of chloroethane exposure result from its use as a general and local anesthetic. It is a central nervous system depressant, causing headache, salivation, nausea, dizziness, muscular incoordination, a feeling of inebriation, and unconsciousness. Cardiac arrhythmia, respiratory failure, cardiac arrest, and death may occur (Lawson, 1965; Finer, 1966; Cole, 1967; Adriani, 1968; Dobkin and Byles, 1971). For humans, a TC_{Lo} of 1,300 ppm has been reported (ITII, 1979). In addition to causing direct myocardial depression, chloroethane may act indirectly on the heart through vagal stimulation. Atropine has been shown to reverse the chloroethane-induced vagal stimulation (Lawson, 1965). Chloroethane is also an eye, respiratory tract, and skin irritant. In a patch test, chloroethane sprayed on skin caused allergic eczema (van Ketel, 1976).

Animal Toxicity

Sayers et al. (1929) exposed groups of six guinea pigs to chloroethane at various concentrations ranging from 24% to 1% for periods of 5-810 minutes. Chloroethane at concentrations of 23%-24% produced unconsciousness and the death of one animal in 5-10 minutes. A 40-minute exposure at 15.3% resulted in the death of two animals, whereas a 30-minute exposure to 9.1% resulted in the death of one animal. Animals dying after exposure to chloroethane had congested livers and hemorrhage and edema of the lungs. All survivors were normal at necropsy. Similar effects were observed in two animals exposed to 4% chloroethane for 540 minutes. Animals exposed to 1% chloroethane for 810 minutes were found to be similar to controls at necropsy (8 days postexposure).

Rats exposed to 220 ppm chloroethane for 4 hours per day for 6 months demonstrated hepatic malfunction, reduced arterial pressure, and inhibition of leukocyte phagocytic activity (Troshina, 1966). All animals exhibited lipid degenerative changes in the liver and thickening of alveolar septa in the lung. Animals exposed for the same period to 20 ppm were similar to controls.

I. INTRODUCTION

A number of studies have investigated the action of chloroethane on the heart (primarily in dogs). Bush et al. (1952) studied effects of chloroethane in dogs and children. In dogs, they found a twofold effect: first, stimulation of the vagus with wandering pacemaker, nodal rhythm, and occasionally ventricular fibrillation; second, direct depression of cardiac muscle which sometimes led to asystole. Only the disturbances of vagal origin were prevented by atropine. In children not premedicated with atropine, the authors noted early features of vagal stimulation identical to those seen in dogs. These effects were immediately reversed by intravenous administration of atropine. Morris et al. (1953) found that chloroethane sensitized the dog heart to adrenaline. Also in the same laboratory, Haid et al. (1954) observed cardiac irregularities of almost every type but found no evidence that ventricular fibrillation occurred spontaneously.

During chloroethane anesthesia, muscle spasms have been reported, especially when hypoxia occurs. Van-Liere et al. (1966), investigating this occurrence, exposed dogs to chloroethane by holding a saturated piece of gauze over a tracheal cannula opening. Subsequently, they monitored the effects of chloroethane on uterine motility. When chloroethane was given at moderate concentrations, there were no changes in amplitude, frequency, or duration of uterine contractions; furthermore, muscle tone remained unchanged. When given at greater concentrations, chloroethane produced a decrease in uterine motility and in muscle tone. When chloroethane was administered at lethal concentrations, blood pressure fell to zero, markedly reducing the supply of blood to the uterus; however, uterine contractions continued, although frequency and amplitude were reduced.

Male and female F344 rats (six per group) and male beagle dogs (two per group) were exposed to 0, 1,600, 4,000, or 10,000 ppm chloroethane for 6 hours per day, 5 days per week for 2 weeks, and groups of five male $B6C3F_1$ mice were exposed for 6 hours to 0 or 4,000 ppm chloroethane (Landry et al., 1982). No toxicologically significant compound-related effects on body weights or clinical chemical, hematologic, urinary, neurologic (dogs only), or gross or microscopic pathologic effects were seen in rats or dogs. Statistically significant increases were observed in liver weight to body weight ratios for male rats exposed to 4,000 or 10,000 ppm chloroethane (4.9% and 7.5%, respectively). Liver nonprotein sulfhydryl concentrations, measured 30 minutes after one 6-hour exposure, were lower than control values in rats exposed to 4,000 ppm (88% of control) and 10,000 ppm (89%) and in mice exposed to 4,000 ppm chloroethane (64% of control).

In a subsequent study, Landry et al. (1987) exposed groups of seven male and seven female $B6C3F_1$ mice to 0, 250, 1,250, or 5,000 ppm chloroethane 23 hours per day for 11 days. No chemical-related neurobehavioral, clinical chemical, or hematologic effects were observed. Exposure-related effects were limited to increased liver weights and a slight increase in hepatocellular vacuolation (glycogen or fat) in mice exposed to 5,000 ppm. No exposure-related effects were observed at concentrations of 1,250 or 250 ppm chloroethane.

The effects of chloroethane exposure on fetal development in mice were investigated by Hanley et al. (1987). Groups of 30 pregnant CF-1 mice were exposed to chloroethane at concentrations of 0, 500, 1,500, or 5,000 ppm for 6 hours per day on days 6-15 of gestation. No significant effects on maternal body weight, body weight gain, liver weight, reproductive parameters, or fetal body weight were observed. No external, visceral, or skeletal malformations were observed in fetal mice. There was a small increase in the incidence of foramina of the skull bones in fetuses from the 5,000-ppm group.

In the BALB/c-3T3 cell transformation assay, chloroethane induced a dose-dependent cytotoxicity but failed to elicit a consistent transformation response (Tu et al., 1985).

Metabolism

Metabolism and disposition data for chloroethane were not found in the literature.

Genetic Toxicology

The only published report on the mutagenic activity of chloroethane is of a positive *Salmonella typhimurium* test conducted within the closed environment of a desiccator; mutation induction was observed in strains TA98, TA100, TA1535, and TA1537 in both the presence and absence of metabolic activation (Riccio et al., 1983).

Bromoethane (NTP, 1989), a structural analog of chloroethane, was mutagenic in *S. typhimurium* when testing was performed in a desiccator (Simmon, 1981; Barber et al., 1981, 1983) but not when tested according to a preincubation protocol without control for volatility (Haworth et al., 1983). In cytogenetic tests with Chinese hamster ovary (CHO) cells, bromoethane induced sister chromatid exchanges (SCEs) but not chromosomal aberrations, in both the presence and absence of S9 (Loveday et al., 1989). No increase in sex-linked recessive lethal mutations was observed in Drosophila fed an 8.2 mM solution of bromoethane (Vogel and Chandler, 1974).

Other structural analogs of chloroethane were also mutagenic in Salmonella when exposure occurred in a closed environment; these were iodoethane (Simmon, 1981; Barber et al., 1981), 1-bromopropane (Barber et al., 1981), and 1,1-dibromoethane (Brem et al., 1974). 1,2-Dichloroethane was mutagenic in the presence of S9 activation in Salmonella base-substitution strains when tested according to a standard preincubation protocol; however, 1,1-dichloroethane was negative when tested according to the same protocol (NTP unpublished data). Another analog, 1,2-dibromoethane, was also mutagenic in Salmonella under a preincubation protocol with and without S9 (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 and sex-linked recessive lethal mutations and reciprocal translocations in adult *Drosophila melanogaster* (Myhr and Caspary, 1989; Mitchell et al., 1989; NTP unpublished data). Both 1,2-dibromoethane and 1,2-dichloroethane induced chromosomal aberrations and SCEs in cultured CHO cells (NTP unpublished data). 1,2-Dichloroethane required S9 for a positive response in the aberration assay, whereas 1,2-dibromoethane was direct-acting. Another structural analog, 1,2-dibromopropane, was positive in the Drosophila sex-linked recessive lethal assay reported by Vogel and Chandler (1974).

These haloalkanes were tested only in a limited number of in vivo mammalian assays, and the results were uniformly negative. 1,2-Dibromoethane, like bromoethane, did not induce micronucleated peripheral blood erythrocytes in mice (NTP unpublished data), and 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

Chloroethane was studied for long-term toxicity and carcinogenicity because of its large production volume, considerable worker and consumer exposure, and the lack of carcinogenicity data. These studies were performed with concurrent studies of bromoethane (NTP, 1989) for structure-activity comparison. In the current studies, chloroethane was administered by inhalation as that is the main route of human exposure.

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF CHLOROETHANE

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

- Vapor Generation System
- Vapor Concentration Monitoring
- Degradation Study of Chloroethane in the Chamber
- Vapor Concentration Uniformity in the Chamber

SINGLE-EXPOSURE STUDIES

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

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

GENETIC TOXICOLOGY

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF CHLOROETHANE

Chloroethane was obtained from Matheson Gas Products (East Rutherford, NJ) or Air Products, Inc. (Tamaqua, PA) (Table 1). Purity and identity analyses were conducted at Midwest Research Institute (MRI) (Kansas City, MO) and Battelle Pacific Northwest Laboratories (Richland, WA). MRI and Battelle Pacific Northwest Laboratories reports on the analyses performed in support of the chloroethane studies are on file at the National Institute of Environmental Health Sciences. The identity of the lots was confirmed by spectroscopic analyses. The infrared and nuclear magnetic resonance spectra (representative spectra are presented in Figures 1 and 2) agreed with the structure of chloroethane and the literature spectra (Sadtler Standard Spectra; Bhacca et al., 1962).

Cumulative data indicated that all lots of the study material were at least 99.5% pure. Trace impurities (total less than 0.4%) were detected in several lots by gas chromatography with a Chromosorb 102 or an OPN/Porasil C column. No bulk chemical stability studies were performed.

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

Vapor Generation System

No additional preparation was necessary before introduction of chloroethane into the vapor generation system (Figure 3). The liquid to be vaporized was forced under pressure, at a metered rate, directly from the shipping container into a stainless steel boiler that was maintained at about 60° C (32° C for the single-exposure studies) by a controlled-temperature water bath. The vapor was routed through a gas metering valve and a purge/expose valve into a pipe at the chamber inlet, where the vapor was mixed with dilution air entering the chamber.

Vapor Concentration Monitoring

A gas chromatograph (Hewlett-Packard Model 5840) with a flame ionization detector was used to monitor the exposure chamber, control chamber, and exposure room. The calibration of the monitor was confirmed and corrected two times per month, or more frequently as necessary, by checking the calibration against volumetrically prepared gas standards. Starting on March 23, 1982, an online standard, 500 ppm hexane, was used daily to establish monitor performance.

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

Single-Exposure Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Lot Numbers			
44480	A031880	A082280; A040181; A042881	A040181; A020982; 75-4-82-CH; A080482; 8-82-18-H; 1-83-13-H; A013183; A061483; A080583; 010684
Date of Initial Use			
4/28/80	9/17/80	3/11/81	3/17/82
Supplier			
Matheson Gas Products (East Rutherford, NJ)	Air Products, Inc. (Tamaqua, PA)	Lot no. A082280--Matheson Gas Products (East Rutherford, NJ); lot nos. A040181 and A042881--Air Products, Inc. (Tamaqua, PA)	Air Products, Inc. (Tamaqua, PA)

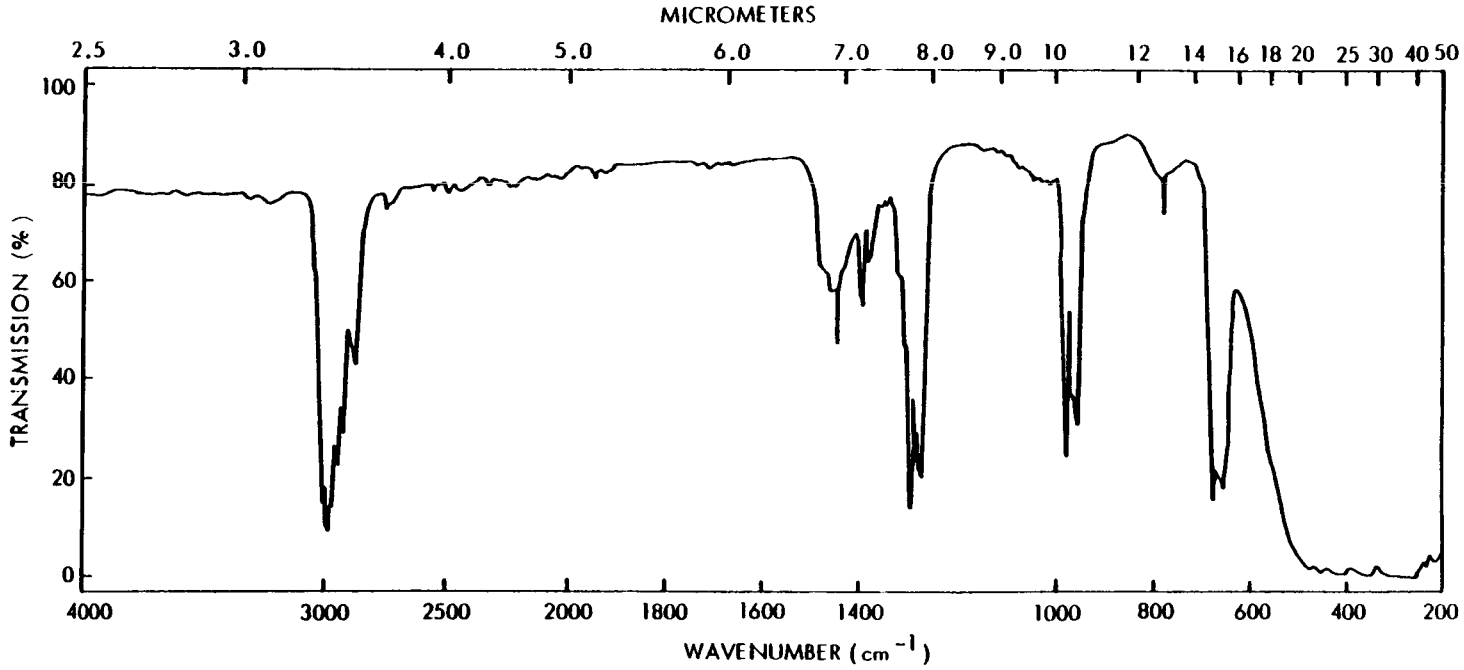

FIGURE 1. INFRARED ABSORPTION SPECTRUM OF CHLOROETHANE (LOT NO. A080583)

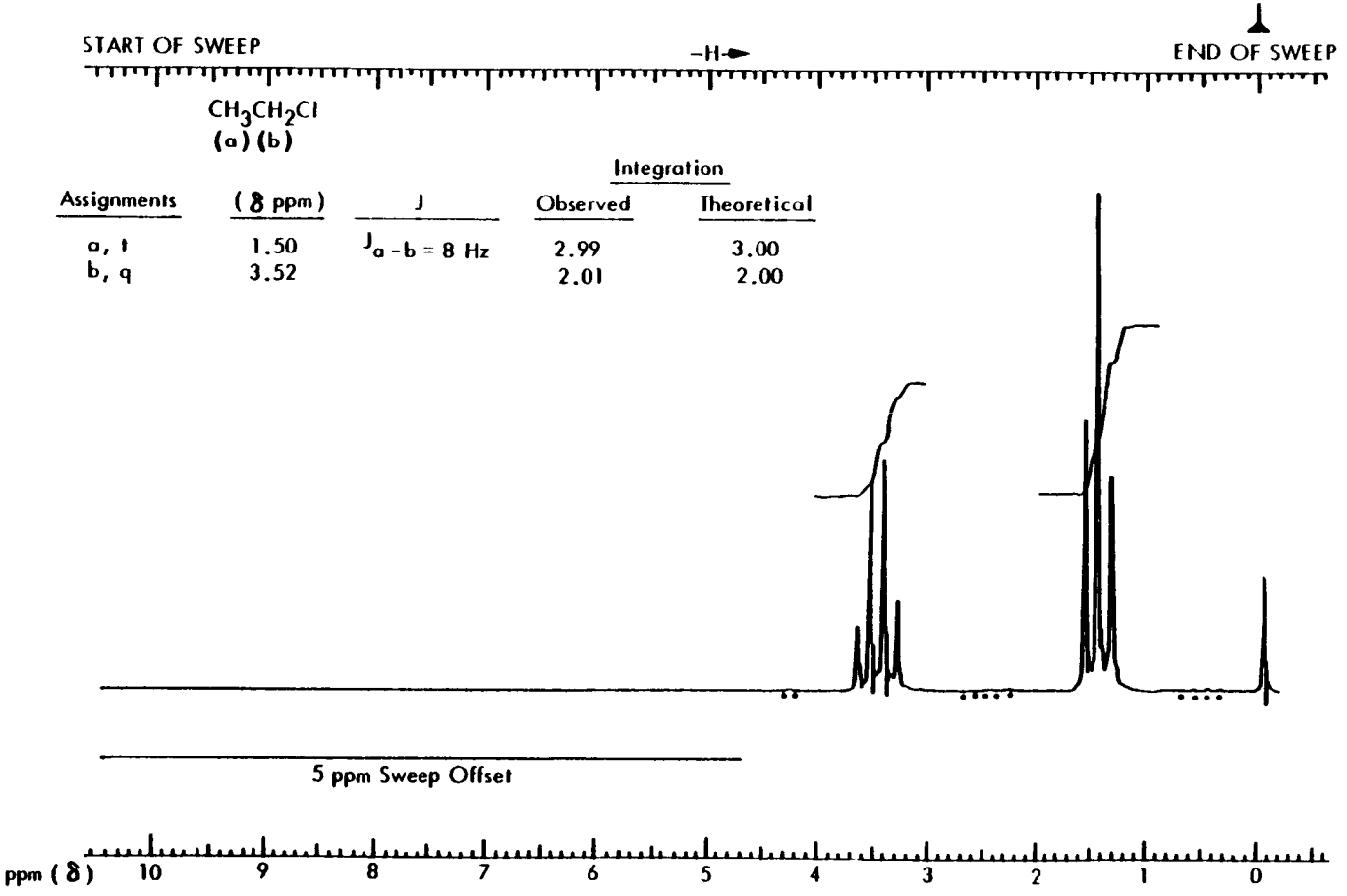

FIGURE 2. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF CHLOROETHANE (LOT NO. A080583)

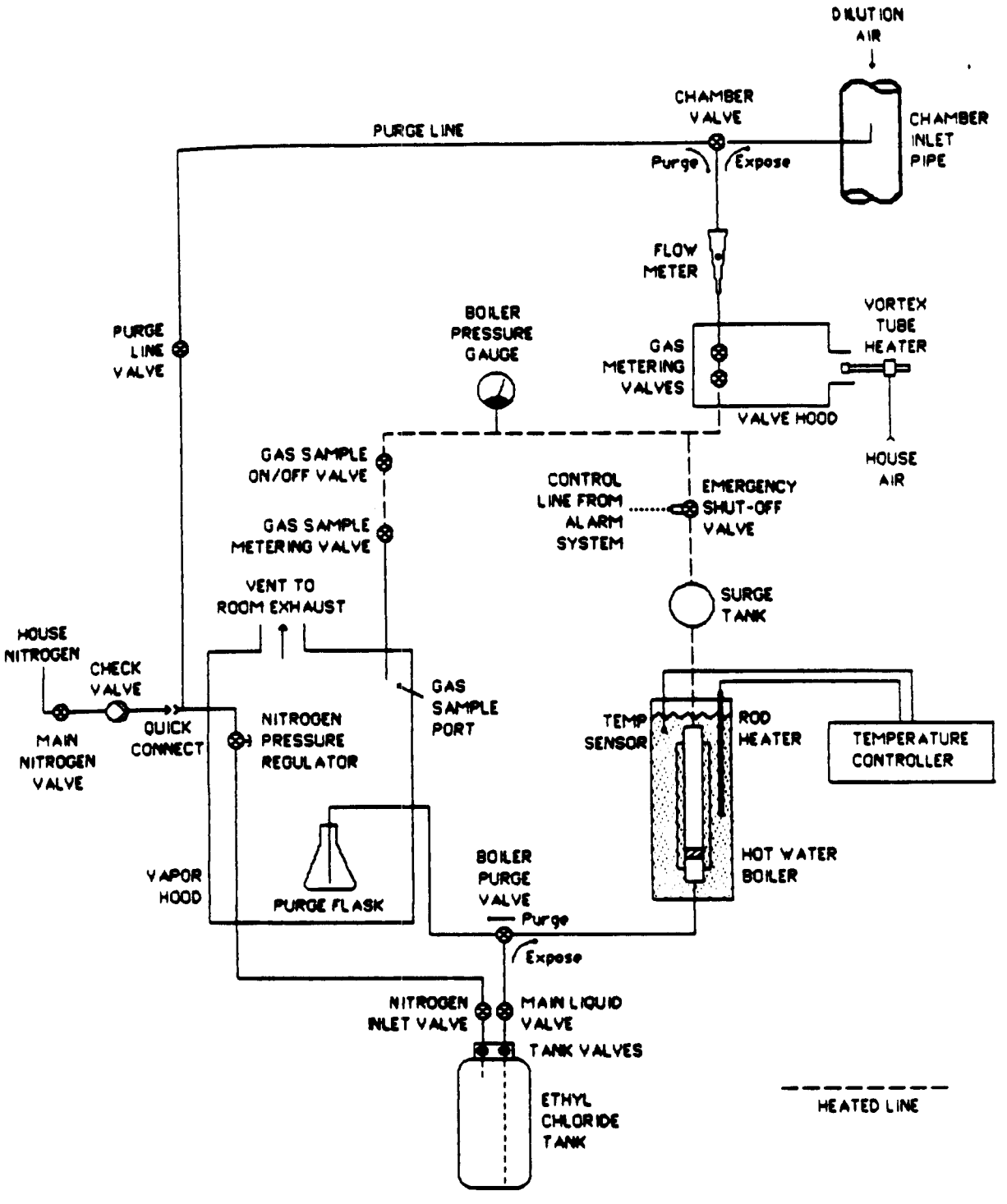

FIGURE 3. CHLOROETHANE VAPOR GENERATION SYSTEM

The same monitor was shared between the chloroethane and methyl methacrylate (another study) chambers until January 14, 1983, the last exposure day for methyl methacrylate. Weekly mean exposure concentrations for the 2-year studies are presented in Figures 4 and 5.

Degradation Study of Chloroethane in the Chamber

Samples of chloroethane exposure chamber atmospheres were examined for the occurrence of degradation products with a Hewlett-Packard Model 5840A gas chromatograph equipped with a flame ionization detector and a Porapak PS 80/100 column. There was no evidence of decomposition of chloroethane in the exposure atmospheres.

Vapor Concentration Uniformity in the Chamber

Uniformity of chloroethane concentration in the exposure chamber was measured before the start of the studies and was checked periodically throughout the studies with a portable photoionization detector. In all instances, the mean values of the concentrations were within ±10% of the target concentration at all 12 positions sampled within the chamber (Tables 2 and 3).

TABLE 2. SUMMARY OF CHAMBER CONCENTRATIONS OF CHLOROETHANE IN THE TWO-YEAR INHALATION STUDIES (a)

	Total Number of Readings	Mean Concentration (ppm) (b)
Rats	7,718	15,051 ± 636
Mice	7,484	15,048 ± 641

(a) Target concentration = 15,000 ppm
(b) Mean ± standard deviation

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

Range of Concentration (percent of target)	Number of Days Mean Concentration Within Range (a)	
	Rats	Mice
>110	0	0
100-110	284	276
90-100	205	201
<90	0	0

(a) Target concentration = 15,000 ppm

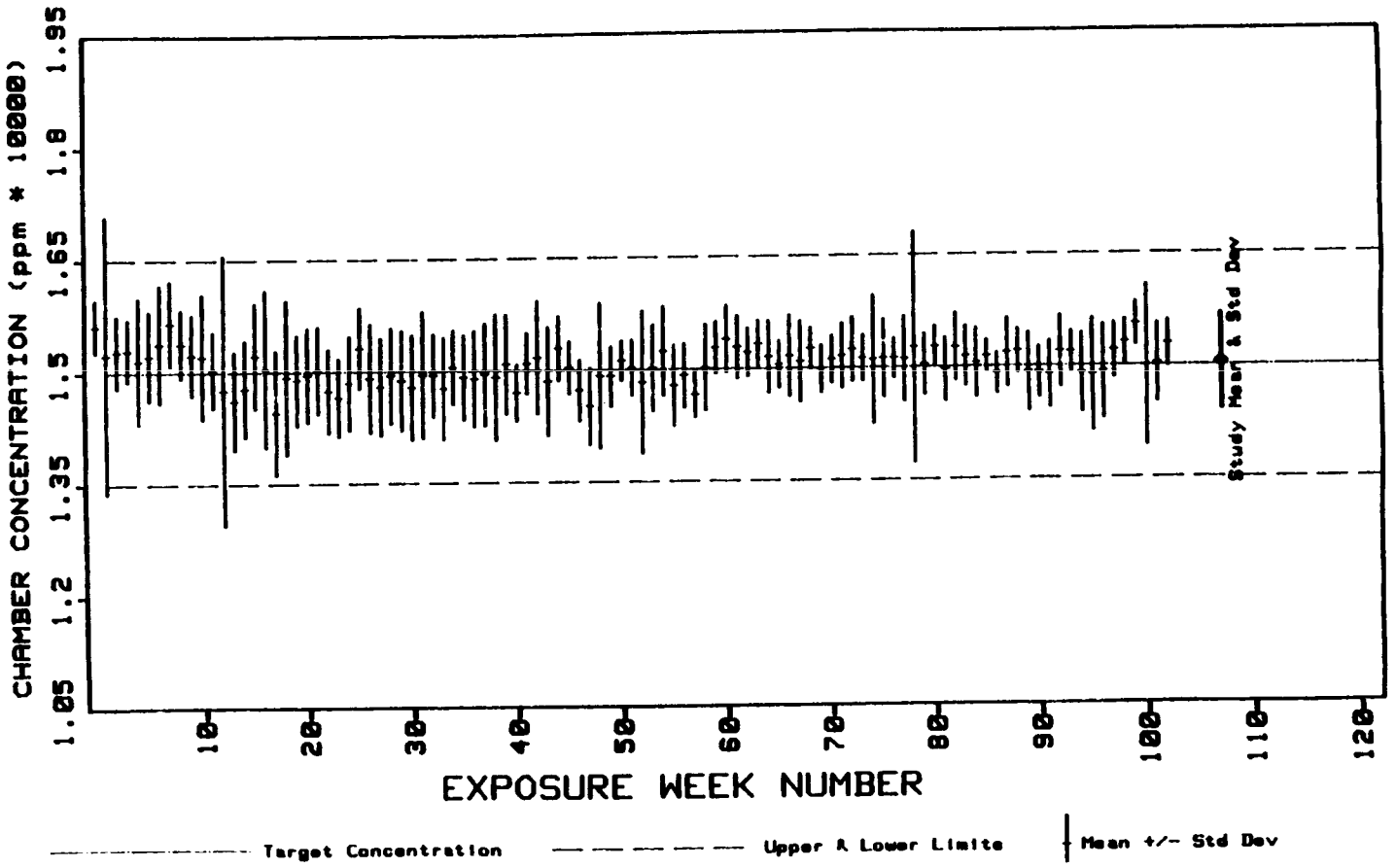

FIGURE 4. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 15,000-ppm CHLOROETHANE RAT EXPOSURE CHAMBER FOR ENTIRE 102-WEEK STUDIES

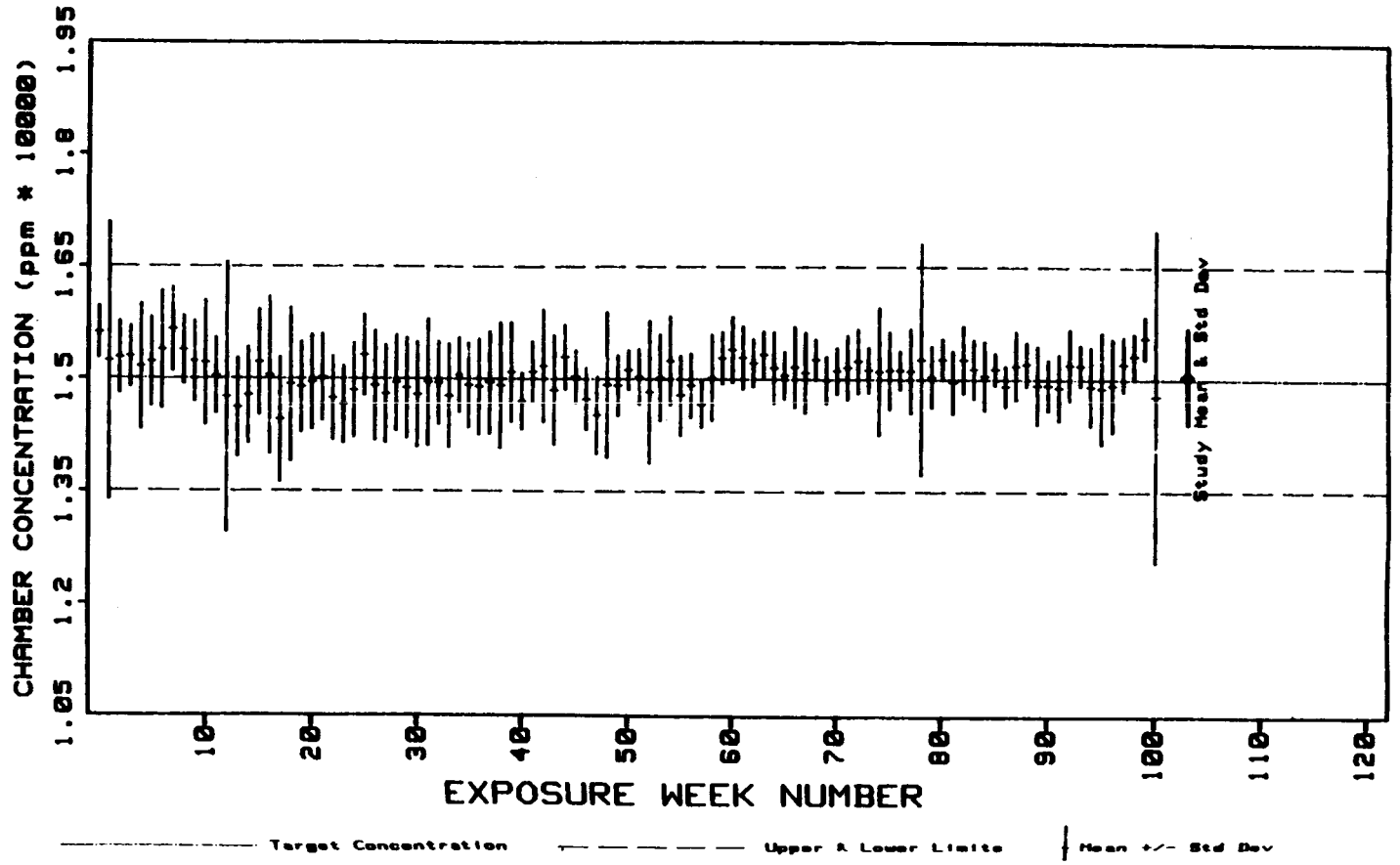

FIGURE 5. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 15,000-ppm CHLOROETHANE MOUSE EXPOSURE CHAMBER FOR ENTIRE 100-WEEK STUDIES

SINGLE-EXPOSURE STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and observed for 26 days before the studies began. The rats were 8-9 weeks old when placed on study, and the mice were 9-10 weeks old.

Groups of five rats and five mice of each sex were exposed for a single 4-hour exposure to air containing chloroethane at the target concentration of 19,000 ppm. Controls were not used. Animals were weighed before exposure and were observed continually during exposure and then three times per day for 14 days. After 14 days, the animals were killed without a formal necropsy. Details of animal maintenance are presented in Table 4.

FOURTEEN-DAY STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories and observed for 21 days before the studies began. The rats were 7-8 weeks old when placed on study, and the mice were 8-9 weeks old.

Groups of five rats and five mice of each sex were exposed to filtered air or to air containing chloroethane at the target concentration of 19,000 ppm for 6 hours per day, 5 days per week for 14 days (10 exposures). Rats and mice were observed continually during exposure and three times per day on nonexposure days. All animals were weighed before the first exposure day, after 1 week, and at necropsy. A necropsy was performed on all animals. Details of animal maintenance are presented in Table 4.

THIRTEEN-WEEK STUDIES

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

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories, observed for 21 days, and assigned to study groups from weight classes 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 chloroethane at target concentrations of 0, 2,500, 5,000, 10,000, or 19,000 ppm, 6 hours per day, 5 days per week for 13 weeks (65 exposures). Further experimental details are summarized in Table 4.

Rats were observed three times per day and mice two times per day; moribund animals were killed. Individual animal weights were recorded once per week. At the end of the 13-week studies, survivors were killed. A necropsy was performed on all animals except those excessively autolyzed or cannibalized. Tissues and groups examined are listed in Table 4.

TWO-YEAR STUDIES

Study Design

Groups of 50 rats of each sex were exposed to air containing chloroethane at concentrations of 0 (chamber controls) or 15,000 ppm, 6 hours per day, 5 days per week for 102 weeks. Groups of 50 mice of each sex were exposed to chloroethane at concentrations of 0 or 15,000 ppm on the same schedule for 100 weeks. Although no chemical-related effects were observed in the 13-week studies, 2-year studies with this chemical were conducted so that structure-activity comparisons could be made with bromoethane in concurrent studies (NTP, 1989). Therefore, only one chemically exposed group (plus a control group) was included for each species and sex in the studies. Actual concentrations are summarized in Tables 2 and 3 and Figures 4 and 5. Rats and mice occupied the same chambers.

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.

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

Single-Exposure Studies	Fourteen-Day Studies	Thirteen-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	50 males and 50 females of each species
Doses			
19,000 ppm chloroethane by inhalation	0 or 19,000 ppm chloroethane by inhalation	0, 2,500, 5,000, 10,000, or 19,000 ppm chloroethane by inhalation	0 or 15,000 ppm chloroethane by inhalation
Date of First Dose			
4/28/80	9/17/80	3/11/81	3/17/82
Date of Last Dose			
N/A	9/30/80	6/9/81	Rats--3/2/84; mice--2/14/84
Duration of Dosing			
Single 4-h exposure	6 h/d for a total of 10 exposures over 14 d	6 h/d, 5 d/wk for 13 wk	6 h/d, 5 d/wk for 102 wk (rats) or 100 wk (mice)
Type and Frequency of Observation			
Observed continually during exposure and then 3 × d for 14 d; weighed initially	Observed continually during exposure and 3 × d on nonexposure days; weighed initially and 1 × wk thereafter	Observed 3 × d (rats) or 2 × d (mice) during exposure; weighed 1 × wk	Observed 2 × d; weighed initially, 1 × wk for 12 wk, and then 1 × mo
Necropsy and Histologic Examinations			
Necropsy and histologic exams not performed	Necropsy performed on all animals; histologic exams performed on 1 female rat and 1 male mouse in the control groups and 2 male rats, 1 female rat, 1 male mouse, and 2 female mice in the exposed groups. Tissues examined include: adrenal glands, bone marrow, brain, colon, esophagus, gallbladder (mice), heart, jejunum, kidneys, larynx, liver, lungs and bronchi, mandibular lymph nodes, nasal cavity, pancreas, parathyroid glands (mice), pituitary gland, prostate/testes or ovaries/uterus, salivary glands, seminal vesicles, skin, spleen, stomach, thymus, thyroid gland (mice), trachea, and urinary bladder	Necropsy performed on all animals; histologic exams performed on all control and high dose animals. Tissues examined include: adrenal glands, bone marrow, brain, colon, esophagus, gallbladder (mice), heart, jejunum, kidneys, larynx, liver, lungs and bronchi, mammary gland, mandibular lymph nodes, nasal cavity, pancreas, parathyroid glands, pituitary gland, prostate/testes or ovaries/uterus, salivary glands, seminal vesicles (mice), skin, spleen, stomach, thymus, thyroid gland, trachea, and urinary bladder; liver weighed at necropsy	Necropsy and histologic exams performed on all animals; the following tissues were examined: adrenal glands, brain, bronchial lymph nodes, cecum, clitoral or preputial gland (rats), colon, duodenum, esophagus, gallbladder (mice), gross lesions, heart, ileum, jejunum, kidneys, larynx, liver, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nose, pancreas, parathyroid glands, pituitary gland, prostate/testes/epididymis or ovaries/uterus, rectum, salivary glands, skin, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, tissue masses with regional lymph nodes, trachea, and urinary bladder
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)	Charles River Breeding Laboratories (Portage, MI)	Frederick Cancer Research Facility (Frederick, MD)
Study Laboratory			
Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories

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

Single-Exposure Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE (Continued)			
Method of Animal Identification			
Individual cage number	Ear tag	Ear tag	Ear tag
Time Held Before Study			
26 d	21 d	21 d	21 d
Age When Placed on Study			
Rats--8-9 wk; mice--9-10 wk	Rats--7-8 wk; mice--8-9 wk	Rats--7-8 wk; mice--8-9 wk	Rats--8 wk; mice--9 wk
Age When Killed			
Rats--10-11 wk; mice--11-12 wk	Rats--9-10 wk; mice--10-11 wk	Rats--20-21 wk; mice--21-22 wk	Rats--112 wk; mice--109 wk
Necropsy or Kill Dates			
5/12/80	10/1/80	6/10/81-6/12/81	Rats--3/14/84-3/15/84; mice--2/14/84-2/15/84
Method of Animal Distribution			
According to a table of random numbers	Same as single-exposure studies	Assigned from weight classes to groups according to tables of random numbers	Same as 13-wk studies
Feed			
NIH 07 Rat and Mouse Ration (Zeigler Bros., Inc., Gardners, PA); available ad libitum during nonexposure 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 (Hazleton Systems, Inc., Aberdeen, MD)	Same as 14-d studies	Same as 14-d studies
Animals per Cage			
1	1	1	1
Other Chemicals on Study in the Same Room			
1,3-Butadiene	None	None	Methyl methacrylate (until 1/14/83)
Chamber Environment			
Temp--exposure, 75°-76° F; nonexposure, 72°-76° F; hum--exposure, 55%-57%; nonexposure, 40%-60%; fluorescent light 12 h/d; 10 chamber air changes/h during exposure	Temp--70°-75° F; hum--46%-76%; fluorescent light 12 h/d; 10 chamber air changes/h during exposure; 20/h during nonexposure	Temp--71°-74° F; hum--40%-65%; fluorescent light 12 h/d; 10 chamber air changes/h during exposure; 20/h during nonexposure	Temp--mean, 76° F; range, 60°-83° F; hum--mean, 60%; range, 38%-88%; fluorescent light 12 h/d; 10 chamber air changes/h

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 5-6 weeks of age and were quarantined 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 at 8-9 weeks of age.

Animal Maintenance

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

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 study 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 missing. Some tissues were excessively autolyzed or missing, 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 microscopically are listed in Table 4.

When the pathology evaluation was completed by the laboratory pathologist and the pathology data entered into the Toxicology Data Management System, the slides, paraffin blocks, and residual formalin-fixed tissues were sent to the NTP Archives. The slides, blocks, and residual wet tissues were audited for accuracy of labeling and animal identification and for thoroughness of tissue trimming. The slides, individual animal necropsy records, and pathology tables were sent to an independent pathology quality assessment laboratory. The individual animal records and pathology tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tissues with a tumor diagnosis, all potential target tissues, and all tissues from a randomly selected 10% of the animals were re-evaluated microscopically by a quality assessment pathologist. Nonneoplastic lesions were evaluated for accuracy and consistency of diagnosis only in the potential target organs, in the randomly selected 10% of animals, and in tissues with unusual incidence patterns or trends. Tissues are generally not evaluated in a "blinded" fashion (i.e., without knowledge of dose group) unless the lesions in question are subtle.

The quality assessment report and slides were submitted to a Pathology Working Group (PWG) Chairperson, who reviewed microscopically all potential target tissues and any other tissues for which there was a disagreement in diagnosis between the laboratory and quality assessment pathologists. Representative examples of potential chemical-related nonneoplastic lesions and neoplasms and examples of disagreements in diagnosis between the laboratory and quality assessment pathologists were shown to the PWG. The PWG, which included the laboratory pathologist, the quality assessment pathologist, and other pathologists experienced in rodent toxicology, examined the tissues without knowledge of dose group or previously rendered diagnoses. When the consensus diagnosis of the PWG differed from that of the laboratory pathologist, the diagnosis was changed to reflect the opinion of the PWG. This procedure has been described, in part, by Maronpot and Boorman (1982) and Boorman et al. (1985). The final pathology data 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).

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 compound-related effect on survival used the method of Cox (1972). 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 a logistic regression 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, tumor prevalence was modeled as a logistic function of chemical exposure and time. Both linear and quadratic terms in time were incorporated initially, and the quadratic term was eliminated if it did not significantly enhance the fit of the model. The exposed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and Haseman (1986). When tumors are incidental, this comparison of the time-specific tumor prevalences also provides a comparison of the time-specific tumor incidences (McKnight and Crowley, 1984).

In addition to logistic regression, alternative methods of statistical analysis were used, and the results of these tests are summarized in the appendixes. One method is the life table test (Cox, 1972). The underlying variable considered by this analysis is time to death due to tumor. If the tumor is rapidly lethal, then time to death due to tumor closely approximates time to tumor onset. In this case, the life table test also provides a comparison of the time-specific tumor incidences. Another method is the Fisher exact test (Gart et al., 1979), a procedure based on the overall proportion of tumor-bearing animals.

Tests of significance include pairwise comparisons of each exposed group with controls (since this was a single-concentration study, no trend tests were carried out). 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 this Report was prepared, the NTP historical data base for inhalation studies comprised only studies from Battelle Pacific Northwest Laboratories, and no other 2-year 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 the gaseous chemical. The chemical was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). The study chemical was equilibrated with air and introduced through valves into sealed desiccators containing minimal glucose agar plates with the *Salmonella*

typhimurium tester strains (TA98, TA100, and TA1535) alone or with S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver). The entire apparatus was incubated at 37° C for 48 hours.

Each test consisted of triplicate plates of concurrent positive and negative controls and of two doses of the study chemical. The high dose was limited by toxicity. All negative assays were repeated, and all positive assays were repeated under the conditions that elicited the positive response. Because this initial investigation was limited by equipment availability to only two doses of study chemical, a second, more extensive test will be conducted in the near future which will allow testing of chloroethane at the usual number of five doses.

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 a low-level increase in revertants. A response was considered negative when no increase in revertant colonies was observed after chemical treatment.

III. RESULTS

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III. RESULTS: RATS

SINGLE-EXPOSURE STUDIES

All rats survived the 4-hour exposure to 19,000 ppm chloroethane. No clinical signs of toxicity were seen. The rats were not exposed at lower concentrations.

FOURTEEN-DAY STUDIES

All rats survived exposure at the sole concentration of 19,000 ppm (Table 5). Initial and final mean body weights of exposed male rats were greater than those of controls, and weight gain did not appear affected by exposure to chloroethane. Mean body weights of exposed and control female rats were similar. No clinical signs of toxicity were seen. In addition, there were no compound-related gross observations at necropsy, nor were there compound-related microscopic findings.

TABLE 5. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-DAY INHALATION STUDIES OF CHLOROETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams)			Final Weight Relative to Controls (percent)
		Initial (b)	Final	Change (c)	
MALE					
0	5/5	139 ± 4	168 ± 7	+29 ± 6	
19,000	5/5	152 ± 4	186 ± 5	+34 ± 2	111
FEMALE					
0	5/5	117 ± 4	136 ± 4	+19 ± 1	
19,000	5/5	116 ± 2	135 ± 2	+19 ± 1	99

(a) Number surviving/number initially in the 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

THIRTEEN-WEEK STUDIES

All rats lived to the end of the studies (Table 6). The final mean body weights of all exposed groups were lower than those of controls; the final mean body weight of rats exposed to 19,000 ppm was 8% lower than that of controls for males and 4% lower for females. No compound-related clinical signs or gross or microscopic pathologic effects were seen. The liver weight to body weight ratio for male rats exposed to 19,000 ppm was significantly greater than that for controls (Table 7).

Dose Selection Rationale: Although no chemically related toxic effects were observed in the short-term studies, concerns about potential flammability and the explosion hazard led to the selection of 0 and 15,000 ppm as the exposure concentrations for male and female rats for the 2-year studies.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of exposed male rats were 4%-8% lower than those of controls after week 33 (Table 8 and Figure 6). Mean body weights of exposed female rats were generally 5%-10% lower than those of controls from week 11 to week 42 and 6%-13% lower from week 47 to the end of the study. No compound-related clinical signs were observed.

TABLE 6. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE THIRTEEN-WEEK INHALATION STUDIES OF CHLOROETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	161 ± 3	348 ± 9	+187 ± 8	
2,500	(d) 10/10	163 ± 2	335 ± 6	+171 ± 5	96
5,000	10/10	161 ± 3	326 ± 7	+165 ± 6	94
10,000	10/10	160 ± 2	332 ± 7	+172 ± 6	95
19,000	10/10	161 ± 3	321 ± 7	+160 ± 7	92
FEMALE					
0	10/10	124 ± 2	200 ± 4	+76 ± 3	
2,500	10/10	123 ± 3	190 ± 4	+67 ± 2	95
5,000	10/10	124 ± 2	187 ± 3	+63 ± 2	94
10,000	10/10	124 ± 3	195 ± 5	+71 ± 4	98
19,000	10/10	124 ± 3	192 ± 3	+68 ± 2	96

(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) One final body weight not taken; weight change is based on the other nine animals.

TABLE 7. LIVER WEIGHTS OF RATS IN THE THIRTEEN-WEEK INHALATION STUDIES OF CHLOROETHANE (a)

Concentration (ppm)	Number Weighed	Final Body Weight (grams)	Liver Weight (mg)	Liver Weight/ Final Body Weight (mg/g)
MALE				
0	10	348 ± 8.9	13,367 ± 620	38.3 ± 1.08
2,500	9	335 ± 6.0	13,553 ± 357	40.5 ± 0.84
5,000	10	326 ± 6.6	12,280 ± 511	37.6 ± 1.18
10,000	10	332 ± 6.8	13,743 ± 488	41.4 ± 1.11
19,000	10	(b) 321 ± 7.3	13,990 ± 534	(c) 43.5 ± 0.78
FEMALE				
0	10	200 ± 3.8	7,091 ± 303	35.3 ± 0.99
2,500	10	190 ± 3.8	7,095 ± 275	37.4 ± 1.21
5,000	10	187 ± 3.1	(b) 6,060 ± 172	32.4 ± 0.87
10,000	10	195 ± 5.3	7,257 ± 321	37.1 ± 0.97
19,000	10	192 ± 2.8	6,541 ± 125	34.1 ± 0.76

(a) Mean ± standard error; P values vs. the controls by Dunnett's test (Dunnett, 1955).
(b) $P<0.05$
(c) $P<0.01$

TABLE 8. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF CHLOROETHANE

Weeks on Study	Chamber Control Av. Wt. (grams)	Chamber Control No. of Survivors	15,000 ppm Av. Wt. (grams)	15,000 ppm Wt. (percent of chamber controls)	15,000 ppm No. of Survivors
MALE					
0	167	50	169	101	50
1	202	50	202	100	50
2	223	50	220	99	50
3	242	50	240	99	50
4	259	50	254	98	50
5	274	50	269	98	50
6	289	50	280	97	50
7	298	50	288	97	50
8	306	50	299	98	50
9	315	50	307	97	50
10	324	50	316	98	50
11	333	50	324	97	50
12	345	50	333	97	50
16	362	50	348	96	50
20	377	50	361	96	50
25	394	50	379	96	50
29	399	50	391	98	50
33	417	50	400	96	50
38	422	50	401	95	50
42	431	50	404	94	50
47	444	50	420	95	50
51	454	50	433	95	50
55	462	50	440	95	50
59	477	50	437	92	50
64	461	50	435	94	48
68	462	50	442	96	47
72	466	48	449	96	46
79	472	42	455	96	42
83	471	39	447	95	39
86	470	38	442	94	36
90	469	37	445	95	28
95	462	31	446	97	24
99	463	22	434	94	20
103	444	17	409	92	10
FEMALE					
0	129	50	129	100	50
1	143	50	142	99	50
2	152	50	150	99	50
3	160	50	159	99	50
4	165	50	163	99	50
5	171	50	170	99	50
6	178	50	173	97	50
7	182	50	176	97	50
8	185	50	180	97	50
9	189	50	183	97	50
10	195	50	187	96	50
11	199	50	190	95	50
12	201	50	191	95	50
16	210	50	201	96	50
20	214	50	203	95	50
25	221	50	209	95	50
29	230	50	216	94	50
33	241	50	224	93	50
38	256	49	235	92	50
42	263	49	238	90	50
47	272	49	243	89	50
51	287	49	255	89	50
55	295	49	263	89	49
59	309	49	270	87	49
64	311	49	278	89	49
68	316	49	285	90	49
72	320	49	290	91	48
79	328	47	298	91	45
83	328	45	299	91	40
86	331	44	299	90	37
90	324	43	303	94	33
95	336	35	310	92	30
99	342	33	312	91	25
103	328	31	296	90	23

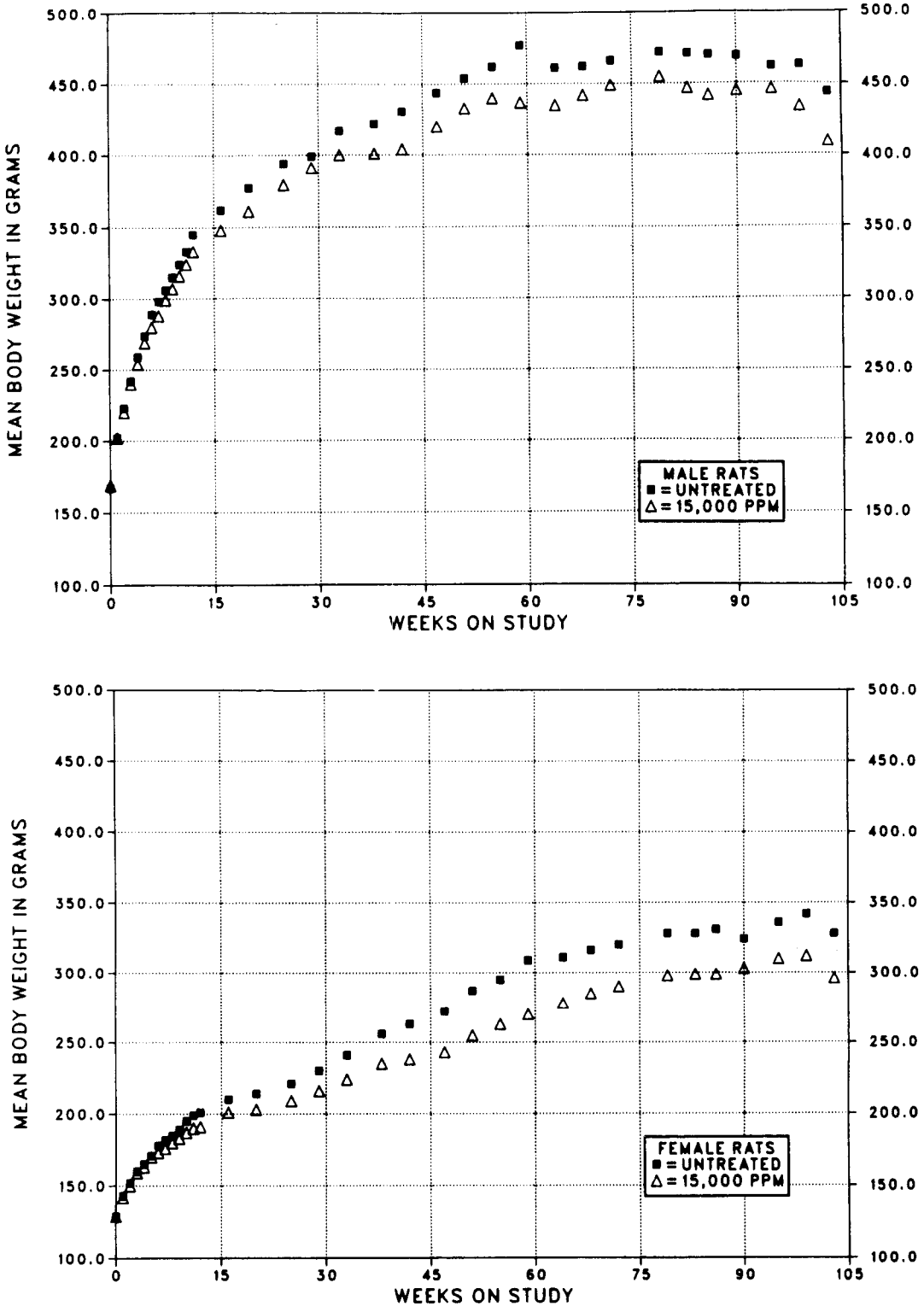


FIGURE 6. GROWTH CURVES FOR RATS EXPOSED TO CHLOROETHANE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female rats exposed to chloroethane at the concentrations used in these studies and for controls are shown in Table 9 and in the Kaplan and Meier curves in Figure 7. Although survival of exposed and control male rats was unusually low at the end of the study, no significant differences in survival were observed between exposed and control groups of either sex. At week 90, survival for rats was not unusually low; survival for male rats was 37/50 (controls) and 31/50 (exposed) and for female rats was 43/50 (controls) and 33/50 (exposed).

Pathology and Statistical Analyses of Results

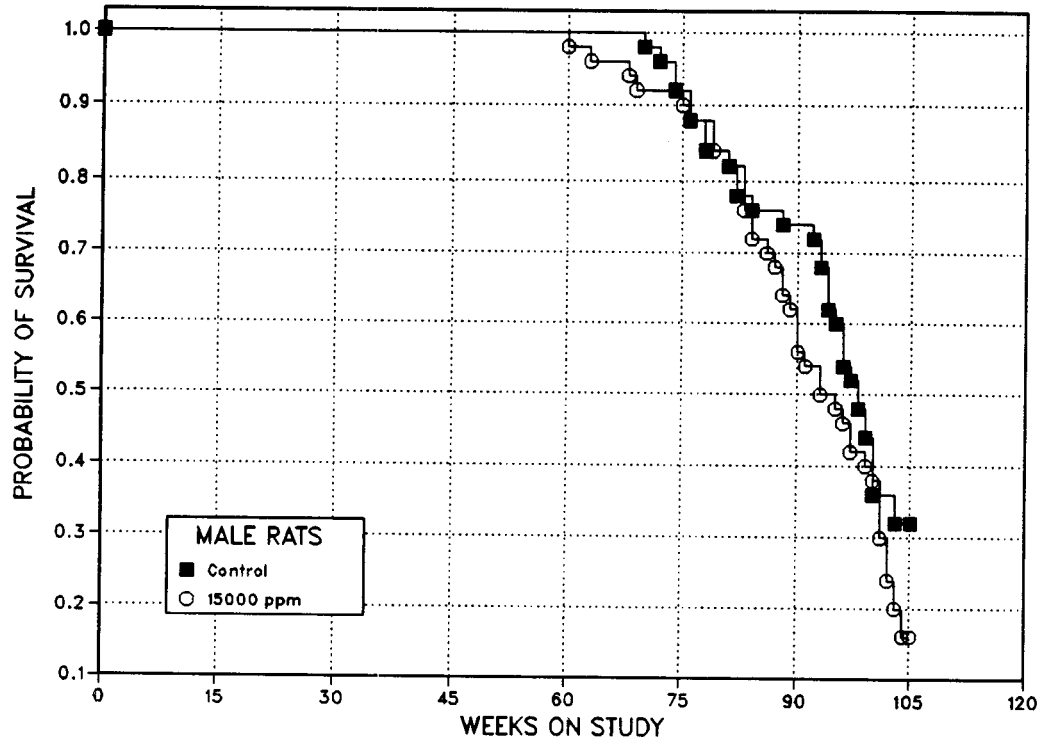
This section describes the statistically significant or biologically noteworthy changes in the incidences of rats with neoplastic or nonneoplastic lesions of the skin, brain, and hematopoietic system.

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 9. SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF CHLOROETHANE

	Chamber Control	15,000 ppm
MALE (a)		
Animals initially in study	50	50
Natural deaths	6	9
Moribund kills	28	33
Animals surviving until study termination	16	8
Survival P value (b)		0.161
FEMALE (a)		
Animals initially in study	50	50
Natural deaths	0	4
Moribund kills	19	24
Animals surviving until study termination	31	22
Survival P value (b)		0.083

(a) First day of termination period: 729
(b) The result of the life table pairwise comparison with the controls is in the dosed column.



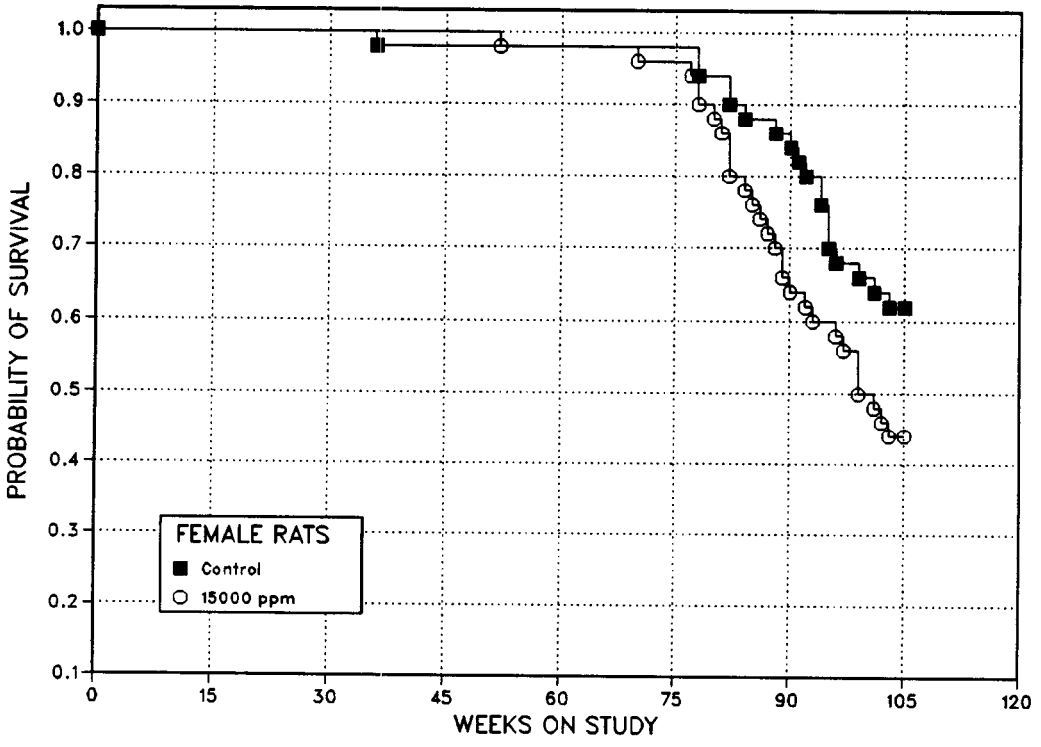


FIGURE 7. KAPLAN-MEIER SURVIVAL CURVES FOR RATS EXPOSED TO CHLOROETHANE BY INHALATION FOR TWO YEARS

Skin: Trichoepitheliomas, sebaceous gland adenomas, basal cell carcinomas, or squamous cell carcinomas were observed only in exposed male rats (Table 10). Keratoacanthomas occurred in four control and two exposed male rats. Trichoepitheliomas, sebaceous adenomas, and basal cell tumors are combined for statistical evaluation because they frequently have similar morphologic features. Basal cells in the epidermis or adnexa can differentiate into several cell types, and therefore, some epithelial tumors of the skin contain varying proportions of basal cells, sebaceous cells, or follicle-like structures. Classification is usually based on the predominant cellular component. Keratoacanthomas were not included in the combination for analysis because they have a characteristic architecture that differs from that of other skin tumors. They are invaginated beneath the epidermis to form a cyst-like structure containing keratin. The wall of the cyst-like structure consists of papillary projections of stratified squamous epithelium. Keratoacanthomas are believed to arise from hair follicles. Keratoacanthomas may progress to squamous cell carcinomas, and therefore, these were combined for statistical evaluation as well.

TABLE 10. SKIN TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE (a)

	Chamber Control	15,000 ppm
Trichoepithelioma		
Overall Rates	0/50 (0%)	1/50 (2%)
Sebaceous Gland Adenoma		
Overall Rates	0/50 (0%)	1/50 (2%)
Basal Cell Carcinoma		
Overall Rates	0/50 (0%)	3/50 (6%)
Trichoepithelioma, Sebaceous Gland Adenoma, or Basal Cell Carcinoma (b)		
Overall Rates	0/50 (0%)	5/50 (10%)
Terminal Rates	0/16 (0%)	1/8 (13%)
Day of First Observation		678
Logistic Regression Test		P=0.016
Squamous Cell Carcinoma		
Overall Rates	0/50 (0%)	2/50 (4%)
Keratoacanthoma		
Overall Rates	4/50 (8%)	2/50 (4%)
Keratoacanthoma or Squamous Cell Carcinoma (c)		
Overall Rates	4/50 (8%)	4/50 (8%)
Terminal Rates	2/16 (13%)	0/8 (0%)
Day of First Observation	682	577
Logistic Regression Test		P=0.578

(a) The statistical analyses used are discussed in Section II (Statistical Methods) and Table B3 (footnotes).
(b) Historical incidence in chamber controls at study laboratory (mean): 2/300 (0.7%); historical incidence in untreated controls (noninhalation) in NTP studies: 30/1,936 (2%)
(c) Historical incidence in chamber controls at study laboratory (mean): 17/300 (6%); historical incidence in untreated controls (noninhalation) in NTP studies: 70/1,936 (4%)

Brain: Malignant astrocytomas were seen in three exposed female rats, and gliosis, a nonneoplastic proliferation of glial cells, was observed in a fourth. Each of the female rats with an astrocytoma died before termination of the study (at weeks 52, 93, and 102), and the brain tumors may have been the primary contributing cause of death. Although this low incidence is not significant relative to concurrent controls, it is significant ($P<0.05$) relative to the incidence observed in chamber controls from previous studies at this laboratory (1/297) and also relative to the historical control incidence of glial cell tumors in untreated control female F344/N rats from previous NTP studies (23/1,969). However, the highest incidence observed in a single untreated control group is 3/50. Three primary tumors of glial cell origin were seen in male rats: a malignant oligodendroglioma in one control, and a benign oligodendroglioma and a malignant astrocytoma in two exposed animals.

Hematopoietic System: The incidences of mononuclear cell leukemia in exposed male and female rats were marginally greater than those in controls (male: control, 33/50; exposed, 36/50; female: 20/50; 25/50). Because mononuclear cell leukemia is a common tumor with variable incidences, the marginal increases in the incidences of leukemia were not considered biologically significant.

SINGLE-EXPOSURE STUDIES

All mice survived the 4-hour exposure to 19,000 ppm chloroethane. No clinical signs of toxicity were seen. The mice were not exposed at lower concentrations.

FOURTEEN-DAY STUDIES

All mice survived exposure at the sole concentration of 19,000 ppm (Table 11). Final mean body weights of exposed mice were higher than those of controls. No clinical signs of toxicity were seen. In addition, there were no compound-related gross observations at necropsy, nor were there compound-related microscopic findings.

TABLE 11. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY INHALATION STUDIES OF CHLOROETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	5/5	24.2 ± 0.4	27.0 ± 0.3	+2.8 ± 0.4	
19,000	5/5	24.4 ± 0.7	28.6 ± 0.9	+4.2 ± 0.2	105.9
FEMALE					
0	5/5	21.0 ± 0.3	21.6 ± 2.4	+0.6 ± 2.2	
19,000	5/5	21.0 ± 0.4	24.2 ± 0.6	+3.2 ± 0.7	112.0

(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

THIRTEEN-WEEK STUDIES

One of 10 male mice exposed to 10,000 ppm chloroethane died before the end of the studies (Table 12). The final mean body weights of all exposed groups were generally higher than those of controls. No compound-related clinical signs were seen. The liver weight to body weight ratio for female mice exposed to 19,000 ppm was significantly greater than that for controls (Table 13); however, no microscopic liver changes were observed. Nasal cavity hemorrhage of minimal severity was observed grossly in 3/10 male and 6/10 female mice exposed to 19,000 but was considered to be an artifact of necropsy and unrelated to exposure to chloroethane because no microscopic lesions associated with exposure to chloroethane were observed in the nasal mucosa of these animals.

Dose Selection Rationale: Although no chemically related toxic effects were observed in the short-term studies, concerns about potential flammability and the explosion hazard led to the selection of 0 and 15,000 ppm as the exposure concentrations for male and female mice for the 2-year studies.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of exposed male mice were up to 13% higher than those of controls throughout the study (Table 14 and Figure 8). Mean body weights of exposed and control female mice were generally similar throughout the study. Exposed females were hyperactive during the daily exposure period. Activity returned to normal soon after exposure ended.

TABLE 12. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE THIRTEEN-WEEK INHALATION STUDIES OF CHLOROETHANE

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	23.8 ± 0.5	30.2 ± 0.5	+6.4 ± 0.5	
2,500	10/10	24.2 ± 0.5	30.8 ± 0.3	+6.6 ± 0.4	102.0
5,000	10/10	24.0 ± 0.6	32.0 ± 0.9	+8.0 ± 0.5	106.0
10,000	(d) 9/10	23.1 ± 0.6	31.0 ± 0.6	+7.7 ± 0.6	102.6
19,000	10/10	23.7 ± 0.4	32.3 ± 0.6	+8.6 ± 0.5	107.0
FEMALE					
0	10/10	19.3 ± 0.6	26.9 ± 0.6	+7.6 ± 0.2	
2,500	10/10	18.5 ± 0.3	27.0 ± 0.4	+8.5 ± 0.3	100.4
5,000	10/10	19.0 ± 0.4	26.2 ± 0.4	+7.2 ± 0.5	97.4
10,000	10/10	20.7 ± 0.5	27.0 ± 0.5	+6.3 ± 0.7	100.4
19,000	10/10	19.6 ± 0.4	29.2 ± 0.5	+9.6 ± 0.3	108.6

(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

TABLE 13. LIVER WEIGHTS OF MICE IN THE THIRTEEN-WEEK INHALATION STUDIES OF CHLOROETHANE (a)

Concentration (ppm)	Number Weighed	Final Body Weight (grams)	Liver Weight (mg)	Liver Weight/ Final Body Weight (mg/g)
MALE				
0	10	30.2 ± 0.47	1,696 ± 31	56.2 ± 0.86
2,500	10	30.8 ± 0.29	1,814 ± 61	58.9 ± 1.74
5,000	10	32.0 ± 0.87	(b) 1,880 ± 44	58.9 ± 1.31
10,000	9	31.0 ± 0.55	1,591 ± 38	(b) 51.3 ± 0.92
19,000	10	(b) 32.3 ± 0.56	(c) 1,932 ± 48	59.8 ± 1.18
FEMALE				
0	10	26.9 ± 0.64	1,557 ± 46	57.9 ± 0.94
2,500	10	27.0 ± 0.36	1,604 ± 35	59.4 ± 1.06
5,000	10	26.2 ± 0.42	1,580 ± 40	60.4 ± 1.51
10,000	10	27.0 ± 0.54	1,540 ± 39	57.1 ± 0.99
19,000	10	(c) 29.2 ± 0.49	(c) 1,993 ± 66	(c) 68.2 ± 1.56

(a) Mean ± standard error; P values vs. the controls by Dunnett's test (Dunnett, 1955).
(b) $P<0.05$
(c) $P<0.01$

TABLE 14. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF CHLOROETHANE

Weeks on Study	Chamber Control		15,000 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of chamber controls)	No. of Survivors
MALE					
0	23.5	50	23.9	102	50
1	25.4	50	26.3	104	50
2	26.4	50	27.7	105	50
3	27.4	49	29.1	106	50
4	27.8	49	30.2	109	50
5	29.5	49	30.5	103	50
6	30.6	49	31.0	101	50
7	28.9	49	30.5	106	50
8	29.3	49	30.6	104	50
9	30.5	49	32.2	106	50
10	30.3	49	32.1	106	50
11	31.2	49	32.4	104	50
12	31.2	49	33.3	107	50
16	32.4	49	33.8	104	50
20	33.5	49	35.0	104	50
25	35.8	49	37.0	103	50
29	37.0	49	38.3	104	50
33	36.6	49	38.0	104	49
38	37.5	49	39.5	105	47
42	38.4	49	40.4	105	44
47	38.5	49	40.4	105	43
51	39.6	49	41.8	106	40
55	40.4	49	42.8	106	34
59	42.4	46	42.7	101	30
64	39.0	46	43.9	113	28
68	39.9	46	42.7	107	27
72	39.8	44	43.7	110	25
79	39.6	40	43.3	109	19
83	41.2	36	43.8	106	17
86	39.5	35	42.2	107	15
90	39.7	33	42.1	106	14
95	39.5	30	41.5	105	13
99	39.9	28	40.2	101	11
FEMALE					
0	19.1	50	18.7	98	50
1	20.7	50	21.5	104	50
2	21.6	50	22.9	106	50
3	23.4	50	23.8	102	50
4	23.5	50	23.7	101	50
5	24.0	50	24.2	101	50
6	24.3	50	25.7	106	50
7	25.2	50	26.8	106	50
8	25.6	49	26.1	102	50
9	26.4	49	27.6	105	50
10	26.8	49	27.7	103	50
11	26.2	49	27.2	104	50
12	26.7	49	28.4	106	50
16	27.6	49	28.9	105	50
20	27.3	48	29.3	107	50
25	29.4	47	29.9	102	50
29	29.3	47	29.9	102	50
33	29.4	47	29.3	100	50
38	29.0	47	30.1	104	50
42	31.0	47	30.8	99	50
47	31.3	47	31.7	101	49
51	33.4	46	31.3	94	49
55	33.3	46	32.1	96	49
59	33.2	46	33.8	102	49
64	33.8	46	30.8	91	49
68	33.5	46	32.8	98	48
72	33.0	45	32.5	98	47
79	33.6	45	32.4	96	42
83	33.1	45	33.2	100	37
86	33.2	43	33.4	101	31
90	33.5	43	31.7	95	22
95	33.0	39	34.9	106	9
99	34.4	34	33.5	97	2

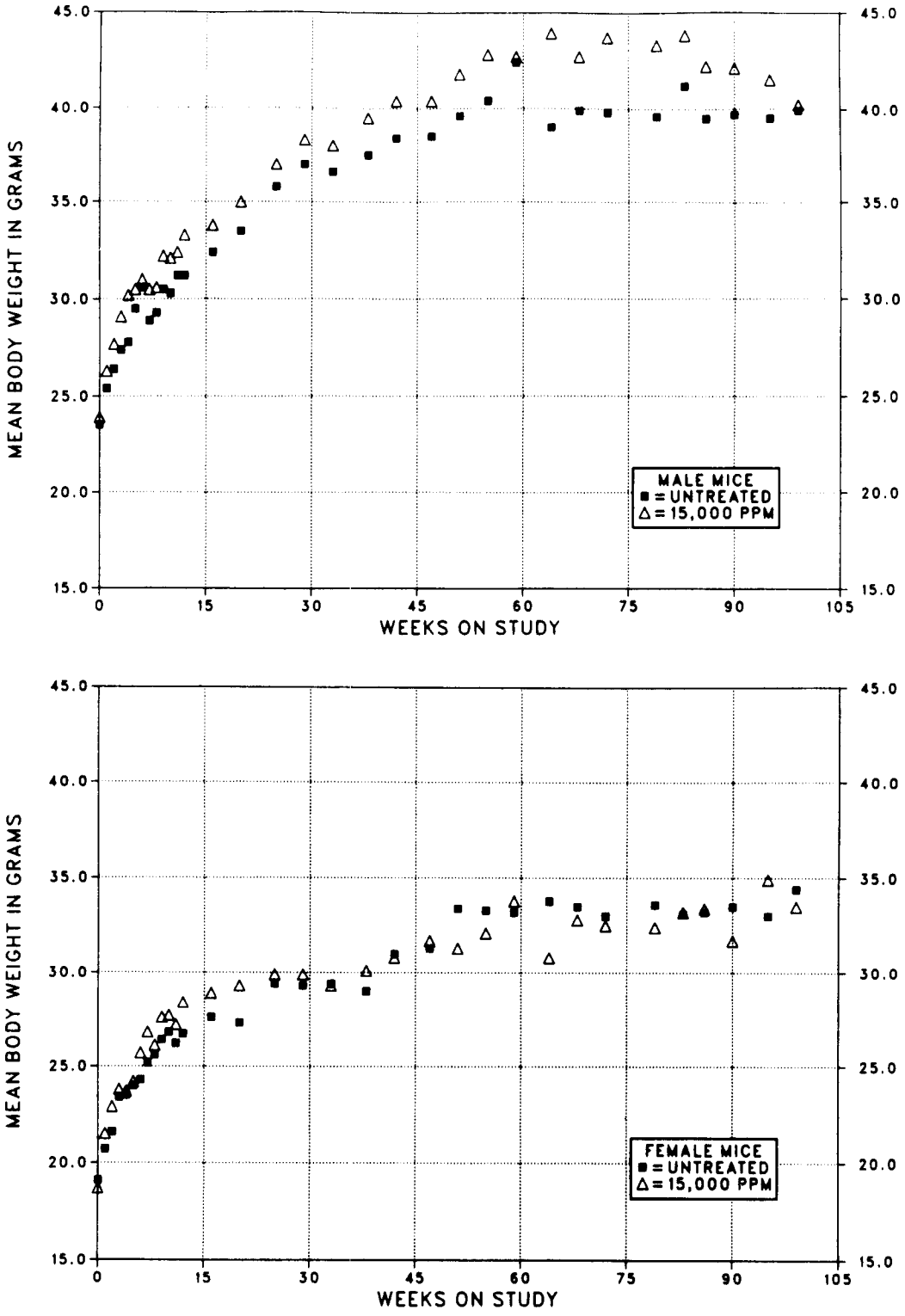


FIGURE 8. GROWTH CURVES FOR MICE EXPOSED TO CHLOROETHANE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female mice exposed to chloroethane at the concentrations used in these studies and for controls are shown in Table 15 and in the Kaplan and Meier curves in Figure 9. Survival of the exposed groups of both male (after day 330) and female (after day 574) mice was significantly lower than that of controls. As a result of poor survival, the mouse study was terminated at week 100.

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, liver, lung, hematopoietic system, kidney, and urogenital tract.

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 15. SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF CHLOROETHANE

	Chamber Control	15,000 ppm
MALE (a)		
Animals initially in study	50	50
Natural deaths	7	14
Moribund kills	15	25
Animals surviving until study termination	28	11
Survival P value (b)		<0.001
FEMALE (a)		
Animals initially in study	50	50
Natural deaths	6	18
Moribund kills	9	30
Accidentally killed	2	0
Animals missing	1	0
Animals surviving until study termination	32	2
Survival P value (b)		<0.001

(a) First day of termination period: 700
(b) The result of the life table pairwise comparison with the controls is in the dosed column.

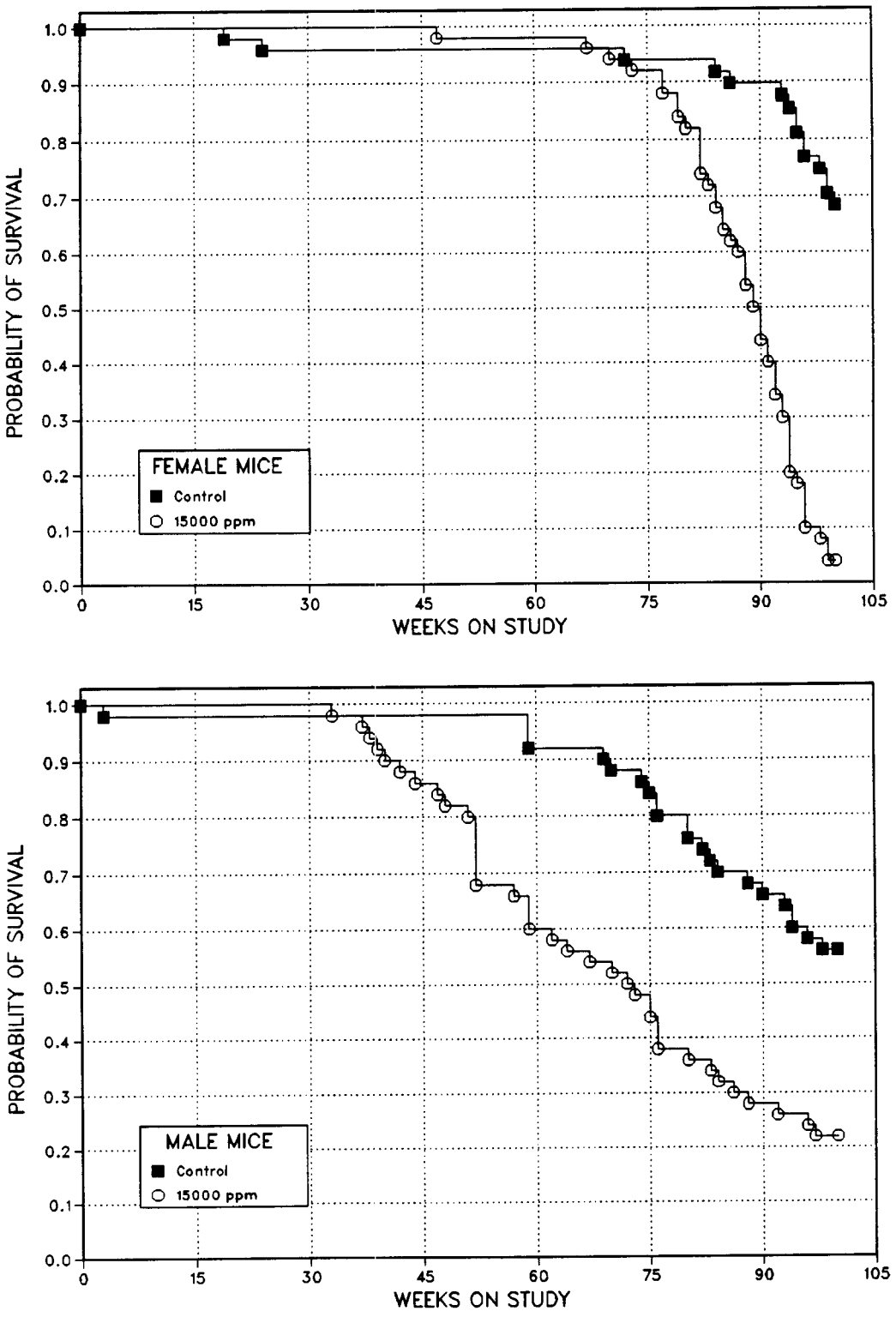


FIGURE 9. KAPLAN-MEIER SURVIVAL CURVES FOR MICE EXPOSED TO CHLOROETHANE BY INHALATION FOR TWO YEARS

Uterus: Exposure of female mice to chloroethane vapor caused the development of uterine carcinomas in 86% of exposed animals (Table 16). The uterine carcinomas were of endometrial gland origin and consisted of anaplastic epithelial cells arranged in irregular glandular structures, complex papillary formations, or solid sheets of cells. The tumors were highly malignant and invaded the myometrium of the uterus and, in 34 animals, metastasized to a wide variety of organs, primarily lung (23), ovary (22), lymph nodes (18), kidney (8), adrenal gland (8), pancreas (7), urinary bladder (7), mesentery (7), spleen (5), heart (4), and to a lesser extent, colon (2), stomach (1), gallbladder (1), small intestine (1), ureter (1), and liver (1).

A uterine carcinoma occurred in a single control female mouse. However, this spontaneous neoplasm was not similar to those occurring in exposed female mice in that it consisted of nests and ribbons of epithelial cells embedded in a homogenous eosinophilic matrix characteristic of a yolk sac carcinoma of ovarian origin. The ovaries of this mouse were normal, and the precise histogenesis of the uterine tumor is uncertain.

Uterine endometrial hyperplasia occurred at a decreased incidence in exposed female mice relative to that in controls (control, 41/49; exposed, 6/50). This lesion is not part of the morphologic continuum of uterine neoplasia, and it is a common degenerative change normally observed in aging animals. The decreased incidence of uterine hyperplasia in exposed female mice is the result of the presence of the uterine carcinomas that obliterated much of the normal tissue.

Liver: The incidence of hepatocellular carcinomas in exposed female mice was significantly greater than that in controls (Table 17). An additional exposed female had a hepatocellular adenoma.

Lung: The incidences of alveolar/bronchiolar adenomas and of alveolar/bronchiolar adenomas or carcinomas (combined) in exposed male mice were significantly greater than those in controls (Table 18).

TABLE 16. UTERINE CARCINOMAS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE (a,b)

	Chamber Control	15,000 ppm
Overall Rates	(c) 0/49 (0%)	43/50 (86%)
Terminal Rates	0/32 (0%)	2/2 (100%)
Day of First Observation		469
Logistic Regression Test		P<0.001

(a) The statistical analyses used are discussed in Section II (Statistical Methods) and Table D3 (footnotes).
(b) Historical incidence of uterine glandular neoplasms 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) One chamber control mouse had a uterine carcinoma not of endometrial origin.

TABLE 17. HEPATOCELLULAR TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE

	Chamber Control	15,000 ppm
Adenoma		
Overall Rates	0/49 (0%)	1/48 (2%)
Carcinoma		
Overall Rates	3/49 (6%)	7/48 (15%)
Terminal Rates	3/32 (9%)	0/2 (0%)
Day of First Observation	700	622
Logistic Regression Test		P=0.025
Adenoma or Carcinoma (a)		
Overall Rates	3/49 (6%)	8/48 (17%)
Terminal Rates	3/32 (9%)	0/2 (0%)
Day of First Observation	700	590
Logistic Regression Test		P=0.025

(a) Historical incidence in chamber controls at study laboratory (mean ± SD): 29/347 (8% ± 4%); historical incidence in untreated controls (noninhalation) in NTP studies: 184/2,032 (9% ± 5%)

TABLE 18. ALVEOLAR/BRONCHIOLAR LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE

	Chamber Control	15,000 ppm
Alveolar Epithelium Hyperplasia		
Overall Rates	0/50 (0%)	1/48 (2%)
Adenoma		
Overall Rates	3/50 (6%)	8/48 (17%)
Terminal Rates	3/28 (11%)	3/11 (27%)
Day of First Observation	700	409
Logistic Regression Test		P=0.015
Carcinoma		
Overall Rates	2/50 (4%)	2/48 (4%)
Adenoma or Carcinoma (a)		
Overall Rates	5/50 (10%)	10/48 (21%)
Terminal Rates	5/28 (18%)	4/11 (36%)
Day of First Observation	700	409
Logistic Regression Test		P=0.008

(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%)

Hematopoietic System: The incidence of lymphomas was marginally increased in exposed female mice (control, 4/49; exposed, 10/50). Granulocytic leukemia was observed in an additional exposed female mouse. The incidence in the control group (4/49, 8%) was lower than that in historical chamber controls at the study laboratory (73/348, 21%) and in noninhalation untreated historical controls (636/2,040, 31%).

Kidney: The incidence of nephropathy was marginally increased in exposed female mice (control, 10/49; exposed, 20/47). No renal neoplasms were observed in exposed or control animals. The nephropathy was characterized by scattered foci of tubular regeneration and minimal glomerulosclerosis. Karyomegaly (nuclear enlargement) of renal tubular epithelial cells was also reported in exposed mice (male: 0/50; 40/49; female: 0/49; 5/47), but the change was extremely subtle and minimal in severity. Mouse cells normally have some degree of variation in nuclear size, but exposed male mice were judged to have more cells with enlarged nuclei than did controls.

Urogenital Tract: Greater than normal incidences of nonneoplastic urogenital lesions were observed in control and exposed male mice, with exposed mice appearing to be more affected. The lesions included inflammation, abscess, ulceration, and, in some cases, necrosis of the prepuce, preputial gland, penis, urinary bladder, and kidney, indicative of an ascending urinary tract infection. The lesions appeared early in the study. The greater incidence in exposed male mice may have been a contributing factor to the reduced survival in exposed male mice.

Chloroethane, at doses of 10, 20, and 42 μg/plate, was tested for induction of reverse gene mutations in *Salmonella typhimurium* strains TA98, TA100, and TA1535 under a newly developed protocol for testing volatile chemicals within the closed environment of a desiccator to ensure adequate exposure (Table 19). The high dose was toxic to all three strains. All strains were tested in both the presence and absence of Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver S9. A positive response was observed in strain TA1535 with and without S9 and in strain TA100 only in the presence of rat liver S9. An increase in revertant colonies was observed in strain TA100 when exposure occurred in the presence of hamster S9, but this was of insufficient magnitude for a positive call. No mutagenic activity was observed in strain TA98 with or without S9.

TABLE 19. MUTAGENICITY OF CHLOROETHANE IN *SALMONELLA TYPHIMURIUM* (a)

Strain	Dose (g/chamber)	Revertants/Plate (b)					
TA100		−S9					
		Trial 1	Trial 2	Trial 3			
	0	128 ± 6.8	131 ± 4.9	112 ± 7.6			
	10	146 ± 5.0	133 ± 10.3	--			
	20	--	--	103 ± 21.1			
Trial summary		Negative	Negative	Negative			
Positive control (c)		738 ± 20	452 ± 28.4	647 ± 6.5			
		+30% S9 (hamster)			+30% S9 (rat)		
		Trial 1	Trial 2	Trial 3	Trial 1	Trial 2	Trial 3
	0	122 ± 9.2	138 ± 5.2	117 ± 7.7	139 ± 3.7	136 ± 7.9	115 ± 2.6
	10	128 ± 7.3	234 ± 8.5	--	368 ± 8.5	209 ± 6.4	--
	20	--	--	168 ± 44.3	--	--	275 ± 9.5
Trial summary		Negative	Equivocal	Equivocal	Positive	Equivocal	Positive
Positive control (c)		919 ± 14.8	862 ± 53.8	879 ± 5.6	1,236 ± 28.2	1,164 ± 80.5	919 ± 23.1
TA1535		−S9					
		Trial 1	Trial 2				
	0	14 ± 1.5	21 ± 1.7				
	10	133 ± 3.6	--				
	20	--	200 ± 17.6				
Trial summary		Positive	Positive				
Positive control (c)		142 ± 31.5	199 ± 10.4				
		+30% S9 (hamster)			+30% S9 (rat)		
		Trial 1	Trial 2	Trial 3	Trial 1	Trial 2	Trial 3
	0	15 ± 3.2	12 ± 2.3	14 ± 0.7	18 ± 1.8	15 ± 0.9	14 ± 0.6
	10	102 ± 2.9	251 ± 12.2	--	375 ± 11.1	203 ± 7.8	--
	20	--	--	346 ± 43.7	--	--	287 ± 6.0
Trial summary		Positive	Positive	Positive	Positive	Positive	Positive
Positive control (c)		290 ± 13.1	228 ± 18.3	242 ± 16.4	206 ± 18	344 ± 8.3	475 ± 15.2
TA98		−S9			+30% S9 (rat)		
	0	19 ± 1.7			21 ± 2.5		
	10	21 ± 1.5			34 ± 1.2		
Trial summary		Negative			Negative		
Positive control (c)		170 ± 4.1			617 ± 223.3		

(a) Study performed at Microbiological Associates, Inc. Cells were incubated in the absence of exogenous metabolic activation (−S9) or with Aroclor 1254-induced S9 from male Syrian hamster liver or male Sprague Dawley rat liver. High dose was limited by toxicity; 0 g/chamber is the negative control. Exposure to chloroethane equilibrated with air was conducted by incubating the plates for 48 hours within the closed environment of a desiccator.
(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 and TA1535.

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 chloroethane by inhalation to male and female F344/N rats and B6C3F$_1$ mice in single 4-hour, 14-day, 13-week, and 2-year studies. The exposure concentrations for male and female rats and mice were as follows: 19,000 ppm for a single 4-hour exposure; 0 and 19,000 ppm for 6 hours per day, 5 days per week for 2 weeks; 0, 2,500, 5,000, 10,000, or 19,000 ppm for 6 hours per day, 5 days per week for 13 weeks; and 0 or 15,000 ppm for 2 years. The inhalation route of exposure was chosen to mimic human exposure.

Short-Term Studies

In the single 4-hour exposure studies and in the 14-day studies, all rats and mice survived at the sole concentration of 19,000 ppm chloroethane. No clinical signs of toxicity were seen. In the 14-day studies, the final mean body weights of exposed male rats, male mice, and female mice were slightly higher than those of controls. Mean body weights of exposed and control female rats were similar. In addition, no compound-related gross or microscopic effects in rats or mice exposed to chloroethane were observed. The absence of compound-induced mortality and toxic effects was the basis for selecting 19,000 ppm as the highest exposure concentration in the 13-week studies.

All rats and mice survived to the end of the 13-week studies, except one male mouse in the 10,000-ppm group which died during week 1. Chloroethane exposure did not produce clinical signs or gross or microscopic pathologic effects. The final mean body weights of exposed rat groups were all slightly lower than those of controls (less than 8%). The final mean body weights of exposed groups of mice were generally higher than those of controls. Although no chemically related toxic effects were observed in the short-term studies, concerns about potential flammability and the explosion hazard led to the selection of 0 and 15,000 ppm as the exposure concentrations for male and female rats and mice for the 2-year studies.

Two-Year Studies in Rats

Male and female rats were exposed to 0 or 15,000 ppm chloroethane for 2 years. In these studies, survival of both control and exposed male rats and exposed female rats was low at the end of the studies (male: control, 16/50; exposed, 8/50; female: 31/50; 22/50). However, there were no statistically significant differences in survival between exposed and control groups of either sex. At week 90, survival was not low (male: 37/50; 31/50; female: 43/50; 33/50). At week 95, survival in all groups was at or above 48%; therefore, these studies are considered adequate for evaluation of carcinogenicity. The unusually high incidences of mononuclear cell leukemia in both exposed and control rats may have contributed to the high mortality. Mean body weights of exposed male rats were similar to those of controls, and mean body weights of exposed female rats were generally 5%-13% lower than those of controls. Chloroethane exposure did not produce clinical signs.

Exposure to chloroethane was associated with development of astrocytomas (uncommon malignant glial cell tumors of the brain) in three exposed female rats and gliosis (a nonneoplastic proliferation of glial cells) in a fourth. The three female rats with astrocytomas died before the end of the study; these tumors may have been the primary cause of death. Although the incidence of malignant astrocytomas is not statistically increased vs. the concurrent controls, the incidence is significant when compared with that reported in inhalation chamber controls from previous studies at the study laboratory (1/297) and relative to the historical incidence of glial cell tumors in untreated control female F344/N rats in NTP noninhalation studies (23/1,969). The greatest incidence reported to date from any one such untreated control group is 3/50. Primary tumors of glial cell origin were also observed in male rats. One control male rat had a malignant oligodendroglioma; a benign oligodendroglioma and a malignant astrocytoma were observed in two exposed males.

In the 2-year bromoethane studies (NTP, 1989), neoplasms of the brain were observed in exposed male and female rats but not in controls. Granular cell tumors were observed in male rats exposed to bromoethane (control, 0/49; 100 ppm, 3/50; 200 ppm, 1/50; 400 ppm, 1/50). In addition, glial cell tumors (a glioma, an astrocytoma, and an oligodendroglioma) were observed in males

exposed to 100 ppm bromoethane. Female rats exposed to bromoethane at the same concentrations as males had a concentration-related incidence of gliomas (0/50; 1/50; 1/48; 3/50). Although in both the chloroethane and bromoethane studies the incidence of brain neoplasms could not be clearly associated with chemical exposure, the total incidence of brain neoplasms for the two structurally related chemicals is 18/398 (4.5%) for male and female rats. This is clearly a greater incidence of brain neoplasms than has been seen in control rats in NTP studies and is deserving of attention.

Low incidences of several types of skin neoplasms occurred only in exposed male rats. These included trichoepitheliomas (1/50), sebaceous gland adenomas (1/50), and basal cell carcinomas (3/50). All are epithelial tumors that arise from the epidermis or adnexal structures. The incidence of each of these morphologic types of skin tumors in exposed rats is not significantly greater than that in controls, but the combined incidence (5/50) is greater than the mean historical incidence of epithelial skin tumors for chamber controls from the study laboratory (2/300, 0.7%) and the historical incidence in untreated controls in previous NTP noninhalation studies (30/1,936, 2%). Keratoacanthomas occurred in 4/50 control and 2/50 exposed male rats; squamous cell carcinomas were observed in 0/50 control and 2/50 exposed males. The combined incidence of these two tumors was not significantly greater than that in controls. Although the skin is directly exposed to chloroethane vapor, the epithelial tumors cannot be related with certainty to chloroethane exposure because the marginally increased incidence in the exposed group is not statistically significant and the neoplasms were of various morphologic types. Skin tumors were not observed in female rats or mice exposed to chloroethane or in rats exposed for 2 years to bromoethane (NTP, 1989).

Two-Year Studies in Mice

Male and female mice were exposed to 0 or 15,000 ppm for 2 years. Survival of exposed male mice was significantly lower than that of controls after week 48; after week 72, survival was reduced to 50%. Because of the reduced number of exposed male mice surviving to the end of the study and the absence of obvious carcinogenic effects, this study was considered inadequate for determination of carcinogenicity. During the study, greater than normal incidences of nonneoplastic urogenital lesions were observed in individually housed control and exposed male mice and may have contributed to the reduced survival. Exposed mice were more severely affected than controls, as indicated during formal clinical observations and histopathologic review. Male rats exposed in the same chamber were unaffected. The condition was generally described as a preputial infection with ascending urinary tract infection. The lesions included inflammation, abscesses, ulceration, and, in some cases, necrosis with involvement of the prepuce, preputial gland, penis, urinary bladder, and kidney. The most common reason for removal of moribund male mice from the study was urinary bladder distention, presumably a result of urethral obstruction. Cultures of bacteria from various sites identified several common organisms commensal in rodents. The etiology of this condition could not be determined, and the apparent contribution of chloroethane exposure to the incidence or the severity of these lesions is not understood. However, chloroethane is a skin irritant and may have exacerbated the condition.

Although survival of exposed male mice was significantly reduced, mean body weights of exposed males were generally higher than those of controls throughout the study. Whether the increase in mean body weight in exposed mice as compared with that in controls (up to 13% greater) is due to the reduced sample size of exposed mice or to the presence or absence of urinary tract infections is not known. No chloroethane-related clinical signs other than those discussed above were observed.

Survival of exposed female mice after week 82 was significantly lower than that of controls; the majority of exposed females died as a result of chloroethane-induced carcinomas of the uterus. An unusual clinical sign, hyperactivity, was observed in exposed female mice, but all control animals, as well as exposed male and female rats and male mice, exhibited normal behavior. The hyperactivity was most intense at the start of each exposure day and was characterized by the

animals' running and climbing about the cages. The activity continued throughout most of the exposure period, with intervals of rest and apparent fatigue gradually increasing until the end of the exposure period. After the daily exposure period was concluded, the behavior of the exposed females was similar to that of controls. The etiology of this hyperactivity is unknown. In spite of the increased activity, mean body weights of exposed female mice were generally similar to those of controls throughout the study.

A highly significant incidence (86%) of uterine carcinomas of endometrial origin, clearly associated with chloroethane exposure, was observed in exposed female mice. Although one control female mouse did have a carcinoma of the uterus, the carcinoma was not considered to be of endometrial origin and was morphologically different from those occurring in exposed mice. The tumors in exposed females were highly malignant and invaded the myometrium of the uterus; 34 metastasized to a wide variety of organs. Adenomas, carcinomas, and squamous cell carcinomas of the uterus were observed in female mice exposed by inhalation to the structurally related bromoethane at concentrations of 100, 200, or 400 ppm (4/50; 5/47; 27/48) for 2 years but not in control mice (NTP, 1989). Although not statistically significant, uterine adenocarcinomas did occur in female mice administered time-weighted-average doses of 148 mg/kg or 299 mg/kg 1,2-dichloroethane per day by gavage for 78 weeks (3/49; 4/47) (NCI, 1978a). In addition, uterine endometrial stromal sarcomas and polyps were observed in low dose and high dose female mice; the incidence of stromal sarcomas and polyps when combined was significantly different from that in controls. However, uterine carcinomas were not observed in female mice in long-term studies with a number of chloroethanes--1,1-dichloroethane (NCI, 1978b), 1,1,1-trichloroethane (NCI, 1977), 1,1,2-trichloroethane (NCI, 1978c), 1,1,1,2-tetrachloroethane (NTP, 1983a), 1,1,2,2-tetrachloroethane (NCI, 1978d), pentachloroethane (NTP, 1983b), and hexachloroethane (NCI, 1978e).

The incidence of hepatocellular carcinomas in female mice exposed to chloroethane was significantly greater than that in controls (control, 3/49; exposed, 7/48). Another exposed female had a hepatocellular adenoma. The incidence of hepatocellular adenomas or carcinomas (combined) in exposed female mice (17%) is greater than the historical incidence in chamber controls from the study laboratory (29/347, 8%) or in untreated control female mice from NTP studies (184/2,032, 9%). The one adenoma reported in an exposed female mouse was observed on day 590. It is possible that if survival of exposed females had not been reduced as a result of chloroethane-induced uterine carcinomas, the incidence of hepatocellular neoplasms might have been greater. Increased incidences of these neoplasms did not occur, however, in male or female rats exposed to chloroethane. Chemical-related hepatocellular carcinomas have been observed in other long-term NCI/NTP chloroethane studies--1,1,1-trichloroethane (NCI, 1977), 1,1,2-trichloroethane (NCI, 1978c), 1,1,1,2-tetrachloroethane (NTP, 1983a), 1,1,2,2-tetrachloroethane (NCI, 1978d), pentachloroethane (NTP, 1983b), and hexachloroethane (NCI, 1978e).

The incidence of alveolar/bronchiolar neoplasms of the lung in exposed male mice was significantly greater than that in controls (adenomas: control, 3/50; exposed, 8/48; adenomas or carcinomas, combined: 5/50; 10/48). Although these neoplasms are relatively common in male mice (historical incidence in chamber controls: 75/348, 22%), the potential expression of alveolar/bronchiolar neoplasms in exposed male mice was probably reduced by the poor survival of exposed animals. This is supported by the fact that adenomas in exposed mice were detected as early as day 409, whereas adenomas or carcinomas in control mice were not observed until day 700.

One would expect that in an inhalation study the respiratory tract would be a likely target. However, the association of exposure to chloroethane with the incidence of alveolar/bronchiolar neoplasms is not clear, especially since there were no supporting nonneoplastic lesions in the lungs of exposed mice and no neoplasms were seen in exposed female mice or rats. The remainder of the respiratory tract, including the nasal cavity, was unaffected by chloroethane exposure as well. In several 2-year inhalation and long-term gavage studies with structurally related compounds, neoplasms of the lung have

been reported. Inhalation exposure of male mice to bromoethane for 2 years produced increased incidences of alveolar/bronchiolar adenomas or carcinomas (combined) (control, 7/50; 100 ppm, 6/50; 200 ppm, 12/50; 400 ppm, 15/50) (NTP, 1989). Neoplasms of the nasal cavity and upper respiratory tract were not observed in bromoethane-exposed male mice. Alveolar/bronchiolar neoplasms were reported for female F344/N rats exposed by inhalation to 40 ppm 1,2-dibromoethane (NTP, 1982) and for male and female $B6C3F_1$ mice exposed to 10 or 40 ppm 1,2-dibromoethane. Neoplasms of the nasal cavity were observed in male and female rats exposed to 10 and 40 ppm 1,2-dibromoethane and in female mice exposed to 40 ppm but not in male mice. Lung neoplasms were significantly increased in male $B6C3F_1$ mice dosed with 1,2-dichloroethane by gavage at 195 mg/kg per day and in female $B6C3F_1$ mice dosed with 1,2-dichloroethane by gavage at 299 mg/kg per day (NCI, 1978a). Long-term gavage administration of 1,1-dichloroethane did not result in alveolar/bronchiolar neoplasms (NCI, 1978b).

Genetic Toxicology

Chloroethane is mutagenic in Salmonella both in the absence and presence of exogenous metabolic activation. Chloroethane's S9-independent mutagenicity is consistent with the activity of an alkylating agent. This activity was observed primarily in the base substitution strains (e.g., TA100 and TA1535) and, because of the volatility of the chemical, only when the test was conducted in desiccators. The above data and the chemical structure of chloroethane suggest a potential for carcinogenic activity that may occur at, but not be limited to, the site of initial contact. The skin, which was the site of malignant and benign epithelial neoplasms in male rats, and the lung, where there was an increase of alveolar/bronchiolar neoplasms in male mice, are both initial contact sites in these inhalation studies.

Audit

The experimental and tabulated data for the NTP Technical Report on chloroethane 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 *equivocal evidence of carcinogenic activity** of chloroethane for male F344/N rats, as indicated by benign and malignant epithelial neoplasms of the skin. For female F344/N rats, there was *equivocal evidence of carcinogenic activity*, as indicated by three uncommon malignant astrocytomas of the brain in the exposed group. The study in male $B6C3F_1$ mice was considered to be an *inadequate study of carcinogenicity* because of reduced survival in the exposed group. However, there was an increased incidence of alveolar/bronchiolar neoplasms of the lung. There was *clear evidence of carcinogenic activity* for female $B6C3F_1$ mice, as indicated by carcinomas of the uterus. A marginally increased incidence of hepatocellular neoplasms was observed in the exposed group.

*Explanation of Levels of Evidence of Carcinogenic Activity is on page 6.
A summary of the Peer Review comments and the public discussion on this Technical Report appears on page 9.

V. REFERENCES

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APPENDIX A

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

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

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	50	50
ALIMENTARY SYSTEM		
Intestine large, colon	(50)	(45)
Mesothelioma malignant, metastatic, testes		1 (2%)
Liver	(50)	(50)
Hepatocellular carcinoma	1 (2%)	
Leukemia mononuclear	31 (62%)	34 (68%)
Lymphoma malignant histiocytic	1 (2%)	
Mesothelioma malignant, metastatic, testes		1 (2%)
Neoplastic nodule, multiple		1 (2%)
Mesentery	*(50)	*(50)
Mesothelioma malignant, metastatic, testes	1 (2%)	1 (2%)
Pancreas	(50)	(49)
Leukemia mononuclear	4 (8%)	7 (14%)
Mesothelioma malignant	1 (2%)	
Mesothelioma malignant, metastatic, testes	1 (2%)	1 (2%)
Stomach	(50)	(50)
Leukemia mononuclear		1 (2%)
Stomach, forestomach	(48)	(49)
Papilloma squamous	1 (2%)	
Serosa, mesothelioma malignant, metastatic, testes		2 (4%)
CARDIOVASCULAR SYSTEM		
Heart	(50)	(50)
Leukemia mononuclear	12 (24%)	14 (28%)
Schwannoma, NOS	1 (2%)	
ENDOCRINE SYSTEM		
Adrenal gland	(50)	(50)
Leukemia mononuclear		1 (2%)
Mesothelioma malignant, metastatic, testes	1 (2%)	
Adrenal gland, cortex	(50)	(50)
Adenoma	1 (2%)	
Leukemia mononuclear	14 (28%)	14 (28%)
Lymphoma malignant histiocytic	1 (2%)	
Adrenal gland, medulla	(36)	(48)
Leukemia mononuclear	8 (22%)	10 (21%)
Pheochromocytoma malignant		1 (2%)
Pheochromocytoma benign	7 (19%)	2 (4%)
Bilateral, pheochromocytoma benign	1 (3%)	7 (15%)
Islets, pancreatic	(48)	(48)
Adenoma	6 (13%)	2 (4%)
Adenoma, multiple		1 (2%)
Parathyroid gland	(31)	(41)
Adenoma	1 (3%)	
Pituitary gland	(49)	(50)
Leukemia mononuclear	7 (14%)	6 (12%)
Pars distalis, adenoma	31 (63%)	25 (50%)
Pars distalis, carcinoma	1 (2%)	
Pars distalis, leukemia mononuclear	3 (6%)	1 (2%)
Pars intermedia, adenoma	1 (2%)	
Thyroid gland	(49)	(47)
C-cell, adenoma	6 (12%)	1 (2%)
C-cell, adenoma, multiple	1 (2%)	
C-cell, carcinoma	2 (4%)	
Follicular cell, carcinoma	2 (4%)	

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

	Chamber Control	15,000 ppm
GENERAL BODY SYSTEM		
Tissue, NOS	*(50)	*(50)
Chordoma		1 (2%)
Leukemia mononuclear		1 (2%)
Sarcoma		1 (2%)
GENITAL SYSTEM		
Preputial gland	(47)	(45)
Adenoma	1 (2%)	1 (2%)
Carcinoma	1 (2%)	2 (4%)
Prostate	(50)	(48)
Sarcoma, metastatic, uncertain primary site		1 (2%)
Seminal vesicle	*(50)	*(50)
Sarcoma, metastatic, uncertain primary site		1 (2%)
Testes	(50)	(50)
Leukemia mononuclear	4 (8%)	2 (4%)
Mesothelioma malignant	1 (2%)	
Bilateral, interstitial cell, adenoma	19 (38%)	8 (16%)
Interstitial cell, adenoma	10 (20%)	17 (34%)
Tunic, mesothelioma malignant		3 (6%)
HEMATOPOIETIC SYSTEM		
Bone marrow	(50)	(48)
Leukemia mononuclear	2 (4%)	7 (15%)
Lymphoma malignant histiocytic	1 (2%)	
Lymph node	(49)	(50)
Sarcoma, metastatic, uncertain primary site		1 (2%)
Mesenteric, leukemia mononuclear	2 (4%)	1 (2%)
Pancreatic, leukemia mononuclear	1 (2%)	
Renal, leukemia mononuclear	3 (6%)	
Lymph node, bronchial	(42)	(48)
Leukemia mononuclear	15 (36%)	12 (25%)
Lymph node, mandibular	(45)	(38)
Leukemia mononuclear	14 (31%)	8 (21%)
Spleen	(50)	(50)
Hemangioma	1 (2%)	
Leukemia mononuclear	30 (60%)	35 (70%)
Mesothelioma malignant	1 (2%)	
Mesothelioma malignant, metastatic, testes		1 (2%)
Thymus	(39)	(41)
Leukemia mononuclear	3 (8%)	2 (5%)
INTEGUMENTARY SYSTEM		
Mammary gland	(13)	(14)
Fibroadenoma	1 (8%)	
Skin	(49)	(46)
Basal cell carcinoma		3 (7%)
Keratoacanthoma	4 (8%)	2 (4%)
Squamous cell carcinoma		1 (2%)
Trichoepithelioma		1 (2%)
Lip, squamous cell carcinoma		1 (2%)
Sebaceous gland, adenoma		1 (2%)
Subcutaneous tissue, fibroma	1 (2%)	2 (4%)
Subcutaneous tissue, fibrous histiocytoma		1 (2%)
Subcutaneous tissue, lipoma		1 (2%)
Subcutaneous tissue, neurofibrosarcoma		1 (2%)

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

	Chamber Control	15,000 ppm
MUSCULOSKELETAL SYSTEM		
None		
NERVOUS SYSTEM		
Brain	(50)	(50)
Astrocytoma malignant		1 (2%)
Granular cell tumor malignant	1 (2%)	
Leukemia mononuclear	2 (4%)	4 (8%)
Oligodendroglioma benign		1 (2%)
Oligodendroglioma malignant	1 (2%)	
RESPIRATORY SYSTEM		
Larynx	(49)	(44)
Leukemia mononuclear		1 (2%)
Lung	(50)	(50)
Leukemia mononuclear	24 (48%)	27 (54%)
Sarcoma, metastatic		1 (2%)
Squamous cell carcinoma		1 (2%)
Mediastinum, mesothelioma benign	1 (2%)	
Nose	(50)	(49)
Leukemia mononuclear	6 (12%)	4 (8%)
SPECIAL SENSES SYSTEM		
Zymbal gland	*(50)	*(50)
Carcinoma	1 (2%)	
URINARY SYSTEM		
Kidney	(50)	(50)
Leukemia mononuclear	12 (24%)	14 (28%)
Lipoma, moderate	1 (2%)	
Lymphoma malignant histiocytic	1 (2%)	
Renal tubule, carcinoma		1 (2%)
Urinary bladder	(50)	(49)
Leukemia mononuclear	1 (2%)	4 (8%)
Mesothelioma malignant, metastatic, testes	1 (2%)	1 (2%)
Sarcoma, metastatic, uncertain primary site		1 (2%)
SYSTEMIC LESIONS		
Multiple organs	*(50)	*(50)
Leukemia mononuclear	33 (66%)	36 (72%)
Mesothelioma malignant	2 (4%)	3 (6%)
Lymphoma malignant histiocytic	1 (2%)	
Hemangioma	1 (2%)	
Mesothelioma benign	1 (2%)	
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	50	50
Moribund sacrifice	28	33
Terminal sacrifice	16	8
Natural death	6	9

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

	Chamber Control	15,000 ppm
TUMOR SUMMARY		
Total animals with primary neoplasms **	49	48
Total primary neoplasms	142	127
Total animals with benign neoplasms	46	44
Total benign neoplasms	95	73
Total animals with malignant neoplasms	39	40
Total malignant neoplasms	46	54
Total animals with secondary neoplasms ***	1	3
Total secondary neoplasms	4	13
Total animals with malignant neoplasms-- uncertain primary site		1
Total animals with neoplasms-- uncertain benign or malignant	1	
Total uncertain neoplasms	1	

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** 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 CHLOROETHANE: CHAMBER CONTROL

WEEKS ON STUDY	0 7 0	0 7 2	0 7 4	0 7 4	0 7 6	0 7 6	0 7 8	0 7 8	0 8 1	0 8 2	0 8 2	0 8 4	0 8 8	0 9 2	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 5	0 9 6	0 9 6	0 9 6	0 9 7	0 9 8
CARCASS ID	1 1 1	3 6 1	4 0 1	4 9 1	2 4 1	2 7 1	4 3 1	4 6 1	4 5 1	0 9 1	1 7 1	4 7 1	3 2 1	5 0 1	1 4 1	3 8 1	1 6 1	4 1 1	1 2 1	2 3 1	0 6 1	1 0 1	3 0 1	1 5 1	0 1 1
ALIMENTARY SYSTEM																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Intestine small, ileum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																						X			
Leukemia mononuclear				X			X	X		X	X		X	X	X		X	X	X		X	X	X		X
Lymphoma malignant histiocytic					X																				
Mesentery																				+					
Mesothelioma malignant, metastatic, testes																				X					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																	X		X						
Mesothelioma malignant																									
Mesothelioma malignant, metastatic, testes																				X					
Pharynx			+																						
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Papilloma squamous																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth														+											
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X						X			X				X		X		X	X			
Schwannoma, NOS																									
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes																				X					
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Leukemia mononuclear				X						X	X		X		X		X		X		X	X			
Lymphoma malignant histiocytic					X																				
Adrenal gland, medulla	M	+	M	+	M	I	+	+	+	+	+	+	I	+	M	+	M	+	+	−	+	+	+	M	+
Leukemia mononuclear				X						X									X		X				
Pheochromocytoma benign		X																X							
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Adenoma										X													X		X
Parathyroid gland	M	M	+	+	+	M	+	M	+	+	+	M	M	+	M	+	+	+	M	+	+	+	+	+	M
Adenoma														X											
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X						X			X								X				
Pars distalis, adenoma	X	X		X	X			X	X				X	X	X	X	X	X	X			X		X	X
Pars distalis, carcinoma																									
Pars distalis, leukemia mononuclear											X				X		X								
Pars intermedia, adenoma									X																
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma												X													
C-cell, adenoma, multiple																									X
C-cell, carcinoma																	X								
Follicular cell, carcinoma																									
GENERAL BODY SYSTEM																									
Tissue, NOS																									
GENITAL SYSTEM																									
Epididymis	+	M	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	I	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle													+						+		+				
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																	X				X				
Mesothelioma malignant																				X					
Bilateral, interstitial cell, adenoma		X										X		X					X						
Interstitial cell, adenoma										X			X				X			X			X		

+: Tissue examined microscopically
: Not examined
−: Present but not examined microscopically
I: Insufficient tissue

M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

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

WEEKS ON STUDY	098	099	099	100	100	100	100	103	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	051	351	441	021	041	081	191	291	251	031	071	131	181	201	211	221	261	281	311	331	341	371	391	421	481	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, jejunum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma																										1
Leukemia mononuclear	X	X		X	X				X	X	X	X	X	X			X	X	X	X	X		X			31
Lymphoma malignant histiocytic																										1
Mesentery																										1
Mesothelioma malignant, metastatic, testes																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear					X							X														4
Mesothelioma malignant																			X							1
Mesothelioma malignant, metastatic, testes																										1
Pharynx			+																							2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	48
Papilloma squamous																X										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth									+								+									3
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X				X				X	X		X														12
Schwannoma, NOS	X																									1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesothelioma malignant, metastatic, testes																										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																	X									1
Leukemia mononuclear	X			X	X				X								X									14
Lymphoma malignant histiocytic																										1
Adrenal gland, medulla	+	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	M	+	+	36
Leukemia mononuclear	X			X					X								X									8
Pheochromocytoma benign										X		X			X						X				X	7
Bilateral, pheochromocytoma benign																				X						1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma									X										X				X			6
Parathyroid gland	+	+	+	M	M	M	+	M	+	M	M	M	+	+	M	+	+	M	+	+	+	+	+	M	+	31
Adenoma																										1
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X				X												X									7
Pars distalis, adenoma		X	X		X		X	X		X	X	X	X			X	X	X		X			X		X	31
Pars distalis, carcinoma																						X				1
Pars distalis, leukemia mononuclear																										3
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell, adenoma							X									X			X			X	X			6
C-cell, adenoma, multiple																										1
C-cell, carcinoma																		X								2
Follicular cell, carcinoma											X							X								2
GENERAL BODY SYSTEM																										
Tissue, NOS							+																			1
GENITAL SYSTEM																										
Epididymis	+	+	M	+	+	+	+	+	+	+	M	M	M	+	+	+	+	I	M	+	M	M	+	M	+	37
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																								X		1
Carcinoma			X																							1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle					+			+											+	+						7
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X								X																	4
Mesothelioma malignant																										1
Bilateral, interstitial cell, adenoma	X	X		X					X	X	X	X	X		X			X			X			X	X	19
Interstitial cell, adenoma			X					X								X			X			X	X			10

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

WEEKS ON STUDY	070	072	074	074	076	076	078	078	081	082	082	084	088	092	093	093	094	094	094	095	096	096	096	097	098
CARCASS ID	11 1	36 1	40 1	49 1	24 1	27 1	43 1	46 1	45 1	09 1	17 1	47 1	32 1	50 1	14 1	38 1	16 1	41 1	12 1	23 1	06 1	10 1	30 1	51 1	01 1
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X						X								
Lymphoma malignant histiocytic					X																				
Lymph node	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenteric, leukemia mononuclear											X				X										
Pancreatic, leukemia mononuclear																						X			
Renal, leukemia mononuclear				X							X											X			
Lymph node, bronchial	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+
Leukemia mononuclear				X						X	X		X		X						X	X			
Lymph node, mandibular	M	M	+	+	+	+	+	+	+	I	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X									X		X		X				X	X			
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Leukemia mononuclear				X			X			X	X		X	X	X		X	X	X		X	X			X
Mesothelioma malignant																									
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	M	+	M	+	+	+	+	+	+	M
Leukemia mononuclear											X										X				
INTEGUMENTARY SYSTEM																									
Mammary gland	+	M	M	+	M	+	M	M	M	M	M	+	M	+	M	M	M	+	+	M	M	M	M	M	M
Fibroadenoma	X																								
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Subcutaneous tissue, fibroma						X																			X
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granular cell tumor malignant																									
Leukemia mononuclear																	X				X				
Oligodendroglioma malignant									X																
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X			X			X	X	X	X		X		X	X	X		X	X			X
Mediastinum, mesothelioma benign																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear													X				X		X		X				
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Ear																						+			
Eye																									
Zymbal gland			+																						
Carcinoma			X																						
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear										X	X		X		X		X				X				
Lipoma, moderate											X														
Lymphoma malignant histiocytic					X																				
Urethra																								+	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																			X						
Mesothelioma malignant, metastatic, testes																				X					

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

WEEKS ON STUDY	098	099	099	100	100	100	100	103	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
CARCASS ID	051	351	441	021	041	081	191	291	251	031	071	131	181	201	211	221	261	281	311	331	341	371	391	421	481	TOTAL: TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										2
Lymphoma malignant histiocytic																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesenteric, leukemia mononuclear																										2
Pancreatic, leukemia mononuclear																										1
Renal, leukemia mononuclear																										3
Lymph node, bronchial	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M	+	+	42
Leukemia mononuclear	X				X				X	X		X		X			X			X						15
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Leukemia mononuclear	X			X	X					X		X		X			X			X						14
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																				X						1
Leukemia mononuclear	X	X		X	X				X	X	X	X	X	X			X	X	X	X	X		X	X		30
Mesothelioma malignant																			X							1
Thymus	+	+	+	+	M	+	+	+	+	+	+	M	+	M	+	+	+	M	+	+	+	+	+	M	M	39
Leukemia mononuclear																	X									3
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	M	M	M	M	M	M	+	+	+	M	M	M	M	M	M	M	M	M	M	+	M	+	+	13
Fibroadenoma																										1
Skin	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Keratoacanthoma			X																				X		X	4
Subcutaneous tissue, fibroma																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granular cell tumor malignant		X																								1
Leukemia mononuclear																										2
Oligodendroglioma malignant																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X		X	X				X	X		X		X			X		X	X						24
Mediastinum, mesothelioma benign																								X		1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X				X																					6
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSES SYSTEM																										
Ear				M																						1
Eye									+																	1
Zymbal gland																										1
Carcinoma																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X			X	X				X					X			X									12
Lipoma, moderate																										1
Lymphoma malignant histiocytic																										1
Urethra																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										1
Mesothelioma malignant, metastatic, testes																										1

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE: 15,000 ppm

WEEKS ON STUDY	0 6 0	0 6 3	0 6 8	0 6 9	0 7 5	0 7 6	0 7 9	0 7 9	0 8 1	0 8 3	0 8 3	0 8 3	0 8 4	0 8 4	0 8 6	0 8 7	0 8 8	0 8 8	0 8 9	0 9 0	0 9 0	0 9 0	0 9 1	0 9 3	0 9 3
CARCASS ID	1 2 7 1	1 4 7 1	1 5 0 1	1 0 2 1	1 2 4 1	1 4 3 1	1 2 0 1	1 0 4 1	1 4 6 1	1 3 0 1	1 3 6 1	1 1 4 1	1 1 7 1	1 4 8 1	1 3 8 1	1 4 9 1	1 1 9 1	1 4 0 1	1 1 8 1	1 0 9 1	1 3 2 1	1 4 5 1	1 2 2 1	1 1 6 1	1 4 4 1
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	M	M	+	+	M
Intestine large	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Mesothelioma malignant, metastatic, testes																									
Intestine large, rectum	+	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	+	A	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X				X			X		X	X			X	X	X	X	X			X	X		X
Mesothelioma malignant, metastatic, testes																									
Neoplastic nodule, multiple																									
Mesentery																									
Mesothelioma malignant, metastatic, testes																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X														X									
Mesothelioma malignant, metastatic, testes																									
Pharynx																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X																							
Stomach, forestomach	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Serosa, mesothelioma malignant, metastatic, testes											X														
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X									X	X			X	X		X	X						X
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X					X			X				X		X
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Leukemia mononuclear											X				X								X		
Pheochromocytoma malignant																X									
Pheochromocytoma benign									X									X							
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Adenoma																									
Adenoma, multiple																									
Parathyroid gland	+	+	M	M	+	+	M	+	+	+	+	+	M	M	+	+	M	+	+	+	M	+	+	+	M
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																X			X						
Pars distalis, adenoma					X			X	X		X		X	X					X	X	X	X	X	X	
Pars distalis, leukemia mononuclear		X																							
Thyroid gland	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																									
GENERAL BODY SYSTEM																									
Tissue, NOS		+	+																						
Chordoma																									
Leukemia mononuclear		X																							
Sarcoma			X																						
GENITAL SYSTEM																									
Epididymis	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Penis																									
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	M	+
Adenoma																									
Carcinoma																							X		
Prostate	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+
Sarcoma, metastatic, uncertain primary site			X																						
Seminal vesicle			+	+									+				+								
Sarcoma, metastatic, uncertain primary site			X																						
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									
Bilateral, interstitial cell, adenoma												X				X									
Interstitial cell, adenoma				X				X		X	X						X			X				X	X
Tunic, mesothelioma malignant											X														

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 15,000 ppm (Continued)

WEEKS ON STUDY	095	096	097	097	099	100	101	101	101	101	102	102	102	103	103	104	104	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	11001	10301	13111	14111	11311	12991	11151	13711	12551	12881	10801	14211	12331	10661	13991	12111	12661	10111	10551	10771	11111	11121	13331	13441	13551	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	43
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+		+	+	A	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	A	+	+	M		+	+	A	+	+	+	+	+	+	+	+	+	45
Intestine large, colon	+	+	+	+	+	+	+	+	A	+	+	+		+	+	A	+	+	+	+	+	+	+	+	+	45
Mesothelioma malignant, metastatic, testes												X														1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	M	+	+		+	+	A	+	+	+	+	+	+	+	+	+	43
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	M	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	M	+	M	+	+	+	M	M	M	+	A	+	+	+	+	+	+	+	+	+	40
Intestine small, jejunum	+	+	+	+	+	+	+	+	A	+	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X	X	X	X	X		X	X	X	X	X		X	X	X	X		X		X	X	X	X	X	34
Mesothelioma malignant, metastatic, testes												X														1
Neoplastic nodule, multiple																									X	1
Mesentery												+														1
Mesothelioma malignant, metastatic, testes												X														1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear									X	X		X					X					X				7
Mesothelioma malignant, metastatic, testes												X														1
Pharynx							+																			1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Serosa, mesothelioma malignant, metastatic, testes												X														2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X								X	X							X					X		X		14
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear										X																1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X								X	X		X		X			X		X			X		X		14
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	48
Leukemia mononuclear	X								X			X			X		X		X			X				10
Pheochromocytoma malignant																										1
Pheochromocytoma benign																										2
Bilateral, pheochromocytoma benign	X		X	X									X									X	X		X	7
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	48
Adenoma							X	X																		2
Adenoma, multiple																			X							1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X										X						X					X				6
Pars distalis, adenoma		X	X		X			X	X				X		X	X		X	X		X		X		X	25
Pars distalis, leukemia mononuclear																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	47
C-cell, adenoma												X														1
GENERAL BODY SYSTEM																										
Tissue, NOS		+					+																			4
Chordoma		X																								1
Leukemia mononuclear																										1
Sarcoma																										1
GENITAL SYSTEM																										
Epididymis	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	M	+	M	+	M	M	+	42
Penis								+																		1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	45
Adenoma												X														1
Carcinoma																							X			2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma, metastatic, uncertain primary site																										1
Seminal vesicle				+										+												6
Sarcoma, metastatic, uncertain primary site																										1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X										X															2
Bilateral, interstitial cell, adenoma						X	X					X							X	X		X				8
Interstitial cell, adenoma	X	X						X			X			X	X		X				X			X	X	17
Tunic, mesothelioma malignant												X														3

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 15,000 ppm (Continued)

WEEKS ON STUDY	0 6 0	0 6 3	0 6 8	0 6 9	0 7 5	0 7 6	0 7 9	0 7 9	0 8 1	0 8 3	0 8 3	0 8 3	0 8 4	0 8 4	0 8 6	0 8 7	0 8 8	0 8 8	0 8 9	0 9 0	0 9 0	0 9 0	0 9 1	0 9 3	0 9 3
CARCASS ID	1 2 7 1	1 4 7 1	1 5 0 1	1 0 2 1	1 2 4 1	1 4 3 1	1 2 0 1	1 0 4 1	1 4 6 1	1 3 0 1	1 3 6 1	1 1 4 1	1 1 7 1	1 4 8 1	1 3 8 1	1 4 9 1	1 1 9 1	1 4 0 1	1 1 8 1	1 0 9 1	1 3 2 1	1 4 5 1	1 2 2 1	1 1 6 1	1 4 4 1
HEMATOPOIETIC SYSTEM																									
Blood															+										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Leukemia mononuclear												X				X									X
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site			X																						
Mesenteric, leukemia mononuclear																									
Lymph node, bronchial	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X													X	X									X
Lymph node, mandibular	+	+	M	+	I	M	+	+	M	M	+	+	+	+	+	+	+	+	+	M	M	M	+	M	+
Leukemia mononuclear											X					X									X
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X				X		X	X		X	X			X	X	X	X	X			X	X		X
Mesothelioma malignant, metastatic, testes																									
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Leukemia mononuclear																									X
INTEGUMENTARY SYSTEM																									
Mammary gland	+	M	M	M	M	M	M	M	+	M	M	+	M	+	+	M	+	M	+	M	M	M	+	M	M
Skin	+	+	+	+	+	+	+	+	+	+	M	+	M	M	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Keratoacanthoma																									
Squamous cell carcinoma										X															
Trichoepithelioma																									
Lip, squamous cell carcinoma																									
Sebaceous gland, adenoma																									
Subcutaneous tissue, fibroma								X									X								
Subcutaneous tissue, fibrous histiocytoma																									
Subcutaneous tissue, lipoma																									
Subcutaneous tissue, neurofibrosarcoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant																									
Leukemia mononuclear		X																	X						
Oligodendroglioma benign																							X		
Spinal cord																									
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	I
Leukemia mononuclear																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X				X			X		X	X			X	X			X			X	X		X
Sarcoma, metastatic			X																						
Squamous cell carcinoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X																							
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye					+	+																			
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X				X	X			X						X
Renal tubule, carcinoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Leukemia mononuclear																									X
Mesothelioma malignant, metastatic, testes																									
Sarcoma, metastatic, uncertain primary site			X																						

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 15,000 ppm (Continued)

WEEKS ON STUDY	095	096	097	097	099	100	101	101	101	101	102	102	102	103	103	104	104	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	1101	1031	1131	1411	1131	1291	1151	1371	1251	1281	1081	1421	1231	1061	1391	1211	1261	1011	1051	1071	1111	1121	1331	1341	1351	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood				+				+								+										4
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear	X			X						X		X														7
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, uncertain primary site																										1
Mesenteric, leukemia mononuclear	X																									1
Lymph node, bronchial	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	48
Leukemia mononuclear	X								X			X		X	X		X		X				X			12
Lymph node, mandibular	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	38
Leukemia mononuclear									X	X	X								X				X			8
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X	X	X	X	X		X	X	X	X	X		X	X	X	X		X	X	X	X	X	X		35
Mesothelioma malignant, metastatic, testes												X														1
Thymus	+	+	M	+	+	+	+	+	M	M	+	M	+	+	+	+	I	+	+	M	M	+	+	+	M	41
Leukemia mononuclear																						X				2
INTEGUMENTARY SYSTEM																										
Mammary gland	M	+	M	M	M	M	+	M	M	+	M	M	+	M	+	M	M	M	M	M	+	M	M	M	M	14
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	46
Basal cell carcinoma				X													X			X						3
Keratoacanthoma			X														X									2
Squamous cell carcinoma																										1
Trichoepithelioma														X												1
Lip, squamous cell carcinoma							X																			1
Sebaceous gland, adenoma												X														1
Subcutaneous tissue, fibroma																										2
Subcutaneous tissue, fibrous histiocytoma																								X		1
Subcutaneous tissue, lipoma									X																	1
Subcutaneous tissue, neurofibrosarcoma			X																							1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant																								X		1
Leukemia mononuclear	X								X																	4
Oligodendroglioma benign																										1
Spinal cord								+																		1
RESPIRATORY SYSTEM																										
Larynx	+	+	+		+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	I	+	+	+	+	+	44
Leukemia mononuclear			X																							1
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X			X	X	X		X	X	X	X			X	X	X	X		X			X	X	X		27
Sarcoma, metastatic																										1
Squamous cell carcinoma						X																				1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X									X				X												4
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSES SYSTEM																										
Eye				+	+		+	+										+								7
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X								X	X	X			X	X				X			X		X		14
Renal tubule, carcinoma											X															1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X																		X			X				4
Mesothelioma malignant, metastatic, testes												X														1
Sarcoma, metastatic, uncertain primary site																										1

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

	Chamber Control	15,000 ppm
Adrenal Medulla: Pheochromocytoma		
Overall Rates (a)	8/36 (22%)	9/48 (19%)
Adjusted Rates (b)	48.9%	56.2%
Terminal Rates (c)	6/13 (46%)	3/7 (43%)
Day of First Observation	500	562
Life Table Test (d)		P=0.175
Logistic Regression Test (d)		P=0.589N
Fisher Exact Test (d)		P=0.450N
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma		
Overall Rates (a)	8/36 (22%)	10/48 (21%)
Adjusted Rates (b)	48.9%	57.5%
Terminal Rates (c)	6/13 (46%)	3/7 (43%)
Day of First Observation	500	562
Life Table Test (d)		P=0.119
Logistic Regression Test (d)		P=0.549
Fisher Exact Test (d)		P=0.543N
Preputial Gland: Adenoma or Carcinoma		
Overall Rates (a)	2/47 (4%)	3/45 (7%)
Adjusted Rates (b)	10.3%	25.0%
Terminal Rates (c)	1/16 (6%)	1/6 (17%)
Day of First Observation	692	633
Life Table Test (d)		P=0.284
Logistic Regression Test (d)		P=0.394
Fisher Exact Test (d)		P=0.479
Pancreatic Islets: Adenoma		
Overall Rates (a)	6/48 (13%)	3/48 (6%)
Adjusted Rates (b)	26.2%	21.7%
Terminal Rates (c)	2/15 (13%)	1/8 (13%)
Day of First Observation	570	701
Life Table Test (d)		P=0.411N
Logistic Regression Test (d)		P=0.310N
Fisher Exact Test (d)		P=0.243N
Pituitary Gland/Pars Distalis: Adenoma		
Overall Rates (a)	31/49 (63%)	25/50 (50%)
Adjusted Rates (b)	83.3%	84.6%
Terminal Rates (c)	10/15 (67%)	5/8 (63%)
Day of First Observation	485	519
Life Table Test (d)		P=0.457
Logistic Regression Test (d)		P=0.158N
Fisher Exact Test (d)		P=0.129N
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma		
Overall Rates (a)	32/49 (65%)	25/50 (50%)
Adjusted Rates (b)	86.7%	84.6%
Terminal Rates (c)	11/15 (73%)	5/8 (63%)
Day of First Observation	485	519
Life Table Test (d)		P=0.498
Logistic Regression Test (d)		P=0.116N
Fisher Exact Test (d)		P=0.090N
Skin: Basal Cell Carcinoma		
Overall Rates (a)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	25.6%
Terminal Rates (c)	0/16 (0%)	1/8 (13%)
Day of First Observation		678
Life Table Test (d)		P=0.055
Logistic Regression Test (d)		P=0.083
Fisher Exact Test (d)		P=0.121

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

	Chamber Control	15,000 ppm
Skin: Trichoepithelioma, Sebaceous Gland Adenoma, or Basal Cell Carcinoma		
Overall Rates (a)	0/50 (0%)	5/50 (10%)
Adjusted Rates (b)	0.0%	36.3%
Terminal Rates (c)	0/16 (0%)	1/8 (13%)
Day of First Observation		678
Life Table Test (d)		P=0.011
Logistic Regression Test (d)		P=0.016
Fisher Exact Test (d)		P=0.028
Skin: Keratoacanthoma		
Overall Rates (a)	4/50 (8%)	2/50 (4%)
Adjusted Rates (b)	19.5%	15.0%
Terminal Rates (c)	2/16 (13%)	0/8 (0%)
Day of First Observation	682	678
Life Table Test (d)		P=0.531N
Logistic Regression Test (d)		P=0.423N
Fisher Exact Test (d)		P=0.339N
Skin: Keratoacanthoma or Squamous Cell Carcinoma		
Overall Rates (a)	4/50 (8%)	4/50 (8%)
Adjusted Rates (b)	19.5%	21.4%
Terminal Rates (c)	2/16 (13%)	0/8 (0%)
Day of First Observation	682	577
Life Table Test (d)		P=0.481
Logistic Regression Test (d)		P=0.578
Fisher Exact Test (d)		P=0.643
Subcutaneous Tissue: Fibroma or Neurofibrosarcoma		
Overall Rates (a)	1/50 (2%)	3/50 (6%)
Adjusted Rates (b)	2.2%	9.3%
Terminal Rates (c)	0/16 (0%)	0/8 (0%)
Day of First Observation	526	552
Life Table Test (d)		P=0.288
Logistic Regression Test (d)		P=0.366
Fisher Exact Test (d)		P=0.309
Testis: Adenoma		
Overall Rates (a)	29/50 (58%)	25/50 (50%)
Adjusted Rates (b)	89.5%	90.3%
Terminal Rates (c)	13/16 (82%)	6/8 (75%)
Day of First Observation	500	479
Life Table Test (d)		P=0.240
Logistic Regression Test (d)		P=0.417N
Fisher Exact Test (d)		P=0.274N
Thyroid Gland: C-Cell Adenoma		
Overall Rates (a)	7/49 (14%)	1/47 (2%)
Adjusted Rates (b)	33.4%	6.7%
Terminal Rates (c)	4/16 (25%)	0/8 (0%)
Day of First Observation	587	709
Life Table Test (d)		P=0.095N
Logistic Regression Test (d)		P=0.051N
Fisher Exact Test (d)		P=0.034N
Thyroid Gland: C-Cell Adenoma or Carcinoma		
Overall Rates (a)	9/49 (18%)	1/47 (2%)
Adjusted Rates (b)	40.8%	6.7%
Terminal Rates (c)	5/16 (31%)	0/8 (0%)
Day of First Observation	587	709
Life Table Test (d)		P=0.044N
Logistic Regression Test (d)		P=0.017N
Fisher Exact Test (d)		P=0.009N

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

	Chamber Control	15,000 ppm
Hematopoietic System: Mononuclear Leukemia		
Overall Rates (a)	33/50 (66%)	36/50 (72%)
Adjusted Rates (b)	87.6%	96.9%
Terminal Rates (c)	12/16 (75%)	7/8 (88%)
Day of First Observation	517	437
Life Table Test (d)		P=0.046
Logistic Regression Test (d)		P=0.214
Fisher Exact Test (d)		P=0.333
All Sites: Malignant Mesothelioma		
Overall Rates (a)	2/50 (4%)	3/50 (6%)
Adjusted Rates (b)	9.3%	11.9%
Terminal Rates (c)	1/16 (6%)	0/8 (0%)
Day of First Observation	665	577
Life Table Test (d)		P=0.390
Logistic Regression Test (d)		P=0.485
Fisher Exact Test (d)		P=0.500
All Sites: All Mesothelioma		
Overall Rates (a)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	15.3%	11.9%
Terminal Rates (c)	2/16 (12%)	0/8 (0%)
Day of First Observation	665	577
Life Table Test (d)		P=0.509
Logistic Regression Test (d)		P=0.633
Fisher Exact Test (d)		P=0.661N

(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 dosed group incidence are the P values corresponding to pairwise comparisons between the 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 logistic regression test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in the dosed group is indicated by (N).

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

Study	No. Examined	No. of Tumors	Diagnosis	Range (b) Low	Range (b) High
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories					
Propylene oxide	50	1	Keratoacanthoma		
Methyl methacrylate	50	2	Keratoacanthoma		
		1	Papilloma, NOS		
Propylene	50	0			
1,2-Epoxybutane	50	1	Keratoacanthoma		
Dichloromethane	50	2	Keratoacanthoma		
		4	Papilloma, NOS		
		1	Trichoepithelioma		
		1	Sebaceous adenocarcinoma		
Tetrachloroethylene	50	3	Keratoacanthoma		
		2	Squamous cell papilloma		
		1	Squamous cell carcinoma		
Total	300				
Benign		17 (5.7%)		0/50	7/50
Malignant		2 (0.7%)		0/50	1/50
Benign or malignant		19 (6.3%)		0/50	8/50
Overall Historical Incidence for Untreated Controls in NTP Studies					
		25	Squamous cell papilloma		
		8	Basal cell tumor		
		3	Trichoepithelioma		
		1	Adnexal adenoma		
		4	Sebaceous adenoma		
		31	Keratoacanthoma		
		14	Squamous cell carcinoma		
		14	Basal cell carcinoma		
Total	1,936				
Benign		72 (3.7%)		0/50	10/49
Malignant		28 (1.4%)		0/50	3/50
Benign or malignant		100 (5.2%)		0/50	12/49

(a) Data as of April 29, 1987, for studies of at least 104 weeks
(b) Range is presented for groups of 35 or more animals.

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

Study	Incidence in Controls
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories	
Propylene oxide	20/50
Methyl methacrylate	19/50
Propylene	16/50
1,2-Epoxybutane	25/50
Dichloromethane	34/50
Tetrachloroethylene	28/50
TOTAL	142/300 (47.3%)
SD (b)	13.31%
Range (c)	
High	34/50
Low	16/50
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	636/1,936 (32.9%)
SD (b)	14.62%
Range (c)	
High	36/50
Low	5/50

(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 CHLOROETHANE

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	50	50
ALIMENTARY SYSTEM		
Intestine large, cecum	(49)	(45)
Parasite metazoan	8 (16%)	4 (9%)
Intestine large, colon	(50)	(45)
Parasite metazoan	5 (10%)	5 (11%)
Intestine large, rectum	(47)	(43)
Parasite metazoan	4 (9%)	5 (12%)
Serosa, inflammation, chronic	1 (2%)	1 (2%)
Serosa, thrombus	1 (2%)	
Liver	(50)	(50)
Angiectasis		1 (2%)
Basophilic focus	18 (36%)	7 (14%)
Clear cell focus	3 (6%)	2 (4%)
Congestion		2 (4%)
Degeneration	2 (4%)	2 (4%)
Degeneration, cystic	3 (6%)	9 (18%)
Degeneration, fatty	9 (18%)	5 (10%)
Fibrosis	1 (2%)	
Hematopoietic cell proliferation		3 (6%)
Hemorrhage	1 (2%)	
Hepatodiaphragmatic nodule	2 (4%)	2 (4%)
Inflammation, granulomatous, focal	6 (12%)	5 (10%)
Necrosis	7 (14%)	4 (8%)
Pigmentation		1 (2%)
Bile duct, hyperplasia	44 (88%)	34 (68%)
Hepatocyte, hyperplasia	3 (6%)	8 (16%)
Pancreas	(50)	(49)
Atrophy	24 (48%)	17 (35%)
Cytomegaly	2 (4%)	1 (2%)
Inflammation		1 (2%)
Pigmentation, hemosiderin	1 (2%)	1 (2%)
Artery, intima, hyperplasia	1 (2%)	
Perivascular, inflammation		3 (6%)
Pharynx	(2)	(1)
Inflammation, suppurative		1 (100%)
Palate, inflammation, chronic	2 (100%)	
Salivary glands	(50)	(50)
Duct, hyperplasia	10 (20%)	15 (30%)
Duct, inflammation, suppurative	2 (4%)	1 (2%)
Stomach, forestomach	(48)	(49)
Hyperkeratosis		1 (2%)
Inflammation, chronic	2 (4%)	
Inflammation, suppurative	3 (6%)	1 (2%)
Ulcer	4 (8%)	1 (2%)
Epithelium, hyperplasia	2 (4%)	2 (4%)
Serosa, inflammation, chronic		1 (2%)
Stomach, glandular	(50)	(50)
Erosion		3 (6%)
Hyperplasia, lymphoid		1 (2%)
Mineralization		2 (4%)
Epithelium, hyperplasia		1 (2%)
Serosa, inflammation, chronic		1 (2%)
Tooth	(3)	
Gingiva, hyperplasia, pseudoepitheliomatous	1 (33%)	
Peridontal tissue, inflammation, suppurative, chronic	2 (67%)	
Pulp, inflammation, suppurative	1 (33%)	

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

	Chamber Control	15,000 ppm
CARDIOVASCULAR SYSTEM		
Heart	(50)	(50)
Inflammation, chronic	43 (86%)	46 (92%)
Artery, mineralization		1 (2%)
Atrium, thrombus	2 (4%)	2 (4%)
Perivascular, inflammation	1 (2%)	
ENDOCRINE SYSTEM		
Adrenal gland, cortex	(50)	(50)
Degeneration, fatty	23 (46%)	26 (52%)
Hematopoietic cell proliferation	2 (4%)	2 (4%)
Hyperplasia	13 (26%)	6 (12%)
Hypertrophy	2 (4%)	
Adrenal gland, medulla	(36)	(48)
Hematopoietic cell proliferation		1 (2%)
Hyperplasia	11 (31%)	16 (33%)
Islets, pancreatic	(48)	(48)
Hyperplasia	3 (6%)	4 (8%)
Parathyroid gland	(31)	(41)
Hyperplasia		3 (7%)
Pituitary gland	(49)	(50)
Pars distalis, cyst	1 (2%)	2 (4%)
Pars distalis, hemorrhage	1 (2%)	1 (2%)
Pars distalis, hyperplasia	10 (20%)	10 (20%)
Pars distalis, inflammation, suppurative		1 (2%)
Pars distalis, necrosis	1 (2%)	
Pars distalis, pigmentation, hemosiderin		1 (2%)
Thyroid gland	(49)	(47)
C-cell, hyperplasia	19 (39%)	23 (49%)
GENERAL BODY SYSTEM		
Tissue, NOS	(1)	(4)
Inflammation, chronic	1 (100%)	1 (25%)
Necrosis	1 (100%)	1 (25%)
GENITAL SYSTEM		
Epididymis	(37)	(42)
Granuloma sperm		1 (2%)
Inflammation, chronic	1 (3%)	
Mineralization	1 (3%)	
Vacuolization cytoplasmic	14 (38%)	15 (36%)
Penis		(1)
Inflammation, suppurative		1 (100%)
Preputial gland	(47)	(45)
Cyst	1 (2%)	1 (2%)
Inflammation, suppurative	10 (21%)	3 (7%)
Duct, hyperplasia		1 (2%)
Prostate	(50)	(48)
Hyperplasia	4 (8%)	11 (23%)
Inflammation, chronic	1 (2%)	
Inflammation, suppurative	16 (32%)	13 (27%)
Seminal vesicle	(7)	(6)
Inflammation, suppurative	7 (100%)	5 (83%)
Testes	(50)	(50)
Atrophy	27 (54%)	29 (58%)
Interstitial cell, hyperplasia	12 (24%)	15 (30%)
Perivascular, inflammation	3 (6%)	8 (16%)
Tunic, hyperplasia		1 (2%)

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

	Chamber Control	15,000 ppm
HEMATOPOIETIC SYSTEM		
Bone marrow	(50)	(48)
Hyperplasia		1 (2%)
Myelofibrosis	1 (2%)	1 (2%)
Lymph node	(49)	(50)
Mesenteric, hematopoietic cell proliferation	1 (2%)	
Mesenteric, inflammation, granulomatous		1 (2%)
Pancreatic, hyperplasia	1 (2%)	
Renal, hematopoietic cell proliferation	1 (2%)	
Lymph node, bronchial	(42)	(48)
Hyperplasia	2 (5%)	2 (4%)
Pigmentation, hemosiderin	1 (2%)	
Lymph node, mandibular	(45)	(38)
Angiectasis	1 (2%)	2 (5%)
Hyperplasia	19 (42%)	11 (29%)
Spleen	(50)	(50)
Fibrosis	3 (6%)	9 (18%)
Hematocyst		1 (2%)
Hematopoietic cell proliferation	2 (4%)	2 (4%)
Thymus	(39)	(41)
Epithelial cell, hyperplasia	1 (3%)	
INTEGUMENTARY SYSTEM		
Mammary gland	(13)	(14)
Galactocele		3 (21%)
Hyperplasia	8 (62%)	10 (71%)
Skin	(49)	(46)
Acanthosis	1 (2%)	
Ectopic tissue		1 (2%)
Inflammation, chronic	1 (2%)	1 (2%)
Pigmentation, hemosiderin	1 (2%)	
Prepuce, abscess	1 (2%)	
Prepuce, epithelium, hyperplasia	1 (2%)	
MUSCULOSKELETAL SYSTEM		
Bone	(50)	(49)
Fibrous osteodystrophy		4 (8%)
Hyperostosis		1 (2%)
NERVOUS SYSTEM		
Brain	(50)	(50)
Hemorrhage, focal	3 (6%)	3 (6%)
Hydrocephalus	1 (2%)	
Necrosis, focal	2 (4%)	
Meninges, hemorrhage	1 (2%)	
Meninges, inflammation, suppurative	1 (2%)	
Meninges, pigmentation, hemosiderin		1 (2%)
Spinal cord		(1)
Degeneration		1 (100%)
RESPIRATORY SYSTEM		
Larynx	(49)	(44)
Inflammation, suppurative	14 (29%)	21 (48%)
Metaplasia, squamous		1 (2%)

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

	Chamber Control	15,000 ppm
RESPIRATORY SYSTEM (Continued)		
Lung	(50)	(50)
Congestion	1 (2%)	5 (10%)
Edema	1 (2%)	2 (4%)
Erythrophagocytosis		1 (2%)
Hemorrhage	4 (8%)	3 (6%)
Infiltration cellular, histiocytic	5 (10%)	13 (26%)
Infiltration cellular, mixed cell	1 (2%)	1 (2%)
Inflammation, chronic, focal	4 (8%)	2 (4%)
Metaplasia, osseous	1 (2%)	2 (4%)
Alveolar epithelium, hyperplasia	6 (12%)	7 (14%)
Artery, mediastinum, mineralization		1 (2%)
Bronchiole, inflammation, suppurative		1 (2%)
Perivascular, infiltration cellular, mononuclear cell	9 (18%)	14 (28%)
Nose	(50)	(49)
Edema	1 (2%)	
Inflammation, suppurative	12 (24%)	13 (27%)
Thrombus	8 (16%)	7 (14%)
Nasolacrimal duct, inflammation, suppurative	12 (24%)	8 (16%)
Respiratory epithelium, hyperplasia	9 (18%)	14 (29%)
Respiratory epithelium, metaplasia, squamous	1 (2%)	
Submucosa, inflammation	22 (44%)	23 (47%)
Vomeronasal organ, inflammation, suppurative	2 (4%)	1 (2%)
Trachea	(50)	(49)
Inflammation, suppurative	2 (4%)	7 (14%)
Epithelium, hyperplasia		1 (2%)
SPECIAL SENSES SYSTEM		
Eye	(1)	(7)
Cataract		1 (14%)
Degeneration	1 (100%)	1 (14%)
Inflammation, chronic		1 (14%)
Synechia		4 (57%)
Bilateral, cataract		3 (43%)
Retina, atrophy		3 (43%)
URINARY SYSTEM		
Kidney	(50)	(50)
Fatty change	1 (2%)	
Hematopoietic cell proliferation	2 (4%)	3 (6%)
Hydronephrosis		1 (2%)
Inflammation, suppurative	4 (8%)	3 (6%)
Nephropathy	49 (98%)	49 (98%)
Pelvis, inflammation, suppurative	2 (4%)	
Pelvis, necrosis	1 (2%)	
Pelvis, epithelium, hyperplasia	1 (2%)	3 (6%)
Urethra	(1)	
Inflammation, suppurative	1 (100%)	
Epithelium, hyperplasia	1 (100%)	
Urinary bladder	(50)	(49)
Hemorrhage		1 (2%)
Inflammation		1 (2%)
Inflammation, suppurative	2 (4%)	1 (2%)
Transitional epithelium, hyperplasia	1 (2%)	2 (4%)

APPENDIX B

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

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

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	50	50
ALIMENTARY SYSTEM		
Intestine large, cecum	(50)	(48)
Sarcoma, metastatic, bone	1 (2%)	
Intestine large, colon	(50)	(49)
Leukemia mononuclear		1 (2%)
Intestine small, ileum	(47)	(43)
Leukemia mononuclear		1 (2%)
Sarcoma, metastatic, tissue, NOS	1 (2%)	
Liver	(50)	(50)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)
Fibrous histiocytoma, metastatic, skeletal muscle		1 (2%)
Hepatocellular carcinoma	1 (2%)	
Leukemia lymphocytic		1 (2%)
Leukemia mononuclear	19 (38%)	25 (50%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Sarcoma, metastatic, bone	1 (2%)	
Mesentery	*(50)	*(50)
Schwannoma malignant, metastatic, stomach		1 (2%)
Pancreas	(49)	(50)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)
Leukemia mononuclear	6 (12%)	4 (8%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Sarcoma, metastatic, tissue, NOS	1 (2%)	
Schwannoma malignant, metastatic, stomach		1 (2%)
Pharynx	*(50)	*(50)
Palate, papilloma squamous		1 (2%)
Stomach, forestomach	(46)	(50)
Leukemia mononuclear	3 (7%)	
Schwannoma malignant		1 (2%)
Stomach, glandular	(50)	(49)
Leukemia mononuclear	3 (6%)	1 (2%)
Tongue	*(50)	*(50)
Papilloma squamous	1 (2%)	1 (2%)
CARDIOVASCULAR SYSTEM		
Heart	(50)	(50)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)
Leukemia lymphocytic		1 (2%)
Leukemia mononuclear	10 (20%)	8 (16%)
ENDOCRINE SYSTEM		
Adrenal gland	(50)	(50)
Capsule, leukemia lymphocytic		1 (2%)
Capsule, lymphoma malignant undifferentiated cell type	1 (2%)	
Adrenal gland, cortex	(50)	(50)
Adenoma	2 (4%)	1 (2%)
Fibrous histiocytoma, metastatic, skeletal muscle		1 (2%)
Leukemia mononuclear	6 (12%)	8 (16%)
Sarcoma, metastatic, bone	1 (2%)	

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

	Chamber Control	15,000 ppm
ENDOCRINE SYSTEM (Continued)		
Adrenal gland, medulla	(35)	(40)
Leukemia mononuclear	7 (20%)	6 (15%)
Pheochromocytoma malignant		1 (3%)
Pheochromocytoma benign	1 (3%)	2 (5%)
Sarcoma, metastic, bone	1 (3%)	
Islets, pancreatic	(49)	(50)
Carcinoma	1 (2%)	
Pituitary gland	(49)	(50)
Pars distalis, adenoma	26 (53%)	30 (60%)
Pars distalis, carcinoma	6 (12%)	3 (6%)
Pars distalis, carcinoma, metastatic, Zymbal gland		1 (2%)
Pars distalis, leukemia mononuclear	4 (8%)	2 (4%)
Thyroid gland	(49)	(48)
Leukemia mononuclear	1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)	
C-cell, adenoma	5 (10%)	2 (4%)
C-cell, carcinoma	3 (6%)	1 (2%)
Follicular cell, adenoma	1 (2%)	
Follicular cell, carcinoma	2 (4%)	3 (6%)
GENERAL BODY SYSTEM		
Tissue, NOS	*(50)	*(50)
Sarcoma	1 (2%)	
GENITAL SYSTEM		
Clitoral gland	(46)	(43)
Adenoma	1 (2%)	4 (9%)
Carcinoma	2 (4%)	1 (2%)
Ovary	(49)	(50)
Granulosa cell tumor malignant		1 (2%)
Leukemia mononuclear	6 (12%)	6 (12%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Uterus	(49)	(50)
Leukemia mononuclear	5 (10%)	2 (4%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Polyp stromal	2 (4%)	7 (14%)
HEMATOPOIETIC SYSTEM		
Bone marrow	(50)	(50)
Leukemia mononuclear	2 (4%)	1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Sarcoma, metastatic, bone	1 (2%)	
Lymph node	(48)	(49)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Mediastinal, leukemia mononuclear	1 (2%)	
Mesenteric, leukemia mononuclear	2 (4%)	1 (2%)
Mesenteric, lymphoma malignant undifferentiated cell type	1 (2%)	
Pancreatic, leukemia mononuclear	1 (2%)	
Renal, lymphoma malignant undifferentiated cell type	1 (2%)	
Lymph node, bronchial	(47)	(47)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)
Fibrous histiocytoma, metastatic, skeletal muscle		1 (2%)
Leukemia mononuclear	8 (17%)	11 (23%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Sarcoma, metastatic, bone	1 (2%)	

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

	Chamber Control	15,000 ppm
HEMATOPOIETIC SYSTEM		
Lymph node, bronchial (Continued)	(47)	(47)
Mesenteric, sarcoma, metastatic, tissue, NOS	1 (2%)	
Lymph node, mandibular	(39)	(43)
Leukemia lymphocytic		1 (2%)
Leukemia mononuclear	5 (13%)	8 (19%)
Lymphoma malignant undifferentiated cell type	1 (3%)	
Spleen	(50)	(50)
Fibrous histiocytoma, metastatic		1 (2%)
Hemangiosarcoma	1 (2%)	
Leukemia mononuclear	19 (38%)	23 (46%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Thymus	(38)	(39)
Leukemia mononuclear	5 (13%)	2 (5%)
Lymphoma malignant undifferentiated cell type	1 (3%)	
INTEGUMENTARY SYSTEM		
Mammary gland	(48)	(50)
Adenocarcinoma		1 (2%)
Adenoma	2 (4%)	1 (2%)
Fibroadenoma	11 (23%)	8 (16%)
Fibroadenoma, multiple	1 (2%)	1 (2%)
Leukemia mononuclear	1 (2%)	
Skin	(47)	(49)
Basal cell carcinoma		1 (2%)
Subcutaneous tissue, fibroma	1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM		
Bone	(50)	(50)
Fibrous histiocytoma, metastatic, skeletal muscle		1 (2%)
Osteosarcoma	1 (2%)	
Periosteum, leukemia mononuclear	3 (6%)	4 (8%)
Skeletal muscle	*(50)	*(50)
Fibrous histiocytoma		1 (2%)
NERVOUS SYSTEM		
Brain	(50)	(50)
Astrocytoma malignant		3 (6%)
Carcinoma, metastatic, pituitary gland	5 (10%)	2 (4%)
Leukemia mononuclear	3 (6%)	3 (6%)
Meninges, carcinoma, metastatic, Zymbal gland		1 (2%)
RESPIRATORY SYSTEM		
Larynx	(50)	(49)
Leukemia lymphocytic		1 (2%)
Lung	(50)	(50)
Basal cell carcinoma, metastatic, skin		1 (2%)
Carcinoma, metastatic, thyroid gland	1 (2%)	
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)
Fibrous histiocytoma, metastatic, skeletal muscle		1 (2%)
Leukemia mononuclear	15 (30%)	16 (32%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Sarcoma, metastatic, bone	1 (2%)	
Sarcoma, metastatic, ear		1 (2%)

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

	Chamber Control	15,000 ppm
RESPIRATORY SYSTEM (Continued)		
Nose	(50)	(50)
Leukemia lymphocytic		1 (2%)
Leukemia mononuclear	3 (6%)	3 (6%)
Trachea	(50)	(49)
Leukemia lymphocytic		1 (2%)
SPECIAL SENSES SYSTEM		
Ear	*(50)	*(50)
Sarcoma		1 (2%)
Eye	*(50)	*(50)
Leukemia mononuclear		1 (2%)
Zymbal gland	*(50)	*(50)
Adenoma		1 (2%)
Carcinoma		1 (2%)
URINARY SYSTEM		
Kidney	(50)	(50)
Fibrous histiocytoma, metastatic, uncertain primary site		1 (2%)
Leukemia lymphocytic		1 (2%)
Leukemia mononuclear	6 (12%)	8 (16%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Sarcoma, metastatic, bone	1 (2%)	
Urinary bladder	(49)	(49)
Leukemia mononuclear	3 (6%)	3 (6%)
SYSTEMIC LESIONS		
Multiple organs	*(50)	*(50)
Leukemia mononuclear	20 (40%)	25 (50%)
Lymphoma malignant undifferentiated cell	1 (2%)	
Hemangiosarcoma	1 (2%)	
Leukemia lymphocytic		1 (2%)
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	50	50
Terminal sacrifice	31	22
Moribund sacrifice	19	24
Natural death		4
TUMOR SUMMARY		
Total animals with primary neoplasms **	45	48
Total primary neoplasms	95	105
Total animals with benign neoplasms	37	38
Total benign neoplasms	56	60
Total animals with malignant neoplasms	33	35
Total malignant neoplasms	39	45
Total animals with secondary neoplasms ***	8	8
Total secondary neoplasms	17	20
Total animals with malignant neoplasms--uncertain primary site		1

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** 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 CHLOROETHANE: CHAMBER CONTROL

WEEKS ON STUDY	036	078	078	082	082	084	088	090	091	092	094	094	095	095	095	096	099	101	103	105	105	105	105	105	105
CARCASS ID	06411	08811	09711	06311	09411	08851	05221	07711	07211	09111	06811	07311	06611	07111	07611	05311	08311	09311	05911	05111	05411	05551	05611	05711	05811
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, bone												X													
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	M	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Intestine small, ileum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+
Sarcoma, metastatic, tissue, NOS																	X								
Intestine small, jejunum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																									
Leukemia mononuclear					X	X		X			X		X	X	X	X		X	X	X					
Lymphoma malignant undifferentiated cell type	X																								
Sarcoma, metastatic, bone												X													
Mesentery					+																				
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X					X				X	X									
Lymphoma malignant undifferentiated cell type	X																								
Sarcoma, metastatic, tissue, NOS																	X								
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+
Leukemia mononuclear					X										X										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X										X										
Tongue																	+								
Papilloma squamous																	X								
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X	X		X			X				X	X									
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, lymphoma malignant undifferentiated cell type	X																								
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma															X										
Leukemia mononuclear						X								X		X			X						
Sarcoma, metastatic, bone												X													
Adrenal gland, medulla	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	M	+	+
Leukemia mononuclear					X	X					X				X	X									
Pheochromocytoma benign																									
Sarcoma, metastatic, bone												X													
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																								X	
Parathyroid gland	+	M	M	M	+	+	M	+	+	+	+	M	+	M	+	+	+	+	+	M	+	+	+	+	+
Pituitary gland	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X		X		X	X					X		X			X		X	X			X	X	
Pars distalis, carcinoma			X						X	X			X					X				X			
Pars distalis, leukemia mononuclear					X									X	X										
Thyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									
Lymphoma malignant undifferentiated cell type	X																								
C-cell, adenoma																				X					
C-cell, carcinoma													X												
Follicular cell, adenoma										X															
Follicular cell, carcinoma																									
GENERAL BODY SYSTEM																									
Tissue, NOS																	+								
Sarcoma																	X								
GENITAL SYSTEM																									
Clitoral gland	M	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	M	+	+	+	+	+
Adenoma																									
Carcinoma				X																					
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X									X	X										
Lymphoma malignant undifferentiated cell type	X																								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X						X			X	X										
Lymphoma malignant undifferentiated cell type	X																								
Polyp stromal		X																							X

+: Tissue examined microscopically
: Not examined
−: Present but not examined microscopically
I: Insufficient tissue

M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

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

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	TOTAL:
CARCASS ID	0601	0611	0621	0651	0671	0691	0701	0741	0751	0781	0791	0801	0811	0821	0841	0871	0881	0891	0901	0921	0951	0961	0981	0991	1001	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+		45
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Sarcoma, metastatic, bone																										1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine small, duodenum	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Sarcoma, metastatic, tissue, NOS																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Hepatocellular carcinoma																						X				1
Leukemia mononuclear		X			X				X		X	X					X	X				X				19
Lymphoma malignant undifferentiated cell type																										1
Sarcoma, metastatic, bone																										1
Mesentery																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+		49
Leukemia mononuclear										X								X								6
Lymphoma malignant undifferentiated cell type																										1
Sarcoma, metastatic, tissue, NOS																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+		48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+		46
Leukemia mononuclear										X																3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Leukemia mononuclear										X																3
Tongue																										1
Papilloma squamous																										1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Leukemia mononuclear					X						X	X						X								10
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Capsule, lymphoma malignant undifferentiated cell type																										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Adenoma	X																									2
Leukemia mononuclear					X							X														6
Sarcoma, metastatic, bone																										1
Adrenal gland, medulla	+	+	I	+	M	+	+	M	M	+	M	+	M	+	+	+	I	+	+	M	+	I	+	M	I	35
Leukemia mononuclear												X						X								7
Pheochromocytoma benign																			X							1
Sarcoma, metastatic, bone																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+		49
Carcinoma																										1
Parathyroid gland	I	+	M	+	M	M	+	M	+	M	+	+	+	+	+	M	M	+	+	+	+	+	+	M	+	34
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma			X			X	X	X	X		X	X		X		X			X	X	X	X	X	X		26
Pars distalis, carcinoma																										6
Pars distalis, leukemia mononuclear																		X								4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Leukemia mononuclear											X															1
Lymphoma malignant undifferentiated cell type																										1
C-cell, adenoma							X			X		X						X								5
C-cell, carcinoma			X											X												3
Follicular cell, adenoma																										1
Follicular cell, carcinoma						X												X								2
GENERAL BODY SYSTEM																										
Tissue, NOS																										1
Sarcoma																										1
GENITAL SYSTEM																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Adenoma	X																									1
Carcinoma								X																		2
Ovary	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Leukemia mononuclear					X						X	X														6
Lymphoma malignant undifferentiated cell type																										1
Uterus	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Leukemia mononuclear											X															5
Lymphoma malignant undifferentiated cell type																										1
Polyp stromal																										2

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

WEEKS ON STUDY	0 3 6	0 7 8	0 7 8	0 8 2	0 8 2	0 8 4	0 8 8	0 9 0	0 9 1	0 9 2	0 9 4	0 9 4	0 9 5	0 9 5	0 9 5	0 9 6	0 9 9	1 0 1	1 0 3	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5
CARCASS ID	0 6 4 1	0 8 6 1	0 9 7 1	0 6 3 1	0 9 4 1	0 8 5 1	0 5 2 1	0 7 7 1	0 7 7 2 1	0 9 1 1	0 6 8 1	0 7 3 1	0 6 6 1	0 7 1 1	0 7 6 1	0 5 3 1	0 8 3 1	0 9 3 1	0 5 9 1	0 5 1 1	0 5 4 1	0 5 5 1	0 5 6 1	0 5 7 1	0 5 8 1
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X										X									
Lymphoma malignant undifferentiated cell type	X																								
Sarcoma, metastatic, bone												X													
Lymph node	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type	X																								
Mediastinal, leukemia mononuclear																									
Mesenteric, leukemia mononuclear															X	X									
Mesenteric, lymphoma malignant undifferentiated cell type	X																								
Pancreatic, leukemia mononuclear											X														
Renal, lymphoma malignant undifferentiated cell type	X																								
Lymph node, bronchial	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X	X							X		X	X									
Lymphoma malignant undifferentiated cell type	X																								
Sarcoma, metastatic, bone												X													
Mesenteric, sarcoma, metastatic, tissue NOS																	X								
Lymph node, mandibular	+	M	M	M	+	+	+	+	M	+	+	I	+	+	+	+	+	+	+	+	+	M	+	+	+
Leukemia mononuclear					X										X	X									
Lymphoma malignant undifferentiated cell type	X																								
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Leukemia mononuclear					X	X		X			X		X	X	X	X		X	X	X					
Lymphoma malignant undifferentiated cell type	X																								
Thymus	+	+	+	+	+	+	M	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M
Leukemia mononuclear						X					X				X	X									
Lymphoma malignant undifferentiated cell type	X																								
INTEGUMENTARY SYSTEM																									
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Fibroadenoma			X	X	X					X		X										X			
Fibroadenoma, multiple																						X			
Leukemia mononuclear						X																			
Skin	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	M
Subcutaneous tissue, fibroma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma												X													
Periosteum, leukemia mononuclear						X									X										
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland			X						X	X			X									X			
Leukemia mononuclear					X										X	X									
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland																									
Leukemia mononuclear					X	X		X			X		X	X	X	X			X	X					
Lymphoma malignant undifferentiated cell type	X																								
Sarcoma, metastatic, bone												X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear													X	X		X									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye			+																						
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X						X		X	X		X									
Lymphoma malignant undifferentiated cell type	X																								
Sarcoma, metastatic, bone												X													
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X									X										

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

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	TOTAL:
CARCASS ID	0601	0611	0621	0651	0671	0691	0701	0741	0751	0781	0791	0801	0811	0821	0841	0871	0881	0891	0901	0921	0951	0961	0981	0991	1001	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										2
Lymphoma malignant undifferentiated cell type																										1
Sarcoma, metastatic, bone																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	48
Lymphoma malignant undifferentiated cell type																										1
Mediastinal, leukemia mononuclear											X															1
Mesenteric, leukemia mononuclear																										2
Mesenteric, lymphoma malignant undifferentiated cell type																										1
Pancreatic, leukemia mononuclear																										1
Renal, lymphoma malignant undifferentiated cell type																										1
Lymph node, bronchial	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Leukemia mononuclear											X	X						X								8
Lymphoma malignant undifferentiated cell type																										1
Sarcoma, metastatic, bone																										1
Mesenteric, sarcoma, metastatic, tissue NOS																										1
Lymph node, mandibular	M	+	+	+	+	+	+	M	+	+	+	M	+	+	+	M	+	+	+	+	+	M	+	+	+	39
Leukemia mononuclear					X						X															5
Lymphoma malignant undifferentiated cell type																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																						X				1
Leukemia mononuclear		X			X				X		X	X				X	X	X								19
Lymphoma malignant undifferentiated cell type																										1
Thymus	M	+	+	+	+	M	+	+	I	+	+	+	M	M	+	+	+	M	+	+	+	M	+	+	M	38
Leukemia mononuclear											X															5
Lymphoma malignant undifferentiated cell type																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma											X	X														2
Fibroadenoma					X			X	X								X				X					11
Fibroadenoma, multiple																										1
Leukemia mononuclear																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Subcutaneous tissue, fibroma	X																									1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Periosteum, leukemia mononuclear											X															3
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pituitary gland																										5
Leukemia mononuclear																										3
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, thyroid gland			X																							1
Leukemia mononuclear					X				X		X	X						X								15
Lymphoma malignant undifferentiated cell type																										1
Sarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										3
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSES SYSTEM																										
Eye									+							+	M									3
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear												X														6
Lymphoma malignant undifferentiated cell type																										1
Sarcoma, metastatic, bone																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear											X															3

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE: 15,000 ppm

WEEKS ON STUDY	052	070	077	078	078	080	081	082	082	082	084	085	086	087	088	089	090	092	093	096	097	099	099	099
CARCASS ID	19401	19311	19111	17761	19991	16551	20011	17211	17791	16411	18611	16111	17711	17781	17701	18411	15881	19511	18711	17411	18511	18211	16011	16911	16311
ALIMENTARY SYSTEM																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																								
Intestine large, rectum	A	+	+	+	+	+	+	M	M	M	+	+	A	+	M	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	M	M	M	+	+
Leukemia mononuclear																								
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site						X																		
Fibrous histiocytoma, metastatic, skeletal muscle														X										
Leukemia lymphocytic																								
Leukemia mononuclear			X				X						X		X		X	X	X		X		X	
Mesentery		+																						
Schwannoma malignant, metastatic, stomach		X																						
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site						X																		
Leukemia mononuclear																X					X			
Schwannoma malignant, metastatic, stomach		X																						
Pharynx																								
Palate, papilloma squamous																								
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma malignant		X																						
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear															X									
Tongue									+															
Papilloma squamous									X															
CARDIOVASCULAR SYSTEM																								
Blood vessel																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site						X																		
Leukemia lymphocytic																								
Leukemia mononuclear			X												X		X		X		X		X	
ENDOCRINE SYSTEM																								
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, leukemia lymphocytic																								
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
Fibrous histiocytoma, metastatic, skeletal muscle														X										
Leukemia mononuclear			X										X		X		X	X	X				X	
Adrenal gland, medulla	+	+	+	+	M	M	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X														X		X		X		X	
Pheochromocytoma malignant																								
Pheochromocytoma benign																								
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	M	M	+	+	+	M	+	+	M	M	M	M	M	M	+	+	+	M	+	M	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X			X		X	X		X	X	X	X	X		X			X		X	X	X		X
Pars distalis, carcinoma																		X						X	
Pars distalis, carcinoma, metastatic, Zymbal gland																X									
Pars distalis, leukemia mononuclear															X								X		
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																									
C-cell, carcinoma																			X						
Follicular cell, carcinoma																									
GENERAL BODY SYSTEM																								
None																								
GENITAL SYSTEM																								
Clitoral gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	M	+	+	+	+	+	M	I	+	M
Adenoma																					X				
Carcinoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor malignant																									
Leukemia mononuclear			X										X		X				X		X		X		
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear															X								X		
Polyp stromal								X				X							X			X			

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 15,000 ppm (Continued)

WEEKS ON STUDY	101	102	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
CARCASS ID	16211	19711	15711	15111	15211	15311	15411	15511	15611	15911	16611	16711	16811	17311	17511	17711	18011	18111	18311	18811	18911	19011	19211	19611	19811	TOTAL: TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear									X																	1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Leukemia mononuclear									X																	1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Fibrous histiocytoma, metastatic, skeletal muscle																										1
Leukemia lymphocytic																X										1
Leukemia mononuclear	X		X	X	X	X	X	X	X			X	X	X	X		X	X				X		X		25
Mesentery																								+		2
Schwannoma malignant, metastatic, stomach																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Leukemia mononuclear			X						X																	4
Schwannoma malignant, metastatic, stomach																										1
Pharynx									+															+		2
Palate, papilloma squamous									X																	1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma malignant																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	49
Leukemia mononuclear																										1
Tongue																										1
Papilloma squamous																										1
CARDIOVASCULAR SYSTEM																										
Blood vessel													+													1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Leukemia lymphocytic																X										1
Leukemia mononuclear			X						X																	8
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, leukemia lymphocytic																X										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																	X									1
Fibrous histiocytoma, metastatic, skeletal muscle																										1
Leukemia mononuclear			X																							8
Adrenal gland, medulla	+	+	+	I	M	+	+	+	+	+	+	I	M	+	+	+	+	+	+	+	+	M	I	+	+	40
Leukemia mononuclear									X																	6
Pheochromocytoma malignant																								X		1
Pheochromocytoma benign							X			X																2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	M	M	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	I	+	M	+	31
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X	X	X	X	X		X	X	X	X	X			X				X			X	X	X	30
Pars distalis, carcinoma														X												3
Pars distalis, carcinoma, metastatic, Zymbal gland																										1
Pars distalis, leukemia mononuclear																										2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C-cell, adenoma														X									X			2
C-cell, carcinoma																										1
Follicular cell, carcinoma	X													X			X									3
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	43
Adenoma			X								X				X											4
Carcinoma													X													1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granulosa cell tumor malignant								X																		1
Leukemia mononuclear																										6
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										2
Polyp stromal				X						X													X			7

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 15,000 ppm
(Continued)

WEEKS ON STUDY	052	070	077	078	078	080	081	082	082	082	084	085	086	087	088	088	089	090	092	093	096	097	099	099	099
CARCASS ID	19401	19311	19911	17611	19991	16651	20001	17211	17791	16411	18611	16111	17111	17811	17001	18411	15581	19511	18711	17411	18511	18211	16001	16991	16331
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear															X										
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenteric, leukemia mononuclear															X										
Lymph node, bronchial	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site						X																			
Fibrous histiocytoma, metastatic, skeletal muscle														X											
Leukemia mononuclear							X								X		X	X	X		X		X		
Lymph node, mandibular	+	+	+	+	+	+	M	+	+	+	M	+	+	M	+	+	M	+	M	+	+	+	+	+	+
Leukemia lymphocytic																									
Leukemia mononuclear			X												X						X		X		
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic						X																			
Leukemia mononuclear			X				X						X		X		X	X	X		X		X		
Thymus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	M	+	+	+
Leukemia mononuclear																							X		
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Adenoma																									
Fibroadenoma										X	X									X					
Fibroadenoma, multiple																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Subcutaneous tissue, fibroma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skeletal muscle														X											
Periosteum, leukemia mononuclear																							X		
Skeletal muscle														+											
Fibrous histiocytoma														X											
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant	X																			X					
Carcinoma, metastatic, pituitary gland																		X					X		
Leukemia mononuclear			X												X				X						
Meninges, carcinoma, metastatic, Zymbal gland																X									
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Leukemia lymphocytic																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma, metastatic, skin																									
Fibrous histiocytoma, metastatic, uncertain primary site						X																			
Fibrous histiocytoma, metastatic, skeletal muscle														X											
Leukemia mononuclear			X				X						X		X		X	X	X		X		X		
Sarcoma, metastatic, ear									X																
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia lymphocytic																									
Leukemia mononuclear			X																X				X		
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Leukemia lymphocytic																									
SPECIAL SENSES SYSTEM																									
Ear									+							+									
Sarcoma									X																
Eye					+										+										
Leukemia mononuclear															X										
Harderian gland																									
Zymbal gland																+							+		
Adenoma																							X		
Carcinoma																X									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, uncertain primary site						X																			
Leukemia lymphocytic																									
Leukemia mononuclear			X										X		X		X					X		X	
Urinary bladder	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear															X								X		

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 15,000 ppm (Continued)

WEEKS ON STUDY	101	102	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	16211	19711	15711	15111	15211	15311	15411	15511	15611	15911	16611	16711	16811	17311	17511	17711	18011	18111	18311	18811	18911	19011	19211	19611	19811	ITSSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	49
Mesenteric, leukemia mononuclear																										1
Lymph node, bronchial	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	47
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Fibrous histiocytoma, metastatic, skeletal muscle																										1
Leukemia mononuclear	X		X					X	X																	11
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	43
Leukemia lymphocytic																X										1
Leukemia mononuclear			X		X			X	X																	8
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic																										1
Leukemia mononuclear	X		X	X	X	X	X	X					X	X	X		X	X						X		23
Thymus	M	+	+	M	M	+	+	+	+	M	+	+	M	+	+	+	+	+	M	+	M	+	+	+	+	39
Leukemia mononuclear			X																							2
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																						X				1
Adenoma													X													1
Fibroadenoma		X	X										X	X					X							8
Fibroadenoma, multiple		X																								1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	49
Basal cell carcinoma									X																	1
Subcutaneous tissue, fibroma																				X						1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, skeletal muscle																										1
Periosteum, leukemia mononuclear			X						X													X				4
Skeletal muscle																										1
Fibrous histiocytoma																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant		X																								3
Carcinoma, metastatic, pituitary gland																										2
Leukemia mononuclear																										3
Meninges, carcinoma, metastatic, Zymbal gland																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia lymphocytic																X										1
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell carcinoma, metastatic, skin									X																	1
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Fibrous histiocytoma, metastatic, skeletal muscle																										1
Leukemia mononuclear	X		X			X		X					X		X		X									16
Sarcoma, metastatic, ear																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia lymphocytic																X										1
Leukemia mononuclear																										3
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia lymphocytic																X										1
SPECIAL SENSES SYSTEM																										
Ear																										2
Sarcoma																										1
Eye				+	+																		+			5
Leukemia mononuclear																										1
Harderian gland					+																					1
Zymbal gland																										2
Adenoma																										1
Carcinoma																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, uncertain primary site																										1
Leukemia lymphocytic																X										1
Leukemia mononuclear			X						X																	8
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear			X																							3

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

	Chamber Control	15,000 ppm
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma		
Overall Rates (a)	1/35 (3%)	3/40 (7%)
Adjusted Rates (b)	5.6%	18.8%
Terminal Rates (c)	1/18 (6%)	3/16 (19%)
Day of First Observation	729	729
Life Table Test (d)		P=0.258
Logistic Regression Test (d)		P=0.258
Fisher Exact Test (d)		P=0.360
Brain: Malignant Astrocytoma		
Overall Rates (a)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	9.1%
Terminal Rates (c)	0/31 (0%)	0/22 (0%)
Day of First Observation		364
Life Table Test (d)		P=0.095
Logistic Regression Test (d)		P=0.128
Fisher Exact Test (d)		P=0.121
Clitoral Gland: Adenoma		
Overall Rates (a)	1/46 (2%)	4/43 (9%)
Adjusted Rates (b)	3.3%	16.3%
Terminal Rates (c)	1/30 (3%)	2/21 (10%)
Day of First Observation	729	672
Life Table Test (d)		P=0.105
Logistic Regression Test (d)		P=0.106
Fisher Exact Test (d)		P=0.160
Clitoral Gland: Adenoma or Carcinoma		
Overall Rates (a)	3/46 (7%)	5/43 (12%)
Adjusted Rates (b)	8.7%	20.7%
Terminal Rates (c)	2/30 (7%)	3/21 (14%)
Day of First Observation	568	672
Life Table Test (d)		P=0.216
Logistic Regression Test (d)		P=0.255
Fisher Exact Test (d)		P=0.319
Mammary Gland: Fibroadenoma		
Overall Rates (a)	11/50 (22%)	8/50 (16%)
Adjusted Rates (b)	28.1%	27.1%
Terminal Rates (c)	6/31 (19%)	3/22 (14%)
Day of First Observation	545	574
Life Table Test (d)		P=0.540N
Logistic Regression Test (d)		P=0.303N
Fisher Exact Test (d)		P=0.306N
Mammary Gland: Adenoma or Fibroadenoma		
Overall Rates (a)	13/50 (26%)	8/50 (16%)
Adjusted Rates (b)	33.9%	27.1%
Terminal Rates (c)	8/31 (26%)	3/22 (14%)
Day of First Observation	545	574
Life Table Test (d)		P=0.386N
Logistic Regression Test (d)		P=0.173N
Fisher Exact Test (d)		P=0.163N
Mammary Gland: Adenoma, Fibroadenoma, or Adenocarcinoma		
Overall Rates (a)	13/50 (26%)	9/50 (18%)
Adjusted Rates (b)	33.9%	31.0%
Terminal Rates (c)	8/31 (26%)	4/22 (18%)
Day of First Observation	545	574
Life Table Test (d)		P=0.493N
Logistic Regression Test (d)		P=0.255N
Fisher Exact Test (d)		P=0.235N

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

	Chamber Control	15,000 ppm
Pituitary Gland/Pars Distalis: Adenoma		
Overall Rates (a)	26/49 (53%)	30/50 (60%)
Adjusted Rates (b)	65.7%	77.2%
Terminal Rates (c)	18/31 (58%)	14/22 (64%)
Day of First Observation	540	490
Life Table Test (d)		P=0.044
Logistic Regression Test (d)		P=0.250
Fisher Exact Test (d)		P=0.311
Pituitary Gland/Pars Distalis: Carcinoma		
Overall Rates (a)	6/49 (12%)	3/50 (6%)
Adjusted Rates (b)	14.8%	10.7%
Terminal Rates (c)	1/31 (3%)	1/22 (5%)
Day of First Observation	545	629
Life Table Test (d)		P=0.380N
Logistic Regression Test (d)		P=0.180N
Fisher Exact Test (d)		P=0.233N
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma		
Overall Rates (a)	32/49 (65%)	33/50 (66%)
Adjusted Rates (b)	72.2%	81.4%
Terminal Rates (c)	19/31 (61%)	15/22 (68%)
Day of First Observation	540	490
Life Table Test (d)		P=0.099
Logistic Regression Test (d)		P=0.525
Fisher Exact Test (d)		P=0.555
Thyroid Gland: C-Cell Adenoma		
Overall Rates (a)	5/49 (10%)	2/48 (4%)
Adjusted Rates (b)	16.1%	9.1%
Terminal Rates (c)	5/31 (16%)	2/22 (9%)
Day of First Observation	729	729
Life Table Test (d)		P=0.370N
Logistic Regression Test (d)		P=0.370N
Fisher Exact Test (d)		P=0.226N
Thyroid Gland: C-Cell Carcinoma		
Overall Rates (a)	3/49 (6%)	1/48 (2%)
Adjusted Rates (b)	8.9%	3.1%
Terminal Rates (c)	2/31 (6%)	0/22 (0%)
Day of First Observation	659	643
Life Table Test (d)		P=0.416N
Logistic Regression Test (d)		P=0.330N
Fisher Exact Test (d)		P=0.316N
Thyroid Gland: C-Cell Adenoma or Carcinoma		
Overall Rates (a)	8/49 (16%)	3/48 (6%)
Adjusted Rates (b)	24.6%	11.9%
Terminal Rates (c)	7/31 (23%)	2/22 (9%)
Day of First Observation	659	643
Life Table Test (d)		P=0.233N
Logistic Regression Test (d)		P=0.171N
Fisher Exact Test (d)		P=0.106N
Thyroid Gland: Follicular Cell Carcinoma		
Overall Rates (a)	2/49 (4%)	3/48 (6%)
Adjusted Rates (b)	6.5%	12.7%
Terminal Rates (c)	2/31 (6%)	2/22 (9%)
Day of First Observation	729	707
Life Table Test (d)		P=0.355
Logistic Regression Test (d)		P=0.380
Fisher Exact Test (d)		P=0.490

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

	Chamber Control	15,000 ppm
Thyroid Gland: Follicular Cell Adenoma or Carcinoma		
Overall Rates (a)	3/49 (6%)	3/48 (6%)
Adjusted Rates (b)	8.7%	12.7%
Terminal Rates (c)	2/31 (6%)	2/22 (9%)
Day of First Observation	643	707
Life Table Test (d)		P=0.513
Logistic Regression Test (d)		P=0.578
Fisher Exact Test (d)		P=0.651
Uterus: Stromal Polyp		
Overall Rates (a)	2/49 (4%)	7/50 (14%)
Adjusted Rates (b)	5.3%	23.1%
Terminal Rates (c)	1/30 (3%)	3/22 (14%)
Day of First Observation	540	573
Life Table Test (d)		P=0.049
Logistic Regression Test (d)		P=0.093
Fisher Exact Test (d)		P=0.085
Hematopoietic System: Leukemia		
Overall Rates (a)	20/50 (40%)	(e) 26/50 (52%)
Adjusted Rates (b)	48.1%	77.5%
Terminal Rates (c)	10/31 (32%)	15/22 (68%)
Day of First Observation	574	535
Life Table Test (d)		P=0.025
Logistic Regression Test (d)		P=0.090
Fisher Exact Test (d)		P=0.158

(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 dosed group incidence are the P values corresponding to pairwise comparisons between the 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 logistic regression test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in the dosed group is indicated by (N).
(e) Includes one diagnosis of lymphocytic leukemia

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 2 gliomas, NOS, 18 astrocytomas, and 3 oligodendrogliomas

TABLE B4b. HISTORICAL INCIDENCE OF LEUKEMIA 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	14/50
Methyl methacrylate	11/50
Propylene	13/49
1,2-Epoxybutane	26/50
Dichloromethane	17/50
Tetrachloroethylene	18/50
TOTAL	99/299 (33.1%)
SD (b)	10.57%
Range (c)	
High	26/50
Low	11/50
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	383/1,983 (19.3%)
SD (b)	6.66%
Range (c)	
High	15/49
Low	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 B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	50	50
ALIMENTARY SYSTEM		
Intestine large	(50)	(49)
Anus, parasite metazoan		1 (2%)
Intestine large, cecum	(50)	(48)
Parasite metazoan	7 (14%)	6 (13%)
Intestine large, colon	(50)	(49)
Parasite metazoan	4 (8%)	7 (14%)
Intestine large, rectum	(48)	(44)
Parasite metazoan	6 (13%)	3 (7%)
Liver	(50)	(50)
Angiectasis	1 (2%)	1 (2%)
Basophilic focus	29 (58%)	22 (44%)
Congestion		1 (2%)
Degeneration	2 (4%)	2 (4%)
Degeneration, fatty	10 (20%)	6 (12%)
Hematopoietic cell proliferation	3 (6%)	5 (10%)
Hepatodiaphragmatic nodule	3 (6%)	
Inflammation, granulomatous, focal	19 (38%)	21 (42%)
Leukocytosis	3 (6%)	1 (2%)
Necrosis	2 (4%)	8 (16%)
Pigmentation		1 (2%)
Thrombus	2 (4%)	
Bile duct, hyperplasia	7 (14%)	12 (24%)
Hepatocyte, hyperplasia	2 (4%)	
Mesentery	(1)	(2)
Fat, inflammation, chronic	1 (100%)	1 (50%)
Pancreas	(49)	(50)
Atrophy	15 (31%)	9 (18%)
Cytomegaly	1 (2%)	2 (4%)
Hyperplasia		1 (2%)
Inflammation	1 (2%)	
Artery, mineralization		1 (2%)
Pharynx		(2)
Palate, inflammation, chronic		1 (50%)
Salivary glands	(48)	(50)
Inflammation, chronic		1 (2%)
Inflammation, suppurative, chronic	1 (2%)	
Duct, hyperplasia	4 (8%)	6 (12%)
Stomach, forestomach	(46)	(50)
Inflammation, chronic	2 (4%)	
Inflammation, suppurative	1 (2%)	
Ulcer	1 (2%)	1 (2%)
Epithelium, hyperplasia	6 (13%)	1 (2%)
Stomach, glandular	(50)	(49)
Mineralization		1 (2%)
Ulcer		1 (2%)
CARDIOVASCULAR SYSTEM		
Blood vessel		(1)
Inflammation		1 (100%)
Heart	(50)	(50)
Inflammation, chronic	42 (84%)	41 (82%)
Artery, mineralization		1 (2%)
Atrium, thrombus		2 (4%)

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

	Chamber Control	15,000 ppm
ENDOCRINE SYSTEM		
Adrenal gland, cortex	(50)	(50)
Degeneration		1 (2%)
Degeneration, fatty	13 (26%)	18 (36%)
Focal cellular change	1 (2%)	
Hematopoietic cell proliferation	5 (10%)	6 (12%)
Hemorrhage		1 (2%)
Hyperplasia	6 (12%)	9 (18%)
Hypertrophy	1 (2%)	1 (2%)
Necrosis	1 (2%)	
Adrenal gland, medulla	(35)	(40)
Hyperplasia	4 (11%)	3 (8%)
Necrosis	1 (3%)	
Islets, pancreatic	(49)	(50)
Hyperplasia	1 (2%)	
Parathyroid gland	(34)	(31)
Hyperplasia		1 (3%)
Pituitary gland	(49)	(50)
Pars distalis, cyst	3 (6%)	4 (8%)
Pars distalis, hemorrhage		1 (2%)
Pars distalis, hyperplasia	10 (20%)	11 (22%)
Pars distalis, infiltration cellular, mixed cell		1 (2%)
Pars distalis, metaplasia, osseous	1 (2%)	
Pars distalis, pigmentation, hemosiderin	1 (2%)	2 (4%)
Thyroid gland	(49)	(48)
Mineralization		1 (2%)
C-cell, hyperplasia	33 (67%)	31 (65%)
GENERAL BODY SYSTEM		
None		
GENITAL SYSTEM		
Clitoral gland	(46)	(43)
Cyst	2 (4%)	
Hyperplasia	1 (2%)	1 (2%)
Inflammation, suppurative	4 (9%)	3 (7%)
Duct, hyperplasia	1 (2%)	1 (2%)
Ovary	(49)	(50)
Atrophy	1 (2%)	4 (8%)
Cyst	2 (4%)	5 (10%)
Interstitium, hyperplasia	2 (4%)	1 (2%)
Uterus	(49)	(50)
Hemorrhage	1 (2%)	
Inflammation, suppurative	1 (2%)	
Endometrium, hyperplasia	1 (2%)	1 (2%)
Endometrium, hyperplasia, cystic	1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM		
Bone marrow	(50)	(50)
Infiltration cellular, histiocytic		1 (2%)
Myelofibrosis	2 (4%)	
Lymph node	(48)	(49)
Mesenteric, angiectasis	1 (2%)	
Mesenteric, inflammation, granulomatous	1 (2%)	
Renal, inflammation, granulomatous	1 (2%)	
Lymph node, bronchial	(47)	(47)
Congestion	1 (2%)	1 (2%)
Hyperplasia	1 (2%)	1 (2%)
Inflammation, granulomatous	1 (2%)	

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

	Chamber Control	15,000 ppm
HEMATOPOIETIC SYSTEM (Continued)		
Lymph node, mandibular	(39)	(43)
Angiectasis	1 (3%)	
Depletion		1 (2%)
Hyperplasia	9 (23%)	8 (19%)
Spleen	(50)	(50)
Fibrosis	1 (2%)	
Hematocyst		1 (2%)
Hematopoietic cell proliferation	1 (2%)	7 (14%)
Inflammation, granulomatous, focal	1 (2%)	2 (4%)
Pigmentation, hemosiderin		2 (4%)
Thymus	(38)	(39)
Epithelial cell, hyperplasia	1 (3%)	
INTEGUMENTARY SYSTEM		
Mammary gland	(48)	(50)
Hyperplasia	45 (94%)	47 (94%)
Skin	(47)	(49)
Acanthosis	2 (4%)	2 (4%)
Inflammation	1 (2%)	
Inflammation, suppurative		3 (6%)
Subcutaneous tissue, inflammation, chronic	1 (2%)	
Subcutaneous tissue, inflammation, granulomatous	1 (2%)	
MUSCULOSKELETAL SYSTEM		
Bone	(50)	(50)
Fibrous osteodystrophy		1 (2%)
NERVOUS SYSTEM		
Brain	(50)	(50)
Gliosis		1 (2%)
Hemorrhage, focal	2 (4%)	2 (4%)
Inflammation		1 (2%)
Necrosis, focal	1 (2%)	1 (2%)
RESPIRATORY SYSTEM		
Larynx	(50)	(49)
Inflammation, suppurative	10 (20%)	7 (14%)
Metaplasia, squamous	1 (2%)	
Epithelium, hyperplasia		2 (4%)
Submucosa, inflammation	1 (2%)	1 (2%)
Lung	(50)	(50)
Congestion		2 (4%)
Edema	1 (2%)	2 (4%)
Foreign body	1 (2%)	
Hemorrhage		4 (8%)
Infiltration cellular, histiocytic	8 (16%)	13 (26%)
Inflammation, chronic, diffuse	1 (2%)	1 (2%)
Inflammation, chronic, focal	4 (8%)	4 (8%)
Inflammation, granulomatous	1 (2%)	
Mineralization		1 (2%)
Necrosis		1 (2%)
Thrombus		1 (2%)
Alveolar epithelium, hyperplasia	4 (8%)	8 (16%)
Bronchiole, epithelium, hyperplasia		1 (2%)
Mediastinum, infiltration cellular, mononuclear cell	1 (2%)	

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

	Chamber Control		15,000 ppm	
RESPIRATORY SYSTEM				
Lung (Continued)	(50)		(50)	
Perivascular, infiltration cellular, mononuclear cell	21	(42%)	19	(38%)
Nose	(50)		(50)	
Inflammation, suppurative	6	(12%)	6	(12%)
Thrombus	2	(4%)	5	(10%)
Nasolacrimal duct, inflammation, suppurative	12	(24%)	10	(20%)
Respiratory epithelium, hyperplasia	4	(8%)	10	(20%)
Respiratory epithelium, metaplasia, squamous	2	(4%)	1	(2%)
Submucosa, inflammation	25	(50%)	34	(68%)
Vomeronasal organ, inflammation, suppurative	1	(2%)	1	(2%)
Trachea	(50)		(49)	
Inflammation, suppurative	2	(4%)	1	(2%)
Epithelium, hyperplasia			1	(2%)
Submucosa, inflammation			2	(4%)
SPECIAL SENSES SYSTEM				
Eye	(3)		(5)	
Cataract	1	(33%)	2	(40%)
Hemorrhage			1	(20%)
Inflammation, chronic			1	(20%)
Synechia	1	(33%)	1	(20%)
Bilateral, cataract	1	(33%)	1	(20%)
Retina, atrophy	1	(33%)	2	(40%)
Harderian gland			(1)	
Inflammation, suppurative			1	(100%)
URINARY SYSTEM				
Kidney	(50)		(50)	
Hydronephrosis			1	(2%)
Inflammation, suppurative	2	(4%)		
Mineralization			1	(2%)
Nephropathy	47	(94%)	42	(84%)
Renal tubule, hyperplasia, focal	1	(2%)	2	(4%)
Urinary bladder	(49)		(49)	
Hemorrhage			1	(2%)

APPENDIX C

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

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

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	50	50
ALIMENTARY SYSTEM		
Esophagus	(50)	(48)
Squamous cell carcinoma	1 (2%)	
Intestine large, colon	(46)	(45)
Lymphoma malignant mixed		1 (2%)
Intestine small, duodenum	(45)	(42)
Hepatocellular carcinoma, metastatic		1 (2%)
Intestine small, ileum	(44)	(43)
Lymphoma malignant mixed		1 (2%)
Liver	(50)	(47)
Hemangiosarcoma		1 (2%)
Hepatocellular carcinoma	5 (10%)	6 (13%)
Hepatocellular carcinoma, multiple	4 (8%)	3 (6%)
Hepatocellular adenoma	5 (10%)	2 (4%)
Hepatocellular adenoma, multiple	1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)	
Pancreas	(49)	(47)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Stomach, forestomach	(49)	(48)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Stomach, glandular	(49)	(48)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Tooth	*(50)	*(50)
Peridontal tissue, lymphoma malignant undifferentiated cell type	1 (2%)	
CARDIOVASCULAR SYSTEM		
Heart	(50)	(48)
Lymphoma malignant undifferentiated cell type	1 (2%)	
ENDOCRINE SYSTEM		
Adrenal gland	(47)	(47)
Capsule, lymphoma malignant undifferentiated cell type	1 (2%)	
Adrenal gland, cortex	(46)	(46)
Adenoma	1 (2%)	
Islets, pancreatic	(49)	(48)
Adenoma	1 (2%)	
Thyroid gland	(49)	(48)
Follicular cell, adenoma		1 (2%)
GENERAL BODY SYSTEM		
None		
GENITAL SYSTEM		
Epididymis	(46)	(39)
Lymphoma malignant undifferentiated cell type	1 (2%)	

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

	Chamber Control	15,000 ppm
HEMATOPOIETIC SYSTEM		
Lymph node	(38)	(40)
Mesenteric, lymphoma malignant mixed		1 (3%)
Mesenteric, lymphoma malignant undifferentiated cell type	1 (3%)	
Lymph node, bronchial	(29)	(30)
Fibrosarcoma, metastatic, skin	1 (3%)	
Hepatocellular carcinoma, metastatic, liver	1 (3%)	
Lymphoma malignant undifferentiated cell type	1 (3%)	
Spleen	(49)	(48)
Hemangiosarcoma		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
INTEGUMENTARY SYSTEM		
Skin	(50)	(49)
Hemangiosarcoma		1 (2%)
Prepuce, fibrous histiocytoma	1 (2%)	
Subcutaneous tissue, lipoma		1 (2%)
Subcutaneous tissue, head, fibrosarcoma	1 (2%)	
MUSCULOSKELETAL SYSTEM		
Bone	(50)	(48)
Cranium, lymphoma malignant undifferentiated cell type	1 (2%)	
Cranium, sternum, fibrosarcoma, metastatic, skin	1 (2%)	
NERVOUS SYSTEM		
None		
RESPIRATORY SYSTEM		
Lung	(50)	(48)
Alveolar/bronchiolar adenoma	3 (6%)	8 (17%)
Alveolar/bronchiolar carcinoma	2 (4%)	1 (2%)
Alveolar/bronchiolar carcinoma, multiple		1 (2%)
Carcinoma, metastatic, harderian gland	1 (2%)	
Fibrosarcoma, metastatic, skin	1 (2%)	
Hepatocellular carcinoma, metastatic, liver	1 (2%)	
Hepatocellular carcinoma, metastatic, multiple, liver	1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)	
Nose	(50)	(49)
Lymphoma malignant undifferentiated cell type	1 (2%)	
SPECIAL SENSES SYSTEM		
Ear	*(50)	*(50)
Fibrosarcoma		1 (2%)
Pinna, squamous cell carcinoma	1 (2%)	
Harderian gland	*(50)	*(50)
Adenocarcinoma	1 (2%)	
Adenoma	2 (4%)	4 (8%)
Carcinoma	1 (2%)	

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

	Chamber Control	15,000 ppm
URINARY SYSTEM		
Kidney	(50)	(49)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Ureter	*(50)	*(50)
Lymphoma malignant undifferentiated cell type	1 (2%)	
SYSTEMIC LESIONS		
Multiple organs	*(50)	*(50)
Lymphoma malignant undifferentiated cell	1 (2%)	
Lymphoma malignant mixed		2 (4%)
Hemangiosarcoma		2 (4%)
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	50	50
Terminal sacrifice	28	11
Natural death	7	14
Moribund sacrifice	15	25
TUMOR SUMMARY		
Total animals with primary neoplasms **	27	20
Total primary neoplasms	31	33
Total animals with benign neoplasms	12	11
Total benign neoplasms	13	17
Total animals with malignant neoplasms	17	13
Total malignant neoplasms	18	16
Total animals with secondary neoplasms ***	3	1
Total secondary neoplasms	7	1

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** 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 CHLOROETHANE: CHAMBER CONTROL

WEEKS ON STUDY	003	059	059	059	069	070	074	075	076	076	080	080	082	083	084	088	090	093	094	094	096	098	100	100	100
CARCASS ID	351	211	361	341	041	231	111	181	461	481	261	491	501	401	151	141	101	051	091	121	291	441	011	021	031
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Gallbladder	+	+	+	M	M	+	+	M	+	+	+	+	+	A	+	M	A	+	-	+	M	+	+	+	+
Intestine large	+	+	+	+	+	+	A	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Intestine large, cecum	M	+	+	+	+	+	A	M	M	+	+	+	+	A	+	+	A	+	+	+	M	M	+	+	+
Intestine large, colon	+	+	+	+	+	+	A	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Intestine large, rectum	M	+	+	+	+	+	A	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	A	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	A	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Intestine small, ileum	M	+	+	+	+	+	A	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Intestine small, jejunum	M	+	+	+	+	+	A	A	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma						X	X				X										X			X	
Hepatocellular carcinoma, multiple					X				X										X						
Hepatocellular adenoma		X																							X
Hepatocellular adenoma, multiple																				X					
Lymphoma malignant undifferentiated cell type														X											
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type														X											
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type														X											
Stomach, glandular	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type														X											
Tooth														+											+
Peridontal tissue, lymphoma malignant undifferentiated cell type														X											
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type														X											
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	I	+	+	+	+	+	+	-	-	A	+	-	+	+	+	+	+	+
Capsule, lymphoma malignant undifferentiated cell type														X											
Adrenal gland, cortex	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	.	A	+	+	+	+	+	+	+	+
Adenoma																									
Adrenal gland, medulla	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	A	+	-	-	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	M	M	M	+	M	M	M	M	+	M	M	M	M	M	M	M	I	M	M	+	M	M	+	M	+
Pituitary gland	+	M	+	+	+	+	+	M	+	+	+	+	+	I	+	+	+	+	-	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
GENERAL BODY SYSTEM																									
Tissue, NOS																									
GENITAL SYSTEM																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	-	+	+	M	+	M
Lymphoma malignant undifferentiated cell type														X											
Penis								+											+						
Preputial gland				+			+	+			+	+	+	+						+	+			+	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Seminal vesicle		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+
Lymph node	M	+	+	+	M	+	M	+	+	+	+	+	+	+	M	+	I	M	+	+	+	I	+	+	+
Mesenteric, lymphoma malignant undifferentiated cell type														X											
Lymph node, bronchial	M	+	+	+	M	+	M	+	+	+	+	+	+	+	M	+	M	M	+	M	+	I	+	+	+
Fibrosarcoma, metastatic, skin			X																						
Hepatocellular carcinoma, metastatic, liver									X																
Lymphoma malignant undifferentiated cell type														X											
Lymph node, mandibular	M	M	+	+	M	M	M	M	M	M	+	M	M	M	M	M	I	M	M	+	M	I	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	A	+	-	-	+	+	+	-	+
Lymphoma malignant undifferentiated cell type														X											
Thymus	+	M	M	+	M	M	+	+	M	+	M	+	+	I	+	M	M	M	I	M	+	M	M	+	+

+: Tissue examined microscopically
: Not examined
-: Present but not examined microscopically
I: Insufficient tissue

M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

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

WEEKS ON STUDY	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
CARCASS ID	0061	0071	0081	1031	1061	1071	1091	2001	2021	2041	2051	2071	2081	3001	3011	3021	3031	3071	3081	3091	4011	4021	4031	4051	4071	TOTAL: TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma							X																			1
Gallbladder	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	I	+	+	+	+	A	+	+	+	40
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, cecum	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma																										5
Hepatocellular carcinoma, multiple																	X									4
Hepatocellular adenoma		X	X											X												5
Hepatocellular adenoma, multiple																										1
Lymphoma malignant undifferentiated cell type																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1
Salivary glands	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1
Tooth																										2
Peridontal tissue, lymphoma malignant undifferentiated cell type																										1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant undifferentiated cell type																										1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Capsule, lymphoma malignant undifferentiated cell type																										1
Adrenal gland, cortex	+		I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma																X										1
Adrenal gland, medulla	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	47
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																					X					1
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	M	M	I	+	M	+	+	M	+	M	+	M	M	+	+	21
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	47
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
GENERAL BODY SYSTEM																										
Tissue, NOS									+																	1
GENITAL SYSTEM																										
Epididymis	+	+	–	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	46
Lymphoma malignant undifferentiated cell type																										1
Penis	+																									3
Preputial gland	+		+		+					+	+	+		+					+						+	19
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	–		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+		46
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	–	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	50
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	M	M	I	+	+	+	+	+	+	+	I	I	+	+	+	+	+	38
Mesenteric, lymphoma malignant undifferentiated cell type																										1
Lymph node, bronchial	M	+	+	+	+	+	+	M	M	M	I	+	M	+	I	M	M	M	I	I	+	+	I	+	+	29
Fibrosarcoma, metastatic, skin																										1
Hepatocellular carcinoma, metastatic, liver																										1
Lymphoma malignant undifferentiated cell type																										1
Lymph node, mandibular	+	+	I	+	M	+	M	+	M	M	M	M	+	M	+	+	+	–	M	I	M	M	+	I	+	19
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	49
Lymphoma malignant undifferentiated cell type																										1
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	I	+	+	M	+	+	+	33

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

WEEKS ON STUDY	003	059	059	059	069	070	074	075	076	076	080	080	082	083	084	088	090	093	094	094	096	098	100	100	100
CARCASS ID	351	211	361	341	041	231	111	181	461	481	261	491	501	401	151	141	101	051	091	121	291	441	011	021	031
INTEGUMENTARY SYSTEM																									
Mammary gland	M	+	M	M	M	M	M	M	M	+	+	+	+	M	+	M	M	M	+	M	M	+	+	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prepuce, fibrous histiocytoma																									
Subcutaneous tissue, head, fibrosarcoma			X																						
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cranium, lymphoma malignant undifferentiated cell type														X											
Cranium, sternum, fibrosarcoma, metastatic, skin			X																						
Skeletal muscle															+										
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, harderian gland			X																						
Fibrosarcoma, metastatic, skin			X																						
Hepatocellular carcinoma, metastatic, liver																			X						
Hepatocellular carcinoma, metastatic, multiple, liver									X																
Lymphoma malignant undifferentiated cell type														X											
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type														X											
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Ear																									
Pinna, squamous cell carcinoma																									
Eye	+																								+
Harderian gland			+											+											+
Adenocarcinoma																									X
Adenoma																									
Carcinoma			X																						
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type														X											
Ureter														+											
Lymphoma malignant undifferentiated cell type														X											
Urinary bladder	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+

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

WEEKS ON STUDY	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
CARCASS ID	061	071	081	131	161	171	191	201	221	241	251	271	281	301	311	321	331	371	381	391	411	421	431	451	471	TOTAL: TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	M	+	M	+	M	M	M	+	M	M	M	M	M	M	M	M	+	M	M	M	+	18
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	50
Prepuce, fibrous histiocytoma																										1
Subcutaneous tissue, head, fibrosarcoma																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cranium, lymphoma malignant undifferentiated cell type																										1
Cranium, sternum, fibrosarcoma, metastatic, skin																										1
Skeletal muscle																	+									2
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma	X			X													X									3
Alveolar/bronchiolar carcinoma						X																X				2
Carcinoma, metastatic, harderian gland																										1
Fibrosarcoma, metastatic, skin																										1
Hepatocellular carcinoma, metastatic, liver																										1
Hepatocellular carcinoma, metastatic, multiple, liver																										1
Lymphoma malignant undifferentiated cell type																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant undifferentiated cell type																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	50
SPECIAL SENSES SYSTEM																										
Ear																		+								1
Pinna, squamous cell carcinoma																		X								1
Eye																										2
Harderian gland								+						+												5
Adenocarcinoma																										1
Adenoma								X						X												2
Carcinoma																										1
URINARY SYSTEM																										
Kidney	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant undifferentiated cell type																										1
Ureter																										1
Lymphoma malignant undifferentiated cell type																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE: 15,000 ppm

WEEKS ON STUDY	0 0 1	0 3 3	0 3 7	0 3 8	0 3 9	0 4 0	0 4 2	0 4 4	0 4 8	0 5 1	0 5 2	0 5 2	0 5 2	0 5 2	0 5 2	0 5 2	0 5 7	0 5 9	0 5 9	0 5 9	0 6 2	0 6 4	0 6 7	0 7 0	0 7 2
CARCASS ID	1 2 7 1	1 4 0 1	1 1 5 1	1 1 4 1	1 1 6 1	1 1 3 1	1 2 6 1	1 0 6 1	1 4 7 1	1 2 2 1	1 2 9 1	1 1 0 1	1 1 7 1	1 2 0 1	1 3 2 1	1 4 1 1	1 1 2 1	1 1 1 1	1 4 2 1	1 5 0 1	1 4 5 1	1 4 8 1	1 3 1 1	1 1 9 1	1 3 9 1
ALIMENTARY SYSTEM																									
Esophagus	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	M	A	+	+	+	+	M	M	A	+	+	M	M	+	+	+	+	+	+	+	+	+	M	+
Intestine large	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Intestine large, rectum	+	A	A	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	A	A	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	A	A	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																									
Intestine small, ileum	+	A	A	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Intestine small, jejunum	+	A	A	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Hepatocellular carcinoma										X			X				X								
Hepatocellular carcinoma, multiple																									
Hepatocellular adenoma																									
Mesentery		A		+	+														+						
Pancreas	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARDIOVASCULAR SYSTEM																									
Heart	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Adrenal gland	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	A	A	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	A		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	M	+	M	+	M	M	M	+	M	M	+	+	+	M	M	M	M	M	M	M	+	M	M
Pituitary gland	+	A	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Thyroid gland	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
GENERAL BODY SYSTEM																									
Tissue, NOS																	+								
GENITAL SYSTEM																									
Epididymis	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	M		+
Penis					+										+					+					+
Preputial gland	+									+	+	+		+	+	+				+	+	+	+	+	
Prostate	+	A	A	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Seminal vesicle		A	+	+	+	+	+	+		+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
Testes	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Blood	+		A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
Bone marrow	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+
Lymph node	+	A	+	+	+	+	+	+	M	+	+	+	+	M	M	M	+	+	+	+	+	+	+	M	+
Mesenteric, lymphoma malignant mixed																									
Lymph node, bronchial	+	A	A	+	+	+	M	+	M	M	+	+	+	M	M	M	+	+	M	+	+	M	+	M	+
Lymph node, mandibular	+	A	A	M	M	M	+	M	M	+	M	+	M	M	M	M	M	+	+	M	+	M	M	M	M
Spleen	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Thymus	+	M	A	+	+	M	+	M	M	+	+	+	+	+	+	-	M	M	M	+	+	+	+	+	M
INTEGUMENTARY SYSTEM																									
Mammary gland	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	+	M	M	M	+	M	M	+	M	M
Skin	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Subcutaneous tissue, lipoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
Spinal cord								+																	
RESPIRATORY SYSTEM																									
Larynx	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
Lung	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																				X					
Alveolar/bronchiolar carcinoma																									
Alveolar/bronchiolar carcinoma, multiple																									
Nose	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	M	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Ear																	+							+	
Fibrosarcoma																								X	
Eye																									
Harderian gland																									
Adenoma																									
URINARY SYSTEM																									
Kidney	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ureter							+																		
Urinary bladder	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 15,000 ppm (Continued)

WEEKS ON STUDY	07 73	07 75	07 75	07 76	07 76	07 76	08 80	08 83	08 84	08 86	08 88	09 92	09 96	09 97	10 00	10 00	10 00	10 00	10 00	10 00	10 00	10 00	10 00	10 00	10 00	10 00	TOTAL:
CARCASS ID	10 91	14 61	14 91	10 71	13 41	13 61	14 41	12 51	13 71	10 81	13 81	12 11	12 41	14 31	11 11	10 21	10 31	10 41	10 51	11 81	12 31	12 81	13 01	13 31	13 51		TISSUES TUMORS
ALIMENTARY SYSTEM																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Gallbladder	+	+	+	+	+	+	+	+	+	+	A	A	+	A	M	M	M	I	M	+	M	M	M	+	+		31
Intestine large	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+		44
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Lymphoma malignant mixed																								X			1
Intestine large, rectum	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+		44
Intestine small	+	A	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+		43
Intestine small, duodenum	+	A	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+		42
Hepatocellular carcinoma, metastatic																			X								1
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+		43
Lymphoma malignant mixed																								X			1
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+		43
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Hemangiosarcoma											X																1
Hepatocellular carcinoma									X						X										X		6
Hepatocellular carcinoma, multiple																		X	X		X						3
Hepatocellular adenoma		X																	X								2
Mesentery																											3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
CARDIOVASCULAR SYSTEM																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
ENDOCRINE SYSTEM																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+		47
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+		46
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+		47
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Parathyroid gland	M	+	M	M	M	+	+	+	+	M	M	M	M	M	+	M	+	+	M	M	M	+	M	M	M		17
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	I	+	+	+	+	+	+	+	+	+		44
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Follicular cell, adenoma																					X						1
GENERAL BODY SYSTEM																											
Tissue, NOS			+													+											3
GENITAL SYSTEM																											
Epididymis	+	+	+	+	+	+	+	+	+	+		+		+	+	M	M	+	M	+	M	+	M	+	+		39
Penis	+								+				+		+												8
Preputial gland		+	+	+	+	+	+	+	+			+	+							+					+		24
Prostate	+	+	+	+	+	+	+	M	+	+	+	A	+	+	I	+	+	+	+	+	+	+	+	+	+		43
Seminal vesicle	+	+	+	+	+	+			+		+	A	M	+	+	+	+	+	+	+	+	+		+	+		41
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+		47
HEMATOPOIETIC SYSTEM																											
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Lymph node	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	M	+	+	M	+		40
Mesenteric, lymphoma malignant mixed									X																		1
Lymph node, bronchial	+	M	M	+	M	+	+	+	M	+	+	M	M	+	+	+	+	+	+	+	M	+	M	M	+		30
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	M	M	M	M	+	M	M	M	+	+	M	+	+	M	+		22
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Hemangiosarcoma											X																1
Thymus	M	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	I	M	+	+	+	M	+	M	M		33
INTEGUMENTARY SYSTEM																											
Mammary gland	M	M	+	+	+	M	+	+	+	M	M	M	M	+	M	M	+	M	M	+	+	M	+	+	M		16
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Hemangiosarcoma																									X		1
Subcutaneous tissue, lipoma																						X					1
MUSCULOSKELETAL SYSTEM																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
NERVOUS SYSTEM																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Spinal cord																											1
RESPIRATORY SYSTEM																											
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Alveolar/bronchiolar adenoma	X			X					X			X								X	X	X					8
Alveolar/bronchiolar carcinoma													X														1
Alveolar/bronchiolar carcinoma, multiple																		X									1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
SPECIAL SENSES SYSTEM																											
Ear											+														+		4
Fibrosarcoma																											1
Eye																			+	+							2
Harderian gland																			+	+		+			+		4
Adenoma																			X	X		X			X		4
URINARY SYSTEM																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Ureter																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+		47

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

	Chamber Control	15,000 ppm
Harderian Gland: Adenoma		
Overall Rates (a)	2/50 (4%)	4/50 (8%)
Adjusted Rates (b)	7.1%	36.4%
Terminal Rates (c)	2/28 (7%)	4/11 (36%)
Day of First Observation	700	700
Life Table Test (d)		P=0.039
Logistic Regression Test (d)		P=0.039
Fisher Exact Test (d)		P=0.339
Harderian Gland: Adenoma, Adenocarcinoma, or Carcinoma		
Overall Rates (a)	4/50 (8%)	4/50 (8%)
Adjusted Rates (b)	12.5%	36.4%
Terminal Rates (c)	3/28 (11%)	4/11 (36%)
Day of First Observation	409	700
Life Table Test (d)		P=0.176
Logistic Regression Test (d)		P=0.264
Fisher Exact Test (d)		P=0.643N
Liver: Hepatocellular Adenoma		
Overall Rates (a)	6/50 (12%)	2/47 (4%)
Adjusted Rates (b)	18.7%	12.9%
Terminal Rates (c)	4/28 (14%)	1/11 (9%)
Day of First Observation	409	519
Life Table Test (d)		P=0.511N
Logistic Regression Test (d)		P=0.317N
Fisher Exact Test (d)		P=0.155N
Liver: Hepatocellular Carcinoma		
Overall Rates (a)	9/50 (18%)	9/47 (19%)
Adjusted Rates (b)	22.6%	52.6%
Terminal Rates (c)	2/28 (7%)	5/11 (45%)
Day of First Observation	479	357
Life Table Test (d)		P=0.092
Logistic Regression Test (d)		P=0.466
Fisher Exact Test (d)		P=0.545
Liver: Hepatocellular Adenoma or Carcinoma		
Overall Rates (a)	15/50 (30%)	10/47 (21%)
Adjusted Rates (b)	37.9%	54.6%
Terminal Rates (c)	6/28 (21%)	5/11 (45%)
Day of First Observation	409	357
Life Table Test (d)		P=0.267
Logistic Regression Test (d)		P=0.365N
Fisher Exact Test (d)		P=0.227N
Lung: Alveolar/Bronchiolar Adenoma		
Overall Rates (a)	3/50 (6%)	8/48 (17%)
Adjusted Rates (b)	10.7%	43.5%
Terminal Rates (c)	3/28 (11%)	3/11 (27%)
Day of First Observation	700	409
Life Table Test (d)		P=0.003
Logistic Regression Test (d)		P=0.015
Fisher Exact Test (d)		P=0.087
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma		
Overall Rates (a)	5/50 (10%)	10/48 (21%)
Adjusted Rates (b)	17.9%	54.4%
Terminal Rates (c)	5/28 (18%)	4/11 (36%)
Day of First Observation	700	409
Life Table Test (d)		P=0.002
Logistic Regression Test (d)		P=0.008
Fisher Exact Test (d)		P=0.113

TABLE C3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE (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 dosed group incidence are the P values corresponding to pairwise comparisons between the 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 logistic regression test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in the dosed group is indicated by (N).

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 CHLOROETHANE

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	50	50
ALIMENTARY SYSTEM		
Esophagus	(50)	(48)
Hyperkeratosis		1 (2%)
Gallbladder	(40)	(31)
Inflammation, chronic	1 (3%)	
Mucosa, hyperplasia		1 (3%)
Intestine large	(46)	(45)
Anus, necrosis, focal		1 (2%)
Intestine small, duodenum	(45)	(42)
Ulcer		1 (2%)
Intestine small, ileum	(44)	(43)
Inflammation, subacute		1 (2%)
Liver	(50)	(47)
Basophilic focus		1 (2%)
Hematopoietic cell proliferation	2 (4%)	3 (6%)
Infiltration cellular, histiocytic, focal	1 (2%)	
Inflammation, acute		1 (2%)
Mineralization, focal		1 (2%)
Necrosis	2 (4%)	5 (11%)
Hepatocyte, cytomegaly	1 (2%)	
Mesentery		(3)
Inflammation, suppurative		1 (33%)
Pancreas	(49)	(47)
Hyperplasia		2 (4%)
Salivary glands	(49)	(48)
Inflammation, chronic	7 (14%)	7 (15%)
Stomach, forestomach	(49)	(48)
Hyperkeratosis	1 (2%)	2 (4%)
Epithelium, hyperplasia		2 (4%)
Stomach, glandular	(49)	(48)
Atrophy	1 (2%)	
Cyst	1 (2%)	1 (2%)
Hyperplasia	1 (2%)	
Inflammation, chronic		1 (2%)
Metaplasia, squamous	1 (2%)	4 (8%)
Mineralization		1 (2%)
Mucosa, necrosis	1 (2%)	
Tooth	(2)	
Abscess	1 (50%)	
CARDIOVASCULAR SYSTEM		
Heart	(50)	(48)
Coronary artery, inflammation, chronic	2 (4%)	
Coronary artery, mineralization	1 (2%)	
Valve, degeneration		2 (4%)
Valve, degeneration, mucoid	7 (14%)	8 (17%)
Valve, mineralization		1 (2%)
ENDOCRINE SYSTEM		
Adrenal gland	(47)	(47)
Capsule, inflammation, necrotizing	1 (2%)	
Subcapsular, hyperplasia	23 (49%)	27 (57%)

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

	Chamber Control	15,000 ppm
ENDOCRINE SYSTEM (Continued)		
Adrenal gland, cortex	(46)	(46)
Degeneration, focal		1 (2%)
Hematopoietic cell proliferation		1 (2%)
Hyperplasia, focal	1 (2%)	2 (4%)
Hypertrophy, focal		1 (2%)
Adrenal gland, medulla	(47)	(47)
Cyst		1 (2%)
Islets, pancreatic	(49)	(48)
Atrophy		1 (2%)
Pituitary gland	(47)	(44)
Pars distalis, hyperplasia	1 (2%)	
Thyroid gland	(49)	(48)
Cyst	1 (2%)	
GENERAL BODY SYSTEM		
Tissue, NOS	(1)	(3)
Hemorrhage, focal	1 (100%)	
GENITAL SYSTEM		
Epididymis	(46)	(39)
Inflammation, necrotizing	1 (2%)	
Penis	(3)	(8)
Inflammation, suppurative	1 (33%)	2 (25%)
Necrosis	2 (67%)	6 (75%)
Endothelium, hyperplasia, pseudoepitheliomatous		1 (13%)
Preputial gland	(19)	(24)
Abscess	3 (16%)	1 (4%)
Cyst	6 (32%)	11 (46%)
Hyperplasia		2 (8%)
Inflammation, chronic	1 (5%)	4 (17%)
Inflammation, necrotizing		3 (13%)
Inflammation, suppurative		5 (21%)
Prostate	(49)	(43)
Inflammation, chronic	1 (2%)	2 (5%)
Inflammation, suppurative	1 (2%)	2 (5%)
Seminal vesicle	(46)	(41)
Dilatation	3 (7%)	10 (24%)
Inflammation, chronic		2 (5%)
Inflammation, necrotizing	1 (2%)	
Inflammation, suppurative	1 (2%)	1 (2%)
Testes	(48)	(47)
Atrophy	4 (8%)	9 (19%)
Inflammation, suppurative		1 (2%)
Vein, angiectasis	1 (2%)	
HEMATOPOIETIC SYSTEM		
Lymph node	(38)	(40)
Hyperplasia		1 (3%)
Infiltration cellular, histiocytic	1 (3%)	
Mediastinal, sinus, infiltration cellular		1 (3%)
Mesenteric, infiltration cellular, histiocytic		1 (3%)
Renal, inflammation, acute		1 (3%)
Lymph node, bronchial	(29)	(30)
Infiltration cellular, histiocytic	1 (3%)	2 (7%)
Lymph node, mandibular	(19)	(22)
Ectasia	1 (5%)	
Erythrophagocytosis		1 (5%)
Hyperplasia, lymphoid		1 (5%)
Infiltration cellular, histiocytic	4 (21%)	3 (14%)

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

	Chamber Control	15,000 ppm
HEMATOPOIETIC SYSTEM (Continued)		
Spleen	(49)	(48)
Atrophy	1 (2%)	1 (2%)
Congestion, acute		1 (2%)
Fibrosis	1 (2%)	
Hematopoietic cell proliferation	6 (12%)	9 (19%)
Hemorrhage	1 (2%)	
Hemorrhage, chronic	1 (2%)	
Hyperplasia, lymphoid	2 (4%)	
Thymus	(33)	(33)
Cyst		1 (3%)
Necrosis, multiple	1 (3%)	
INTEGUMENTARY SYSTEM		
Mammary gland	(18)	(16)
Inflammation, chronic	1 (6%)	
Duct, ectasia	1 (6%)	
Skin	(50)	(49)
Hyperplasia, lymphoid		1 (2%)
Hair follicle, atrophy	11 (22%)	6 (12%)
Hair follicle, degeneration	1 (2%)	
Hair follicle, ectasia	1 (2%)	
Prepuce, abscess	3 (6%)	
Prepuce, cyst		1 (2%)
Prepuce, hyperkeratosis		1 (2%)
Prepuce, inflammation, chronic		3 (6%)
Prepuce, inflammation, necrotizing	1 (2%)	2 (4%)
Prepuce, inflammation, suppurative	1 (2%)	4 (8%)
Prepuce, ulcer	10 (20%)	18 (37%)
Subcutaneous tissue, hyperplasia, lymphoid	1 (2%)	1 (2%)
Subcutaneous tissue, infiltration cellular, histiocytic	1 (2%)	
Subcutaneous tissue, inflammation, acute		1 (2%)
Subcutaneous tissue, inflammation, chronic	1 (2%)	1 (2%)
Subcutaneous tissue, inflammation, suppurative	1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM		
Skeletal muscle	(2)	
Inflammation, necrotizing	1 (50%)	
NERVOUS SYSTEM		
Brain	(50)	(48)
Infiltration cellular, lymphocytic, focal	1 (2%)	
Inflammation, suppurative		1 (2%)
Thalamus, mineralization	19 (38%)	17 (35%)
RESPIRATORY SYSTEM		
Larynx	(50)	(48)
Dilatation	1 (2%)	
Submucosa, cyst		1 (2%)
Submucosa, inflammation, chronic	1 (2%)	

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

	Chamber Control	15,000 ppm
RESPIRATORY SYSTEM (Continued)		
Lung	(50)	(48)
Bronchiectasis	1 (2%)	
Hemorrhage	1 (2%)	1 (2%)
Hyperplasia, lymphoid	1 (2%)	
Inflammation, acute	1 (2%)	1 (2%)
Inflammation, chronic, multifocal	9 (18%)	2 (4%)
Inflammation, chronic active	1 (2%)	
Alveolar epithelium, hyperplasia, focal		1 (2%)
Alveolus, adenomatosis, focal	1 (2%)	
Alveolus, infiltration cellular, histiocytic	1 (2%)	
Bronchiole, hyperplasia, multifocal		1 (2%)
Glands, ectasia	3 (6%)	4 (8%)
Interstitium, inflammation, chronic		1 (2%)
Submucosa, bronchus, glands, ectasia		1 (2%)
Nose	(50)	(49)
Glands, cyst	2 (4%)	1 (2%)
Glands, hyperplasia	1 (2%)	
Nasolacrimal duct, inflammation, suppurative	1 (2%)	
Olfactory epithelium, hyperplasia		1 (2%)
Septum, developmental malformation		1 (2%)
Submucosa, inflammation, chronic		3 (6%)
Trachea	(50)	(47)
Glands, dilatation		4 (9%)
SPECIAL SENSES SYSTEM		
Eye	(2)	(2)
Cornea, inflammation, subacute	1 (50%)	
Cornea, necrosis, focal	1 (50%)	
URINARY SYSTEM		
Kidney	(50)	(49)
Cyst	1 (2%)	
Hydronephrosis		1 (2%)
Infarct		2 (4%)
Inflammation, chronic	1 (2%)	2 (4%)
Inflammation, suppurative	2 (4%)	8 (16%)
Necrosis		3 (6%)
Nephropathy	27 (54%)	21 (43%)
Capsule, inflammation, necrotizing	1 (2%)	
Pelvis, inflammation, suppurative	2 (4%)	1 (2%)
Renal tubule, karyomegaly		40 (82%)
Renal tubule, mineralization		1 (2%)
Ureter	(1)	(1)
Mucosa, inflammation, chronic		1 (100%)
Urinary bladder	(47)	(47)
Inflammation, acute	1 (2%)	2 (4%)
Inflammation, chronic	2 (4%)	3 (6%)
Inflammation, necrotizing		1 (2%)
Inflammation, suppurative	2 (4%)	2 (4%)
Lumen, concretion		1 (2%)
Transitional epithelium, hyperplasia	1 (2%)	2 (4%)
Transitional epithelium, necrosis		6 (13%)

APPENDIX D

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

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

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	49	50
ALIMENTARY SYSTEM		
Gallbladder	(39)	(32)
Carcinoma, metastatic		1 (3%)
Carcinoma, metastatic, uterus		1 (3%)
Lymphoma malignant histiocytic		1 (3%)
Lymphoma malignant lymphocytic		1 (3%)
Lymphoma malignant mixed	1 (3%)	1 (3%)
Lymphoma malignant undifferentiated cell type	1 (3%)	
Intestine large, cecum	(41)	(41)
Lymphoma malignant mixed		2 (5%)
Intestine large, colon	(47)	(44)
Carcinoma, metastatic, uterus		2 (5%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Intestine large, rectum	(46)	(44)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Intestine small	(45)	(42)
Carcinoma, metastatic, uterus		1 (2%)
Intestine small, duodenum	(44)	(41)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Intestine small, ileum	(44)	(41)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)
Lymphoma malignant mixed		1 (2%)
Intestine small, jejunum	(44)	(40)
Lymphoma malignant histiocytic		1 (3%)
Lymphoma malignant lymphocytic		1 (3%)
Lymphoma malignant mixed		1 (3%)
Liver	(49)	(48)
Carcinoma, metastatic, uterus		1 (2%)
Hepatocellular carcinoma	3 (6%)	5 (10%)
Hepatocellular carcinoma, multiple		2 (4%)
Hepatocellular adenoma		1 (2%)
Leukemia granulocytic		1 (2%)
Lymphoma malignant histiocytic		2 (4%)
Lymphoma malignant lymphocytic	2 (4%)	1 (2%)
Lymphoma malignant mixed	1 (2%)	3 (6%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Mesentery	*(49)	*(50)
Carcinoma, metastatic, uncertain primary site		1 (2%)
Carcinoma, metastatic, uterus		5 (10%)
Carcinoma, metastatic, multiple, uterus		2 (4%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Pancreas	(48)	(49)
Carcinoma, metastatic, uterus		7 (14%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)
Lymphoma malignant mixed	1 (2%)	2 (4%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Salivary glands	(48)	(47)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		3 (6%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)

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

	Chamber Control	15,000 ppm
ALIMENTARY SYSTEM (Continued)		
Stomach	(48)	(48)
Carcinoma, metastatic, uterus		1 (2%)
Stomach, forestomach	(48)	(48)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Papilloma squamous		2 (4%)
Stomach, glandular	(49)	(47)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
CARDIOVASCULAR SYSTEM		
Heart	(49)	(50)
Carcinoma, metastatic, uterus		3 (6%)
Carcinoma, metastatic, multiple, uterus		1 (2%)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
ENDOCRINE SYSTEM		
Adrenal gland	(49)	(48)
Carcinoma, metastatic, uterus		1 (2%)
Lymphoma malignant mixed		1 (2%)
Capsule, carcinoma, metastatic, uterus		4 (8%)
Capsule, lymphoma malignant histiocytic		1 (2%)
Capsule, lymphoma malignant mixed	1 (2%)	1 (2%)
Capsule, lymphoma malignant undifferentiated cell type		1 (2%)
Subcapsular, lymphoma malignant		1 (2%)
Adrenal gland, cortex	(49)	(48)
Carcinoma, metastatic, uterus		3 (6%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type		1 (2%)
Adrenal gland, medulla	(49)	(47)
Carcinoma, metastatic, uterus		1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)
Lymphoma malignant mixed		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Pheochromocytoma, NOS	1 (2%)	2 (4%)
Islets, pancreatic	(48)	(49)
Lymphoma malignant mixed		1 (2%)
Pituitary gland	(49)	(45)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Pars distalis, adenoma	11 (22%)	1 (2%)
Thyroid gland	(48)	(48)
Lymphoma malignant mixed		1 (2%)
Follicular cell, adenoma		2 (4%)
GENERAL BODY SYSTEM		
Tissue, NOS	*(49)	*(50)
Adenoacanthoma, metastatic, mammary gland	1 (2%)	
Carcinoma, metastatic, uterus		2 (4%)
Lymphoma malignant mixed	1 (2%)	1 (2%)

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

	Chamber Control	15,000 ppm
GENITAL SYSTEM		
Ovary	(49)	(48)
Adenocarcinoma		1 (2%)
Carcinoma, metastatic, uterus		21 (44%)
Carcinoma, metastatic, multiple, uterus		1 (2%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)
Lymphoma malignant mixed	1 (2%)	2 (4%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Bilateral, lymphoma malignant mixed		1 (2%)
Uterus	(49)	(50)
Carcinoma	1 (2%)	42 (84%)
Carcinoma, multiple		1 (2%)
Fibrosarcoma		1 (2%)
Lymphoma malignant histiocytic		2 (4%)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		3 (6%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Cervix, polyp	1 (2%)	
Endometrium, polyp stromal	1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM		
Bone marrow	(49)	(50)
Leukemia granulocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Lymph node	(46)	(45)
Carcinoma, metastatic, uterus		1 (2%)
Iliac, lymphoma malignant mixed		1 (2%)
Mediastinal, lymphoma malignant mixed	1 (2%)	1 (2%)
Mediastinal, lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Mesenteric, carcinoma, metastatic, uterus		1 (2%)
Mesenteric, lymphoma malignant histiocytic		1 (2%)
Mesenteric, lymphoma malignant lymphocytic		2 (4%)
Mesenteric, lymphoma malignant		1 (2%)
Mesenteric, lymphoma malignant mixed	1 (2%)	2 (4%)
Mesenteric, lymphoma malignant undifferentiated cell type		2 (4%)
Renal, carcinoma, metastatic, uterus		2 (4%)
Renal, lymphoma malignant lymphocytic		1 (2%)
Renal, lymphoma malignant mixed	1 (2%)	2 (4%)
Renal, lymphoma malignant undifferentiated cell type		2 (4%)
Lymph node, bronchial	(37)	(38)
Adenoacanthoma, metastatic, mammary gland	1 (3%)	
Carcinoma, metastatic, uterus		13 (34%)
Carcinoma, metastatic, multiple, uterus		1 (3%)
Lymphoma malignant histiocytic		1 (3%)
Lymphoma malignant lymphocytic	1 (3%)	1 (3%)
Lymphoma malignant	1 (3%)	
Lymphoma malignant mixed	1 (3%)	3 (8%)
Lymphoma malignant undifferentiated cell type	1 (3%)	2 (5%)
Lymph node, mandibular	(41)	(26)
Lymphoma malignant histiocytic		1 (4%)
Lymphoma malignant lymphocytic	1 (2%)	2 (8%)
Lymphoma malignant mixed		3 (12%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (4%)

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

	Chamber Control	15,000 ppm
HEMATOPOIETIC SYSTEM (Continued)		
Spleen	(49)	(49)
Carcinoma, metastatic, uterus		5 (10%)
Leukemia granulocytic		1 (2%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	2 (4%)
Lymphoma malignant		1 (2%)
Lymphoma malignant mixed	1 (2%)	3 (6%)
Lymphoma malignant undifferentiated cell type	1 (2%)	2 (4%)
Thymus	(39)	(25)
Lymphoma malignant lymphocytic		1 (4%)
Lymphoma malignant mixed		1 (4%)
Lymphoma malignant undifferentiated cell type	1 (3%)	
INTEGUMENTARY SYSTEM		
Mammary gland	(42)	(38)
Adenoacanthoma	1 (2%)	1 (3%)
Adenocarcinoma	2 (5%)	
Lymphoma malignant lymphocytic		1 (3%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Skin	(48)	(50)
Lymphoma malignant mixed		1 (2%)
Sarcoma	1 (2%)	
Subcutaneous tissue, hemangiosarcoma	1 (2%)	
Subcutaneous tissue, lymphoma malignant histiocytic		1 (2%)
Subcutaneous tissue, lymphoma malignant lymphocytic	1 (2%)	
Subcutaneous tissue, lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM		
Bone	(49)	(50)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
Cranium, osteosarcoma	1 (2%)	
Skeletal muscle	*(49)	*(50)
Adenoacanthoma, metastatic, mammary gland	1 (2%)	
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		1 (2%)
NERVOUS SYSTEM		
Brain	(49)	(50)
Meninges, lymphoma malignant mixed		1 (2%)
RESPIRATORY SYSTEM		
Larynx	(46)	(49)
Lymphoma malignant mixed		2 (4%)
Lung	(49)	(50)
Adenoacanthoma, metastatic, multiple, mammary gland	1 (2%)	
Alveolar/bronchiolar adenoma	1 (2%)	2 (4%)
Alveolar/bronchiolar adenoma, multiple	1 (2%)	
Alveolar/bronchiolar carcinoma	2 (4%)	2 (4%)
Alveolar/bronchiolar carcinoma, multiple	1 (2%)	
Carcinoma, metastatic, uterus		12 (24%)
Carcinoma, metastatic, multiple, uncertain primary site		1 (2%)

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

	Chamber Control	15,000 ppm
RESPIRATORY SYSTEM		
Lung (Continued)	(49)	(50)
Carcinoma, metastatic, multiple, uterus		11 (22%)
Leukemia granulocytic		1 (2%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic	2 (4%)	1 (2%)
Lymphoma malignant mixed	1 (2%)	3 (6%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Nose	(49)	(50)
Lymphoma malignant mixed		2 (4%)
Mucosa, adenocarcinoma		1 (2%)
Trachea	(46)	(49)
Lymphoma malignant mixed		2 (4%)
SPECIAL SENSES SYSTEM		
Ear	*(49)	*(50)
Squamous cell carcinoma	1 (2%)	
Pinna, fibrosarcoma	1 (2%)	
Harderian gland	*(49)	*(50)
Adenocarcinoma		2 (4%)
Adenoma	2 (4%)	
URINARY SYSTEM		
Kidney	(49)	(47)
Carcinoma, metastatic, uterus		8 (17%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)
Lymphoma malignant mixed	1 (2%)	2 (4%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)
Ureter	*(49)	*(50)
Carcinoma, metastatic, uterus		1 (2%)
Urinary bladder	(46)	(43)
Carcinoma, metastatic, uterus		7 (16%)
Lymphoma malignant histiocytic		1 (2%)
Lymphoma malignant lymphocytic		1 (2%)
Lymphoma malignant mixed		2 (5%)
Lymphoma malignant undifferentiated cell type	1 (2%)	
SYSTEMIC LESIONS		
Multiple organs	*(49)	*(50)
Hemangiosarcoma	1 (2%)	
Lymphoma malignant mixed	1 (2%)	3 (6%)
Lymphoma malignant undifferentiated cell	1 (2%)	2 (4%)
Lymphoma malignant lymphocytic	2 (4%)	2 (4%)
Lymphoma malignant	1 (2%)	1 (2%)
Leukemia granulocytic		1 (2%)
Lymphoma malignant histiocytic		2 (4%)
ANIMAL DISPOSITION SUMMARY		
Animals initially in study	50	50
Terminal sacrifice	32	2
Moribund sacrifice	9	30
Natural death	6	18
Accidently killed	2	
Missing	1	

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

	Chamber Control	15,000 ppm
TUMOR SUMMARY		
Total animals with primary neoplasms **	28	47
Total primary neoplasms	38	80
Total animals with benign neoplasms	15	9
Total benign neoplasms	17	9
Total animals with malignant neoplasms	18	47
Total malignant neoplasms	20	69
Total animals with secondary neoplasms ***	1	35
Total secondary neoplasms	4	122
Total animals with malignant neoplasms--uncertain primary site		1
Total animal with neoplasms--uncertain benign or malignant	1	2
Total uncertain neoplasms	1	2

* Number of animals receiving complete necropsy examinations; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** 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 CHLOROETHANE: CHAMBER CONTROL

WEEKS ON STUDY	00 08	00 11	00 24	00 47	00 72	00 84	00 86	00 93	00 94	00 94	00 95	00 95	00 96	00 96	00 98	00 99	00 99	00 99	01 00	01 01	01 01	01 01	01 01	01 01	01 01	01 01
CARCASS ID	09 31	05 51	07 81	07 31	07 51	09 01	08 51	08 41	07 61	10 01	08 91	06 21	09 91	08 01	08 31	09 21	05 31	05 71	05 11	05 21	05 41	05 61	05 81	05 91	05 91	06 01
ALIMENTARY SYSTEM																										
Esophagus		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Gallbladder		+	A	+	+	A	+	A	M	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																	X									
Lymphoma malignant undifferentiated cell type											X															
Intestine large		+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum		+	+	+	+	+	+	A	+	M	+	M	+	+	+	+	+	+	M	M	M	+	M	M	+	+
Intestine large, colon		+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum		M	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small		+	M	+	+	+	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum		+	M	+	+	+	+	A	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum		M	M	+	+	+	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic											X															
Intestine small, jejunum		M	M	+	+	+	+	A	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+
Liver		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																										
Lymphoma malignant lymphocytic											X															
Lymphoma malignant mixed																	X									
Lymphoma malignant undifferentiated cell type												X														
Pancreas		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic											X															
Lymphoma malignant mixed																	X									
Lymphoma malignant undifferentiated cell type												X														
Salivary glands		+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type												X														
Stomach		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Stomach, forestomach		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type												X														
Stomach, glandular		+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type												X														
Tooth																										
CARDIOVASCULAR SYSTEM																										
Heart		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																										
Adrenal gland		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, lymphoma malignant mixed																	X									
Adrenal gland, cortex		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic											X															
Adrenal gland, medulla		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic											X															
Lymphoma malignant undifferentiated cell type												X														
Pheochromocytoma, NOS																										
Islets, pancreatic		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland		+	M	M	+	+	M	M	M	M	M	M	+	M	M	M	M	M	+	+	–	+	+	+	+	M
Pituitary gland		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Pars distalis, adenoma								X											X	X						X
Thyroid gland		+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
GENERAL BODY SYSTEM																										
Tissue, NOS		+															+									
Adenoacanthoma, metastatic, mammary gland		X																								
Lymphoma malignant mixed																	X									
GENITAL SYSTEM																										
Clitoral gland															–											
Ovary		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic											X															
Lymphoma malignant mixed																	X									
Lymphoma malignant undifferentiated cell type												X														
Uterus		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma					X																					
Lymphoma malignant undifferentiated cell type												X														
Cervix, polyp																X										
Endometrium, polyp stromal													X													
HEMATOPOIETIC SYSTEM																										
Blood		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type												X														
Lymph node		+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, lymphoma malignant mixed																	X									
Mediastinal, lymphoma malignant undifferentiated cell type												X														
Mesenteric, lymphoma malignant mixed																	X									
Renal, lymphoma malignant mixed																	X									

+: Tissue examined microscopically
: Not examined
–: Present but not examined microscopically
I: Insufficient tissue

M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

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

WEEKS ON STUDY	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	TOTAL:
CARCASS ID	06111	06311	06411	06511	06611	06711	06811	06911	07011	07111	07211	07411	07711	07911	08111	08211	08611	08711	08811	09111	09411	09511	09611	09711	09811	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	M	+	M	+	+	+	+	M	+	+	39
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant lymphocytic																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma												X		X	X											3
Lymphoma malignant lymphocytic																	X									2
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Pancreas	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant undifferentiated cell type																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	.	+	+	+	+	+	+	+	48
Stomach, forestomach	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant undifferentiated cell type																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1
Tooth									+																	1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Capsule, lymphoma malignant mixed																										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Lymphoma malignant undifferentiated cell type																										1
Pheochromocytoma, NOS												X														1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	48
Parathyroid gland	M	+	M	M	+	+	+	M	+	+	+	+	+	+	+	+	+	M	M	M	+	+	+	+	M	27
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma									X			X							X		X	X	X		X	11
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
GENERAL BODY SYSTEM																										
Tissue, NOS																										2
Adenoacanthoma, metastatic, mammary gland																										1
Lymphoma malignant mixed																										1
GENITAL SYSTEM																										
Clitoral gland																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma																										1
Lymphoma malignant undifferentiated cell type																										1
Cervix, polyp																										1
Endometrium, polyp stromal																										1
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1
Lymph node	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Mediastinal, lymphoma malignant mixed																										1
Mediastinal, lymphoma malignant undifferentiated cell type																										1
Mesenteric, lymphoma malignant mixed																										1
Renal, lymphoma malignant mixed																										1

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

WEEKS ON STUDY	008	019	024	047	072	084	086	093	094	094	095	095	096	096	098	099	099	100	101	101	101	101	101	101	101
CARCASS ID	0931	0551	0781	0731	0751	0901	0851	0841	0761	1001	0891	0621	0991	0801	0831	0921	0531	0557	0511	0521	0541	0561	0581	0591	0601
HEMATOPOIETIC SYSTEM (Continued)																									
Lymph node, bronchial		+	M	+	+	+	+	+	M	I	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Adenoacanthoma, metastatic, mammary gland		X																							
Lymphoma malignant lymphocytic											X														
Lymphoma malignant																									
Lymphoma malignant mixed																	X								
Lymphoma malignant undifferentiated cell type												X													
Lymph node, mandibular		+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+
Lymphoma malignant lymphocytic											X														
Lymphoma malignant undifferentiated cell type												X													
Spleen		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																	X								
Lymphoma malignant undifferentiated cell type												X													
Thymus		M	M	+	+	+	M	+	M	M	M	+	M	+	+	+	+	M	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type												X													
INTEGUMENTARY SYSTEM																									
Mammary gland		+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	M
Adenoacanthoma		X																							
Adenocarcinoma																									
Lymphoma malignant undifferentiated cell type												X													
Skin		+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma																		X							
Subcutaneous tissue, hemangiosarcoma																				X					
Subcutaneous tissue, lymphoma malignant lymphocytic											X														
Subcutaneous tissue, lymphoma malignant undifferentiated cell type												X													
MUSCULOSKELETAL SYSTEM																									
Bone		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type												X													
Cranium, osteosarcoma										X															
Skeletal muscle		+				+																			
Adenoacanthoma, metastatic, mammary gland		X																							
NERVOUS SYSTEM																									
Brain		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
Larynx		+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
Lung		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
Adenoacanthoma, metastatic, multiple, mammary gland		X																							
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar adenoma, multiple																									
Alveolar/bronchiolar carcinoma																X						X			
Alveolar/bronchiolar carcinoma, multiple																									
Lymphoma malignant lymphocytic											X														
Lymphoma malignant mixed																	X								
Lymphoma malignant undifferentiated cell type												X													
Nose		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea		+	I	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Ear								+						+								+			
Squamous cell carcinoma								X																	
Pinna, fibrosarcoma														X											
Eye																									
Harderian gland																									+
Adenoma																									X
URINARY SYSTEM																									
Kidney		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic											X														
Lymphoma malignant mixed																	X								
Lymphoma malignant undifferentiated cell type												X													
Urinary bladder		+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type												X													

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

WEEKS ON STUDY	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	101	TOTAL:
CARCASS ID	06611	06631	06641	06651	06661	06671	06681	06691	07011	07111	07211	07411	07711	07911	08111	08211	08611	08711	08811	09111	09411	09511	09611	09711	09811	TISSUES TUMORS
HEMATOPOIETIC SYSTEM (Cont'd)																										
Lymph node, bronchial	+	+	+	M	M	M	M	+	M	+	M	+	+	+	+	+	+	+	+	M	+	M	+	+	+	37
Adenoacanthoma, metastatic, mammary gland																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant																	X									1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Lymph node, mandibular	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	M	+	M	+	+	+	+	41
Lymphoma malignant lymphocytic																										1
Lymphoma malignant undifferentiated cell type																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																	X									1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	39
Lymphoma malignant undifferentiated cell type																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Adenoacanthoma																										1
Adenocarcinoma		X												X												2
Lymphoma malignant undifferentiated cell type																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Sarcoma																										1
Subcutaneous tissue, hemangiosarcoma																										1
Subcutaneous tissue, lymphoma malignant lymphocytic																										1
Subcutaneous tissue, lymphoma malignant undifferentiated cell type																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1
Cranium, osteosarcoma																										1
Skeletal muscle																										2
Adenoacanthoma, metastatic, mammary gland																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	I	+	+	+	46
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoacanthoma, metastatic, multiple, mammary gland																										1
Alveolar/bronchiolar adenoma					X																					1
Alveolar/bronchiolar adenoma, multiple																									X	1
Alveolar/bronchiolar carcinoma																										2
Alveolar/bronchiolar carcinoma, multiple																					X					1
Lymphoma malignant lymphocytic																	X									2
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	46
SPECIAL SENSES SYSTEM																										
Ear																										3
Squamous cell carcinoma																										1
Pinna, fibrosarcoma																										1
Eye										+																1
Harderian gland		+																								2
Adenoma		X																								2
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	46
Lymphoma malignant undifferentiated cell type																										1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE: 15,000 ppm

WEEKS ON STUDY	047	067	070	073	077	077	079	079	082	082	082	082	083	084	084	085	085	086	087	088	088	088	089	089
CARCASS ID	19601	19801	17201	16001	18101	19201	16801	15501	17901	19101	17101	18201	18801	19901	19701	16201	17601	19001	20001	18501	15701	18401	17301	19301	19401
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	M	+	A	+	+	M	+	A	+	+	+	+	A	+	+	+	+	+	+	M	M
Carcinoma, metastatic, uterus																									
Carcinoma, metastatic																									
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Intestine large	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine large, cecum	+	M	+	+	A	M	+	+	+	+	+	A	+	+	+	+	M	+	+	A	+	+	+	+	+
Lymphoma malignant mixed																									
Intestine large, colon	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uterus																									
Lymphoma malignant histiocytic																						X			
Lymphoma malignant mixed																									
Intestine large, rectum	+	+	+	+	A	+	+	+	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																						X			
Lymphoma malignant mixed																									
Intestine small	+	+	+	+	A	+	+	+	A	+	+	A	+	+	+	+	A	+	+	A	+	+	+	+	+
Carcinoma, metastatic, uterus																									
Intestine small, duodenum	+	+	+	+	A	+	+	+	A	+	+	A	+	+	+	+	A	+	+	A	M	+	+	+	+
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Intestine small, ileum	+	+	+	+	A	+	+	+	A	+	+	A	+	+	+	+	A	+	+	A	+	+	+	+	+
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Intestine small, jejunum	+	+	+	+	A	+	+	+	A	+	+	A	+	+	+	+	A	+	+	A	+	+	+	+	+
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uterus				X																					
Hepatocellular carcinoma																									
Hepatocellular carcinoma, multiple																									X
Hepatocellular adenoma																	X								
Leukemia granulocytic																									
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type									X																
Mesentery										+										+		+			
Carcinoma, metastatic, uterus																									
Carcinoma, metastatic, uncertain primary site																									
Carcinoma, metastatic, uterus										X															
Carcinoma, metastatic, multiple, uterus																									
Lymphoma malignant histiocytic																						X			
Lymphoma malignant mixed																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uterus				X								X					X			X					
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type									X																
Salivary glands	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type									X																
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uterus				X																					
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Papilloma squamous																		X							
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uterus												X								X					
Carcinoma, metastatic, multiple, uterus																									
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uterus										X															
Lymphoma malignant mixed																									
Capsule, carcinoma, metastatic, uterus				X																					
Capsule, lymphoma malignant histiocytic																						X			
Capsule, lymphoma malignant mixed						X																			
Capsule, lymphoma malignant undifferentiated cell type																X									
Subcapsular, lymphoma malignant															X										

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 15,000 ppm (Continued)

WEEKS ON STUDY	090	090	090	091	091	092	092	092	093	093	094	094	094	094	094	095	096	096	096	096	098	099	099	100	100	TOTAL: TISSUES TUMORS
CARCASS ID	15611	17511	17811	16911	19511	16511	16111	16711	15411	16611	18611	17711	15811	17411	17011	18311	15911	16411	18011	18911	15111	15311	16311	15211	18711	
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	I	A	M	+	A	M	A	+	+	+	M	+	+	A	M	+	A	+	+	A	+	+	+	+	+	32
Carcinoma, metastatic, uterus																						X				1
Carcinoma, metastatic																		X								1
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Intestine large	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, cecum	+	M	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	41
Lymphoma malignant mixed									X						X											2
Intestine large, colon	+	+	+	+	M	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	44
Carcinoma, metastatic, uterus							X										X									2
Lymphoma malignant histiocytic																										1
Lymphoma malignant mixed									X																	1
Intestine large, rectum	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant histiocytic																										1
Lymphoma malignant mixed									X																	1
Intestine small	+	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Carcinoma, metastatic, uterus														X												1
Intestine small, duodenum	+	+	+	+	M	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
Intestine small, ileum	+	+	+	+	A	A	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	41
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
Intestine small, jejunum	+	+	+	+	A	A	A	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	40
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
Liver	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, uterus																										1
Hepatocellular carcinoma	X			X							X				X						X					5
Hepatocellular carcinoma, multiple																			X							2
Hepatocellular adenoma																										1
Leukemia granulocytic	X																									1
Lymphoma malignant histiocytic										X																2
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											3
Lymphoma malignant undifferentiated cell type																										1
Mesentery		+	+	+	+			+	+	+			+			+										12
Carcinoma, metastatic, uterus													X													1
Carcinoma, metastatic, uncertain primary site										X																1
Carcinoma, metastatic, uterus		X	X													X										4
Carcinoma, metastatic, muitiple, uterus				X				X																		2
Lymphoma malignant histiocytic																										1
Lymphoma malignant mixed									X																	1
Pancreas	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, uterus		X			X																		X			7
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											2
Lymphoma malignant undifferentiated cell type																										1
Salivary glands	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											3
Lymphoma malignant undifferentiated cell type																										1
Stomach	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, uterus																										1
Stomach, forestomach	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
Papilloma squamous			X																							2
Stomach, glandular	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	47
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, uterus																			X							3
Carcinoma, metastatic, multiple, uterus																					X					1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, uterus																										1
Lymphoma malignant mixed															X											1
Capsule, carcinoma, metastatic, uterus				X										X									X			4
Capsule, lymphoma malignant histiocytic																										1
Capsule, lymphoma malignant mixed																										1
Capsule, lymphoma malignant undifferentiated cell type																										1
Subcapsular, lymphoma malignant																										1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 15,000 ppm (Continued)

WEEKS ON STUDY	0467	0677	0703	0773	0779	0799	0799	0800	0822	0822	0822	0823	0834	0844	0855	0855	0866	0877	0888	0888	0888	0899	0899
CARCASS ID	19661	19681	17201	16001	18111	19211	16811	15511	17911	19111	17111	18121	18821	19911	19771	16221	17611	19011	20011	18511	15711	18411	17311	19311	19411
ENDOCRINE SYSTEM (Continued)																									
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
Carcinoma, metastatic, uterus																									
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant undifferentiated cell type									X																
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uterus																									
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type									X																
Pheochromocytoma, NOS													X	X											
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Parathyroid gland	+	M	+	M	M	M	M	M	M	+	+	M	+	M	M	+	M	M	M	M	+	+	M	M	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	-	+	+	+	M	+
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Pars distalis, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Follicular cell, adenoma																								X	
GENERAL BODY SYSTEM																									
Tissue, NOS					+																				
Carcinoma, metastatic, uterus																									
Lymphoma malignant mixed																									
GENITAL SYSTEM																									
Ovary	+	+	+	+	M	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Carcinoma, metastatic, uterus				X					X			X				X		X	X				X		
Carcinoma, metastatic, multiple, uterus										X															
Lymphoma malignant histiocytic																							X		
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type										X															
Bilateral, lymphoma malignant mixed						X																			
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma		X		X		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X
Carcinoma, multiple																									
Fibrosarcoma						X																			
Lymphoma malignant histiocytic																							X		
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type									X																
Endometrium, polyp stromal																									
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia granulocytic																									
Lymphoma malignant mixed																									
Lymph node	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	
Carcinoma, metastatic, uterus																									
Iliac, lymphoma malignant mixed						X																			
Mediastinal, lymphoma malignant mixed						X																			
Mediastinal, lymphoma malignant undifferentiated cell type									X																
Mesenteric, carcinoma, metastatic, uterus										X															
Mesenteric, lymphoma malignant histiocytic																							X		
Mesenteric, lymphoma malignant lymphocytic			X																						
Mesenteric, lymphoma malignant														X											
Mesenteric, lymphoma malignant mixed						X																			
Mesenteric, lymphoma malignant undifferentiated cell type									X						X										
Renal, carcinoma, metastatic, uterus												X				X									
Renal, lymphoma malignant lymphocytic			X																						
Renal, lymphoma malignant mixed						X																			
Renal, lymphoma malignant undifferentiated cell type									X						X										
Lymph node, bronchial	+	+	+	+	M	+	M	+	+	+	I	+	+	+	M	+	M	+	M	+	M	+	M	+	M
Carcinoma, metastatic, uterus				X							X							X		X					
Carcinoma, metastatic, multiple, uterus																									
Lymphoma malignant histiocytic																							X		
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type									X						X										
Lymph node, mandibular	M	M	+	+	M	+	M	+	+	+	M	+	+	M	M	M	M	M	M	M	+	+	M	M	+
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type									X																

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 15,000 ppm
(Continued)

WEEKS ON STUDY	0 9 0	0 9 0	0 9 0	0 9 1	0 9 1	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 5	0 9 6	0 9 6	0 9 6	0 9 6	0 9 8	0 9 9	0 9 9	1 0 0	1 0 0	TOTAL:
CARCASS ID	1 5 6 1	1 7 5 1	1 7 8 1	1 6 9 1	1 9 5 1	1 6 5 1	1 6 1 1	1 6 7 1	1 5 4 1	1 6 6 1	1 8 6 1	1 7 7 1	1 5 8 1	1 7 4 1	1 7 0 1	1 8 3 1	1 5 9 1	1 6 4 1	1 8 0 1	1 8 9 1	1 5 1 1	1 5 5 3 1	1 6 3 1	1 5 2 1	1 8 7 1	TISSUES / TUMORS
ENDOCRINE SYSTEM (Cont'd)																										
Adrenal gland, cortex	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	48
Carcinoma, metastatic, uterus			X															X			X					3
Lymphoma malignant lymphocytic																										1
Lymphoma malignant undifferentiated cell type																										1
Adrenal gland, medulla	+	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	47
Carcinoma, metastatic, uterus																		X								1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Pheochromocytoma, NOS																										2
Islets, pancreatic	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	49
Lymphoma malignant mixed															X											1
Parathyroid gland	M	+	+	M	M	+	M	M	M	M	+	M	M	+	+	M	+	M	M	+	M	M	M	+	+	19
Pituitary gland	+	+	+	+	I	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	45
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
Pars distalis, adenoma												X														1
Thyroid gland	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	48
Lymphoma malignant mixed															X											1
Follicular cell, adenoma																				X						2
GENERAL BODY SYSTEM																										
Tissue, NOS									+													+	+			4
Carcinoma, metastatic, uterus																						X	X			2
Lymphoma malignant mixed									X																	1
GENITAL SYSTEM																										
Ovary	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma			X																							1
Carcinoma, metastatic, uterus		X	X	X		X	X	X					X	X		X		X			X	X	X	X		21
Carcinoma, metastatic, multiple, uterus																										1
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											2
Lymphoma malignant undifferentiated cell type																										1
Bilateral, lymphoma malignant mixed																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	50
Carcinoma	X	X	X		X	X	X	X		X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	42
Carcinoma, multiple				X																						1
Fibrosarcoma																										1
Lymphoma malignant histiocytic										X																2
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											3
Lymphoma malignant undifferentiated cell type																										1
Endometrium, polyp stroma,									X																	1
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	50
Leukemia granulocytic	X																									1
Lymphoma malignant mixed									X																	1
Lymph node	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Carcinoma, metastatic, uterus		X																								1
Iliac, lymphoma malignant mixed																										1
Mediastinal, lymphoma malignant mixed																										1
Mediastinal, lymphoma malignant undifferentiated cell type																										1
Mesenteric, carcinoma, metastatic, uterus																										1
Mesenteric, lymphoma malignant histiocytic																										1
Mesenteric, lymphoma malignant lymphocytic																								X		2
Mesenteric, lymphoma malignant																										1
Mesenteric, lymphoma malignant mixed															X											2
Mesenteric, lymphoma malignant undifferentiated cell type																										2
Renal, carcinoma, metastatic, uterus																										2
Renal, lymphoma malignant lymphocytic																										1
Renal, lymphoma malignant mixed															X											2
Renal, lymphoma malignant undifferentiated cell type																										2
Lymph node, bronchial	+	M	+	+	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Carcinoma, metastatic, uterus			X		X	X							X	X		X		X			X		X			13
Carcinoma, metastatic, multiple, uterus				X																						1
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											3
Lymphoma malignant undifferentiated cell type																										2
Lymph node, mandibular	+	M	M	I	+	+	A	M	+	+	+	+	M	M	+	+	M	+	+	M	+	+	M	+	+	26
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																								X		2
Lymphoma malignant mixed									X						X											3
Lymphoma malignant undifferentiated cell type																										1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 15,000 ppm (Continued)

WEEKS ON STUDY	047	067	070	073	077	077	079	079	080	082	082	082	082	083	084	084	085	085	086	087	088	088	088	089	089
CARCASS ID	19601	19801	17201	16001	18101	19201	16801	15501	17901	19101	17101	18201	18801	19901	19701	16201	17601	19001	20001	18501	15701	18401	17301	19301	19401
HEMATOPOIETIC SYSTEM (Cont'd)																									
Spleen	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+
Carcinoma, metastatic, uterus											X	X													
Leukemia granulocytic																									
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant															X										
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type										X						X									
Thymus	+	I	+	+	+	I	+	+	+	+	+	M	M	M	+	+	+	+	M	+	M	M	+	+	+
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
INTEGUMENTARY SYSTEM																									
Mammary gland	M	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	M	+	+
Adenoacanthoma																									
Lymphoma malignant lymphocytic			X																						
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Subcutaneous tissue, lymphoma malignant histiocytic																						X			
Subcutaneous tissue, lymphoma malignant undifferentiated cell type											X														
MUSCULOSKELETAL SYSTEM																									
Bone	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic			X																						
Skeletal muscle			+																						
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Meninges, lymphoma malignant mixed																									
RESPIRATORY SYSTEM																									
Larynx	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									X
Alveolar/bronchiolar carcinoma				X				X			X	X							X	X				X	
Carcinoma, metastatic, uterus																									
Carcinoma, metastatic, multiple, uterus																									
Carcinoma, metastatic, multiple, uncertain primary site																	X								
Carcinoma, metastatic, multiple, uterus																									
Leukemia granulocytic																						X			
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed						X																			
Lymphoma malignant undifferentiated cell type										X															
Nose	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
Lymphoma malignant mixed																									
Mucosa, adenocarcinoma																									
Trachea	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+
Lymphoma malignant mixed																									
SPECIAL SENSES SYSTEM																									
Eye																									
Harderian gland														+			+								
Adenocarcinoma														X			X								
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
Carcinoma, metastatic, uterus				X							X	X											X		
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type										X															
Ureter					+																				+
Carcinoma, metastatic, uterus																									X
Urinary bladder	+	+	+	+	+	+	+	-	+	+	-	A	+	-	+	+	+	-	+	M	+	+	+	-	+
Carcinoma, metastatic, uterus											X				X				X		X				
Lymphoma malignant histiocytic																						X			
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed																									

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 15,000 ppm (Continued)

WEEKS ON STUDY	0 9 0	0 9 0	0 9 0	0 9 1	0 9 1	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 5	0 9 6	0 9 6	0 9 6	0 9 6	0 9 8	0 9 9	0 9 9	1 0 0	1 0 0	TOTAL:
CARCASS ID	1 5 6 1	1 7 5 1	1 7 8 1	1 6 9 1	1 9 5 1	1 6 5 1	1 6 1 1	1 6 7 1	1 5 4 1	1 6 6 1	1 8 6 1	1 7 7 1	1 5 8 1	1 7 4 1	1 7 0 1	1 8 3 1	1 5 9 1	1 6 4 1	1 8 0 1	1 8 9 1	1 5 1 1	1 5 3 1	1 6 3 1	1 5 2 1	1 8 7 1	TISSUES / TUMORS
HEMATOPOIETIC SYSTEM (Cont'd)																										
Spleen	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, uterus					X													X		X						5
Leukemia granulocytic	X																									1
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																								X		2
Lymphoma malignant																										1
Lymphoma malignant mixed									X						X											3
Lymphoma malignant undifferentiated cell type																										2
Thymus	M	M	I	M	M	M	A	+	M	+	I	+	M	I	+	I	M	M	M	+	M	M	+	+	+	25
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed															X											1
INTEGUMENTARY SYSTEM																										
Mammary gland	M	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	M	M	M	+	M	+	+	+	+	38
Adenoacanthoma																							X			1
Lymphoma malignant lymphocytic																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed									X																	1
Subcutaneous tissue, lymphoma malignant histiocytic																										1
Subcutaneous tissue, lymphoma malignant undifferentiated cell type																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Skeletal muscle									+																	2
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X																	1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	50
Meninges, lymphoma malignant mixed									X																	1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant mixed									X						X											2
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma											X								X							2
Alveolar/bronchiolar carcinoma																								X		2
Carcinoma, metastatic, uterus							X						X	X				X		X						12
Carcinoma, metastatic, multiple, uterus																					X	X	X			3
Carcinoma, metastatic, multiple, uncertain primary site										X																1
Carcinoma, metastatic, multiple, uterus		X	X	X	X			X								X			X							8
Leukemia granulocytic	X																									1
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											3
Lymphoma malignant undifferentiated cell type																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	-	+	+	+	50
Lymphoma malignant mixed									X						X											2
Mucosa, adenocarcinoma								X																		1
Trachea	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	+	49
Lymphoma malignant mixed									X						X											2
SPECIAL SENSES SYSTEM																										
Eye																					+					1
Harderian gland																										2
Adenocarcinoma																										2
URINARY SYSTEM																										
Kidney	+	-	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	47
Carcinoma, metastatic, uterus												X		X		X	X									8
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											2
Lymphoma malignant undifferentiated cell type																										1
Ureter																										2
Carcinoma, metastatic, uterus																										1
Urinary bladder	+	+	+	+	A	A	A	+	+	+	-	+	+	+	+	M	+	+	+	A	+	+	+	+	+	43
Carcinoma, metastatic, uterus			X										X				X									7
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed									X						X											2

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

	Chamber Control	15,000 ppm
Liver: Hepatocellular Carcinoma		
Overall Rates (a)	3/49 (6%)	7/48 (15%)
Adjusted Rates (b)	9.4%	47.7%
Terminal Rates (c)	3/32 (9%)	0/2 (0%)
Day of First Observation	700	622
Life Table Test (d)		P<0.001
Logistic Regression Test (d)		P=0.025
Fisher Exact Test (d)		P=0.150
Liver: Hepatocellular Adenoma or Carcinoma		
Overall Rates (a)	3/49 (6%)	8/48 (17%)
Adjusted Rates (b)	9.4%	49.2%
Terminal Rates (c)	3/32 (9%)	0/2 (0%)
Day of First Observation	700	590
Life Table Test (d)		P<0.001
Logistic Regression Test (d)		P=0.025
Fisher Exact Test (d)		P=0.093
Lung: Alveolar/Bronchiolar Carcinoma		
Overall Rates (a)	3/49 (6%)	2/50 (4%)
Adjusted Rates (b)	8.9%	51.9%
Terminal Rates (c)	2/32 (6%)	1/2 (50%)
Day of First Observation	688	622
Life Table Test (d)		P=0.112
Logistic Regression Test (d)		P=0.479
Fisher Exact Test (d)		P=0.490N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma		
Overall Rates (a)	5/49 (10%)	4/50 (8%)
Adjusted Rates (b)	15.0%	60.7%
Terminal Rates (c)	4/32 (13%)	1/2 (50%)
Day of First Observation	688	622
Life Table Test (d)		P=0.008
Logistic Regression Test (d)		P=0.216
Fisher Exact Test (d)		P=0.487N
Pituitary Gland/Pars Distalis: Adenoma		
Overall Rates (a)	11/49 (22%)	1/45 (2%)
Adjusted Rates (b)	32.9%	7.1%
Terminal Rates (c)	10/32 (31%)	0/2 (0%)
Day of First Observation	657	653
Life Table Test (d)		P=0.707N
Logistic Regression Test (d)		P=0.250N
Fisher Exact Test (d)		P=0.003N
Uterus: Carcinoma		
Overall Rates (a)	(e) 0/49 (0%)	43/50 (86%)
Adjusted Rates (b)	0%	100.0%
Terminal Rates (c)	0/32 (0%)	2/2 (100%)
Day of First Observation		469
Life Table Test (d)		P<0.001
Logistic Regression Test (d)		P<0.001
Fisher Exact Test (d)		P<0.001
Hematopoietic System: Lymphoma		
Overall Rates (a)	4/49 (8%)	10/50 (20%)
Adjusted Rates (b)	10.7%	65.8%
Terminal Rates (c)	1/32 (3%)	1/2 (50%)
Day of First Observation	663	486
Life Table Test (d)		P<0.001
Logistic Regression Test (d)		P=0.086
Fisher Exact Test (d)		P=0.080

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF CHLOROETHANE (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 dosed group incidence are the P values corresponding to pairwise comparisons between the 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 logistic regression test regards these lesions as nonfatal. The Fisher exact test compares directly the overall incidence rates. A lower incidence in the dosed group is indicated by (N).
(e) One chamber control mouse had a uterine carcinoma not of endometrial origin.

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

Study	Incidence of 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	4/335 (1.2%)
SD (b)	2.36%
Range (c)	
High	3/48
Low	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	(d) 5/2,011 (0.2%)
SD (b)	0.68%
Range (c)	
High	1/47
Low	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.
(d) Includes one adenoma, NOS; one squamous cell carcinoma was also observed.

TABLE D4b. HISTORICAL INCIDENCE OF HEPATOCELLULAR TUMORS IN FEMALE 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	1/50	2/50	3/50
Methyl methacrylate	7/50	0/50	7/50
Propylene	0/50	2/50	2/50
1,2-Epoxybutane	2/50	2/50	4/50
Dichloromethane	2/50	1/50	3/50
Ethylene oxide	1/49	5/49	6/49
Tetrachloroethylene	3/48	1/48	4/48
TOTAL	16/347 (4.6%)	13/347 (3.7%)	29/347 (8.4%)
SD (b)	4.59%	3.21%	3.59%
Range (c)			
High	7/50	5/49	7/50
Low	0/50	0/50	2/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	107/2,032 (5.3%)	(d) 81/2,032 (4.0%)	(d) 184/2,032 (9.1%)
SD (b)	4.34%	2.42%	4.70%
Range (c)			
High	9/49	4/48	10/49
Low	0/50	0/50	1/50

(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.
(d) One hepatoblastoma was also observed.

TABLE D4c. HISTORICAL INCIDENCE OF HEMATOPOIETIC SYSTEM TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls	
	Lymphoma	Lymphoma or Leukemia
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories		
Propylene oxide	12/50	12/50
Methyl methacrylate	8/50	8/50
Propylene	16/50	16/50
1,2-Epoxybutane	13/50	13/50
Dichloromethane	7/50	7/50
Ethylene oxide	9/49	9/49
Tetrachloroethylene	8/49	8/49
TOTAL	73/348 (21.0%)	73/348 (21.0%)
SD (b)	6.55%	6.55%
Range (c)		
High	16/50	16/50
Low	7/50	7/50
Overall Historical Incidence for Untreated Controls in NTP Studies		
TOTAL	617/2,040 (30.2%)	636/2,040 (31.2%)
SD (b)	13.32%	12.83%
Range (c)		
High	37/50	38/50
Low	5/50	6/50

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

	Chamber Control	15,000 ppm
Animals initially in study	50	50
Animals removed	50	50
Animals examined histopathologically	49	50
ALIMENTARY SYSTEM		
Esophagus	(49)	(50)
Hyperkeratosis	1 (2%)	
Gallbladder	(39)	(32)
Inflammation, chronic	2 (5%)	
Inflammation, suppurative		1 (3%)
Wall, necrosis		1 (3%)
Intestine large	(48)	(45)
Anus, ulcer	1 (2%)	
Intestine large, cecum	(41)	(41)
Inflammation, acute		1 (2%)
Inflammation, necrotizing		1 (2%)
Intestine large, colon	(47)	(44)
Inflammation, necrotizing		1 (2%)
Intestine small, duodenum	(44)	(40)
Fibrosis		1 (3%)
Intestine small, ileum	(44)	(40)
Atrophy		1 (3%)
Liver	(49)	(48)
Basophilic focus	1 (2%)	
Eosinophilic focus		2 (4%)
Focal cellular change		2 (4%)
Hematopoietic cell proliferation	7 (14%)	3 (6%)
Inclusion body intranuclear		2 (4%)
Infarct		1 (2%)
Inflammation, chronic	1 (2%)	
Necrosis	1 (2%)	7 (15%)
Pancreas	(48)	(49)
Atrophy	2 (4%)	1 (2%)
Fibrosis		2 (4%)
Inflammation, chronic	4 (8%)	2 (4%)
Inflammation, necrotizing		2 (4%)
Karyomegaly		2 (4%)
Salivary glands	(48)	(47)
Inflammation, chronic	12 (25%)	3 (6%)
Stomach, forestomach	(48)	(48)
Acanthosis		1 (2%)
Hemorrhage, acute		1 (2%)
Hyperkeratosis	1 (2%)	9 (19%)
Stomach, glandular	(49)	(47)
Cyst	1 (2%)	
Metaplasia, squamous, focal	1 (2%)	1 (2%)
Necrosis, coagulative		1 (2%)
Ulcer	1 (2%)	
Mucosa, dilatation		1 (2%)
Tooth	(1)	
Peridontal tissue, abscess	1 (100%)	
CARDIOVASCULAR SYSTEM		
Heart	(49)	(50)
Coronary artery, inflammation, chronic	1 (2%)	1 (2%)
Endocardium, thrombus		1 (2%)
Myocardium, fibrosis		2 (4%)
Myocardium, mineralization		1 (2%)
Myocardium, necrosis		1 (2%)
Valve, degeneration, mucoid	7 (14%)	7 (14%)

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

	Chamber Control		15,000 ppm	
ENDOCRINE SYSTEM				
Adrenal gland	(49)		(48)	
Capsule, inflammation, necrotizing	1	(2%)	1	(2%)
Subcapsular, hyperplasia	45	(92%)	45	(94%)
Adrenal gland, cortex	(49)		(48)	
Accessory adrenal cortical nodule			1	(2%)
Atrophy	1	(2%)		
Congestion			1	(2%)
Cyst			1	(2%)
Degeneration	40	(82%)	25	(52%)
Fibrosis	40	(82%)	21	(44%)
Hematopoietic cell proliferation			3	(6%)
Hemorrhage, acute			1	(2%)
Hyperplasia	2	(4%)		
Inflammation, chronic			1	(2%)
Inflammation, suppurative			1	(2%)
Adrenal gland, medulla	(49)		(47)	
Cyst			2	(4%)
Hyperplasia	1	(2%)		
Islets, pancreatic	(48)		(49)	
Atrophy			3	(6%)
Inflammation, chronic	1	(2%)		
Pituitary gland	(49)		(45)	
Cyst			1	(2%)
Pars distalis, cyst			1	(2%)
Pars distalis, hemorrhage	1	(2%)		
Pars distalis, hyperplasia	10	(20%)	4	(9%)
Pars distalis, hyperplasia, focal	2	(4%)		
Thyroid gland	(48)		(48)	
Atrophy	1	(2%)		
Follicular cell, hyperplasia	2	(4%)		
Follicular cell, hyperplasia, focal	2	(4%)		
GENERAL BODY SYSTEM				
None				
GENITAL SYSTEM				
Clitoral gland	(1)			
Cyst multilocular	1	(100%)		
Ovary	(49)		(48)	
Abscess	1	(2%)		
Atrophy	1	(2%)		
Cyst	17	(35%)	12	(25%)
Inflammation, chronic	1	(2%)	1	(2%)
Inflammation, suppurative	1	(2%)		
Necrosis, liquifactive	1	(2%)		
Corpus luteum, cyst			1	(2%)
Periovarian tissue, inflammation, chronic	4	(8%)	1	(2%)
Uterus	(49)		(50)	
Inflammation, necrotizing			1	(2%)
Endometrium, hyperplasia	2	(4%)		
Endometrium, hyperplasia, cystic	39	(80%)	6	(12%)
Endometrium, inflammation, chronic	1	(2%)		
Endometrium, inflammation, suppurative	3	(6%)	2	(4%)
Lymphatic, ectasia			1	(2%)

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

	Chamber Control	15,000 ppm
HEMATOPOIETIC SYSTEM		
Bone marrow	(49)	(50)
Hyperplasia		2 (4%)
Myelofibrosis	36 (73%)	6 (12%)
Lymph node	(46)	(45)
Infiltration cellular, histiocytic	1 (2%)	
Mediastinal, hyperplasia, lymphoid, chronic	1 (2%)	
Mesenteric, edema, acute	1 (2%)	
Mesenteric, hemorrhage, acute	1 (2%)	
Mesenteric, infiltration cellular, histiocytic	1 (2%)	
Sinus, ectasia		1 (2%)
Lymph node, bronchial	(37)	(38)
Erythrophagocytosis		1 (3%)
Hemorrhage		1 (3%)
Hyperplasia, lymphoid	3 (8%)	2 (5%)
Infiltration cellular, histiocytic	2 (5%)	2 (5%)
Lymph node, mandibular	(41)	(26)
Ectasia	1 (2%)	
Erythrophagocytosis		2 (8%)
Hyperplasia, lymphoid	3 (7%)	
Infiltration cellular, histiocytic	14 (34%)	4 (15%)
Inflammation, chronic		1 (4%)
Inflammation, subacute		1 (4%)
Spleen	(49)	(49)
Atrophy	1 (2%)	
Erythrophagocytosis	2 (4%)	
Hematopoietic cell proliferation	11 (22%)	17 (35%)
Hyperplasia, lymphoid	4 (8%)	2 (4%)
Thymus	(39)	(25)
Cyst	1 (3%)	1 (4%)
Infiltration cellular		1 (4%)
INTEGUMENTARY SYSTEM		
Mammary gland	(42)	(38)
Inflammation	2 (5%)	2 (5%)
Duct, ectasia	3 (7%)	3 (8%)
Skin	(48)	(50)
Epidermis, atrophy	1 (2%)	1 (2%)
Hair follicle, atrophy	14 (29%)	19 (38%)
Subcutaneous tissue, edema		1 (2%)
Subcutaneous tissue, infiltration cellular, histiocytic		1 (2%)
Subcutaneous tissue, inflammation, chronic		1 (2%)
MUSCULOSKELETAL SYSTEM		
Bone	(49)	(50)
Cranium, developmental malformation	1 (2%)	
Skeletal muscle	(2)	(2)
Intercostal, abscess	1 (50%)	
NERVOUS SYSTEM		
Brain	(49)	(50)
Hemorrhage, acute	1 (2%)	
Inflammation, chronic		1 (2%)
Cerebrum, infiltration cellular, histiocytic	1 (2%)	
Thalamus, mineralization	9 (18%)	10 (20%)
Ventricle, dilatation	1 (2%)	

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

	Chamber Control	15,000 ppm
RESPIRATORY SYSTEM		
Larynx	(46)	(49)
Epithelium, hyperplasia, focal		1 (2%)
Lung	(49)	(50)
Hemorrhage		5 (10%)
Inflammation, acute	1 (2%)	12 (24%)
Inflammation, chronic, multifocal	23 (47%)	1 (2%)
Inflammation, subacute		1 (2%)
Metaplasia, osseous		1 (2%)
Thrombus		2 (4%)
Alveolar epithelium, hyperplasia, diffuse		1 (2%)
Alveolus, adenomatosis, focal		2 (4%)
Alveolus, edema		1 (2%)
Alveolus, erythrophagocytosis		2 (4%)
Alveolus, infiltration cellular, histiocytic	1 (2%)	6 (12%)
Bronchiole, hyperplasia, multifocal	1 (2%)	1 (2%)
Bronchus, inflammation, suppurative	1 (2%)	
Glands, ectasia	2 (4%)	1 (2%)
Interstitium, inflammation, chronic		1 (2%)
Interstitium, inflammation, subacute		1 (2%)
Pleura, inflammation, chronic		1 (2%)
Vein, metaplasia, osseous, focal	1 (2%)	
Nose	(49)	(50)
Glands, dilatation		2 (4%)
Mucosa, hyperplasia		1 (2%)
Mucosa, inflammation, suppurative	2 (4%)	1 (2%)
Nasolacrimal duct, hyperplasia		1 (2%)
Nasolacrimal duct, inflammation, suppurative		1 (2%)
Respiratory epithelium, hyperplasia	2 (4%)	2 (4%)
Respiratory epithelium, metaplasia, squamous	1 (2%)	2 (4%)
Submucosa, inflammation, chronic, diffuse		1 (2%)
Trachea	(46)	(49)
Glands, dilatation	1 (2%)	1 (2%)
Submucosa, inflammation, chronic	1 (2%)	
SPECIAL SENSES SYSTEM		
None		
URINARY SYSTEM		
Kidney	(49)	(47)
Cyst		1 (2%)
Hematopoietic cell proliferation	1 (2%)	1 (2%)
Hydronephrosis		6 (13%)
Hypoplasia	1 (2%)	
Inflammation, chronic	8 (16%)	
Inflammation, suppurative	2 (4%)	
Nephropathy	10 (20%)	20 (43%)
Capsule, inflammation, suppurative	1 (2%)	
Glomerulus, amyloid deposition		1 (2%)
Renal tubule, karyomegaly		5 (11%)
Renal tubule, mineralization		1 (2%)
Renal tubule, pigmentation, bile		2 (4%)
Ureter		(2)
Transitional epithelium, necrosis		1 (50%)
Urinary bladder	(46)	(43)
Edema		1 (2%)
Inflammation, chronic	17 (37%)	5 (12%)
Inflammation, necrotizing		1 (2%)

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 13. Blood was taken from 10 $B6C3F_1$ mice killed in a moribund state between months 12 and 18. 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) *M. pul.* (*Mycoplasma pulmonis*) (24 mo)
Rats	PVM KRV (Kilham rat virus) H-1 (Toolan's H-1 virus) Sendai	RCV (rat coronavirus) (13 mo)	RCV/SDV (sialodacryoadenitis virus) (24 mo) *M. pul.* (24 mo)

Results

One of 10 control rats had a positive titer for KRV at 24 months.

APPENDIX F

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

Pelleted Diet: January 1982 to February 1984

(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)	23.40 ± 0.98	21.8-26.3	26
Crude fat (percent by weight)	5.03 ± 0.58	3.3-5.7	26
Crude fiber (percent by weight)	3.43 ± 0.51	2.9-5.6	26
Ash (percent by weight)	6.53 ± 0.43	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)	12,207 ± 480	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)	16.7 ± 3.19	12.0-27.0	26
Riboflavin (ppm)	7.6 ± 0.85	6.1-8.2	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)	0.98 ± 0.05	0.87-1.10	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)	0.53 ± 0.15	0.17-0.77	26
Cadmium (ppm) (a)	<0.10		26
Lead (ppm)	0.79 ± 0.62	0.33-3.37	26
Mercury (ppm) (a)	<0.05		26
Selenium (ppm)	0.30 ± 0.07	0.13-0.40	26
Aflatoxins (ppb) (a)	<5.0		26
Nitrate nitrogen (ppm) (b)	8.75 ± 4.49	0.10-22.0	26
Nitrite nitrogen (ppm) (b)	2.08 ± 2.01	0.10-7.20	26
BHA (ppm) (c)	4.34 ± 4.68	2.0-17.0	26
BHT (ppm) (c)	2.47 ± 2.53	0.9-12.0	26
Aerobic plate count (CFU/g) (d)	40,477 ± 33,886	4,900-130,000	26
Coliform (MPN/g) (e)	46.27 ± 123	3.0-460	26
E. coli (MPN/g) (a)	≤3.0		26
Total nitrosamines (ppb) (f)	5.17 ± 5.82	1.7-30.9	26
N-Nitrosodimethylamine (ppb) (f)	4.15 ± 5.82	0.8-30.0	26
N-Nitrosopyrrolidine (ppb) (f)	1.02 ± 0.25	0.81-1.7	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) Fifteen 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. 346 for the 2-year studies of chloroethane (ethyl chloride) in rats and mice were audited for the National Institute of Environmental Health Sciences (NIEHS) at the National Toxicology Program (NTP) Archives by Dynamac Corporation and Integrated Laboratory Systems. The audits included a review of:

(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 individual data for a random 10% sample of animals in each study group were reviewed in detail.
(4) All chemistry records.
(5) All postmortem records for individual animals concerning date of death, disposition code, condition code, 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 10% 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 10% sample of animals to verify their incorporation into final pathology tables.
(9) Correlation between the data, factual information, and procedures for the 2-year studies presented in the draft Technical Report and the records available at the NTP Archives.

Procedures and events during the exposure phase of the studies were documented adequately in the archival records with the exception that clinical observation records for July 1982 were not present. 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 100% of the group mean body weight values showed 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, 57/66 in rats and 34/35 in mice correlated with necropsy observations; residual wet tissues from the 10 animals with noncorrelations contained no untrimmed potential lesions. Survival records for unscheduled-death animals were found to be correct, except for the disposition codes (moribund kill vs. found dead) for 2/123 rats and 4/127 mice; the wet tissues for these animals contained correct identifiers, and these differences had no impact on the overall survival data of their study groups.

Review of the pathology specimens showed that identifiers (ear tags) were saved and read correctly for all 55 rats and 48 mice examined. The archival records showed that ear tags on individual animals were inspected and occasionally found to be absent during the studies; such animals were retagged with their originally assigned number. Inspection of the residual wet tissues for 55 rats and 48 mice detected 16 and 9 untrimmed potential lesions in rats and mice, respectively. One untrimmed potential lesion in a control male rat and three in control and exposed female mice involved target organs. The intestinal segments were partially unopened in 35/55 rats and 42/48 mice examined; however, no lesions were evident in the unopened segments by external examination. Gross observations made at necropsy correlated with microscopic observations, except for 8 in rats and 10 in mice; these were spread across study groups.

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

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