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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

# TOXICOLOGY AND CARCINOGENESIS STUDIES OF 2-CHLOROACETOPHENONE

(CAS NO. 532-27-4)

# IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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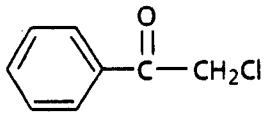

## 2-CHLOROACETOPHENONE

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.

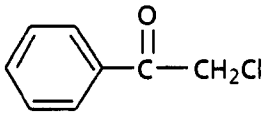
Dr. Longnecker, the second principal reviewer, agreed with the conclusions. He asked whether dosed animals were left in the inhalation chamber following the exposure period. Since the Report stated that 10 hours were required for 2-chloroacetophenone concentration to drop to 1% of target concentration, 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

# I. INTRODUCTION



**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) | Intravenous (c) | Inhalation (b) | Inhalation (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

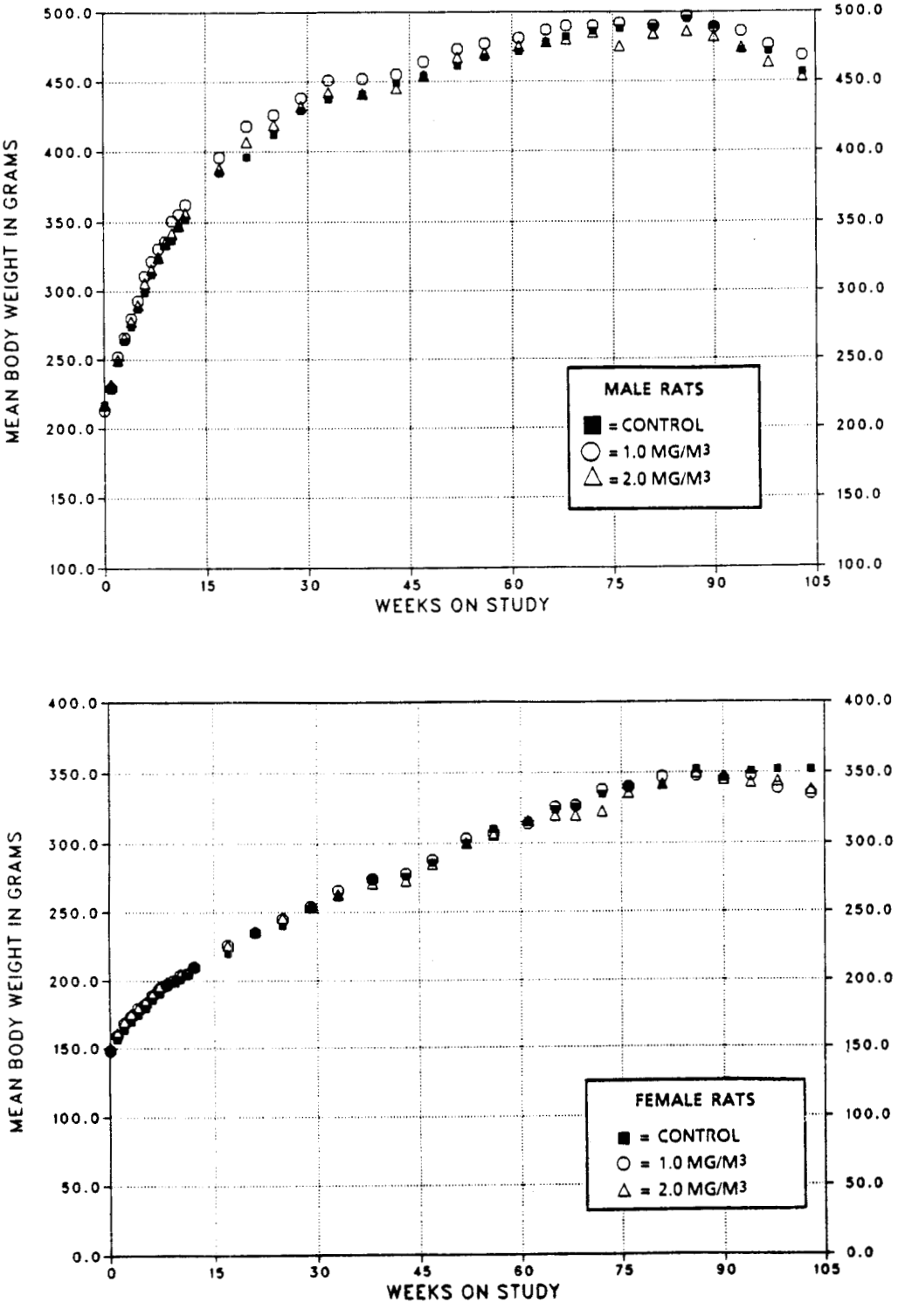



**FIGURE 1. GROWTH CURVES FOR RATS EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS**

### 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.

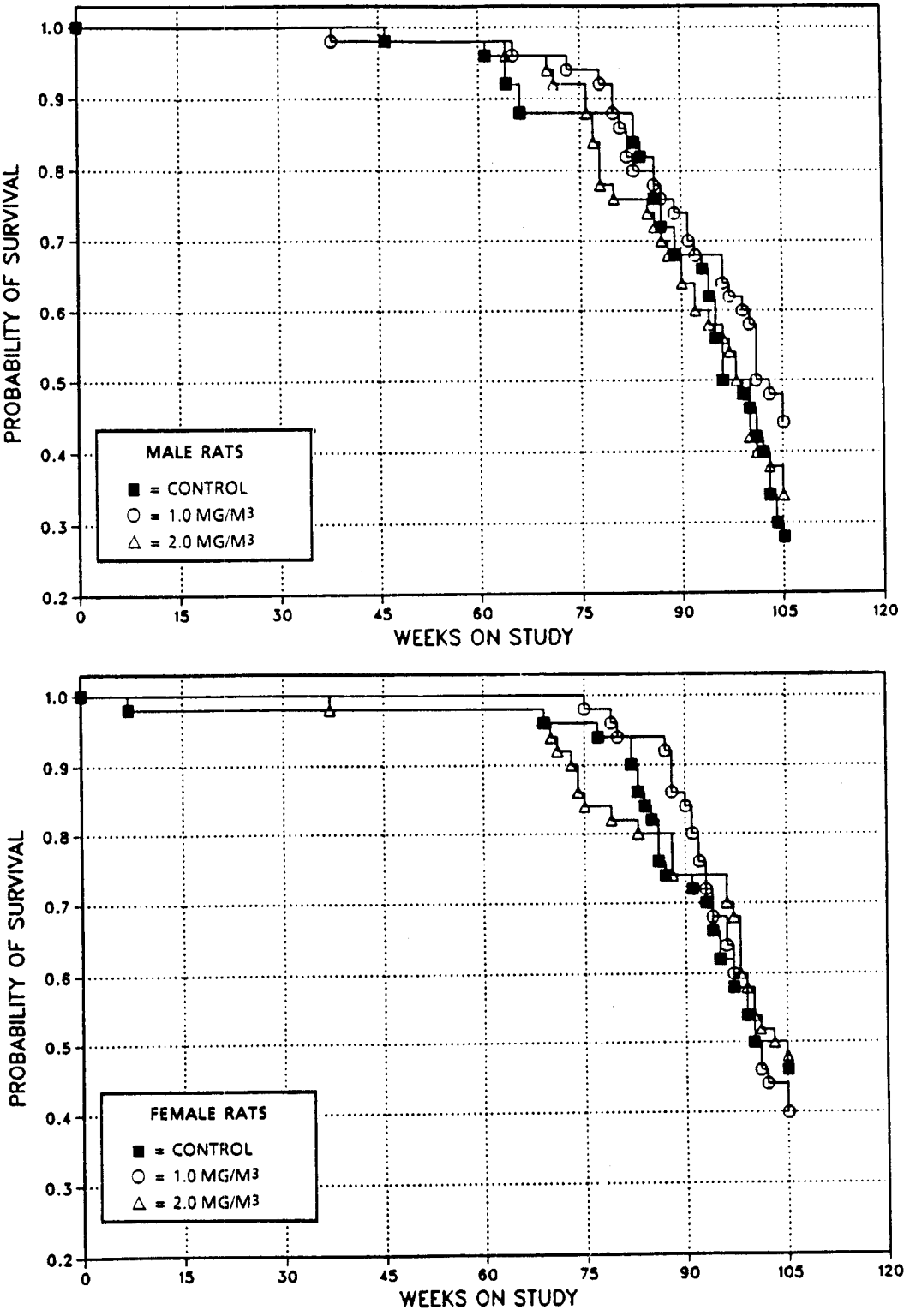



**FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR RATS EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS**

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%)

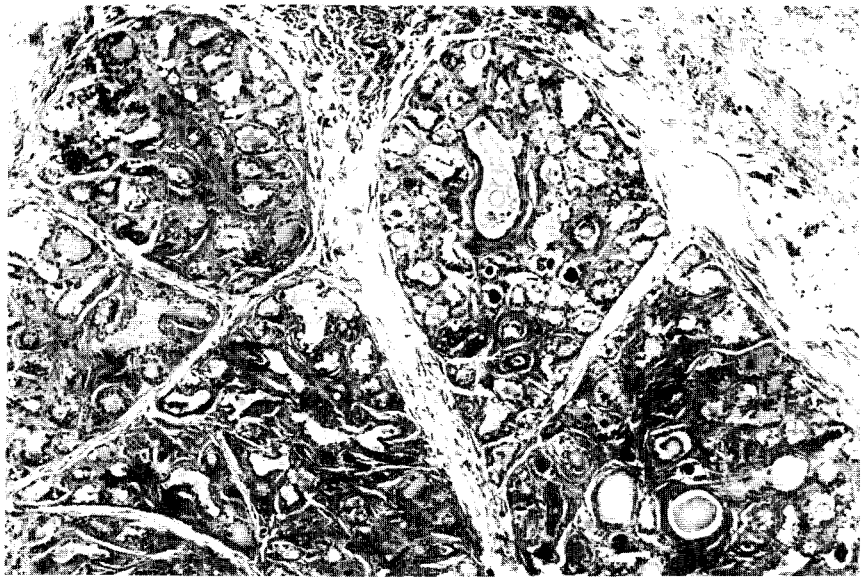


Figure 3. Mammary gland fibroadenoma in a female F344/N rat exposed to 1 mg/m$^3$ 2-chloroacetophenone by inhalation for 2 years.

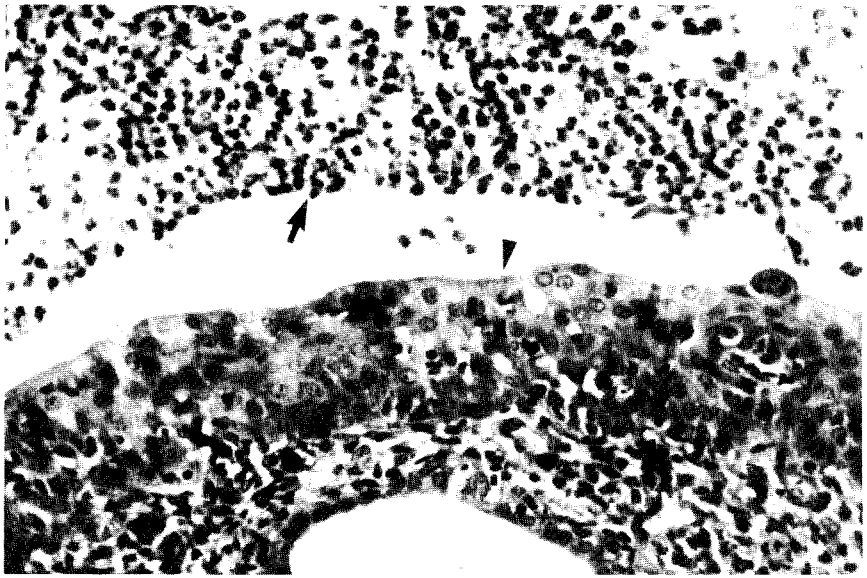


Figure 4. Suppurative inflammation and squamous metaplasia of the nasal passage in a male F344/N rat exposed to 2 mg/m$^3$ 2-chloroacetophenone by inhalation for 2 years. Exudate composed primarily of neutrophils is present in the lumen (arrow), whereas the underlying nasal epithelium has undergone metaplasia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

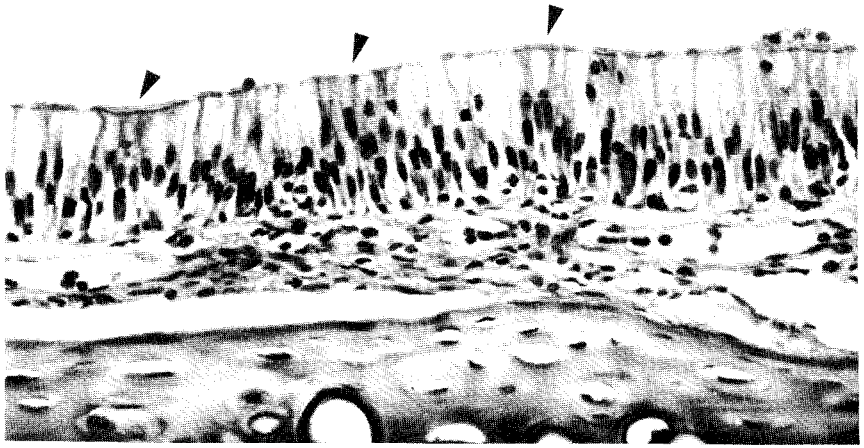


Figure 5. Hyperplasia of the respiratory epithelium of the nasal passage in a female F344/N rat exposed to 1 mg/m$^3$ 2-chloroacetophenone by inhalation for 2 years. The epithelium is thickened and hypercellular. Cilia are evident along the luminal surfaces of the epithelial cells (arrowheads).

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 | |

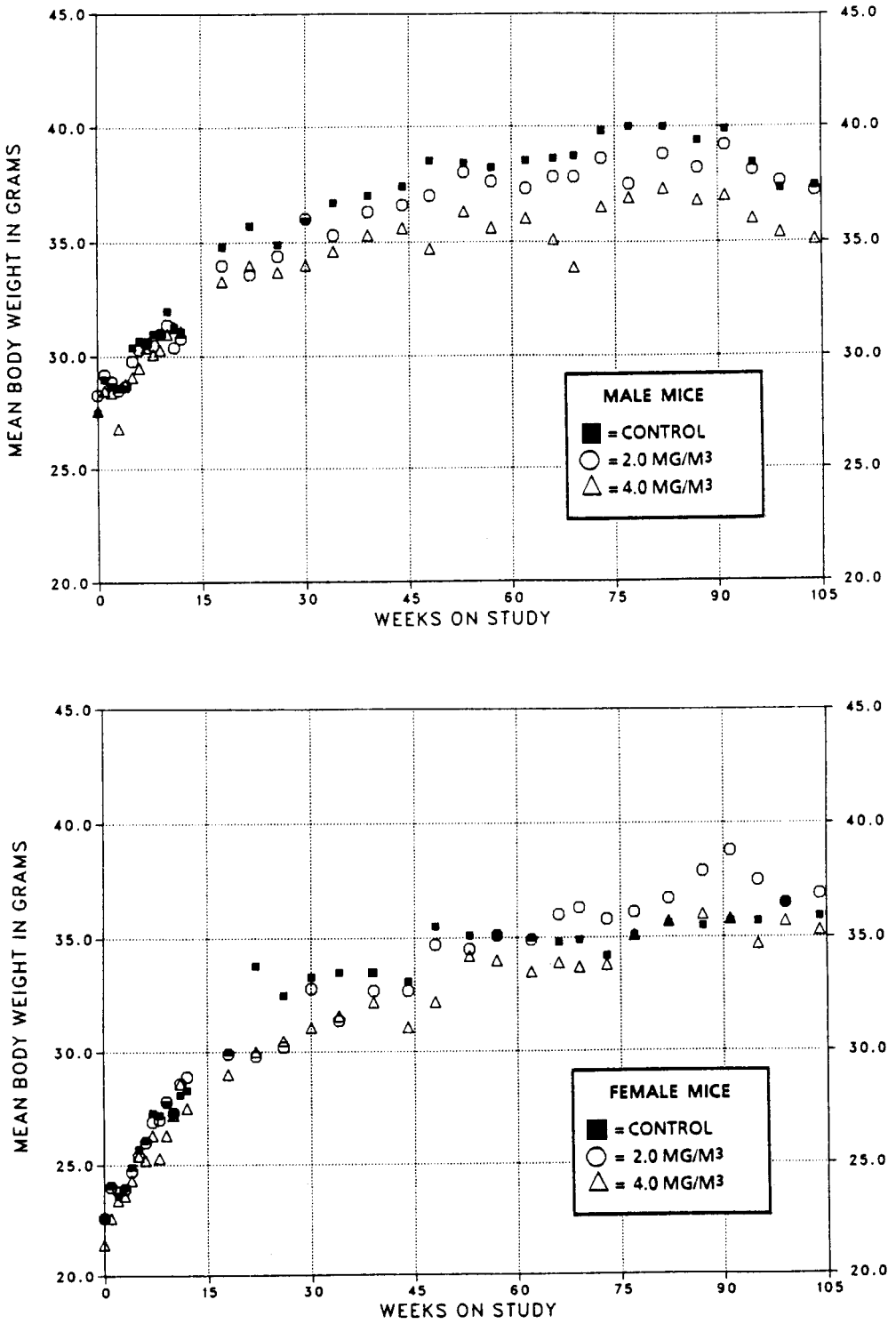



**FIGURE 7. GROWTH CURVES FOR MICE EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS**

### 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

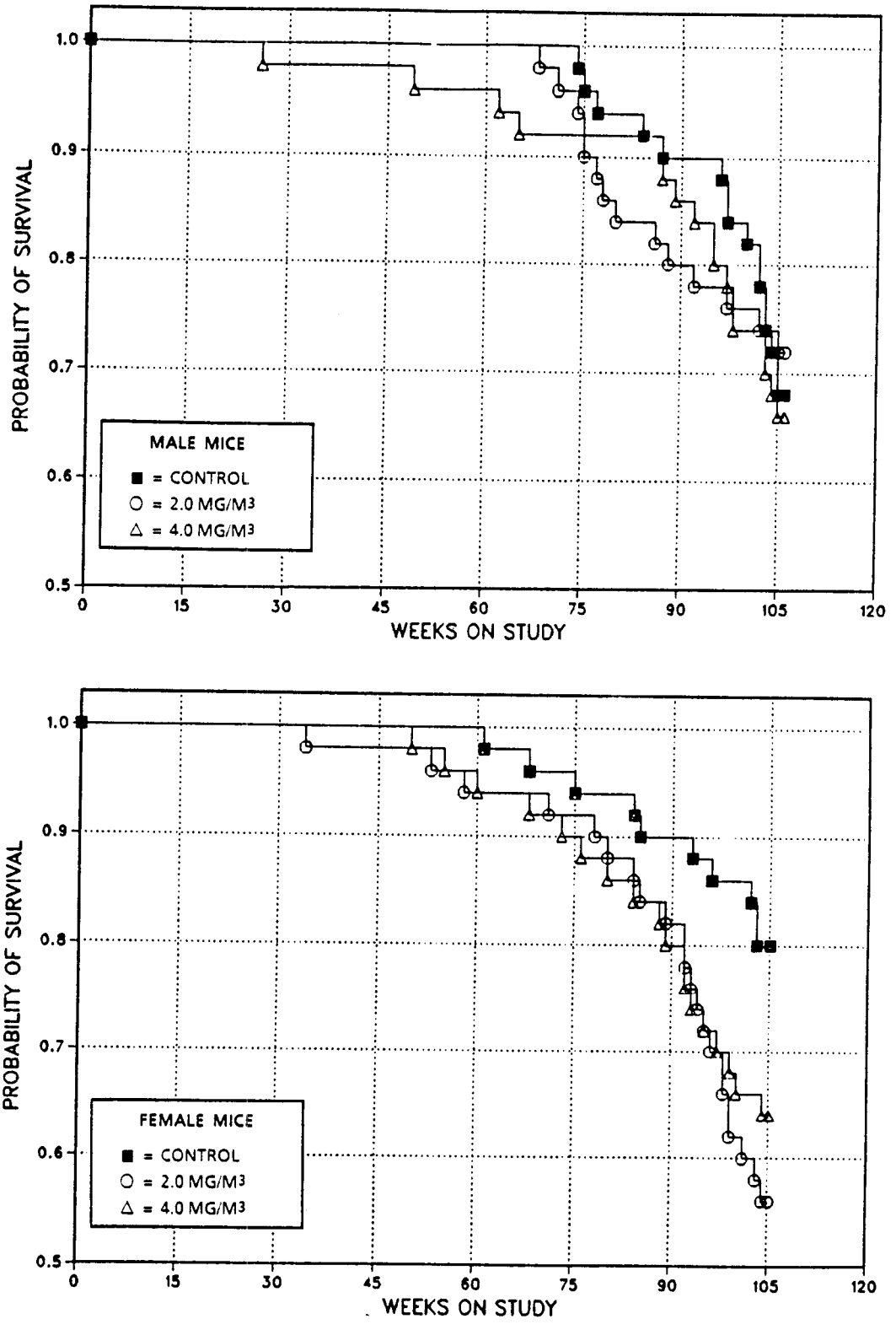



FIGURE 8. KAPLAN-MEIER SURVIVAL CURVES FOR MICE EXPOSED TO 2-CHLOROACETOPHENONE BY INHALATION FOR TWO YEARS

## 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.

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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 | 41 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 | + | + | + | + | + | 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 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | TOTAL: 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 | 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 | 51 1 | 05 1 |
| **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 | 09 9 | 10 0 | 10 1 | 10 1 | 10 2 | 10 3 | 10 3 | 10 3 | 10 4 | 10 4 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | 10 5 | TOTAL: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 34 1 | 26 1 | 19 1 | 07 1 | 21 1 | 46 1 | 11 1 | 12 1 | 27 1 | 43 1 | 09 1 | 06 1 | 08 1 | 10 1 | 13 1 | 17 1 | 24 1 | 25 1 | 29 1 | 33 1 | 38 1 | 39 1 | 42 1 | 44 1 | 48 1 | 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 | 12201 | 12261 | 11771 | 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 | | | | | | | | | | | | | | | | | | | | | | | | + | |
| 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 |
| 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 |
| 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 |
| 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: 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 | |
| **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 | 0 3 8 | 0 6 5 | 0 7 3 | 0 7 8 | 0 8 0 | 0 8 0 | 0 8 1 | 0 8 2 | 0 8 2 | 0 8 3 | 0 8 6 | 0 8 7 | 0 8 9 | 0 9 1 | 0 9 1 | 0 9 2 | 0 9 6 | 0 9 6 | 0 9 7 | 0 9 9 | 1 0 0 | 1 0 1 | 1 0 1 | 1 0 1 | 1 0 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 1 2 9 1 | 1 3 6 1 | 1 2 5 1 | 1 0 1 1 | 1 0 8 1 | 1 4 1 1 | 1 3 4 1 | 1 2 0 1 | 1 2 6 1 | 1 1 7 1 | 1 4 8 1 | 1 3 0 1 | 1 2 4 1 | 1 1 2 1 | 1 3 8 1 | 1 4 5 1 | 1 0 7 1 | 1 4 0 1 | 1 0 3 1 | 1 1 0 1 | 1 2 3 1 | 1 0 2 1 | 1 1 4 1 | 1 1 5 1 | 1 2 7 1 |
| **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: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 1191 | 1161 | 1281 | 1041 | 1051 | 1061 | 1091 | 1111 | 1131 | 1181 | 1211 | 1221 | 1311 | 1321 | 1331 | 1351 | 1371 | 1391 | 1421 | 1431 | 1441 | 1461 | 1471 | 1491 | 1501 | TISSUES TUMORS |
| 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 | 090 | 090 | 092 | 092 | 094 | 096 | 097 | 098 | 098 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 22801 | 24111 | 23211 | 23511 | 23711 | 21811 | 22611 | 21111 | 20701 | 23811 | 20111 | 21411 | 24511 | 24211 | 22411 | 20081 | 24911 | 25011 | 20411 | 21911 | 22201 | 24331 | 21511 | 21311 | 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 1 | 205 1 | 225 1 | 202 1 | 203 1 | 206 1 | 209 1 | 210 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 | X | 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 | 22801 | 24111 | 23211 | 23511 | 23711 | 21811 | 22611 | 21111 | 20711 | 23811 | 20111 | 21411 | 24511 | 24211 | 22411 | 20811 | 24911 | 25011 | 20411 | 21911 | 22011 | 24331 | 21151 | 21131 | 24411 |
| 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 | | | | | | | | | X | | | | | | | |
| Thymoma malignant | | | | | | | | | | | | 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/m³ | 2 mg/m³ |
|---|---|---|---|
| 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 | 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 | 07011 | 06711 | 07411 | 08111 | 09931 | 07911 | 08011 | 07511 | 09511 | 08411 | 06911 | 08811 | 07111 | 09411 | 05511 | 07311 | 05311 | 05111 | 08511 | 08911 | 10011 | 06211 | 09811 | 06411 | 06811 |
| **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 | 07881 | 05441 | 05561 | 05771 | 05881 | 05991 | 06001 | 06111 | 06631 | 06551 | 07211 | 07661 | 07711 | 08211 | 08331 | 08661 | 08711 | 09001 | 09111 | 09212 | 09661 | 09771 | 09991 | 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 | 10011 | 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 | 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 | 09921 | 09961 | 09971 | 09991 | 05221 | TISSUES TUMORS |
| **HEMATOPOIETIC SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | + | | 1 |
| Blood | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Bone marrow | | | | | | | | | | | | | | | | | | | | | | | | X | | 2 |
| Leukemia mononuclear | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Lymph node | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Axillary, lymphoma malignant histiocytic | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Mesenteric, leukemia mononuclear | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Pancreatic, leukemia mononuclear | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | 44 |
| Lymph node, bronchial | X | X | X | X | | | | X | | | | | X | | | | | | | | | X | | | | 15 |
| Leukemia mononuclear | + | + | + | + | + | + | + | + | M | + | + | + | + | M | + | + | + | + | + | + | + | + | + | + | + | 46 |
| Lymph node, mandibular | X | X | X | X | | | | | | | | | X | | | | | | | | X | X | | | | 14 |
| Leukemia mononuclear | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymphoma malignant histiocytic | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Spleen | X | X | X | X | X | X | | X | | | | X | X | | | | | X | | X | X | X | X | X | | 26 |
| Leukemia mononuclear | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Lymphoma malignant histiocytic | + | + | + | + | + | + | + | + | + | + | + | + | M | + | + | + | + | + | + | + | + | + | M | M | + | 38 |
| Thymus | | | X | X | | | | | | | | | | | | | | | | | | | | | | 4 |
| Leukemia mononuclear | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **INTEGUMENTARY SYSTEM** | + | + | + | + | + | + | + | + | + | + | + | + | + | I | + | + | + | + | + | + | + | + | + | + | + | 48 |
| Mammary gland | | | | | | | | | | | | | | | | | | | | | | | X | | X | 2 |
| Adenocarcinoma | | X | X | | X | X | | | X | X | | | | | | | | X | | | | | | | X | 11 |
| Fibroadenoma | | | | | | | | | | | | | | | | | | | | X | | | | | | 1 |
| Fibroadenoma, multiple | | | | X | | | | | | | | | | | | | | | | | | | | | | 1 |
| Leukemia mononuclear | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 49 |
| Skin | | | | | | | | | | | | | | | | | | | | | | | | | | 1 |
| Keratoacanthoma | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 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 | 19601 | 16201 | 15101 | 19001 | 17301 | 15801 | 19801 | 18801 | 15601 | 15701 | 15301 | 16901 | 18901 | 19501 | 17701 | 18101 | 18001 | 16601 | 17601 | 19901 | 16801 | 17401 | 18401 | 17901 | 16401 |
| **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 | 205 | 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 | 201 1 | 155 1 | 159 1 | 160 1 | 163 1 | 185 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 | 19611 | 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 | 20001 | 15511 | 15991 | 16001 | 16331 | 16511 | 16711 | 17001 | 17111 | 17211 | 17511 | 17881 | 18211 | 18311 | 18611 | 18711 | 19111 | 19211 | 19331 | 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 | 25201 | 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 | 30011 | 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 | 25201 | 25901 | 27401 | 27801 | 28601 | 26901 | 26701 | 26001 | 29901 | 28001 | 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 | | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenoma | | | | | | | | | | | | | | | | | | | X | | | | | | |
| Fibroadenoma | | | 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 | 106 | TOTAL: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 26811 | 25111 | 25331 | 25441 | 26021 | 26331 | 26651 | 27001 | 27212 | 27331 | 27551 | 27771 | 27791 | 28111 | 28331 | 28441 | 28551 | 28881 | 28891 | 29001 | 29111 | 29331 | 29441 | 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/m$^3$ | 2 mg/m$^3$ |
|---|---|---|---|
| **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/m$^3$ | 2 mg/m$^3$ |
|---|---|---|---|
| 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | | | | | | | | | |
| Hepatocellular carcinoma, multiple | | | X | | 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 | 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 | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | 46 |
| 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | 092 | 097 | 102 | 105 | 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 | 10101 | 10301 | 10401 | 10501 | 10701 | 10801 | 10901 | 11001 | 11101 | 11201 | 11301 |
| **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. TISSUES TUMORS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 11401 | 11501 | 11601 | 11701 | 11801 | 11901 | 12101 | 12301 | 12501 | 12701 | 12901 | 13001 | 13101 | 13401 | 13701 | 13801 | 14001 | 14101 | 14201 | 14301 | 14401 | 14501 | 14601 | 14901 | 15001 | |
| **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 | 0 6 8 | 0 7 1 | 0 7 4 | 0 7 5 | 0 7 5 | 0 7 7 | 0 7 8 | 0 8 0 | 0 8 6 | 0 8 8 | 0 9 2 | 0 9 7 | 1 0 2 | 1 0 5 | 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 1 3 5 1 | 1 2 2 1 | 1 0 2 1 | 1 2 6 1 | 1 3 2 1 | 1 2 4 1 | 1 2 8 1 | 1 4 7 1 | 1 3 6 1 | 1 4 8 1 | 1 2 0 1 | 1 3 9 1 | 1 3 3 1 | 1 0 6 1 | 1 0 1 1 | 1 0 3 1 | 1 0 4 1 | 1 0 5 1 | 1 0 7 1 | 1 0 8 1 | 1 0 9 1 | 1 1 0 1 | 1 1 1 1 | 1 1 2 1 | 1 1 3 1 |
| **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 | | | | | | | | |
| 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 | 12231 | 12551 | 12771 | 12991 | 13011 | 13311 | 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 | 087 | 089 | 092 | 095 | 095 | 097 | 098 | 098 | 103 | 103 | 104 | 105 | 106 | 106 | 106 | 106 | 106 | 106 | 106 | 106 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 21551 | 20441 | 22771 | 24771 | 23991 | 22551 | 21991 | 22881 | 22221 | 24221 | 23811 | 20551 | 21881 | 24111 | 22991 | 20881 | 21611 | 20111 | 20221 | 20331 | 20661 | 20771 | 20991 | 21101 | 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. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 21 21 | 21 31 | 21 41 | 21 71 | 22 01 | 22 11 | 22 31 | 22 41 | 22 61 | 23 01 | 23 11 | 23 21 | 23 31 | 23 41 | 23 51 | 23 61 | 23 71 | 24 01 | 24 31 | 24 41 | 24 51 | 24 61 | 24 81 | 24 91 | 25 01 | | TISSUES TUMORS |
| 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 | 106 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 21511 | 20411 | 22711 | 24711 | 23911 | 22511 | 21911 | 22811 | 22211 | 24211 | 23811 | 20511 | 21811 | 24111 | 22911 | 20811 | 21611 | 20111 | 20211 | 20311 | 20611 | 20711 | 20911 | 21011 | 21111 |
| **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 | 21201 | 21331 | 21441 | 21171 | 22201 | 22211 | 22231 | 22241 | 22261 | 23011 | 23111 | 23211 | 23311 | 23411 | 23511 | 23611 | 23711 | 24011 | 24311 | 24411 | 24511 | 24611 | 24811 | 24911 | 25011 | 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/m³ | 4 mg/m³ |
|---|---|---|---|
| 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 | 09931 | 07411 | 07611 | 05551 | 05711 | 05111 | 07011 | 07111 | 08011 | 07911 | 05211 | 05311 | 05411 | 05611 | 05811 | 05911 | 06011 | 06111 | 06211 | 06311 | 06411 | 06511 | 06611 | 06711 | 06811 |
| **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 | 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 | 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CARCASS ID | 09311 | 07411 | 07611 | 05511 | 05711 | 05111 | 07011 | 07111 | 08011 | 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 | TISSUES TUMORS |
| **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 | + | + | + | + | A | 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 | 15511 | 15611 | 15811 | 15911 | 16311 | 16411 | 16811 | 16911 | 17211 | 17411 | 17611 | 17711 | 17911 | 18111 | 18211 | 18411 | 18511 | 18611 | 18911 | 19011 | 19111 | 19511 | 19611 | 19811 | 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 | 18011 | 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 | 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 | 27111 | 27221 | 27441 | 27551 | 27761 | 27771 | 27881 | 27991 | 28001 | 28111 | 28311 | 28551 | 28661 | 28771 | 29021 | 29331 | 29551 | 29661 | 29771 | 29881 | 29991 | 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 | 30101 | 26511 | 26601 | 26631 | 25811 | 27311 | 25511 | 25211 | 29411 | 25111 | 25311 | 25411 | 25711 | 26111 | 26211 | 26641 |
| **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 | 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 | 26611 | 26711 | 26811 | 26911 | 27111 | 27211 | 27411 | 27511 | 27611 | 27711 | 27811 | 27911 | 28011 | 28111 | 28311 | 28511 | 28611 | 28711 | 29211 | 29311 | 29511 | 29611 | 29711 | 29811 | 29911 | 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 | 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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 |
| **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 | 28001 | 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/m$^3$ | 4 mg/m$^3$ |
|---|---|---|---|
| **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/m³ | 4 mg/m³ |
|---|---|---|---|
| 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)<br>Reo 3 (reovirus type 3)<br>GDVII (Theiler's encephalomyelitis virus)<br>Poly (polyoma virus)<br>MVM (minute virus of mice)<br>Ectro (infectious ectromelia)<br>Sendai | M. Ad. (mouse adenovirus)<br>LCM (lymphocytic choriomeningitis virus)<br>**Immunofluorescence Assay**<br>EDIM (epizootic diarrhea of infant mice) (24 mo) | MHV (mouse hepatitis virus)<br>GDVII (22,23,24 mo)<br>PVM (24 mo)<br>Sendai (24 mo)<br>Reo 3 (24 mo)<br>Ectro (24 mo)<br>M. Ad. (24 mo)<br>*M. pul. (Mycoplasma pulmonis)* (24 mo)<br>*M. arth. (Mycoplasma arthritidis)* (24 mo) |
| | | **Complement Fixation** | |
| Rats | PVM<br>KRV (Kilham rat virus)<br>H-1 (Toolan's H-1 virus)<br>Sendai | RCV (rat coronavirus) | RCV/SDA sialodacryoadenitis virus (12,18,22, 24 mo)<br>PVM (24 mo)<br>Sendai (24 mo)<br>*M. pul.* (24 mo)<br>*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 ($\mu^3$) | 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 ($\mu^3$) | 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 ($\mu^3$) | 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 ($\mu^3$) | 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.

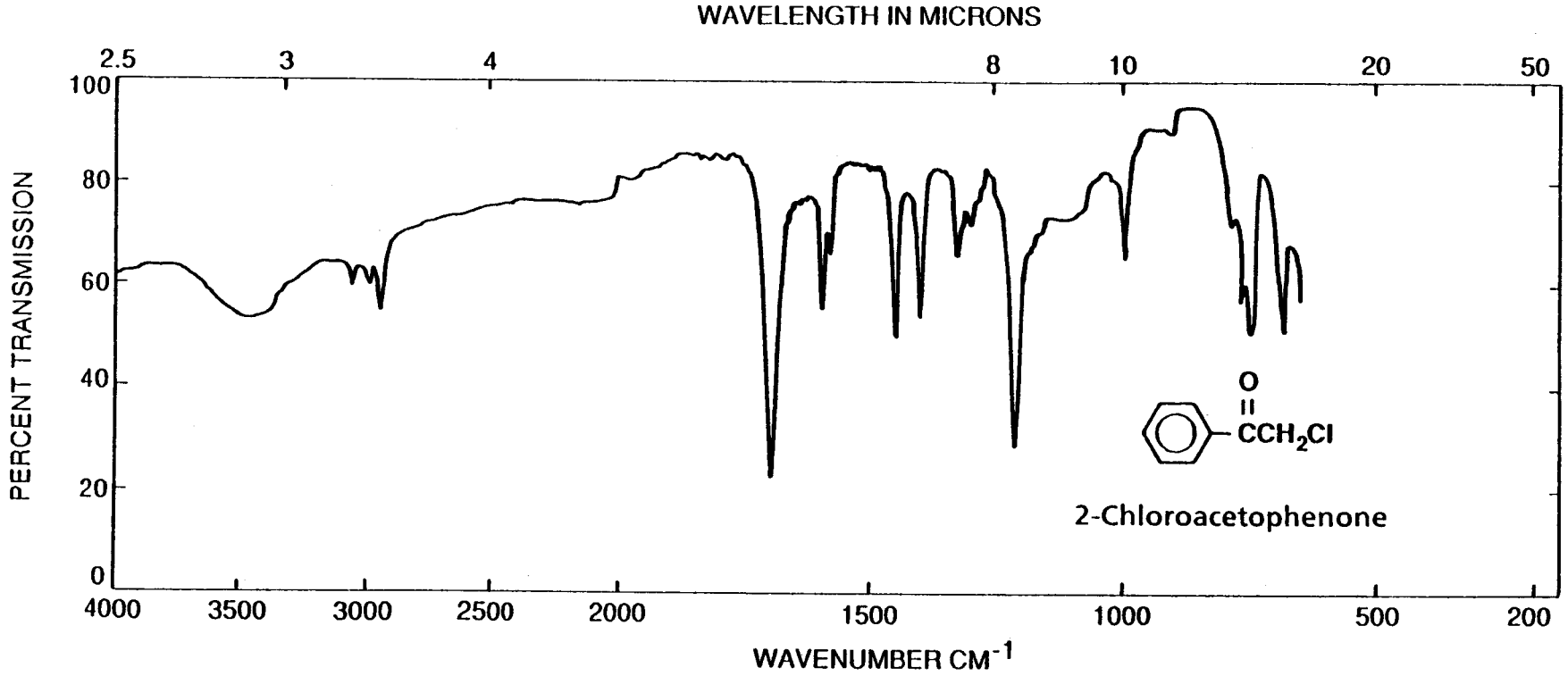


FIGURE H1. INFRARED ABSORPTION SPECTRUM OF 2-CHLOROACETOPHENONE (LOT NO. APG-30-MD)

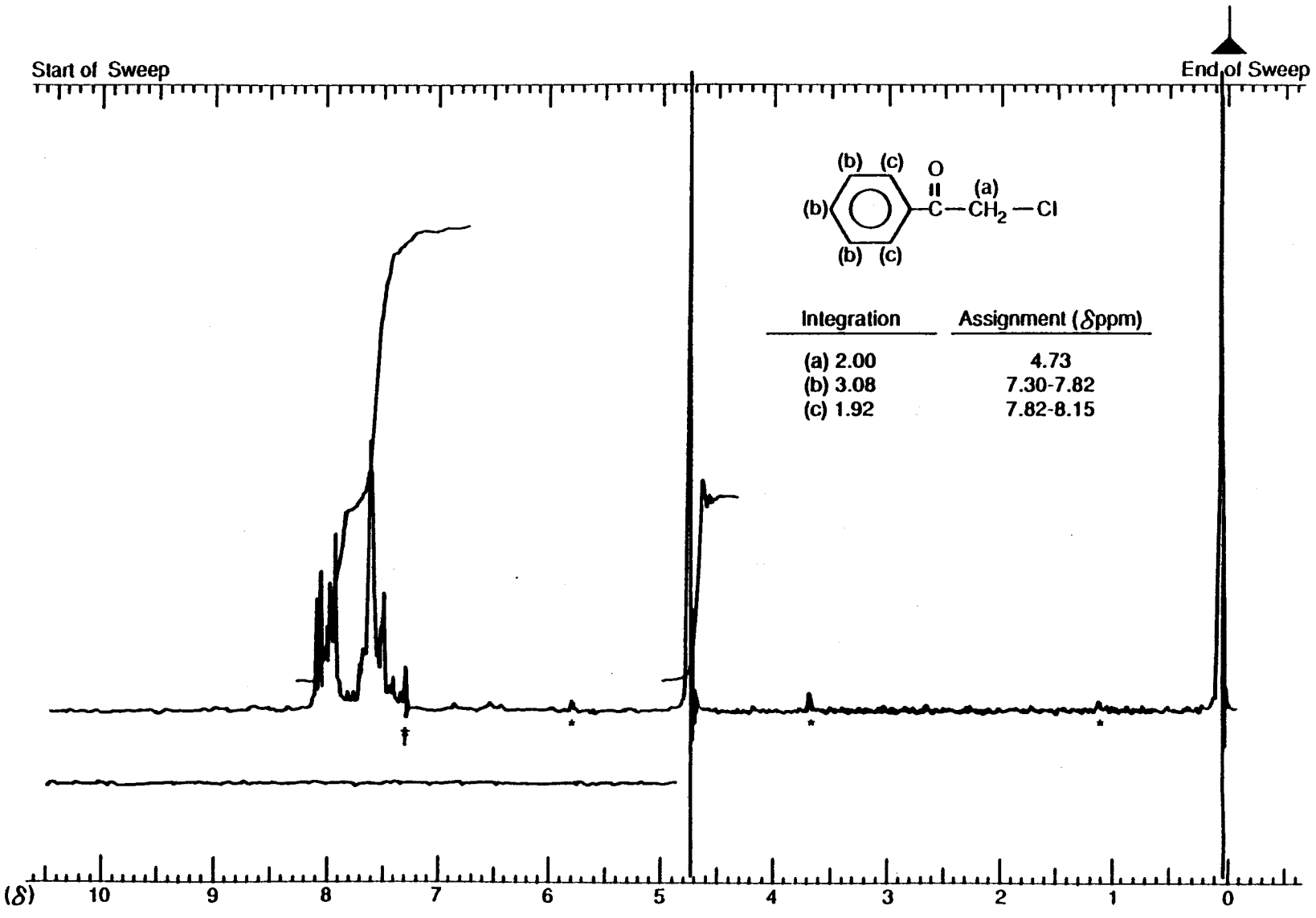


FIGURE H2. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF 2-CHLOROACETOPHENONE (LOT NO. APG-30-MD)

## 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 |

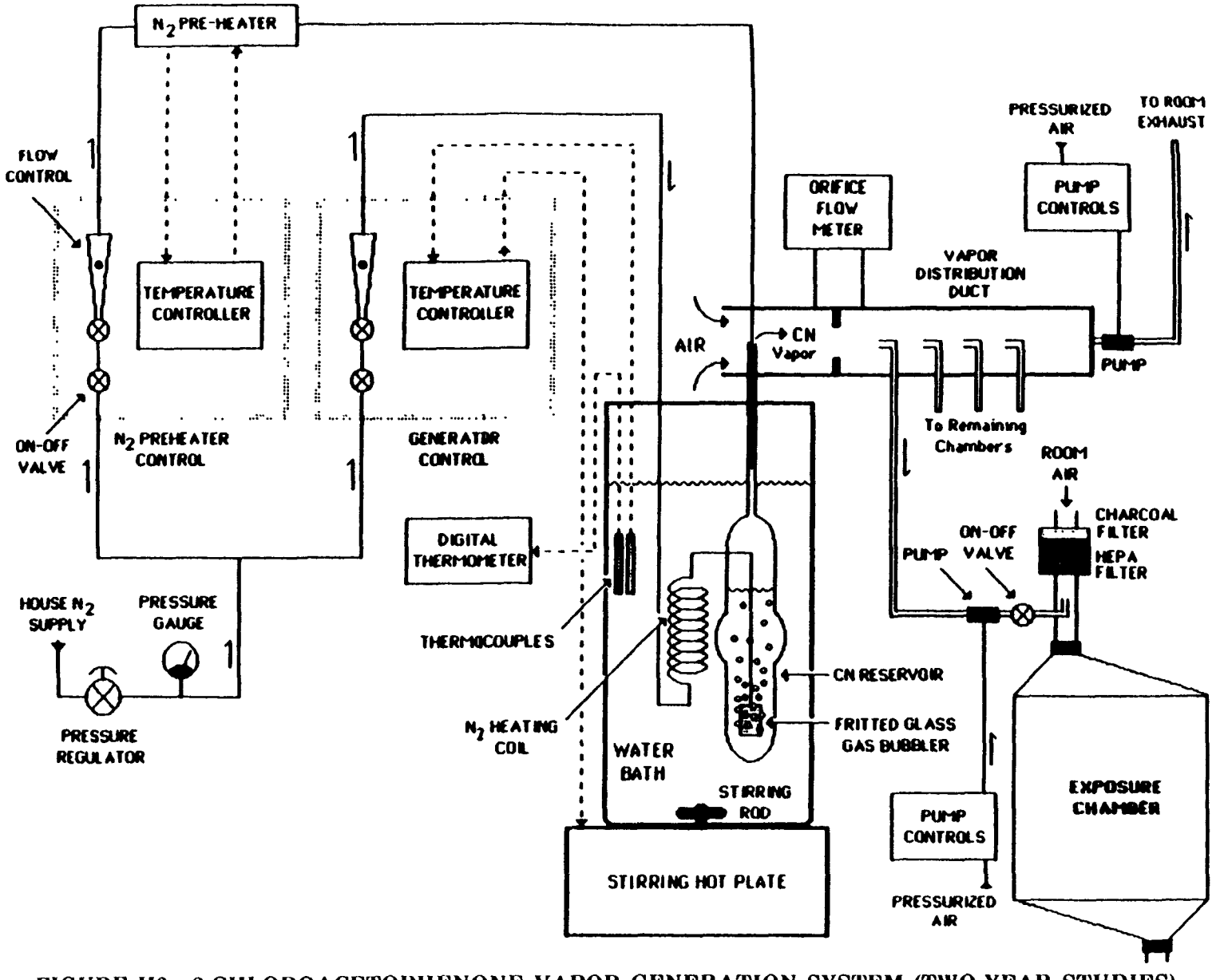


FIGURE H3. 2-CHLOROACETOPHENONE VAPOR GENERATION SYSTEM (TWO-YEAR STUDIES)

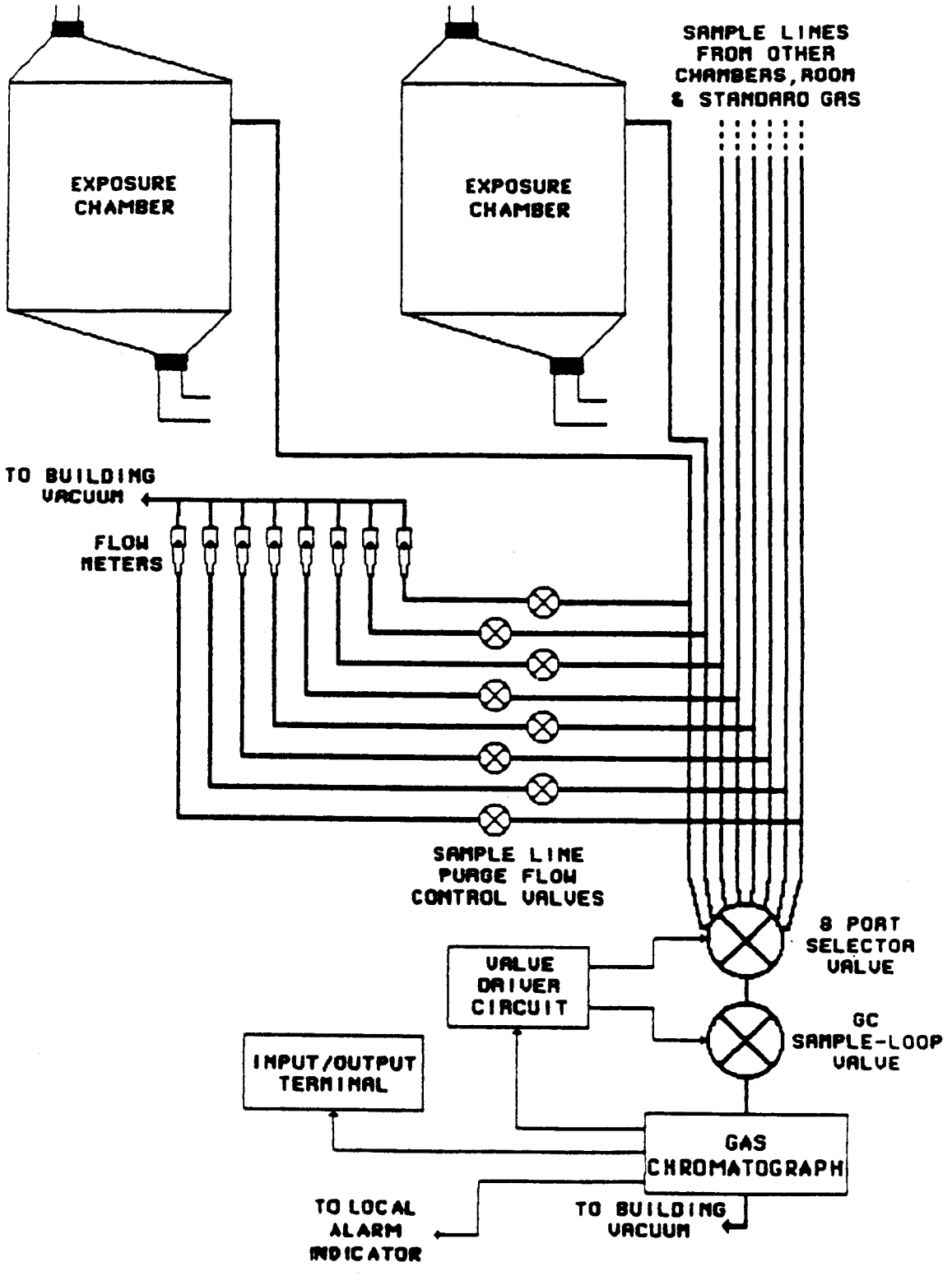


FIGURE H4. CHAMBER CONCENTRATION MONITORING SYSTEM

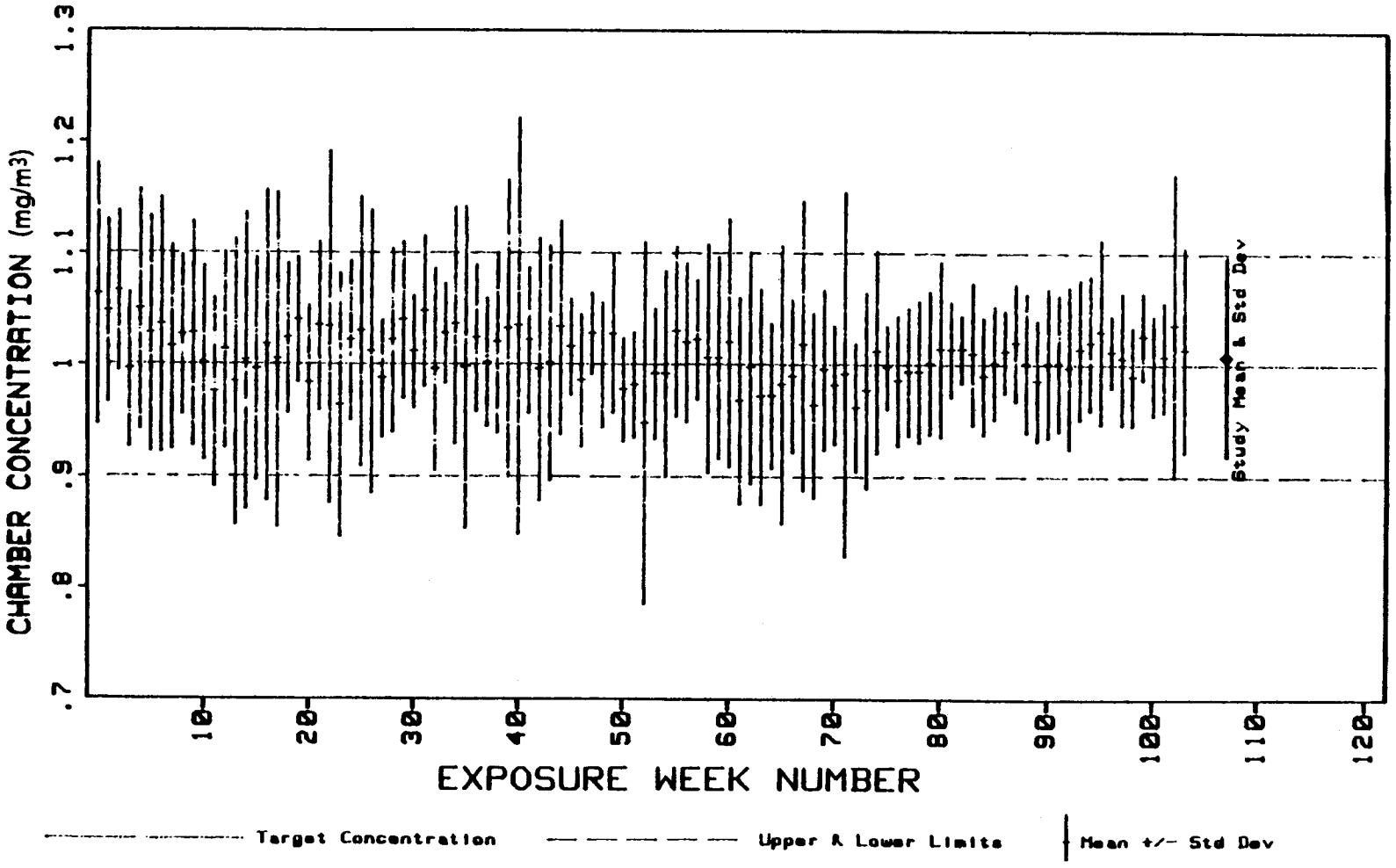


**FIGURE H5. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 1 mg/m$^3$ 2-CHLOROACETOPHENONE RAT EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES**

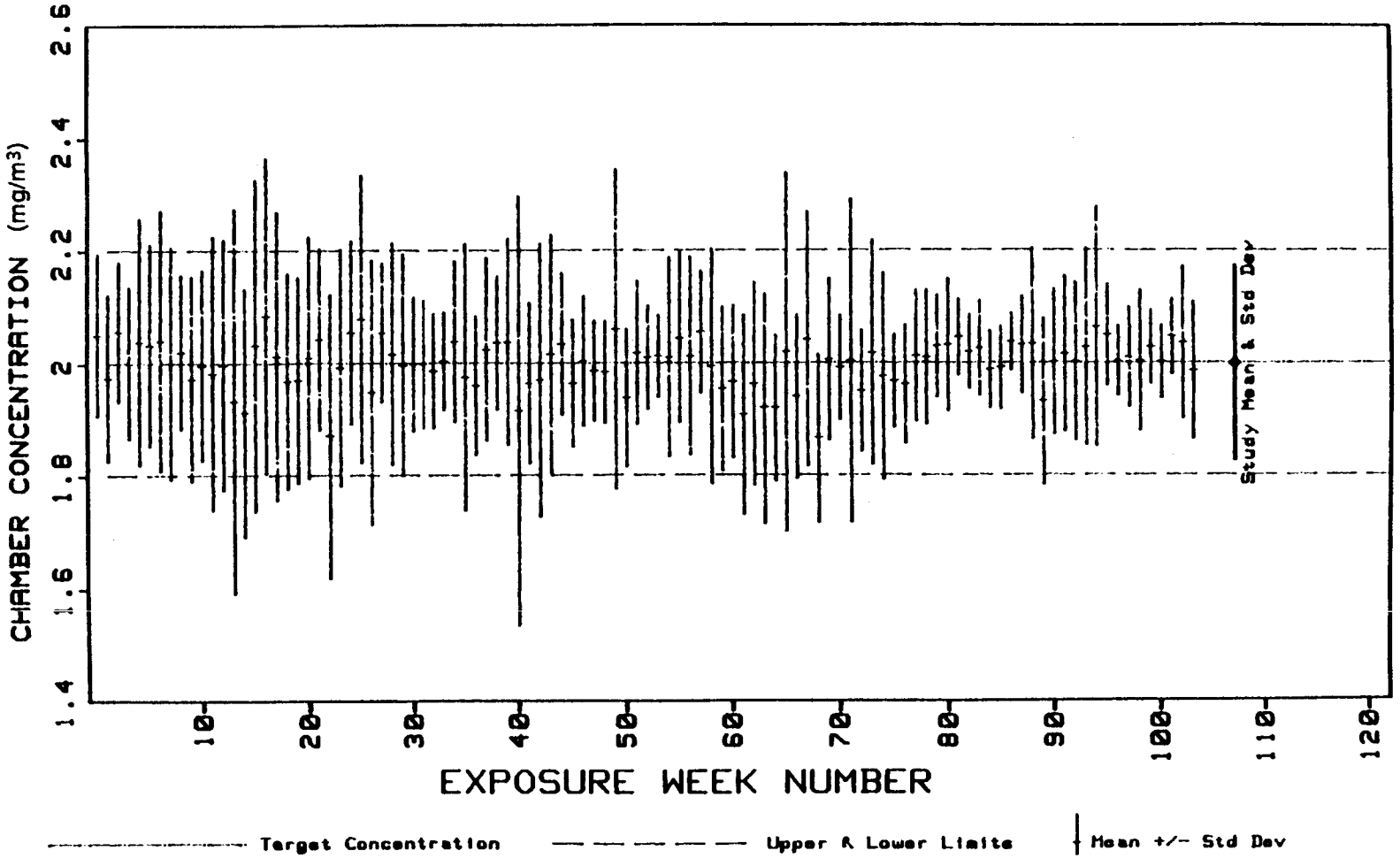


**FIGURE H6. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 2 mg/m³ 2-CHLOROACETOPHENONE RAT EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES**

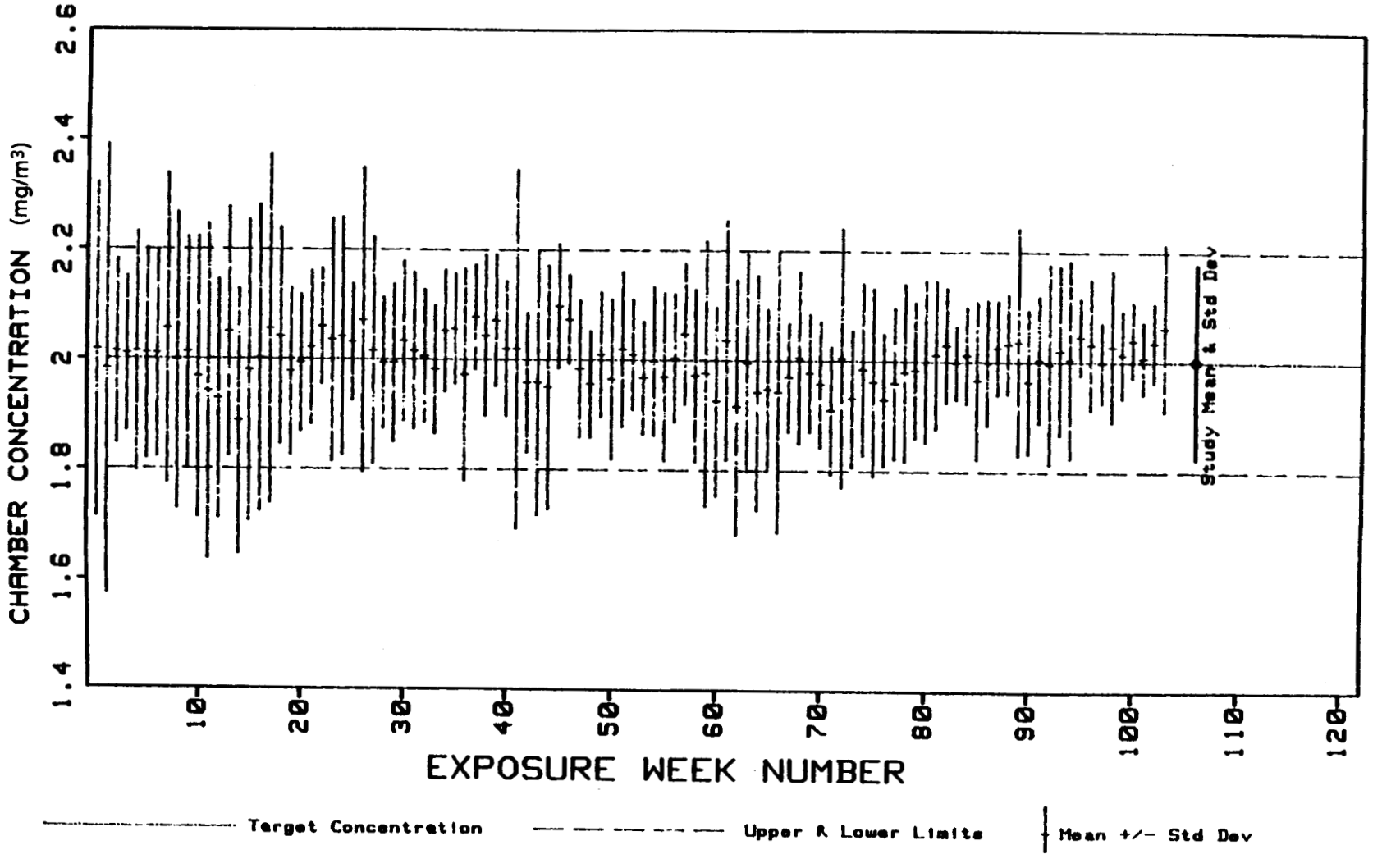


**FIGURE H7. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 2 mg/m$^3$ 2-CHLOROACETOPHENONE MOUSE EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES**

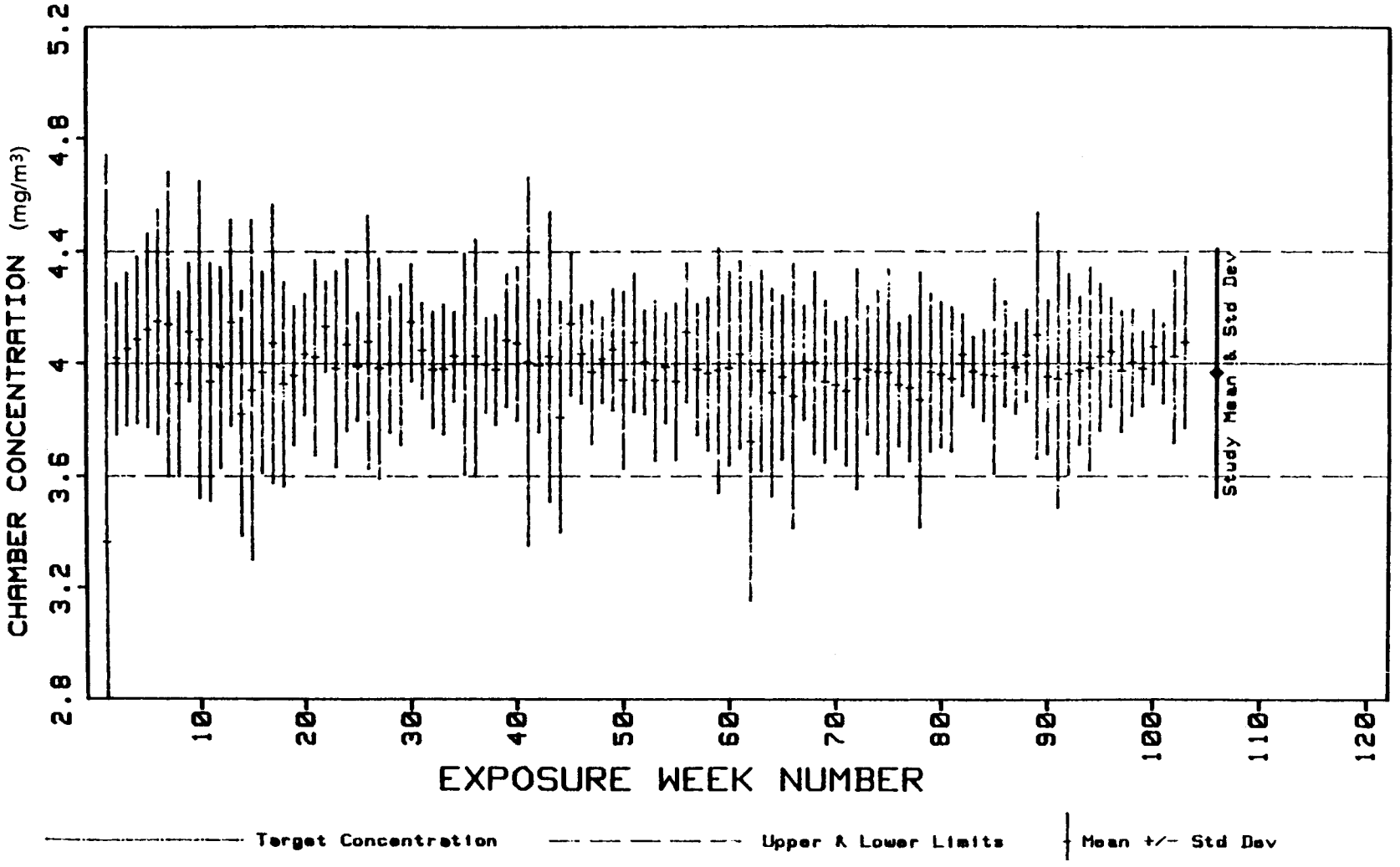


**FIGURE H8. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION IN THE 4 mg/m$^3$ 2-CHLOROACETOPHENONE MOUSE EXPOSURE CHAMBER FOR ENTIRE 2-YEAR STUDIES**

**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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