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TOXICOLOGY AND CARCINOGENESIS STUDIES OF 2-CHLOROACETOPHENONE

(CAS NO. 532-27-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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

NTP TECHNICAL REPORT

ON THE

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(CAS NO. 532-27-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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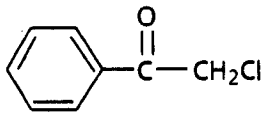

2-CHLOROACETOPHENONE

CAS No. 532-27-4

C_8H_7ClO Molecular weight 154.6

Synonyms: α-chloroacetophenone; 2-chloro-1-phenylethanone; CN; phenacyl chloride; phenylchloromethylketone

Trade Names: Mace®; Chemical Mace®

ABSTRACT

2-Chloroacetophenone is a potent lacrimator that has been used as a riot control agent and in tear gas formulations for personal protection devices. Toxicology and carcinogenesis studies were conducted by exposing groups of F344/N rats and B6C3F$_1$ mice of each sex to air containing 2-chloroacetophenone vapor for 14 days, 13 weeks, 15 months, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium* and Chinese hamster ovary (CHO) cells.

Fourteen-Day Studies: In 14-day studies, exposure concentrations of 2-chloroacetophenone ranged from 4.8 to 64 mg/m^3. All rats exposed to 19, 43, or 64 mg/m^3 died during the first week of the studies and 1/5 male rats exposed to 10 mg/m^3 died during the second week of the study. Rats exposed to 10 mg/m^3 lost weight; the final mean body weights of male or female rats exposed to 4.8 mg/m^3, the lowest concentration used, were 23% or 15% lower than that of controls. During the exposure, rats showed partial closure of the eyelids, excessive lacrimation (dacryorrhea), dyspnea, and erythema. All mice exposed to 10 mg/m^3 or higher concentrations of 2-chloroacetophenone died during the first week of the studies. The final mean body weights of mice exposed to 4.8 mg/m^3 were similar to those of controls. Dacryorrhea was observed in exposed mice.

Thirteen-Week Studies: The exposure concentrations of 2-chloroacetophenone ranged from 0.25 to 4 mg/m^3 for rats and mice. All rats lived to the end of the studies. The final mean body weights of rats exposed to 4 mg/m^3 were 9% lower than those of controls. Eye irritation during exposure was evident in rats exposed to 0.5 mg/m^3 or higher concentrations of 2-chloroacetophenone. One of 10 female mice exposed to 4 mg/m^3 and 1/10 female mice exposed to 0.5 mg/m^3 died before the end of the study. The final mean body weights of exposed mice were 7%-12% lower than that of controls for males and 12%-15% lower for females. No chemical-related gross or microscopic lesions were observed in rats or mice.

In the 2-year studies, groups of 60 rats of each sex were exposed to a vapor of 0 (chamber control), 1, or 2 mg/m^3 (0, 0.15, or 0.3 ppm) 2-chloroacetophenone, 6 hours per day, 5 days per week. Groups of 60 mice of each sex were exposed to 0 (chamber control), 2, or 4 mg/m^3 (0, 0.3, or 0.6 ppm) on the same schedule. Ten animals from each group were killed and examined at 15 months; the remaining animals continued on study for 2 years.

Fifteen-Month Studies: In the 15-month studies, minimal-to-mild focal squamous metaplasia and hyperplasia of the respiratory epithelium were seen at increased incidences in rats exposed to 2 mg/m^3. No exposure-related lesions were observed in mice of either sex.

Body Weight and Survival in the Two-Year Studies: Mean body weights and survival of exposed and chamber control rats were similar throughout most of the studies (survival--male: control, 14/50; 1 mg/m^3, 22/50; 2 mg/m^3, 17/50; female: 23/50; 20/50; 24/50). Mean body weights of male mice exposed to 4 mg/m^3 were about 5%-12% lower than those of controls after week 30; small differences between mean body weights of exposed and control female mice were not clearly exposure related. The survival of female mice exposed to 2 mg/m^3 was significantly lower than that of chamber controls after week 98. No other differences in survival were observed between any groups of mice (male: control, 34/50; 2 mg/m^3, 36/50; 4 mg/m^3, 33/50; female: 40/50; 28/50; 32/50).

Nonneoplastic and Neoplastic Effects in the Two-Year Studies: Fibroadenomas of the mammary gland occurred in female rats with positive trends, and the incidence in the 2 mg/m^3 group was greater than that in chamber controls (control, 12/50; 1 mg/m^3, 19/50; 2 mg/m^3, 23/50). The incidences of adenomas or adenocarcinomas of the mammary gland were not increased in the exposed groups.

Minimal-to-mild suppurative inflammation of the nasal mucosa was observed at increased incidences in exposed male rats. Hyperplasia and squamous metaplasia of the nasal respiratory epithelium were observed at increased incidences in exposed male and female rats. In mice, squamous metaplasia of the respiratory epithelium of the nasal passage was seen in four females and two males exposed to 4 mg/m^3 2-chloroacetophenone.

Inflammation, ulcers, and squamous hyperplasia of the forestomach were observed at increased incidences in exposed female rats.

There were no exposure-related increased incidences of neoplastic lesions in mice.

Genetic Toxicology: 2-Chloroacetophenone was not mutagenic in *S. typhimurium* strains TA98, TA100, TA1535, or TA1537 with or without exogenous metabolic activation. In cytogenetic tests with CHO cells, 2-chloroacetophenone did not induce sister chromatid exchanges with or without activation, but a weak positive increase in chromosomal aberrations was observed in the absence of metabolic activation.

Conclusions: Under the conditions of these 2-year inhalation studies, there was *no evidence of carcinogenic activity** of 2-chloroacetophenone for male rats exposed to 1 or 2 mg/m^3. There was *equivocal evidence of carcinogenic activity* for female F344/N rats, based on a marginal increase in fibroadenomas of the mammary gland. There was *no evidence of carcinogenic activity* for male or female B6C3F$_1$ mice exposed to 2 or 4 mg/m^3 2-chloroacetophenone.

*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 10.

SUMMARY OF THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Male F344/N Rats	Female F344/N Rats	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Exposure concentrations			
0, 1, or 2 mg/m^3 2-chloroacetophenone, 6 h/d, 5 d/wk	0, 1, or 2 mg/m^3 2-chloroacetophenone, 6 h/d, 5 d/wk	0, 2, or 4 mg/m^3 2-chloroacetophenone, 6 h/d, 5 d/wk	0, 2, or 4 mg/m^3 2-chloroacetophenone, 6 h/d, 5 d/wk
Body weights in the 2-year study			
Exposed and chamber control groups similar	Exposed and chamber control groups similar	High exposure group lower than chamber controls	Exposed and chamber control groups similar
Survival rates in the 2-year study			
14/50; 22/50; 17/50	23/50; 20/50; 24/50	34/50; 36/50; 33/50	40/50; 28/50; 32/50
Nonneoplastic effects			
Nasal passage: inflammation, hyperplasia, and squamous metaplasia of the respiratory epithelium	Forestomach: inflammation, ulcers, squamous metaplasia; nasal passage: hyperplasia and squamous metaplasia of the respiratory epithelium	None	None
Neoplasms			
None	Fibroadenomas of the mammary gland: 12/50; 19/50; 23/50	None	None
Level of evidence of carcinogenic activity			
No evidence	Equivocal evidence	No evidence	No evidence

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

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

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

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

- **Some Evidence of Carcinogenic Activity** is demonstrated by studies that are interpreted as showing a 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 2-Chloroacetophenone is based on 13-week studies that began in September 1981 and ended in December 1981 and on 2-year studies that began in September 1982 and ended in September 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 2-chloroacetophenone on November 20, 1989, 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 2-CHLOROACETOPHENONE

On November 20, 1989, the draft Technical Report on the toxicology and carcinogenesis studies of 2-chloroacetophenone 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. R. Melnick, NIEHS, began the discussion by reviewing the experimental design, results, and proposed conclusions (no evidence of carcinogenic activity for male rats; equivocal evidence for female rats; no evidence of carcinogenic activity for male or female mice).

Dr. McKnight, a principal reviewer, agreed with the conclusions for male rats and male and female mice but disagreed with the conclusion for female rats. She thought that the dose-related increases in fibroadenomas, adenomas, and adenocarcinomas of the mammary gland in female rats were strong enough to support some evidence of carcinogenic activity. Dr. Melnick said that, based on findings of a marginal increase of a commonly occurring benign neoplasm at an incidence that fell well within the historical range for untreated controls, the conclusion of equivocal evidence was judged appropriate. Dr. McKnight inquired as to how zero dose was administered to control animals. Dr. Melnick said that the chamber controls were treated in the same manner as the dosed animals, except that they did not receive vapors.

Dr. Longnecker, the second principal reviewer, agreed with the conclusions. He asked whether dosed animals were left in the inhalation chamber following the exposure period. Since the Report stated that 10 hours were required for 2-chloroacetophenone concentration to drop to 1% of target concentration, total exposure would have been increased for animals that remained in the chambers. Dr. Melnick responded that animals remained in the chambers and that details concerning the additional exposure would be better explained in the Report.

Most of the discussion was concerned with the significance of the mammary gland neoplasms observed in female rats. Dr. Silbergeld argued that both a significant trend test and pairwise comparison between control and high dose groups for fibroadenomas supported some evidence. On the other hand, Dr. Ashby thought that higher incidences in the control groups of more recent studies weakened the argument for equivocal evidence.

Dr. McKnight moved that the Technical Report on 2-chloroacetophenone be accepted with the conclusions as written for male rats and male and female mice, no evidence of carcinogenic activity. Dr. Longnecker seconded the motion, which was accepted unanimously. Dr. McKnight moved that the conclusion for female rats be changed from equivocal evidence of carcinogenic activity to some evidence of carcinogenic activity, based on statistically significant, dose-related increases in fibroadenomas or adenomas of the mammary glands, with incidences in both the low and high dose groups higher than ever seen in a chamber control group. Dr. Longnecker seconded the motion, which was defeated by six negative votes (Drs. Ashby, Carlson, Davis, Garman, Gold, and Hayden) to five affirmative votes (Drs. Klaassen, Longnecker, McKnight, Silbergeld, and Zeise). Dr. Gold moved that the conclusion be accepted as written, equivocal evidence of carcinogenic activity. Dr. Davis seconded the motion, which was accepted by seven affirmative votes (Drs. Ashby, Carlson, Davis, Garman, Gold, Hayden, and Longnecker) to four negative votes (Drs. Klaassen, McKnight, Silbergeld, and Zeise).

I. INTRODUCTION

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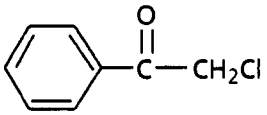

2-CHLOROACETOPHENONE

CAS No. 532-27-4

C_8H_7ClO Molecular weight 154.6

Synonyms: α-chloroacetophenone; 2-chloro-1-phenylethanone; CN; phenacyl chloride; phenylchloromethylketone

Trade Names: Mace®; Chemical Mace®

Chemical and Physical Properties, Production, and Use

2-Chloroacetophenone, a colorless-to-grey, crystalline solid (boiling point, 244°-245° C; melting point, 58°-59° C; vapor pressure, 0.0054 mm mercury at 20° C) with a floral odor, is practically insoluble in water but freely soluble in alcohol, ether, or benzene (Merck, 1983; ACGIH, 1986). 2-Chloroacetophenone has been synthesized by chlorination of acetophenone with selenium oxychloride (Schaefer and Sonnenberg, 1963). At room temperature and one atmosphere pressure, 1 mg/m^3 2-chloroacetophenone is equivalent to 0.16 ppm.

2-Chloroacetophenone is a potent lacrimator that has been used in tear gas formulations for riot control and in personal protection devices. It is also an irritant to the upper respiratory passages and to the skin. Amoore and Hautala (1983) reported that the odor threshold for 2-chloroacetophenone by humans is 0.035 ppm, the nose irritation threshold is 0.034 ppm, and the eye irritation threshold is 0.022 ppm. Because these values are only slightly less than the threshold limit value (TLV) of 0.05 ppm (approximately 0.3 mg/m^3) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH, 1986), it was estimated that less than 50% of distracted persons would perceive the presence of 2-chloroacetophenone at concentrations below the TLV. Reist and Rex (1977), however, reported that the odor detection threshold for 2-chloroacetophenone is 1.34 ppm, which is about 25 times the TLV for this compound. Persons at greatest risk of exposure to 2-chloroacetophenone are police and workers in facilities that produce 2-chloroacetophenone or tear gas formulations containing 2-chloroacetophenone. Approximately 2,300 workers in the United States are potentially exposed to 2-chloroacetophenone (National Occupational Exposure Survey, NIOSH, unpublished data).

2-Chloroacetophenone has been used as the active agent in tear gas used for riot control because it is a potent peripheral sensory irritant. By stimulating sensory nerve receptors in skin and mucosa of the eyes and respiratory tract, it causes burning in the eyes and excess lacrimation, blepharospasm, a burning sensation in the nose and throat, salivation, rhinorrhea, sneezing, coughing, labored breathing, and a stinging or burning sensation on exposed skin (Punte et al., 1962a; Grant, 1974; Sanford, 1976; Ballantyne and Swanston, 1978; Beswick, 1983). These symptoms occur almost instantaneously on exposure to 2-chloroacetophenone and generally resolve within about 20 minutes after exposure has ceased; however, severe and permanent corneal injury has been demonstrated in laboratory animals.

Animal Toxicity

Some LD_{50} and LC_{50} values for 2-chloroacetophenone in rabbits, mice, rats, and guinea pigs are presented in Table 1 (Punte et al., 1962b; Ballantyne and Swanston, 1978). Exposure concentrations in the inhalation studies by Ballantyne and Swanston ranged from 250 to 750 mg/m^3 for 15-60 minutes. The most notable species difference in these short-term studies is that mice are less sensitive than rats, rabbits, or guinea pigs to short-term intravenous or inhalation exposure to 2-chloroacetophenone. The cause of death in the inhalation studies was attributed to asphyxia after lung damage (pulmonary congestion, hemorrhage, and edema). Signs of intoxication in animals exposed to 2-chloroacetophenone were lacrimation, salivation, lethargy, and labored breathing (Punte et al., 1962b).

The short-term inhalation toxicity of 2-chloroacetophenone was greater than that of two other sensory irritants, 2-chlorobenzylidene malononitrile (CS) and dibenz[*b*,*f*]-1,4-oxazepine in rats, mice, rabbits, and guinea pigs after oral, intraperitoneal, intravenous, or inhalation exposure (Ballantyne, 1977; Ballantyne and Swanston, 1978). Gaskins et al. (1972) reported that the oral LD_{50} of 2-chloroacetophenone (1%-4% solutions) in rats ranged from 50 to 250 mg/kg, depending on the vehicle and concentration used.

Ocular effects resulting from exposure of rabbits to solutions containing 2-chloroacetophenone have been studied extensively. Ballantyne et al. (1975) reported that application of 0.1 ml of solutions of 1%, 2%, 5%, or 10% 2-chloroacetophenone dissolved in polyethylene glycol 300 into the conjunctival sac of rabbits (doses equivalent to 1, 2, 5, or 10 mg) caused lacrimation, blepharitis, chemosis, conjunctivitis, iritis, keratitis, and vascularization of the cornea. Damage to the cornea, including loss of epithelium, inflammatory cell infiltration, and vascularization, was marked and persistent at concentrations of 5% and higher. In addition, increases in corneal thickness and increases in intraocular tension were detected after application of 0.02% and 0.25% 2-chloroacetophenone, respectively. Gaskins et al. (1972) observed permanent corneal damage in rabbits exposed to 10%, but not to 4% or less, 2-chloroacetophenone dissolved in 1,1,1-trichloroethane. Thatcher et al. (1971) reported that 0.1 ml of Mace® (a tear gas mixture containing 0.9% 2-chloroacetophenone dissolved in 5% 1,1,1-trichloroethane, 4% mixed hydrocarbons, and 85%-90% fluorocarbon 113) or an aerosol of 2-chloroacetophenone in fluorocarbon 113 caused ocular injury in New Zealand white rabbits, including conjunctivitis, corneal edema, and corneal epithelial loss, when applied directly to the eyes or when sprayed from an aerosol can held 1-2 feet from the exposed animals. Direct instillation of liquid Mace® into the eyes of

TABLE 1. SOME LD_{50} AND LC_{50} VALUES OF 2-CHLOROACETOPHENONE IN RATS, MICE, RABBITS, AND GUINEA PIGS

Species	Route of Administration (a)					
	Oral (b)	Intraperitoneal (b)	Intravenous (b)	(c)	Inhalation (b)	(c)
Rat	127	36	41		8,750	3,700
Mouse			81		18,200	73,500
Rabbit	118		31	20	11,480	
Guinea pig	158	17			13,140	3,500

(a) Values are LD_{50} in milligrams per kilogram body weight except for inhalation, for which median lethal toxicity values (LCt_{50}) are given as the product of concentration (mg/m^3) and time (min).
(b) Ballantyne and Swanston, 1978
(c) Punte et al., 1962b

anesthetized rabbits or monkeys, or direct spraying from 6 feet at a restrained monkey, caused severe and permanent corneal damage (MacLeod, 1969). Most ocular lesions, including loss of the corneal epithelium, stromal edema, and corneal vascularization, healed within 4-7 days after exposure; however, corneal opacities and melanosis were evident 60 days after exposure. When animals were not anesthetized or restrained, the ocular lesions were milder and transient. In mice exposed to 2-chloroacetophenone vapor for 5 minutes inside a desiccator (equilibrated for 10 minutes with 1 g of 2-chloroacetophenone), there was a rapid exocytosis of secretory granules from both the secretory cells and the intralobular ductal epithelial cells of the exorbital lacrimal gland; however, within 60 minutes, the exorbital lacrimal gland appeared normal (Berkley and Hazlett, 1987).

Solid 2-chloroacetophenone (5 mg) also caused marked damage to the cornea, iris, conjunctiva, and eyelids; the no-effect level on the cornea was between 0.1 and 0.25 mg (Ballantyne et al., 1975). Punte et al. (1962b) observed severe conjunctival congestion in rabbit eyes instilled with 0.5 or 1 mg of 2-chloroacetophenone. Fifteen-minute exposure to aerosols of 2-chloroacetophenone (720 mg/m^3) did not damage the cornea or iris but did cause irritation of the eyelids and conjunctiva. The ocular effects of 2-chloroacetophenone were more marked and of longer duration than those of dibenz[*b*,*f*]-1,4-oxazepine.

The concentration of 2-chloroacetophenone producing a 50% depression in respiratory rate (RD_{50}) in mice was 52 µg/liter, a value about five times greater than that for CS (Ballantyne and Swanston, 1978). Alarie and Keller (1973) suggested that sensory irritants, such as 2-chloroacetophenone, decrease respiratory rates in mice as a result of a reflex action after stimulation of the nasal trigeminal nerve endings.

2-Chloroacetophenone produced a more marked and persistent contact dermatitis than that caused by 2-chlorobenzylidene malononitrile Ballantyne and Swanston, 1978). Dorsal application of 0.1 ml of solutions of 12.5% 2-chloroacetophenone in acetone or corn oil to rabbits, guinea pigs, or mice caused erythema, edema, and desquamation. Histologic examination of the skin 3 days after application of 2-chloroacetophenone revealed epidermal necrosis, edema, and acute inflammatory cell infiltration of the dermis. Gaskins et al. (1972) reported that direct application of a 4% solution of 2-chloroacetophenone in trioctyl phosphate to rabbit skin produced purpura and necrotic eschar after 5 or 6 days. Topical administration (0.2 ml of 1% or 0.5% acetone solution) or intradermal administration (0.5 ml containing 10-25 µg) of 2-chloroacetophenone or *o*-chlorobenzylidene malononitrile caused contact sensitization or delayed hypersensitivity in guinea pigs (Chung and Giles, 1972). Skin reactions of sensitized guinea pigs to challenging doses of 2-chloroacetophenone included erythema, edema, induration, necrosis, and eschar formation.

The toxicity of 2-chloroacetophenone has been considered to be due to its alkylation of tissue nucleophilic sites. Cucinell et al. (1971) suggested that 2-chloroacetophenone toxicity may be due to the alkylation and consequent inhibition of sulfhydryl-containing enzymes because inhibition of lactate dehydrogenase (LDH) activity by 2-chloroacetophenone in vitro was not reversed by glutathione and because intravenous administration of sodium thiosulfate did not protect rats from lethal doses of 2-chloroacetophenone given by interperitoneal injection. After exposure to CS, glutathione partially reversed the inhibition of LDH activity, and thiosulfate protected rats challenged with LD_{50} doses of this compound.

2-Chloroacetophenone has been shown to inhibit enzymes involved in phospholipid synthesis (Kageyama et al., 1986), glucose metabolism (Castro, 1966), and human plasma cholinesterase (Castro, 1968). The inhibition of cholinesterase activity may not involve interaction with sulfhydryl groups on the enzyme because the inhibition was reversible by dialysis or dilution.

Rutledge and Deitrich (1971) found that the metabolism of norepinephrine was altered in brain cortical slices prepared from rabbits receiving 300 mg/kg 2-chloroacetophenone by intraperitoneal injection. They suggested that 2-chloroacetophenone inhibited aldehyde dehydrogenase

because the rate of formation of phenolic acids was decreased, whereas the rate of formation of phenolic glycols was increased. Dithiothreitol and glutathione antagonized the inhibition of rat brain aldehyde dehydrogenase activity by 2-chloroacetophenone.

Developmental Toxicity

Incubation of chick embryos in the primitive streak stage with 0.5-3 mM 2-chloroacetophenone for 15-120 minutes increased the frequency of abnormalities in the nervous system, including improper differentiation and incomplete closure of the brain (Lakshmi, 1962). Well-differentiated closed neural tubes were observed in embryos incubated with 2-chloroacetophenone and subsequently exposed to sulfhydryl agents (Mulherkar et al., 1965, 1967). Embryos incubated at the head-process stage with 2-chloroacetophenone showed normal development. Thus, the inhibitory effect of 2-chloroacetophenone on morphogenesis of the nervous system in chick embryos was reversible. No developmental toxicity studies have been reported for 2-chloroacetophenone in mammals.

Carcinogenicity

Gwynn and Salaman (1953) reported that 2-chloroacetophenone was a cocarcinogen because it increased the incidence of epidermal papillomas in skin of mice previously given dermal applications of 0.3 ml of 0.15% 9,10-dimethyl-1,2-benzanthracene (DMBA) dissolved in acetone. Twenty-one days after exposure to DMBA, mice received applications of 0.3 ml of 0.4%-0.8% 2-chloroacetophenone in acetone twice per week for 12 weeks and then once per week for 15 weeks. Twenty epidermal neoplasms were observed in 9/12 mice that received the DMBA plus 2-chloroacetophenone applications, compared with 1 neoplasm in 12 control mice that received DMBA followed by dermal applications of acetone on the same dosing schedule. Epidermal hyperplasia was also observed at the site of application of 2-chloroacetophenone.

No neoplasms were produced in mice that had received dermal applications of a solution of 0.003 M (0.05%) 2-chloroacetophenone in acetone twice per week for 5 months (ACGIH, 1986).

Genetic Toxicology

2-Chloroacetophenone was not mutagenic to *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537 with or without liver S9 obtained from Aroclor-induced male Sprague Dawley rats or Syrian hamsters (Zeiger et al., 1987; Appendix I). In Chinese hamster ovary cells, 2-chloroacetophenone did not induce sister chromatid exchanges but did produce a weak positive response for induction of chromosomal aberrations in the absence of exogenous metabolic activation (Appendix I).

Human Effects

In humans, the estimated respiratory LC_{50} for 2-chloroacetophenone is 8,000-11,000 mg · min/m^3 (Sanford, 1976; ACGIH, 1986). Volunteers exposed to various airborne concentrations of 2-chloroacetophenone responded to the short-term irritant properties of this compound after 1 minute of exposure at 210 mg/m^3, 2 minutes of exposure at 120 mg/m^3, or 3 minutes of exposure at 90 mg/m^3 (Punte et al., 1962a). Symptoms in humans exposed to 2-chloroacetophenone include irritation to the eyes, respiratory tract, and skin. Irritation resulting from dermal exposure to 2-chloroacetophenone was characterized by purpura, erythema, edema, desquamation, and vesication (Penneys et al., 1969; Penneys, 1971; Holland and White, 1972). In addition to primary irritant dermatitis, exposure to 2-chloroacetophenone or Mace® has also been shown to cause allergic contact dermatitis in humans (Penneys et al., 1969; Penneys, 1971; Frazier, 1976). Thus, 2-chloroacetophenone is also a potent cutaneous sensitizer in humans, causing a delayed hypersensitivity reaction. Some prisoners sprayed with 2-chloroacetophenone during a disturbance at San Quentin Prison in April 1981 required hospitalization because of severe laryngotracheobronchitis, chemical skin burns, conjunctivitis, and apparent allergic reactions (Thorburn, 1982).

I. INTRODUCTION

Study Rationale

2-Chloroacetophenone was nominated for toxicology and carcinogenesis studies by the National Cancer Institute because of its use as a riot control agent and because there was a lack of long-term toxicology and carcinogenicity information on this compound. The inhalation route of exposure was selected because that is the primary route of human exposure.

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF 2-CHLOROACETOPHENONE

GENERATION AND MONITORING OF CHAMBER CONCENTRATIONS

- Generation System
- Concentration Monitoring
- Chamber Atmosphere Characterization

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

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

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF 2-CHLOROACETOPHENONE

2-Chloroacetophenone formulated with the anti-agglomerant magnesium oxide was obtained in one lot (lot no. APG-30-MD) from the U.S. Army (Aberdeen Proving Ground, Aberdeen, MD). Purity and identity analyses were conducted on representative samples at Midwest Research Institute (Kansas City, MO) (Appendix H).

The study chemical was identified as 2-chloroacetophenone by infrared, ultraviolet/visible, and nuclear magnetic resonance spectroscopic analyses.

The 2-chloroacetophenone content of the formulation was found to be approximately 85%, as determined by elemental analysis, Karl Fischer water analysis, thin-layer chromatography, and gas chromatography and by gravimetric analysis (to quantitate the amount of material insoluble in methylene chloride or acetone).

Material insoluble in methylene chloride and acetone represented 11.2% of the sample by weight. Analysis by X-ray diffraction, X-ray emission spectroscopy, and spark source mass spectroscopy indicated that the insoluble material was primarily magnesium oxide, with traces of silicon dioxide and iron.

Karl Fischer analysis indicated the presence of 2.2% water. Gas chromatography with one system detected 11 impurities with a total relative peak area of approximately 1.7%, with the largest impurity of 0.8%. In accordance with National Toxicology Program (NTP) practice for impurities whose concentrations do not exceed 1%, the chromatographic impurities were not identified.

Stability studies performed by gas chromatography indicated that 2-chloroacetophenone was stable after storage for 2 weeks in the dark at 25° C; a 4% decrease was observed after storage at 60° C.

Periodic analysis of 2-chloroacetophenone stored at −20° C throughout the studies indicated no significant degradation of the study material by gas chromatographic and infrared spectroscopic analyses.

GENERATION AND MONITORING OF CHAMBER CONCENTRATIONS

Generation System

A single generator produced 2-chloroacetophenone vapor, which was carried by a distribution duct to each of the chambers (Hazleton 2000®, Lab Products, Inc.), except for the control chambers. In the generator, 2-chloroacetophenone was heated to the liquid state. Preheated nitrogen was then bubbled through the molten liquid at a controlled rate, volatilizing the 2-chloroacetophenone and leaving the magnesium oxide in the generator (Appendix H).

Concentration Monitoring

An HP 5840 gas chromatograph equipped with a 3% phenyl/cyanopropyl column and with an electron capture detector was used to monitor each exposure chamber, each control chamber, and the exposure room. An automated multiplexed eight-port stream-select valve sampled multiple positions, automatically cycling through all eight ports about once every 30 minutes. Excellent control of 2-chloroacetophenone chamber concentrations was achieved; less than 3% of the daily mean concentrations deviated by ±10% from the target concentrations. Weekly mean exposure concentrations for the 2-year studies are presented in Figures H5 through H8. A summary of the chamber concentrations is presented in Table H2; Table H3 summarizes the distribution of mean daily concentrations.

Chamber Atmosphere Characterization

Uniformity of the concentration of 2-chloroacetophenone in each exposure chamber was measured before the start of the studies and was checked at approximately 3-month intervals with an HP 5840 gas chromatographic system equipped with an electron-capture detector. 2-Chloroacetophenone concentrations for mouse and rat chambers were within 10% and 12%, respectively, of the mean target concentration at all five positions sampled; the relative standard deviation did not exceed 5.5%. Therefore, the

concentration of 2-chloroacetophenone vapor in the chambers was considered to be uniform.

Acetophenone is present as a volatile impurity in the bulk chemical at a level of 0.08%. During the short-term studies, acetophenone concentrations in the chambers were increased because of decomposition in the generator and reached levels of 22% of the 2-chloroacetophenone concentrations. Before the long-term studies, the generation system was modified to eliminate degradation of the 2-chloroacetophenone. During the studies, acetophenone concentrations in the chambers were further reduced below detectable levels by sparging the molten chemical for 1 week prior to use for vapor generation. No other impurities were observed in the chamber atmosphere.

Some discoloration of the study material in the generator reservoir occurred during the 2-year studies, but analysis by high-performance liquid chromatography, gas chromatography/mass spectroscopy, and ultraviolet/visible spectroscopy indicated that changes in the study material during the generation process were limited primarily to the enhanced removal of the more volatile impurities and the formation of small amounts of nonvolatile condensation products, which were not detected in the chamber atmosphere.

The chamber atmospheres were not evaluated for the presence of aerosolized 2-chloroacetophenone. However, the saturation concentration at 68° F is approximately 50 mg/m^3, so it is unlikely that aerosolized chemical could have been present.

During the first 4 months of the 2-year studies, a slow buildup to the target concentration was observed. The time to reach 90% of the target concentration (T_{90}) ranged from 15 to 120 minutes. The problem was traced to the configuration of the inlet to the chamber from the distribution line. This was modified, and the T_{90} was reduced to 20 minutes. On January 24, 1983, the length of the exposure was redefined as 6 hours plus the T_{90} of 20 minutes.

After the generator was turned off, the time required for the concentration in the chamber atmosphere to reach 10% of the original target concentration was approximately 2 hours and the time to reach 1% of the original target concentration was approximately 10 hours. This long concentration-decay appeared to be due to the slow volatilization of the 2-chloroacetophenone that condensed on the chamber walls and resulted in a 5%-25% increase in total exposure to 2-chloroacetophenone.

FOURTEEN-DAY STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Harlan Industries and were observed for 21 days before chemical exposure. Groups of five rats and five mice of each sex were exposed to air containing 2-chloroacetophenone concentrations of 0 (chamber control), 4.8, 10, 19, 43, or 64 mg/m^3 for 6 hours per day for 10 days of exposure over 14 days. Rats and mice were observed three times per day and were weighed before exposure, once per week thereafter, and at necropsy. A necropsy was performed on all animals. Histopathologic examinations were performed on two rats and three mice of each sex exposed to 4.8 mg/m^3 and one male and one female rat exposed to 10 mg/m^3 Further details are presented in Table 2.

THIRTEEN-WEEK STUDIES

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

Seven- to 8-week-old male and female F344/N rats and B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories. Animals were observed for 22 days, distributed to weight classes, and assigned to groups according to tables of random numbers. Feed was available ad libitum during nonexposure periods; water was available at all times. Further experimental details are summarized in Table 2.

Groups of 10 rats and 10 mice of each sex were exposed to air containing 2-chloroacetophenone

TABLE 2. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Fourteen-Day Studies	Thirteen-Week Studies	Fifteen-Month and Two-Year Studies
EXPERIMENTAL DESIGN		
Size of Study Groups		
5 males and 5 females of each species	10 males and 10 females of each species	60 males and 60 females of each species
Chamber Concentrations		
0, 4.8, 10, 19, 43, or 64 mg/m^3 2-chloroacetophenone by inhalation	0, 0.25, 0.5, 1, 2, or 4 mg/m^3 2-chloroacetophenone by inhalation	Rats--0, 1, or 2 mg/m^3 2-chloroacetophenone by inhalation; mice--0, 2, 4 mg/m^3
Date of First Exposure		
5/13/81	9/17/81	Rats--9/29/82; mice--9/21/82
Date of Last Exposure		
5/26/81	12/15/81	Rats--9/21/84; mice--9/14/84
Duration of Exposure		
6 h/d for 10 exposures over 14 d	6 h/d, 5 d/wk for 13 wk for 64 (0.25 mg/m^3 group) or 65 exposures	6 h/d 5 d/wk for 15 mo or 103 wk
Type and Frequency of Observation		
Observed 3 × d; weighed initially and 1 × wk thereafter	Observed 2 or 3 × d; weighed initially and 1 × wk thereafter	Observed 2 × d; weighed initially, 1 × wk for 12 wk, and 1 × mo thereafter
Necropsy, Histologic Examinations, and Supplemental Studies		
Necropsy performed on all animals; histologic exams performed on 2 rats of each sex exposed to 5 mg/m^3, 1 rat of each sex exposed to 10 mg/m^3, and 3 mice of each sex exposed to 5 mg/m^3	Necropsy performed on all controls and animals exposed to 4 mg/m^3 and all animals dying before the end of the studies. Tissues examined histologically for all controls and animals exposed to 4 mg/m^3 and all animals dying before the end of the studies	2 y--necropsy performed on all animals; complete histologic exams performed on all male rats and female control rats, female rats exposed to 2 mg/m^3, and all mice. Tissues examined include: adrenal glands, brain, cecum, colon, duodenum, epididymis/prostate/testes or ovaries/uterus, esophagus, eyes (rats), gallbladder (mice), gross lesions and tissue masses with regional lymph nodes, heart, ileum, jejunum, kidneys, larynx, liver, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nasal passage and turbinates, pancreas, parathyroid glands, pituitary gland, preputial or clitoral gland (rats), rectum, salivary glands, skin, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, trachea, tracheobronchial lymph nodes, and urinary bladder. Tissues examined for female rats exposed to 1 mg/m^3 include: adrenal glands, pituitary gland, and stomach. 15 mo--organ weights and blood samples for hematologic analyses obtained at necropsy for animals killed at 15 mo. Complete histologic exams performed on high dose and control animals

TABLE 2. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF 2-CHLOROACETOPHENONE (Continued)

Fourteen-Day Studies	Thirteen-Week Studies	Fifteen-Month and Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE		
Strain and Species		
F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice
Animal Source		
Harlan Industries (Indianapolis, IN)	Charles River Breeding Laboratories (Portage, MI)	Charles River Breeding Laboratories (Portage, MI)
Study Laboratory		
Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories
Method of Animal Identification		
Ear tag and cage number	Ear tag and cage number	Ear tag and cage number
Time Held Before Study		
21 d	22 d	28 d
Age When Placed on Study		
Rats--7 wk; mice--9 wk	7-8 wk	Rats--8-9 wk; mice--9-10 wk
Age When Killed		
Rats--9 wk; mice--11 wk	20-21 wk	15 mo: rats--73-74 wk; mice--74-75 wk; 2 y: rats--113-114 wk; mice--114-115 wk
Necropsy Dates		
5/27/81	12/16/81-12/18/81	15 mo: rats--12/28/83; mice--12/19/83; 2 y: rats--10/2/84-10/4/84; mice--9/24/84-9/28/84
Method of Animal Distribution		
According to a table of random numbers	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers	Same as 13-wk studies
Diet		
NIH 07 Rat and Mouse Ration (Zeigler Bros., Inc., Gardners, PA); available ad libitum during nonexposure periods	Same as 14-d studies	Same as 14-d studies
Water		
Automatic watering system (Edstrom Industries, Waterford, WI); available ad libitum	Same as 14-d studies	Same as 14-d studies
Cages		
Stainless steel, wire-bottom cages (Hazleton Systems, Inc., Aberdeen, MD)	Same as 14-d studies	Same as 14-d studies
Animals per Cage		
1	1	1
Other Chemicals on Study in the Same Room		
None	None	None
Chamber Environment		
Temp--71°-73° F; hum--41%-64%; fluorescent light 12 h/d	Temp--69°-77° F; hum--25%-78%; fluorescent light 12 h/d	Temp--68°-82° F (rats) or 67°-79° F (mice); hum--29%-82% (rats) or 28%- 80% (mice); fluorescent light 12 h/d

at target concentrations of 0 (chamber control), 0.25, 0.5, 1, 2, or 4 mg/m^3, 6 hours per day, 5 days per week for 65 or 64 (0.25 mg/m^3 groups) exposures. The chamber doors, except for the time required for animal maintenance, were left closed for 24 hours per day because of the persistence of 2-chloroacetophenone. Animals were observed two or three times per day; moribund animals were killed. 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. Liver weights were recorded at necropsy. Histologic examinations were performed on animals that died before the end of the studies, controls, and animals exposed to 4 mg/m^3. Tissues and groups examined are listed in Table 2.

TWO-YEAR STUDIES

Study Design

Groups of 60 rats of each sex were exposed to 2-chloroacetophenone at target concentrations of 0 (chamber controls), 1, or 2 mg/m^3, 6 hours per day, 5 days per week for 103 weeks. Groups of 60 mice of each sex were exposed to 0 (chamber controls), 2, or 4 mg/m^3 on the same schedule. Although the control of chamber concentration was very good throughout the studies, mice in the 4 mg/m^3 groups were inadvertently exposed to 1 mg/m^3 2-chloroacetophenone for the first 5 days of the studies. Conditions in the control chambers were similar to those maintained in the exposure chambers, except that the control chambers did not receive 2-chloroacetophenone vapors from the distribution ducts.

During month 15, up to 10 anesthetized animals (rats, phenobarbital; mice, diethyl ether) from each group had blood samples taken from the lumbar aorta (rats) or supraorbital sinus (mice). The erythrocyte and leukocyte counts, hemoglobin concentration, hematocrit, and leukocyte differential count were determined. The animals were killed, and the brain, liver, and right kidney were weighed; histologic examinations were performed on control and high dose animals.

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 Charles River Breeding Laboratories. Breeding stock for the foundation colonies at the production facility originated at the National Institutes of Health Repository. Animals shipped for study were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. Rats were shipped to the study laboratory at 4-5 weeks of age and mice at 5-6 weeks of age. The animals were quarantined at the study laboratory for 4 weeks. Thereafter, a complete necropsy was performed on five animals of each sex and species to assess their health status. The rats were placed on study at 8-9 weeks of age and the mice at 9-10 weeks of age. The health of the animals was monitored during the course of the studies according to the protocols of the NTP Sentinel Animal Program (Appendix E).

Animal Maintenance

Rats and mice were housed individually. Feed (Appendix F) was available ad libitum during nonexposure periods; water was available at all times. Cages were rotated within the chambers during these studies. Chamber doors for all groups were kept closed Monday through Friday. The excreta pans beneath cage compartments were changed once per day to control the ammonia levels. Further details of animal maintenance are given in Table 2.

Clinical Examinations and Pathology

All animals were observed two times per day. Body weights were recorded once per week for the first 12 weeks of the studies and once per month thereafter. Mean body weights were calculated for each group. Animals found moribund and those surviving to the end of the studies were humanely killed. A necropsy was performed on all animals, including those found dead.

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. Complete histopathologic examinations were performed on all male rats and male and female mice. For female rats, histopathologic examination of tissues was performed according to an "inverse pyramid" design (McConnell, 1983a,b). That is, complete histopathologic examinations (Table 2) were performed on all high dose and control animals and on low dose animals dying before the end of the studies. In addition, histopathologic examinations were performed on all grossly visible lesions in all dose groups. Potential target organs for chemically related neoplastic and nonneoplastic effects were identified from the short-term studies or by examination of the pathology data from high dose and control groups in the 2-year studies; these target organs/tissues in the lower dose group were examined histopathologically (Table 2).

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 (rats: forestomach [females], lung, mammary gland [females], nasal passage; mice: forestomach [females], lung, kidney [males], nasal passage), 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 and in the randomly selected 10% of animals.

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. For the studies in rats, the PWG examined sections of forestomach, mammary gland, and nasal passage and examples of incidental tumor discrepancies. For the studies in mice, the PWG examined sections of forestomach, kidney, lung, and nasal passage. The PWG included the laboratory pathologist (for the studies in rats), the quality assessment pathologist, and other pathologists experienced in rodent toxicology, who 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 dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) life table test for a dose-related trend. When significant survival differences were detected, additional analyses using

these procedures were carried out to determine the time point at which significant differences in the survival curves were first detected. All reported P values for the survival analysis are two-sided.

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

Analysis of Tumor Incidence: The majority of tumors in this study were considered to be incidental to the cause of death or not rapidly lethal. Thus, the primary statistical method used was 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 dosed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and Haseman (1986). When tumors are incidental, this comparison of the time-specific tumor prevalences also provides a comparison of the time-specific tumor incidences (McKnight and Crowley, 1984).

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

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

Analysis of Continuous Variables: The statistical analysis of organ weight data was carried out by using the nonparametric multiple comparison procedures of Dunn (1964) or Shirley (1977) to assess the significance of pairwise comparisons between dosed and vehicle control groups. Jonckheere's test (Jonckheere, 1954) was used to evaluate the significance of dose-response trends and to determine whether Dunn's or Shirley's test was more appropriate for pairwise comparisons.

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.

III. RESULTS

RATS

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

FIFTEEN-MONTH STUDIES

TWO-YEAR STUDIES

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

MICE

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

FIFTEEN-MONTH STUDIES

TWO-YEAR STUDIES

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

GENETIC TOXICOLOGY

III. RESULTS: RATS

FOURTEEN-DAY STUDIES

All rats exposed to 19, 43, or 64 mg/m^3 2-chloroacetophenone and 1/5 male rats exposed to 10 mg/m^3 died before the end of the studies (Table 3). Rats exposed to 10 mg/m^3 lost weight. Rats exposed to 4.8 mg/m^3 gained less weight than controls; the final mean body weights of males or females were 23% or 15% lower than that of controls. During the exposure to 2-chloroacetophenone, rats had dacryorrhea and dyspnea; erythema was seen in all rats exposed to 10, 19, 43, or 64 mg/m^3; and partially closed eyelids were observed in all rats exposed to 19, 43, or 64 mg/m^3. Epistaxis was seen in two exposed males and seven exposed females.

THIRTEEN-WEEK STUDIES

All rats lived to the end of the studies (Table 4). The final mean body weights of male or female rats exposed to 4 mg/m^3 were 9% lower than those of controls. Compound-related clinical signs in rats exposed to 0.5 mg/m^3 or higher concentrations of 2-chloroacetophenone included eye irritation during exposure. The liver weight to body weight ratio for female rats exposed to 4 mg/m^3 was slightly greater than that for controls; however, exposure had no effect on absolute liver weights. No compound-related lesions were observed.

TABLE 3. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-DAY INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Concentration (mg/m^3)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	5/5	146 ± 3	204 ± 5	+58 ± 6	
4.8	5/5	132 ± 4	157 ± 7	+25 ± 5	77
10	(d) 4/5	122 ± 4	103 ± 4	−18 ± 3	50
19	(e) 0/5	130 ± 3	(f)	(f)	(f)
43	(g) 0/5	131 ± 4	(f)	(f)	(f)
64	(h) 0/5	143 ± 3	(f)	(f)	(f)
FEMALE					
0	5/5	113 ± 2	144 ± 3	+31 ± 2	
4.8	5/5	110 ± 5	123 ± 5	+13 ± 3	85
10	5/5	100 ± 4	84 ± 3	−16 ± 3	58
19	(i) 0/5	115 ± 3	(f)	(f)	(f)
43	(j) 0/5	106 ± 1	(f)	(f)	(f)
64	(k) 0/5	115 ± 4	(f)	(f)	(f)

(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 studies.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Day of death: 8
(e) Day of death: 4,5,5,6,6
(f) No data are reported due to 100% mortality in this group.
(g) Day of death: 2,2,3,4,4
(h) Day of death: 2,2,2,2,3
(i) Day of death: 5,5,5,6,7
(j) Day of death: 3,4,4,4,4
(k) Day of death: all 2

TABLE 4. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE THIRTEEN-WEEK INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Concentration (mg/m^3)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	187 ± 5	359 ± 4	+172 ± 4	
0.25	10/10	178 ± 5	358 ± 4	+180 ± 5	100
0.5	10/10	185 ± 6	365 ± 11	+180 ± 8	102
1	10/10	170 ± 6	364 ± 4	+194 ± 8	101
2	10/10	166 ± 5	348 ± 8	+182 ± 6	97
4	10/10	194 ± 4	328 ± 5	+134 ± 6	91
FEMALE					
0	10/10	139 ± 2	(d) 213 ± 4	+74 ± 4	
0.25	10/10	139 ± 3	204 ± 6	+65 ± 4	96
0.5	10/10	139 ± 3	206 ± 3	+67 ± 1	97
1	10/10	138 ± 2	211 ± 4	+73 ± 3	99
2	10/10	137 ± 3	211 ± 4	+74 ± 3	99
4	10/10	135 ± 3	194 ± 4	+59 ± 2	91

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean. Subsequent calculations based on animals weighed at theend of the study.
(c) Mean body weight change of the animals weighed at the end of the study ± standard error of the mean
(d) The final body weight was not recorded for one animal.

Dose Selection Rationale: Because of the lower weight gains at 4 mg/m^3 in the 13-week studies and the mortality and body weight effects at higher concentrations in the 14-day studies, exposure concentrations selected for rats for the 2-year studies were 1 and 2 mg/m^3, 6 hours per day, 5 days per week.

FIFTEEN-MONTH STUDIES

The liver, brain, or kidney weights and the hematology data were not clearly affected by exposure to 2-chloroacetophenone (Table 5). The lymphocyte count of male rats exposed to 2 mg/m^3 was significantly greater than that of chamber controls (Table G1). Minimal-to-mild focal squamous metaplasia and hyperplasia of the respiratory epithelium were seen at increased incidences in rats exposed to 2 mg/m^3 (metaplasia--male: control, 0/10; 1 mg/m^3, 0/10; 2 mg/m^3, 2/10; female: 0/10; 0/10; 3/10; hyperplasia--male: 0/10; 1/10; 5/10; female: 1/10; 1/10; 9/10). The lesions were similar to those observed in the 2-year studies (see p. 34). One female rat exposed at 2 mg/m^3 had a mammary gland fibroadenoma.

TABLE 5. ORGAN WEIGHT TO BODY WEIGHT RATIOS FOR RATS IN THE FIFTEEN-MONTH INHALATION STUDIES OF 2-CHLOROACETOPHENONE (a)

Organ	Chamber Control	1 mg/m^3	2 mg/m^3
MALE			
Body weight (grams)	474 ± 6.6	487 ± 9.5	471 ± 10.8
Liver	32.8 ± 0.75	30.7 ± 0.47	31.9 ± 0.98
Brain	4.1 ± 0.07	4.1 ± 0.09	4.1 ± 0.07
Right kidney	6.5 ± 0.20	6.2 ± 0.10	6.0 ± 0.11
FEMALE			
Body weight (grams)	326 ± 8.9	*296 ± 6.5	315 ± 10.5
Liver	32.8 ± 0.65	32.5 ± 1.44	30.8 ± 0.85
Brain	5.6 ± 0.11	*6.1 ± 0.15	5.9 ± 0.18
Right kidney	6.2 ± 0.17	6.5 ± 0.29	6.1 ± 0.12

(a) Mean ± standard error in milligrams per gram unless otherwise specified for groups of 10 animals; P values vs. the controls by Dunn's test (Dunn, 1964) or Shirley's test (Shirley, 1977).
*P<0.05

TWO-YEAR STUDIES

Sentinel Animal Program

Results of the tests for serum antibodies to murine infectious organisms are shown in Appendix E. Positive serologic reactions were seen for pneumonia virus of mice (PVM) in 1/10 sentinel rats at month 6 and in 2/10 at month 22, for *mycoplasma arthritidis* in 2/10 rats at month 24, and for rat coronavirus or sialodacryoadenitis virus (RCV/SDA) at all timepoints sampled. There was no evidence of clinical disease associated with these positive serologic reactions in sentinel rats or in any of the rats studied. Similarly, there were no histologic lesions that could be attributed to infection with these organisms.

Body Weights and Clinical Signs

Mean body weights of exposed and chamber control rats were similar throughout most of the studies (Table 6 and Figure 1). No compound-related clinical signs were observed.

TABLE 6. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Weeks on Study	Chamber Control		1 mg/m^3			2 mg/m^3		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of chamber controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of chamber controls)	No. of Survivors
MALE								
0	217	50	213	98	50	217	100	50
1	229	50	229	100	50	232	101	50
2	248	50	252	102	50	250	101	50
3	263	50	266	101	50	266	101	50
4	274	50	280	102	50	278	101	50
5	287	50	293	102	50	290	101	50
6	299	50	311	104	50	306	102	50
7	312	50	322	103	50	316	101	50
8	323	50	331	102	50	325	101	50
9	333	50	336	101	50	335	101	50
10	337	50	351	104	50	342	101	50
11	346	50	356	103	50	348	101	50
12	352	50	363	103	50	357	101	50
17	385	50	396	103	50	388	101	50
21	396	50	418	106	50	407	103	50
25	412	50	426	103	50	419	102	50
29	429	50	438	102	50	432	101	50
33	437	50	451	103	50	442	101	50
38	441	50	452	102	49	441	100	50
43	449	50	455	101	49	445	99	50
47	454	49	464	102	49	454	100	49
52	461	49	473	103	49	467	101	49
56	467	49	477	102	49	470	101	49
61	471	48	481	102	49	475	101	49
65	478	44	487	102	48	478	100	48
68	482	44	490	102	48	480	100	48
72	486	44	490	101	48	485	100	46
76	488	44	492	101	47	475	97	44
81	489	44	490	100	43	484	99	38
86	495	38	497	100	39	486	98	36
90	490	34	489	100	37	482	98	32
94	472	31	486	103	34	474	100	29
98	471	25	476	101	31	463	98	25
103	456	17	468	103	24	453	99	19
Mean for Weeks								
1-12	300		307	102		304	101	
17-52	429		441	103		433	101	
56-103	479		485	101		475	99	
FEMALE								
0	147	50	148	101	50	150	102	50
1	156	50	159	102	50	161	103	50
2	163	50	168	103	50	169	104	50
3	169	50	173	102	50	175	104	50
4	174	50	179	103	50	179	103	50
5	179	50	182	102	50	184	103	50
6	185	50	189	102	50	190	103	50
7	190	50	194	102	50	196	103	50
8	196	49	197	101	50	199	102	50
9	199	49	200	101	50	200	101	50
10	201	49	204	101	50	205	102	50
11	204	49	205	100	50	206	101	50
12	209	49	210	100	50	211	101	50
17	(a) 220	49	226	114	50	226	114	50
21	234	49	235	100	50	236	101	50
25	240	49	245	102	50	246	103	50
29	253	49	254	100	50	254	100	50
33	261	49	266	102	50	263	101	50
38	274	49	274	100	50	271	99	49
43	276	49	278	101	50	273	99	49
47	286	49	288	101	50	285	100	49
52	300	49	303	101	50	300	100	49
56	310	49	307	99	50	306	99	49
61	316	49	314	99	50	316	100	49
65	324	49	326	101	50	320	99	49
68	326	48	327	100	50	320	98	49
72	335	48	338	101	50	323	96	46
76	340	48	340	100	49	336	99	42
81	341	47	347	102	47	342	100	41
86	352	38	348	99	47	350	99	40
90	346	37	345	100	42	345	100	37
94	351	33	348	99	34	343	98	37
98	352	29	339	96	30	344	98	30
103	352	25	335	95	22	338	96	25
Mean for Weeks								
1-12	185		188	102		190	103	
17-52	260		263	101		262	101	
56-103	337		334	99		332	99	

(a) Based on weights of 26 animals

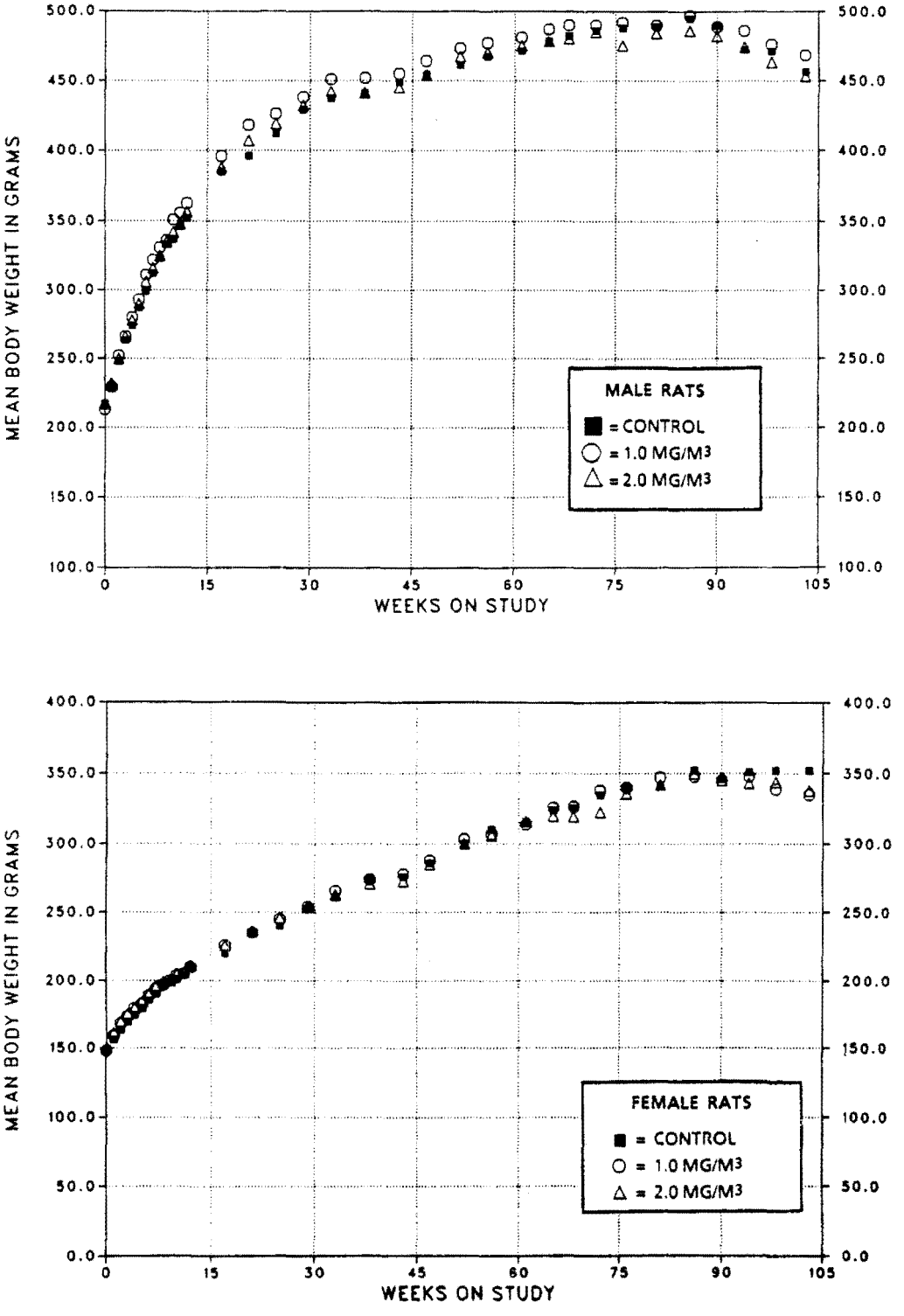

FIGURE 1. GROWTH CURVES FOR RATS EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female rats exposed to 2-chloroacetophenone at the concentrations used in these studies and for chamber controls are shown in Table 7 and in the Kaplan and Meier curves in Figure 2. No significant differences in survival were observed between any groups of either sex. Survival was lower than usual for 2-year studies in F344/N rats; however, at week 90, survival was 64%-74% for males and 74%-84% for females.

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 mammary gland, anterior pituitary gland, parathyroid gland, nasal passage, and forestomach.

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.

Mammary Gland: Fibroadenomas in female rats occurred with a positive trend; the incidence

TABLE 7. SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE

	Chamber Control	1 mg/m^3	2 mg/m^3
MALE (a)			
Animals initially in study	50	50	50
Natural deaths	10	6	9
Moribund kills	26	22	24
Animals surviving until study termination	14	22	17
Mean survival (days)	652	669	651
Survival P values (b)	0.815	0.183	0.851
FEMALE (a)			
Animals initially in study	50	50	50
Natural deaths	5	2	4
Moribund kills	22	28	22
Animals surviving until study termination	23	20	24
Mean survival (days)	667	686	667
Survival P values (b)	0.874	0.932	0.945

(a) First day of termination period: 735
(b) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

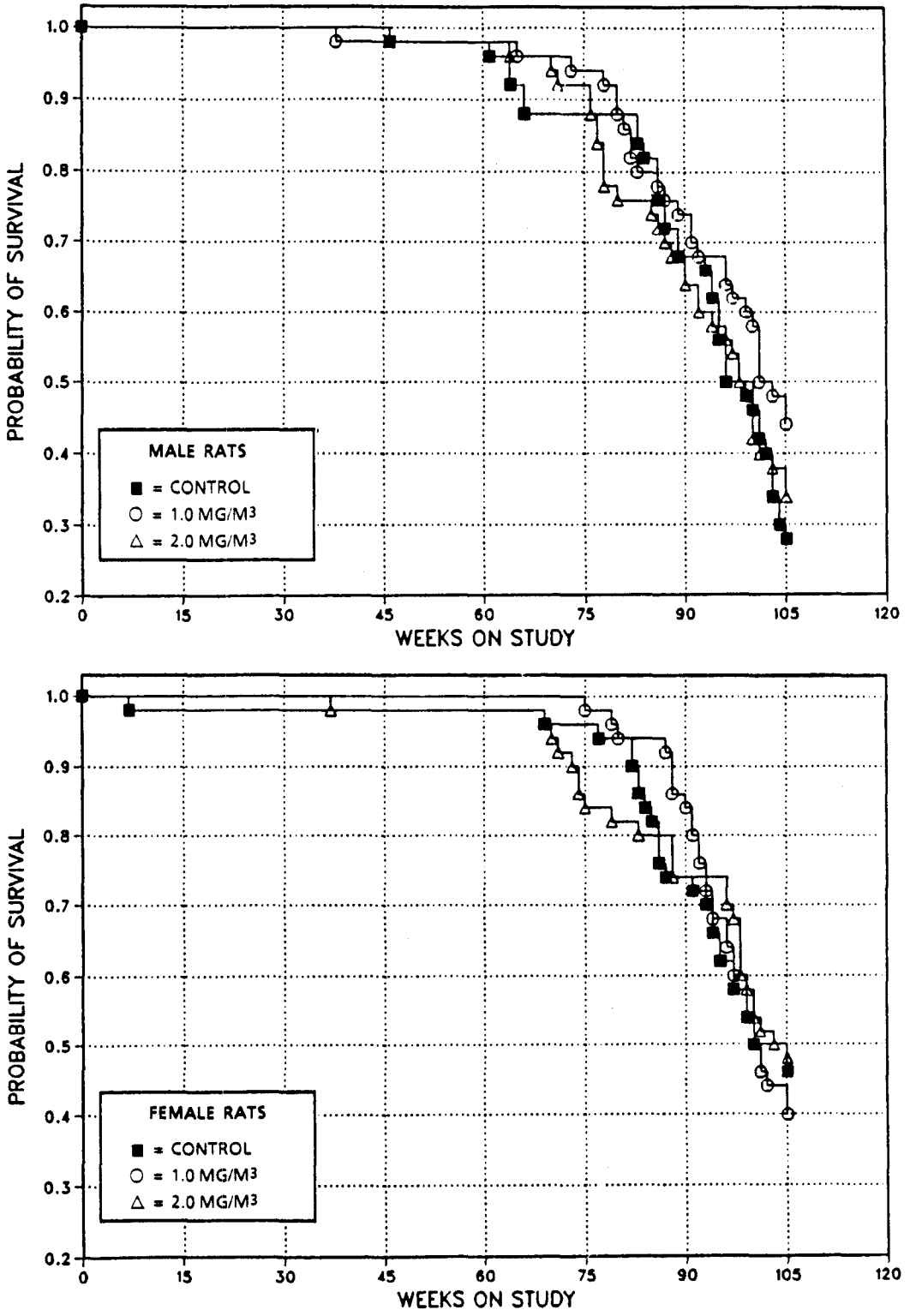

FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR RATS EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS

in the group exposed to 2 mg/m^3 was increased relative to that in chamber controls (Table 8). Adenomas or adenocarcinomas were not increased in exposed female rats. The incidences of fibroadenomas in groups exposed to 1 or 2 mg/m^3 exceeded the highest incidences previously observed in chamber controls at the study laboratory but not the highest observed in untreated historical controls at all laboratories combined (Table B4a).

Lesions diagnosed as hyperplasia were focal groups of small or medium ducts/ductules with prominent epithelium; some were prominently dilated. These lesions are common in aged female rats and are not part of a morphologic continuum with fibroadenomas. Fibroadenomas were well-circumscribed benign neoplasms consisting of acini and ductules of well-differentiated epithelium separated by abundant but variable amounts of dense connective tissue (Figure 3). The adenomas were composed of similar epithelial structures but lacked the proliferating connective tissue stroma seen in the fibroadenomas. The adenocarcinomas were poorly circumscribed malignant neoplasms with variable growth patterns. They were distinguished from adenomas by the degree of differentiation of the glandular epithelium and by the degree of cellular pleomorphism and atypia.

TABLE 8. MAMMARY GLAND LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (a)

	Chamber Control	1 mg/m^3	2 mg/m^3
Hyperplasia			
Overall Rates	6/48 (13%)	9/50 (18%)	11/50 (22%)
Fibroadenoma			
Overall Rates	12/50 (24%)	19/50 (38%)	23/50 (46%)
Terminal Rates	8/23 (35%)	11/20 (55%)	11/24 (46%)
Day of First Observation	533	553	490
Logistic Regression Tests	P=0.013	P=0.117	P=0.017
Adenoma			
Overall Rates	0/50 (0%)	2/50 (4%)	1/50 (2%)
Fibroadenoma or Adenoma			
Overall Rates	12/50 (24%)	20/50 (40%)	23/50 (46%)
Terminal Rates	8/23 (35%)	11/20 (55%)	11/24 (46%)
Day of First Observation	533	553	490
Logistic Regression Tests	P=0.013	P=0.082	P=0.017
Adenocarcinoma			
Overall Rates	2/50 (4%)	2/50 (4%)	1/50 (2%)
Fibroadenoma, Adenoma, or Adenocarcinoma (b)			
Overall Rates	13/50 (26%)	22/50 (44%)	23/50 (46%)
Terminal Rates	9/23 (39%)	11/20 (55%)	11/24 (46%)
Day of First Observation	533	553	490
Logistic Regression Tests	P=0.022	P=0.058	P=0.028

(a) For a complete explanation of the entries in this table, see Table B3 (footnotes); the statistical analyses used are discussed in Section II (Statistical Methods).
(b) Historical incidence for chamber controls at study laboratory (mean ± SD): 76/349 (22% ± 9%); historical incidence for untreated controls in NTP studies: 552/1,643 (34% ± 12%)

Anterior Pituitary Gland: The incidences of adenomas and adenomas or carcinomas (combined) in the pars distalis of female rats exposed to 1 mg/m^3 were marginally greater than those in chamber controls; the incidences of hyperplasia were lower in the exposed females than in the controls (Table 9).

Parathyroid Gland: Adenomas were seen in 2/33 male rats exposed to 1 mg/m^3 and 1/44 male rats exposed to 2 mg/m^3.

Nasal Passage: Suppurative inflammation of the nasal mucosa was observed at increased incidences in exposed male, but not female, rats (Table 10). The inflammation was focal, generally minimal to mild in severity, and characterized by an infiltrate of neutrophils and variable numbers of macrophages in the lamina propria (Figure 4). Minimal-to-mild hyperplasia and squamous metaplasia of the respiratory epithelium occurred at increased incidences in exposed male and female rats. The mean severity of the hyperplasia in females and squamous metaplasia in males and females also was greater in the 2 mg/m^3 rats. Hyperplasia of the respiratory epithelium was characterized by increased cellularity (primarily goblet cells) and by height of the cells, especially in the dorsolateral region of the nasal passage, the naso-turbinates, and the nasal septum (Figure 5). Squamous metaplasia consisted of foci of two to six layers of nonkeratinized squamous epithelial cells, most frequently located along the margins of the naso- and maxilloturbinates.

Although compound-related nonneoplastic effects were observed in the nasal passage, no primary epithelial neoplasms were seen in the nasal passage of chamber control or exposed rats. A fibrosarcoma occurred in the nasal passage of a control female.

Forestomach: Inflammation, ulcers, and squamous hyperplasia (Figure 6) were observed at increased incidences in exposed female rats (Table 10). No forestomach neoplasms were observed in exposed or chamber control rats of either sex.

TABLE 9. ANTERIOR PITUITARY GLAND LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (a)

	Chamber Control	1 mg/m^3	2 mg/m^3
Hyperplasia			
Overall Rates	13/49 (27%)	6/48 (13%)	7/49 (14%)
Adenoma			
Overall Rates	27/49 (55%)	40/48 (83%)	30/49 (61%)
Terminal Rates	14/23 (61%)	14/18 (78%)	19/24 (79%)
Day of First Observation	533	553	512
Logistic Regression Tests	P=0.270	P=0.003	P=0.316
Carcinoma			
Overall Rates	3/49 (6%)	0/48 (0%)	5/49 (10%)
Adenoma or Carcinoma (b)			
Overall Rates	30/49 (61%)	40/48 (83%)	35/49 (71%)
Terminal Rates	16/23 (70%)	14/18 (78%)	21/24 (88%)
Day of First Observation	533	553	512
Logistic Regression Tests	P=0.124	P=0.018	P=0.160

(a) For a complete explanation of the entries in this table, see Table B3 (footnotes); the statistical analyses used are discussed in Section II (Statistical Methods).
(b) Historical incidence for chamber controls at study laboratory (mean ± SD): 181/340 (53% ± 8%); historical incidence for untreated controls in NTP studies: 771/1,617 (48% ± 11%)

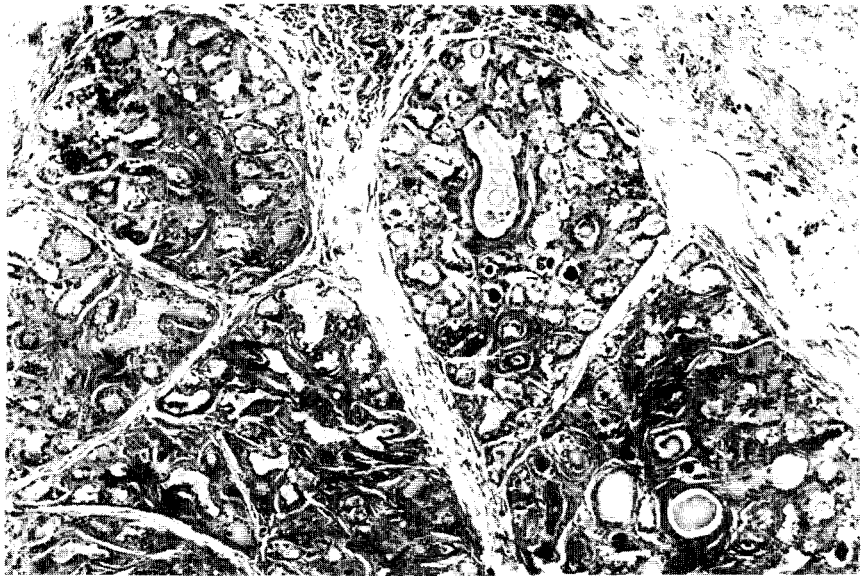

Figure 3. Mammary gland fibroadenoma in a female F344/N rat exposed to 1 mg/m^3 2-chloroacetophenone by inhalation for 2 years.

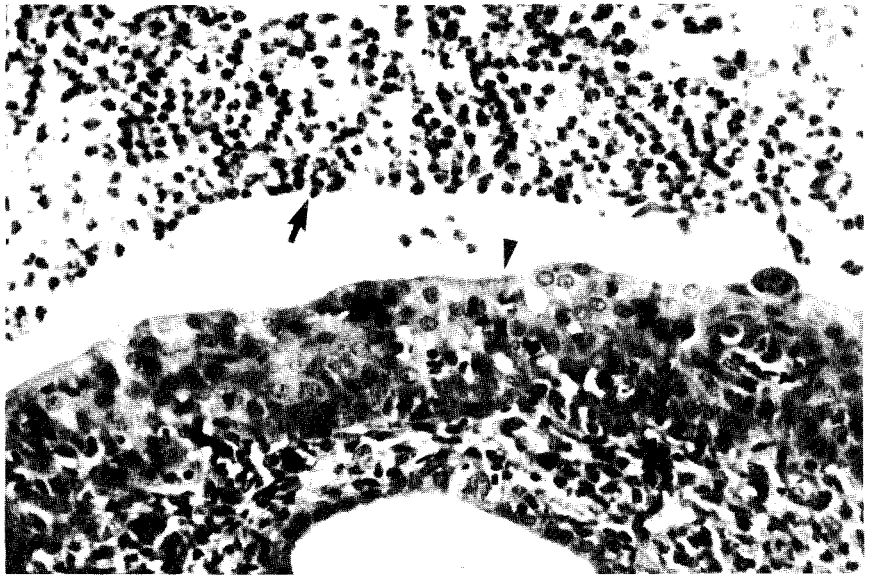

Figure 4. Suppurative inflammation and squamous metaplasia of the nasal passage in a male F344/N rat exposed to 2 mg/m^3 2-chloroacetophenone by inhalation for 2 years. Exudate composed primarily of neutrophils is present in the lumen (arrow), whereas the underlying nasal epithelium has undergone metaplasia to stratified squamous epithelium (arrowhead).

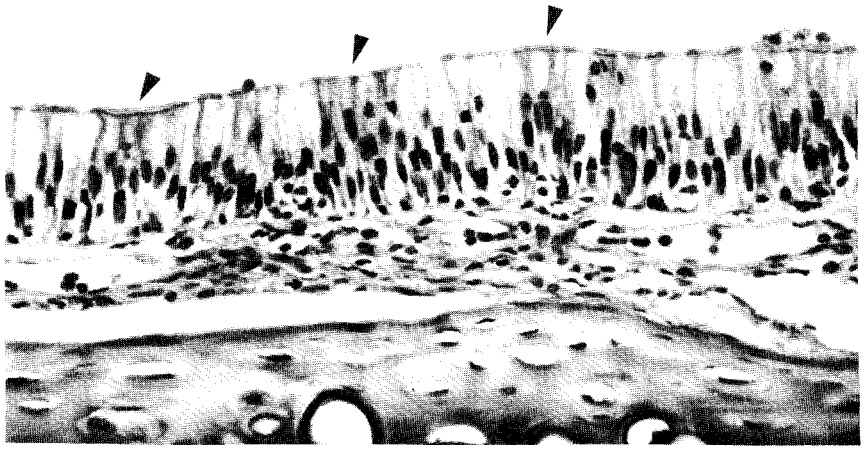

Figure 5. Hyperplasia of the respiratory epithelium of the nasal passage in a female F344/N rat exposed to 1 mg/m^3 2-chloroacetophenone by inhalation for 2 years. The epithelium is thickened and hypercellular. Cilia are evident along the luminal surfaces of the epithelial cells (arrowheads).

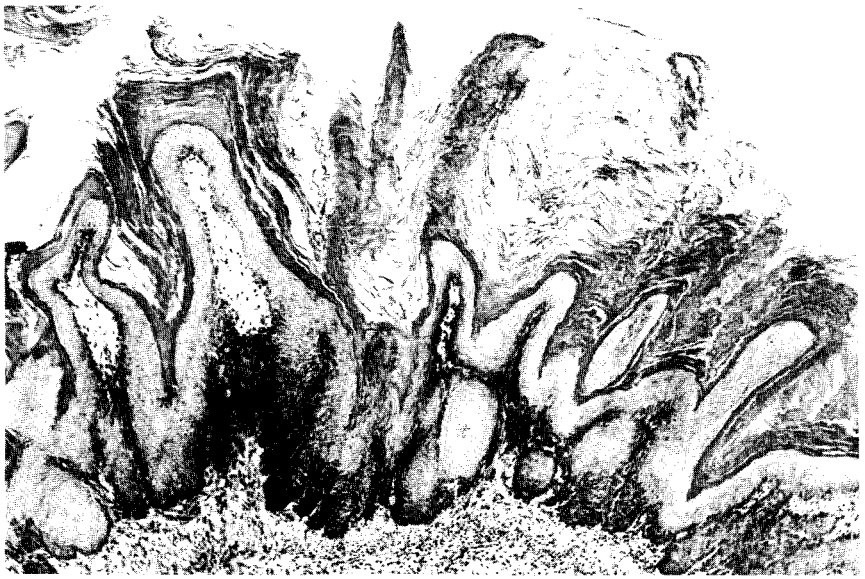

Figure 6. Marked hyperplasia of the stratified squamous epithelium of the forestomach in a female F344/N rat exposed to 1 mg/m^3 2-chloroacetophenone by inhalation for 2 years. The epithelium is thickened, highly folded, and covered by a thick layer of keratin.

TABLE 10. NUMBERS OF RATS WITH SELECTED LESIONS OF THE NASAL PASSAGE AND FORESTOMACH IN THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE (a)

Site/Lesion	Male			Female		
	Chamber Control	1 mg/m^3	2 mg/m^3	Chamber Control	1 mg/m^3	2 mg/m^3
Nasal passage						
Suppurative inflammation	26	36	**46	29	27	33
Nasal respiratory epithelium						
Hyperplasia	12 (1.5)	17 (1.3)	**44 (1.6)	20 (1.2)	*31 (1.5)	**38 (2.2)
Squamous metaplasia	2 (1.0)	*11 (1.3)	**27 (1.8)	1 (1.0)	*7 (1.6)	**26 (1.7)
Number examined	46	50	49	48	50	49
Forestomach						
Inflammation	4	3	6	1	*7	*8
Ulcer	4	2	3	1	4	5
Squamous hyperplasia	6	4	7	2	6	8
Number examined	46	49	49	47	49	49

(a) Number of animals with specified lesion; mean severity grade (1 = minimal; 2 = mild; 3 = moderate; 4 = marked) for animals with lesion is in parentheses; P values vs. controls by Fisher exact test.
*P<0.05
**P<0.01

FOURTEEN-DAY STUDIES

All mice exposed to 10 mg/m^3 or more died before the end of the studies (Table 11). The final mean body weights of mice exposed to 4.8 mg/m^3 were similar to those of controls. During the exposure to 2-chloroacetophenone, mice had dacryorrhea. Reddened lungs were seen in 7 exposed males and 2 exposed females that died. No compound-related lesions were seen in mice exposed to 4.8 mg/m^3.

THIRTEEN-WEEK STUDIES

One of 10 female mice exposed to 4 mg/m^3 and 1/10 female mice exposed to 0.5 mg/m^3 died before the end of the studies (Table 12). The final mean body weights of exposed mice were 7%-12% lower than those of chamber controls for males and 12%-15% lower for females. Compound-related clinical signs in mice exposed to 0.5 mg/m^3 or higher concentrations of 2-chloroacetophenone included eye irritation during exposure. No compound-related lesions were observed.

Dose Selection Rationale: Because of 100% mortality in mice exposed to 10 mg/m^3 in the 14-day studies and the absence of effects at 4 mg/m^3 in the 13-week studies, exposure concentrations selected for mice for the 2-year studies were 2 and 4 mg/m^3, 6 hours per day, 5 days per week.

FIFTEEN-MONTH STUDIES

Relative liver, brain, and kidney weights were not clearly affected by exposure to 2-chloroacetophenone (Table 13). Hematologic findings were not considered biologically meaningful (Table G2). No exposure-related lesions were observed in mice of either sex.

TABLE 11. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Concentration (mg/m^3)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	5/5	24.0 ± 0.6	25.8 ± 0.6	+1.8 ± 0.4	
4.8	5/5	24.6 ± 1.3	25.6 ± 1.0	+1.0 ± 0.3	99
10	(d) 0/5	24.0 ± 0.7	(e)	(e)	(e)
19	(f) 0/5	23.6 ± 0.7	(e)	(e)	(e)
43	(g) 0/5	23.6 ± 0.6	(e)	(e)	(e)
64	(h) 0/5	23.4 ± 0.7	(e)	(e)	(e)
FEMALE					
0	5/5	20.2 ± 0.5	23.2 ± 0.7	+3.0 ± 0.3	
4.8	5/5	20.6 ± 0.7	22.4 ± 1.2	+1.8 ± 0.6	97
10	(i) 0/5	20.4 ± 0.7	(e)	(e)	(e)
19	(j) 0/5	18.2 ± 0.4	(e)	(e)	(e)
43	(f) 0/5	18.8 ± 0.5	(e)	(e)	(e)
64	(h) 0/5	21.0 ± 0.8	(e)	(e)	(e)

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean
(c) Mean body weight change of the group ± standard error of the mean
(d) Day of death: all 7
(e) No data are reported due to 100% mortality in this group.
(f) Day of death: 4,5,5,5,5
(g) Day of death: 3,4,4,4,5
(h) Day of death: all 2
(i) Day of death: 5,5,6,6,6
(j) Day of death: all 5

TABLE 12. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE THIRTEEN-WEEK INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Concentration (mg/m^3)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	23.8 ± 0.3	33.8 ± 0.9	+10.0 ± 0.6	
0.25	10/10	24.0 ± 0.4	31.0 ± 1.1	+7.0 ± 1.1	92
0.5	10/10	23.6 ± 0.3	31.5 ± 0.5	+7.9 ± 0.7	93
1	10/10	24.0 ± 0.4	29.8 ± 0.7	+5.8 ± 0.9	88
2	10/10	22.5 ± 0.6	30.7 ± 0.8	+8.2 ± 0.6	91
4	10/10	23.9 ± 0.4	31.2 ± 0.9	+7.3 ± 0.6	92
FEMALE					
0	10/10	19.5 ± 0.4	(d) 31.0 ± 0.6	+11.4 ± 0.5	
0.25	10/10	20.3 ± 0.2	26.3 ± 0.7	+6.0 ± 0.7	85
0.5	(e) 9/10	20.2 ± 0.2	26.8 ± 0.8	+6.7 ± 0.7	86
1	10/10	19.8 ± 0.4	26.9 ± 0.8	+7.1 ± 0.7	87
2	10/10	20.1 ± 0.5	27.2 ± 0.4	+7.1 ± 0.5	88
4	(f) 9/10	20.2 ± 0.4	27.4 ± 0.6	+7.2 ± 0.4	88

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean. Subsequent calculations based on animals weighed at the end of the study.
(c) Mean body weight change of animals weighed at the end of the study ± standard error of the mean
(d) The final mean body weight was not recorded for one animal.
(e) Week of death: 1
(f) Week of death: 4

TABLE 13. ORGAN WEIGHT TO BODY WEIGHT RATIOS FOR MICE IN THE FIFTEEN-MONTH INHALATION STUDIES OF 2-CHLOROACETOPHENONE (a)

Organ	Chamber Control	2 mg/m^3	4 mg/m^3
MALE			
Number weighed	10	9	10
Body weight (grams)	36.9 ± 0.57	36.5 ± 1.02	34.4 ± 1.11
Brain	12.6 ± 0.17	12.8 ± 0.41	13.3 ± 0.44
Liver	51.6 ± 2.07	57.3 ± 9.43	51.9 ± 4.75
Right kidney	21.6 ± 0.50	21.5 ± 0.70	21.9 ± 0.62
FEMALE			
Number weighed	9	10	9
Body weight (grams)	32.8 ± 1.12	34.7 ± 1.22	31.2 ± 1.72
Brain	14.6 ± 0.46	14.5 ± 0.45	*16.8 ± 0.98
Liver	53.4 ± 1.30	**48.6 ± 1.56	*49.4 ± 0.95
Right kidney	15.3 ± 0.54	14.9 ± 0.40	15.9 ± 0.81

(a) Mean ± standard error in milligrams per gram unless otherwise specified; P values vs. the controls by Dunn's test (1964) or Shirley's test (Shirley, 1977).
*$P<0.05$
**$P<0.01$

TWO-YEAR STUDIES

Sentinel Animal Program

Results of the tests for serum antibodies to murine infectious organisms are shown in Appendix E. There was a positive serologic reaction for Sendai in 1/10 mice at month 6. Since samples from mice after month 6 and all samples from rats were negative for this viral infection, it was considered to be a false positive. No clinical signs or lesions of this disease were observed.

Body Weights and Clinical Signs

Mean body weights of male mice exposed to 4 mg/m^3 were 5%-12% lower than those of chamber controls after week 30; small differences between mean body weights of exposed female mice and those of chamber controls were not clearly exposure related (Table 14 and Figure 7). Rapid, shallow breathing of mice exposed to 4 mg/m^3 was observed for the first 6 months of the studies and for mice of each sex exposed to 2 mg/m^3 from months 3 through 6.

TABLE 14. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Weeks on Study	Chamber Control		2 mg/m^3			4 mg/m^3		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of chamber controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of chamber controls)	No. of Survivors
MALE								
0	27.5	50	28.3	103	50	27.6	100	50
1	29.0	50	29.2	101	50	28.5	98	50
2	28.7	50	28.9	101	50	28.4	99	50
3	28.6	50	28.5	100	50	26.8	94	50
4	28.6	50	28.7	100	50	28.8	101	50
5	30.4	50	29.8	98	50	29.1	96	50
6	30.7	50	30.3	99	50	29.5	96	50
7	30.6	50	30.6	100	50	30.4	99	50
8	31.0	50	30.5	98	50	30.1	97	50
9	31.0	50	31.0	100	50	30.3	98	50
10	32.0	50	31.4	98	50	31.0	97	50
11	31.3	50	30.4	97	50	31.3	100	50
12	31.1	50	30.8	99	50	31.1	100	50
18	34.8	50	34.0	98	50	33.3	96	50
22	35.7	50	33.6	94	50	34.0	95	50
26	34.9	50	34.4	99	50	33.7	97	49
30	35.9	50	36.0	100	50	34.0	95	49
34	36.7	50	35.3	96	50	34.6	94	49
39	37.0	50	36.3	98	50	35.3	95	49
44	37.4	50	36.6	98	50	35.6	95	49
48	38.5	50	37.0	96	50	34.7	90	49
53	38.4	50	38.0	99	50	36.3	95	48
57	38.2	50	37.6	98	50	35.6	93	48
62	38.5	50	37.3	97	50	36.0	94	47
66	38.6	50	37.8	98	50	35.1	91	46
69	38.7	50	37.8	98	49	33.9	88	46
73	39.8	50	38.6	97	48	36.5	92	46
77	40.0	47	37.5	94	43	36.9	92	46
82	40.0	47	38.8	97	42	37.3	93	46
87	39.4	45	38.2	97	41	36.8	93	44
91	39.9	45	39.2	98	40	37.0	93	43
95	38.4	44	38.1	99	39	36.0	94	40
99	37.3	42	37.6	101	38	35.4	95	37
104	37.4	35	37.2	99	37	35.1	94	34
Mean for weeks								
1-12	30.3		30.0	99		29.6	98	
18-48	36.4		35.4	97		34.4	95	
53-104	38.8		38.0	98		36.0	93	
FEMALE								
0	22.6	50	22.6	100	50	21.4	95	50
1	24.1	50	24.0	100	50	22.6	94	50
2	23.6	50	23.8	101	50	23.4	99	50
3	24.0	50	23.9	100	50	23.6	98	50
4	24.9	50	24.7	99	50	24.3	98	50
5	25.7	50	25.4	99	50	25.4	99	50
6	26.1	50	26.0	100	50	25.2	97	50
7	27.3	50	26.9	99	50	26.3	96	50
8	27.2	50	27.0	99	50	25.3	93	50
9	27.7	50	27.8	100	50	26.3	95	50
10	27.3	50	27.3	100	50	27.2	100	50
11	28.1	50	28.6	102	50	28.6	102	50
12	28.3	50	28.9	102	50	27.5	97	50
18	30.0	50	29.9	100	50	29.0	97	50
22	33.8	50	29.8	88	50	30.0	89	50
26	32.5	50	30.2	93	50	30.5	94	50
30	33.3	50	32.8	98	50	31.1	93	50
34	33.5	50	31.4	94	49	31.6	94	50
39	33.5	50	32.7	98	49	32.2	96	50
44	33.1	50	32.7	99	49	31.1	94	50
48	35.5	50	34.7	98	49	32.2	91	50
53	35.1	50	34.5	98	48	34.2	97	49
57	35.1	50	35.1	100	48	34.0	97	48
62	35.0	49	34.9	100	47	33.5	96	47
66	34.8	49	36.0	103	47	33.9	97	47
69	34.9	48	36.3	104	47	33.7	97	46
73	34.2	48	35.8	105	46	33.8	99	45
77	35.1	47	36.1	103	46	35.1	100	44
82	35.6	47	36.7	103	44	35.7	100	43
87	35.5	45	37.9	107	42	36.0	101	41
91	35.7	45	38.8	109	40	35.8	100	39
95	35.7	43	37.5	105	35	34.7	97	36
99	36.5	43	36.5	100	31	35.7	98	34
104	35.9	40	36.9	103	28	35.3	98	32
Mean for weeks								
1-12	26.2		26.2	100		25.5	97	
18-48	33.2		31.8	96		31.0	93	
53-104	35.3		36.4	103		34.7	98	

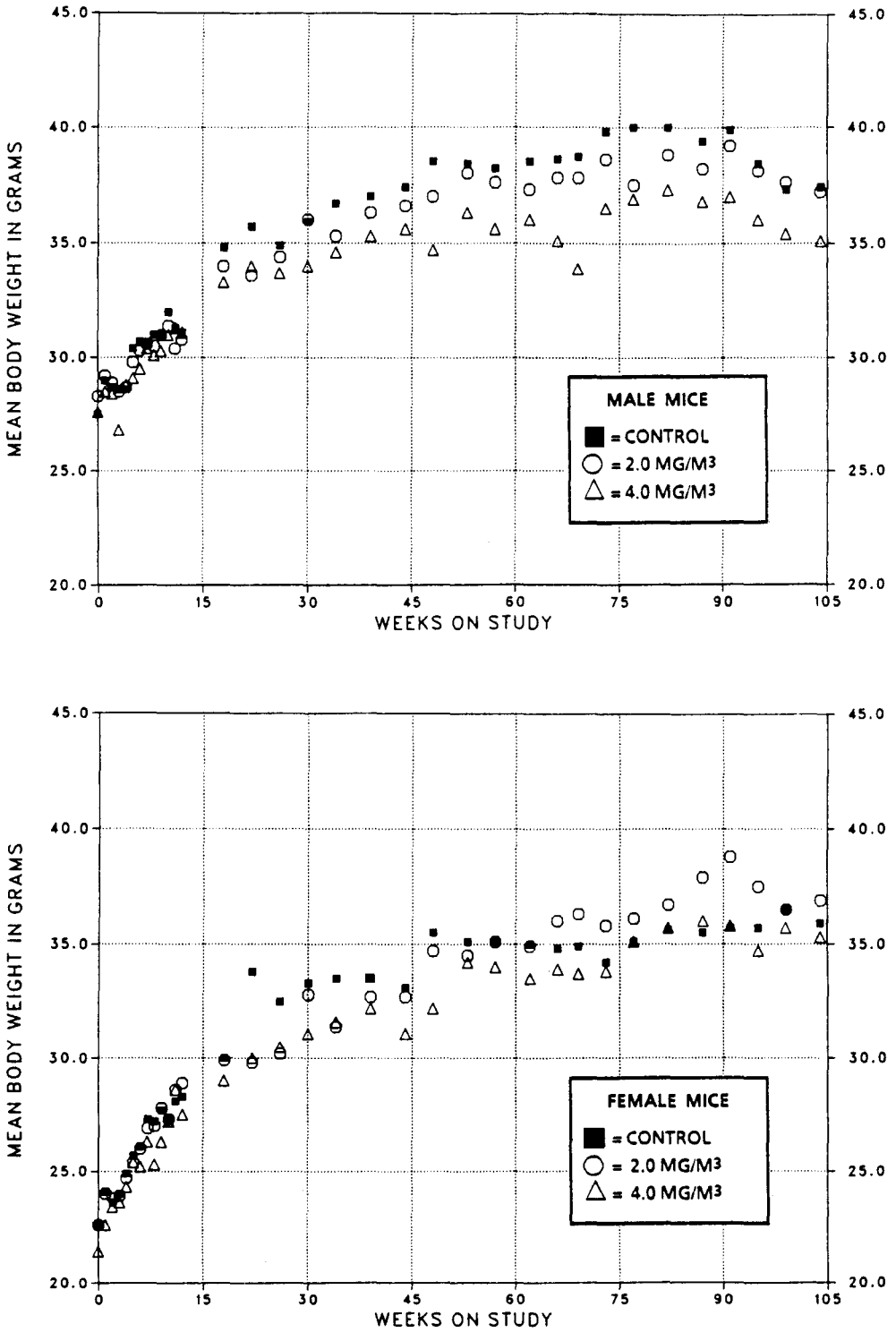

FIGURE 7. GROWTH CURVES FOR MICE EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female mice exposed to 2-chloroacetophenone at the concentrations used in these studies and for chamber controls are shown in Table 15 and in the Kaplan and Meier curves in Figure 8. The survival of female mice exposed to 2 mg/m^3 was significantly lower than that of chamber controls after week 98. No other differences in survival were observed between any groups.

Pathology and Statistical Analyses of Results

This section describes the biologically noteworthy changes in the incidences of mice with nonneoplastic lesions of the nasal passage. No statistically significant increases in the incidences of neoplastic lesions were observed.

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

Nasal Passage: Squamous metaplasia of the respiratory epithelium was seen in 4/49 female and 2/48 male mice exposed to 4 mg/m^3 2-chloroacetophenone. It was characterized by foci of nonkeratinized squamous epithelium two to six cell layers thick, usually located on the margins of the naso- or maxilloturbinates.

TABLE 15. SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE

	Chamber Control	2 mg/m^3	4 mg/m^3
MALE (a)			
Animals initially in study	50	50	50
Natural deaths	5	9	11
Moribund kills	11	5	6
Animals surviving until study termination	34	36	33
Mean survival (days)	711	692	689
Survival P values (b)	0.807	0.982	0.869
FEMALE (a)			
Animals initially in study	50	50	50
Natural deaths	2	(c) 10	8
Moribund kills	8	13	10
Animals surviving until study termination	40	28	32
Mean survival (days)	709	676	678
Survival P values (b)	0.095	0.017	0.099

(a) First day of termination period: male--736; female--735
(b) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.
(c) Includes one animal dying during the termination period

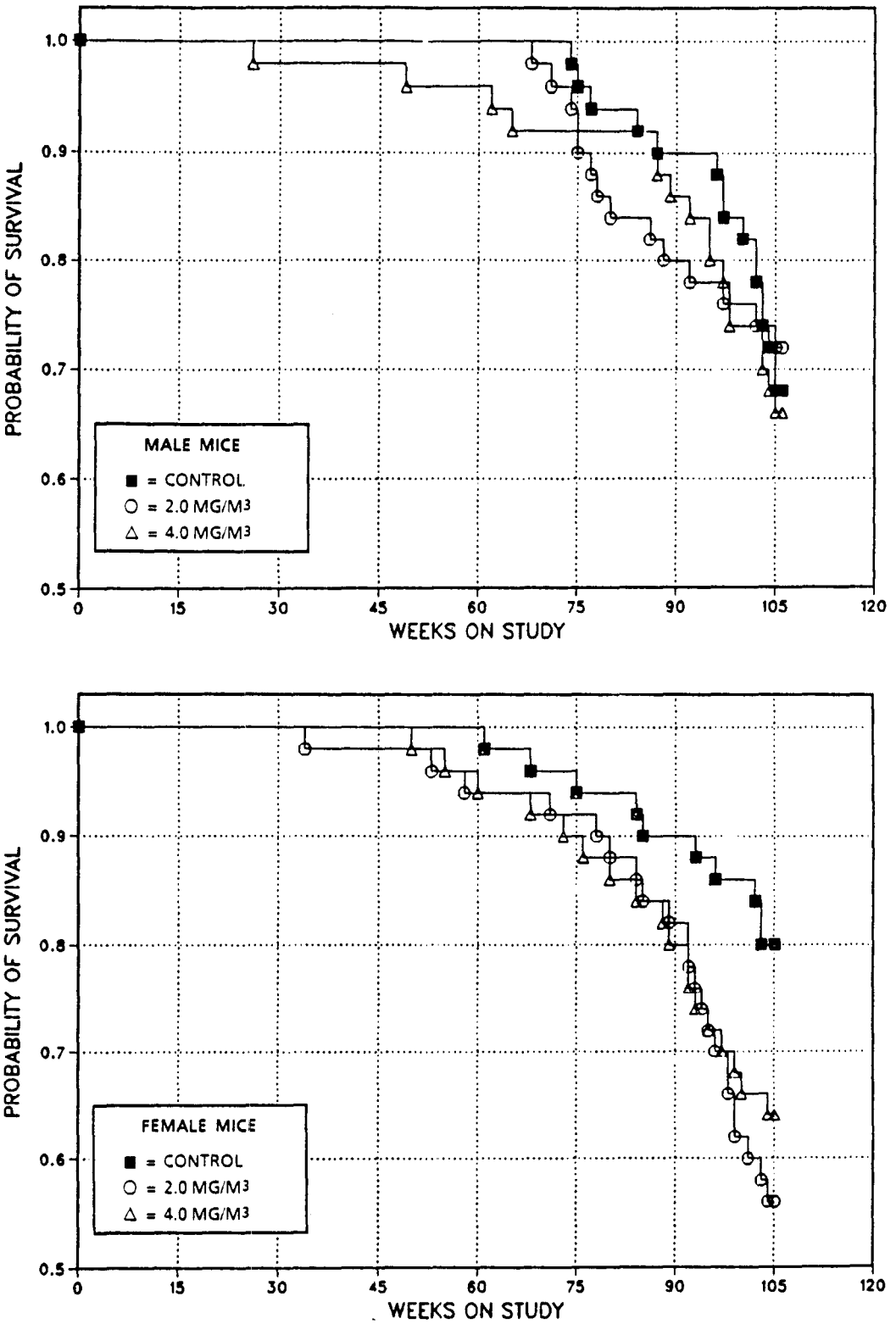

FIGURE 8. KAPLAN-MEIER SURVIVAL CURVES FOR MICE EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS

GENETIC TOXICOLOGY

2-Chloroacetophenone, within a dose range of 0.1 to 333.0 µg/plate, was not mutagenic when tested in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537 according to a pre-incubation protocol with or without Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver S9 (Zeiger et al., 1987; Table I1). No induction of sister chromatid exchanges was observed in Chinese hamster ovary (CHO) cells treated with 2-chloroacetophenone at concentrations of 0.016-0.5 µg/ml in the absence of S9 or 0.16-5.0 µg/ml in the presence of Aroclor 1254-induced male Sprague Dawley rat liver S9 (Table I2). The only genotoxic effect observed for 2-chloroacetophenone was a weak positive response in the CHO cell chromosomal aberration test conducted without S9 activation; in this test, the highest dose tested, 3.0 µg/ml, induced a highly significant increase in aberrations, along with marked toxicity (only 65 cells scored) (Table I3). The experimental procedures and results are presented in Appendix I.

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

Toxicology and carcinogenesis studies of 2-chloroacetophenone, a potent lacrimator used in tear gas formulations, were conducted by exposing male and female F344/N rats and $B6C3F_1$ mice to air containing vapors of this chemical. 2-Chloroacetophenone was selected for study because it has been used as a riot control agent and because there was limited information on its long-term toxicology and potential carcinogenicity. The inhalation route of exposure was selected because that is the primary route of human exposure. The lot of 2-chloroacetophenone used in these studies was obtained from the U.S. Army and found to be about 85% pure; the major impurities were water (2.2%) and nonvolatile magnesium oxide (11.2%). Eleven organic impurities, detected by gas chromatographic analyses, totaled less than 2% of the material.

The selection of exposure concentrations of 2-chloroacetophenone for the 2-year studies (1 or 2 mg/m^3 for rats and 2 or 4 mg/m^3 for mice) was based on the increased number of deaths and decreased body weights of animals exposed to 2-chloroacetophenone in the 14-day and 13-week inhalation studies (2 mg/m^3 is equivalent to 0.3 ppm, and 4 mg/m^3 is equivalent to 0.6 ppm). In the 14-day studies, exposure of rats to 19 mg/m^3 or higher concentrations and exposure of mice to 10 mg/m^3 or higher concentrations caused 100% mortality; for rats exposed to 10 mg/m^3, there was 20% mortality for males and a 16%-18% loss in mean body weight for males and females. In the 13-week studies, there were no clearly exposure-related deaths and no gross or microscopic lesions observed in rats or mice exposed to 2-chloroacetophenone at concentrations ranging from 0.25 to 4 mg/m^3. The final mean body weights of rats exposed to 4 mg/m^3 were 9% lower than those of chamber controls.

In the 2-year studies in rats, exposure had no apparent effect on survival or body weight. At the end of the studies, survival in all groups of rats was lower than usual for untreated F344/N rats of similar age (Haseman et al., 1985); however, at week 90, survival was about 70% for males and nearly 80% for females. In mice, mean body weights of high dose males were lower than those of chamber controls; no apparent exposure-related effect occurred in low dose males or in females. The only significant difference in survival for mice was a lower rate for low dose females after week 98.

There were no clearly compound-related neoplastic effects in rats exposed to 1 or 2 mg/m^3 2-chloroacetophenone for 2 years. Fibroadenomas of the mammary gland in female rats occurred with a significant positive trend, and the incidence in the group exposed to 2 mg/m^3 was significantly increased relative to that in chamber controls. Fibroadenomas are the most common benign neoplasms of the mammary gland in rats. The historical incidences for chamber control female rats at the study laboratory range from 5/50 to 17/50, with a mean of 20% ± 9%; the incidences in the 1 and 2 mg/m^3 groups exceed the highest incidence in historical chamber controls. Additionally, one female rat exposed to 2 mg/m^3 in the 15-month study had a fibroadenoma. The increased incidences of fibroadenomas in female rats exposed to 2-chloroacetophenone are considered to represent equivocal, rather than some, evidence of carcinogenic activity for the following reasons: the incidences in the two exposure groups do not show a strong concentration-related effect; the incidences do not exceed the highest incidence in untreated historical controls at all National Toxicology Program (NTP) laboratories combined (range: 5/50 to 30/50; mean: 32% ± 12%); and there was no chemically related increased incidence of malignant mammary gland neoplasms. The historical incidence of mammary gland fibroadenomas in female F344/N rats may be slightly underestimated for comparison of the rate of this lesion in the 2-chloroacetophenone study with that of other 2-year studies. Rao et al. (1990) reported that there has been a gradual increase in the rate of mammary gland tumors observed in untreated female F344/N rats for 2-year studies begun during the period from 1971 to 1981; the 2-year studies of 2-chloroacetophenone were started in 1982.

The incidence of neoplasms (primarily adenomas) of the anterior pituitary gland (pars distalis) was increased in female rats exposed to 1 mg/m^3. Although the incidence in this group exceeds the highest incidence in historical chamber controls (31/49), the incidence in the concurrent controls (30/49) is also unusually high. The

marginal increase in the 1 mg/m^3 female rats is not considered to be chemically related because the incidences in the two exposure groups are not concentration related, because the incidence in females exposed to 2 mg/m^3 is not significantly increased relative to that in controls, because the incidences of this common neoplasm in groups of historical controls are highly variable, and because there were decreases in the incidences of hyperplasia in exposed groups rather than corroborating increases. Further, additional female rats with hyperplasia or adenoma of the pars distalis were observed in the 15-month control and 2 mg/m^3 groups (hyperplasia: control, 3/10; 2 mg/m^3, 4/10; adenoma: 3/10; 1/10) but not in the 1 mg/m^3 group.

Adenomas of the parathyroid gland were observed in 2/33 male rats exposed to 1 mg/m^3 and in 1/44 male rats exposed to 2 mg/m^3. Although these values are not significantly increased compared with that in controls, their occurrence is noteworthy because neoplasms of the parathyroid gland are uncommon in male F344/N rats; the historical incidence is approximately 0.4% (5/1,197) in untreated control male F344/N rats (Table A4). These lesions are not considered to be chemically related because of their low numbers and the lack of a concentration-related response.

There were no increased incidences of neoplastic lesions in B6C3F$_1$ mice exposed to 2-chloroacetophenone for 2 years.

2-Chloroacetophenone has been known to be a potent lacrimator and an irritant to the eyes, upper respiratory passages, and the skin of laboratory animals (Punte et al., 1962b; Thatcher et al., 1971; Gaskins et al., 1972; Ballantyne et al., 1975; Ballantyne and Swanston, 1978) and humans (Punte et al., 1962a; Penneys et al., 1969; Penneys, 1971; Holland and White, 1972). Thus, it appears that 2-chloroacetophenone is most toxic to tissues of primary contact.

In the current studies, excessive lacrimation (dacryorrhea) and clinical signs indicative of irritation to the eyes and respiratory tract were observed in the 14-day studies at exposure concentrations of 4 mg/m^3 or higher. Although there was some indication of eye irritation in rats during the 13-week studies at concentrations as low as 0.5 mg/m^3, there were no long-term compound-related clinical signs at the exposure concentrations used in the 2-year studies. Concentration-related adverse effects occurred in the nasal mucosa of rats exposed to 2-chloroacetophenone for 2 years. Nasal lesions caused by exposure to 2-chloroacetophenone were observed primarily in the anterior nasal section and included inflammation in male rats and hyperplasia and squamous metaplasia of the respiratory epithelium in male and female rats.

The irritant effects of 2-chloroacetophenone on the nasal mucosa may have been exacerbated by viral infection; serologic determinations for sentinel or control animals were positive for antibodies to rat coronavirus or sialodacryoadenitis virus at months 6, 12, 18, and 24 of the studies. Squamous metaplasia of the respiratory epithelium was also observed in exposed mice but at a much lower incidence than in rats. The incidences of eye or skin lesions were not increased in the exposed groups of rats or mice compared with those in controls, although 2-chloroacetophenone has been reported to be a promoter of neoplasms initiated by 9,10-dimethyl-1,2-benzanthracene in mouse skin (Gwynn and Salaman, 1953).

Exposure-related increased incidences of forestomach ulceration, inflammation, and epithelial hyperplasia around the ulcerated areas were observed in female rats. It is uncertain whether these were direct effects of the chemical, which may have been ingested during grooming, or perhaps of effects related to stress. No apparent differences in the incidences of these lesions between the control and exposed groups occurred in male rats.

2-Chloroacetophenone was not mutagenic in *Salmonella typhimurium* (Zeiger et al., 1987) and did not induce sister chromatid exchanges in Chinese hamster ovary cells; however, it did produce an increase in chromosomal aberrations in the absence of S9 activation and at a toxic concentration.

The experimental and tabulated data for the NTP Technical Report on 2-chloroacetophenone were examined for accuracy, consistency, completeness, and compliance with Good Laboratory

Practice regulations. As summarized in Appendix J, 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.

Under the conditions of these 2-year inhalation studies, there was *no evidence of carcinogenic activity** of 2-chloroacetophenone for male rats exposed to 1 or 2 mg/m^3. There was *equivocal evidence of carcinogenic activity* for female F344/N rats, based on a marginal increase in fibroadenomas of the mammary gland. There was *no evidence of carcinogenic activity* for male or female B6C3F$_1$ mice exposed to 2 or 4 mg/m^3 2-chloroacetophenone.

*Explanation of Levels of Evidence of Carcinogenic Activity is on page 8.
A summary of the Peer Review comments and the public discussion on this Technical Report appears on page 12.

V. REFERENCES

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APPENDIX A

SUMMARY OF LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	1 mg/m^3	2 mg/m^3
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine large, colon	(44)	(47)	(46)
Leukemia mononuclear	1 (2%)		
Intestine small, duodenum	(43)	(45)	(45)
Adenocarcinoma	1 (2%)		
Peyer's patch, leukemia mononuclear	1 (2%)		
Intestine small, ileum	(41)	(45)	(43)
Peyer's patch, leukemia mononuclear	2 (5%)	1 (2%)	
Intestine small, jejunum	(43)	(44)	(40)
Peyer's patch, leukemia mononuclear	1 (2%)		
Liver	(49)	(50)	(50)
Adenoma	1 (2%)		
Leukemia mononuclear	28 (57%)	26 (52%)	26 (52%)
Mesentery	*(50)	*(50)	*(50)
Leukemia mononuclear		1 (2%)	
Mesothelioma malignant, metastatic, testes		1 (2%)	
Fat, leukemia mononuclear			1 (2%)
Pancreas	(47)	(50)	(49)
Leukemia mononuclear	7 (15%)	4 (8%)	
Mesothelioma malignant, metastatic, testes		1 (2%)	
Acinus, adenoma		1 (2%)	
Pharynx	*(50)	*(50)	*(50)
Palate, papilloma squamous	3 (6%)		
Salivary glands	(46)	(49)	(49)
Leukemia mononuclear		1 (2%)	
Stomach, forestomach	(46)	(49)	(49)
Leukemia mononuclear	3 (7%)	1 (2%)	
Stomach, glandular	(48)	(49)	(49)
Leukemia mononuclear	2 (4%)	3 (6%)	
CARDIOVASCULAR SYSTEM			
Heart	(49)	(50)	(50)
Leukemia mononuclear	12 (24%)	13 (26%)	10 (20%)
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(47)	(49)	(50)
Adenoma	1 (2%)	2 (4%)	1 (2%)
Leukemia mononuclear	13 (28%)	15 (31%)	10 (20%)
Adrenal gland, medulla	(46)	(49)	(50)
Leukemia mononuclear	14 (30%)	13 (27%)	10 (20%)
Pheochromocytoma malignant	2 (4%)	1 (2%)	2 (4%)
Pheochromocytoma benign	11 (24%)	10 (20%)	16 (32%)
Bilateral, pheochromocytoma benign	3 (7%)	5 (10%)	4 (8%)
Islets, pancreatic	(47)	(50)	(48)
Adenoma	3 (6%)	6 (12%)	1 (2%)
Adenoma, multiple		1 (2%)	
Carcinoma	1 (2%)		
Parathyroid gland	(35)	(33)	(44)
Adenoma		2 (6%)	1 (2%)
Pituitary gland	(47)	(50)	(48)
Pars distalis, adenoma	31 (66%)	35 (70%)	32 (67%)
Pars distalis, carcinoma	1 (2%)		1 (2%)
Pars distalis, leukemia mononuclear	8 (17%)	10 (20%)	8 (17%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
ENDOCRINE SYSTEM (Continued)			
Thyroid gland	(45)	(46)	(48)
Leukemia mononuclear		1 (2%)	
C-cell, adenoma	5 (11%)	5 (11%)	2 (4%)
C-cell, carcinoma	2 (4%)	1 (2%)	1 (2%)
Follicular cell, adenocarcinoma		2 (4%)	1 (2%)
Follicular cell, adenoma	1 (2%)		
GENERAL BODY SYSTEM			
Tissue, NOS	*(50)	*(50)	*(50)
Chordoma	1 (2%)		
Sarcoma	1 (2%)		
GENITAL SYSTEM			
Epididymis	(40)	(36)	(39)
Leukemia mononuclear		1 (3%)	
Penis	*(50)	*(50)	*(50)
Leukemia mononuclear		1 (2%)	
Preputial gland	(45)	(48)	(50)
Adenoma	2 (4%)	6 (13%)	5 (10%)
Carcinoma		1 (2%)	
Leukemia mononuclear		1 (2%)	
Squamous cell carcinoma	1 (2%)		
Prostate	(49)	(49)	(47)
Adenoma	1 (2%)		
Testes	(50)	(50)	(50)
Leukemia mononuclear	1 (2%)	3 (6%)	1 (2%)
Bilateral, interstitial cell, adenoma	18 (36%)	21 (42%)	20 (40%)
Interstitial cell, adenoma	11 (22%)	10 (20%)	7 (14%)
Tunic, mesothelioma benign	2 (4%)	2 (4%)	
Tunic, mesothelioma malignant		1 (2%)	
HEMATOPOIETIC SYSTEM			
Bone marrow	(46)	(49)	(50)
Leukemia mononuclear	9 (20%)	11 (22%)	4 (8%)
Lymph node	(48)	(50)	(49)
Mediastinal, leukemia mononuclear	1 (2%)	1 (2%)	
Mesenteric, leukemia mononuclear	4 (8%)	3 (6%)	2 (4%)
Pancreatic, leukemia mononuclear		1 (2%)	
Renal, leukemia mononuclear	2 (4%)	3 (6%)	3 (6%)
Lymph node, bronchial	(44)	(48)	(46)
Leukemia mononuclear	14 (32%)	16 (33%)	10 (22%)
Sarcoma, metastatic	1 (2%)		
Lymph node, mandibular	(45)	(43)	(45)
Leukemia mononuclear	12 (27%)	15 (35%)	6 (13%)
Spleen	(48)	(49)	(49)
Leukemia mononuclear	29 (60%)	25 (51%)	27 (55%)
Thymus	(33)	(38)	(41)
Leukemia mononuclear	8 (24%)	8 (21%)	2 (5%)
Thymoma malignant			1 (2%)
INTEGUMENTARY SYSTEM			
Mammary gland	(23)	(20)	(23)
Adenocarcinoma		1 (5%)	
Adenoma			1 (4%)
Fibroadenoma		1 (5%)	

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m³	2 mg/m³
INTEGUMENTARY SYSTEM (Continued)			
Skin	(46)	(49)	(47)
Basal cell adenoma			1 (2%)
Basal cell carcinoma	1 (2%)		1 (2%)
Keratoacanthoma	4 (9%)	2 (4%)	4 (9%)
Papilloma squamous		1 (2%)	1 (2%)
Squamous cell carcinoma		1 (2%)	
Subcutaneous tissue, fibroma	1 (2%)	2 (4%)	1 (2%)
Subcutaneous tissue, lipoma			1 (2%)
Subcutaneous tissue, neurofibrosarcoma	1 (2%)		1 (2%)
MUSCULOSKELETAL SYSTEM			
Bone	(47)	(50)	(50)
Femur, osteosarcoma		1 (2%)	
Skeletal muscle	*(50)	*(50)	*(50)
Hemangioma			1 (2%)
NERVOUS SYSTEM			
Brain	(49)	(50)	(50)
Astrocytoma malignant			1 (2%)
Carcinoma, metastatic, pituitary gland	1 (2%)		1 (2%)
Glioma benign	1 (2%)		
Glioma malignant	1 (2%)		
Granular cell tumor benign			1 (2%)
Leukemia mononuclear	8 (16%)	7 (14%)	4 (8%)
RESPIRATORY SYSTEM			
Lung	(49)	(50)	(50)
Alveolar/bronchiolar adenoma	1 (2%)	1 (2%)	1 (2%)
Alveolar/bronchiolar carcinoma	1 (2%)	1 (2%)	
Carcinoma, metastatic, thyroid gland	1 (2%)		
Leukemia mononuclear	23 (47%)	22 (44%)	18 (36%)
Neoplasm, NOS, metastatic, tissue nos	1 (2%)		
Osteosarcoma, metastatic, bone		1 (2%)	
Osteosarcoma, metastatic, uncertain primary site	1 (2%)		
Sarcoma, metastatic, eye		1 (2%)	
Sarcoma, metastatic, tissue, NOS	1 (2%)		
Squamous cell carcinoma, metastatic, skin		1 (2%)	
Nose	(46)	(50)	(49)
Carcinoma, metastatic, skin			1 (2%)
Leukemia mononuclear	2 (4%)	3 (6%)	2 (4%)
Trachea	(46)	(48)	(49)
Carcinoma, metastatic, thyroid gland	1 (2%)		
SPECIAL SENSES SYSTEM			
Eye	(50)	*(50)	(50)
Leukemia mononuclear	12 (24%)		11 (22%)
Sarcoma		1 (2%)	
Zymbal gland	*(50)	*(50)	*(50)
Carcinoma		1 (2%)	

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
URINARY SYSTEM			
Kidney	(49)	(49)	(50)
Leukemia mononuclear	11 (22%)	15 (31%)	7 (14%)
Lipoma	1 (2%)		
Renal tubule, adenoma	1 (2%)		1 (2%)
Urinary bladder	(49)	(50)	(49)
Leukemia mononuclear	5 (10%)	8 (16%)	1 (2%)
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Leukemia mononuclear	29 (58%)	26 (52%)	27 (54%)
Mesothelioma benign	2 (4%)	2 (4%)	
Mesothelioma malignant		1 (2%)	
Hemangioma			1 (2%)
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Moribund	26	22	24
Dead	10	6	9
Terminal sacrifice	14	22	17
TUMOR SUMMARY			
Total animals with primary neoplasms **	48	50	49
Total primary neoplasms	145	151	138
Total animals with benign neoplasms	44	48	48
Total benign neoplasms	102	113	102
Total animals with malignant neoplasms	34	35	30
Total malignant neoplasms	43	38	36
Total animals with secondary neoplasms ***	4	4	2
Total secondary neoplasms	7	5	2
Total animals with malignant neoplasms--uncertain primary site	1		

* Number of animals receiving complete necropsy examination; 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 2-CHLOROACETOPHENONE: CHAMBER CONTROL

WEEKS ON STUDY	046	061	064	064	066	066	083	083	084	086	086	086	087	087	089	089	093	094	094	095	095	095	096	096	096
CARCASS ID	16 1	01 1	49 1	32 1	30 1	23 1	02 1	50 1	20 1	18 1	22 1	31 1	03 1	14 1	37 1	45 1	04 1	41 1	28 1	35 1	36 1	47 1	40 1	15 1	05 1
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Intestine large, cecum	M	M	M	M	M	M	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Intestine large, colon	+	+	+	A	A	A	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	A	+
Leukemia mononuclear																X									
Intestine large, rectum	+	+	A	M	A	A	+	+	+	+	+	+	+	+	A	M	+	A	M	+	+	+	+	M	+
Intestine small	+	+	A	A	A	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Intestine small, duodenum	+	+	A	A	A	A	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	A	+
Adenocarcinoma																									
Peyer's patch, leukemia mononuclear																X									
Intestine small, ileum	+	+	A	A	A	A	+	+	+	+	+	+	+	+	A	+	A	A	+	+	+	+	+	A	+
Peyer's patch, leukemia mononuclear											X					X									
Intestine small, jejunum	+	+	A	A	A	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Peyer's patch, leukemia mononuclear																X									
Liver	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Leukemia mononuclear				X	X						X	X	X	X		X	X			X	X	X	X		X
Mesentery														+											
Pancreas	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Leukemia mononuclear											X	X	X				X			X	X				
Pharynx								+											+						
Palate, papilloma squamous								X											X						
Salivary glands	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Stomach	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	A	A	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Leukemia mononuclear											X					X									
Stomach, glandular	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X					X									
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X						X	X	X			X	X				X		X		
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Adrenal gland, cortex	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Adenoma																									
Leukemia mononuclear				X								X	X	X		X	X			X	X				
Adrenal gland, medulla	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	A	+
Leukemia mononuclear				X								X	X			X	X			X	X		X		
Pheochromocytoma malignant																X									
Pheochromocytoma benign												X								X		X	X		
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Adenoma																									
Carcinoma																									
Parathyroid gland	M	I	+	M	+	A	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+
Pituitary gland	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X		X					X	X	X		X		X		X			X		X	X		X	X
Pars distalis, carcinoma																									
Pars distalis, leukemia mononuclear											X		X			X	X			X	X				
Thyroid gland	+	+	A	M	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
C cell, adenoma										X									X						
C cell, carcinoma							X			X															
Follicular cell, adenoma											X														
GENERAL BODY SYSTEM																									
Tissue, NOS							+																		
Chordoma																									
Sarcoma							X																		
GENITAL SYSTEM																									
Epididymis	+	M	M	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	M	+
Preputial gland	+	+	M	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Squamous cell carcinoma																									
Prostate	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									X
Seminal vesicle			+																						
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X																				
Bilateral, interstitial cell, adenoma							X	X			X				X								X	X	
Interstitial cell, adenoma												X		X			X			X	X	X			
Tunic, mesothelioma benign																									

+ 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	099	100	101	101	102	103	103	103	104	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	341	261	191	071	211	461	111	121	271	431	091	061	081	101	131	171	241	251	291	331	381	391	421	441	481	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, cecum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	40
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Leukemia mononuclear																										1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	40
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Adenocarcinoma		X																								1
Peyer's patch, leukemia mononuclear																										1
Intestine small, ileum	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Peyer's patch, leukemia mononuclear																										2
Intestine small, jejunum	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Peyer's patch, leukemia mononuclear																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																					X					1
Leukemia mononuclear				X		X		X	X	X	X		X	X	X	X	X	X		X		X		X		28
Mesentery															+											2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Leukemia mononuclear								X																		7
Pharynx																		+								3
Palate, papilloma squamous																		X								3
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear								X																		3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear																										2
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear						X		X	X							X										12
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma						X																				1
Leukemia mononuclear						X		X	X	X			X													13
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear						X		X	X	X			X				X									14
Pheochromocytoma malignant												X														2
Pheochromocytoma benign		X		X	X				X			X											X		X	11
Bilateral, pheochromocytoma benign								X							X									X		3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma										X		X										X				3
Carcinoma																		X								1
Parathyroid gland	M	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M	+	+	M	+	M	M	M	+	+	35
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma	X	X	X	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											X		X													8
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
C-cell, adenoma														X				X			X					5
C-cell, carcinoma																										2
Follicular cell, adenoma																										1
GENERAL BODY SYSTEM																										
Tissue, NOS				+																						2
Chordoma				X																						1
Sarcoma																										1
GENITAL SYSTEM																										
Epididymis	+	+	M	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	40
Preputial gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	45
Adenoma						X																X				2
Squamous cell carcinoma												X														1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																										1
Seminal vesicle				+																		+				3
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										1
Bilateral, interstitial cell, adenoma					X			X	X			X	X		X	X				X		X	X		X	X	18
Interstitial cell, adenoma	X									X	X			X			X									11
Tunic, mesothelioma benign																X								X		2

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

WEEKS ON STUDY	046	061	064	064	066	066	083	083	084	086	086	086	087	087	089	089	093	094	094	095	095	095	096	096	096
CARCASS ID	161	011	491	321	301	231	021	501	201	181	221	311	031	141	371	451	041	411	281	351	361	471	401	151	051
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Leukemia mononuclear											X		X	X		X	X			X	X				
Lymph node	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Mediastinal, leukemia mononuclear											X														
Mesenteric, leukemia mononuclear				X	X						X									X					
Renal, leukemia mononuclear				X																					
Lymph node, bronchial	+	+	M	+	M	A	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	A	+
Leukemia mononuclear				X							X	X	X	X		X				X	X				
Sarcoma, metastatic							X																		
Lymph node, mandibular	+	M	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	A	+
Leukemia mononuclear				X							X	X	X			X	X			X	X				
Spleen	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Leukemia mononuclear				X	X					X	X	X	X	X		X	X			X	X	X	X		X
Thymus	+	+	+	I	M	A	M	M	+	M	+	+	+	+	+	+	+	M	M	+	+	M	+	A	+
Leukemia mononuclear											X	X	X				X			X	X				
INTEGUMENTARY SYSTEM																									
Mammary gland	M	M	+	M	A	M	+	M	M	M	M	M	M	+	+	M	+	M	+	M	+	M	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma																									
Keratoacanthoma																									
Subcutaneous tissue, fibroma	X																								
Subcutaneous tissue, neurofibrosarcoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland																									
Glioma benign																				X					
Glioma malignant								X																	
Leukemia mononuclear					X						X					X	X			X	X				
Spinal cord		+																							
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Lung	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, thyroid gland							X																		
Leukemia mononuclear				X	X						X	X	X	X		X	X			X	X	X	X		
Neoplasm, NOS, metastatic, tissue, NOS																									
Osteosarcoma, metastatic, uncertain primary site																									
Sarcoma, metastatic, tissue, NOS							X																		
Nose	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+
Leukemia mononuclear																				X					
Trachea	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Carcinoma, metastatic, thyroid gland							X																		
SPECIAL SENSES SYSTEM																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X		X			X	X			X	X	X			
Harderian gland																							+		
URINARY SYSTEM																									
Kidney	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X	X						X	X	X			X	X			X	X				
Lipoma																									
Renal tubule, adenoma																									
Urinary bladder	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X						X			X	X				

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

WEEKS ON STUDY	099	100	101	101	102	103	103	103	104	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	341	261	191	071	211	461	111	121	271	431	091	061	081	101	131	171	241	251	291	331	381	391	421	441	481	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear								X	X																	9
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Mediastinal, leukemia mononuclear																										1
Mesenteric, leukemia mononuclear																										4
Renal, leukemia mononuclear										X																2
Lymph node, bronchial	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	44
Leukemia mononuclear						X		X		X	X		X									X				14
Sarcoma, metastatic																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Leukemia mononuclear						X			X	X														X		12
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear				X		X		X	X	X	X		X	X	X	X	X	X		X		X		X		29
Thymus	+	+	M	+	+	M	+	+	M	+	+	+	M	M	+	+	M	+	M	+	+	+	+	+	+	33
Leukemia mononuclear								X			X															8
INTEGUMENTARY SYSTEM																										
Mammary gland	M	+	+	+	+	+	+	M	M	M	+	+	M	+	M	M	M	M	M	+	+	M	+	+	M	23
Skin	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	I	+	I	+	+	+	46
Basal cell carcinoma														X												1
Keratoacanthoma			X			X					X			X												4
Subcutaneous tissue, fibroma																										1
Subcutaneous tissue, neurofibrosarcoma			X																							1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, pituitary gland																				X						1
Glioma benign																										1
Glioma malignant																										1
Leukemia mononuclear								X		X																8
Spinal cord																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma																									X	1
Alveolar/bronchiolar carcinoma									X																	1
Carcinoma, metastatic, thyroid gland																										1
Leukemia mononuclear						X		X	X	X	X		X			X	X	X		X				X		23
Neoplasm, NOS, metastatic, tissue, NOS				X																						1
Osteosarcoma, metastatic, uncertain primary site													X													1
Sarcoma, metastatic, tissue, NOS																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear																X										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Carcinoma, metastatic, thyroid gland																										1
SPECIAL SENSES SYSTEM																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear						X		X	X	X										X						12
Harderian gland																										1
URINARY SYSTEM																										
Kidney	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear						X		X																		11
Lipoma																						X				1
Renal tubule, adenoma									X																	1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear								X																		5

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 1 mg/m³

WEEKS ON STUDY	038	065	073	078	080	080	081	082	082	083	086	087	089	091	091	092	096	096	097	099	100	101	101	101	101
CARCASS ID	12901	13611	12511	10111	10811	14111	13411	12001	12611	11711	14811	13011	12411	11211	13811	14511	10711	14011	10311	11011	12311	10211	11411	11511	12711
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Intestine large	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine large, cecum	M	M	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Intestine large, rectum	A	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	A	+	+	+	+	+	A	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine small, duodenum	A	+	+	I	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+	A	+	+	A	+
Peyer's patch, leukemia mononuclear																						X			
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	A	+	+	A	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X	X			X	X	X		X	X	X				X	X	X	X	X			X
Mesentery																				+				+	
Leukemia mononuclear																									
Mesothelioma malignant, metastatic, testes																								X	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear														X											
Mesothelioma malignant, metastatic, testes																								X	
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Leukemia mononuclear														X											
Stomach	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									
Stomach, glandular	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X							X		X					X			X			X
ENDOCRINE SYSTEM																									
Adrenal gland	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Leukemia mononuclear					X				X			X		X				X			X	X			X
Adrenal gland, medulla	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X				X			X		X							X	X			X
Pheochromocytoma malignant																									
Pheochromocytoma benign														X							X			X	X
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X									X					X	X	X				X
Adenoma, multiple									X																
Parathyroid gland	M	M	+	+	+	M	+	+	M	+	M	+	+	+	M	+	M	M	+	+	+	M	+	+	+
Adenoma																					X		X		
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X		X				X	X	X	X			X	X	X	X	X	X	X		X	X		X
Pars distalis, leukemia mononuclear									X			X		X					X			X			X
Thyroid gland	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Leukemia mononuclear																									
C-cell, adenoma						X	X																		
C-cell, carcinoma																									
Follicular cell, adenocarcinoma																									
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Epididymis	M	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	I	+	+	M	+	+	+	+	+
Leukemia mononuclear																									
Penis																						+			
Leukemia mononuclear																						X			
Preputial gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+
Adenoma															X										
Carcinoma																									
Leukemia mononuclear																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle																+							+		
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																						X			
Bilateral, interstitial cell, adenoma			X																		X	X		X	X
Interstitial cell, adenoma				X		X	X					X		X				X							
Tunic, mesothelioma benign																						X			
Tunic, mesothelioma malignant																								X	

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1 mg/m³ (Continued)

WEEKS ON STUDY	103	105	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	11991	11611	12811	10411	10511	10611	10911	11111	11311	11811	12111	12211	13111	13211	13311	13511	13711	13911	14211	14311	14411	14611	14711	14911	15011	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	44
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	I	+	+	42
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Peyer's patch, leukemia mononuclear																										1
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X	X		X	X	X	X	X						X						X	X			X	26
Mesentery			+																							3
Leukemia mononuclear			X																							1
Mesothelioma malignant, metastatic, testes																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear			X			X																X				4
Mesothelioma malignant, metastatic, testes																										1
Acinus, adenoma					X																					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear			X																							1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X	X																							3
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X	X			X	X														X	X				13
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma											X											X				2
Leukemia mononuclear	X	X	X			X	X														X	X				15
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X		X			X	X														X	X				13
Pheochromocytoma malignant																				X						1
Pheochromocytoma benign	X									X			X			X			X		X				10
Bilateral, pheochromocytoma benign		X	X			X		X														X				5
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma									X																	6
Adenoma, multiple																										1
Parathyroid gland	+	M	M	M	+	+	+	+	+	+	+	+	M	M	I	+	+	+	+	+	M	I	+	+	+	33
Adenoma																										2
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma	X	X		X	X	X	X	X	X	X	X	X			X	X			X	X	X		X	X	X	35
Pars distalis, leukemia mononuclear		X	X			X																X				10
Thyroid gland	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear			X																							1
C-cell, adenoma															X						X				X	5
C-cell, carcinoma	X																									1
Follicular cell, adenocarcinoma				X							X															2
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis	+	+	+		+	+	+	+	I	+	+	+	+	+	M	+	M	+	+	+	M	M	+	M	I	36
Leukemia mononuclear						X																				1
Penis																										1
Leukemia mononuclear																										1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma		X			X										X			X		X						6
Carcinoma																			X							1
Leukemia mononuclear						X																				1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	49
Seminal vesicle					●																					3
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X				X																				3
Bilateral, interstitial cell, adenoma	X	X	X	X		X				X			X	X	X		X	X	X		X	X		X	X	21
Interstitial cell, adenoma									X			X				X				X						10
Tunic, mesothelioma benign												X														2
Tunic, mesothelioma malignant																										1

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1 mg/m³ (Continued)

WEEKS ON STUDY	038	065	073	078	080	080	081	082	082	083	086	087	089	091	091	092	096	096	097	099	100	101	101	101	101
CARCASS ID	12901	13611	12511	01011	08101	14111	13411	12001	12611	11711	14811	13011	12411	11211	13811	14511	10711	14011	10311	11011	12311	10211	11141	11151	12771
HEMATOPOIETIC SYSTEM																									
Bone marrow	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear										X			X						X			X			X
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, leukemia mononuclear														X											
Mesenteric, leukemia mononuclear																			X			X			
Pancreatic, leukemia mononuclear														X											
Renal, leukemia mononuclear														X					X						
Lymph node, bronchial	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Leukemia mononuclear					X					X		X	X	X					X			X			X
Lymph node, mandibular	+	+	+	M	+	+	+	M	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+
Leukemia mononuclear					X				X	X		X	X	X					X			X			X
Spleen	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X			X	X	X		X	X	X				X	X	X	X	X			X
Thymus	A	+	+	+	+	+	+	M	M	M	+	+	+	+	+	+	+	A	+	M	+	+	M	+	+
Leukemia mononuclear					X							X		X					X			X			
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	M	M	M	M	M	M	M	M	M	M	M	+	M	+	M	M	+	M	+	M	+	M
Adenocarcinoma																									
Fibroadenoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma														X	X										
Papilloma squamous																									
Squamous cell carcinoma																					X				
Subcutaneous tissue, fibroma				X			X																		
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Femur, osteosarcoma	X																								
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear												X		X					X			X			X
RESPIRATORY SYSTEM																									
Larynx	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma														X											
Leukemia mononuclear					X				X	X		X	X	X				X	X		X	X			X
Osteosarcoma, metastatic, bone	X																								
Sarcoma, metastatic, eye																									
Squamous cell carcinoma, metastatic, skin																					X				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear														X								X			
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
SPECIAL SENSES SYSTEM																									
Eye																							+		
Sarcoma																									
Harderian gland																				+					
Zymbal gland						+																			
Carcinoma						X																			
URINARY SYSTEM																									
Kidney	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X							X		X					X			X			X
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear												X		X					X			X			

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 1 mg/m³ (Continued)

WEEKS ON STUDY	103	105	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL: TISSUES TUMORS
CARCASS ID	11901	11611	12811	10411	10511	10611	10911	11111	11311	11811	12111	12211	13111	13211	13311	13511	13711	13911	14211	14311	14411	14611	14711	14911	15011	
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X	X			X	X														X					11
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, leukemia mononuclear																										1
Mesenteric, leukemia mononuclear	X																									3
Pancreatic, leukemia mononuclear																										1
Renal, leukemia mononuclear					X																					3
Lymph node, bronchial	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear	X	X	X			X	X								X						X	X				16
Lymph node, mandibular	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	43
Leukemia mononuclear	X					X	X								X						X	X				15
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X	X		X	X	X	X	X						X						X	X			X	25
Thymus	M	+	+	M	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	38
Leukemia mononuclear		X				X																X				8
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	+	M	+	+	+	M	+	+	+	M	I	M	M	+	M	M	+	+	M	+	M	+	M	20
Adenocarcinoma																X										1
Fibroadenoma																						X				1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Keratoacanthoma																										2
Papilloma squamous									X																	1
Squamous cell carcinoma																										1
Subcutaneous tissue, fibroma																										2
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Femur, osteosarcoma																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X				X																				7
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																							X			1
Alveolar/bronchiolar carcinoma																										1
Leukemia mononuclear	X	X	X		X	X	X	X							X						X	X			X	22
Osteosarcoma, metastatic, bone																										1
Sarcoma, metastatic, eye														X												1
Squamous cell carcinoma, metastatic, skin																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																						X				3
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPECIAL SENSES SYSTEM																										
Eye														+												2
Sarcoma														X												1
Harderian gland							+																			2
Zymoal gland																										1
Carcinoma																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X	X			X	X								X						X	X			X	15
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X	X			X																X				8

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 2 mg/m³

WEEKS ON STUDY	046	064	070	071	076	076	077	077	078	078	078	080	085	086	087	088	088	090	090	092	092	094	096	097	098	098
CARCASS ID	22881	24111	23211	23531	23711	21811	22611	21111	20711	23811	20111	21411	24511	24421	22441	20081	24911	25011	20411	21911	22201	24331	21511	21131	24411
ALIMENTARY SYSTEM																										
Esophagus	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	M	M	M	+	A	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Intestine large, colon	+	+	+	+	+	A	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Intestine small	+	+	+	A	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Intestine small, duodenum	+	+	+	A	+	A	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Intestine small, ileum	+	+	+	A	+	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+
Intestine small, jejunum	+	+	+	M	+	A	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X				X			X	X	X		X		X	X	X	X
Mesentery									+																
Fat, leukemia mononuclear									X																
Pancreas	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																										
CARDIOVASCULAR SYSTEM																										
Blood vessel						+																				
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear													X					X	X		X				X	
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Leukemia mononuclear													X			X	X	X		X					X	
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear													X			X	X	X		X					X	
Pheochromocytoma malignant								X																		X
Pheochromocytoma benign						X		X			X		X							X				X		
Bilateral, pheochromocytoma benign																										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	A	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+
Adenoma																X										
Parathyroid gland	+	M	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma		X	X	X	X		X		X	X	X			X	X	X	X		X		X	X	X	X	X
Pars distalis, carcinoma												X														
Pars distalis, leukemia mononuclear									X								X	X		X				X		
Thyroid gland	+	M	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																										
C-cell, carcinoma																										
Follicular cell, adenocarcinoma																										
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis	M	+	+	+	+	+	+	+	M	M	A	+	+	+	+	+	+	+	+	M	+	+	+	M	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma															X										
Prostate	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Seminal vesicle					+																				
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																										
Bilateral, interstitial cell, adenoma																		X		X			X			
Interstitial cell, adenoma		X						X				X			X									X		

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 2 mg/m³
(Continued)

WEEKS ON STUDY	100	100	100	100	101	103	105	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	246 1	247 1	248 1	211 7 1	240 1	233 3 1	205 1	225 1	202 1	203 1	206 1	209 1	211 0 1	211 2 1	211 6 1	221 1	222 1	223 1	227 1	229 1	230 1	231 1	234 1	236 1	239 1	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	39
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, jejunum	+	+	+	A	+	+	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	40
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X		X		X		X	X	X					X	X		X	X	X		X	X	X	X	26
Mesentery																					+		+			3
Fat, leukemia mononuclear																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	49
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth																									+	1
CARDIOVASCULAR SYSTEM																										
Blood vessel						+													+				+			4
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X		X																				X	X	10
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma									X																	1
Leukemia mononuclear	X	X		X												X										10
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X		X												X										10
Pheochromocytoma malignant																										2
Pheochromocytoma benign				X	X	X							X	X				X					X	X	X	X	16
Bilateral, pheochromocytoma benign		X										X			X						X					4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																										1
Parathyroid gland	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	44
Adenoma													X													1
Pituitary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma		X		X	X	X	X	X					X					X	X	X	X	X	X	X		32
Pars distalis, carcinoma																										1
Pars distalis, leukemia mononuclear	X	X		X																						8
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C cell, adenoma									X							X										2
C cell, carcinoma																		X								1
Follicular cell, adenocarcinoma																		X								1
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis	+	M	+	+	+	+	+	+	+	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	I	39
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma												X						X					X	X		5
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Seminal vesicle														+												2
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear				X																						1
Bilateral, interstitial cell, adenoma		X	X			X	X		X	X	X	X	X		X	X	Y	X	X	X				X	X	20
Interstitial cell, adenoma														X							X					7

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 2 mg/m³
(Continued)

WEEKS ON STUDY	046	064	070	071	076	076	077	077	078	078	078	080	085	086	087	088	090	090	092	092	094	096	097	098	098
CARCASS ID	22881	24111	23211	23511	23711	21811	22261	21111	20711	23811	20111	21411	24511	24211	22411	20811	24911	25011	20411	21911	22011	24311	21151	21131	24441
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X				X				X	X							
Lymph node	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenteric, leukemia mononuclear																	X	X							
Renal, leukemia mononuclear																	X	X						X	
Lymph node, bronchial	M	+	+	+	+	+	+	+	+	+	A	+	+	M	+	+	+	+	+	+	+	M	+	+	+
Leukemia mononuclear									X				X				X	X		X				X	
Lymph node, mandibular	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X				X				X	X						X	
Spleen	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X				X		X	X	X	X		X		X	X	X	X
Thymus	+	+	+	+	M	M	+	M	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X																
Thymoma malignant												X						X							
INTEGUMENTARY SYSTEM																									
Mammary gland	+	M	I	M	+	M	M	M	+	+	M	M	I	M	+	+	+	M	M	+	M	M	M	+	+
Adenoma																									
Skin	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Basal cell adenoma																									X
Basal cell carcinoma																									X
Keratoacanthoma																	X								
Papilloma squamous				X																					
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, lipoma																				X					
Subcutaneous tissue, neurofibrosarcoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																									
Hemangioma																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant		X																							
Carcinoma, metastatic, pituitary gland												X													
Granular cell tumor benign																									
Leukemia mononuclear																	X	X							
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																		X							
Leukemia mononuclear									X				X		X	X	X	X		X		X	X	X	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, skin																									X
Leukemia mononuclear																	X	X							
Trachea	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Ear																									
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X				X			X	X	X		X			X	X	
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X								X	X		X				X	
Renal tubule, adenoma																									X
Urinary bladder	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Leukemia mononuclear																		X							

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 2 mg/m³
(Continued)

WEEKS ON STUDY	100	100	100	100	101	103	105	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	24611	24711	24811	21711	24011	23311	20511	22511	20211	20311	20611	20911	21011	21211	21611	22111	22211	22311	22711	22911	23011	23111	23411	23611	23911	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear																										4
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesenteric, leukemia mononuclear																										2
Renal, leukemia mononuclear																										3
Lymph node, bronchial	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear	X	X		X																X						10
Lymph node, mandibular	+	M	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	45
Leukemia mononuclear	X																									6
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X		X		X		X	X	X					X	X		X	X	X		X	X	X	X	27
Thymus	+	+	+	M	+	+	-	+	+	+	+	+	+	+	+	M	+	+	+	M	M	+	+	+	+	41
Leukemia mononuclear																										2
Thymoma malignant																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	M	+	M	M	+	+	M	M	M	M	+	+	M	+	+	+	+	+	+	M	M	M	I	+	+	23
Adenoma																									X	1
Skin	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Basal cell adenoma																										1
Basal cell carcinoma																										1
Keratoacanthoma											X							X							X	4
Papilloma squamous																										1
Subcutaneous tissue, fibroma																									X	1
Subcutaneous tissue, lipoma																										1
Subcutaneous tissue, neurofibrosarcoma															X											1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																			+							1
Hemangioma																			X							1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant																										1
Carcinoma, metastatic, pituitary gland																										1
Granular cell tumor benign									X																	1
Leukemia mononuclear	X			X																						4
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lung	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Leukemia mononuclear	X	X		X											X	X			X				X		X	18
Nose	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, skin																										1
Leukemia mononuclear																										2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSES SYSTEM																										
Ear				+																						1
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X		X																						11
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X		X																						7
Renal tubule, adenoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear																										1

TABLE A3. ANALYSIS OF PRIMARY NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	1 mg/m^3	2 mg/m^3
Adrenal Medulla: Pheochromocytoma			
Overall Rates (a)	14/46 (30%)	15/49 (31%)	20/50 (40%)
Adjusted Rates (b)	56.1%	51.2%	71.1%
Terminal Rates (c)	5/14 (36%)	8/22 (36%)	10/17 (59%)
Day of First Observation	602	631	532
Life Table Tests (d)	P=0.186	P=0.303N	P=0.229
Logistic Regression Tests (d)	P=0.124	P=0.483N	P=0.165
Cochran-Armitage Trend Test (d)	P=0.185		
Fisher Exact Test (d)		P=0.581	P=0.222
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma			
Overall Rates (a)	15/46 (33%)	16/49 (33%)	21/50 (42%)
Adjusted Rates (b)	57.3%	54.7%	72.2%
Terminal Rates (c)	5/14 (36%)	9/22 (41%)	10/17 (59%)
Day of First Observation	602	631	532
Life Table Tests (d)	P=0.197	P=0.290N	P=0.238
Logistic Regression Tests (d)	P=0.130	P=0.479N	P=0.173
Cochran-Armitage Trend Test (d)	P=0.193		
Fisher Exact Test (d)		P=0.585	P=0.230
Preputial Gland: Adenoma			
Overall Rates (a)	2/45 (4%)	6/48 (13%)	5/50 (10%)
Adjusted Rates (b)	12.3%	23.7%	25.7%
Terminal Rates (c)	1/13 (8%)	4/22 (18%)	4/17 (24%)
Day of First Observation	715	631	605
Life Table Tests (d)	P=0.248	P=0.308	P=0.293
Logistic Regression Tests (d)	P=0.199	P=0.209	P=0.238
Cochran-Armitage Trend Test (d)	P=0.232		
Fisher Exact Test (d)		P=0.156	P=0.264
Preputial Gland: Adenoma, Carcinoma, or Squamous Cell Carcinoma			
Overall Rates (a)	3/45 (7%)	7/48 (15%)	5/50 (10%)
Adjusted Rates (b)	19.6%	27.9%	25.7%
Terminal Rates (c)	2/13 (15%)	5/22 (23%)	4/17 (24%)
Day of First Observation	715	631	605
Life Table Tests (d)	P=0.410	P=0.389	P=0.466
Logistic Regression Tests (d)	P=0.336	P=0.267	P=0.391
Cochran-Armitage Trend Test (d)	P=0.372		
Fisher Exact Test (d)		P=0.186	P=0.418
Pancreatic Islets: Adenoma			
Overall Rates (a)	3/47 (6%)	7/50 (14%)	1/48 (2%)
Adjusted Rates (b)	19.3%	20.1%	2.9%
Terminal Rates (c)	2/14 (14%)	1/22 (5%)	0/17 (0%)
Day of First Observation	722	556	612
Life Table Tests (d)	P=0.279N	P=0.278	P=0.266N
Logistic Regression Tests (d)	P=0.274N	P=0.190	P=0.305N
Cochran-Armitage Trend Test (d)	P=0.271N		
Fisher Exact Test (d)		P=0.185	P=0.301N
Pancreatic Islets: Adenoma or Carcinoma			
Overall Rates (a)	4/47 (9%)	7/50 (14%)	1/48 (2%)
Adjusted Rates (b)	26.1%	20.1%	2.9%
Terminal Rates (c)	3/14 (21%)	1/22 (5%)	0/17 (0%)
Day of First Observation	722	556	612
Life Table Tests (d)	P=0.169N	P=0.426	P=0.143N
Logistic Regression Tests (d)	P=0.171N	P=0.309	P=0.177N
Cochran-Armitage Trend Test (d)	P=0.168N		
Fisher Exact Test (d)		P=0.299	P=0.174N

TABLE A3. ANALYSIS OF PRIMARY NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
Pharynx: Squamous Papilloma			
Overall Rates (e)	3/50 (6%)	0/50 (0%)	0/50 (0%)
Adjusted Rates (b)	12.0%	0.0%	0.0%
Terminal Rates (c)	1/14 (7%)	0/22 (0%)	0/17 (0%)
Day of First Observation	577		
Life Table Tests (d)	P=0.036N	P=0.100N	P=0.126N
Logistic Regression Tests (d)	P=0.037N	P=0.121N	P=0.121N
Cochran-Armitage Trend Test (d)	P=0.037N		
Fisher Exact Test (d)		P=0.121N	P=0.121N
Pituitary Gland/Pars Distalis: Adenoma			
Overall Rates (a)	31/47 (66%)	35/50 (70%)	32/48 (67%)
Adjusted Rates (b)	84.4%	86.8%	77.7%
Terminal Rates (c)	8/13 (62%)	17/22 (77%)	8/16 (50%)
Day of First Observation	318	449	444
Life Table Tests (d)	P=0.491N	P=0.273N	P=0.523N
Logistic Regression Tests (d)	P=0.495	P=0.452	P=0.550
Cochran-Armitage Trend Test (d)	P=0.515		
Fisher Exact Test (d)		P=0.417	P=0.557
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma			
Overall Rates (a)	32/47 (68%)	35/50 (70%)	33/48 (69%)
Adjusted Rates (b)	87.5%	86.8%	78.3%
Terminal Rates (c)	9/13 (69%)	17/22 (77%)	8/16 (50%)
Day of First Observation	318	449	444
Life Table Tests (d)	P=0.489N	P=0.215N	P=0.521N
Logistic Regression Tests (d)	P=0.497	P=0.547	P=0.554
Cochran-Armitage Trend Test (d)	P=0.517		
Fisher Exact Test (d)		P=0.506	P=0.560
Skin: Keratoacanthoma			
Overall Rates (e)	4/50 (8%)	2/50 (4%)	4/50 (8%)
Adjusted Rates (b)	21.2%	5.4%	20.1%
Terminal Rates (c)	1/14 (7%)	0/22 (0%)	3/17 (18%)
Day of First Observation	706	631	630
Life Table Tests (d)	P=0.550N	P=0.243N	P=0.586N
Logistic Regression Tests (d)	P=0.576	P=0.306N	P=0.647
Cochran-Armitage Trend Test (d)	P=0.579		
Fisher Exact Test (d)		P=0.339N	P=0.643N
Testis: Interstitial Cell Adenoma			
Overall Rates (a)	29/50 (58%)	31/50 (62%)	27/50 (54%)
Adjusted Rates (b)	89.3%	85.4%	92.3%
Terminal Rates (c)	11/14 (79%)	17/22 (77%)	15/17 (88%)
Day of First Observation	577	505	444
Life Table Tests (d)	P=0.255N	P=0.182N	P=0.281N
Logistic Regression Tests (d)	P=0.406N	P=0.558	P=0.452N
Cochran-Armitage Trend Test (d)	P=0.381N		
Fisher Exact Test (d)		P=0.419	P=0.420N
Thyroid Gland: C-Cell Adenoma			
Overall Rates (a)	5/45 (11%)	5/46 (11%)	2/48 (4%)
Adjusted Rates (b)	25.7%	18.1%	11.8%
Terminal Rates (c)	3/14 (21%)	3/21 (14%)	2/17 (12%)
Day of First Observation	602	559	735
Life Table Tests (d)	P=0.139N	P=0.471N	P=0.171N
Logistic Regression Tests (d)	P=0.165N	P=0.614N	P=0.210N
Cochran-Armitage Trend Test (d)	P=0.154N		
Fisher Exact Test (d)		P=0.616N	P=0.192N

TABLE A3. ANALYSIS OF PRIMARY NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
Thyroid Gland: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	6/45 (13%)	6/46 (13%)	3/48 (6%)
Adjusted Rates (b)	27.4%	21.4%	17.6%
Terminal Rates (c)	3/14 (21%)	3/21 (14%)	3/17 (18%)
Day of First Observation	577	559	735
Life Table Tests (d)	P=0.164N	P=0.462N	P=0.196N
Logistic Regression Tests (d)	P=0.185N	P=0.606N	P=0.232N
Cochran-Armitage Trend Test (d)	P=0.173N		
Fisher Exact Test (d)		P=0.605N	P=0.211N
Hematopoietic System: Mononuclear Leukemia			
Overall Rates (e)	29/50 (58%)	26/50 (52%)	27/50 (54%)
Adjusted Rates (b)	83.2%	65.1%	80.3%
Terminal Rates (c)	9/14 (64%)	9/22 (41%)	11/17 (65%)
Day of First Observation	447	540	540
Life Table Tests (d)	P=0.323N	P=0.102N	P=0.329N
Logistic Regression Tests (d)	P=0.390N	P=0.297N	P=0.435N
Cochran-Armitage Trend Test (d)	P=0.382N		
Fisher Exact Test (d)		P=0.344N	P=0.420N
All Sites: Mesothelioma			
Overall Rates (e)	2/50 (4%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	14.3%	11.3%	0.0%
Terminal Rates (c)	2/14 (14%)	1/22 (5%)	0/17 (0%)
Day of First Observation	735	702	
Life Table Tests (d)	P=0.172N	P=0.655	P=0.194N
Logistic Regression Tests (d)	P=0.188N	P=0.590	P=0.194N
Cochran-Armitage Trend Test (d)	P=0.202N		
Fisher Exact Test (d)		P=0.500	P=0.247N

(a) Number of tumor-bearing animals/number of animals examined microscopically at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals killed at the end of the study
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) Number of tumor-bearing animals/number of animals examined grossly at the site

TABLE A4. HISTORICAL INCIDENCE OF PARATHYROID GLAND NEOPLASMS IN MALE F344/N RATS (a)

Study	Incidence of Adenomas in Controls
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories (b)	
Propylene oxide	0/44
Methyl methacrylate	0/50
Propylene	0/45
1,2-Epoxybutane	0/49
Dichloromethane	0/49
Tetrachloroethylene	0/47
Bromoethane	0/46
TOTAL	0/330
SD (c)	0.00%
Range (d)	
High	0/50
Low	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies	
TOTAL	5/1,197 (0.4%)
SD (c)	0.87%
Range (d)	
High	1/36
Low	0/50

(a) Data as of May 12, 1988, for studies of at least 104 weeks; no malignant tumors have been observed.
(b) Denominators for chamber controls represent the number of thyroid glands examined.
(c) Standard deviation
(d) 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 2-CHLOROACETOPHENONE

	Chamber Control	1 mg/m^3	2 mg/m^3
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine large	(45)	(48)	(50)
Anus, parasite metazoan			1 (2%)
Intestine large, cecum	(40)	(44)	(39)
Parasite metazoan	2 (5%)	3 (7%)	3 (8%)
Intestine large, colon	(44)	(47)	(46)
Diverticulum			1 (2%)
Hyperplasia, lymphoid		1 (2%)	
Inflammation			1 (2%)
Parasite metazoan	10 (23%)	4 (9%)	4 (9%)
Intestine large, rectum	(40)	(42)	(47)
Parasite metazoan		2 (5%)	1 (2%)
Intestine small, ileum	(41)	(45)	(43)
Hyperplasia, lymphoid		7 (16%)	
Parasite metazoan		2 (4%)	
Liver	(49)	(50)	(50)
Angiectasis	4 (8%)	7 (14%)	5 (10%)
Basophilic focus	22 (45%)	18 (36%)	21 (42%)
Clear cell focus	1 (2%)		
Congestion	1 (2%)		
Degeneration			1 (2%)
Degeneration, cystic	2 (4%)	7 (14%)	8 (16%)
Degeneration, fatty	6 (12%)	3 (6%)	8 (16%)
Eosinophilic focus	1 (2%)	1 (2%)	1 (2%)
Hematopoietic cell proliferation	1 (2%)	5 (10%)	3 (6%)
Hemorrhage		1 (2%)	
Hepatodiaphragmatic nodule	3 (6%)	3 (6%)	4 (8%)
Inflammation, granulomatous, focal	12 (24%)	19 (38%)	16 (32%)
Leukocytosis		1 (2%)	1 (2%)
Necrosis	8 (16%)	8 (16%)	5 (10%)
Thrombus		1 (2%)	1 (2%)
Bile duct, hyperplasia	32 (65%)	32 (64%)	29 (58%)
Hepatocyte, hyperplasia	4 (8%)		1 (2%)
Hepatocyte, hyperplasia, focal	1 (2%)	1 (2%)	
Hepatocyte, necrosis	3 (6%)		2 (4%)
Mesentery	(2)	(3)	(3)
Fat, inflammation, chronic	2 (100%)	2 (67%)	3 (100%)
Fat, necrosis	2 (100%)	1 (33%)	2 (67%)
Pancreas	(47)	(50)	(49)
Inflammation			3 (6%)
Acinus, atrophy	18 (38%)	15 (30%)	25 (51%)
Acinus, cytomegaly	2 (4%)		
Salivary glands	(46)	(49)	(49)
Hemorrhage	1 (2%)		
Inflammation	4 (9%)	6 (12%)	6 (12%)
Necrosis			1 (2%)
Duct, hyperplasia	11 (24%)	16 (33%)	13 (27%)
Duct, inflammation, suppurative			1 (2%)
Duct, metaplasia, squamous			1 (2%)
Parotid gland, atrophy			1 (2%)
Stomach, forestomach	(46)	(49)	(49)
Hyperplasia, squamous	6 (13%)	4 (8%)	7 (14%)
Inflammation	4 (9%)	3 (6%)	6 (12%)
Mineralization			1 (2%)
Ulcer	4 (9%)	2 (4%)	3 (6%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
ALIMENTARY SYSTEM (Continued)			
Stomach, glandular	(48)	(49)	(49)
Ectopic tissue	1 (2%)	1 (2%)	
Erosion		1 (2%)	1 (2%)
Inflammation	4 (8%)	5 (10%)	1 (2%)
Mineralization	2 (4%)		3 (6%)
Ulcer	3 (6%)	2 (4%)	
Tooth			(1)
Inflammation, chronic			1 (100%)
CARDIOVASCULAR SYSTEM			
Blood vessel			(4)
Inflammation			2 (50%)
Mineralization			2 (50%)
Heart	(49)	(50)	(50)
Inflammation, chronic	47 (96%)	44 (88%)	41 (82%)
Mineralization	1 (2%)		3 (6%)
Pigmentation, hemosiderin	1 (2%)		
Atrium, thrombus	5 (10%)	2 (4%)	4 (8%)
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(47)	(49)	(50)
Degeneration, fatty	19 (40%)	30 (61%)	18 (36%)
Focal cellular change	3 (6%)	3 (6%)	3 (6%)
Hematopoietic cell proliferation	2 (4%)	3 (6%)	3 (6%)
Hyperplasia	6 (13%)	2 (4%)	3 (6%)
Hypertrophy	1 (2%)		
Inflammation, chronic			1 (2%)
Necrosis			1 (2%)
Pigmentation, hemosiderin			1 (2%)
Thrombus			1 (2%)
Adrenal gland, medulla	(46)	(49)	(50)
Hematopoietic cell proliferation			1 (2%)
Hyperplasia	20 (43%)	15 (31%)	14 (28%)
Inflammation, chronic			1 (2%)
Necrosis			1 (2%)
Pigmentation, hemosiderin			1 (2%)
Islets, pancreatic	(47)	(50)	(48)
Cytomegaly			1 (2%)
Hyperplasia		1 (2%)	1 (2%)
Parathyroid gland	(35)	(33)	(44)
Hyperplasia	4 (11%)		4 (9%)
Pituitary gland	(47)	(50)	(48)
Pars distalis, angiectasis			1 (2%)
Pars distalis, cyst		1 (2%)	1 (2%)
Pars distalis, hemorrhage			1 (2%)
Pars distalis, hyperplasia	7 (15%)	10 (20%)	6 (13%)
Pars intermedia, degeneration, cystic			1 (2%)
Pars intermedia, hyperplasia			1 (2%)
Thyroid gland	(45)	(46)	(48)
C-cell, hyperplasia	11 (24%)	5 (11%)	10 (21%)
Follicular cell, hyperplasia		1 (2%)	
GENERAL BODY SYSTEM			
None			

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
GENITAL SYSTEM			
Epididymis	(40)	(36)	(39)
Granuloma sperm	1 (3%)		
Inflammation, chronic			1 (3%)
Mineralization			1 (3%)
Necrosis			1 (3%)
Vacuolization cytoplasmic	8 (20%)		4 (10%)
Serosa, hyperplasia			1 (3%)
Preputial gland	(45)	(48)	(50)
Cyst	1 (2%)	2 (4%)	
Hyperplasia		1 (2%)	1 (2%)
Inflammation, suppurative	17 (38%)	15 (31%)	23 (46%)
Duct, ectasia			1 (2%)
Duct, hyperplasia		1 (2%)	
Prostate	(49)	(49)	(47)
Hemorrhage	1 (2%)		
Inflammation, suppurative	18 (37%)	23 (47%)	15 (32%)
Epithelium, hyperplasia	7 (14%)	3 (6%)	9 (19%)
Seminal vesicle	(3)	(3)	(2)
Hemorrhage	1 (33%)		
Inflammation, suppurative	2 (67%)	3 (100%)	2 (100%)
Testes	(50)	(50)	(50)
Atrophy	8 (16%)	11 (22%)	14 (28%)
Mineralization			1 (2%)
Interstitial cell, hyperplasia	13 (26%)	9 (18%)	12 (24%)
Perivascular, inflammation	5 (10%)	3 (6%)	2 (4%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(46)	(49)	(50)
Depletion			1 (2%)
Myelofibrosis	2 (4%)	3 (6%)	
Lymph node	(48)	(50)	(49)
Mesenteric, angiectasis	1 (2%)		
Renal, hyperplasia			1 (2%)
Lymph node, bronchial	(44)	(48)	(46)
Angiectasis			2 (4%)
Congestion	1 (2%)	1 (2%)	
Hyperplasia	2 (5%)		1 (2%)
Inflammation, granulomatous		1 (2%)	2 (4%)
Pigmentation, hemosiderin	1 (2%)		
Lymph node, mandibular	(45)	(43)	(45)
Angiectasis		1 (2%)	1 (2%)
Congestion	1 (2%)		
Hematopoietic cell proliferation	1 (2%)		
Hyperplasia	16 (36%)	16 (37%)	15 (33%)
Inflammation, granulomatous		1 (2%)	1 (2%)
Spleen	(48)	(49)	(49)
Developmental malformation			1 (2%)
Ectopic tissue		1 (2%)	
Fibrosis	6 (13%)	8 (16%)	8 (16%)
Hematopoietic cell proliferation		3 (6%)	3 (6%)
Hemorrhage			1 (2%)
Necrosis		2 (4%)	1 (2%)
INTEGUMENTARY SYSTEM			
Mammary gland	(23)	(20)	(23)
Galactocele	7 (30%)	4 (20%)	10 (43%)
Hyperplasia	10 (43%)	8 (40%)	8 (35%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
INTEGUMENTARY SYSTEM (Continued)			
Skin	(46)	(49)	(47)
Acanthosis		2 (4%)	
Cyst epithelial inclusion	1 (2%)		
Inflammation, suppurative	1 (2%)		
Prepuce, inflammation, suppurative	1 (2%)	1 (2%)	
Subcutaneous tissue, inflammation, chronic	5 (11%)	1 (2%)	1 (2%)
Subcutaneous tissue, inflammation, suppurative		1 (2%)	
Subcutaneous tissue, necrosis			1 (2%)
MUSCULOSKELETAL SYSTEM			
Bone	(47)	(50)	(50)
Fibrous osteodystrophy	1 (2%)		3 (6%)
Hyperostosis			1 (2%)
NERVOUS SYSTEM			
Brain	(49)	(50)	(50)
Compression		2 (4%)	
Hemorrhage	1 (2%)	7 (14%)	2 (4%)
Metaplasia, osseous	1 (2%)		
Thrombus			1 (2%)
Spinal cord	(1)		
Hemorrhage	1 (100%)		
RESPIRATORY SYSTEM			
Larynx	(48)	(48)	(49)
Inflammation, suppurative	15 (31%)	14 (29%)	21 (43%)
Metaplasia, squamous		2 (4%)	3 (6%)
Lung	(49)	(50)	(50)
Congestion		3 (6%)	4 (8%)
Foreign body			1 (2%)
Hemorrhage	2 (4%)	5 (10%)	7 (14%)
Infiltration cellular, mixed cell		1 (2%)	1 (2%)
Inflammation, chronic, diffuse	1 (2%)		1 (2%)
Inflammation, chronic, focal	13 (27%)	13 (26%)	5 (10%)
Inflammation, granulomatous, focal			2 (4%)
Leukocytosis		2 (4%)	2 (4%)
Metaplasia, osseous	1 (2%)		
Mineralization	2 (4%)		2 (4%)
Pigmentation, hemosiderin	3 (6%)		2 (4%)
Thrombus		1 (2%)	
Alveolar epithelium, hyperplasia	5 (10%)	5 (10%)	6 (12%)
Alveolus, infiltration cellular, histiocytic	11 (22%)	7 (14%)	8 (16%)
Alveolus, inflammation, suppurative			1 (2%)
Artery, intima, inflammation, chronic			1 (2%)
Bronchiole, inflammation, suppurative		1 (2%)	1 (2%)
Bronchiole, epithelium, hyperplasia	1 (2%)	1 (2%)	2 (4%)
Bronchus, inflammation, suppurative			2 (4%)
Bronchus, epithelium, hyperplasia			1 (2%)
Bronchus, epithelium, metaplasia, squamous			1 (2%)
Peribronchial, infiltration cellular, mononuclear cell	1 (2%)		
Peribronchiolar, infiltration cellular, mononuclear cell			1 (2%)
Perivascular, infiltration cellular, mononuclear cell	9 (18%)	7 (14%)	13 (26%)

TABLE A5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
RESPIRATORY SYSTEM (Continued)			
Nose	(46)	(50)	(49)
Foreign body	3 (7%)	2 (4%)	3 (6%)
Inflammation	30 (65%)	34 (68%)	44 (90%)
Inflammation, suppurative	26 (57%)	36 (72%)	46 (94%)
Thrombus	7 (15%)	3 (6%)	5 (10%)
Mucosa, cyst		1 (2%)	
Nasolacrimal duct, inflammation, suppurative	9 (20%)	5 (10%)	14 (29%)
Olfactory epithelium, degeneration	4 (9%)		6 (12%)
Olfactory epithelium, metaplasia	4 (9%)	2 (4%)	7 (14%)
Respiratory epithelium, hyperplasia	12 (26%)	17 (34%)	44 (90%)
Respiratory epithelium, metaplasia, squamous	2 (4%)	11 (22%)	27 (55%)
Vomeronasal organ, inflammation, suppurative	2 (4%)	4 (8%)	6 (12%)
Trachea	(46)	(48)	(49)
Inflammation	1 (2%)		1 (2%)
Inflammation, suppurative	1 (2%)	6 (13%)	5 (10%)
Mineralization			2 (4%)
Epithelium, hyperplasia	1 (2%)	1 (2%)	
Epithelium, metaplasia, squamous	4 (9%)	6 (13%)	4 (8%)
SPECIAL SENSES SYSTEM			
Eye	(50)	(2)	(50)
Synechia			1 (2%)
Anterior chamber, inflammation, suppurative	2 (4%)		2 (4%)
Cornea, hyperplasia			1 (2%)
Cornea, inflammation, suppurative	2 (4%)		3 (6%)
Cornea, mineralization			3 (6%)
Lens, degeneration	6 (12%)		7 (14%)
Lens, mineralization			2 (4%)
Retina, atrophy	1 (2%)		2 (4%)
Sclera, inflammation			1 (2%)
Harderian gland	(1)	(2)	
Inflammation, suppurative		2 (100%)	
URINARY SYSTEM			
Kidney	(49)	(49)	(50)
Cyst	1 (2%)		
Hematopoietic cell proliferation			1 (2%)
Hydronephrosis			1 (2%)
Mineralization	2 (4%)		
Nephropathy	48 (98%)	49 (100%)	48 (96%)
Pelvis, inflammation, suppurative			2 (4%)
Renal tubule, hyperplasia	2 (4%)	3 (6%)	1 (2%)
Renal tubule, inflammation, suppurative			1 (2%)
Urinary bladder	(49)	(50)	(49)
Calculus gross observation	2 (4%)		
Calculus micro observation only	2 (4%)		
Hemorrhage	2 (4%)		1 (2%)
Inflammation, suppurative	3 (6%)	2 (4%)	1 (2%)
Mineralization	1 (2%)		
Transitional epithelium, hyperplasia	5 (10%)	3 (6%)	

APPENDIX B

SUMMARY OF LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	1 mg/m³	2 mg/m³
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine large, cecum	(47)	*(50)	(41)
Leiomyoma			1 (2%)
Intestine large, colon	(48)	*(50)	(48)
Leukemia mononuclear		2 (4%)	
Intestine small, ileum	(46)	*(50)	(45)
Peyer's patch, leukemia mononuclear	1 (2%)		1 (2%)
Intestine small, jejunum	(48)	*(50)	(46)
Peyer's patch, leukemia mononuclear			1 (2%)
Liver	(49)	*(50)	(49)
Leukemia mononuclear	27 (55%)	21 (42%)	20 (41%)
Lymphoma malignant histiocytic	1 (2%)		
Mesentery	*(50)	*(50)	*(50)
Lymphoma malignant histiocytic	1 (2%)		
Sarcoma	1 (2%)		
Fat, leukemia mononuclear	1 (2%)	1 (2%)	
Pancreas	(49)	*(50)	(47)
Leukemia mononuclear	6 (12%)	4 (8%)	2 (4%)
Acinus, adenoma			1 (2%)
Salivary glands	(49)	*(50)	(49)
Leukemia mononuclear	4 (8%)	2 (4%)	1 (2%)
Stomach, forestomach	(47)	(49)	(49)
Leukemia mononuclear	4 (9%)	3 (6%)	2 (4%)
Stomach, glandular	(49)	(50)	(49)
Leukemia mononuclear	3 (6%)	2 (4%)	1 (2%)
Tongue	*(50)	*(50)	*(50)
Papilloma squamous			1 (2%)
CARDIOVASCULAR SYSTEM			
Heart	(49)	*(50)	(50)
Leukemia mononuclear	8 (16%)	10 (20%)	8 (16%)
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(49)	(50)	(48)
Adenoma	5 (10%)	4 (8%)	4 (8%)
Carcinoma			1 (2%)
Leukemia mononuclear	13 (27%)	15 (30%)	9 (19%)
Sarcoma, metastatic, uterus			1 (2%)
Adrenal gland, medulla	(49)	(50)	(48)
Ganglioneuroma	1 (2%)		
Leukemia mononuclear	9 (18%)	14 (28%)	8 (17%)
Pheochromocytoma benign	3 (6%)	4 (8%)	3 (6%)
Bilateral, pheochromocytoma benign	2 (4%)		
Islets, pancreatic	(48)	*(50)	(46)
Adenoma	2 (4%)		1 (2%)
Carcinoma			2 (4%)
Parathyroid gland	(32)	*(50)	(38)
Adenoma			1 (3%)
Pituitary gland	(49)	*(50)	(49)
Pars distalis, adenoma	27 (55%)	40 (80%)	30 (61%)
Pars distalis, carcinoma	3 (6%)		5 (10%)
Pars distalis, leukemia mononuclear	7 (14%)	9 (18%)	4 (8%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
ENDOCRINE SYSTEM (Continued)			
Thyroid gland	(47)	*(50)	(45)
Bilateral, C-cell, adenoma	1 (2%)		
C-cell, adenoma	1 (2%)	3 (6%)	6 (13%)
Follicular cell, adenocarcinoma	2 (4%)		
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Clitoral gland	(45)	*(50)	(42)
Adenoma	5 (11%)	2 (4%)	2 (5%)
Adenoma, multiple			1 (2%)
Carcinoma		1 (2%)	1 (2%)
Ovary	(49)	*(50)	(49)
Adenoma	1 (2%)		
Granulosa cell tumor malignant			1 (2%)
Granulosa theca tumor malignant	1 (2%)		
Granulosa theca tumor benign	1 (2%)		
Leukemia mononuclear	6 (12%)	3 (6%)	5 (10%)
Lymphoma malignant histiocytic	1 (2%)		
Uterus	(49)	*(50)	(48)
Adenocarcinoma			1 (2%)
Adenoma	2 (4%)		
Deciduoma benign			1 (2%)
Fibroma	1 (2%)		
Leukemia mononuclear	4 (8%)	2 (4%)	1 (2%)
Lymphoma malignant histiocytic	1 (2%)		
Polyp stromal	6 (12%)	6 (12%)	5 (10%)
Sarcoma stromal		1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(49)	*(50)	(47)
Leukemia mononuclear	2 (4%)	2 (4%)	5 (11%)
Lymph node	(49)	*(50)	(49)
Axillary, lymphoma malignant histiocytic	1 (2%)		
Mesenteric, leukemia mononuclear	1 (2%)	2 (4%)	2 (4%)
Pancreatic, leukemia mononuclear	1 (2%)	1 (2%)	
Renal, leukemia mononuclear			1 (2%)
Lymph node, bronchial	(44)	*(50)	(41)
Leukemia mononuclear	15 (34%)	10 (20%)	11 (27%)
Lymph node, mandibular	(46)	*(50)	(47)
Leukemia mononuclear	14 (30%)	12 (24%)	9 (19%)
Lymphoma malignant histiocytic	1 (2%)		
Spleen	(49)	*(50)	(49)
Leukemia mononuclear	26 (53%)	22 (44%)	20 (41%)
Lymphoma malignant histiocytic	1 (2%)		
Thymus	(38)	*(50)	(46)
Leukemia mononuclear	4 (11%)	7 (14%)	4 (9%)
INTEGUMENTARY SYSTEM			
Mammary gland	(48)	(50)	(50)
Adenocarcinoma	2 (4%)	2 (4%)	1 (2%)
Adenoma		2 (4%)	1 (2%)
Fibroadenoma	11 (23%)	15 (30%)	21 (42%)
Fibroadenoma, multiple	1 (2%)	4 (8%)	2 (4%)
Leukemia mononuclear	1 (2%)	1 (2%)	3 (6%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
INTEGUMENTARY SYSTEM (Continued)			
Skin	(49)	*(50)	(47)
Keratoacanthoma	1 (2%)		1 (2%)
Papilloma squamous			1 (2%)
Thoracic, subcutaneous tissue, ventral, leukemia mononuclear	4 (8%)	1 (2%)	4 (9%)
MUSCULOSKELETAL SYSTEM			
Skeletal muscle	*(50)	*(50)	*(50)
Schwannoma malignant			1 (2%)
NERVOUS SYSTEM			
Brain	(49)	*(50)	(50)
Carcinoma, metastatic, pituitary gland	3 (6%)		5 (10%)
Glioma benign			1 (2%)
Leukemia mononuclear	5 (10%)	5 (10%)	2 (4%)
RESPIRATORY SYSTEM			
Lung	(49)	*(50)	(49)
Alveolar/bronchiolar adenoma	1 (2%)	1 (2%)	
Alveolar/bronchiolar carcinoma			1 (2%)
Carcinoma, metastatic, adrenal gland			1 (2%)
Leukemia mononuclear	24 (49%)	19 (38%)	17 (35%)
Lymphoma malignant histiocytic	1 (2%)		
Neoplasm, NOS, metastatic, uncertain primary site		1 (2%)	
Sarcoma, metastatic, uterus			1 (2%)
Mediastinum, hemangioma	1 (2%)		
Mediastinum, sarcoma			1 (2%)
Nose	(48)	(50)	(49)
Fibrosarcoma	1 (2%)		
Leukemia mononuclear	4 (8%)	3 (6%)	
SPECIAL SENSES SYSTEM			
Eye	(49)	*(50)	(48)
Leukemia mononuclear	8 (16%)		8 (17%)
Zymbal gland	*(50)	*(50)	*(50)
Carcinoma	1 (2%)		
URINARY SYSTEM			
Kidney	(49)	*(50)	(49)
Leukemia mononuclear	11 (22%)	11 (22%)	7 (14%)
Capsule, sarcoma, metastatic, uterus			1 (2%)
Renal tubule, adenoma		1 (2%)	
Urinary bladder	(48)	*(50)	(48)
Leukemia mononuclear	5 (10%)	4 (8%)	2 (4%)
Transitional epithelium, papilloma	1 (2%)	1 (2%)	
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Leukemia mononuclear	27 (54%)	23 (46%)	20 (40%)
Hemangioma	1 (2%)		
Lymphoma malignant histiocytic	1 (2%)		

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Moribund	22	28	22
Terminal sacrifice	23	20	24
Dead	5	2	4
TUMOR SUMMARY			
Total animals with primary neoplasms **	45	50	48
Total primary neoplasms	113	110	120
Total animals with benign neoplasms	39	47	43
Total benign neoplasms	74	83	84
Total animals with malignant neoplasms	32	26	29
Total malignant neoplasms	39	27	36
Total animals with secondary neoplasms ***	3	1	7
Total secondary neoplasms	3	1	9
Total animals with malignant neoplasms--uncertain primary site		1	

* Number of animals receiving complete necropsy examination; 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 2-CHLOROACETOPHENONE: CHAMBER CONTROL

WEEKS ON STUDY	07 09	06 09	07 07	08 02	08 02	08 03	08 03	08 04	08 05	08 06	08 06	08 06	08 07	09 01	09 03	09 04	09 04	09 05	09 05	09 07	09 07	09 09	09 09	10 00	10 00
CARCASS ID	07 01	06 71	07 41	08 11	09 31	07 91	08 01	07 51	09 51	08 41	06 91	08 81	07 11	09 41	05 51	07 31	05 31	05 11	08 51	08 91	10 01	06 21	09 81	06 41	06 81
ALIMENTARY SYSTEM																									
Esophagus	+	A	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	M	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Intestine small	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	M	I	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peyer's patch, leukemia mononuclear																	X								
Intestine small, jejunum	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X				X			X		X		X	X		X		X	X	X	X	X
Lymphoma malignant histiocytic					X																				
Mesentery					+		+								+		+								
Lymphoma malignant histiocytic					X																				
Sarcoma															X										
Fat, leukemia mononuclear																	X								
Pancreas	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X			X							X	X								
Pharynx																			+						
Salivary glands	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X			X								X								
Stomach	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+
Leukemia mononuclear						X																X	X		
Stomach, glandular	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																X	X						X		
Tooth	+																								
CARDIOVASCULAR SYSTEM																									
Heart	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X			X							X	X				X		X		
ENDOCRINE SYSTEM																									
Adrenal gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																					X				
Leukemia mononuclear						X			X					X		X	X		X		X	X	X		
Adrenal gland, medulla	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Ganglioneuroma																									
Leukemia mononuclear						X			X							X	X				X	X	X		
Pheochromocytoma benign											X														
Bilateral, pheochromocytoma benign														X											X
Islets, pancreatic	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	M	M	M	M	M	M	+	M	+	M	+	+	M	+	+	+	+	M	M	M	+	+	M	+	M
Pituitary gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X	X			X	X		X			X				X	X	X	X	X		X		
Pars distalis, carcinoma																									
Pars distalis, leukemia mononuclear																X					X	X	X		X
Thyroid gland	M	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, C-cell, adenoma																									
C-cell, adenoma																									
Follicular cell, adenocarcinoma			X																						
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Clitoral gland	M	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+
Adenoma							X						X												
Ovary	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X																				
Granulosa theca tumor malignant																									
Granulosa theca tumor benign																									
Leukemia mononuclear																X	X				X		X		
Lymphoma malignant histiocytic					X																				
Uterus	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Fibroma																		X							
Leukemia mononuclear																X							X		
Lymphoma malignant histiocytic					X																				
Polyp stromal					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 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	106	TOTAL:
CARCASS ID	06661	07811	05411	05561	05571	05581	05591	06601	06611	06631	06651	07211	07611	07711	08211	08311	08611	08711	09011	09111	09211	09611	09711	09911	05211	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, colon	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	I	M	+	+	+	+	+	+	+	44
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Peyer's patch, leukemia mononuclear																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X	X	X	X	X		X				X	X					X		X	X	X	X	X		27
Lymphoma malignant histiocytic																										1
Mesentery		+	+																							6
Lymphoma malignant histiocytic																										1
Sarcoma																										1
Fat, leukemia mononuclear																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear				X	X																					6
Pharynx																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear				X																						4
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Leukemia mononuclear				X																						4
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear																										3
Tooth																										1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear		X		X																						8
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma	X				X		X													X						5
Leukemia mononuclear	X	X		X																X						13
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Ganglioneuroma									X																	1
Leukemia mononuclear		X		X																						9
Pheochromocytoma benign								X			X															3
Bilateral, pheochromocytoma benign																										2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	48
Adenoma					X			X																		2
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	M	+	M	+	32
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma		X	X			X	X	X	X	X	X	X	X	X							X		X	X	X	27
Pars distalis, carcinoma	X				X															X						3
Pars distalis, leukemia mononuclear		X		X																						7
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Bilateral, C-cell, adenoma								X																		1
C-cell, adenoma																					X					1
Follicular cell, adenocarcinoma												X														2
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	45
Adenoma					X															X					X	5
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																										1
Granulosa theca tumor malignant						X																				1
Granulosa theca tumor benign											X															1
Leukemia mononuclear				X														X								6
Lymphoma malignant histiocytic																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma	X																						X			2
Fibroma																										1
Leukemia mononuclear		X	X																							4
Lymphoma malignant histiocytic																										1
Polyp stromal														X												6

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

WEEKS ON STUDY	007	069	077	082	082	083	083	084	085	086	086	086	087	091	093	094	094	095	095	097	097	099	099	100	100
CARCASS ID	07001	06711	07411	08111	09311	07911	08011	07511	09511	08411	06911	08811	07111	09411	05511	07311	05311	05111	08511	08911	10101	06211	09811	06411	06811
HEMATOPOIETIC SYSTEM																									
Blood																									
Bone marrow	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																						X			
Lymph node	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Axillary, lymphoma malignant histiocytic					X																				
Mesenteric, leukemia mononuclear																							X		
Pancreatic, leukemia mononuclear																	X								
Lymph node, bronchial	+	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	I	+	+	+	I	+
Leukemia mononuclear						X			X					X		X	X				X	X	X		
Lymph node, mandibular	+	A	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X										X	X				X	X	X		X
Lymphoma malignant histiocytic					X																				
Spleen	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X			X			X		X		X	X				X	X	X	X	X
Lymphoma malignant histiocytic					X																				
Thymus	+	A	M	M	M	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	M	+	M
Leukemia mononuclear																X	X								
INTEGUMENTARY SYSTEM																									
Mammary gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Fibroadenoma			X								X									X				
Fibroadenoma, multiple																									
Leukemia mononuclear																									
Skin	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																				X					
Thoracic, subcutaneous tissue, ventral, leukemia mononuclear						X										X						X			
MUSCULOSKELETAL SYSTEM																									
Bone	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland																									
Leukemia mononuclear																X	X						X		
RESPIRATORY SYSTEM																									
Larynx	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Lung	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Leukemia mononuclear						X			X			X		X		X	X				X	X	X	X	X
Lymphoma malignant histiocytic					X																				
Mediastinum, hemangioma																									
Nose	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma										X															
Leukemia mononuclear																X	X						X		
Trachea	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X							X	X					X	X		
Harderian gland																									
Lacrimal gland											+													+	
Zymbal gland			+																						-
Carcinoma			X																						
URINARY SYSTEM																									
Kidney	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear									X			X				X	X					X	X		X
Urinary bladder	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X										X	X						X		
Transitional epithelium, papilloma																									

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	106	TOTAL
CARCASS ID	06661	07881	05441	05661	05771	05881	05991	06601	06611	06631	06651	07221	07661	07771	08211	08331	08661	08771	09091	09111	09221	09661	09771	09991	05221	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood																								+		1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear																								X		2
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Axillary, lymphoma malignant histiocytic																										1
Mesenteric, leukemia mononuclear																										1
Pancreatic, leukemia mononuclear																										1
Lymph node, bronchial	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	44
Leukemia mononuclear	X	X	X	X				X					X									X				15
Lymph node, mandibular	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear	X	X	X	X									X								X	X				14
Lymphoma malignant histiocytic																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X	X	X	X	X		X				X	X					X		X	X	X	X	X		26
Lymphoma malignant histiocytic																										1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	M	+	38
Leukemia mononuclear			X	X																						4
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma																							X		X	2
Fibroadenoma		X	X		X	X			X	X								X							X	11
Fibroadenoma, multiple																				X						1
Leukemia mononuclear				X																						1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Keratoacanthoma																										1
Thoracic, subcutaneous tissue, ventral, leukemia mononuclear				X																						4
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, pituitary gland	X				X															X						3
Leukemia mononuclear		X		X																						5
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma						X																				1
Leukemia mononuclear	X	X	X	X	X			X				X	X					X		X	X	X		X		24
Lymphoma malignant histiocytic																										1
Mediastinum, hemangioma								X																		1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibrosarcoma																										1
Leukemia mononuclear				X																						4
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPECIAL SENSES SYSTEM																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear		X		X																				X		8
Harderian gland			+	+						+	+														+	5
Lacrimal gland																									+	3
Zymbal gland																										1
Carcinoma																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X	X	X																		X					11
Urinary bladder	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear				X																						5
Transitional epithelium, papilloma														X												1

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 1 mg/m³

WEEKS ON STUDY	075	079	080	087	088	088	088	090	091	091	092	092	093	093	094	094	096	096	097	097	099	099	099	100	100
CARCASS ID	19611	16211	15111	19011	17311	15811	19811	18811	15611	15711	15311	16911	18911	19511	17711	18111	18001	16611	17611	19911	16811	17411	18411	17911	16411
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	M	+	+	+	+
Leukemia mononuclear							X															X			
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X		X				X	X			X	X	X		X		X		X	X	X	X	X	X	X
Mesentery																						+			
Fat, leukemia mononuclear																						X			
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear								X				X							X						
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+
Leukemia mononuclear																	X		X						
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X										X		X						
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																			X						
Tooth														+											
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X		X				X					X	X				X		X			X			X
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma												X					X								
Leukemia mononuclear	X		X				X	X				X	X				X		X	X		X	X		
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X				X	X				X	X				X		X	X		X	X		
Pheochromocytoma benign								X																	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Parathyroid gland	+	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	X	X	X	X	X	X
Pars distalis, leukemia mononuclear								X				X					X		X	X	X		X		
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma								X						X											
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Clitoral gland	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+
Leukemia mononuclear							X						X												
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																			X			X			
Polyp stromal			X			X			X		X												X		
Sarcoma stromal				X																					
Vagina																									

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1 mg/m³ (Continued)

WEEKS ON STUDY	101	101	102	105	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	161 1	185 1	154 1	152 1	200 1	155 1	159 1	160 1	163 1	165 1	167 1	170 1	171 1	172 1	175 1	178 1	182 1	183 1	186 1	187 1	191 1	192 1	193 1	194 1	197 1	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+																					29
Intestine large	+	+	+	+	+																					29
Intestine large, cecum	+	+	A	+	+																					28
Intestine large, colon	+	+	+	+	+																					28
Leukemia mononuclear																										2
Intestine large, rectum	+	+	+	+	+																					28
Intestine small	+	+	A	+	+																					29
Intestine small, duodenum	+	+	A	+	+																					29
Intestine small, ileum	+	+	A	+	+																					27
Intestine small, jejunum	+	+	A	+	+																					28
Liver	+	+	+	+	+			+	+		+			+		+		+		+		+	+	+	+	41
Leukemia mononuclear		X	X								X					X							X			21
Mesentery									+																	2
Fat, leukemia mononuclear																										1
Pancreas	+	+	+	+	+																					30
Leukemia mononuclear		X																								4
Salivary glands	+	+	+	+	+																					29
Leukemia mononuclear																										2
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear																										3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X																								2
Tooth																										1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+																					30
Leukemia mononuclear		X																								10
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma							X																		X	4
Leukemia mononuclear		X					X				X												X			15
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X					X				X												X			14
Pheochromocytoma benign		X					X											X								4
Islets, pancreatic	+	+	+	+	+																					29
Parathyroid gland	+	+	M	I	M																					22
Pituitary gland	+	+	+	+	+	+	+		+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma	X	X	X	X	X	X				X			X	X	X		X	X	X	X	X	X	X	X	X	40
Pars distalis, leukemia mononuclear		X					X																			9
Thyroid gland	+	+	M	+	+	+																				30
C-cell, adenoma						X																				3
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Clitoral gland	+	+	+	+	M									M		+	+				+	+	+			33
Adenoma																	X					X				2
Carcinoma				X																						1
Ovary	+	+	+	+	+	+			+																	31
Leukemia mononuclear		X																								3
Uterus	+	+	+	+	+		+			+										+						33
Leukemia mononuclear																										2
Polyp stromal																				X						6
Sarcoma stromal																										1
Vagina																					+					1

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1 mg/m³ (Continued)

WEEKS ON STUDY	075	079	080	087	088	088	088	090	091	091	092	092	093	093	094	094	096	096	097	097	099	099	099	100	100
CARCASS ID	19601	16211	15111	19011	17311	15811	19811	18811	15611	15711	15311	16911	18911	19511	17711	18111	18011	16611	17611	19911	16811	17411	18411	17911	16411
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear								X														X			
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenteric, leukemia mononuclear							X																		
Pancreatic, leukemia mononuclear																						X			
Lymph node, bronchial	+	M	+	+	+	+	+	+	M	M	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+
Leukemia mononuclear			X				X	X				X					X		X	X		X			
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X		X				X	X				X	X						X	X		X			X
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X		X				X	X			X	X	X		X		X		X	X	X	X	X	X	X
Thymus	+	M	+	+	+	+	+	+	+	+	M	+	I	+	+	+	+	+	+	M	+	+	M	+	+
Leukemia mononuclear			X				X					X							X		X	X			
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
Adenocarcinoma																									
Adenoma																X									
Fibroadenoma		X		X	X										X						X		X		
Fibroadenoma, multiple														X											
Leukemia mononuclear																									
Skin	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	M
Thoracic, subcutaneous tissue, ventral, leukemia mononuclear												X													
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear								X									X			X		X			
RESPIRATORY SYSTEM																									
Larynx	I	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	I	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Leukemia mononuclear	X		X				X	X				X	X		X		X		X	X	X	X		X	X
Neoplasm, NOS, metastatic, uncertain primary site																		X							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
Leukemia mononuclear																	X		X						
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye					+																				
Harderian gland																								+	+
Lacrimal gland								+																	
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X	X				X	X						X	X		X			X
Renal tubule, adenoma																			X						
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X												X			X			
Transitional epithelium, papilloma																									

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 1 mg/m³ (Continued)

WEEKS ON STUDY	101	101	102	105	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	16111	18511	15411	15211	20011	15511	15911	16011	16311	16511	16711	17011	17111	17211	17511	17811	18211	18311	18611	18711	19111	19211	19311	19411	19711	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+																					30
Leukemia mononuclear																										2
Lymph node	+	+	+	+	+		+																			31
Mesenteric, leukemia mononuclear		X																								2
Pancreatic, leukemia mononuclear																										1
Lymph node, bronchial	+	+	+	+	+		+																			26
Leukemia mononuclear		X					X																			10
Lymph node, mandibular	+	+	+	+	+																					30
Leukemia mononuclear		X	X																							12
Spleen	+	+	+	+	+				+		+					+	+						+			35
Leukemia mononuclear		X	X						X		X					X							X			22
Thymus	+	+	+	M	+																					24
Leukemia mononuclear		X																								7
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma	X	X																								2
Adenoma										X																2
Fibroadenoma					X		X	X	X	X		X				X				X				X		15
Fibroadenoma, multiple													X	X								X				4
Leukemia mononuclear							X																			1
Skin	+	+	+	+	+																					27
Thoracic, subcutaneous tissue, ventral, leukemia mononuclear																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+																					30
NERVOUS SYSTEM																										
Brain	+	+	+	+	+																					30
Leukemia mononuclear		X																								5
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+																					27
Lung	+	+	+	+	+		+				+	+			+	+	+	+	+				+	+		40
Alveolar/bronchiolar adenoma																X										1
Leukemia mononuclear		X	X				X				X					X										19
Neoplasm, NOS, metastatic, uncertain primary site																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear		X																								3
Trachea	+	+	+	+	+																					29
SPECIAL SENSES SYSTEM																										
Eye																								+		2
Harderian gland																										2
Lacrimal gland														+	+											3
URINARY SYSTEM																										
Kidney	+	+	+	+	+		+							+			+		+	+			+		+	37
Leukemia mononuclear		X					X																X			11
Renal tubule, adenoma																										1
Urinary bladder	+	+	+	+	+					+																31
Leukemia mononuclear		X																								4
Transitional epithelium, papilloma										X																1

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 2 mg/m³

WEEKS ON STUDY	037	069	070	071	073	074	074	075	079	083	088	088	088	096	096	097	098	098	098	098	099	100	100	101	103
CARCASS ID	25211	25911	27411	27811	28611	26911	26711	26011	29911	28011	26111	28711	27111	29611	29211	28211	26411	26611	25711	29711	29511	25511	25611	25811	27611
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine large, cecum	M	M	M	M	M	M	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Leiomyoma																									
Intestine large, colon	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine large, rectum	+	+	+	A	I	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine small	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Intestine small, duodenum	+	+	M	A	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	A	+
Intestine small, ileum	+	+	+	A	+	+	M	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+
Peyer's patch, leukemia mononuclear																				X					
Intestine small, jejunum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	A	+
Peyer's patch, leukemia mononuclear																				X					
Liver	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X		X	X						X	X	X	X			X		X		X	X
Mesentery					+			+																	
Pancreas	+	+	+	A	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Leukemia mononuclear																				X					
Acinus, adenoma																									
Salivary glands	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X																		
Stomach, glandular	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									
Tongue																									
Papilloma squamous																									
Tooth																									
CARDIOVASCULAR SYSTEM																									
Blood vessel																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X		X	X								X				X					X
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Adenoma																									
Carcinoma																		X							
Leukemia mononuclear							X	X							X	X				X		X			X
Sarcoma, metastatic, uterus										X															
Adrenal gland, medulla	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X	X							X					X		X			X
Pheochromocytoma benign																								X	
Islets, pancreatic	+	+	+	A	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Adenoma																									
Carcinoma																									
Parathyroid gland	+	+	+	+	+	+	+	M	+	M	+	+	+	+	M	+	M	M	+	+	+	+	+	+	M
Adenoma																									
Pituitary gland	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma						X			X		X	X			X	X	X	X	X	X	X				
Pars distalis, carcinoma								X																X	X
Pars distalis, leukemia mononuclear							X									X				X		X			
Thyroid gland	+	+	+	A	+	+	+	+	+	+	+	+	+	+	M	+	A	A	+	+	+	+	+	A	+
C cell, adenoma																					X		X		
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Clitoral gland	+	M	+	M	+	+	+	M	+	+	+	M	M	+	+	+	+	M	+	+	+	+	+	M	+
Adenoma																							X		
Adenoma, multiple																									
Carcinoma														X											
Ovary	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor malignant																						X			
Leukemia mononuclear					X		X															X			
Oviduct																									
Uterus	+	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Deciduoma benign																									
Leukemia mononuclear																									
Polyp stromal														X									X		
Sarcoma stromal										X															

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 2 mg/m³
(Continued)

WEEKS ON STUDY	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL
CARCASS ID	26811	25111	25311	25411	26211	26311	26511	27011	27211	27311	27511	27711	27911	28111	28311	28411	28511	28811	28911	29011	29111	29311	29411	29811	30101	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	M	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	M	+	+	+	45
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Leiomyoma											X															1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	M	+	+	+	43
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	45
Peyer's patch, leukemia mononuclear																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Peyer's patch, leukemia mononuclear																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X						X				X			X	X				X	X	X		X			20
Mesentery																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Leukemia mononuclear	X																									2
Acinus, adenoma													X													1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X																									1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	49
Leukemia mononuclear	X																									2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X																									1
Tongue																	+									1
Papilloma squamous																	X									1
Tooth																									+	1
CARDIOVASCULAR SYSTEM																										
Blood vessel			+													+										2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X													X												8
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma								X									X	X			X					4
Carcinoma																										1
Leukemia mononuclear	X													X												9
Sarcoma, metastatic, uterus																										1
Adrenal gland, medulla	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear	X													X												8
Pheochromocytoma benign								X											X							3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	46
Adenoma																									X	1
Carcinoma											X													X		2
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	M	+	M	+	M	+	M	+	+	38
Adenoma																									X	1
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma		X		X	X	X	X	X	X	X		X		X	X	X		X		X	X	X	X	X	X	30
Pars distalis, carcinoma			X										X													5
Pars distalis, leukemia mononuclear																										4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
C cell, adenoma	X							X									X	X								6
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Clitoral gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Adenoma																		X								2
Adenoma, multiple									X																	1
Carcinoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Granulosa cell tumor malignant																										1
Leukemia mononuclear	X													X												5
Oviduct																						+				1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma												X														1
Deciduoma benign																						X				1
Leukemia mononuclear	X																									1
Polyp stromal			X		X									X												5
Sarcoma stromal																										1

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 2 mg/m³ (Continued)

WEEKS ON STUDY	037	069	070	071	073	074	074	075	079	083	088	088	088	096	096	097	098	098	098	099	100	100	101	103
CARCASS ID	25211	25911	27411	27811	28611	26911	26711	26001	29911	28011	26111	28711	27111	29611	29211	28211	26411	26611	25711	29711	29511	25511	25611	25811	27611
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	I
Leukemia mononuclear					X									X	X	X						X			
Lymph node	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenteric, leukemia mononuclear							X															X			
Renal, leukemia mononuclear																						X			
Lymph node, bronchial	+	+	+	A	+	+	+	+	+	+	+	M	+	+	+	M	+	+	M	+	+	+	+	+	+
Leukemia mononuclear					X		X	X						X	X					X		X			X
Lymph node, mandibular	+	+	+	A	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+
Leukemia mononuclear							X								X	X				X		X			X
Spleen	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X		X	X						X	X	X	X			X		X		X	X
Thymus	+	+	+	A	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X													X		X			
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																			X						
Adenoma																									
Fibroadenoma			X		X	X					X	X	X				X	X	X		X	X	X		
Fibroadenoma, multiple																									
Leukemia mononuclear																						X		X	
Skin	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Papilloma squamous																						X			
Thoracic, subcutaneous tissue, ventral, leukemia mononuclear							X													X					
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+																								
Schwannoma malignant	X																								
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland								X															X	X	
Glioma benign																									
Leukemia mononuclear							X	X																	
RESPIRATORY SYSTEM																									
Larynx	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, adrenal gland																	X								
Leukemia mononuclear					X		X	X						X	X	X				X		X		X	X
Sarcoma, metastatic, uterus										X															
Mediastinum, sarcoma																							X		
Nose	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
SPECIAL SENSES SYSTEM																									
Eye	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
Leukemia mononuclear					X			X							X	X				X		X			
Harderian gland								+																	
Lacrimal gland																						+			
URINARY SYSTEM																									
Kidney	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear							X	X							X					X		X			
Capsule, sarcoma, metastatic, uterus										X															
Urinary bladder	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																								X	

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 2 mg/m³ (Continued)

WEEKS ON STUDY	105	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	26811	25111	25311	25411	26211	26311	26511	27001	27211	27311	27511	27711	27911	28111	28311	28411	28511	28811	28911	29011	29111	29311	29411	29811	30101	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Leukemia mononuclear																										5
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesenteric, leukemia mononuclear																										2
Renal, leukemia mononuclear																										1
Lymph node, bronchial	+	I	+	+	M	+	+	M	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	41
Leukemia mononuclear	X														X					X						11
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Leukemia mononuclear	X														X					X						9
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X						X				X			X	X				X	X	X		X			20
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	I	+	+	+	+	+	+	+	+	+	46
Leukemia mononuclear	X																									4
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma															X											1
Adenoma																										1
Fibroadenoma	X		X			X								X	X			X		X	X	X	X			21
Fibroadenoma, multiple								X									X									2
Leukemia mononuclear	X																									3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	47
Keratoacanthoma																		X								1
Papilloma squamous																										1
Thoracic, subcutaneous tissue, ventral, leukemia mononuclear	X										X															4
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Schwannoma malignant																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pituitary gland			X										X													5
Glioma benign													X													1
Leukemia mononuclear																										2
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar carcinoma									X																	1
Carcinoma, metastatic, adrenal gland																										1
Leukemia mononuclear	X						X				X			X	X					X			X			17
Sarcoma, metastatic, uterus																										1
Mediastinum, sarcoma																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPECIAL SENSES SYSTEM																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear														X	X											8
Harderian gland	+	+								+	+											+	+			8
Lacrimal gland																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear	X													X												7
Capsule, sarcoma, metastatic, uterus																										1
Urinary bladder	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leukemia mononuclear																				X						2

TABLE B3. ANALYSIS OF PRIMARY NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	1 mg/m^3	2 mg/m^3
Adrenal Cortex: Adenoma			
Overall Rates (a)	5/49 (10%)	4/50 (8%)	4/48 (8%)
Adjusted Rates (b)	19.2%	14.9%	16.7%
Terminal Rates (c)	3/23 (13%)	2/20 (10%)	4/24 (17%)
Day of First Observation	679	640	735
Life Table Tests (d)	P=0.399N	P=0.542N	P=0.473N
Logistic Regression Tests (d)	P=0.411N	P=0.479N	P=0.470N
Cochran-Armitage Trend Test (d)	P=0.441N		
Fisher Exact Test (d)		P=0.487N	P=0.513N
Adrenal Cortex: Adenoma or Carcinoma			
Overall Rates (a)	5/49 (10%)	4/50 (8%)	5/48 (10%)
Adjusted Rates (b)	19.2%	14.9%	19.1%
Terminal Rates (c)	3/23 (13%)	2/20 (10%)	4/24 (17%)
Day of First Observation	679	640	682
Life Table Tests (d)	P=0.528N	P=0.542N	P=0.595N
Logistic Regression Tests (d)	P=0.556N	P=0.479N	P=0.609N
Cochran-Armitage Trend Test (d)	P=0.556		
Fisher Exact Test (d)		P=0.487N	P=0.617
Adrenal Medulla: Pheochromocytoma			
Overall Rates (a)	5/49 (10%)	4/50 (8%)	3/48 (6%)
Adjusted Rates (b)	16.6%	15.6%	12.1%
Terminal Rates (c)	2/23 (9%)	2/20 (10%)	2/23 (9%)
Day of First Observation	602	626	705
Life Table Tests (d)	P=0.288N	P=0.512N	P=0.350N
Logistic Regression Tests (d)	P=0.301N	P=0.476N	P=0.371N
Cochran-Armitage Trend Test (d)	P=0.299N		
Fisher Exact Test (d)		P=0.487N	P=0.369N
Clitoral Gland: Adenoma			
Overall Rates (a)	5/45 (11%)	(e) 2/33 (6%)	3/42 (7%)
Adjusted Rates (b)	17.8%		11.8%
Terminal Rates (c)	3/22 (14%)		2/23 (9%)
Day of First Observation	577		700
Life Table Test (d)			P=0.340N
Logistic Regression Test (d)			P=0.396N
Fisher Exact Test (d)			P=0.396N
Clitoral Gland: Adenoma or Carcinoma			
Overall Rates (a)	5/45 (11%)	(e) 3/33 (9%)	4/42 (10%)
Adjusted Rates (b)	17.8%		14.2%
Terminal Rates (c)	3/22 (14%)		2/23 (9%)
Day of First Observation	577		666
Life Table Test (d)			P=0.470N
Logistic Regression Test (d)			P=0.547N
Fisher Exact Test (d)			P=0.544N
Pancreatic Islets: Adenoma or Carcinoma			
Overall Rates (a)	2/48 (4%)	(e) 0/29 (0%)	3/46 (7%)
Adjusted Rates (b)	9.1%		13.0%
Terminal Rates (c)	2/22 (9%)		3/23 (13%)
Day of First Observation	735		735
Life Table Test (d)			P=0.521
Logistic Regression Test (d)			P=0.521
Fisher Exact Test (d)			P=0.480

TABLE B3. ANALYSIS OF PRIMARY NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m³	2 mg/m³
Mammary Gland: Fibroadenoma			
Overall Rates (f)	12/50 (24%)	19/50 (38%)	23/50 (46%)
Adjusted Rates (b)	42.2%	64.4%	61.9%
Terminal Rates (c)	8/23 (35%)	11/20 (55%)	11/24 (46%)
Day of First Observation	533	553	490
Life Table Tests (d)	P=0.031	P=0.070	P=0.038
Logistic Regression Tests (d)	P=0.013	P=0.117	P=0.017
Cochran-Armitage Trend Test (d)	P=0.014		
Fisher Exact Test (d)		P=0.097	P=0.018
Mammary Gland: Adenoma or Fibroadenoma			
Overall Rates (f)	12/50 (24%)	20/50 (40%)	23/50 (46%)
Adjusted Rates (b)	42.2%	65.4%	61.9%
Terminal Rates (c)	8/23 (35%)	11/20 (55%)	11/24 (46%)
Day of First Observation	533	553	490
Life Table Tests (d)	P=0.033	P=0.050	P=0.038
Logistic Regression Tests (d)	P=0.013	P=0.082	P=0.017
Cochran-Armitage Trend Test (d)	P=0.015		
Fisher Exact Test (d)		P=0.066	P=0.018
Mammary Gland: Adenoma, Fibroadenoma, or Adenocarcinoma			
Overall Rates (f)	13/50 (26%)	22/50 (44%)	23/50 (46%)
Adjusted Rates (b)	46.0%	68.2%	61.9%
Terminal Rates (c)	9/23 (39%)	11/20 (55%)	11/24 (46%)
Day of First Observation	533	553	490
Life Table Tests (d)	P=0.054	P=0.037	P=0.057
Logistic Regression Tests (d)	P=0.022	P=0.058	P=0.028
Cochran-Armitage Trend Test (d)	P=0.026		
Fisher Exact Test (d)		P=0.046	P=0.030
Pituitary Gland/Pars Distalis: Adenoma			
Overall Rates (a)	27/49 (55%)	40/48 (83%)	30/49 (61%)
Adjusted Rates (b)	73.1%	90.2%	84.8%
Terminal Rates (c)	14/23 (61%)	14/18 (78%)	19/24 (79%)
Day of First Observation	533	553	512
Life Table Tests (d)	P=0.427	P=0.017	P=0.442
Logistic Regression Tests (d)	P=0.270	P=0.003	P=0.316
Cochran-Armitage Trend Test (d)	P=0.296		
Fisher Exact Test (d)		P=0.002	P=0.341
Pituitary Gland/Pars Distalis: Carcinoma			
Overall Rates (a)	3/49 (6%)	0/48 (0%)	5/49 (10%)
Adjusted Rates (b)	12.3%	0.0%	16.8%
Terminal Rates (c)	2/23 (9%)	0/18 (0%)	2/24 (8%)
Day of First Observation	731		523
Life Table Tests (d)	P=0.271	P=0.161N	P=0.374
Logistic Regression Tests (d)	P=0.252	P=0.152N	P=0.355
Cochran-Armitage Trend Test (d)	P=0.253		
Fisher Exact Test (d)		P=0.125N	P=0.357
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma			
Overall Rates (a)	30/49 (61%)	40/48 (83%)	35/49 (71%)
Adjusted Rates (b)	80.0%	90.2%	91.7%
Terminal Rates (c)	16/23 (70%)	14/18 (78%)	21/24 (88%)
Day of First Observation	533	553	512
Life Table Tests (d)	P=0.318	P=0.043	P=0.323
Logistic Regression Tests (d)	P=0.124	P=0.018	P=0.160
Cochran-Armitage Trend Test (d)	P=0.156		
Fisher Exact Test (d)		P=0.013	P=0.196

TABLE B3. ANALYSIS OF PRIMARY NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
Thyroid Gland: C-Cell Adenoma			
Overall Rates (a)	2/47 (4%)	(e) 3/30 (10%)	6/45 (13%)
Adjusted Rates (b)	8.7%		21.6%
Terminal Rates (c)	2/23 (9%)		3/24 (13%)
Day of First Observation	735		687
Life Table Test (d)			P=0.151
Logistic Regression Test (d)			P=0.122
Fisher Exact Test (d)			P=0.120
Uterus: Stromal Polyp			
Overall Rates (f)	6/49 (12%)	6/50 (12%)	5/48 (10%)
Adjusted Rates (b)	16.2%	16.3%	17.8%
Terminal Rates (c)	1/23 (4%)	1/20 (5%)	3/24 (13%)
Day of First Observation	573	560	666
Life Table Tests (d)	P=0.425N	P=0.588N	P=0.476N
Logistic Regression Tests (d)	P=0.455N	P=0.575	P=0.514N
Cochran-Armitage Trend Test (d)	P=0.451N		
Fisher Exact Test (d)		P=0.606N	P=0.515N
Hematopoietic System: Mononuclear Leukemia			
Overall Rates (f)	27/50 (54%)	23/50 (46%)	20/50 (40%)
Adjusted Rates (b)	72.4%	57.0%	53.8%
Terminal Rates (c)	13/23 (57%)	5/20 (25%)	8/24 (33%)
Day of First Observation	577	519	505
Life Table Tests (d)	P=0.120N	P=0.360N	P=0.128N
Logistic Regression Tests (d)	P=0.096N	P=0.236N	P=0.114N
Cochran-Armitage Trend Test (d)	P=0.096N		
Fisher Exact Test (d)		P=0.274N	P=0.115N

(a) Number of tumor-bearing animals/number of animals examined microscopically at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals killed at the end of the study
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) Incomplete sampling of tissues
(f) Number of tumor-bearing animals/number of animals examined grossly at the site

TABLE B4a. HISTORICAL INCIDENCE OF MAMMARY GLAND NEOPLASMS IN FEMALE F344/N RATS (a)

Study	Incidence in Controls		
	Fibroadenoma	Adenocarcinoma	Fibroadenoma or Adenocarcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	7/50	1/50	8/50
Methyl methacrylate	10/50	0/50	10/50
Propylene	9/49	0/49	9/49
1,2-Epoxybutane	(b) 16/50	1/50	(b) 17/50
Dichloromethane	5/50	1/50	6/50
Tetrachloroethylene	7/50	2/50	8/50
Bromoethane	(b) 17/50	4/50	(b) 18/50
TOTAL	71/349 (20.3%)	9/349 (2.6%)	76/349 (21.8%)
SD (c)	9.25%	2.76%	9.39%
Range (d)			
High	17/50	4/50	18/50
Low	5/50	0/50	6/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	(e) 520/1,643 (31.6%)	(f) 49/1,643 (3.0%)	(e,f) 552/1,643 (33.6%)
SD (c)	12.23%	2.07%	11.95%
Range (d)			
High	30/50	4/50	32/50
Low	5/50	0/50	6/50

(a) Data as of May 12, 1988, for studies of at least 104 weeks
(b) Includes one adenoma, NOS
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.
(e) Includes 11 adenomas, NOS, 2 cystadenomas, NOS, and 1 papillary cystadenoma, NOS
(f) Includes two carcinomas, NOS, two papillary adenocarcinomas, and one cystadenocarcinoma, NOS

TABLE B4b. HISTORICAL INCIDENCE OF ANTERIOR PITUITARY GLAND NEOPLASMS IN FEMALE F344/N RATS (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	25/48	0/48	25/48
Methyl methacrylate	30/50	1/50	31/50
Propylene	18/44	1/44	19/44
1,2-Epoxybutane	25/49	6/49	31/49
Dichloromethane	24/49	1/49	25/49
Tetrachloroethylene	19/50	4/50	23/50
Bromoethane	26/50	1/50	27/50
TOTAL	167/340 (49.1%)	14/340 (4.1%)	181/340 (53.2%)
SD (b)	7.42%	4.37%	7.50%
Range (c)			
High	30/50	6/49	31/49
Low	19/50	0/48	19/44
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	(d) 731/1,617 (45.2%)	(e) 42/1,617 (2.6%)	(d,e) 771/1,617 (47.7%)
SD (b)	10.79%	2.76%	11.00%
Range (c)			
High	33/47	6/50	33/47
Low	10/49	0/50	12/49

(a) Data as of May 12, 1988, 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 39 chromophobe adenomas
(e) Includes three adenocarcinomas, NOS, and three chromophobe carcinomas

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	1 mg/m^3	2 mg/m^3
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine large	(49)	(29)	(48)
Anus, parasite metazoan	1 (2%)		
Intestine large, cecum	(47)	(28)	(41)
Inflammation			1 (2%)
Parasite metazoan	3 (6%)	1 (4%)	4 (10%)
Ulcer			1 (2%)
Intestine large, colon	(48)	(28)	(48)
Parasite metazoan	2 (4%)	3 (11%)	4 (8%)
Intestine large, rectum	(44)	(28)	(43)
Parasite metazoan	2 (5%)		4 (9%)
Intestine small, ileum	(46)	(27)	(45)
Hyperplasia, lymphoid	4 (9%)	2 (7%)	6 (13%)
Parasite metazoan		1 (4%)	
Liver	(49)	(41)	(49)
Angiectasis		4 (10%)	3 (6%)
Basophilic focus	31 (63%)	25 (61%)	33 (67%)
Clear cell focus	1 (2%)		
Degeneration, fatty	13 (27%)	13 (32%)	10 (20%)
Eosinophilic focus		2 (5%)	
Hematopoietic cell proliferation	7 (14%)	2 (5%)	5 (10%)
Hemorrhage	1 (2%)		
Hepatodiaphragmatic nodule	5 (10%)	6 (15%)	4 (8%)
Inflammation, granulomatous, focal	26 (53%)	25 (61%)	26 (53%)
Leukocytosis	1 (2%)		3 (6%)
Necrosis	7 (14%)	2 (5%)	7 (14%)
Pigmentation, hemosiderin			1 (2%)
Bile duct, hyperplasia	17 (35%)	8 (20%)	13 (27%)
Hepatocyte, hyperplasia	1 (2%)	1 (2%)	2 (4%)
Hepatocyte, hyperplasia, focal		2 (5%)	
Mesentery	(6)	(2)	(2)
Hemorrhage	1 (17%)		
Inflammation, granulomatous, suppurative, multifocal	1 (17%)		
Fat, inflammation, chronic	2 (33%)	1 (50%)	1 (50%)
Fat, necrosis	1 (17%)	1 (50%)	1 (50%)
Pancreas	(49)	(30)	(47)
Inflammation	4 (8%)		2 (4%)
Acinus, atrophy	15 (31%)	6 (20%)	14 (30%)
Acinus, cytomegaly	2 (4%)	1 (3%)	1 (2%)
Pharynx	(1)		
Palate, inflammation, chronic	1 (100%)		
Salivary glands	(49)	(29)	(49)
Inflammation, suppurative		1 (3%)	4 (8%)
Duct, hyperplasia	14 (29%)	8 (28%)	19 (39%)
Stomach, forestomach	(47)	(49)	(49)
Hyperplasia, squamous	2 (4%)	6 (12%)	8 (16%)
Inflammation	1 (2%)	7 (14%)	8 (16%)
Ulcer	1 (2%)	4 (8%)	5 (10%)
Stomach, glandular	(49)	(50)	(49)
Erosion			1 (2%)
Inflammation	1 (2%)	1 (2%)	2 (4%)
Mineralization			1 (2%)
Ulcer		1 (2%)	

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m³	2 mg/m³
ALIMENTARY SYSTEM (Continued)			
Tooth	(1)	(1)	(1)
Inflammation, chronic			1 (100%)
Inflammation, suppurative		1 (100%)	1 (100%)
Inflammation, suppurative, chronic	1 (100%)		
CARDIOVASCULAR SYSTEM			
Blood vessel			(2)
Inflammation			2 (100%)
Heart	(49)	(30)	(50)
Inflammation, chronic	38 (78%)	16 (53%)	37 (74%)
Atrium, thrombus	1 (2%)	1 (3%)	
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(49)	(50)	(48)
Degeneration		2 (4%)	1 (2%)
Degeneration, cystic			1 (2%)
Degeneration, fatty	22 (45%)	29 (58%)	28 (58%)
Focal cellular change	8 (16%)	5 (10%)	3 (6%)
Hematopoietic cell proliferation	5 (10%)	7 (14%)	10 (21%)
Hyperplasia	10 (20%)	2 (4%)	11 (23%)
Hypertrophy		1 (2%)	1 (2%)
Inflammation, chronic			1 (2%)
Necrosis		1 (2%)	1 (2%)
Bilateral, hypertrophy		1 (2%)	
Adrenal gland, medulla	(49)	(50)	(48)
Hematopoietic cell proliferation	1 (2%)		1 (2%)
Hyperplasia	15 (31%)	10 (20%)	11 (23%)
Parathyroid gland	(32)	(22)	(38)
Hyperplasia		1 (5%)	2 (5%)
Pituitary gland	(49)	(48)	(49)
Cyst	1 (2%)		
Pars distalis, angiectasis	1 (2%)		
Pars distalis, cyst	1 (2%)		
Pars distalis, degeneration, cystic	3 (6%)		2 (4%)
Pars distalis, hyperplasia	13 (27%)	5 (10%)	7 (14%)
Pars distalis, hyperplasia, focal		1 (2%)	
Pars distalis, infiltration cellular, mixed cell	1 (2%)		
Pars distalis, mineralization		1 (2%)	
Pars intermedia, hyperplasia			1 (2%)
Thyroid gland	(47)	(30)	(45)
Cyst	1 (2%)		
C cell, hyperplasia	24 (51%)	14 (47%)	21 (47%)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Clitoral gland	(45)	(33)	(42)
Cyst	2 (4%)		
Hyperplasia	2 (4%)	3 (9%)	
Inflammation, chronic	1 (2%)		1 (2%)
Inflammation, suppurative	6 (13%)	10 (30%)	7 (17%)
Duct, hyperplasia	2 (4%)		
Duct, inflammation, suppurative	1 (2%)		

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
GENITAL SYSTEM (Continued)			
Ovary	(49)	(31)	(49)
Atrophy	8 (16%)	3 (10%)	6 (12%)
Cyst	6 (12%)	4 (13%)	1 (2%)
Infiltration cellular, mixed cell			1 (2%)
Interstitium, hyperplasia	1 (2%)		
Oviduct			(1)
Cyst			1 (100%)
Uterus	(49)	(33)	(48)
Dilatation		1 (3%)	
Inflammation, suppurative	1 (2%)		
Prolapse		1 (3%)	
Endometrium, cyst			1 (2%)
Endometrium, cyst, multiple	1 (2%)	1 (3%)	
Endometrium, inflammation, suppurative			1 (2%)
Vagina		(1)	
Hypertrophy		1 (100%)	
Inflammation, chronic		1 (100%)	
HEMATOPOIETIC SYSTEM			
Bone marrow	(49)	(30)	(47)
Depletion	1 (2%)		
Myelofibrosis	2 (4%)		2 (4%)
Lymph node	(49)	(31)	(49)
Axillary, hematopoietic cell proliferation	1 (2%)		
Mesenteric, inflammation, granulomatous			1 (2%)
Pancreatic, inflammation, granulomatous		1 (3%)	
Lymph node, bronchial	(44)	(26)	(41)
Hematopoietic cell proliferation			1 (2%)
Hyperplasia	1 (2%)		2 (5%)
Inflammation, granulomatous	1 (2%)		1 (2%)
Lymph node, mandibular	(46)	(30)	(47)
Hematopoietic cell proliferation	1 (2%)		1 (2%)
Hyperplasia	15 (33%)	8 (27%)	17 (36%)
Spleen	(49)	(35)	(49)
Fibrosis	2 (4%)	1 (3%)	1 (2%)
Hematopoietic cell proliferation	5 (10%)	1 (3%)	3 (6%)
Hyperplasia, lymphoid		1 (3%)	1 (2%)
Inflammation, granulomatous, focal		1 (3%)	1 (2%)
INTEGUMENTARY SYSTEM			
Mammary gland	(48)	(50)	(50)
Galactocele	10 (21%)	8 (16%)	3 (6%)
Hyperplasia	6 (13%)	9 (18%)	11 (22%)
Inflammation, chronic	1 (2%)		
Inflammation, suppurative	1 (2%)		1 (2%)
Skin	(49)	(27)	(47)
Acanthosis	1 (2%)		
Inflammation, suppurative	1 (2%)	1 (4%)	2 (4%)
Subcutaneous tissue, inflammation, chronic	2 (4%)	1 (4%)	
Subcutaneous tissue, necrosis		1 (4%)	
Subcutaneous tissue, thrombus		1 (4%)	

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
MUSCULOSKELETAL SYSTEM			
Bone	(49)	(30)	(50)
Fibrous osteodystrophy		1 (3%)	
Fracture	1 (2%)		
Inflammation, suppurative, chronic	1 (2%)		
Osteopetrosis	3 (6%)	4 (13%)	3 (6%)
NERVOUS SYSTEM			
Brain	(49)	(30)	(50)
Compression			1 (2%)
Hemorrhage	1 (2%)	2 (7%)	2 (4%)
Hydrocephalus		1 (3%)	
Pigmentation, hemosiderin	1 (2%)		
RESPIRATORY SYSTEM			
Larynx	(48)	(27)	(49)
Hyperplasia		1 (4%)	2 (4%)
Inflammation	2 (4%)		
Inflammation, suppurative	18 (38%)	1 (4%)	22 (45%)
Metaplasia, squamous	1 (2%)		2 (4%)
Epithelium, hyperplasia			1 (2%)
Lung	(49)	(40)	(49)
Congestion	1 (2%)		
Hemorrhage	4 (8%)	7 (18%)	1 (2%)
Infiltration cellular, mixed cell	1 (2%)		1 (2%)
Inflammation, chronic, diffuse			1 (2%)
Inflammation, chronic, focal	5 (10%)	9 (23%)	9 (18%)
Metaplasia, squamous			1 (2%)
Pigmentation, hemosiderin	1 (2%)		2 (4%)
Thrombus		1 (3%)	
Alveolar epithelium, hyperplasia	1 (2%)	4 (10%)	6 (12%)
Alveolus, infiltration cellular, histiocytic	11 (22%)	6 (15%)	11 (22%)
Bronchiole, epithelium, hyperplasia			1 (2%)
Bronchus, mineralization			1 (2%)
Bronchus, epithelium, hyperplasia			1 (2%)
Mediastinum, inflammation, granulomatous		1 (3%)	
Perivascular, infiltration cellular, mononuclear cell	14 (29%)	10 (25%)	14 (29%)
Pleura, hyperplasia			1 (2%)
Nose	(48)	(50)	(49)
Foreign body	3 (6%)	1 (2%)	1 (2%)
Inflammation	41 (85%)	41 (82%)	42 (86%)
Inflammation, suppurative	29 (60%)	27 (54%)	33 (67%)
Thrombus	7 (15%)	2 (4%)	3 (6%)
Nasolacrimal duct, inflammation, suppurative	7 (15%)	11 (22%)	7 (14%)
Olfactory epithelium, degeneration	2 (4%)		1 (2%)
Olfactory epithelium, metaplasia	4 (8%)	3 (6%)	3 (6%)
Respiratory epithelium, hyperplasia	20 (42%)	31 (62%)	38 (78%)
Respiratory epithelium, metaplasia, squamous	1 (2%)	7 (14%)	26 (53%)
Respiratory epithelium, ulcer		1 (2%)	
Vomeronasal organ, inflammation		2 (4%)	
Vomeronasal organ, inflammation, suppurative	6 (13%)	3 (6%)	5 (10%)
Trachea	(48)	(29)	(48)
Inflammation	2 (4%)		
Inflammation, suppurative	3 (6%)	2 (7%)	4 (8%)
Epithelium, hyperplasia	2 (4%)	1 (3%)	
Epithelium, metaplasia, squamous	3 (6%)	2 (7%)	1 (2%)

TABLE B5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	1 mg/m^3	2 mg/m^3
SPECIAL SENSES SYSTEM			
Eye	(49)	(2)	(48)
Synechia	1 (2%)	1 (50%)	3 (6%)
Cornea, inflammation, suppurative	1 (2%)		
Lens, degeneration	3 (6%)	1 (50%)	8 (17%)
Lens, mineralization	1 (2%)	1 (50%)	4 (8%)
Retina, atrophy	6 (12%)	1 (50%)	9 (19%)
Harderian gland	(5)	(2)	(8)
Inflammation	1 (20%)		
Inflammation, suppurative	2 (40%)	2 (100%)	6 (75%)
Metaplasia, squamous	2 (40%)		3 (38%)
Lacrimal gland	(3)	(3)	(1)
Acinus, atrophy	3 (100%)	3 (100%)	1 (100%)
URINARY SYSTEM			
Kidney	(49)	(37)	(49)
Cyst	1 (2%)	1 (3%)	
Hematopoietic cell proliferation	1 (2%)		
Hydronephrosis			2 (4%)
Nephropathy	48 (98%)	37 (100%)	48 (98%)
Papilla, necrosis			1 (2%)
Renal tubule, hyperplasia		1 (3%)	1 (2%)
Urinary bladder	(48)	(31)	(48)
Inflammation, chronic			1 (2%)
Transitional epithelium, hyperplasia			1 (2%)

APPENDIX C

SUMMARY OF LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	2 mg/m^3	4 mg/m^3
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Gallbladder	(41)	(36)	(32)
Hepatocellular carcinoma, metastatic, liver		1 (3%)	
Lymphoma malignant mixed	1 (2%)		
Intestine small, duodenum	(46)	(44)	(42)
Adenoma	1 (2%)		
Intestine small, ileum	(48)	(44)	(44)
Lymphoma malignant lymphocytic		1 (2%)	3 (7%)
Lymphoma malignant mixed		1 (2%)	1 (2%)
Intestine small, jejunum	(46)	(43)	(43)
Adenocarcinoma	1 (2%)		
Lymphoma malignant lymphocytic		1 (2%)	1 (2%)
Liver	(50)	(48)	(49)
Hemangiosarcoma		1 (2%)	3 (6%)
Hemangiosarcoma, multiple			1 (2%)
Hepatocellular carcinoma	6 (12%)	9 (19%)	8 (16%)
Hepatocellular carcinoma, multiple	5 (10%)	3 (6%)	4 (8%)
Hepatocellular adenoma	4 (8%)	5 (10%)	7 (14%)
Hepatocellular adenoma, multiple	1 (2%)	3 (6%)	2 (4%)
Lymphoma malignant histiocytic	2 (4%)		1 (2%)
Lymphoma malignant mixed	1 (2%)	1 (2%)	1 (2%)
Mesentery	*(50)	*(50)	*(50)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed			1 (2%)
Pancreas	(50)	(45)	(47)
Hemangioma	1 (2%)		
Lymphoma malignant histiocytic	1 (2%)		1 (2%)
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)	1 (2%)	2 (4%)
Salivary glands	(50)	(48)	(49)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)	1 (2%)	
Stomach, forestomach	(49)	(46)	(45)
Lymphoma malignant mixed		1 (2%)	
Papilloma squamous	2 (4%)	1 (2%)	
Stomach, glandular	(50)	(44)	(47)
Lymphoma malignant mixed	1 (2%)		
Tooth	*(50)	*(50)	*(50)
Lymphoma malignant mixed			1 (2%)
CARDIOVASCULAR SYSTEM			
Heart	(50)	(49)	(49)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant mixed		2 (4%)	1 (2%)
ENDOCRINE SYSTEM			
Adrenal gland	(50)	(45)	(47)
Capsule, lymphoma malignant histiocytic			1 (2%)
Capsule, lymphoma malignant lymphocytic		1 (2%)	
Subcapsular, adenoma	1 (2%)		1 (2%)
Adrenal gland, cortex	(50)	(45)	(47)
Hepatocellular carcinoma, metastatic, liver		1 (2%)	
Lymphoma malignant mixed	1 (2%)		

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
ENDOCRINE SYSTEM (Continued)			
Adrenal gland, medulla	(48)	(44)	(41)
Lymphoma malignant mixed	1 (2%)		
Pheochromocytoma, NOS	1 (2%)		
Pheochromocytoma benign			1 (2%)
Bilateral, pheochromocytoma malignant			1 (2%)
Islets, pancreatic	(50)	(42)	(46)
Adenoma		1 (2%)	
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant mixed	1 (2%)		
Pituitary gland	(44)	(37)	(46)
Lymphoma malignant mixed			1 (2%)
Pars distalis, adenoma		1 (3%)	
Thyroid gland	(50)	(45)	(48)
Follicular cell, adenoma		1 (2%)	1 (2%)
GENERAL BODY SYSTEM			
Tissue, NOS	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic		1 (2%)	
GENITAL SYSTEM			
Epididymis	(47)	(41)	(42)
Lymphoma malignant mixed	1 (2%)		
Sarcoma	1 (2%)		
Preputial gland	*(50)	*(50)	*(50)
Sarcoma			1 (2%)
Prostate	(50)	(44)	(43)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)		1 (2%)
Seminal vesicle	*(50)	*(50)	*(50)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)		1 (2%)
Testes	(50)	(44)	(47)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)		1 (2%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(50)	(48)	(49)
Sternal, lymphoma malignant histiocytic			1 (2%)
Lymph node	(48)	(46)	(47)
Inguinal, lymphoma malignant histiocytic	1 (2%)		
Mediastinal, lymphoma malignant lymphocytic		1 (2%)	1 (2%)
Mesenteric, lymphoma malignant histiocytic	1 (2%)		1 (2%)
Mesenteric, lymphoma malignant lymphocytic			4 (9%)
Mesenteric, lymphoma malignant mixed	1 (2%)	1 (2%)	3 (6%)
Renal, lymphoma malignant histiocytic			1 (2%)
Renal, lymphoma malignant lymphocytic			1 (2%)
Renal, lymphoma malignant mixed			2 (4%)
Lymph node, bronchial	(35)	(38)	(36)
Lymphoma malignant histiocytic			1 (3%)
Lymphoma malignant lymphocytic	1 (3%)		1 (3%)
Lymphoma malignant mixed	1 (3%)	2 (5%)	1 (3%)
Lymph node, mandibular	(41)	(29)	(38)
Hemangiosarcoma, metastatic, spleen	1 (2%)		
Lymphoma malignant histiocytic	1 (2%)		1 (3%)
Lymphoma malignant lymphocytic	1 (2%)		
Lymphoma malignant mixed	1 (2%)	1 (3%)	2 (5%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
HEMATOPOIETIC SYSTEM (Continued)			
Spleen	(50)	(47)	(49)
Hemangiosarcoma	1 (2%)		
Lymphoma malignant histiocytic	2 (4%)		1 (2%)
Lymphoma malignant lymphocytic	2 (4%)	3 (6%)	2 (4%)
Lymphoma malignant mixed	1 (2%)	1 (2%)	2 (4%)
Sarcoma		1 (2%)	
Thymus	(28)	(33)	(29)
Lymphoma malignant histiocytic			1 (3%)
Lymphoma malignant mixed	1 (4%)		1 (3%)
INTEGUMENTARY SYSTEM			
Skin	(50)	(47)	(47)
Lymphoma malignant mixed		1 (2%)	
Subcutaneous tissue, lymphoma malignant histiocytic	1 (2%)		
Subcutaneous tissue, lymphoma malignant mixed	1 (2%)		
Tail, schwannoma, NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
Bone	(50)	(50)	(49)
Lymphoma malignant histiocytic	1 (2%)		1 (2%)
Lymphoma malignant mixed			1 (2%)
Skeletal muscle	*(50)	*(50)	*(50)
Lymphoma malignant mixed			1 (2%)
NERVOUS SYSTEM			
Brain	(50)	(49)	(48)
Meninges, lymphoma malignant mixed			1 (2%)
RESPIRATORY SYSTEM			
Larynx	(50)	(47)	(47)
Lymphoma malignant mixed		1 (2%)	
Lung	(50)	(49)	(49)
Alveolar/bronchiolar adenoma	7 (14%)	8 (16%)	4 (8%)
Alveolar/bronchiolar carcinoma	6 (12%)	3 (6%)	9 (18%)
Hepatocellular carcinoma, metastatic, liver	3 (6%)	6 (12%)	4 (8%)
Lymphoma malignant histiocytic	1 (2%)		1 (2%)
Lymphoma malignant lymphocytic		2 (4%)	1 (2%)
Lymphoma malignant mixed	1 (2%)	3 (6%)	1 (2%)
Nose	(50)	(48)	(48)
Lymphoma malignant mixed			1 (2%)
SPECIAL SENSES SYSTEM			
Harderian gland	*(50)	*(50)	*(50)
Adenoma	3 (6%)	7 (14%)	3 (6%)
Sarcoma	1 (2%)		
Lacrimal gland	*(50)	*(50)	*(50)
Lymphoma malignant mixed		1 (2%)	
URINARY SYSTEM			
Kidney	(50)	(49)	(49)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant lymphocytic	2 (4%)	1 (2%)	1 (2%)
Lymphoma malignant mixed	1 (2%)	2 (4%)	1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)		
Cortex, adenoma	1 (2%)	1 (2%)	

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
URINARY SYSTEM (Continued)			
Urinary bladder	(49)	(44)	(47)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)	1 (2%)	1 (2%)
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Hemangioma	1 (2%)		
Lymphoma malignant lymphocytic	2 (4%)	3 (6%)	4 (8%)
Lymphoma malignant histiocytic	2 (4%)		1 (2%)
Hemangiosarcoma	1 (2%)	1 (2%)	4 (8%)
Lymphoma malignant mixed	1 (2%)	3 (6%)	3 (6%)
Lymphoma malignant undifferentiated cell	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Dead	5	9	11
Terminal sacrifice	34	36	33
Moribund	11	5	6
TUMOR SUMMARY			
Total animals with primary neoplasms **	33	35	39
Total primary neoplasms	49	52	54
Total animals with benign neoplasms	17	21	17
Total benign neoplasms	21	28	19
Total animals with malignant neoplasms	23	23	29
Total malignant neoplasms	27	23	35
Total animals with secondary neoplasms ***	4	6	4
Total secondary neoplasms	4	8	4
Total animals with neoplasms-- uncertain benign or malignant	1	1	
Total uncertain neoplasms	1	1	

* Number of animals receiving complete necropsy examination; 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 2-CHLOROACETOPHENONE: CHAMBER CONTROL

WEEKS ON STUDY	074	075	077	084	087	096	097	097	100	102	102	103	103	104	105	105	106	106	106	106	106	106	106	106	106	106	106
CARCASS ID	371	431	161	041	471	121	351	331	271	011	421	131	301	501	411	171	021	031	051	061	071	081	091	101	111
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	+	M	M	+	+	M	+	+	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							
Intestine large	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Adenoma															X										
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma						X			X							X								X	
Hepatocellular carcinoma, multiple			X		X									X	X										
Hepatocellular adenoma				X															X						
Hepatocellular adenoma, multiple	X																								
Lymphoma malignant histiocytic							X		X																
Lymphoma malignant mixed		X																							
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Lymphoma malignant histiocytic							X																		
Lymphoma malignant mixed		X																							
Pharynx																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							
Tooth																					+		+		+
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcapsular, adenoma																								X	
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							
Adrenal gland, medulla	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+
Lymphoma malignant mixed		X																							
Pheochromocytoma, NOS																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic							X																		
Lymphoma malignant mixed		X																							
Parathyroid gland	+	+	+	M	M	+	M	M	M	+	+	M	M	+	+	M	+	M	+	M	M	M	+	M	M
Pituitary gland	A	M	I	+	+	+	I	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GENERAL BODY SYSTEM																									
Tissue, NOS	+																								
GENITAL SYSTEM																									
Epididymis	M	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							
Sarcoma																		X							
Penis														+											
Preputial gland								+		+			+								+		+	+	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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 C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	141	151	181	191	201	211	221	231	241	251	261	281	291	311	321	341	361	381	391	401	441	451	461	481	491	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	49
Gallbladder	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Lymphoma malignant mixed																										1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	46
Adenoma																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma			X																							1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma								X													X					6
Hepatocellular carcinoma, multiple																									X	5
Hepatocellular adenoma															X		X									4
Hepatocellular adenoma, multiple																										1
Lymphoma malignant histiocytic																										2
Lymphoma malignant mixed																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma			X																							1
Lymphoma malignant histiocytic																										1
Lymphoma malignant mixed																										1
Pharynx					+																					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papilloma squamous						X										X										2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed																										1
Tooth															+					+						5
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcapsular, adenoma																										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant mixed																										1
Pheochromocytoma, NOS		X																								1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Lymphoma malignant mixed																										1
Parathyroid gland	+	+	+	+	+	+	+	M	+	M	+	+	M	+	+	+	M	+	M	M	M	M	+	M	M	26
Pituitary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GENERAL BODY SYSTEM																										
Tissue, NOS																										1
GENITAL SYSTEM																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	47
Lymphoma malignant mixed																										1
Sarcoma																										1
Penis																										1
Preputial gland					+												+				+				+	10
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed																										1
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant mixed																										1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed																										1

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

WEEKS ON STUDY	074	075	077	084	087	096	097	097	100	102	102	103	103	104	105	105	106	106	106	106	106	106	106	106	106
CARCASS ID	371	431	161	041	471	121	351	331	271	011	421	131	301	501	411	171	021	031	051	061	071	081	091	101	111
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Inguinal, lymphoma malignant histiocytic							X																		
Mesenteric, lymphoma malignant histiocytic							X																		
Mesenteric, lymphoma malignant mixed		X																							
Lymph node, bronchial	+	+	+	M	M	+	M	M	+	+	+	M	+	+	M	+	+	+	+	+	+	+	M	+	M
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed		X																							
Lymph node, mandibular	M	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Hemangiosarcoma, metastatic, spleen																									
Lymphoma malignant histiocytic							X																		
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed		X																							
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymphoma malignant histiocytic							X		X																
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed		X																							
Thymus	+	+	+	M	M	M	M	+	+	M	M	M	M	M	M	M	+	M	M	M	+	M	+	+	M
Lymphoma malignant mixed		X																							
INTEGUMENTARY SYSTEM																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, lymphoma malignant histiocytic							X																		
Subcutaneous tissue, lymphoma malignant mixed		X																							
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic									X																
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma															X				X						X
Alveolar/bronchiolar carcinoma															X										
Hepatocellular carcinoma, metastatic, liver														X	X										
Lymphoma malignant histiocytic							X																		
Lymphoma malignant mixed		X																							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye	A	A	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+
Harderian gland						+																			
Adenoma						X																			
Sarcoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed		X																							
Lymphoma malignant undifferentiated cell type					X																				
Cortex, adenoma																				X					
Urinary bladder	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed		X																							

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

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	141	151	181	191	201	211	221	231	241	251	261	281	291	311	321	341	361	381	391	401	441	451	461	481	491	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	48
Inguinal, lymphoma malignant histiocytic																										1
Mesenteric, lymphoma malignant histiocytic																										1
Mesenteric, lymphoma malignant mixed																										1
Lymph node, bronchial	M	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	M	M	35
Lymphoma malignant lymphocytic									X																	1
Lymphoma malignant mixed																										1
Lymph node, mandibular	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+		41
Hemangiosarcoma, metastatic, spleen															X											1
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic					X																					1
Lymphoma malignant mixed																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma															X											1
Lymphoma malignant histiocytic																										2
Lymphoma malignant lymphocytic					X				X																	2
Lymphoma malignant mixed																										1
Thymus	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	M	M	+	+	+	+	28
Lymphoma malignant mixed																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	M	M	M	+	M	+	M	M	+	+	M	M	M	M	M	M	+	M	M	M	M	M	M	5
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, lymphoma malignant histiocytic																										1
Subcutaneous tissue, lymphoma malignant mixed																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma														X					X		X			X		7
Alveolar/bronchiolar carcinoma	X			X							X			X											X	6
Hepatocellular carcinoma, metastatic, liver																									X	3
Lymphoma malignant histiocytic																										1
Lymphoma malignant mixed																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSES SYSTEM																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Harderian gland												+					+		+							4
Adenoma												X					X									3
Sarcoma																			X							1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic					X				X																	2
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Cortex, adenoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant mixed																										1

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 2 mg/m³

WEEKS ON STUDY	068	071	074	075	075	077	078	080	086	088	088	092	097	102	105	106	106	106	106	106	106	106	106	106	106	106	106	106
CARCASS ID	13501	12201	10201	12601	13201	12401	12801	14701	13601	14801	12001	13901	13301	10601	10111	10031	10441	10551	10771	10081	10991	11011	11111	11221	11331
ALIMENTARY SYSTEM																									
Esophagus	A	+	+	I	+	A	+	+	I	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	M	A	+	+	A	+	A	M	A	+	A	A	A	+	+	+	+	M	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver											X														
Intestine large	A	+	+	+	+	A	+	+	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A		M	M	M	A	+	A	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	A	+	+	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	A	+	+	+	+	A	+	+	A	+	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	A	+	A	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	A	+	A	A	+	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	+	+	A	+	A	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																									
Intestine small, jejunum	A	+	+	+	+	A	+	A	A	+	+	M	A	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Liver	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																						X			
Hepatocellular carcinoma	X	X	X	X			X																	X	X
Hepatocellular carcinoma, multiple					X				X		X														
Hepatocellular adenoma										X										X				X	
Hepatocellular adenoma, multiple								X					X												
Lymphoma malignant mixed													X												
Pancreas	A	+	+	+	+	M	+	A	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed													X												
Salivary glands	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Stomach	A	+	+	+	+	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	A	+	+	+	+	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed												X													
Papilloma squamous												X													
Stomach, glandular	A	+	+	+	+	A	+	A	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Tooth																									
CARDIOVASCULAR SYSTEM																									
Blood vessel	A	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed												X	X												
ENDOCRINE SYSTEM																									
Adrenal gland	A	+	+	+	+	A	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Capsule, lymphoma malignant lymphocytic								X																	
Adrenal gland, cortex	A	+	+	+	+	A	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic, liver											X														
Adrenal gland, medulla	A	+	+	+	+	A	+	+	+	+	+	A	I	A	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	A	+	+	+	+	A	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	A	+	M	+	M	A	+	M	M	M	+	M	+	M	+	+	M	M	+	M	M	+	+	M	+
Pituitary gland	A	+	I	+	+	M	+	M	I	+	+	I	+	A	+	+	+	+	+	M	+	+	M	+	+
Pars distalis, adenoma																									
Thyroid gland	A	+	+	+	+	A	+	+	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																			X						
GENERAL BODY SYSTEM																									
Tissue, NOS								•																	
Lymphoma malignant lymphocytic								X																	
GENITAL SYSTEM																									
Epididymis	A	+	+	+	+	A	+	A	M	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Preputial gland												+						+					+		
Prostate	A	+	+	+	+	A	+	A	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	A	+	+	+		A	+	A	+	+	+	A	+	A		+	+			+	+	+			
Testes	A	+	+	+	+	A	+	A	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 2 mg/m³ (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL.
CARCASS ID	1141	1151	1161	1171	1181	1191	1211	1231	1251	1271	1291	1301	1311	1341	1371	1381	1401	1411	1421	1431	1441	1451	1461	1491	1501	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	44
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	M	+	+	36
Hepatocellular carcinoma, metastatic, liver																										1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	40
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant lymphocytic																									X	1
Lymphoma malignant mixed																		X								1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Lymphoma malignant lymphocytic																									X	1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hemangiosarcoma																										1
Hepatocellular carcinoma														X								X				9
Hepatocellular carcinoma, multiple																										3
Hepatocellular adenoma		X																		X						5
Hepatocellular adenoma, multiple							X																			3
Lymphoma malignant mixed																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymphoma malignant mixed																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant mixed																		X								1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant mixed																										1
Papilloma squamous																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Tooth									+																	1
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant mixed																										2
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Capsule, lymphoma malignant lymphocytic																										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Hepatocellular carcinoma, metastatic, liver																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Islets, pancreatic	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	I	+	I	+	+	+	+	I	+	+	42
Adenoma																			X							1
Parathyroid gland	+	M	M	M	+	M	+	+	M	M	+	+	+	+	M	M	M	+	+	M	M	+	M	+	+	24
Pituitary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	I	+	+	+	+	+	I	+	37
Pars distalis, adenoma							X																			1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Follicular cell, adenoma																										1
GENERAL BODY SYSTEM																										
Tissue, NOS																										1
Lymphoma malignant lymphocytic																										1
GENITAL SYSTEM																										
Epididymis	+	M	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Preputial gland	+		M						+																	5
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	44
Seminal vesicle		+				+																				15
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 2 mg/m³ (Continued)

WEEKS ON STUDY	06 8	07 1	07 4	07 5	07 5	07 7	07 8	08 0	08 6	08 8	08 8	09 2	09 7	10 2	10 5	10 6	10 6	10 6	10 6	10 6	10 6	10 6	10 6	10 6	10 6	10 6
CARCASS ID	13 51	12 21	10 21	12 61	13 21	12 41	12 81	14 71	13 61	14 81	12 01	13 91	13 31	10 61	10 11	10 31	10 41	10 51	10 71	10 81	10 91	11 01	11 11	11 21	11 31
HEMATOPOIETIC SYSTEM																									
Blood	A	+	+	+	+	A	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	A	+	+	+	+	A	+	+	+	+	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, lymphoma malignant lymphocytic								X																	
Mesenteric, lymphoma malignant mixed																									
Lymph node, bronchial	A	+	+	+	+	A	+	M	+	+	M	M	+	A	+	+		M	M	+	M	+	+	+	+
Lymphoma malignant mixed													X												
Lymph node, mandibular	A	M	M	M	+	A	M	M	+	+	+	M	M	A	+	M		+	+	+	+	M	+	+	+
Lymphoma malignant mixed																									
Spleen	A	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic								X																	
Lymphoma malignant mixed												X													
Sarcoma																	X								
Thymus	A	+	M	M	M	M	M	M	A	M	+	A	+	A	+	+	I	+	M	+	+	+	+	+	M
INTEGUMENTARY SYSTEM																									
Mammary gland	A	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	+	+	+	+	+	+	+	M	M
Skin	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed													X												
Tail, schwannoma, NOS																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
Larynx	A	+	+	+	+	+	+	+	+	+	+	I	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed													X												
Lung	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma												X		X			X			X					
Alveolar/bronchiolar carcinoma																				X					
Hepatocellular carcinoma, metastatic, liver	X			X	X				X		X														
Lymphoma malignant lymphocytic								X																	
Lymphoma malignant mixed												X	X												
Nose	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	A	+	+	+	+	+	+	+	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Harderian gland												+						+				+			
Adenoma												X						X				X			
Lacrimal gland																									
Lymphoma malignant mixed																									
URINARY SYSTEM																									
Kidney	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed													X												
Cortex, adenoma																									
Urinary bladder	A	+	+	+	+	A	+	A	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 2 mg/m³ (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL. TISSUES TUMORS
CARCASS ID	11441	11551	11661	11771	11881	11991	12011	12311	12551	12771	12991	13011	13111	13411	13711	13811	14011	14111	14211	14311	14411	14511	14611	14911	15011	
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Mediastinal, lymphoma malignant lymphocytic																										1
Mesenteric, lymphoma malignant mixed																		X								1
Lymph node, bronchial	M	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Lymphoma malignant mixed																		X								2
Lymph node, mandibular	+	+	M	+	+	M	+	+	+	+	+	+	+	M	M	+	+	+	M	+	M	+	M	M	+	29
Lymphoma malignant mixed																		X								1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic																				X					X	3
Lymphoma malignant mixed																										1
Sarcoma																										1
Thymus	+	+	M	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	33
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	+	M	M	M	+	+	+	+	+	+	+	+	M	+	M	M	M	M	M	M	M	+	M	19
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant mixed																										1
Tail, schwannoma, NOS												X														1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant mixed																										1
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma	X			X		X														X						8
Alveolar/bronchiolar carcinoma	X														X											3
Hepatocellular carcinoma, metastatic, liver														X												6
Lymphoma malignant lymphocytic																									X	2
Lymphoma malignant mixed																		X								3
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
SPECIAL SENSES SYSTEM																										
Harderian gland	+					+							+	+												7
Adenoma	X					X							X	X												7
Lacrimal gland																		+								1
Lymphoma malignant mixed																		X								1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																									X	1
Lymphoma malignant mixed																		X								2
Cortex, adenoma											X															1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant mixed																		X								1

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 4 mg/m³

WEEKS ON STUDY	026	049	062	065	087	089	092	095	095	097	098	098	103	103	104	105	106	106	106	106	106	106	106
CARCASS ID	21511	20411	22271	24771	23991	22551	21991	22281	22211	24221	23811	20511	21881	24111	22991	20881	21611	20111	20221	20331	20661	20771	20991	21011	21111
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	A	+	M	M	A	+	M	+	+	M	M	+	+	M	+	+	+	+	+	M	+	+
Intestine large	+	+	+	+	+	+	M	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine large, cecum	+	M	M	+	+	+	M	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	M	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine large, rectum	M	+	+	+	+	+	M	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine small	+	A	+	+	+	+	M	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	A	+	M	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	M	+
Intestine small, ileum	+	A	+	+	+	+	M	A	+	A	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic			X																			X			
Lymphoma malignant mixed											X														
Intestine small, jejunum	+	A	+	+	+	A	M	A	+	A	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																						X			
Liver	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma													X						X						
Hemangiosarcoma, multiple					X																				
Hepatocellular carcinoma		X		X						X		X	X						X		X				
Hepatocellular carcinoma, multiple						X																	X		
Hepatocellular adenoma		X						X			X			X			X	X					X	
Hepatocellular adenoma, multiple																						X			
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								
Mesentery	+																								
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed	X																								
Pancreas	+	+	M	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed	X										X														
Salivary glands	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Stomach	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	M	+	+	+	M	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth	+																								
Lymphoma malignant mixed	X																								
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, lymphoma malignant histiocytic																									
Subcapsular, adenoma																									
Adrenal gland, cortex	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	M	+	+	+	M	+	I	I	+	+	+	+	+	+	+	+	+	+	I	+	+	+	I
Pheochromocytoma benign																									
Bilateral, pheochromocytoma malignant																							X		
Islets, pancreatic	+	+	M	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	M	+	M	M	M	M	M	M	+	M	M	+	M	+	+	M	+	+	M	+	M	+
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	I	+	+	+	I	+	+	+	+	+
Lymphoma malignant mixed	X																								
Thyroid gland	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									X
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Epididymis	+	+	+	+	+	+	M	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland									+		+	+		+											
Sarcoma																									
Prostate	+	+	M	+	+	M	M	+	+	A	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								
Seminal vesicle	+	+		+	+	+		+	+		+	+	+	+	+	+	+	+	+	+		+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								
Testes	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL, TISSUES TUMORS
CARCASS ID	21211	21311	21411	21711	22201	22111	22331	22441	22661	23001	23111	23211	23311	23411	23551	23661	23771	24001	24431	24441	24551	24661	24881	24991	25001		
ALIMENTARY SYSTEM																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Gallbladder	M	A	A	+	M	+	+	+	M	+	I	+	+	M	M	A	+	+	+	+	+	+	+	+	+		32
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		44
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Intestine small, duodenum	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		42
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		44
Lymphoma malignant lymphocytic																					X						3
Lymphoma malignant mixed																											1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		43
Lymphoma malignant lymphocytic																											1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Hemangiosarcoma	X																										3
Hemangiosarcoma, multiple																											1
Hepatocellular carcinoma																X											8
Hepatocellular carcinoma, multiple		X									X																4
Hepatocellular adenoma																											7
Hepatocellular adenoma, multiple																			X								2
Lymphoma malignant histiocytic							X																				1
Lymphoma malignant mixed																											1
Mesentery							+														+						3
Lymphoma malignant histiocytic							X																				1
Lymphoma malignant lymphocytic																					X						1
Lymphoma malignant mixed																											1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Lymphoma malignant histiocytic							X																				1
Lymphoma malignant lymphocytic																					X						1
Lymphoma malignant mixed																											2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Lymphoma malignant histiocytic							X																				1
Stomach	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Stomach, forestomach	+	+	+	+	+	+	M	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Stomach, glandular	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Tooth																			+		+						3
Lymphoma malignant mixed																											1
CARDIOVASCULAR SYSTEM																											
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Lymphoma malignant histiocytic							X																				1
Lymphoma malignant mixed																											1
ENDOCRINE SYSTEM																											
Adrenal gland	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Capsule, lymphoma malignant histiocytic							X																				1
Subcapsular, adenoma																			X								1
Adrenal gland, cortex	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Adrenal gland, medulla	+	+	+	+	+	I	+	I	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		41
Pheochromocytoma benign							X																				1
Bilateral, pheochromocytoma malignant																											1
Islets, pancreatic	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Parathyroid gland	M	+	M	M	M	M	M	+	+	M	M	M	M	M	+	M	M	+	+	M	M	+	M	M	M		18
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+		46
Lymphoma malignant mixed																											1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Follicular cell, adenoma																											1
GENERAL BODY SYSTEM																											
None																											
GENITAL SYSTEM																											
Epididymis	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	M	+	+	I	+	M	+		42
Preputial gland			+				+														+	+					8
Sarcoma			X																								1
Prostate	M	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		43
Lymphoma malignant histiocytic							X																				1
Lymphoma malignant mixed																											1
Seminal vesicle	+	+	+	+	+	+	+		+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+		44
Lymphoma malignant histiocytic							X																				1
Lymphoma malignant mixed																											1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Lymphoma malignant histiocytic							X																				1
Lymphoma malignant mixed																											1

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	026	049	062	065	087	087	089	092	095	095	097	098	098	103	103	104	105	106	106	106	106	106	106	106	106
CARCASS ID	2151	2041	2271	2471	2391	2251	2191	2281	2221	2421	2381	2051	2181	2411	2291	2081	2161	2011	2021	2031	2061	2071	2091	2101	2111
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sternal, lymphoma malignant histiocytic																									
Lymph node	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, lymphoma malignant lymphocytic			X																						
Mesenteric, lymphoma malignant histiocytic																									
Mesenteric, lymphoma malignant lymphocytic			X																			X			
Mesenteric, lymphoma malignant mixed	X										X														
Renal, lymphoma malignant histiocytic																									
Renal, lymphoma malignant lymphocytic			X																						
Renal, lymphoma malignant mixed	X										X														
Lymph node, bronchial	+	M	+	+	+	M	M	M	M	M	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed	X																								
Lymph node, mandibular	+	+	M	M	M	+	M	+	+	M	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								
Spleen	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed	X										X														
Thymus	+	+	+	+	M	M	M	M	M	A	M	M	M	M	+	M	+	+	+	+	+	M	M	M	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								
INTEGUMENTARY SYSTEM																									
Mammary gland	M	M	+	+	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	+	M	+
Skin	M	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								
Skeletal muscle	+																								
Lymphoma malignant mixed	X																								
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Meninges, lymphoma malignant mixed	X																								
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	A	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma									X								X								
Alveolar/bronchiolar carcinoma								X												X				X	
Hepatocellular carcinoma, metastatic, liver						X				X			X										X		
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic			X																						
Lymphoma malignant mixed	X																								
Nose	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed	X																								
Trachea	+	+	+	+	+	+	A	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye	+	A	+	A	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Harderian gland																				+					
Adenoma																				X					
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																						X			
Lymphoma malignant mixed	X																								
Urinary bladder	+	+	+	+	+	+	M	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed	X																								

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL
CARCASS ID	2121	2131	2141	2171	2201	2211	2231	2241	2261	2301	2311	2321	2331	2341	2351	2361	2371	2401	2431	2441	2451	2461	2481	2491	2501	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Sternal, lymphoma malignant histiocytic							X																			1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	47
Mediastinal, lymphoma malignant lymphocytic																										1
Mesenteric, lymphoma malignant histiocytic							X																			1
Mesenteric, lymphoma malignant lymphocytic	X																				X					4
Mesenteric, lymphoma malignant mixed													X													3
Renal, lymphoma malignant histiocytic							X																			1
Renal, lymphoma malig lymphocytic																										1
Renal, lymphoma malignant mixed																										2
Lymph node, bronchial	+	M	+	M	+	+	+	+	+	M	+	+	+	+	M	+	M	+	+	+	M	+	+	+	+	36
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	M	+	+	M	M	+	+	+	+	38
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant mixed													X													2
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant lymphocytic	X																				X					2
Lymphoma malignant mixed																										2
Thymus	M	M	+	M	+	+	+	+	+	+	M	+	+	+	M	+	M	+	+	M	+	+	+	+	+	29
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant mixed																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	M	+	M	M	+	M	+	M	M	+	M	M	+	+	M	+	M	+	M	M	M	M	+	+	M	15
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant mixed																										1
Skeletal muscle																										1
Lymphoma malignant mixed																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Meninges, lymphoma malignant mixed																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma																	X						X			4
Alveolar/bronchiolar carcinoma				X			X		X				X					X		X						9
Hepatocellular carcinoma, metastatic, liver																										4
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant mixed																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPECIAL SENSES SYSTEM																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	45
Harderian gland					+																				+	3
Adenoma					X																				X	3
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant histiocytic							X																			1
Lymphoma malignant mixed																										1

TABLE C3. ANALYSIS OF PRIMARY NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	2 mg/m^3	4 mg/m^3
Harderian Gland: Adenoma			
Overall Rates (a)	3/50 (6%)	7/50 (14%)	3/50 (6%)
Adjusted Rates (b)	8.0%	18.8%	9.1%
Terminal Rates (c)	2/34 (6%)	6/36 (17%)	3/33 (9%)
Day of First Observation	666	676	736
Life Table Tests (d)	P=0.547	P=0.171	P=0.642
Logistic Regression Tests (d)	P=0.533	P=0.132	P=0.637
Cochran-Armitage Trend Test (d)	P=0.571N		
Fisher Exact Test (d)		P=0.159	P=0.661N
Liver: Hepatocellular Adenoma			
Overall Rates (e)	5/50 (10%)	8/48 (17%)	9/49 (18%)
Adjusted Rates (b)	12.5%	20.1%	22.6%
Terminal Rates (c)	3/34 (9%)	5/36 (14%)	4/33 (12%)
Day of First Observation	514	559	339
Life Table Tests (d)	P=0.155	P=0.285	P=0.187
Logistic Regression Tests (d)	P=0.183	P=0.294	P=0.232
Cochran-Armitage Trend Test (d)	P=0.152		
Fisher Exact Test (d)		P=0.250	P=0.183
Liver: Hepatocellular Carcinoma			
Overall Rates (e)	11/50 (22%)	12/48 (25%)	12/49 (24%)
Adjusted Rates (b)	25.9%	25.6%	29.0%
Terminal Rates (c)	4/34 (12%)	4/36 (11%)	6/33 (18%)
Day of First Observation	535	470	339
Life Table Tests (d)	P=0.410	P=0.487	P=0.451
Logistic Regression Tests (d)	P=0.517N	P=0.521N	P=0.564
Cochran-Armitage Trend Test (d)	P=0.431		
Fisher Exact Test (d)		P=0.455	P=0.478
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (e)	16/50 (32%)	19/48 (40%)	20/49 (41%)
Adjusted Rates (b)	36.0%	39.6%	45.6%
Terminal Rates (c)	7/34 (21%)	8/36 (22%)	10/33 (30%)
Day of First Observation	514	470	339
Life Table Tests (d)	P=0.225	P=0.351	P=0.249
Logistic Regression Tests (d)	P=0.294	P=0.471	P=0.304
Cochran-Armitage Trend Test (d)	P=0.211		
Fisher Exact Test (d)		P=0.284	P=0.241
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (e)	7/50 (14%)	8/49 (16%)	4/49 (8%)
Adjusted Rates (b)	19.9%	21.0%	11.0%
Terminal Rates (c)	6/34 (18%)	6/36 (17%)	2/33 (6%)
Day of First Observation	730	676	661
Life Table Tests (d)	P=0.249N	P=0.538	P=0.286N
Logistic Regression Tests (d)	P=0.268N	P=0.437	P=0.301N
Cochran-Armitage Trend Test (d)	P=0.238N		
Fisher Exact Test (d)		P=0.483	P=0.274N
Lung: Alveolar/Bronchiolar Carcinoma			
Overall Rates (e)	6/50 (12%)	3/49 (6%)	9/49 (18%)
Adjusted Rates (b)	17.1%	8.3%	26.0%
Terminal Rates (c)	5/34 (15%)	3/36 (8%)	8/33 (24%)
Day of First Observation	730	736	643
Life Table Tests (d)	P=0.200	P=0.217N	P=0.264
Logistic Regression Tests (d)	P=0.181	P=0.242N	P=0.236
Cochran-Armitage Trend Test (d)	P=0.210		
Fisher Exact Test (d)		P=0.254N	P=0.274

TABLE C3. ANALYSIS OF PRIMARY NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (e)	11/50 (22%)	9/49 (18%)	13/49 (27%)
Adjusted Rates (b)	31.4%	23.6%	35.5%
Terminal Rates (c)	10/34 (29%)	7/36 (19%)	10/33 (30%)
Day of First Observation	730	676	643
Life Table Tests (d)	P=0.326	P=0.355N	P=0.372
Logistic Regression Tests (d)	P=0.288	P=0.469N	P=0.329
Cochran-Armitage Trend Test (d)	P=0.339		
Fisher Exact Test (d)		P=0.421N	P=0.385
Circulatory System: Hemangiosarcoma			
Overall Rates (a)	1/50 (2%)	1/50 (2%)	4/50 (8%)
Adjusted Rates (b)	2.9%	2.8%	10.5%
Terminal Rates (c)	1/34 (3%)	1/36 (3%)	2/33 (6%)
Day of First Observation	736	736	604
Life Table Tests (d)	P=0.096	P=0.749N	P=0.172
Logistic Regression Tests (d)	P=0.097	P=0.749N	P=0.178
Cochran-Armitage Trend Test (d)	P=0.101		
Fisher Exact Test (d)		P=0.753N	P=0.181
Circulatory System: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	2/50 (4%)	1/50 (2%)	4/50 (8%)
Adjusted Rates (b)	5.9%	2.8%	10.5%
Terminal Rates (c)	2/34 (6%)	1/36 (3%)	2/33 (6%)
Day of First Observation	736	736	604
Life Table Tests (d)	P=0.228	P=0.480N	P=0.323
Logistic Regression Tests (d)	P=0.227	P=0.480N	P=0.329
Cochran-Armitage Trend Test (d)	P=0.238		
Fisher Exact Test (d)		P=0.500N	P=0.339
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	6/50 (12%)	6/50 (12%)	8/50 (16%)
Adjusted Rates (b)	14.0%	15.1%	20.6%
Terminal Rates (c)	2/34 (6%)	3/36 (8%)	5/33 (15%)
Day of First Observation	520	559	182
Life Table Tests (d)	P=0.307	P=0.596	P=0.361
Logistic Regression Tests (d)	P=0.440	P=0.551N	P=0.543
Cochran-Armitage Trend Test (d)	P=0.330		
Fisher Exact Test (d)		P=0.620N	P=0.387

(a) Number of tumor-bearing animals/number of animals examined grossly at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals killed at the end of the study
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) Number of tumor-bearing animals/number of animals examined microscopically at the site

TABLE C4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	2 mg/m³	4 mg/m³
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine small, ileum	(48)	(44)	(44)
Hyperplasia, lymphoid	2 (4%)		3 (7%)
Liver	(50)	(48)	(49)
Cytomegaly			1 (2%)
Hematopoietic cell proliferation, multifocal			1 (2%)
Infarct			1 (2%)
Inflammation, chronic, multifocal		1 (2%)	3 (6%)
Necrosis	1 (2%)	2 (4%)	
Sinusoid, ectasia		1 (2%)	
Pancreas	(50)	(45)	(47)
Atrophy		1 (2%)	
Pharynx	(1)		
Epithelium, hyperplasia, focal	1 (100%)		
Salivary glands	(50)	(48)	(49)
Hyperplasia, lymphoid	4 (8%)		6 (12%)
Infiltration cellular, lymphocytic		1 (2%)	1 (2%)
Inflammation, chronic, multifocal	3 (6%)	1 (2%)	2 (4%)
Stomach, forestomach	(49)	(46)	(45)
Congestion		1 (2%)	
Cyst	1 (2%)	1 (2%)	
Erosion	1 (2%)		
Hyperkeratosis	3 (6%)	1 (2%)	2 (4%)
Hyperplasia			1 (2%)
Hyperplasia, lymphoid	1 (2%)		
Hyperplasia, squamous		1 (2%)	2 (4%)
Inflammation, chronic, focal	1 (2%)		
Ulcer, multiple	1 (2%)		
Stomach, glandular	(50)	(44)	(47)
Dysplasia	1 (2%)		
Hyperplasia		1 (2%)	1 (2%)
Ulcer, multiple	2 (4%)		
Tooth	(5)	(1)	(3)
Abscess	3 (60%)	1 (100%)	2 (67%)
Developmental malformation	1 (20%)		1 (33%)
Dysplasia	1 (20%)		
CARDIOVASCULAR SYSTEM			
Heart	(50)	(49)	(49)
Cardiomyopathy, focal			1 (2%)
Hyperplasia, lymphoid			1 (2%)
Inflammation, acute			1 (2%)
Atrium, thrombus	1 (2%)	1 (2%)	
Myocardium, necrosis			1 (2%)
Valve, degeneration, mucoid			1 (2%)
ENDOCRINE SYSTEM			
Adrenal gland	(50)	(45)	(47)
Subcapsular, hyperplasia	17 (34%)	5 (11%)	6 (13%)
Adrenal gland, cortex	(50)	(45)	(47)
Hyperplasia, focal	5 (10%)		
Hypertrophy		1 (2%)	
Adrenal gland, medulla	(48)	(44)	(41)
Degeneration, focal			1 (2%)
Pituitary gland	(44)	(37)	(46)
Pars distalis, hyperplasia	1 (2%)	1 (3%)	2 (4%)

TABLE C4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
ENDOCRINE SYSTEM (Continued)			
Thyroid gland	(50)	(45)	(48)
Cyst		1 (2%)	
Follicular cell, hyperplasia, focal	5 (10%)		5 (10%)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Penis	(1)		
Inflammation, suppurative	1 (100%)		
Preputial gland	(10)	(5)	(8)
Abscess	3 (30%)		3 (38%)
Cyst	3 (30%)	3 (60%)	2 (25%)
Inflammation	3 (30%)	1 (20%)	2 (25%)
Inflammation, suppurative		1 (20%)	
Prostate	(50)	(44)	(43)
Abscess	2 (4%)		2 (5%)
Seminal vesicle	(49)	(15)	(44)
Dilatation	2 (4%)		2 (5%)
Inflammation, suppurative	1 (2%)		1 (2%)
Testes	(50)	(44)	(47)
Atrophy	4 (8%)	8 (18%)	4 (9%)
HEMATOPOIETIC SYSTEM			
Lymph node	(48)	(46)	(47)
Hyperplasia, lymphoid	1 (2%)		
Iliac, hyperplasia, lymphoid	1 (2%)		
Iliac, inflammation, chronic	1 (2%)		
Mediastinal, hyperplasia, lymphoid			2 (4%)
Mesenteric, autolysis	1 (2%)		
Mesenteric, hematopoietic cell proliferation		1 (2%)	
Mesenteric, hyperplasia, lymphoid	2 (4%)		3 (6%)
Mesenteric, hyperplasia, re cell		1 (2%)	
Mesenteric, inflammation, chronic	2 (4%)		
Mesenteric, inflammation, suppurative	1 (2%)		
Lymph node, bronchial	(35)	(38)	(36)
Hyperplasia, lymphoid	1 (3%)	2 (5%)	4 (11%)
Lymph node, mandibular	(41)	(29)	(38)
Hyperplasia, lymphoid	6 (15%)	2 (7%)	4 (11%)
Infiltration cellular, histiocytic	1 (2%)		1 (3%)
Inflammation, chronic		1 (3%)	
Spleen	(50)	(47)	(49)
Ectopic tissue		2 (4%)	
Hematopoietic cell proliferation	10 (20%)	5 (11%)	5 (10%)
Hyperplasia, lymphoid	3 (6%)	4 (9%)	3 (6%)
Inflammation, acute			1 (2%)
INTEGUMENTARY SYSTEM			
Mammary gland	(5)	(19)	(15)
Duct, cyst			1 (7%)

TABLE C4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
INTEGUMENTARY SYSTEM (Continued)			
Skin	(50)	(47)	(47)
Abscess		1 (2%)	
Atrophy		1 (2%)	
Hyperplasia, lymphoid		1 (2%)	1 (2%)
Hair follicle, atrophy	1 (2%)	4 (9%)	2 (4%)
Prepuce, inflammation, suppurative			1 (2%)
Prepuce, ulcer	8 (16%)	1 (2%)	
Subcutaneous tissue, hyperplasia, lymphoid			1 (2%)
Subcutaneous tissue, inflammation, suppurative			1 (2%)
MUSCULOSKELETAL SYSTEM			
Bone	(50)	(50)	(49)
Coccygeal, inflammation, suppurative, multifocal	1 (2%)		
NERVOUS SYSTEM			
Brain	(50)	(49)	(48)
Thalamus, mineralization	19 (38%)	21 (43%)	9 (19%)
Ventricle, dilatation			1 (2%)
RESPIRATORY SYSTEM			
Larynx	(50)	(47)	(47)
Epithelium, hyperplasia, focal		1 (2%)	
Lung	(50)	(49)	(49)
Congestion, acute	1 (2%)		
Hyperplasia, lymphoid		1 (2%)	4 (8%)
Infiltration cellular, histiocytic			1 (2%)
Inflammation, chronic, multifocal	21 (42%)	19 (39%)	16 (33%)
Inflammation, suppurative			1 (2%)
Leukocytosis	1 (2%)	1 (2%)	1 (2%)
Alveolar epithelium, hyperplasia	3 (6%)	4 (8%)	1 (2%)
Alveolus, pigmentation, diffuse			1 (2%)
Bronchiole, hyperplasia	1 (2%)		1 (2%)
Venule, thrombus			1 (2%)
Nose	(50)	(48)	(48)
Foreign body	1 (2%)		
Glands, hyperplasia, focal			1 (2%)
Glands, inflammation, suppurative, focal	2 (4%)		
Mucosa, inflammation, suppurative	2 (4%)		2 (4%)
Olfactory epithelium, atrophy			1 (2%)
Respiratory epithelium, metaplasia, squamous			2 (4%)
Trachea	(50)	(46)	(47)
Glands, cyst		1 (2%)	
SPECIAL SENSES SYSTEM			
Eye	(45)		(45)
Inflammation, necrotizing	1 (2%)		

TABLE C4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
URINARY SYSTEM			
Kidney	(50)	(49)	(49)
Cyst	1 (2%)	3 (6%)	
Infarct		1 (2%)	
Infiltration cellular, lymphocytic	41 (82%)	38 (78%)	42 (86%)
Inflammation, chronic, multifocal			1 (2%)
Inflammation, suppurative	2 (4%)	1 (2%)	2 (4%)
Nephropathy	6 (12%)	5 (10%)	10 (20%)
Pelvis, dilatation	1 (2%)		
Pelvis, inflammation, suppurative	4 (8%)		1 (2%)
Renal tubule, hyperplasia, focal	1 (2%)		
Renal tubule, inflammation, suppurative	2 (4%)		
Urinary bladder	(49)	(44)	(47)
Calculus micro observation only	1 (2%)		
Dilatation			1 (2%)
Hyperplasia, lymphoid	1 (2%)		
Inflammation, chronic	5 (10%)		1 (2%)
Inflammation, suppurative	3 (6%)	1 (2%)	
Lumen, hemorrhage			1 (2%)

APPENDIX D

SUMMARY OF LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	2 mg/m^3	4 mg/m^3
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Gallbladder	(45)	(33)	(39)
Lymphoma malignant histiocytic			1 (3%)
Intestine large, cecum	(49)	(41)	(42)
Lymphoma malignant mixed		1 (2%)	
Intestine large, colon	(50)	(47)	(46)
Lymphoma malignant lymphocytic		1 (2%)	
Lymphoma malignant mixed		1 (2%)	
Intestine large, rectum	(49)	(47)	(47)
Lymphoma malignant lymphocytic		1 (2%)	
Intestine small, ileum	(50)	(45)	(43)
Lymphoma malignant histiocytic	2 (4%)		1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)	1 (2%)
Lymphoma malignant mixed		1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type			1 (2%)
Peyer's patch, lymphoma malignant lymphocytic	1 (2%)		
Intestine small, jejunum	(50)	(44)	(43)
Lymphoma malignant histiocytic	2 (4%)		
Liver	(50)	(49)	(49)
Hepatoblastoma		1 (2%)	
Hepatocellular carcinoma	6 (12%)	5 (10%)	4 (8%)
Hepatocellular carcinoma, multiple	2 (4%)		
Hepatocellular adenoma	4 (8%)	5 (10%)	2 (4%)
Hepatocellular adenoma, multiple		3 (6%)	1 (2%)
Histiocytic sarcoma			2 (4%)
Lymphoma malignant histiocytic	4 (8%)		2 (4%)
Lymphoma malignant lymphocytic		3 (6%)	2 (4%)
Lymphoma malignant mixed	1 (2%)	2 (4%)	1 (2%)
Mesentery	*(50)	*(50)	*(50)
Carcinoma, metastatic, uterus			1 (2%)
Histiocytic sarcoma			2 (4%)
Lymphoma malignant histiocytic	1 (2%)		2 (4%)
Lymphoma malignant lymphocytic	7 (14%)	5 (10%)	3 (6%)
Lymphoma malignant mixed	1 (2%)	1 (2%)	2 (4%)
Lymphoma malignant undifferentiated cell type			1 (2%)
Pancreas	(50)	(48)	(48)
Lymphoma malignant histiocytic	4 (8%)		2 (4%)
Lymphoma malignant lymphocytic	4 (8%)	4 (8%)	1 (2%)
Lymphoma malignant mixed		1 (2%)	
Salivary glands	(50)	(50)	(48)
Histiocytic sarcoma			1 (2%)
Lymphoma malignant histiocytic	3 (6%)		2 (4%)
Lymphoma malignant lymphocytic	10 (20%)	5 (10%)	2 (4%)
Lymphoma malignant mixed	1 (2%)	2 (4%)	2 (4%)
Lymphoma malignant undifferentiated cell type			1 (2%)
Stomach, forestomach	(49)	(48)	(48)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant lymphocytic		2 (4%)	
Lymphoma malignant mixed		2 (4%)	
Papilloma squamous		1 (2%)	2 (4%)
Squamous cell carcinoma	1 (2%)		
Stomach, glandular	(50)	(47)	(48)
Lymphoma malignant histiocytic	2 (4%)		
Lymphoma malignant lymphocytic	1 (2%)	2 (4%)	1 (2%)
Lymphoma malignant mixed		2 (4%)	

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
CARDIOVASCULAR SYSTEM			
Heart	(50)	(50)	(49)
Histiocytic sarcoma			1 (2%)
Lymphoma malignant histiocytic	1 (2%)		1 (2%)
Lymphoma malignant lymphocytic	3 (6%)		
Lymphoma malignant mixed		1 (2%)	
ENDOCRINE SYSTEM			
Adrenal gland	(50)	(46)	(48)
Lymphoma malignant mixed		1 (2%)	
Bilateral, lymphoma malignant lymphocytic		1 (2%)	
Capsule, lymphoma malignant lymphocytic	1 (2%)		
Subcapsular, adenoma		1 (2%)	
Adrenal gland, cortex	(46)	(44)	(46)
Lymphoma malignant histiocytic	1 (2%)		1 (2%)
Lymphoma malignant lymphocytic	2 (4%)		
Lymphoma malignant mixed		1 (2%)	1 (2%)
Adrenal gland, medulla	(44)	(38)	(39)
Lymphoma malignant lymphocytic	2 (5%)		
Lymphoma malignant mixed		1 (3%)	1 (3%)
Pheochromocytoma, NOS		1 (3%)	
Islets, pancreatic	(48)	(46)	(46)
Adenoma			1 (2%)
Lymphoma malignant histiocytic			2 (4%)
Lymphoma malignant mixed	1 (2%)		
Pituitary gland	(45)	(43)	(45)
Pars distalis, adenoma	20 (44%)	15 (35%)	12 (27%)
Pars distalis, carcinoma			1 (2%)
Pars intermedia, adenoma	1 (2%)	1 (2%)	1 (2%)
Thyroid gland	(49)	(46)	(49)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)	
Follicular cell, adenoma			2 (4%)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Ovary	(50)	(44)	(45)
Granulosa cell tumor, NOS	1 (2%)		1 (2%)
Hemangiosarcoma			1 (2%)
Histiocytic sarcoma			2 (4%)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant lymphocytic	2 (4%)	2 (5%)	
Lymphoma malignant mixed		3 (7%)	
Mixed tumor benign			1 (2%)
Bilateral, carcinoma, metastatic, uterus			1 (2%)
Uterus	(50)	(49)	(49)
Carcinoma			1 (2%)
Hemangiosarcoma			1 (2%)
Histiocytic sarcoma	1 (2%)		
Leiomyoma			1 (2%)
Lymphoma malignant lymphocytic		1 (2%)	
Lymphoma malignant mixed		2 (4%)	
Polyp		1 (2%)	
Sarcoma	1 (2%)		
Endometrium, polyp	3 (6%)	1 (2%)	2 (4%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
HEMATOPOIETIC SYSTEM			
Bone marrow	(50)	(48)	(49)
Sternal, lymphoma malignant histiocytic	1 (2%)		
Lymph node	(50)	(48)	(46)
Iliac, lymphoma malignant histiocytic	1 (2%)		2 (4%)
Iliac, lymphoma malignant lymphocytic		2 (4%)	1 (2%)
Iliac, lymphoma malignant mixed		1 (2%)	
Inguinal, histiocytic sarcoma			1 (2%)
Mediastinal, histiocytic sarcoma			2 (4%)
Mediastinal, lymphoma malignant histiocytic	3 (6%)		3 (7%)
Mediastinal, lymphoma malignant lymphocytic	3 (6%)	2 (4%)	2 (4%)
Mediastinal, lymphoma malignant mixed	1 (2%)		
Mesenteric, hepatocellular carcinoma, metastatic, liver		1 (2%)	
Mesenteric, histiocytic sarcoma	1 (2%)		2 (4%)
Mesenteric, lymphoma malignant histiocytic	1 (2%)		2 (4%)
Mesenteric, lymphoma malignant lymphocytic	1 (2%)	2 (4%)	1 (2%)
Mesenteric, lymphoma malignant mixed		1 (2%)	
Pancreatic, lymphoma malignant mixed		1 (2%)	
Renal, histiocytic sarcoma			1 (2%)
Renal, lymphoma malignant histiocytic	3 (6%)		3 (7%)
Renal, lymphoma malignant lymphocytic		5 (10%)	1 (2%)
Renal, lymphoma malignant mixed	1 (2%)	1 (2%)	
Lymph node, bronchial	(26)	(38)	(36)
Histiocytic sarcoma			3 (8%)
Lymphoma malignant histiocytic	4 (15%)		3 (8%)
Lymphoma malignant lymphocytic	6 (23%)	9 (24%)	3 (8%)
Lymphoma malignant mixed	1 (4%)	1 (3%)	1 (3%)
Lymphoma malignant undifferentiated cell type			1 (3%)
Lymph node, mandibular	(45)	(41)	(40)
Histiocytic sarcoma			2 (5%)
Lymphoma malignant histiocytic	6 (13%)		2 (5%)
Lymphoma malignant lymphocytic	11 (24%)	7 (17%)	5 (13%)
Lymphoma malignant mixed	2 (4%)	2 (5%)	2 (5%)
Lymphoma malignant undifferentiated cell type			1 (3%)
Squamous cell carcinoma, metastatic, ear	1 (2%)		
Spleen	(50)	(48)	(49)
Hemangiosarcoma		1 (2%)	
Histiocytic sarcoma			3 (6%)
Lymphoma malignant histiocytic	5 (10%)		2 (4%)
Lymphoma malignant lymphocytic	13 (26%)	12 (25%)	5 (10%)
Lymphoma malignant mixed	2 (4%)	5 (10%)	3 (6%)
Lymphoma malignant undifferentiated cell type			1 (2%)
Sarcoma		1 (2%)	
Thymus	(42)	(37)	(35)
Lymphoma malignant histiocytic	2 (5%)		1 (3%)
Lymphoma malignant lymphocytic	3 (7%)	7 (19%)	1 (3%)
Lymphoma malignant mixed	1 (2%)	4 (11%)	
INTEGUMENTARY SYSTEM			
Mammary gland	(39)	(37)	(39)
Adenoacanthoma		1 (3%)	
Adenocarcinoma	4 (10%)	1 (3%)	1 (3%)
Fibroadenoma	1 (3%)		
Lymphoma malignant mixed		2 (5%)	

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
INTEGUMENTARY SYSTEM (Continued)			
Skin	(50)	(50)	(48)
Hemangiosarcoma		1 (2%)	
Histiocytic sarcoma			1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	3 (6%)	
Lymphoma malignant mixed		2 (4%)	
Papilloma squamous		1 (2%)	
Subcutaneous tissue, sarcoma		1 (2%)	
MUSCULOSKELETAL SYSTEM			
Bone	(50)	(48)	(50)
Rib, osteosarcoma		1 (2%)	
Skeletal muscle	*(50)	*(50)	*(50)
Head, lymphoma malignant lymphocytic		1 (2%)	
NERVOUS SYSTEM			
Brain	(50)	(49)	(50)
Carcinoma, metastatic, pituitary gland			1 (2%)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant lymphocytic	2 (4%)	2 (4%)	
Lymphoma malignant mixed		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
RESPIRATORY SYSTEM			
Lung	(50)	(47)	(49)
Adenocarcinoma, metastatic, multiple, harderian gland			1 (2%)
Alveolar/bronchiolar adenoma	4 (8%)	1 (2%)	4 (8%)
Alveolar/bronchiolar adenoma, multiple			1 (2%)
Alveolar/bronchiolar carcinoma	3 (6%)	1 (2%)	1 (2%)
Carcinoma, metastatic, liver		1 (2%)	
Carcinoma, metastatic, uterus			1 (2%)
Hepatocellular carcinoma, metastatic, liver	2 (4%)	2 (4%)	
Histiocytic sarcoma			3 (6%)
Lymphoma malignant histiocytic	4 (8%)		2 (4%)
Lymphoma malignant lymphocytic	11 (22%)	10 (21%)	4 (8%)
Lymphoma malignant mixed	2 (4%)	5 (11%)	1 (2%)
Lymphoma malignant undifferentiated cell type			1 (2%)
Osteosarcoma, metastatic, multiple, bone		1 (2%)	
Vein, mediastinum, hemangiosarcoma, metastatic, uterus			1 (2%)
Trachea	(49)	(46)	(49)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant mixed		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
Peritracheal tissue, lymphoma malignant mixed		1 (2%)	
SPECIAL SENSES SYSTEM			
Ear	*(50)	*(50)	*(50)
Squamous cell carcinoma	1 (2%)		
Harderian gland	*(50)	*(50)	*(50)
Adenocarcinoma			1 (2%)
Carcinoma		1 (2%)	

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
URINARY SYSTEM			
Kidney	(50)	(50)	(48)
Histiocytic sarcoma			1 (2%)
Lymphoma malignant histiocytic	3 (6%)		2 (4%)
Lymphoma malignant lymphocytic	12 (24%)	6 (12%)	3 (6%)
Lymphoma malignant mixed	2 (4%)	3 (6%)	1 (2%)
Lymphoma malignant undifferentiated cell type			1 (2%)
Osteosarcoma, metastatic, multiple, bone		1 (2%)	
Urinary bladder	(50)	(47)	(48)
Lymphoma malignant histiocytic	2 (4%)		1 (2%)
Lymphoma malignant lymphocytic	7 (14%)	6 (13%)	3 (6%)
Lymphoma malignant mixed	1 (2%)	3 (6%)	1 (2%)
Lymphoma malignant undifferentiated cell type			1 (2%)
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic	13 (26%)	14 (28%)	6 (12%)
Lymphoma malignant histiocytic	7 (14%)		3 (6%)
Lymphoma malignant mixed	2 (4%)	5 (10%)	3 (6%)
Hemangiosarcoma		2 (4%)	2 (4%)
Lymphoma malignant undifferentiated cell			1 (2%)
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Moribund	8	13	10
Terminal sacrifice	40	27	32
Dead	2	10	8
TUMOR SUMMARY			
Total animals with primary neoplasms **	42	40	38
Total primary neoplasms	76	65	82
Total animals with benign neoplasms	29	24	24
Total benign neoplasms	33	30	30
Total animals with malignant neoplasms	30	29	25
Total malignant neoplasms	42	34	51
Total animals with secondary neoplasms ***	2	4	4
Total secondary neoplasms	3	6	6
Total animals with neoplasms-- uncertain benign or malignant	1	1	1
Total uncertain neoplasms	1	1	1

* Number of animals receiving complete necropsy examination; 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 2-CHLOROACETOPHENONE: CHAMBER CONTROL

WEEKS ON STUDY	061	068	075	084	085	093	096	102	103	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	093 31	074 11	076 11	055 11	057 11	051 11	070 11	071 11	080 11	079 11	052 11	053 11	054 11	056 11	058 11	059 11	060 11	061 11	062 11	063 11	064 11	065 11	066 11	067 11	068 11
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	M	+	+	+	+	+	+	A	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic									X																
Peyer's patch, lymphoma malignant lymphocytic																	X								
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma	X									X						X									
Hepatocellular carcinoma, multiple									X																
Hepatocellular adenoma																									X
Lymphoma malignant histiocytic								X																	
Lymphoma malignant mixed		X																							
Mesentery				●									+	+		+		+							
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic													X			X		X							
Lymphoma malignant mixed																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic							X	X																	
Lymphoma malignant lymphocytic													X				X								
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic				X				X																	
Lymphoma malignant lymphocytic													X		X	X	X	X	X						
Lymphoma malignant mixed																									
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Lymphoma malignant histiocytic							X																		
Squamous cell carcinoma					X																				
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic							X																		
Lymphoma malignant lymphocytic																	X								
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic								X																	
Lymphoma malignant lymphocytic																X	X								
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, lymphoma malignant lymphocytic																									
Adrenal gland, cortex	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Lymphoma malignant histiocytic								X																	
Lymphoma malignant lymphocytic													X			X									
Adrenal gland, medulla	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Lymphoma malignant lymphocytic													X			X									
Islets, pancreatic	+	+	+	+	+	+	+	+	M	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Parathyroid gland	M	M	M	+	+	+	M	+	+	M	+	+	+	+	+	M	+	+	M	M	+	+	M	+	+
Pituitary gland	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma									X	X						X			X	X			X	X	
Pars intermedia, adenoma											X														
Thyroid gland	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	+
Granulosa cell tumor, NOS																									
Lymphoma malignant lymphocytic																X	X								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																									X
Sarcoma																	X								
Endometrium, polyp																									

+: 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	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	06891	07211	07311	07511	07711	07811	08111	08211	08311	08411	08511	08611	08711	08811	08911	09011	09111	09211	09411	09511	09611	09711	09811	09911	10001	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	M	+	45
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																			X	X						2
Lymphoma malignant lymphocytic																										1
Peyer's patch, lymphoma malignant lymphocytic																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic						X													X							2
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma	X					X						X														6
Hepatocellular carcinoma, multiple																							X			2
Hepatocellular adenoma															X						X			X		4
Lymphoma malignant histiocytic										X									X	X						4
Lymphoma malignant mixed																										1
Mesentery			+	+	+	+	+					+		+		+	+	+						+		16
Lymphoma malignant histiocytic						X																				1
Lymphoma malignant lymphocytic												X		X		X	X									7
Lymphoma malignant mixed					X																					1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic										X										X						4
Lymphoma malignant lymphocytic														X		X										4
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																				X						3
Lymphoma malignant lymphocytic								X				X				X	X									10
Lymphoma malignant mixed					X																					1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																										1
Squamous cell carcinoma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																			X							2
Lymphoma malignant lymphocytic																										1
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic												X														3
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, lymphoma malignant lymphocytic																						X				1
Adrenal gland, cortex	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	46
Lymphoma malignant histiocytic																										1
Lymphoma malignant lymphocytic																										2
Adrenal gland, medulla	M	+	I	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	I	+	44
Lymphoma malignant lymphocytic																										2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant mixed					X																					1
Parathyroid gland	M	+	M	M	M	M	+	M	M	+	+	M	M	+	M	M	M	M	M	+	+	+	M	+	M	25
Pituitary gland	M	M	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	45
Pars distalis, adenoma			X	X	X			X		X		X	X	X	X	X				X				X	X	20
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
Lymphoma malignant lymphocytic																X										1
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	-	+	+	50
Granulosa cell tumor, NOS																						X				1
Lymphoma malignant lymphocytic																										2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	50
Histiocytic sarcoma																										1
Sarcoma																										1
Endometrium, polyp							X										X		X							3

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

WEEKS ON STUDY	061	068	075	084	085	093	096	102	103	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	09311	07411	07611	05511	05711	05111	07011	07111	08101	07911	05211	05311	05411	05611	05811	05911	06011	06111	06211	06311	06411	06511	06611	06711	06811	
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sternal, lymphoma malignant histiocytic																										
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	
Iliac, lymphoma malignant histiocytic																										
Mediastinal, lymphoma malignant histiocytic							X																			
Mediastinal, lymphoma malignant lymphocytic																			X							
Mediastinal, lymphoma malignant mixed		X																								
Mesenteric, histiocytic sarcoma																									X	
Mesenteric, lymphoma malignant histiocytic																										
Mesenteric, lymphoma malignant lymphocytic															X											
Renal, lymphoma malignant histiocytic								X																		
Renal, lymphoma malignant mixed		X																								
Lymph node, bronchial	M	+	+	+	+	M	+	M	M	M	+	+	+	M	+	+	M	M	M	+	+	M	M	M	M	
Lymphoma malignant histiocytic							X																			
Lymphoma malignant lymphocytic													X		X	X										
Lymphoma malignant mixed		X																								
Lymph node, mandibular	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	
Lymphoma malignant histiocytic				X			X	X																		
Lymphoma malignant lymphocytic													X		X	X	X	X	X							
Lymphoma malignant mixed		X																								
Squamous cell carcinoma, metastatic, ear																										
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic							X	X																		
Lymphoma malignant lymphocytic									X				X		X	X	X	X	X							
Lymphoma malignant mixed		X																								
Thymus	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic								X																		
Lymphoma malignant lymphocytic															X	X										
Lymphoma malignant mixed		X																								
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	M	+	M	+	+	M	+	+	M	M	+	+	+	+	+	M	+	+	+	
Adenocarcinoma																									X	
Fibroadenoma																							X			
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant lymphocytic																X										
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant lymphocytic																										
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Alveolar/bronchiolar adenoma					X																					
Alveolar/bronchiolar carcinoma					X					X																
Hepatocellular carcinoma, metastatic, liver																										
Lymphoma malignant histiocytic							X	X																		
Lymphoma malignant lymphocytic													X			X	X	X	X							
Lymphoma malignant mixed		X																								
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Trachea	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																										
SPECIAL SENSES SYSTEM																										
Ear																										
Squamous cell carcinoma																										
Eye	A	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	
Harderian gland																										
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic								X																		
Lymphoma malignant lymphocytic													X		X	X	X	X	X							
Lymphoma malignant mixed		X																								
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	
Lymphoma malignant histiocytic																										
Lymphoma malignant lymphocytic													X		X		X		X							
Lymphoma malignant mixed																										

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 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 TISSUES TUMORS
CARCASS ID	0691	0721	0731	0751	0771	0781	0811	0821	0831	0841	0851	0861	0871	0881	0891	0901	0911	0921	0941	0951	0961	0971	0981	0991	1001	
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sternal, lymphoma malignant histiocytic																			X							1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Iliac, lymphoma malignant histiocytic																				X						1
Mediastinal, lymphoma malignant histiocytic																			X	X						3
Mediastinal, lymphoma malignant lymphocytic														X			X									3
Mediastinal, lymphoma malig. mixed																										1
Mesenteric, histiocytic sarcoma																										1
Mesenteric, lymphoma malignant histiocytic																				X						1
Mesenteric, lymphoma malignant lymphocytic																										1
Renal, lymphoma malignant histiocytic										X										X						3
Renal, lymphoma malignant mixed																										1
Lymph node, bronchial	+	+	M	M	M	M	M	M	M	+	I	+	+	M	I	+	M	+	+	+	+	+	+	+	+	26
Lymphoma malignant histiocytic										X									X	X						4
Lymphoma malignant lymphocytic												X				X						X				6
Lymphoma malignant mixed																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	M	+	+	M	+	+	+	+	45
Lymphoma malignant histiocytic						X				X										X						6
Lymphoma malignant lymphocytic								X				X				X	X					X				11
Lymphoma malignant mixed					X																					2
Squamous cell carcinoma, metastatic, ear						X																				1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic										X									X	X						5
Lymphoma malignant lymphocytic								X				X		X		X	X					X				13
Lymphoma malignant mixed					X																					2
Thymus	+	+	+	M	+	+	+	+	+	M	+	M	M	+	+	+	+	+	+	M	+	+	+	+	M	42
Lymphoma malignant histiocytic																			X							2
Lymphoma malignant lymphocytic														X												3
Lymphoma malignant mixed																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	+	M	+	+	M	+	+	+	+	+	+	+	+	M	+	M	+	M	+	+	+	+	+	+	+	39
Adenocarcinoma						X											X					X				4
Fibroadenoma																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic												X										X				2
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma								X	X													X				4
Alveolar/bronchiolar carcinoma							X																			3
Hepatocellular carcinoma, metastatic, liver						X																	X			2
Lymphoma malignant histiocytic										X									X							4
Lymphoma malignant lymphocytic								X				X		X		X	X					X				11
Lymphoma malignant mixed					X																					2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																			X							1
SPECIAL SENSES SYSTEM																										
Ear						+																				1
Squamous cell carcinoma						X																				1
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Harderian gland														+												1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																			X	X						3
Lymphoma malignant lymphocytic								X				X		X		X	X					X				12
Lymphoma malignant mixed					X																					2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																			X	X						2
Lymphoma malignant lymphocytic								X						X		X										7
Lymphoma malignant mixed					X																					1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 2 mg/m³

WEEKS ON STUDY	0 3 4	0 5 3	0 5 8	0 7 1	0 7 8	0 8 0	0 8 4	0 8 5	0 8 9	0 9 2	0 9 2	0 9 3	0 9 4	0 9 5	0 9 6	0 9 8	0 9 8	0 9 9	0 9 9	1 0 1	1 0 3	1 0 4	1 0 5	1 0 6	1 0 6
CARCASS ID	1 7 3 1	1 8 7 1	1 5 4 1	1 6 5 1	2 0 0 1	1 9 2 1	1 6 0 1	1 9 9 1	1 6 1 1	1 9 4 1	1 6 6 1	1 8 0 1	1 5 7 1	1 9 7 1	1 6 2 1	1 9 3 1	1 7 0 1	1 7 1 1	1 7 8 1	1 8 8 1	1 6 7 1	1 7 5 1	1 8 3 1	1 5 1 1	1 5 2 1
ALIMENTARY SYSTEM																									
Esophagus	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	+	I	+	+	A	+	+	+	+	M	A	+	A	+	A	M	A	+	+	A	A	M	+	+
Intestine large	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Intestine large, cecum	A	M	M		+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	A	+	+
Lymphoma malignant mixed										X															
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X															
Intestine large, rectum	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+
Lymphoma malignant lymphocytic		X																							
Intestine small	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	A	+	+
Intestine small, duodenum	A	+	+	+	+	A	+	+			A	+	+	+	+	+	A	+	+	+	+	A	A	+	+
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	A	+	+
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X															
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	A	M	+	+	+	+	A	+	+	+	+	A	A	+	+
Liver	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatoblastoma								X																	
Hepatocellular carcinoma				X										X		X									
Hepatocellular adenoma												X													
Hepatocellular adenoma, multiple			X																					X	
Lymphoma malignant lymphocytic		X													X										X
Lymphoma malignant mixed										X								X							
Mesentery			+		+	+	+			+		+								+			+		
Lymphoma malignant lymphocytic												X													
Lymphoma malignant mixed										X															
Pancreas	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X															
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic		X																			X				
Lymphoma malignant mixed										X								X							
Stomach	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X								X							
Papilloma squamous																							X		
Stomach, glandular	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X								X							
CARDIOVASCULAR SYSTEM																									
Blood vessel	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed										X															
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	M	+	+
Lymphoma malignant mixed																		X							
Bilateral, lymphoma malignant lymphocytic		X																							
Subcapsular, adenoma																									
Adrenal gland, cortex	A	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	M	+	+
Lymphoma malignant mixed										X															
Adrenal gland, medulla	A	+	+	+	+	+	A	+	+	+	A	+	+	M	+	+	A	I	I	+	+	+	M	+	+
Lymphoma malignant mixed										X															
Pheochromocytoma, NOS																									
Islets, pancreatic	A	+	+	+	+	+	+	+	+	+	A	I	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	M	+	M	M	M	M	M	M	M	M	M	+	M	M	+	M	M	+	M	M	M	M	+
Pituitary gland	M	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	I	+	+
Pars distalis, adenoma																	X				X	X		X	X
Pars intermedia, adenoma																									
Thyroid gland	A	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	A	+	+
Lymphoma malignant lymphocytic		X																							
GENERAL BODY SYSTEM																									
Tissue, NOS																									
GENITAL SYSTEM																									
Clitoral gland																					+				
Ovary	A	+	+	M	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X								X						X	
Uterus	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed										X								X							
Polyp																									
Endometrium, polyp																						X			

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 2 mg/m³
(Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL
CARCASS ID	15331	15551	15661	15881	15991	16331	16441	16881	16991	17221	17441	17661	17771	17991	18111	18821	18441	18551	18661	18991	19011	19111	19951	19661	19881	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	M	+	I	+	+	+	+	+	+	+	M		+	+	+	+	+	+	M	+	+	+	+	+	+	33
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Lymphoma malignant mixed																										1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic																										1
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatoblastoma																										1
Hepatocellular carcinoma																			X			X				5
Hepatocellular adenoma												X				X	X								X	5
Hepatocellular adenoma, multiple	X																									3
Lymphoma malignant lymphocytic																										3
Lymphoma malignant mixed																										2
Mesentery			+	+	+		+									+										13
Lymphoma malignant lymphocytic			X		X		X									X										5
Lymphoma malignant mixed																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant lymphocytic			X				X														X					4
Lymphoma malignant mixed																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic			X				X																		X	5
Lymphoma malignant mixed																										2
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant lymphocytic							X																			2
Lymphoma malignant mixed																										2
Papilloma squamous																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic							X																			2
Lymphoma malignant mixed																										2
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed																										1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant mixed																										1
Bilateral, lymphoma malignant lymphocytic																										1
Subcapsular, adenoma															X											1
Adrenal gland, cortex	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant mixed																										1
Adrenal gland, medulla	+	I	+		+	+	+	+	+	+	+		+	+		+	+	+	+	+	+	+	+	+	+	38
Lymphoma malignant mixed																										1
Pheochromocytoma, NOS																	X									1
Islets, pancreatic	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Parathyroid gland	+	M	+	M	M	M	M	+	M	M	+	M	M	M	M	M	M	+	M	+	M	M	+	M	+	14
Pituitary gland	+	+	+	+	I	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	M	+	43
Pars distalis, adenoma	X	X	X			X	X		X		X	X								X			X			15
Pars intermedia, adenoma								X																		1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant lymphocytic																										1
GENERAL BODY SYSTEM																										
Tissue, NOS				+																						1
GENITAL SYSTEM																										
Clitoral gland																										1
Ovary	+	+	I	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant lymphocytic																									X	2
Lymphoma malignant mixed																										3
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																									X	1
Lymphoma malignant mixed																										2
Polyp												X														1
Endometrium, polyp																										1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 2 mg/m³
(Continued)

WEEKS ON STUDY	034	053	058	071	078	080	084	085	089	092	092	093	094	095	096	098	098	099	099	101	103	104	105	106	106
CARCASS ID	17311	18711	15411	16511	20001	19211	16001	19911	16111	19411	16611	18001	15711	19711	16211	19311	17011	17111	17811	18811	16711	17511	18311	15111	15211
HEMATOPOIETIC SYSTEM																									
Blood	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Iliac, lymphoma malignant lymphocytic																									
Iliac, lymphoma malignant mixed																								X	
Mediastinal, lymphoma malignant lymphocytic		X																							
Mesenteric, hepatocellular carcinoma, metastatic, liver				X																					
Mesenteric, lymphoma malignant lymphocytic																									
Mesenteric, lymphoma malignant mixed																								X	
Pancreatic, lymphoma malignant mixed																								X	
Renal, lymphoma malignant lymphocytic											X				X										
Renal, lymphoma malignant mixed																								X	
Lymph node, bronchial	M	+	+		+	M	+	M	+	+	+	M	M	I	+	I		+	+	+	+	I	+		+
Lymphoma malignant lymphocytic		X									X										X				
Lymphoma malignant mixed										X															
Lymph node, mandibular	+	M	+		M	+	+	M	+	+	+	+	+	+	+	M	+	M	+	+	+	+	M	+	+
Lymphoma malignant lymphocytic												X									X				
Lymphoma malignant mixed										X														X	
Spleen	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																	X								
Lymphoma malignant lymphocytic		X										X			X						X				X
Lymphoma malignant mixed										X								X						X	
Sarcoma																									
Thymus	A	+	+	+	+	M	M	+	+	+	+	M	+	+	I	M	I	M	+	+	M	M	A	+	+
Lymphoma malignant lymphocytic		X																							X
Lymphoma malignant mixed										X														X	
INTEGUMENTARY SYSTEM																									
Mammary gland	+	M	+	M	M	+	M	+	+	+	+	+	+	M	M	M	+	+	+	+	+	+	I	+	+
Adenoacanthoma									X																
Adenocarcinoma																					X				
Lymphoma malignant mixed										X								X							
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X								X							
Papilloma squamous																									
Subcutaneous tissue, sarcoma						X																			
MUSCULOSKELETAL SYSTEM																									
Bone	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Rib osteosarcoma									X																
Skeletal muscle		+																							
Head, lymphoma malignant lymphocytic		X																							
NERVOUS SYSTEM																									
Brain	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic		X																							
Lymphoma malignant mixed										X															
RESPIRATORY SYSTEM																									
Larynx	A	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	A	+	+
Lung	A	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	A	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, liver								X																	
Hepatocellular carcinoma, metastatic, liver				X																					
Lymphoma malignant lymphocytic											X	X			X						X				
Lymphoma malignant mixed										X								X						X	
Osteosarcoma, metastatic, multiple, bone									X																
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
Trachea	A	+	+	+	+	+	+	I	+	+	+	+	+	+	M	+	+	+	+	+	+	+	A	+	+
Lymphoma malignant mixed										X															
Peritracheal tissue, lymphoma malignant mixed																		X							
SPECIAL SENSES SYSTEM																									
Eye														M											
Harderian gland																									
Carcinoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic		X										X									X				
Lymphoma malignant mixed										X															
Osteosarcoma, metastatic, multiple, bone									X																
Urinary bladder	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
Lymphoma malignant lymphocytic		X										X													X
Lymphoma malignant mixed										X								X						X	

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 2 mg/m³ (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL TISSUES TUMORS
CARCASS ID	15311	15511	15611	15811	15911	16311	16411	16811	16911	17211	17411	17611	17711	17911	18111	18211	18411	18511	18611	18911	19011	19111	19511	19611	19811	
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Bone marrow	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Iliac, lymphoma malignant lymphocytic			X				X																			2
Iliac, lymphoma malignant mixed																										1
Mediastinal, lymphoma malignant lymphocytic			X																							2
Mesenteric, hepatocellular carcinoma, metastatic, liver																										1
Mesenteric, lymphoma malignant lymphocytic			X				X																			2
Mesenteric, lymphoma malignant mixed																										1
Pancreatic, lymphoma malignant mixed																										1
Renal, lymphoma malig lymphocytic			X		X		X																			5
Renal, lymphoma malignant mixed																										1
Lymph node, bronchial	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Lymphoma malignant lymphocytic			X				X					X				X					X				X	9
Lymphoma malignant mixed																										1
Lymph node, mandibular	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Lymphoma malignant lymphocytic			X		X		X					X				X										7
Lymphoma malignant mixed																										2
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Hemangiosarcoma																										1
Lymphoma malignant lymphocytic			X		X		X									X	X				X				X	12
Lymphoma malignant mixed	X	X																								5
Sarcoma		X																								1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	37
Lymphoma malignant lymphocytic			X				X					X									X				X	7
Lymphoma malignant mixed	X	X																								4
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	M	+	M	+	+	+	M	+	+	M	+	+	M	+	+	+	+	+	+	37
Adenoacanthoma																										1
Adenocarcinoma																										1
Lymphoma malignant mixed																										2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma							X																			1
Lymphoma malignant lymphocytic							X																		X	3
Lymphoma malignant mixed																										2
Papilloma squamous			X																							1
Subcutaneous tissue, sarcoma																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Rib, osteosarcoma																										1
Skeletal muscle																										1
Head, lymphoma malignant lymphocytic																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																	X									2
Lymphoma malignant mixed																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Alveolar/bronchiolar adenoma											X															1
Alveolar/bronchiolar carcinoma																								X		1
Carcinoma, metastatic, liver																										1
Hepatocellular carcinoma, metastatic, liver																			X							2
Lymphoma malignant lymphocytic			X				X					X				X					X				X	10
Lymphoma malignant mixed	X	X																								5
Osteosarcoma, metastatic, multiple, bone																										1
Nose	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant mixed																										1
Peritracheal tissue, lymphoma malignant mixed																										1
SPECIAL SENSES SYSTEM																										
Eye																										
Harderian gland												+														1
Carcinoma												X														1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																	X				X				X	6
Lymphoma malignant mixed	X	X																								3
Osteosarcoma, metastatic, multiple, bone																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	47
Lymphoma malignant lymphocytic			X				X																		X	6
Lymphoma malignant mixed																										3

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE: 4 mg/m³

WEEKS ON STUDY	0 5 0	0 5 5	0 6 0	0 6 8	0 7 3	0 7 6	0 8 0	0 8 4	0 8 8	0 8 9	0 9 2	0 9 2	0 9 3	0 9 5	0 9 7	0 9 9	1 0 0	1 0 4	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6
CARCASS ID	2 8 4 1	2 5 6 1	2 5 9 1	2 8 9 1	2 9 0 1	2 9 1 1	2 7 0 1	2 8 8 1	2 8 2 1	3 0 0 1	2 6 5 1	2 6 0 1	2 6 3 1	2 5 8 1	2 7 3 1	2 5 5 1	2 5 2 1	2 9 4 1	2 5 1 1	2 5 3 1	2 5 4 1	2 5 7 1	2 6 1 1	2 6 2 1	2 6 4 1
ALIMENTARY SYSTEM																									
Esophagus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	A	A	+	M	M	+	A	A	A	M	+	+	A	+	+	A	+	+	M	+	+	+	+
Lymphoma malignant histiocytic																									
Intestine large	+	+	+	+	+	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	M	M	+	M	+	+	+	A	A	M	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	M	+	+	+	+	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	A	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	A	+	+	A	+	+	A	A	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	A	+	+	I	+	+	A	A	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+
Intestine small, ileum	+	+	A	+	+	A	+	+	A	A	M	+	+	+	A	+	+	A	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type																									
Intestine small, jejunum	+	+	A	+	+	A	+	+	A	A	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma		X							X		X														
Hepatocellular adenoma																									X
Hepatocellular adenoma, multiple																					X				
Histiocytic sarcoma												X		X											
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																									X
Mesentery														+		+	+				+	+		+	+
Carcinoma, metastatic, uterus																X									
Histiocytic sarcoma														X			X								
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																					X				
Lymphoma malignant mixed																									X
Lymphoma malignant undifferentiated cell type																									
Pancreas	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
Salivary glands	+	+	+	+	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																					X				
Lymphoma malignant mixed																									X
Lymphoma malignant undifferentiated cell type																									
Stomach	+	+	+	+	+	+	+	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																									
Stomach, glandular	+	+	+	+	+	+	+	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Tooth															+										+
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																	X								
Lymphoma malignant histiocytic																									
ENDOCRINE SYSTEM																									
Adrenal gland	M	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	M	+	+	+	+	+	+	I	+	A	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant mixed																									
Adrenal gland, medulla	M	+	+	+	+	+	I	I	+	A	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+
Lymphoma malignant mixed																									
Islets, pancreatic	+	+	M	+	+	+	+	+	+	A	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Lymphoma malignant histiocytic																									
Parathyroid gland	M	+	+	M	M	M	M	M	+	M	+	+	+	+	M	+	M	+	+	M	+	M	M	M	M
Pituitary gland	+	+	+	+	+	M	I	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma													X	X			X			X	X				
Pars distalis, carcinoma								X																	
Pars intermedia, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																					X	X			
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Ovary	+	+	A	+	+	+	+	+	+	A	I	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Granulosa cell tumor, NOS																									
Hemangiosarcoma																									
Histiocytic sarcoma												X		X											
Lymphoma malignant histiocytic																									
Mixed tumor benign																									
Bilateral, carcinoma, metastatic, uterus																X									
Uterus	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																X									
Hemangiosarcoma				X																					
Leiomyoma																									
Endometrium, polyp																			X						

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	TOTAL:
CARCASS ID	2 6 6 1	2 6 7 1	2 6 8 1	2 6 9 1	2 7 1 1	2 7 2 1	2 7 4 1	2 7 5 1	2 7 6 1	2 7 7 1	2 7 8 1	2 7 9 1	2 8 0 1	2 8 1 1	2 8 3 1	2 8 5 1	2 8 6 1	2 8 7 1	2 9 2 1	2 9 3 1	2 9 5 1	2 9 6 1	2 9 7 1	2 9 8 1	2 9 9 1	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	48
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Lymphoma malignant histiocytic					X																					1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	41
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant lymphocytic												X														1
Lymphoma malignant mixed																							X			1
Lymphoma malignant undifferentiated cell type																								X		1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma							X																			4
Hepatocellular adenoma														X												2
Hepatocellular adenoma, multiple																										1
Histiocytic sarcoma																										2
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic							X					X														2
Lymphoma malignant mixed																										1
Mesentery				+	+	+	+	+	+	+		+			+							+	+	+		19
Carcinoma, metastatic, uterus																										1
Histiocytic sarcoma																										2
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic							X					X														3
Lymphoma malignant mixed																							X			2
Lymphoma malignant undifferentiated cell type																								X		1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic												X														1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																										1
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic												X														2
Lymphoma malignant mixed																							X			2
Lymphoma malignant undifferentiated cell type																								X		1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Papilloma squamous																		X		X						2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant lymphocytic												X														1
Tooth																										2
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										1
Lymphoma malignant histiocytic					X																					1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant mixed																							X			1
Adrenal gland, medulla	I	+	+	+	+	+		+	I	+	+	M	+	+	+	I	I	+	+	+	+	+	+	+	+	39
Lymphoma malignant mixed																							X			1
Islets, pancreatic	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Adenoma	X																									1
Lymphoma malignant histiocytic					X																	X				2
Parathyroid gland	M	M	+	M	M	M	M	M	M	M	M	+	+	+	+	M	M	M	M	+	+	M	M	M	+	19
Pituitary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	45
Pars distalis, adenoma				X	X			X	X		X										X				X	12
Pars distalis, carcinoma																										1
Pars intermedia, adenoma																X										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell, adenoma																										2
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	45
Granulosa cell tumor, NOS												X														1
Hemangiosarcoma																				X						1
Histiocytic sarcoma																										2
Lymphoma malignant histiocytic																						X				1
Mixed tumor benign			X																							1
Bilateral, carcinoma, metastatic, uterus																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma																										1
Hemangiosarcoma																										1
Leiomyoma								X																		1
Endometrium, polyp															X											2

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	050	055	060	068	073	076	080	084	088	089	092	092	093	095	097	099	100	104	106	106	106	106	106	106	106
CARCASS ID	28401	25611	25911	28911	29011	29111	27011	28811	28211	30011	26511	26011	26311	25811	27311	25511	25211	29411	25111	25311	25411	25711	26111	26211	26411
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	M	+	+	+	+	+	+	+	A	+	+	M	+	+	+	+	+	+	+	+	+	M	+	
Iliac, lymphoma malignant histiocytic																									
Iliac, lymphoma malignant lymphocytic																									
Inguinal, histiocytic sarcoma														X											
Mediastinal, histiocytic sarcoma														X			X								
Mediastinal, lymphoma malignant histiocytic																									
Mediastinal, lymphoma malignant lymphocytic																									
Mesenteric, histiocytic sarcoma														X			X								
Mesenteric, lymphoma malignant histiocytic																									
Mesenteric, lymphoma malignant lymphocytic																									
Renal, histiocytic sarcoma														X											
Renal, lymphoma malignant histiocytic																									
Renal, lymphoma malignant lymphocytic																									
Lymph node, bronchial	+	M	+	+	M	+	+	M	+	A	+	+	M	+	M	M	+	+	M	+	+	+	+	M	+
Histiocytic sarcoma												X		X			X								
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																					X				
Lymphoma malignant mixed																									X
Lymphoma malignant undifferentiated cell type																									
Lymph node, mandibular	M	M	+	+	+	M	+	+	+	A	+	M	M	+	+	+	+	+	+	M	+	+	+	M	+
Histiocytic sarcoma														X			X								
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic															X						X				
Lymphoma malignant mixed																									X
Lymphoma malignant undifferentiated cell type																									
Spleen	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma												X		X			X								
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																					X				
Lymphoma malignant mixed																									X
Lymphoma malignant undifferentiated cell type																									
Thymus	+	M	M	M	M	+	+	+	M	A	M	+	+	M	M	+	M	M	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant lymphocytic																									
INTEGUMENTARY SYSTEM																									
Mammary gland	M	+	+	M	+	+	M	+	+	M	+	+	M	+	M	M	M	+	+	+	+	+	+	+	+
Adenocarcinoma								X																	
Skin	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma														X											
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																+									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland								X																	
Lymphoma malignant histiocytic																									
Lymphoma malignant undifferentiated cell type																									

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	TOTAL:
CARCASS ID	2 6 6 1	2 6 7 1	2 6 8 1	2 6 9 1	2 7 1 1	2 7 2 1	2 7 4 1	2 7 5 1	2 7 6 1	2 7 7 1	2 7 8 1	2 7 9 1	2 8 0 1	2 8 1 1	2 8 3 1	2 8 5 1	2 8 6 1	2 8 7 1	2 9 2 1	2 9 3 1	2 9 5 1	2 9 6 1	2 9 7 1	2 9 8 1	2 9 9 1	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Iliac, lymphoma malignant histiocytic																X						X				2
Iliac, lymphoma malignant lymphocytic												X														1
Inguinal, histiocytic sarcoma																										1
Mediastinal, histiocytic sarcoma																										2
Mediastinal, lymphoma malignant histiocytic					X											X						X				3
Mediastinal, lymphoma malignant lymphocytic												X							X							2
Mesenteric, histiocytic sarcoma																										2
Mesenteric, lymphoma malignant histiocytic					X																	X				2
Mesenteric, lymphoma malignant lymphocytic							X																			1
Renal, histiocytic sarcoma																										1
Renal, lymphoma malignant histiocytic					X											X						X				3
Renal, lymphoma malig lymphocytic							X																			1
Lymph node, bronchial	+	+	M	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	M	+	M	+	+	36
Histiocytic sarcoma																										3
Lymphoma malignant histiocytic					X											X						X				3
Lymphoma malignant lymphocytic							X					X														3
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																								X		1
Lymph node, mandibular	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	40
Histiocytic sarcoma																										2
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic			X				X					X														5
Lymphoma malignant mixed																							X			2
Lymphoma malignant undifferentiated cell type																								X		1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										3
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic			X				X					X							X							5
Lymphoma malignant mixed		X																					X			3
Lymphoma malignant undifferentiated cell type																								X		1
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	M	+	35
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant lymphocytic												X														1
INTEGUMENTARY SYSTEM																										
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	39
Adenocarcinoma																										1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pituitary gland																										1
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant undifferentiated cell type																								X		1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	050	055	060	068	073	076	080	084	088	089	092	092	093	093	095	097	099	100	104	106	106	106	106	106	106	106	106
CARCASS ID	28401	25611	25911	28901	29011	29111	27011	28811	28211	30101	26511	26001	26331	25811	27311	25511	25211	29411	25111	25531	25541	25571	26111	26211	26411
RESPIRATORY SYSTEM																											
Larynx	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, multiple, harderian gland																										X	
Alveolar/bronchiolar adenoma																				X							
Alveolar/bronchiolar adenoma, multiple																											
Alveolar/bronchiolar carcinoma																											
Carcinoma, metastatic, uterus																X											
Histiocytic sarcoma											X		X				X										
Lymphoma malignant histiocytic																											
Lymphoma malignant lymphocytic																					X						
Lymphoma malignant mixed																											X
Lymphoma malignant undifferentiated cell type																											
Vein, mediastinum, hemangiosarcoma, metastatic, uterus				X																							
Nose	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																											
SPECIAL SENSES SYSTEM																											
Eye	A	+	A	A	+	A	+	+	A	+	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+
Harderian gland																										+	
Adenocarcinoma																										X	
URINARY SYSTEM																											
Kidney	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma												X															
Lymphoma malignant histiocytic																											
Lymphoma malignant lymphocytic																											
Lymphoma malignant mixed																											X
Lymphoma malignant undifferentiated cell type																											
Urinary bladder	+	+	+	+	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																											
Lymphoma malignant lymphocytic																											
Lymphoma malignant mixed																											X
Lymphoma malignant undifferentiated cell type																											

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 4 mg/m³ (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL.
CARCASS ID	26661	26671	26681	26691	27711	27721	27741	27751	27761	27771	27781	27791	28011	28111	28311	28511	28611	28711	29211	29311	29511	29611	29711	29811	29911	TISSUES TUMORS
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, multiple, harderian gland																										1
Alveolar/bronchiolar adenoma									X										X					X		4
Alveolar/bronchiolar adenoma, multiple																		X								1
Alveolar/bronchiolar carcinoma																									X	1
Carcinoma, metastatic, uterus																										1
Histiocytic sarcoma																										3
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic			X				X					X														4
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																								X		1
Vein, mediastinum, hemangiosarcoma, metastatic, uterus																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																								X		1
SPECIAL SENSES SYSTEM																										
Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Harderian gland																										1
Adenocarcinoma																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Histiocytic sarcoma																										1
Lymphoma malignant histiocytic					X																	X				2
Lymphoma malignant lymphocytic			X									X							X							3
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																								X		1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant histiocytic																X										1
Lymphoma malignant lymphocytic			X				X					X														3
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																								X		1

TABLE D3. ANALYSIS OF PRIMARY NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	2 mg/m^3	4 mg/m^3
Liver: Hepatocellular Adenoma			
Overall Rates (a)	4/50 (8%)	8/49 (16%)	3/49 (6%)
Adjusted Rates (b)	10.0%	25.0%	9.4%
Terminal Rates (c)	4/40 (10%)	6/28 (21%)	3/32 (9%)
Day of First Observation	735	403	735
Life Table Tests (d)	P=0.550	P=0.066	P=0.621N
Logistic Regression Tests (d)	P=0.490N	P=0.160	P=0.621N
Cochran-Armitage Trend Test (d)	P=0.447N		
Fisher Exact Test (d)		P=0.168	P=0.511N
Liver: Hepatocellular Carcinoma			
Overall Rates (a)	8/50 (16%)	5/49 (10%)	4/49 (8%)
Adjusted Rates (b)	18.3%	14.1%	9.7%
Terminal Rates (c)	5/40 (13%)	2/28 (7%)	1/32 (3%)
Day of First Observation	423	493	382
Life Table Tests (d)	P=0.234N	P=0.478N	P=0.280N
Logistic Regression Tests (d)	P=0.093N	P=0.246N	P=0.119N
Cochran-Armitage Trend Test (d)	P=0.143N		
Fisher Exact Test (d)		P=0.290N	P=0.188N
Liver: Hepatocellular Carcinoma or Hepatoblastoma			
Overall Rates (a)	8/50 (16%)	6/49 (12%)	4/49 (8%)
Adjusted Rates (b)	18.3%	16.1%	9.7%
Terminal Rates (c)	5/40 (13%)	2/28 (7%)	1/32 (3%)
Day of First Observation	423	493	382
Life Table Tests (d)	P=0.243N	P=0.592N	P=0.280N
Logistic Regression Tests (d)	P=0.091N	P=0.335N	P=0.119N
Cochran-Armitage Trend Test (d)	P=0.149N		
Fisher Exact Test (d)		P=0.403N	P=0.188N
Liver: Hepatocellular Adenoma, Hepatocellular Carcinoma, or Hepatoblastoma			
Overall Rates (a)	12/50 (24%)	14/49 (29%)	7/49 (14%)
Adjusted Rates (b)	27.7%	38.4%	18.4%
Terminal Rates (c)	9/40 (23%)	8/28 (29%)	4/32 (13%)
Day of First Observation	423	403	382
Life Table Tests (d)	P=0.303N	P=0.156	P=0.295N
Logistic Regression Tests (d)	P=0.119N	P=0.434	P=0.144N
Cochran-Armitage Trend Test (d)	P=0.151N		
Fisher Exact Test (d)		P=0.387	P=0.166N
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	4/50 (8%)	1/47 (2%)	5/49 (10%)
Adjusted Rates (b)	9.5%	3.7%	15.6%
Terminal Rates (c)	3/40 (8%)	1/27 (4%)	5/32 (16%)
Day of First Observation	590	735	735
Life Table Tests (d)	P=0.313	P=0.291N	P=0.371
Logistic Regression Tests (d)	P=0.347	P=0.208N	P=0.423
Cochran-Armitage Trend Test (d)	P=0.411		
Fisher Exact Test (d)		P=0.201N	P=0.487
Lung: Alveolar/Bronchiolar Carcinoma			
Overall Rates (a)	3/50 (6%)	1/47 (2%)	1/49 (2%)
Adjusted Rates (b)	6.9%	3.7%	3.1%
Terminal Rates (c)	1/40 (3%)	1/27 (4%)	1/32 (3%)
Day of First Observation	590	735	735
Life Table Tests (d)	P=0.270N	P=0.418N	P=0.376N
Logistic Regression Tests (d)	P=0.221N	P=0.323N	P=0.311N
Cochran-Armitage Trend Test (d)	P=0.209N		
Fisher Exact Test (d)		P=0.332N	P=0.316N

TABLE D3. ANALYSIS OF PRIMARY NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	6/50 (12%)	2/47 (4%)	6/49 (12%)
Adjusted Rates (b)	14.1%	7.4%	18.8%
Terminal Rates (c)	4/40 (10%)	2/27 (7%)	6/32 (19%)
Day of First Observation	590	735	735
Life Table Tests (d)	P=0.424	P=0.273N	P=0.468
Logistic Regression Tests (d)	P=0.464	P=0.183N	P=0.524
Cochran-Armitage Trend Test (d)	P=0.555		
Fisher Exact Test (d)		P=0.155N	P=0.606
Mammary Gland: Adenocarcinoma			
Overall Rates (e)	4/50 (8%)	1/50 (2%)	1/50 (2%)
Adjusted Rates (b)	10.0%	3.3%	2.3%
Terminal Rates (c)	4/40 (10%)	0/28 (0%)	0/32 (0%)
Day of First Observation	735	720	583
Life Table Tests (d)	P=0.154N	P=0.299N	P=0.245N
Logistic Regression Tests (d)	P=0.115N	P=0.269N	P=0.190N
Cochran-Armitage Trend Test (d)	P=0.101N		
Fisher Exact Test (d)		P=0.181N	P=0.181N
Mammary Gland: Fibroadenoma or Adenocarcinoma			
Overall Rates (e)	5/50 (10%)	1/50 (2%)	1/50 (2%)
Adjusted Rates (b)	12.5%	3.3%	2.3%
Terminal Rates (c)	5/40 (13%)	0/28 (0%)	0/32 (0%)
Day of First Observation	735	720	583
Life Table Tests (d)	P=0.086N	P=0.202N	P=0.156N
Logistic Regression Tests (d)	P=0.060N	P=0.177N	P=0.117N
Cochran-Armitage Trend Test (d)	P=0.049N		
Fisher Exact Test (d)		P=0.102N	P=0.102N
Pituitary Gland/Pars Distalis: Adenoma			
Overall Rates (a)	20/45 (44%)	15/43 (35%)	12/45 (27%)
Adjusted Rates (b)	52.4%	54.7%	35.6%
Terminal Rates (c)	18/36 (50%)	12/24 (50%)	9/30 (30%)
Day of First Observation	715	685	646
Life Table Tests (d)	P=0.178N	P=0.431	P=0.190N
Logistic Regression Tests (d)	P=0.113N	P=0.567	P=0.119N
Cochran-Armitage Trend Test (d)	P=0.049N		
Fisher Exact Test (d)		P=0.243N	P=0.061N
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma			
Overall Rates (a)	20/45 (44%)	15/43 (35%)	13/45 (29%)
Adjusted Rates (b)	52.4%	54.7%	37.1%
Terminal Rates (c)	18/36 (50%)	12/24 (50%)	9/30 (30%)
Day of First Observation	715	685	583
Life Table Tests (d)	P=0.244N	P=0.431	P=0.262N
Logistic Regression Tests (d)	P=0.151N	P=0.567	P=0.158N
Cochran-Armitage Trend Test (d)	P=0.077N		
Fisher Exact Test (d)		P=0.243N	P=0.095N
Uterus: Endometrial Polyp			
Overall Rates (e)	3/50 (6%)	2/49 (4%)	2/49 (4%)
Adjusted Rates (b)	7.5%	6.9%	6.3%
Terminal Rates (c)	3/40 (7%)	1/28 (4%)	2/32 (6%)
Day of First Observation	735	722	735
Life Table Tests (d)	P=0.509N	P=0.655N	P=0.602N
Logistic Regression Tests (d)	P=0.508N	P=0.632N	P=0.602N
Cochran-Armitage Trend Test (d)	P=0.415N		
Fisher Exact Test (d)		P=0.510N	P=0.510N

TABLE D3. ANALYSIS OF PRIMARY NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m³	4 mg/m³
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (e)	22/50 (44%)	19/50 (38%)	13/50 (26%)
Adjusted Rates (b)	48.6%	52.7%	39.2%
Terminal Rates (c)	17/40 (43%)	12/28 (43%)	12/32 (38%)
Day of First Observation	473	371	673
Life Table Tests (d)	P=0.191N	P=0.342	P=0.189N
Logistic Regression Tests (d)	P=0.069N	P=0.412N	P=0.091N
Cochran-Armitage Trend Test (d)	P=0.038N		
Fisher Exact Test (d)		P=0.342N	P=0.046N
All Sites: Histiocytic Sarcoma			
Overall Rates (e)	1/50 (2%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	2.5%	0.0%	8.0%
Terminal Rates (c)	1/40 (3%)	0/28 (0%)	0/32 (0%)
Day of First Observation	735		641
Life Table Tests (d)	P=0.144	P=0.571N	P=0.243
Logistic Regression Tests (d)	P=0.177	P=0.571N	P=0.317
Cochran-Armitage Trend Test (d)	P=0.176		
Fisher Exact Test (d)		P=0.500N	P=0.309

(a) Number of tumor-bearing animals/number of animals examined microscopically at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals surviving until study termination
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) Number of tumor-bearing animals/number of animals examined grossly at the site

TABLE D4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE

	Chamber Control	2 mg/m^3	4 mg/m^3
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Esophagus	(49)	(49)	(48)
Epithelium, hyperplasia, focal			1 (2%)
Gallbladder	(45)	(33)	(39)
Inflammation, suppurative		2 (6%)	
Intestine large, cecum	(49)	(41)	(42)
Hyperplasia, lymphoid	1 (2%)		
Ulcer, multifocal			1 (2%)
Intestine small, duodenum	(48)	(43)	(41)
Ulcer			1 (2%)
Intestine small, ileum	(50)	(45)	(43)
Amyloid deposition	3 (6%)		1 (2%)
Peyer's patch, hyperplasia, lymphoid	1 (2%)		
Liver	(50)	(49)	(49)
Cyst			1 (2%)
Cytomegaly			1 (2%)
Inflammation, chronic, multifocal	2 (4%)	3 (6%)	1 (2%)
Inflammation, suppurative		1 (2%)	
Necrosis		1 (2%)	
Hepatocyte, vacuolization cytoplasmic, focal	1 (2%)		1 (2%)
Serosa, inflammation, suppurative		1 (2%)	
Vein, thrombus			1 (2%)
Mesentery	(16)	(13)	(19)
Hyperplasia, lymphoid	1 (6%)		2 (11%)
Inflammation, chronic	2 (13%)	1 (8%)	2 (11%)
Inflammation, suppurative		2 (15%)	
Fat, necrosis		1 (8%)	
Vein, thrombus		1 (8%)	
Pancreas	(50)	(48)	(48)
Amyloid deposition, focal			1 (2%)
Atrophy	2 (4%)	2 (4%)	2 (4%)
Cyst	1 (2%)	1 (2%)	
Degeneration, focal	1 (2%)		
Fibrosis, focal		1 (2%)	
Hyperplasia, lymphoid			1 (2%)
Inflammation, chronic		1 (2%)	
Inflammation, suppurative		1 (2%)	
Necrosis, coagulative		1 (2%)	
Salivary glands	(50)	(50)	(48)
Hyperplasia, lymphoid	1 (2%)		
Inflammation, chronic, multifocal		2 (4%)	
Duct, hyperplasia		1 (2%)	
Stomach, forestomach	(49)	(48)	(48)
Developmental malformation	1 (2%)		
Hyperkeratosis			1 (2%)
Hyperplasia, squamous	2 (4%)		6 (13%)
Inflammation, chronic		1 (2%)	
Stomach, glandular	(50)	(47)	(48)
Atrophy	1 (2%)		
Cyst	1 (2%)		
Tooth			(2)
Dysplasia			1 (50%)
CARDIOVASCULAR SYSTEM			
Blood vessel	(50)	(49)	(49)
Aorta, inflammation, chronic	1 (2%)		

TABLE D4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
CARDIOVASCULAR SYSTEM (Continued)			
Heart	(50)	(50)	(49)
Amyloid deposition, multifocal			1 (2%)
Atrium, inflammation, suppurative		1 (2%)	
Atrium, thrombus		2 (4%)	
Myocardium, fibrosis		1 (2%)	
ENDOCRINE SYSTEM			
Adrenal gland	(50)	(46)	(48)
Subcapsular, hyperplasia	49 (98%)	42 (91%)	46 (96%)
Adrenal gland, cortex	(46)	(44)	(46)
Amyloid deposition			1 (2%)
Cyst			2 (4%)
Degeneration	41 (89%)	39 (89%)	37 (80%)
Fibrosis	37 (80%)	23 (52%)	36 (78%)
Focal cellular change		1 (2%)	
Adrenal gland, medulla	(44)	(38)	(39)
Amyloid deposition			1 (3%)
Degeneration	1 (2%)		
Hyperplasia	1 (2%)		
Hyperplasia, focal	1 (2%)		
Pituitary gland	(45)	(43)	(45)
Pars distalis, cyst			1 (2%)
Pars distalis, hyperplasia	11 (24%)	10 (23%)	13 (29%)
Thyroid gland	(49)	(46)	(49)
Inflammation, chronic			1 (2%)
C-cell, hyperplasia	3 (6%)	1 (2%)	
Follicle, cyst		2 (4%)	1 (2%)
Follicular cell, hyperplasia	8 (16%)	6 (13%)	11 (22%)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Ovary	(50)	(44)	(45)
Abscess		1 (2%)	1 (2%)
Cyst	22 (44%)	15 (34%)	14 (31%)
Inflammation, chronic		5 (11%)	2 (4%)
Inflammation, suppurative		1 (2%)	
Uterus	(50)	(49)	(49)
Congestion	1 (2%)		
Inflammation, necrotizing	1 (2%)	2 (4%)	3 (6%)
Endometrium, hyperplasia, cystic	35 (70%)	35 (71%)	28 (57%)
Endometrium, metaplasia, squamous			2 (4%)
Lumen, dilatation	1 (2%)		2 (4%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(50)	(48)	(49)
Sternal, hyperplasia			1 (2%)
Sternal, myelofibrosis	21 (42%)	19 (40%)	18 (37%)
Lymph node	(50)	(48)	(46)
Mediastinal, hyperplasia, lymphoid	1 (2%)		
Mediastinal, inflammation, chronic			1 (2%)
Mesenteric, abscess		1 (2%)	
Mesenteric, hyperplasia, lymphoid			1 (2%)

TABLE D4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
HEMATOPOIETIC SYSTEM (Continued)			
Lymph node, bronchial	(26)	(38)	(36)
Amyloid deposition			1 (3%)
Hemorrhage, acute		1 (3%)	
Hyperplasia, lymphoid	3 (12%)	1 (3%)	1 (3%)
Inflammation, chronic			1 (3%)
Lymph node, mandibular	(45)	(41)	(40)
Hemorrhage, acute	1 (2%)	1 (2%)	
Hyperplasia, lymphoid	5 (11%)	5 (12%)	4 (10%)
Spleen	(50)	(48)	(49)
Amyloid deposition			1 (2%)
Atrophy		1 (2%)	
Congestion			1 (2%)
Hematopoietic cell proliferation	4 (8%)	8 (17%)	3 (6%)
Hyperplasia, lymphoid	3 (6%)	6 (13%)	6 (12%)
Necrosis	1 (2%)		
Pigmentation, hemosiderin		2 (4%)	
Capsule, inflammation, chronic		1 (2%)	
Capsule, inflammation, suppurative	1 (2%)		
Thymus	(42)	(37)	(35)
Amyloid deposition			1 (3%)
Inflammation, chronic, diffuse			1 (3%)
INTEGUMENTARY SYSTEM			
Mammary gland	(39)	(37)	(39)
Inflammation, chronic		1 (3%)	
Duct, dilatation	1 (3%)		
Skin	(50)	(50)	(48)
Ulcer	1 (2%)		1 (2%)
Hair follicle, atrophy	5 (10%)	8 (16%)	7 (15%)
Subcutaneous tissue, inflammation, subacute	1 (2%)		
MUSCULOSKELETAL SYSTEM			
Bone	(50)	(48)	(50)
Cranium, developmental malformation	1 (2%)		
Skeletal muscle		(1)	(1)
Inflammation, suppurative, focal			1 (100%)
NERVOUS SYSTEM			
Brain	(50)	(49)	(50)
Hemorrhage, acute, multifocal			1 (2%)
Hyperplasia, lymphoid	1 (2%)		1 (2%)
Inflammation, chronic, focal		1 (2%)	
Hypothalamus, atrophy	4 (8%)	1 (2%)	2 (4%)
Thalamus, atrophy		1 (2%)	
Thalamus, mineralization	5 (10%)	12 (24%)	10 (20%)
Ventricle, dilatation	1 (2%)		
RESPIRATORY SYSTEM			
Larynx	(50)	(47)	(49)
Epithelium, erosion	1 (2%)		
Epithelium, hyperplasia	1 (2%)		

TABLE D4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF 2-CHLOROACETOPHENONE (Continued)

	Chamber Control	2 mg/m^3	4 mg/m^3
RESPIRATORY SYSTEM (Continued)			
Lung	(50)	(47)	(49)
Hemorrhage			1 (2%)
Hyperplasia, lymphoid	1 (2%)		3 (6%)
Inflammation, chronic		2 (4%)	
Inflammation, chronic, multifocal	26 (52%)	19 (40%)	18 (37%)
Inflammation, suppurative, multifocal		1 (2%)	
Leukocytosis	1 (2%)		2 (4%)
Alveolar epithelium, hyperplasia		2 (4%)	4 (8%)
Alveolus, amyloid deposition, multifocal			1 (2%)
Alveolus, infiltration cellular, histiocytic	1 (2%)	2 (4%)	
Nose	(50)	(48)	(49)
Mucosa, inflammation, suppurative	2 (4%)	1 (2%)	3 (6%)
Olfactory epithelium, cytoplasmic alteration			1 (2%)
Respiratory epithelium, hyperplasia			2 (4%)
Respiratory epithelium, metaplasia, squamous			4 (8%)
Trachea	(49)	(46)	(49)
Glands, cyst			1 (2%)
Peritracheal tissue, inflammation, suppurative		1 (2%)	
SPECIAL SENSES SYSTEM			
Eye	(47)		(42)
Sclera, inflammation, chronic, focal			1 (2%)
Harderian gland	(1)	(1)	(1)
Hyperplasia	1 (100%)		
URINARY SYSTEM			
Kidney	(50)	(50)	(48)
Amyloid deposition		1 (2%)	2 (4%)
Cyst, multiple		1 (2%)	
Hyperplasia, lymphoid	2 (4%)		1 (2%)
Infiltration cellular, lymphocytic	2 (4%)		1 (2%)
Inflammation, chronic	4 (8%)	11 (22%)	2 (4%)
Nephropathy	1 (2%)	3 (6%)	5 (10%)
Renal tubule, crystals			1 (2%)
Renal tubule, cytomegaly			1 (2%)
Renal tubule, dilatation		2 (4%)	1 (2%)
Urinary bladder	(50)	(47)	(48)
Hyperplasia, lymphoid	1 (2%)		1 (2%)
Inflammation, chronic	7 (14%)	13 (28%)	

APPENDIX E

SENTINEL ANIMAL PROGRAM

APPENDIX E. SENTINEL ANIMAL PROGRAM

Methods

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

Fifteen B6C3F$_1$ mice and 15 F344/N rats of each sex were selected at the time of randomization and allocation of the animals to the various study groups. Five animals of each designated sentinel group were killed at 6, 12, and 18 months on study. In these studies, sera from 5 moribund study mice were collected at 22 and 23 months and from 10 moribund study rats at 22 months. 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) **Immunofluorescence Assay** EDIM (epizootic diarrhea of infant mice) (24 mo)	MHV (mouse hepatitis virus) GDVII (22,23,24 mo) PVM (24 mo) Sendai (24 mo) Reo 3 (24 mo) Ectro (24 mo) M. Ad. (24 mo) *M. pul. (Mycoplasma pulmonis)* (24 mo) *M. arth. (Mycoplasma arthritidis)* (24 mo)
		Complement Fixation	
Rats	PVM KRV (Kilham rat virus) H-1 (Toolan's H-1 virus) Sendai	RCV (rat coronavirus)	RCV/SDA sialodacryoadenitis virus (12,18,22, 24 mo) PVM (24 mo) Sendai (24 mo) *M. pul.* (24 mo) *M. arth.* (24 mo)

Results

Results are presented in Table E1.

TABLE E1. MURINE ANTIBODY DETERMINATIONS FOR RATS AND MICE IN THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE (a)

Interval (months)	Number of Animals	Positive Serologic Reaction for
RATS		
6	1/10	PVM
	7/10	RCV
12	9/9	RCV/SDA
18	8/10	RCV/SDA
(b) 22	2/10	PVM
	9/10	RCV/SDA
24	8/10	RCV/SDA
	2/10	*M. arth.*
MICE		
6	1/10	Sendai (c)
12	0/10	None positive
18	0/10	None positive
(b) 22	0/3	None positive
(b) 23	0/2	None positive
24	0/10	None positive

(a) Blood samples were taken from sentinel animals at 6, 12, and 18 months after the start of dosing and from the control animals just before they were killed; samples were sent to Microbiological Associates, Inc. (Bethesda, MD) for determination of antibody titers.
(b) Blood samples were taken from moribund animals at 22 and 23 months.
(c) Since samples from mice after 6 months and all samples from rats were negative for this viral infection, the one sample that was positive at 6 months was considered to be a false positive.

APPENDIX F

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

Pellet Diet: June 1982 to June 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)	23.19 ± 1.21	21.3-26.3	18
Crude fat (percent by weight)	5.24 ± 0.39	4.4-5.7	18
Crude fiber (percent by weight)	3.42 ± 0.60	2.8-5.6	18
Ash (percent by weight)	6.51 ± 0.36	5.7-7.2	18
Amino Acids (percent of total diet)			
Arginine	1.320 ± 0.072	1.310-1.390	5
Cystine	0.319 ± 0.088	0.218-0.400	5
Glycine	1.146 ± 0.063	1.060-1.210	5
Histidine	0.571 ± 0.026	0.531-0.603	5
Isoleucine	0.914 ± 0.030	0.881-0.944	5
Leucine	1.946 ± 0.056	1.850-1.990	5
Lysine	1.280 ± 0.067	1.200-1.370	5
Methionine	0.436 ± 0.165	0.306-0.699	5
Phenylalanine	0.938 ± 0.158	0.665-1.050	5
Threonine	0.855 ± 0.035	0.824-0.898	5
Tryptophan	0.277 ± 0.221	0.156-0.671	5
Tyrosine	0.618 ± 0.086	0.564-0.769	5
Valine	1.108 ± 0.043	1.050-1.170	5
Essential Fatty Acids (percent of total diet)			
Linoleic	2.290 ± 0.313	1.830-2.520	5
Linolenic	0.258 ± 0.040	0.210-0.308	5
Vitamins			
Vitamin A (IU/kg)	12,706 ± 3,788	8,800-24,000	18
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)	17.72 ± 3.32	13.0-24.0	18
Riboflavin (ppm)	7.6 ± 0.85	6.10-8.20	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	5.60-8.80	5
Folic acid (ppm)	2.62 ± 0.89	1.80-3.70	5
Biotin (ppm)	0.254 ± 0.053	0.19-0.32	5
Vitamin B_{12} (ppb)	24.21 ± 12.66	10.6-38.0	5
Choline (ppm)	3,122 ± 416.8	2,400-3,430	5
Minerals			
Calcium (percent)	1.27 ± 0.12	1.11-1.54	18
Phosphorus (percent)	0.96 ± 0.05	0.90 -1.10	18
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	81.70-99.40	5
Zinc (ppm)	52.78 ± 4.94	46.10-58.20	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)	0.50 ± 0.14	0.17-0.72	18
Cadmium (ppm) (a)	<0.10		18
Lead (ppm)	0.89 ± 0.74	0.33-3.37	18
Mercury (ppm) (a)	<0.05		18
Selenium (ppm)	0.31 ± 0.07	0.13-0.42	18
Aflatoxins (ppb) (a)	<5.0		18
Nitrate nitrogen (ppm) (b)	7.98 ± 3.78	0.10-15.0	18
Nitrite nitrogen (ppm) (b)	1.60 ± 1.85	0.10-7.20	18
BHA (ppm) (c)	4.89 ± 5.43	2.00-17.0	18
BHT (ppm) (c)	3.11 ± 2.91	1.00-12.0	18
Aerobic plate count (CFU/g) (d)	41,500 ± 33,838	6,600-130,000	18
Coliform (MPN/g) (e,f)	12.47 ± 15.27	<3.0-43.0	17
Coliform (MPN/g) (g)	37.33 ± 107	<3.00-460.0	18
E. coli (MPN/g)	<3.00		18
Total nitrosamines (ppb) (h)	6.09 ± 6.75	1.80-30.90	18
N-Nitrosodimethylamine (ppb) (h)	5.03 ± 6.76	0.80-30.00	18
N-Nitrosopyrrolidine (ppb) (h)	1.07 ± 0.28	0.81-1.70	18
Pesticides (ppm)			
α-BHC (a,i)	<0.01		18
β-BHC (a)	<0.02		18
γ-BHC (a)	<0.01		18
δ-BHC (a)	<0.01		18
Heptachlor (a)	<0.01		18
Aldrin (a)	<0.01		18
Heptachlor epoxide (a)	<0.01		18
DDE (a)	<0.01		18
DDD (a)	<0.01		18
DDT (a)	<0.01		18
HCB (a)	<0.01		18
Mirex (a)	<0.01		18
Methoxychlor (a)	<0.05		18
Dieldrin (a)	<0.01		18
Endrin (a)	<0.01		18
Telodrin (a)	<0.01		18
Chlordane (a)	<0.05		18
Toxaphene (a)	<0.1		18
Estimated PCBs (a)	<0.2		18
Ronnel (a)	<0.01		18
Ethion (a)	<0.02		18
Trithion (a)	<0.05		18
Diazinon (a)	<0.1		18
Methyl parathion (a)	<0.02		18
Ethyl parathion (a)	<0.02		18
Malathion (j)	0.09 ± 0.06	0.05-0.25	18
Endosulfan I (a)	<0.01		18
Endosulfan II (a)	<0.01		18
Endosulfan sulfate (a)	<0.03		18

(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) Excludes one high value of 460 MPN/g obtained for the lot milled on September 23, 1982
(g) Includes high value noted in (f)
(h) All values were corrected for percent recovery.
(i) BHC = hexachlorocyclohexane or benzene hexachloride
(j) Eleven lots contained more than 0.05 ppm.

APPENDIX G

RESULTS OF HEMATOLOGIC ANALYSES IN THE FIFTEEN-MONTH STUDIES OF 2-CHLOROACETOPHENONE

TABLE G1. HEMATOLOGIC DATA FOR RATS IN THE FIFTEEN-MONTH INHALATION STUDIES OF 2-CHLOROACETOPHENONE (a)

Analysis	Control	1 mg/m^3	2 mg/m^3
MALE			
Erythrocytes (10^6/mm^3)	7.92 ± 0.220	8.01 ± 0.073	7.90 ± 0.155
Hemoglobin (g/dl)	16.1 ± 0.35	16.2 ± 0.14	16.0 ± 0.31
Hematocrit (ml/dl)	38.7 ± 0.74	38.9 ± 0.41	38.7 ± 0.69
Mean cell volume (μ^3)	49.4 ± 0.75	48.8 ± 0.29	49.3 ± 0.42
Mean corpuscular hemoglobin (pg)	20.3 ± 0.29	20.2 ± 0.13	20.2 ± 0.11
Mean corpuscular hemoglobin concentration (percent)	41.5 ± 0.22	41.6 ± 0.15	41.2 ± 0.19
Nucleated erythrocytes (10^3/mm^3)	0.01 ± 0.009	0.02 ± 0.006	*0.03 ± 0.007
Leukocytes (10^3/mm^3)	4.4 ± 0.32	4.6 ± 0.19	4.8 ± 0.32
Segmented neutrophils (10^3/mm^3)	2.1 ± 0.24	2.0 ± 0.21	1.8 ± 0.18
Lymphocytes (10^3/mm^3)	2.2 ± 0.12	2.3 ± 0.12	*2.8 ± 0.18
Monocytes (10^3/mm^3)	0.07 ± 0.016	0.09 ± 0.014	0.12 ± 0.022
Eosinophils (10^3/mm^3)	0.06 ± 0.015	0.08 ± 0.012	0.08 ± 0.009
FEMALE			
Erythrocytes (10^6/mm^3)	7.14 ± 0.279	7.25 ± 0.217	7.29 ± 0.275
Hemoglobin (g/dl)	15.8 ± 0.57	16.1 ± 0.42	15.9 ± 0.53
Hematocrit (ml/dl)	38.6 ± 1.28	39.1 ± 1.03	39.5 ± 1.28
Mean cell volume (μ^3)	54.3 ± 0.47	54.3 ± 0.58	54.6 ± 0.76
Mean corpuscular hemoglobin (pg)	22.1 ± 0.12	22.2 ± 0.24	*21.8 ± 0.29
Mean corpuscular hemoglobin concentration (percent)	40.9 ± 0.32	41.2 ± 0.15	40.3 ± 0.21
Nucleated erythrocytes (10^3/mm^3)	0.03 ± 0.007	0.05 ± 0.021	0.02 ± 0.005
Leukocytes (10^3/mm^3)	2.6 ± 0.18	*4.4 ± 1.20	2.7 ± 0.14
Segmented neutrophils (10^3/mm^3)	0.9 ± 0.10	1.2 ± 0.14	1.0 ± 0.09
Lymphocytes (10^3/mm^3)	1.5 ± 0.10	*3.0 ± 1.14	1.6 ± 0.07
Monocytes (10^3/mm^3)	0.05 ± 0.009	0.10 ± 0.031	0.05 ± 0.008
Eosinophils (10^3/mm^3)	0.04 ± 0.008	0.06 ± 0.011	0.06 ± 0.014

(a) Mean ± standard error for groups of 10 animals; P values vs. the controls by Dunn's test (Dunn, 1964) or Shirley's test (Shirley, 1977).
*P<0.05

TABLE G2. HEMATOLOGIC DATA FOR MICE IN THE FIFTEEN-MONTH INHALATION STUDIES OF 2-CHLOROACETOPHENONE (a)

Analysis	Control	2 mg/m^3	4 mg/m^3
MALE			
Number examined	10	9	10
Erythrocytes (10^6/mm^3)	9.28 ± 0.293	8.95 ± 0.116	9.50 ± 0.309
Hemoglobin (g/dl)	15.8 ± 0.35	15.3 ± 0.18	15.9 ± 0.35
Hematocrit (ml/dl)	42.8 ± 1.07	41.4 ± 0.33	44.4 ± 1.06
Mean cell volume (μ^3)	47.4 ± 0.27	47.1 ± 0.54	47.9 ± 0.31
Mean corpuscular hemoglobin (pg)	17.2 ± 0.12	17.1 ± 0.07	*16.9 ± 0.08
Mean corpuscular hemoglobin concentration (percent)	36.8 ± 0.22	36.9 ± 0.33	**35.8 ± 0.24
Nucleated erythrocytes (10^3/mm^3)	0.02 ± 0.009	0.000 ± 0.000	*0.000 ± 0.000
Leukocytes (10^3/mm^3)	6.8 ± 0.49	7.1 ± 0.29	*8.8 ± 0.53
Segmented neutrophils (10^3/mm^3)	1.9 ± 0.17	1.7 ± 0.26	2.0 ± 0.28
Lymphocytes (10^3/mm^3)	4.7 ± 0.44	5.2 ± 0.25	**6.5 ± 0.41
Monocytes (10^3/mm^3)	0.14 ± 0.025	0.09 ± 0.027	0.09 ± 0.013
Eosinophils (10^3/mm^3)	0.05 ± 0.013	0.08 ± 0.019	**0.21 ± 0.036
FEMALE			
Number examined	9	10	9
Erythrocytes (10^6/mm^3)	9.04 ± 0.094	8.57 ± 0.265	9.27 ± 0.375
Hemoglobin (g/dl)	15.9 ± 0.15	*14.9 ± 0.42	15.7 ± 0.43
Hematocrit (ml/dl)	42.0 ± 0.46	41.0 ± 1.02	43.6 ± 1.14
Mean cell volume (μ^3)	47.0 ± 0.17	**48.7 ± 0.50	**48.2 ± 0.28
Mean corpuscular hemoglobin (pg)	17.6 ± 0.11	17.4 ± 0.11	**17.1 ± 0.08
Mean corpuscular hemoglobin concentration (percent)	37.8 ± 0.26	**36.2 ± 0.23	**35.9 ± 0.24
Nucleated erythrocytes (10^3/mm^3)	0.000 ± 0.000	0.000 ± 0.000	0.006 ± 0.006
Leukocytes (10^3/mm^3)	7.6 ± 1.17	7.0 ± 1.30	6.4 ± 0.60
Segmented neutrophils (10^3/mm^3)	2.9 ± 0.75	2.2 ± 0.49	1.7 ± 0.26
Lymphocytes (10^3/mm^3)	4.5 ± 0.84	4.5 ± 0.80	4.5 ± 0.38
Monocytes (10^3/mm^3)	0.17 ± 0.046	0.16 ± 0.061	0.10 ± 0.023
Eosinophils (10^3/mm^3)	0.08 ± 0.027	0.09 ± 0.040	0.14 ± 0.030

(a) Mean ± standard error; P values vs. the controls by Dunn's test (Dunn, 1964) or Shirley's test (Shirley, 1977).
*P<0.05
**P<0.01

APPENDIX H

CHEMICAL CHARACTERIZATION, GENERATION, AND MONITORING OF CHAMBER CONCENTRATIONS OF 2-CHLOROACETOPHENONE FOR THE TOXICOLOGY STUDIES

APPENDIX H. CHEMICAL CHARACTERIZATION

Procurement and Characterization of 2-Chloroacetophenone

2-Chloroacetophenone formulated with the antiagglomerant magnesium oxide was obtained in one lot (lot no. APG-30-MD) from the U.S. Army (Aberdeen Proving Ground, Aberdeen, MD) as a cream-colored, microcrystalline powder that melted at 54.9°-56.1° C. Purity and identity analyses were conducted on representative samples at Midwest Research Institute (MRI) (Kansas City, MO). MRI reports on the analyses performed in support of the 2-chloroacetophenone studies are on file at the National Institute of Environmental Health Sciences.

The study chemical was identified as 2-chloroacetophenone by spectroscopic analyses. The infrared (Figure H1), ultraviolet/visible, and nuclear magnetic resonance (Figure H2) spectra were consistent with those expected for the structure and with the literature spectra (Sadtler Standard Spectra).

The 2-chloroacetophenone content of the formulation was determined by elemental analysis, Karl Fischer water analysis, thin-layer chromatography, and gas chromatography and by gravimetric analysis to quantitate the amount of insoluble material present. Thin-layer chromatography was performed on silica gel plates (precoated to a thickness of 0.25 mm) with two solvent systems: 100% toluene (system 1) and hexanes:dioxane (88:12) (system 2). Visualization was at 254 nm and with a 2,4-dinitrophenylhydrazine in hydrochloric acid-ethanol spray. Gas chromatographic analysis was performed with flame ionization detection and nitrogen as the carrier at a flow rate of 70 ml/minute and with either a 3% Dexsil 400 column (system 1) or a 3% OV-17 column (system 2).

The results of elemental analysis were lower than theoretical values for carbon, chlorine, and hydrogen, as expected because of the presence of magnesium oxide. Karl Fischer analysis indicated the presence of 2.2% water. Both thin-layer chromatographic systems detected three trace impurities, one at the origin. Gas chromatographic system 1 detected 11 impurities, 2 before and 9 after the major peak. Two impurities after the major peak had relative areas of 0.77% and 0.53%; the remaining nine impurities had a combined relative area of 0.44%. Gas chromatographic system 2 indicated 10 impurities, 1 before and 9 after the major peak. Two unresolved impurity peaks after the major peak had a relative area of 0.78%. Another impurity after the major peak had an area 0.37% of the major peak area. The remaining seven impurities had a combined relative area of 0.2%.

Material insoluble in methylene chloride and acetone represented 11.2% of the sample by weight. Analysis by X-ray diffraction, X-ray emission spectroscopy, and spark source mass spectroscopy indicated that magnesium oxide was the main component of the material, with traces of silicon dioxide and iron.

Stability studies performed by gas chromatography with the same column as previously described for system 1 indicated a 4% reduction in 2-chloroacetophenone content after storage in the dark for 2 weeks at 60° C but no change occurred at 5° or 25° C.

2-Chloroacetophenone was initially stored at room temperature in metal pails. Beginning in August 1981, the chemical was stored in a freezer at about −20° C. Approximately once per month, portions of the chemical were transferred to a hood and held at room temperature until needed for vapor generation. Periodic analysis of 2-chloroacetophenone by gas chromatography and infrared spectroscopy indicated no notable degradation of the study material throughout the studies.

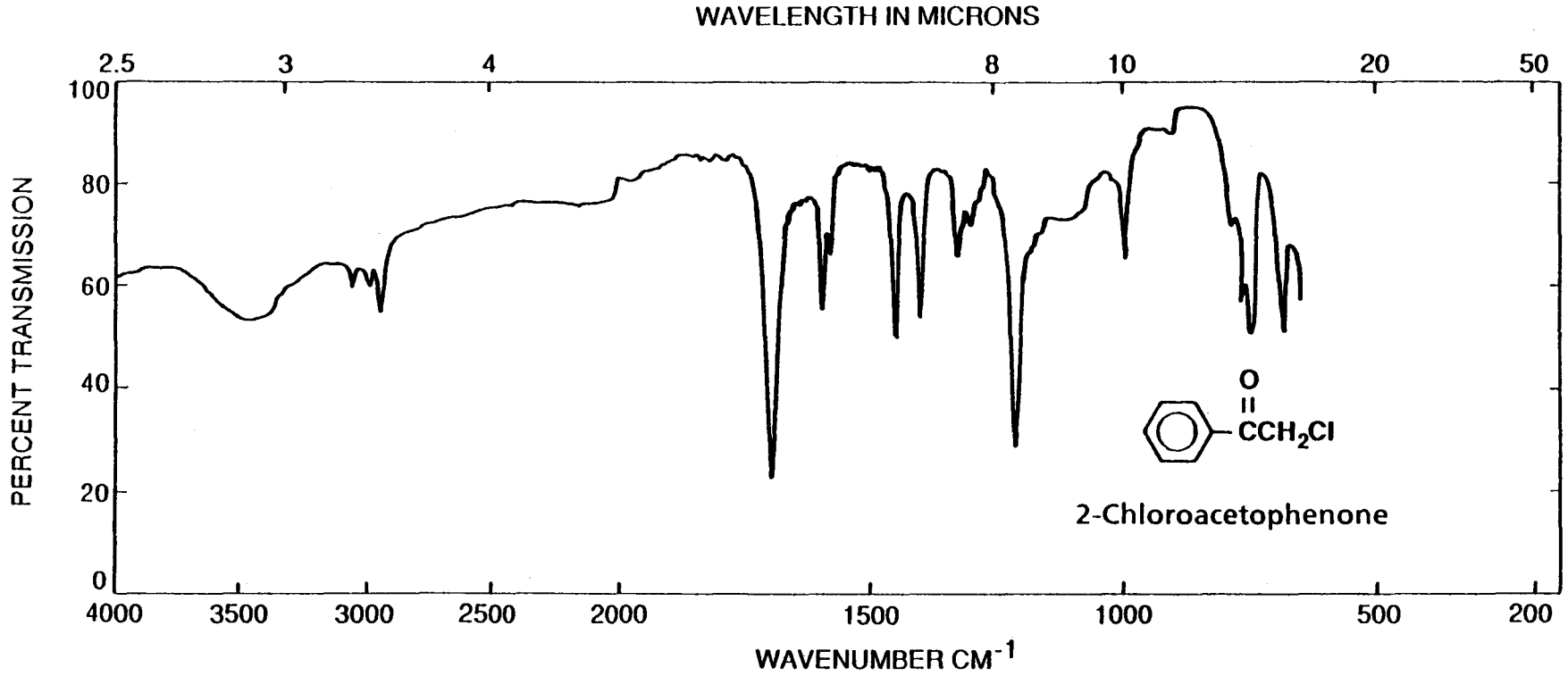

FIGURE H1. INFRARED ABSORPTION SPECTRUM OF 2-CHLOROACETOPHENONE (LOT NO. APG-30-MD)

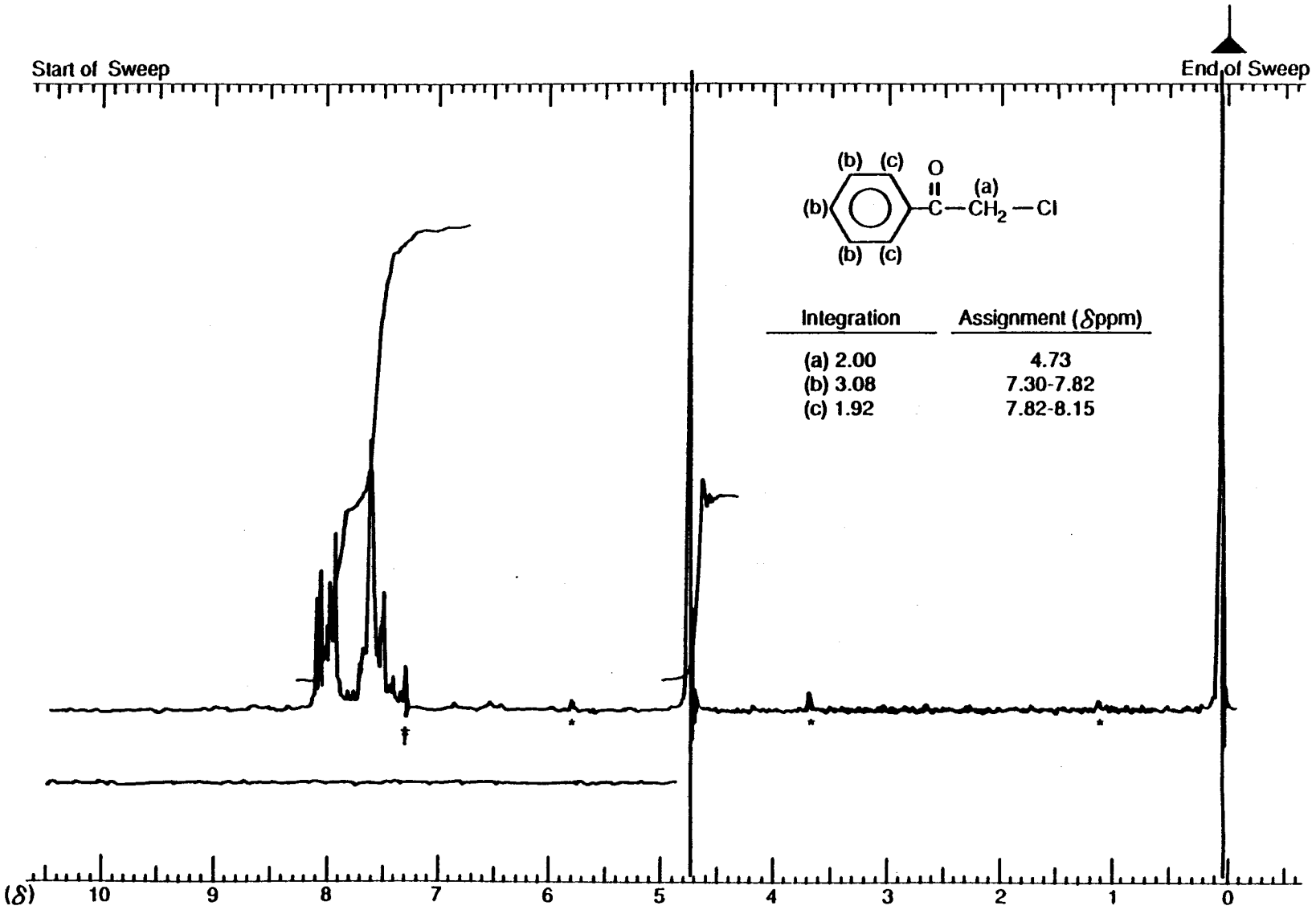

FIGURE H2. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF 2-CHLOROACETOPHENONE (LOT NO. APG-30-MD)

Generation and Measurement of Chamber Concentrations

Generation System: A single generator produced 2-chloroacetophenone vapor, which was carried by a distribution duct to each chamber (Hazleton 2000®, Lab Products, Inc.), except for the control chambers. 2-Chloroacetophenone was heated to the liquid state in the generator. Preheated nitrogen was then bubbled through the molten liquid at a controlled rate (Table H1). The concentration of 2-chloroacetophenone in the chambers was controlled by adjusting the pumping rate from the distribution line, by controlling the chamber air flow, or by changing the nitrogen flow through the generator. For the 14-day studies, the generator was charged only once; for the 13-week and 2-year studies, the generators were periodically disassembled, cleaned, and reloaded to prevent clogging. The generation and distribution system was modified several times to improve stability of 2-chloroacetophenone output, to reduce 2-chloroacetophenone condensation in the distribution duct, and to minimize 2-chloroacetophenone degradation. During the 2-year studies, two identical generators were attached to the same distribution duct to allow for cleaning and reloading. Figure H3 shows the generation system for the 2-year studies.

Concentration Monitoring: An HNU Systems Inc. Model PI201 Photoionization Detector (PID) monitored 2-chloroacetophenone concentrations throughout the 14-day studies. The PID was calibrated by pulling grab samples from chambers operating at stable concentrations into a chloroform-filled bubbler and analyzing the bubbler samples on an analytical gas chromatograph. During the 13-week studies, grab samples were collected in a bubbler and analyzed with an HP 5840 gas chromatograph with a 3% phenyl/cyanopropyl column and electron-capture detector. During the 2-year studies, a similar system was used, except that an automated multiplexed eight-port stream-select valve sampled multiple positions, automatically cycling through all eight ports about once every 30 minutes (Figure H4). Samples of the atmosphere in each chamber were continuously drawn by vacuum through heated polytetrafluoroethylene sample lines at a rate of 1.5 liters/minute to a point near the input of the eight-port stream-select valve. The constant flow assured fresh sample at the input to the valve. The sample lines were maintained at 75° ± 5° F. The calibration of the monitor was confirmed at least twice per month by the analysis of grab samples from each exposure chamber. Generally, duplicate grab samples were obtained from each chamber using bubblers filled with isooctane and a calibrated pump. The bubbler contents were then analyzed on an off-line calibrated gas chromatograph. An off-line standard (tetrachlorobenzene vapor from a diffusion tube) was introduced in February 1984 to check for day-to-day variations. Weekly mean exposure concentrations for the 2-year studies are presented in Figures H5 through H8. A summary of the chamber concentrations is presented in Table H2; Table H3 summarizes the distribution of mean daily concentrations.

TABLE H1. VAPOR GENERATION SYSTEM IN THE INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Fourteen-Day Studies	Thirteen-Week Studies	Fifteen-Month and Two-Year Studies
2-Chloroacetophenone was melted in a water bath at 80° C and poured into a glass jar enclosed in an aluminum cannister and attached to the vapor generator. Chemical was maintained at 105° ± 3° C throughout the entire exposure period. Preheated nitrogen was bubbled through a glass frit into the molten chemical. Nitrogen/2-chloroacetophenone vapor was conducted through heated steel tubes and then cooled and diluted by chamber dilution air	Powdered 2-chloroacetophenone was placed in a glass jar and enclosed in an aluminum cannister that was then attached to the vapor generator. The chemical was melted and kept at 100° ± 10° C by a mantle heater. Preheated nitrogen was bubbled through a glass frit for the highest concentration or above the molten compound for the other chambers. The nitrogen/chemical vapor was carried to the chambers through heated tubes. During nonexposure periods, the temperature was reduced to 80° C and the system was continuously purged with nitrogen	Powdered 2-chloroacetophenone was added to a 250-ml glass bubbler and then kept at 59°-62° C in a water bath. Preheated nitrogen was bubbled through a glass frit into the chemical. Nitrogen/2-chloroacetophenone vapor was diluted by nitrogen at 80° C, cooled, and diluted after leaving the bubbler by distribution with duct air. A small flow of nitrogen was maintained through the reservoir during nonexposure periods. Study material was heated for 1 wk accompanied by nitrogen purging before being used in the generating system

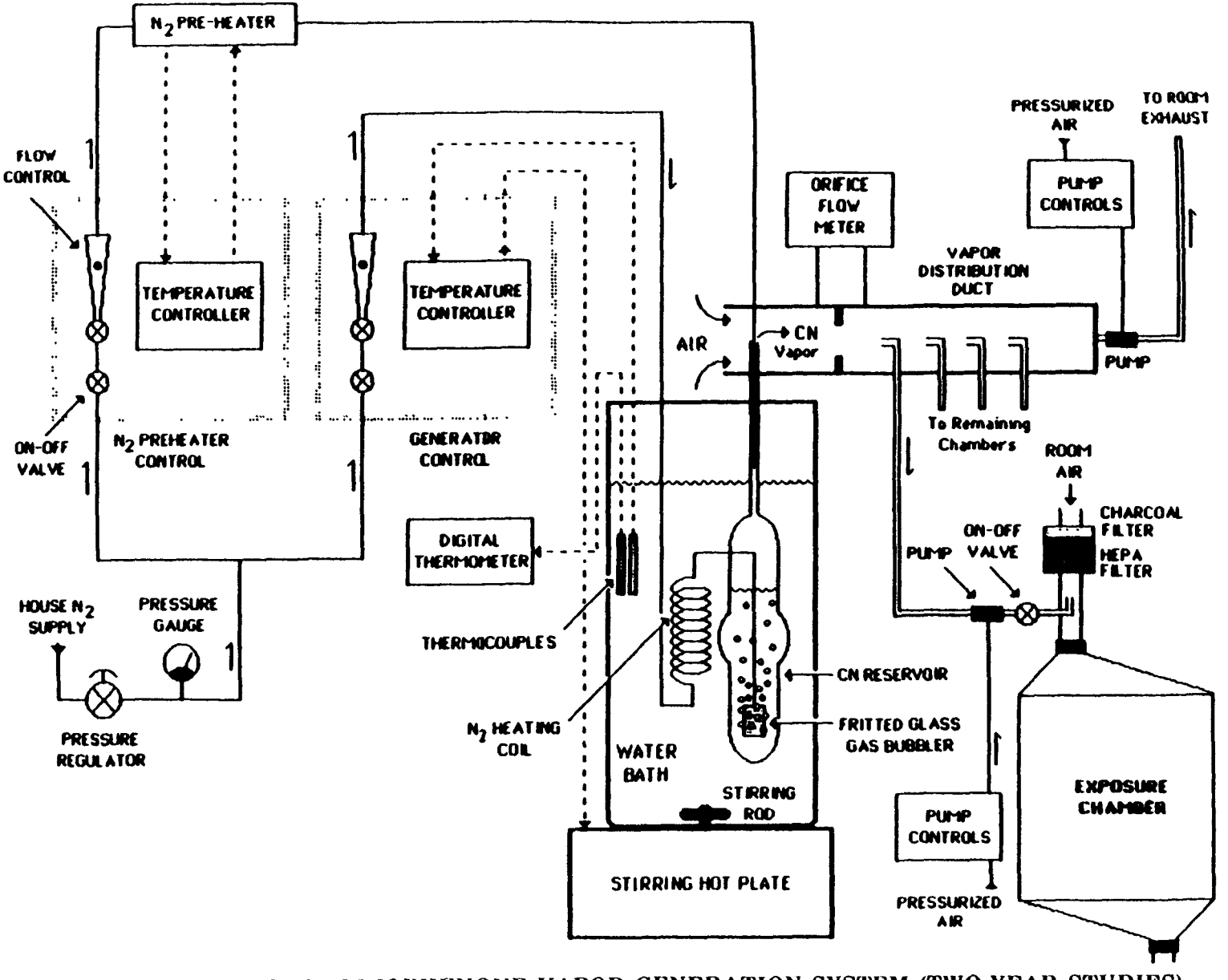

FIGURE H3. 2-CHLOROACETOPHENONE VAPOR GENERATION SYSTEM (TWO-YEAR STUDIES)

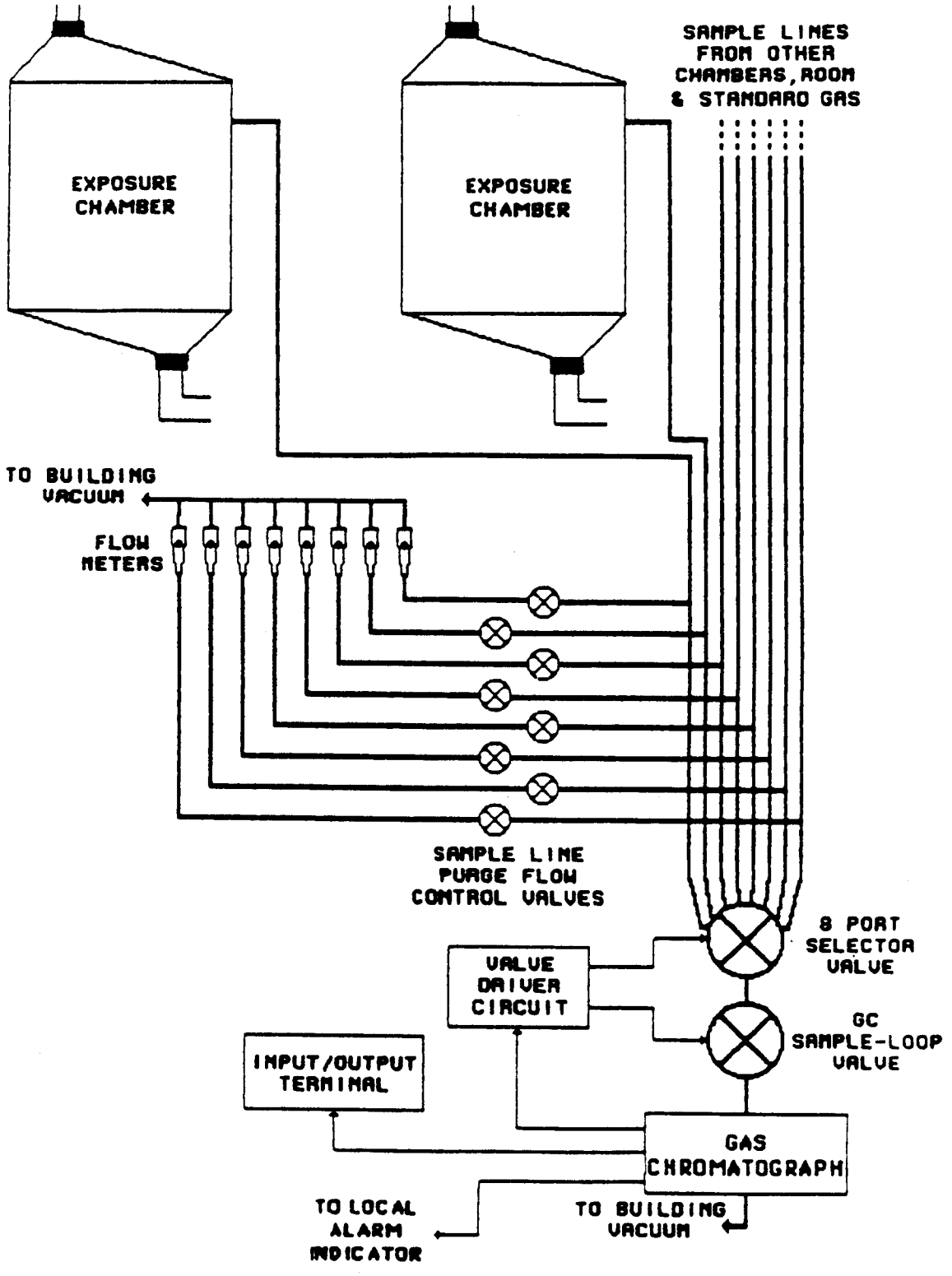

FIGURE H4. CHAMBER CONCENTRATION MONITORING SYSTEM

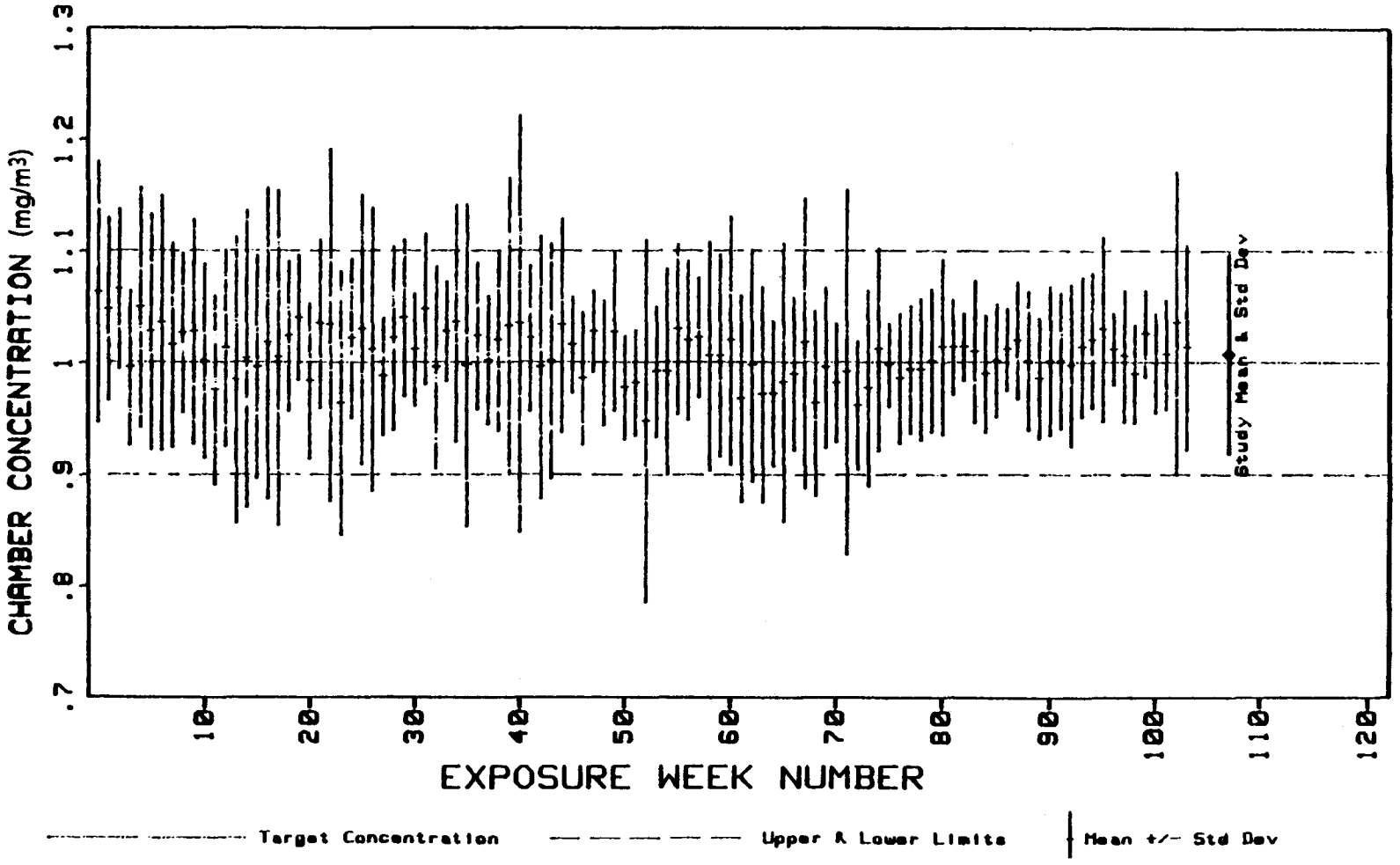

FIGURE H5. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 1 mg/m^3 2-CHLOROACETOPHENONE RAT EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES

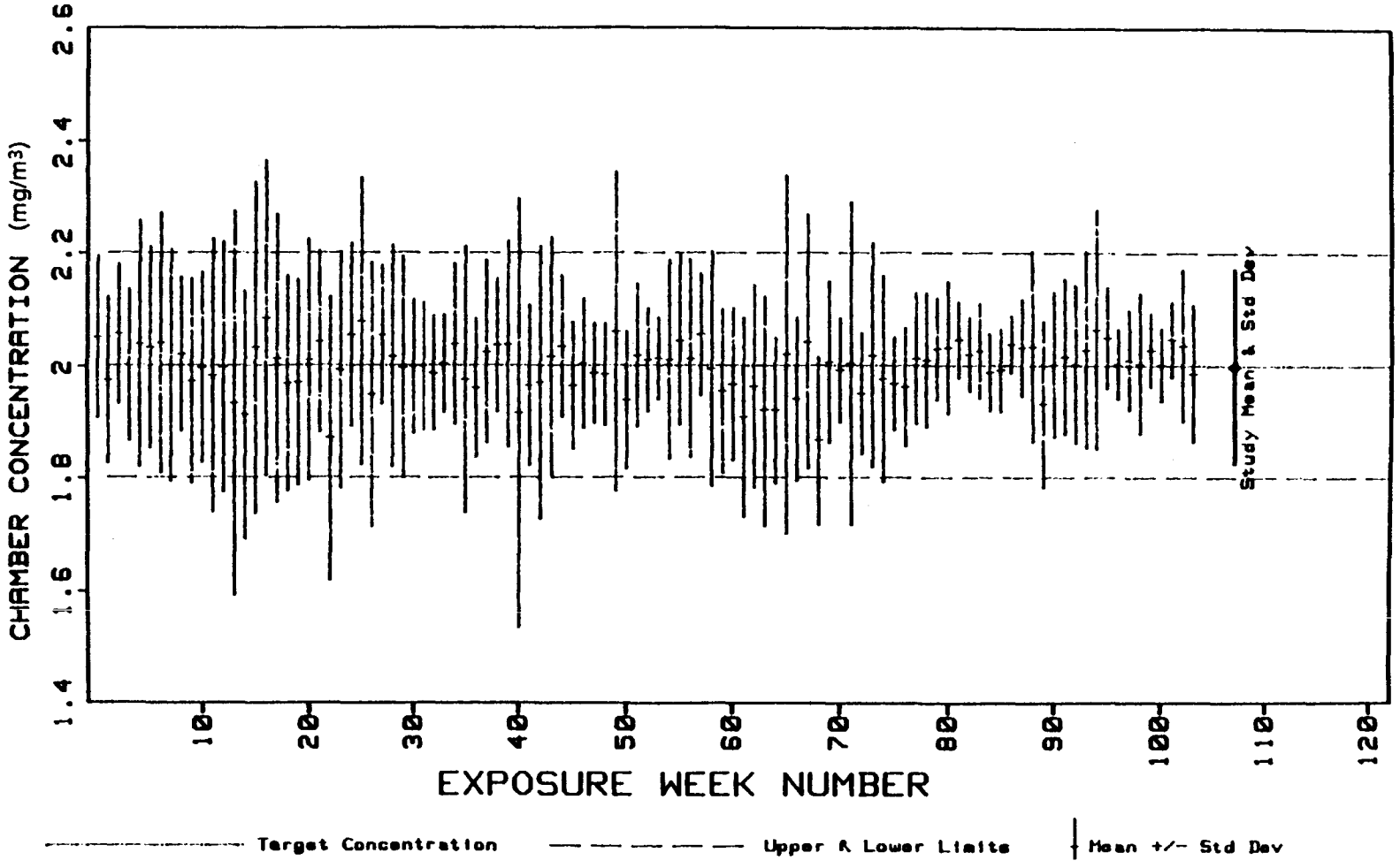

FIGURE H6. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 2 mg/m^3 2-CHLOROACETOPHENONE RAT EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES

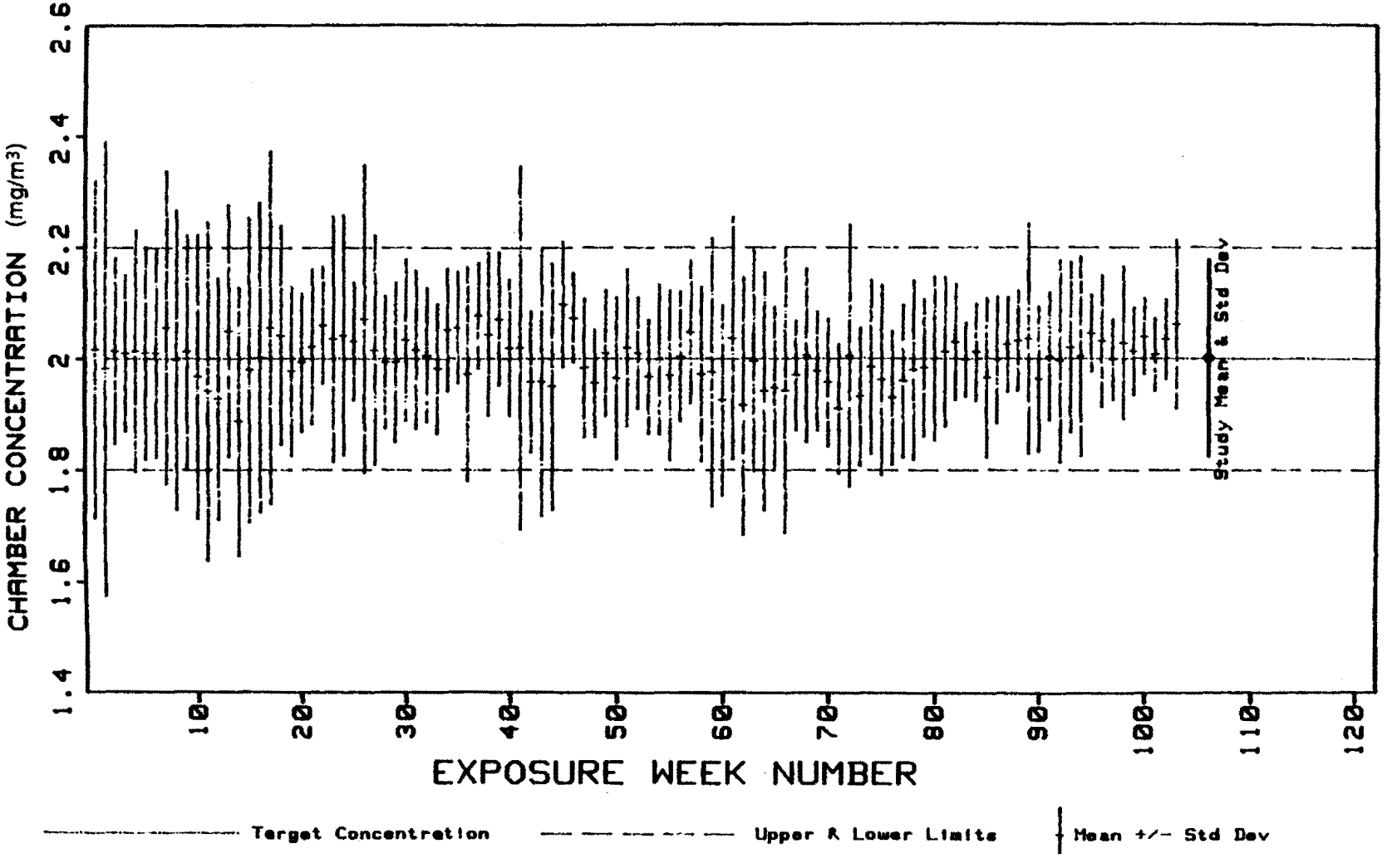

FIGURE H7. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 2 mg/m^3 2-CHLOROACETOPHENONE MOUSE EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES

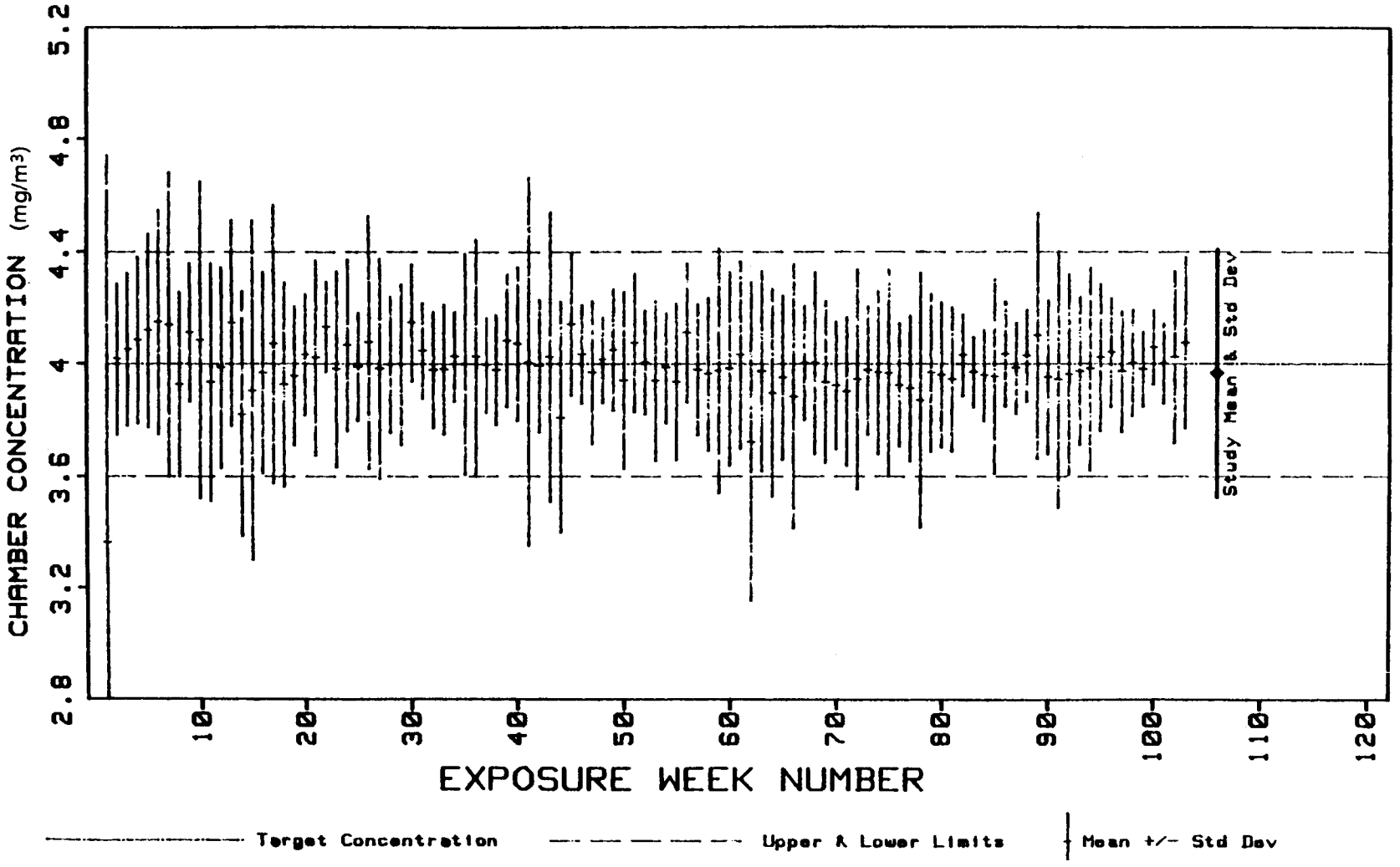

FIGURE H8. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 4 mg/m^3 2-CHLOROACETOPHENONE MOUSE EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES

TABLE H2. SUMMARY OF CHAMBER CONCENTRATIONS IN THE TWO-YEAR INHALATION STUDIES OF 2-CHLOROACETOPHENONE

Target Concentration (mg/m^3)	Total Number of Readings	Average Concentration (a) (mg/m^3)
Rat Chambers		
1	5,413	1.01 ± 0.09
2	5,432	2.00 ± 0.17
Mouse Chambers		
2	5,418	2.00 ± 0.18
4	5,419	3.97 ± 0.44

(a) Mean ± standard deviation

TABLE H3. DISTRIBUTION OF MEAN DAILY CONCENTRATIONS OF 2-CHLOROACETOPHENONE DURING THE TWO-YEAR INHALATION STUDIES (a)

Range of Concentration (percent of target)	Number of Days Mean Within Specified Range		
	1 mg/m^3	2 mg/m^3	4 mg/m^3
Rat Chambers			
120-130	0	1	
110-120	6	6	
100-110	269	245	
90-100	218	238	
80-90	2	5	
Mouse Chambers			
110-120		4	5
100-110		215	224
90-100		270	263
80-90		1	4
70-80		1	0
<70		5	0

APPENDIX I

GENETIC TOXICOLOGY

OF 2-CHLOROACETOPHENONE

METHODS

Salmonella Protocol: Testing was performed as reported by Zeiger et al. (1987). Chemicals were sent to the laboratories as coded aliquots from Radian Corporation (Austin, TX). The study chemical was incubated with the *Salmonella typhimurium* tester strains (TA98, TA100, TA1535, and TA1537) either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver) for 20 minutes at 37° C before the addition of soft agar supplemented with L-histidine and D-biotin and subsequent plating on minimal glucose agar plates. Incubation was continued for an additional 48 hours.

Chemicals were tested in a series (four strains used). Each test consisted of triplicate plates of concurrent positive and negative controls and of at least five doses of the study chemical. The high dose was limited by toxicity or solubility but did not exceed 333 µg/plate. All negative assays were repeated, and all positive assays were repeated under the conditions that elicited the positive response.

A positive response was defined as a reproducible, dose-related increase in histidine-independent (revertant) colonies in any one strain/activation combination. An equivocal response was defined as an increase in revertants which was not dose related, not reproducible, or of insufficient magnitude to support a determination of mutagenicity. A response was considered negative when no increase in revertant colonies was observed after chemical treatment.

Chinese Hamster Ovary Cytogenetics Assays: Testing was performed as reported by Galloway et al. (1985) and is described briefly below. Chemicals were sent to the laboratories as coded aliquots from Radian Corporation (Austin, TX). Chemicals were tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCEs) and chromosomal aberrations both in the presence and absence of Aroclor 1254-induced male Sprague Dawley rat liver S9 and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine (BrdU)-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least three doses of the study chemical; the high dose was limited by toxicity or solubility but did not exceed 5 mg/ml.

In the SCE test without S9, CHO cells were incubated for 26 hours with the study chemical in McCoy's 5A medium supplemented with 10% fetal bovine serum, L-glutamine (2 mM), and antibiotics. BrdU was added 2 hours after culture initiation. After 26 hours, the medium containing the study chemical was removed and replaced with fresh medium plus BrdU and colcemid, and incubation was continued for 2 more hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with the chemical, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing BrdU and no study chemical; incubation proceeded for an additional 26 hours, with colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9.

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

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

Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind, and those from a single test were read by the same person. For the SCE test, 50 second-division metaphase cells were usually scored for frequency of SCEs per cell from each dose; 200 first-division metaphase cells were scored at each dose for the chromosomal aberration test. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

Statistical analyses were conducted on both the slopes of the dose-response curves and the individual dose points. An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001. Chromosomal aberration data are presented as percentage of cells with aberrations. As with SCEs, both the dose-response curve and individual dose points were statistically analyzed. A statistically significant ($P<0.003$) trend test or a significantly increased dose point ($P<0.05$) was sufficient to indicate a chemical effect.

RESULTS

2-Chloroacetophenone, within a dose range of 0.1 to 333.0 µg/plate, was not mutagenic when tested in *S. typhimurium* strains TA98, TA100, TA1535, or TA1537 according to a preincubation protocol with or without Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver S9 (Zeiger et al., 1987; Table I1). No induction of SCEs was observed in CHO cells treated with 2-chloroacetophenone at concentrations of 0.016-0.5 µg/ml in the absence of S9 or 0.16-5.0 µg/ml in the presence of Aroclor 1254-induced male Sprague Dawley rat liver S9 (Table I2). The only genotoxic effect observed for 2-chloroacetophenone was a weakly positive response in the CHO cell chromosomal aberration test conducted without S9 activation; in this test, the highest dose tested, 3.0 µg/ml, induced a highly significant increase in aberrations along with marked toxicity (only 65 cells scored) (Table I3).

TABLE I1. MUTAGENICITY OF 2-CHLOROACETOPHENONE IN *SALMONELLA TYPHIMURIUM* (a)

Strain	Dose (µg/plate)	Revertants/Plate (b) −S9 Trial 1	−S9 Trial 2	+10% S9 (hamster) Trial 1	+10% S9 (hamster) Trial 2	+10% S9 (rat) Trial 1	+10% S9 (rat) Trial 2
TA100	0	105 ± 8.5	88 ± 0.6	122 ± 10.1	91 ± 11.3	133 ± 1.0	113 ± 7.6
	0.1	126 ± 11.8	--	--	--	--	--
	0.3	118 ± 3.1	111 ± 12.7	--	--	--	--
	1	145 ± 12.4	112 ± 6.4	--	107 ± 4.9	127 ± 9.0	--
	3	137 ± 4.9	113 ± 10.1	139 ± 0.9	123 ± 10.0	123 ± 10.3	122 ± 11.1
	10	145 ± 13.5	131 ± 9.3	141 ± 1.3	111 ± 12.9	135 ± 9.9	124 ± 9.2
	33	--	Toxic	137 ± 14.2	120 ± 10.7	146 ± 6.8	138 ± 2.2
	100	--	--	159 ± 6.4	115 ± 17.3	153 ± 3.8	127 ± 4.0
	333	--	--	(c) 80 ± 40.3	--	--	Toxic
Trial summary		Equivocal	Equivocal	Negative	Negative	Negative	Negative
Positive control (d)		418 ± 10.1	292 ± 25.8	1,567 ± 87.1	1,007 ± 48.7	717 ± 159.7	518 ± 13.3
TA1535	0	29 ± 3.8	20 ± 4.4	12 ± 1.9	11 ± 2.4	9 ± 2.0	9 ± 1.7
	0.1	28 ± 3.6	--	--	--	--	--
	0.3	25 ± 6.5	24 ± 5.2	--	--	--	--
	1	33 ± 2.7	22 ± 2.3	--	10 ± 2.7	9 ± 3.7	--
	3	25 ± 2.3	17 ± 1.5	9 ± 3.0	9 ± 2.6	10 ± 2.1	9 ± 3.2
	10	18 ± 1.3	9 ± 2.0	7 ± 0.3	6 ± 1.3	9 ± 1.7	8 ± 2.2
	33	--	Toxic	11 ± 2.8	8 ± 10.7	12 ± 1.3	10 ± 2.5
	100	--	--	6 ± 0.9	8 ± 3.8	10 ± 2.6	6 ± 1.8
	333	--	--	(c) 0 ± 0.0	--	--	Toxic
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control (d)		561 ± 17.6	342 ± 28.3	484 ± 13.0	461 ± 24.5	181 ± 29.5	169 ± 11.6
TA1537	0	6 ± 0.9	3 ± 0.3	11 ± 1.8	9 ± 0.0	11 ± 2.1	6 ± 3.0
	0.1	8 ± 2.6	--	--	--	--	--
	0.3	6 ± 1.7	4 ± 1.2	--	--	--	--
	1	8 ± 1.3	5 ± 1.8	--	7 ± 1.8	11 ± 3.5	--
	3	6 ± 1.2	3 ± 0.6	13 ± 0.0	9 ± 1.5	12 ± 2.5	7 ± 1.0
	10	7 ± 0.7	5 ± 0.9	8 ± 2.0	5 ± 0.3	9 ± 2.6	8 ± 1.5
	33	--	Toxic	6 ± 0.7	7 ± 2.6	9 ± 3.0	10 ± 1.0
	100	--	--	9 ± 1.9	7 ± 0.6	5 ± 2.1	7 ± 2.2
	333	--	--	(c) 5 ± 1.5	--	--	Toxic
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control (d)		222 ± 69.7	124 ± 9.3	410 ± 9.2	162 ± 7.8	115 ± 11.2	115 ± 12.4
TA98	0	16 ± 2.3	15 ± 1.2	33 ± 4.3	31 ± 1.2	30 ± 0.9	30 ± 4.9
	0.1	11 ± 1.0	--	--	--	--	--
	0.3	15 ± 1.0	18 ± 1.9	--	--	--	--
	1	12 ± 1.7	12 ± 2.2	--	32 ± 0.7	30 ± 4.6	--
	3	13 ± 3.2	17 ± 0.3	26 ± 3.0	30 ± 3.5	33 ± 1.9	29 ± 4.3
	10	15 ± 0.9	21 ± 5.4	35 ± 4.5	33 ± 1.7	34 ± 2.9	37 ± 2.3
	33	--	Toxic	32 ± 4.1	33 ± 2.6	36 ± 2.4	35 ± 1.5
	100	--	--	34 ± 6.3	35 ± 0.3	26 ± 3.8	27 ± 4.5
	333	--	--	(c) 21 ± 5.5	--	--	Toxic
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control (d)		845 ± 25.8	637 ± 62.7	1,440 ± 143.0	990 ± 51.5	445 ± 115.4	389 ± 47.8

(a) Study performed at SRI International. The detailed protocol is presented in Haworth et al. (1983); data are presented in Zeiger et al. (1987). Cells and study compound or solvent (dimethyl sulfoxide) 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 or solubility but did not exceed 10 mg/plate; 0 µg/plate dose is the solvent control.
(b) Revertants are presented as mean ± standard error from three plates.
(c) Slight toxicity
(d) 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, sodium azide was used with TA100 and TA1535, and 9-aminoacridine was used with TA1537.

TABLE I2. INDUCTION OF SISTER CHROMATID EXCHANGES IN CHINESE HAMSTER OVARY CELLS BY 2-CHLOROACETOPHENONE (a)

Compound	Dose (μg/ml)	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hours in BrdU	Relative SCEs/Chromosome (percent) (b)
−S9 (c)--Summary: Negative								
Dimethyl sulfoxide		50	1,037	438	0.42	8.8	26.0	
2-Chloroacetophenone	0.016	50	1,042	411	0.39	8.2	26.0	−6.62
	0.05	50	1,043	439	0.42	8.8	26.0	−0.35
	0.16	50	1,042	397	0.38	7.9	26.0	−9.80
	0.5	50	1,050	428	0.40	8.6	26.0	−3.50
Mitomycin C	0.0007	50	1,048	537	0.51	10.7	26.0	21.32
	0.005	10	210	273	1.30	27.3	26.0	207.79
Trend test: P=0.75								
+S9 (d)--Summary: Negative								
Dimethyl sulfoxide		50	1,048	454	0.43	9.1	26.0	
2-Chloroacetophenone	0.16	50	1,046	386	0.36	7.7	26.0	−14.82
	0.5	50	1,050	466	0.44	9.3	26.0	2.45
	1.6	50	1,052	453	0.43	9.1	26.0	−0.60
	5	50	1,052	407	0.38	8.1	26.0	−10.69
Cyclophosphamide	0.1	50	1,050	592	0.56	11.8	26.0	30.15
	0.6	10	210	244	1.16	24.4	26.0	168.21
Trend test: P=0.69								

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

TABLE I3. INDUCTION OF CHROMOSOMAL ABERRATIONS IN CHINESE HAMSTER OVARY CELLS BY 2-CHLOROACETOPHENONE (a)

Trial 1					Trial 2				
Dose (µg/ml)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs	Dose (µg/ml)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs
−S9 (b)--Harvest time: 12 h					−S9 (b)--Harvest time: 12 h				
Dimethyl sulfoxide					Dimethyl sulfoxide				
	200	2	0.01	1.0		200	2	0.01	1.0
2-Chloroacetophenone					2-Chloroacetophenone				
0.16	200	2	0.01	1.0	0.5	200	4	0.02	1.5
0.5	200	8	0.04	4.0	1.0	200	2	0.01	1.0
1.6	200	7	0.04	3.0	1.6	200	7	0.04	3.5
					3.0	65	38	0.58	*43.1
Summary: Equivocal					Summary: Weak positive				
Mitomycin C					Mitomycin C				
0.0625	200	41	0.21	18.5	0.125	200	39	0.20	18.0
0.25	50	23	0.46	40.0	0.250	50	18	0.36	32.0
Trend test for total Abs: P=0.028					Trend test for total Abs: P<0.001				
+S9 (c)--Harvest time: 13 h									
Dimethyl sulfoxide									
	200	2	0.01	1.0					
2-Chloroacetophenone									
1.6	200	1	0.01	0.5					
5	200	2	0.01	1.0					
10	200	0	0.00	0.0					
Summary: Negative									
Cyclophosphamide									
2.5	200	37	0.19	17.0					
7.5	50	21	0.42	36.0					
Trend test for total Abs: P=0.82									

(a) Study performed at Environmental Health Research and Testing, Inc. Abs = aberrations. A detailed presentation of the technique for detecting chromosomal aberrations is found in Galloway et al. (1985). Briefly, Chinese hamster ovary cells were incubated with study compound or solvent (dimethyl sulfoxide) as indicated in (b) and (c). Cells were arrested in first metaphase by addition of colcemid and harvested by mitotic shake-off, fixed, and stained in 6% Giemsa.
(b) In the absence of S9, cells were incubated with study compound or solvent for 8-10 hours at 37° C. Cells were then washed, and fresh medium containing colcemid was added for an additional 2-3 hours followed by harvest.
(c) In the presence of S9, cells were incubated with study compound or solvent for 2 hours at 37° C. Cells were then washed, medium was added, and incubation was continued for 8-10 hours. Colcemid was added for the last 2-3 hours of incubation before harvest. S9 was from the liver of Aroclor 1254-induced male Sprague Dawley rats.
*P<0.05

APPENDIX J

AUDIT SUMMARY

APPENDIX J. AUDIT SUMMARY

The pathology specimens, experimental data, study documents, and draft NTP Technical Report No. 379 for the 2-year studies of 2-chloroacetophenone in rats and mice were audited for the National Institute of Environmental Health Sciences (NIEHS) at the National Toxicology Program (NTP) Archives. The audit included review of:

(1) All records concerning animal receipt, quarantine, randomization, and disposition prior to start of dosing.
(2) All inlife records including protocol, correspondence, animal identification, animal husbandry, environmental conditions, dosing, external masses, mortality, 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 study 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 or near the last inlife observation with gross observations and microscopic diagnoses, consistency of data entry on necropsy record forms, and correlation between gross observations and microscopic diagnoses.
(6) Inventory for wet tissue bags from all animals and residual wet tissues from a random 20% sample of animals in high and control groups, plus other relevant cases, to evaluate the integrity of individual animal identity and the thoroughness of necropsy and trimming procedure performance.
(7) Blocks and slides of tissues from a random 20% sample of animals from high and control groups, plus animals with less than complete or correct identification, to examine for proper inventory, labeling, matching of tissue sections, and preservation.
(8) All microscopic diagnoses for a random 10% sample of animals, plus 100% of the changes in diagnoses made to preliminary pathology tables, to verify their incorporation into the final pathology tables.
(9) The extent of correlation between the data, factual information, and procedures for the 2-year studies as presented in the draft Technical Report and the study records available at the NTP Archives.

Procedures and events for the exposure phase of the studies were documented adequately by records at the Archives. Review of the archival records indicated that protocol-specified procedures for animal care were followed adequately. Records that documented the generation, analysis, distribution, and delivery of doses to animals were complete and accurate. Recalculation of 63 group mean body weight values in the Technical Report for rats and mice, including several that appeared to be outliers, showed that all were correct.

Data entries on necropsy forms were made appropriately. The thoroughness for observation of external masses for rats and mice combined was adequate, both inlife and at necropsy. The date of death recorded for each unscheduled-death animal had matching entries among the inlife records for 176/180 rats and 98/100 mice; the 6 differences in date-of-death entries were all 10 days or less and were inconsequential. The reason for animal removal recorded among the inlife records was in agreement with the disposition code recorded at necropsy for 299/300 rats and 293/300 mice; the 8 mode-of-death discrepancies involved moribund animals that died before they could be killed and had no effect on overall survival values. The condition code for each animal was consistent with the disposition code and gross observations assigned at necropsy.

An individual animal identifier (ear tag) was present and correct in the residual tissue bag for 65/65 rats and 85/90 mice examined. Review of the entire data trail for the five mice whose ear tag did not agree fully with the wet tissue bag label indicated that four mice had been misbagged after tissue trimming and that the remaining mouse had a broken ear tag; however, individual animal data for

these animals had not been mixed up. A total of 16 untrimmed potential lesions were found in the wet tissues of 65 rats, and 5 were found in those of 90 mice examined. Intestinal segments were opened incompletely for 34/65 rats and 32/90 mice examined; however, no untrimmed potential lesions were evident by external examination, and other organs had been opened or incised properly. Each gross observation made at necropsy had a corresponding microscopic diagnosis for all but 9 in rats and 26 in mice. Blocks and slides were present and corresponding tissue sections matched each other properly. All post-Pathology Working Group changes in diagnoses had been incorporated into the final pathology tables. The P values and incidences of neoplasms given in the Technical Report were the same as those in the final pathology tables at the Archives.

This summary describes general audit findings and the extent to which the data and factual information presented in the Technical Report are supported by records at the NTP Archives. Full details are presented in audit reports that are on file at the NIEHS.

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