NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 255

TOXICOLOGY AND CARCINOGENESIS STUDIES OF 1,2-DICHLOROBENZENE (o-DICHLOROBENZENE)

(CAS NO. 95-50-1)

IN F344/N RATS AND B6C3F$_1$ MICE (GAVAGE STUDIES)

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

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of chemically induced disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is comprised of four charter DHHS agencies: the National Cancer Institute, National Institutes of Health; the National Institute of Environmental Health Sciences, National Institutes of Health; the National Center for Toxicological Research, Food and Drug Administration; and the National Institute for Occupational Safety and Health, Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP TECHNICAL REPORT
ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES OF 1,2-DICHLOROBENZENE (o-Dichlorobenzene)

(CAS NO. 95-50-1)

IN F344/N RATS AND B6C3F$_1$ MICE
(GAVAGE STUDIES)

NATIONAL TOXICOLOGY PROGRAM
Box 12233
Research Triangle Park
North Carolina 27709

October 1985

NTP TR 255
NIH Publication No. 86-2511

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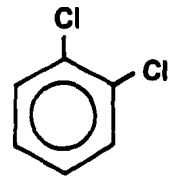
TOXICOLOGY AND CARCINOGENESIS STUDIES OF 1,2-DICHLOROBENZENE



1,2-DICHLOROBENZENE

CAS NO. 95-50-1
$C_6H_4Cl_2$ Mol. Wt. 147.01

ABSTRACT

In 13-week studies using F344/N rats and B6C3F$_1$ mice, 500 mg/kg of 1,2-dichlorobenzene (>99% pure) decreased survival in male and female mice and female rats when administered in corn oil by gavage five times per week. At this dose, 1,2-dichlorobenzene produced centrolobular necrosis of the liver, hepatocellular degeneration, and depletion of lymphocytes in the thymus and spleen of both sexes of rats and mice. At a dose of 250 mg/kg, necrosis of individual hepatocytes was observed in both sexes of rats and in male mice. Minimal hepatocellular necrosis was observed in a few rats at a dose of 125 mg/kg, but no hepatic alterations were observed in mice at this dose. Renal tubular degeneration was observed in male rats at 500 mg/kg, and multifocal mineralization of the myocardial fibers of the heart and skeletal muscle were seen in mice. The only hematologic changes considered notable were slight decreases in hemoglobin and hematocrit in the 500 mg/kg male and female rats and in red blood cell counts in the 500 mg/kg male rats; no other marked hematological changes were observed in either species.

Two-year toxicology and carcinogenesis studies of 1,2-dichlorobenzene were conducted by administering the test chemical in corn oil by gavage five times per week for 103 weeks to groups of 50 male and 50 female F344/N rats and B6C3F$_1$ mice at doses of 60 and 120 mg/kg. Groups of 50 rats and 50 mice of each sex received corn oil by gavage on the same schedule and served as vehicle controls.

Survivals of female rats, male mice, and female mice were comparable to those of the corresponding vehicle controls in the 2-year study, but survival of high dose male rats was ($P<0.001$) shorter than that of the vehicle controls. In this group there were three accidental deaths and five deaths probably due to the gavage process; in addition aspiration of 1,2-dichlorobenzene in corn oil into the lungs may have been a contributing factor to the deaths of 12 high dose male rats. The 120 mg/kg dose level of 1,2-dichlorobenzene did not affect body weight in rats or mice of either sex or survival of mice or female rats. An increase in tubular regeneration in the kidney of high dose male mice was observed in the 2-year study (control, 8/48, 17%; low dose, 12/50, 24%; high dose, 17/49, 35%). No other compound-related nonneoplastic histological lesions were noted in the 2-year study.

The incidence of pheochromocytoma of the adrenal gland in low dose male rats was elevated ($P<0.05$, life table test) relative to controls (9/50, 16/50, 6/49). However, the incidence in the high dose group was lower than that of the controls and the dose-response trend was not statistically significant. Therefore, the increase in pheochromocytoma in the low dose male rats is not regarded as related to administration of 1,2-dichlorobenzene.

A dose-related increase ($P<0.05$) in malignant histiocytic lymphoma was observed in male mice (control, 0/50, 0%; low dose, 1/50, 2%; high dose, 4/50, 8%) and in female mice (0/49, 0%; 0/50, 0%; 3/49, 6%); however, comparisons of the numbers of animals with all types of lymphomas is considered to be a more appropriate comparison. 1,2-Dichlorobenzene did not increase the incidence of all types of lymphomas (combined) in male mice (8/50, 16%; 2/50, 4%; 4/50, 8%) or female mice (11/49, 22%; 11/50, 22%; 13/49, 27%). Therefore, the increase in histiocytic lymphomas was discounted.

Under the conditions of these two-year gavage studies, there was no evidence of carcinogenicity of 1,2-dichlorobenzene for male or female F344/N rats or B6C3F$_1$ mice receiving 60 or 120 mg/kg per day.

CONTRIBUTORS

These carcinogenesis studies were conducted at Battelle Columbus Laboratories under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The 2-year studies were begun in February 1979 and ended in March 1981.

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SUMMARY OF PEER REVIEW COMMENTS ON THE TOXICOLOGY AND CARCINOGENESIS STUDIES OF 1,2-DICHLOROBENZENE

On 22 September 1982 the draft Technical Report on the toxicology and carcinogenesis studies of 1,2-dichlorobenzene underwent peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. This public review meeting began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina. The following precis represents the critiques made by the principal reviewers, as well as comments from and discussion by the Peer Review Panel, NTP staff, and attendees.

Dr. Scala, a principal reviewer for the technical report on the carcinogenesis studies of 1,2-dichlorobenzene, agreed with the conclusions. He opined that the estimated maximum tolerated dose must have been nearly achieved, and that there was a likely risk of significant liver and/or kidney damage at higher doses. A discussion followed on whether or not an MTD had been achieved. Dr. Holland said the statement in the conclusion should be stricken, while Dr. Swenberg said the survival curve, particularly for male rats, indicated an MTD had been reached. NTP agreed to remove the comment on MTD from the conclusion. Dr. Scala called attention to the variable survival rates between the two 14-day studies in mice.

As a second principal reviewer, Dr. Whittemore agreed with the conclusions as stated. She said the survival differences in mice between the two 14-day studies deserved more comment [page 33]. She noted a dose-related trend in kidney tubular regeneration in male mice and asked about the biological significance. There was discussion about the degree and significance of porphyria or porphyrin excretion observed in the 13-week studies. Dr. Vore asked that a statement be included in the report about the apparent increase in porphyrin excretion in female rats [page 28].

Dr. Scala moved that the report on the carcinogenesis studies of 1,2-dichlorobenzene be accepted with the revisions discussed. Dr. Vore seconded the motion and the technical report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

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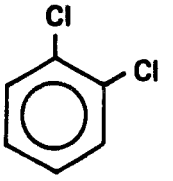

1,2-DICHLOROBENZENE

CAS NO. 95-50-1
$C_6H_4Cl_2$ Mol. Wt. 147.01

The major use of 1,2-dichlorobenzene (*o*-dichlorobenzene) is as an intermediate in the synthesis of several organic compounds (e.g., 3,4-dichloroaniline) and in the synthesis of the herbicides propanil, diuron, and neburon (Fishbein, 1979). It is used as an industrial solvent for toluene diisocyanate, an additive to degreasing agents, a heat-exchange medium, a deodorant for garbage and sewage, an ingredient in paint removers, an engine cleaner and de-inking solvent, and a solvent and intermediate in dye manufacture (Fishbein, 1979; IARC, 1982; Colour Index, 1971; Merck, 1976; Clayton and Clayton, 1981). 1,2-Dichlorobenzene is also used as an insecticide and a fumigant to control peach tree borers, bark beetles, grubs, and termites and to kill mites and other insects in poultry houses and animal sleeping quarters. Because of its properties as both an insecticide and a solvent, 1,2-dichlorobenzene has been used in low-pressure aerosol formulations of insecticides (Kirk-Othmer, 1981; Farm Chemicals Handbook, 1977). Approximately 49 million pounds of 1,2-dichlorobenzene were produced in the United States in 1980 (USITC, 1981). First reported commercial production began in 1921 (U.S. Tariff Commission, 1922).

1,2-Dichlorobenzene has been identified in the drinking water of various cities in the United States (Dowty et al., 1975; Kavlock et al., 1979). Because of the volatility of this compound, the primary route of occupational exposure is inhalation. The Occupational Safety and Health Administration set 50 ppm as the highest acceptable time-weighted average (TWA) concentration for an 8-hour exposure in a 40-hour work-week (OSHA, 1980).

The ability of animals to metabolize chlorinated benzenes appears to decrease as the number of chlorine atoms increases (Matthews, 1982). 1,2-Dichlorobenzene is metabolized and excreted rapidly. In the rabbit, the metabolites of 1,2-dichlorobenzene are 2,3- and 3,4-dichlorophenol, 3,4-dichlorophenylmercapturic acid, and 3,4- and 4,5-dichlorocatechol (Azouz et al., 1955). 3,4-Dichlorophenol is the major phenol produced. The presence of catechol and mercapturic acid metabolites suggests the possibility of an epoxide intermediate. In this species, the excretion of metabolites appears to be complete 6 days after oral dosing. In the Sprague-Dawley rat, 42% of the dose is excreted as urinary metabolites in 24 hours (Reid and Krishna, 1973).

Chlorobenzene, bromobenzene, iodobenzene, and 1,2-dichlorobenzene, administered to rats as single intraperitoneal doses, bind covalently to liver protein and produce centrilobular necrosis (Reid and Krishna, 1973; Brodie et al., 1971). In contrast, 1,4-dichlorobenzene, which is metabolized and excreted more slowly than mono- and 1,2-dichlorobenzene, is not hepatotoxic and does not bind covalently to liver protein.

Hepatic necrosis occurred in Sprague-Dawley rats within 24 hours after a single injection of

approximately 216 mg/kg of 1,2-dichlorobenzene. The centrilobular necrosis was accentuated by pretreatment with chemicals that increase hepatic drug metabolizing enzymes (Reid and Krishna, 1973). These data suggest that the hepatic necrosis produced by these chemicals is mediated by an active epoxide (Brodie et al., 1971). 1,4-Dichlorobenzene is not metabolized to catechols or mercapturic acid (Azouz et al., 1955) and is less hepatotoxic than 1,2-dichlorobenzene (Reid and Krishna, 1973); both findings support this hypothesis. 1,2-Dichlorobenzene has also been shown to bind covalently to kidney protein and to produce necrosis of the proximal convoluted tubules within 24 hours after an intraperitoneal injection to male Sprague-Dawley rats.

The oral LD50 value for 1,2-dichlorobenzene in rats has been reported as 500 mg/kg by Ben-Dyke et al. (1970) and as 2,138 mg/kg by Varshavskaya (1966) (strain and sex unspecified in both studies). This four-fold difference might be explained by knowing the strain and sex used in these studies.

Hollingsworth et al. (1958) administered oral doses of 18.8, 188, or 376 mg/kg of 1,2-dichlorobenzene to groups of 10 young female rats (strain not specified) 5 days per week for 27.4 weeks. None of these doses affected weight gain or mortality. However, the 376 mg/kg dose caused a significant increase in liver weight, an increase in kidney weight, and a decrease in spleen weight. Microscopic examination of the liver showed slight to moderate cloudy swelling. Hematologic and bone marrow values were reported to be normal. Significant increases in liver and kidney weights were also reported at 188 mg/kg, but no changes were found at 18.8 mg/kg.

Two inhalation experiments were also performed by Hollingsworth et al. (1958). In the first, 1,2-dichlorobenzene was administered to rats for 1-10 hours at concentrations of 539, 821, 941, or 977 ppm. A 10-hour exposure to 977 ppm killed all animals tested. Some deaths were observed during a 7-hour exposure to 977 ppm, a 7-, 4-, or 2-hour exposure to 941 ppm, and a 7-hour exposure to 821 ppm. At 539 ppm for 7 hours, no animals died. However, animals exposed to 539 ppm for 3 or 6.5 hours and killed 1 or 3 days later showed marked centrolobular necrosis of the liver and cloudy swelling of the kidney tubular epithelium. During exposure, rats exhibited drowsiness, unsteadiness, eye irritation, difficulty in breathing, and anesthesia. In a second inhalation experiment, exposure to 93 ppm 1,2-dichlorobenzene 7 hours a day, 5 days per week for 6-7 months produced a marked decrease in the body weight of male rats but not of female rats or guinea pigs. There were no other marked effects in rats, monkeys, rabbits, or guinea pigs as determined by histological examination of the organs, examination of behavior, hematological evaluation, or urinalysis. Based on these results, Hollingsworth recommended that the vapor concentration of 1,2-dichlorobenzene be maintained below 75 ppm in the industrial setting.

1,2-Dichlorobenzene has been produced commercially in the United States since at least 1921 (U.S. Tariff Commission, 1922). Hollingsworth et al. (1958) reported that there was no evidence of organic disease or hematological alterations in men who had been exposed industrially to air containing 1,2-dichlorobenzene at concentrations of 1 to 44 ppm (average of 15 ppm) for an unspecified number of years. Factory workers exposed to higher concentrations of 1,2-dichlorobenzene (65-100 ppm) reported irritation of the eyes and respiratory tract (Elkins, 1950).

A few epidemiological reports indicate a possible association of blood disorders with exposure to dichlorobenzenes. Gadrat et al. (1962) reported an incident of acute hemolytic anemia in an 18-year old woman who had been exposed for 6 months to a dry cleaning solvent containing 1,2-dichlorobenzene. Although the authors attributed the anemia to an idiosyncratic reaction to 1,2-dichlorobenzene, the woman was also exposed to "white spirit," an undefined mixture of aliphatic and aromatic hydrocarbons. Another report containing case histories of five patients with blood disorders suggested a possible association between leukemia and exposure to dichlorobenzenes (Girard et al., 1969). The authors reported two incidents of chronic lymphatic leukemia, two of myeloblastic leukemia, and one of myeloproliferative syndrome in patients with previous exposure to dichlorobenzenes. One of the subjects with chronic lymphatic leukemia had been exposed for 16 years to a glue containing 2% 1,2-dichlorobenzene. The other had been exposed for 10 years to a solvent containing 80% 1,2-dichlorobenzene. Myeloblastic leukemia occurred in a 55-year-old woman who had cleaned clothes for several years with 1-2 liters per year of the same solvent and in a 15-year old girl who had removed stains from her own clothes for a period of time with a solution containing 37% 1,2-dichlorobenzene. No evidence of benzene exposure was found in any of these

cases. The authors were unable to conclude that the chlorinated benzenes were the causative agents for these blood disorders, but suggested that workers exposed to these solvents should be carefully monitored. The International Agency for Research on Cancer (1982) considered these data inadequate to evaluate the carcinogenicity of 1,2-dichlorobenzene for humans.

Another chlorinated benzene, hexachlorobenzene, was responsible for an outbreak of porphyria cutanea tarda in approximately 3,000 people in Turkey in 1956 (Cam and Nigogosyan, 1963). The symptoms of the disease included cutaneous lesions, neurological manifestations, and excretion of large amounts of porphyrins in the urine. The porphyrinuria can be reproduced in rats (Ockner and Schmid, 1961). Rimington and Ziegler (1963) reported that large doses of a number of other chlorinated benzenes including 1,2-dichlorobenzene (455 mg/kg/day for 15 days) also produced porphyrinuria in rats. However, recent work has shown that, although hexachlorobenzene causes porphyria in female rats at dietary concentrations as low as 50 ppm (Carlson, 1977), dietary concentrations of 50-200 ppm 1,4-dichlorobenzene and 1,2,4-trichlorobenzene did not produce hepatic porphyria. Moreover, pentachlorobenzene did not affect tissue or urinary porphyrins at doses as high as 1,000 ppm in the diet (Linder et al., 1980). Therefore, although hexachlorobenzene is clearly porphyrogenic, there is less evidence that other chlorinated benzenes cause porphyria.

1,2-Dichlorobenzene did not produce point mutations in *Salmonella typhimurium* when tested at unspecified concentrations without activation (Anderson et al., 1972). A preliminary report indicated that it was also inactive with and without activation by Aroclor 1254® induced rat liver microsomes in *S. typhimurium* strains TA98, TA100, TA1535, and TA1537 at unspecified doses (Lawlor and Haworth, 1979). These negative findings are supported by recent NTP studies described in Appendix I, (Tables I1-I4). In the NTP studies, 1,2-dichlorobenzene was negative in *S. typhimurium* strains TA98, TA100, TA1535, and TA1537 when tested with and without metabolic activation by Aroclor 1254® induced Sprague-Dawley rat and Syrian hamster liver 9,000 g supernatant fractions at doses as high as 333 μg/plate. No published information on the teratogenicity or reproductive effects of 1,2-dichlorobenzene was found.

No studies of the carcinogenicity of 1,2-dichlorobenzene have been reported in the literature. IARC (1982) evaluated the available oral and inhalation data on 1,2-dichlorobenzene in rodents (Hollingsworth, 1958) and considered the studies to be too short in duration and to involve too few animals to be of significance in evaluating the possible carcinogenicity of this compound.

Another chlorinated benzene derivative, monochlorobenzene, was tested for toxic and carcinogenic potential by gavage administration to male and female rats and mice at doses up to 750 mg/kg body weight/day for 13 weeks, and at doses up to 120 mg/kg/day (high dose of 60 mg/kg/day for male mice) for 103 weeks (NTP, 1983). In the 13 week study, doses of 250-750 mg/kg/day caused death, hepatocellular necrosis, renal tubular injury, thymic necrosis, or lymphoid or myeloid depletion of the bone marrow, spleen, or thymus in both rats and mice. The dose of 120 mg/kg/day in the 103-week studies caused an increased incidence of neoplastic nodules of the liver in male rats. Increased tumor incidences associated with long term chlorobenzene treatment were not observed in the female rats or in male or female mice. No other toxic lesions attributed to chlorobenzene were detected in the 103-week studies.

The NTP is currently conducting two year toxicology and carcinogenesis studies of benzene in male and female F344 rats and B6C3F$_1$ mice at doses of 0 (control), 25 (male and female mice, female rats), and 50, 100, or 200 (male rats only) mg/kg/day by gavage. A report is expected to be published in 1984.

1,2-Dichlorobenzene was tested because of its extensive production and use and the absence of previous tests to determine its carcinogenic potential. The 13-week studies were expanded to include hematological evaluation of the animals because of the few reports suggesting that human exposure to 1,2-dichlorobenzene might be associated with hematological disorders, including leukemia (Gadrat et al., 1962; Girard et al., 1969). Clinical chemistry and urinary porphyrin values were obtained to assess the effects of this chemical on the liver and kidney and to assess the potential of the chemical to produce hepatic porphyria.

II. MATERIALS AND METHODS

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THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

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Source and Specifications of Test Animals

Animal Maintenance

Clinical Examinations and Pathology

Data Recording and Statistical Methods

CHEMICAL ANALYSES

1,2-Dichlorobenzene (>99% pure) was obtained from ICC Solvent Chemical Company (New York, NY) in one batch (Lot No. SC61377). Purity and identity analyses were conducted at Midwest Research Institute. Results of elemental analyses agreed with theoretical values (Appendix K). Acidic components (assumed to be hydrochloric acid) were found to be present at a concentration of 10.8 ppm. One gas chromatography system detected seven impurities with areas totalling less than 0.07% of the major peak area. Two other systems detected one impurity with an area that was approximately 0.7% of the major peak area; this impurity, identified as 1,4-dichlorobenzene by gas chromatography/mass spectrometry and by gas chromatographic retention time, was determined to be present in the 1,2-dichlorobenzene at 0.84% ± 0.05% (v/v) by quantitation against standards. Infrared, ultraviolet, and nuclear magnetic resonance spectra were consistent with those in the literature.

The bulk chemical was stored at 22°C in the dark. Results of periodic reanalyses of the bulk 1,2-dichlorobenzene at Battelle Columbus Laboratories by gas chromatography and infrared spectroscopy showed no notable change in the test material, indicating that these storage conditions were satisfactory over the course of these studies.

DOSAGE PREPARATION

The high dose stock solution was prepared by adding a weighed amount of 1,2-dichlorobenzene to the appropriate volume of corn oil and mixing them for 15 minutes in a graduated cylinder equipped with a stirring bar. Other dose solutions were prepared by diluting the high dose stock solution with corn oil.

1,2-Dichlorobenzene in corn oil was found to be stable for 7 days at room temperature (Appendix L). Once formulated, solutions were stored for no longer than 14 days (at 4°C until the day of first use and thereafter at room temperature). All formulated solutions whose concentrations were analyzed conformed to specifications (Appendix M).

FOURTEEN-DAY STUDIES

No single-dose study was performed. In the 14-day studies, 4-week-old male and female F344/N rats and 5-week-old B6C3F$_1$ (C57BL/6N × C3H/HeN MTV-) mice were obtained from Harlan Industries (Indianapolis, IN) and held for 2 weeks before the studies began. Rats were assigned to cages according to a table of random numbers. The cages were then assigned to groups according to another table of random numbers.

Groups of five male and five female rats received 1,2-dichlorobenzene in corn oil by gavage at doses of 0, 60, 125, 250, 500, or 1,000 mg/kg body weight daily for 14 consecutive days and were killed on day 20. Two studies with mice were conducted. In the first study, groups of five males and five females received 14 consecutive daily doses of 0, 250, 500, 1,000, 2,000, or 4,000 mg/kg 1,2-dichlorobenzene in corn oil by gavage and were killed on day 16. In the second study, groups of five males and five females received doses of 0, 30, 60, 125, 250, or 500 mg/kg on the same schedule.

The rats and mice were observed twice daily for mortality and were weighed weekly. Further details of animal maintenance are presented in Table 1. Necropsies were performed on all animals. Tissues from two male and two female rats in the highest surviving dose group were examined histologically. In the first mouse study, livers from one female at 1,000 mg/kg and three male and three female mice at 500 mg/kg were examined microscopically. In the second study, livers from four males and four females were examined microscopically.

THIRTEEN-WEEK STUDIES

Thirteen-week studies were conducted to evaluate the toxicity of 1,2-dichlorobenzene and to determine the doses of test chemical to be used in the 2-year studies.

Four-week-old male and female F344/N rats and 6-week-old male and female B6C3F$_1$ mice were obtained from Harlan Industries, observed for 2 weeks, and then assigned to cages according to a table of random numbers. Cages were then assigned to test groups according to another table of random numbers.

Groups of 10 rats and 10 mice of each sex were administered 1,2-dichlorobenzene in corn oil by gavage, 5 days per week for 13 weeks, at doses of 0, 30, 60, 125, 250, or 500 mg/kg. Diets and water were available *ad libitum*.

Animals were checked for mortality and signs of morbidity twice daily. Moribund animals were killed and necropsies were performed. Each animal was given a weekly clinical examination, including palpation for tissue masses or swelling. Body weight data were collected once per week. Further details of animal maintenance are presented in Table 1.

One week before the rats and mice were killed, animals from the control and 500 mg/kg groups were placed in metabolism cages and urine was collected for 24 hours. The urine was analyzed for urinary uroporphyrins and coproporphyrins (Appendix N).

One day before the animals were killed, blood was withdrawn from the orbital venous plexus of all rats and mice and analyzed for hemoglobin, hematocrit, total and differential white blood cell count, red blood cell count, mean corpuscular volume, platelet count, and reticulocyte count on the day of collection (Appendix E). On the day the animals were killed, they were anesthetized with sodium pentobarbital and blood samples were withdrawn by cardiac puncture. Serum was stored at -20°C prior to analysis for alkaline phosphatase, serum glutamic pyruvic transaminase (SGPT), gamma-glutamyltranspeptidase (GGTP) on mice; and these plus bilirubin, cholesterol, triglycerides, blood urea nitrogen, glucose, total protein, and total globulin fractions on rats. The methodology for these analyses is described in Appendix J. Alpha$_1$ and alpha$_2$ globulin fractions were combined because of the low concentrations present. Liver samples were analyzed for total porphyrin content by the method of Abritti and DeMatteis (1971-1972).

Necropsies were performed on all animals not completely autolyzed or cannibalized. Organ weights were taken for the lungs, heart, liver, spleen, thymus, right kidney, brain, right testicle, right ovary, and uterus. The following specimens were examined histologically for control and high dose groups: gross lesions, tissue masses, abnormal lymph nodes, skin, thigh muscle, mandibular or mesenteric lymph nodes, mammary gland, salivary gland, bone marrow, sternebrae, femur, or vertebrae, thymus, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, small intestine, colon, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, prostate/testes or ovaries/uterus, brain, and pituitary. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

Additional histopathologic examinations were limited to the kidneys, thymus, and liver for rats administered 125 or 250 mg/kg; to the thymus, liver, spleen, heart, and thigh muscle for mice administered 250 mg/kg; and to the liver for mice administered 125 mg/kg.

TWO-YEAR STUDIES

Study Design

Groups of 50 rats and 50 mice of each sex were administered 1,2-dichlorobenzene in corn oil by gavage at doses of 0, 60, or 120 mg/kg body weight. Doses were administered 5 days per week for 103 weeks.

Source and Specifications of Test Animals

Four-week-old male and female F344/N rats and 4.5-week-old male and female B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories (Portage, MI), observed for 17-18

days, and then assigned to cages according to a table of random numbers. The cages were then assigned to control and dosed groups according to another table of random numbers.

A quality control skin grafting program to monitor the genetic integrity of inbred mice used to produce the hybrid B6C3F· test animal has been in effect since early 1978. In mid-1981, data were obtained showing incompatibility between the NIH C3H reference colony and the C3H colony from Charles River. In August, 1981, inbred parental lines of mice were further tested for genetic homogenity via isozyme and protein electrophoregrams which demonstrate phenotypic expressions of known genetic loci.

The C57BL/6 mice were homogeneous at all loci tested. Eighty-five percent of the C3H mice monitored were variant at one to three loci, indicating some heterogeneity in the C3H line from this supplier. Nevertheless, the genome of this line is more homogeneous than those of randomly bred stocks. The $B6C3F_1$ mice used in these studies were the offspring of males obtained from the Charles River C3H colony. The influence of the potential genetic nonuniformity in the hybrid mice on the study results is not known. However, the studies are considered to be valid since matched, concurrent controls were included in the study.

Animal Maintenance

Rats and mice were housed five per cage. Feed and water were available *ad libitum*. The temperature in the animal rooms was 20°-26°C and the humidity was 40%-60%. Fifteen changes of room air per hour were provided. Fluorescent lighting provided illumination 12 hours per day. Further details of animal maintenance are provided in Table 1.

Clinical Examinations and Pathology

All animals were observed twice daily for signs of morbidity or mortality. Clinical signs were recorded intermittently until month 18 and at monthly intervals thereafter. Body weights by cage were recorded every week for the first 13 weeks and monthly thereafter. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. Moribund animals and animals that survived to the end of the bioassay were killed with carbon dioxide and necropsies were performed.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph nodes, skin, mandibular or mesenteric lymph nodes, mammary gland, salivary gland, bone marrow, sternebrae, femur or vertebrae, thymus, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, small intestine, colon, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, prostate/testes or ovaries/uterus, brain, and pituitary. Eyes, thigh muscle, and spinal cord were examined grossly at necropsy but were examined microscopically only if they were found to be grossly abnormal.

Necropsies were performed on all animals unless precluded in whole or in part by autolysis or cannibalization. Undamaged tissues were saved from those animals on which total necropsies were performed. The number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

Neoplastic nodules were classified according to the recommendations of Squire and Levitt (1975) and the National Academy of Sciences (1980). When the pathology examination was completed, the slides, individual animal data records, and summary tables were sent to an independent quality assurance laboratory. Individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechniques were evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10% of the animals were evaluated by an experienced rodent pathologist. Slides of all target tissues and any other slides about which the original and quality assurance pathologist disagreed were submitted to the Chairperson of the Pathology Working Group (PWG) for evaluation. Representative slides selected by the PWG Chairperson were reviewed blindly by the PWG's experienced rodent pathologists, who reached a consensus and compared their findings with the original diagnoses. When conflicts were found, the PWG sent the appropriate slides and their comments to the original pathologist for review. (This procedure has been described, in part, by Maronpot and Boorman, 1982.) The final diagnosis represents a consensus of contractor pathologists and the NTP Pathology Working Group.

Data Recording and Statistical Methods

Data from this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Urinary volumes in dosed versus control rats in the 13-week study were analyzed by the Wilcoxon Rank Sum test (Lehman, 1975). Hematologic data, clinical chemistry data, and organ weights were analyzed for a dose-related effect using simple linear regression (Chatterjee and Brice, 1977). Values for dosed groups were compared with those of the controls by the multiple comparison procedure of Gabriel (1978).

Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time that they died from other than natural causes or were found to be missing; animals dying from natural causes were not statistically 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) extensions of Cox's methods for testing for a dose-related trend. All the reported P values for the survival analyses are two-sided.

The incidence of neoplastic or nonneoplastic lesions has been 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 included only those animals for which that site was examined histologically. However, when lesions were detectable grossly (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 necropsies were performed.

For the statistical analysis of tumor incidence data, two different methods of adjusting for intercurrent mortality were employed. Each used the classical method for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high- and low-dose groups with controls and tests for overall dose-response trends.

The first method of analysis (life table test) assumed that all tumors of a given type observed in animals dying before the end of the study were "fatal"; i.e., they either directly or indirectly caused the death of the animal. According to this approach, the proportions of tumor-bearing animals in the dosed and control groups were compared at each point in time at which an animal died with a tumor of interest. The denominators of these proportions were the total number of animals at risk in each group. These results, including the data from animals killed at the end of the study, were then combined by the Mantel-Haenszel method to obtain an overall P-value. This method of adjusting for intercurrent mortality is the life table method of Cox (1972) and of Tarone (1975).

The second method of analysis (incidental tumor test) assumed that all tumors of a given type observed in animals dying before the end of the study were "incidental"; i.e., they were merely observed at autopsy in animals dying of an unrelated cause. According to this approach, the proportions of animals found to have tumors in dosed and control groups were compared in each of five time intervals: 0-52 weeks, 53-78 weeks, 79-82 weeks, 93 weeks to the week before the terminal kill, and the terminal kill period. The denominators of these proportions were the number of animals on which autopsies were performed during the time interval. The individual time interval comparisons were then combined by the previously described methods to obtain a single overall result. (See Peto et al., 1980, for the computational details of both methods.)

In addition to these tests, one other set of statistical analyses was carried out and reported in the tables analyzing primary tumors: the Fisher's exact test for pairwise comparisons and Cochran-Armitage linear trend test for dose-response trends (Armitage, 1971; Gart et al., 1979). These tests were based on the overall proportion of tumor-bearing animals. All reported P values for tumor incidence analyses are one-sided.

For studies in which there is little effect of compound administration on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death.

TABLE 1. EXPERIMENTAL DESIGN, ANIMALS, AND ANIMAL MAINTENANCE

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Experimental Design			
Size of Test Groups	5 males and 5 females of each species	10 females and 10 males of each species	50 males and 50 females of each species plus 15 sentinel animals/sex/species
Doses	Rats: 0, 60, 125, 250, 500, or 1,000 mg/kg body weight in corn oil by gavage (dose volume: 5 ml/kg body weight) Mice: First study: 0, 250, 500, 1,000, 2,000, or 4000 mg/kg Mice: Rerun: 0, 30, 60, 125, 250, or 500 mg/kg body weight by gavage (dose volume: 5 ml/kg body weight)	0, 30, 60, 125, 250, or 500 mg/kg body weight in corn oil by gavage 5 days per week (dose volume: 5 ml/kg)	0, 60, 120 mg/kg body weight in corn oil by gavage 5 days per week (dose volume: 5 ml/kg body weight)
Duration of Dosing	14 consecutive days; killed on day 16 (mice) and day 20 (rats)	13 weeks	103 weeks (5 days per week)
Type and Frequency of Observations	Observed twice daily for clinical signs of toxicity	Observed twice daily for clinical signs of toxicity; individual animal weights and cage group food consumption measured weekly	Observed twice daily for mortality and moribundity; weighed once per week for 13 weeks and monthly thereafter
Necropsy, Histological Examination, and Special Analyses	Necropsies performed on all animals; tissues from 2 male and 2 female rats in highest surviving dose group (500 mg/kg) examined microscopically; in the first mouse study, livers examined microscopically in 1 female at 1,000 mg/kg and in 3 male and 3 female mice at 500 mg/kg; in the second mouse study, livers from 4 males and 4 females in the 500 mg/kg groups examined microscopically	Necropsies performed on all animals; all controls and high-dose animals examined histopathologically *Hematology:* profiles (hemoglobin, RBC, WBC, hematocrit, MCV, platelet count, and recticulocyte count) obtained on blood collected by orbital bleeding from all animals one day before death *Clinical Chemistry:* Alkaline phosphatase, SGPT and GGTP for mice and rats; bilirubin, cholesterol, triglycerides, BUN, glucose, total protein, and globulins for rats only) determined on blood collected by cardiac puncture at time of death	Necropsies performed on all animals; following tissues examined in all groups: tissues masses, gross lesions, abnormal lymph nodes, blood smears, mandibular or mesenteric lymph nodes, mammary gland, salivary gland, bone marrow, sternebrae, femur or vertebrae, thymus, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, small intestine, colon, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, prostate/testes or ovaries/uterus, brain, pituitary, spinal cord, thigh muscle, eyes (if grossly abnormal)

TABLE 1. EXPERIMENTAL DESIGN, ANIMALS, AND ANIMAL MAINTENANCE (Continued)

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
		Urinalysis: Uroporphyrins and coproporphyrins determined in urine collected for 24 hours from survivors in the control and high-dose groups 1 week before termination. Urine samples from individual rats and pools of 3 to 5 mice of the same dose level and sex examined *Liver porphyrins:* Total liver porphyrin determined from all animals *Organ to body weight ratios:* Following organs weighed from all animals at necropsy: Lung, heart, liver, spleen, thymus, right kidney, brain, right testicle or right ovary, and uterus	
Animals and Animal Maintenance			
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)	Harlan Industries	Charles River (Portage, MI)
Time Held Before Start of Test	14 days	Rats: 15 days; mice: 14 days	Rats: 17 days; mice: 18 days
Age When Placed on Study	Rats: 6 weeks; mice: 7 weeks	Rats: 6 weeks; mice: 8 weeks	Rats: 7 weeks; mice: 7.5 weeks
Age When Killed	Rats: 8 weeks; mice: 9 weeks	Rats: 19 weeks; mice: 21 weeks	Rats: 111-112 weeks; mice: 112-113 weeks
Method of Animal Distribution	Animals assigned by species and sex to cages according to a table of random numbers; cages assigned to control and dose groups according to another table of random numbers	Same as 14-day study	Same as 14-day study
Feed	Purina® Lab Chow (pelleted)	Same as 14-day study	Purina® Lab Chow 3/79 to 10/79 Zeigler Bros. NIH07 10/79 to 3/81

TABLE 1. EXPERIMENTAL DESIGN, ANIMALS, AND ANIMAL MAINTENANCE (Continued)

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Animals and Animal Maintenance			
Bedding	Absorb-Dri® (Lab Products, Inc., Rochelle, NJ)	Same as 14-day study	Same as 14-day study
Water	Edstrom® automatic watering system (Waterford, WI)	Same as 14-day study	Same as 14-day study
Cages	Polycarbonate (Lab Products, Inc.); changed twice per week; neither cages nor racks were rotated	Same as 14-day study	Same as 14-day study
Cage Filters	Spun-bonded polyester filter (Dupont 2024) (Snow Filtration Co., Cincinnati, OH); changed every every two weeks	Same as 14-day study	Same as 14-day study
Animals Per Cage	Five	Same as 14-day study	Same as 14-day study
Animal Room Environment	21°-23°C; 40%-60% relative humidity; 12 hours of fluorescent light per day; 15 room air changes per hour	Same as 14-day study	23 ± 3°C; 40%-60% relative humidity; 12 hours of fluorescent light per day; 15 room air changes per hour
Other Chemicals on Test in Same Room	—	None	None
Chemical/Vehicle Mixture Preparation	Weighed quantity of 1,2-dichlorobenzene adjusted to the highest dose level by addition of corn oil in a volumetric flask (q.s.); lower dose levels prepared by dilution of a measured volume of the high-dose formulation with corn oil	Same as 14-day study	Same as 14-day study
Maximum Storage Time	14 days	—	14 days
Storage Conditions	Room temperature	—	4°C until day of first use, room temperature thereafter.

III. RESULTS

RATS

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

FOURTEEN-DAY STUDIES

All rats receiving 1,000 mg/kg 1,2-dichlorobenzene died. A dose-related decrease in weight gain was observed in male and female rats (Table 2). In male rats, final body weight was depressed more than 10% compared to controls at a dose of 500 mg/kg.

THIRTEEN-WEEK STUDIES

A dose-related decrease in weight gain was observed in male rats during the 13-week study; however, except for the 500 mg/kg male rats, final body weights were within 7% of controls (Table 3). Two female rats receiving 500 mg/kg 1,2-dichlorobenzene died, one at week 6 and one at week 9. One male each from the control, 30 mg/kg, and 125 mg/kg groups also died, presumably because of a gavage error. 1,2-Dichlorobenzene increased liver weights in male and female rats in a dose-related manner (Appendix F, Tables F6 and F7). Significant increases in liver weight/body weight ratios were observed at the 125, 250, and 500 mg/kg doses in males and females. Decreases in the absolute organ weight and the organ weight/body weight

TABLE 2. SURVIVAL AND MEAN BODY WEIGHTS OF RATS ADMINISTERED 1,2-DICHLOROBENZENE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weights Relative to Controls *(b)* (Percent)
		Initial	Final	Change	
Males					
0	5/5	109.8	149.0	+39.2	
60	5/5	110.8	148.6	+37.8	0
125	5/5	110.6	140.6	+30.0	- 6
250	5/5	115.8	144.4	+28.6	- 3
500	5/5	109.8	130.8	+21.0	-12
1,000	0/5 *(c)*	107.2	—	—	—
Females					
0	5/5	95.8	120.8	+25.0	
60	5/5	96.8	119.2	+22.4	- 1
125	5/5	95.0	111.6	+16.6	- 8
200	5/5	95.0	111.0	+16.0	- 8
500	5/5	96.4	110.2	+13.8	- 9
1,000	0/5 *(d)*	97.0	—	—	

(a) Number surviving/number per group.

(b) Weight Relative to Control = $\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$

(c) Deaths occurred on day 4.

(d) One animal died on day 3, one on day 4, and three on day 5.

TABLE 3. SURVIVAL AND MEAN BODY WEIGHTS OF RATS ADMINISTERED 1,2-DICHLOROBENZENE BY GAVAGE FOR 13 WEEKS

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weights Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
Males					
0	9/10	93.3 ± 4.4	293.1 ± 7.8	+199.8 ± 4.9	
30	9/10	104.1 ± 2.9	305.4 ± 3.6	+201.3 ± 3.9	+ 4
60	10/10	97.7 ± 5.9	292.9 ± 6.3	+195.2 ± 6.1	0
125	9/10	99.7 ± 3.4	281.4 ± 5.9	+181.7 ± 5.0	- 4
250	9/9 *(d)*	98.9 ± 4.9	275.8 ± 8.3	+176.9 ± 7.2	- 6
500	10/10	101.8 ± 5.4	236.1 ± 12.1	+134.3 ± 11.4	-19
Females					
0	10/10	83.7 ± 1.1	181.3 ± 5.0	+97.6 ± 4.7	
30	10/10	89.8 ± 2.0	181.4 ± 5.1	+91.6 ± 3.6	0
60	10/10	85.5 ± 1.8	178.1 ± 5.7	+92.6 ± 5.1	- 2
125	10/10	86.4 ± 1.3	175.3 ± 3.8	+88.9 ± 2.9	- 3
250	10/10	88.2 ± 2.1	175.0 ± 4.6	+86.8 ± 3.3	- 3
500	8/10	86.9 ± 2.4	169.4 ± 5.1	+82.5 ± 3.1	- 7

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study.

(b) Mean weight change of the survivors of the group

(c) Weight of the dosed group relative to that of the controls =

$$\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$$

(d) One animal in this group was missexed.

ratio for thymus in male rats at the 500 mg/kg dose may reflect general toxicity or organ-specific toxicity. However, slight increases in organ weight/body weight ratios for lungs, kidney and brain in male rats receiving 500 mg/kg without a corresponding effect on organ weight probably reflect the effect of the chemical on body weight.

Only minimal changes were observed in hematology and clinical chemistry parameters in the 13-week study. Minimal decreases in the hematocrit, the amount of hemoglobin, the number of red blood cells (significant only in males), and mean corpuscular volume were observed in male and female rats at the 500 mg/kg dose (Appendix F, Tables F1 and F2). The number of reticulocytes was increased slightly in high dose females. A minimal decrease in the number of lymphocytes and a small increase in the percentage of segmented neutrophils were observed in high dose males. These hematologic changes presumably reflect toxicity at the high dose. The number of platelets was increased at 60, 125, and 500 mg/kg in female but not in male rats. The reason for the increase in platelets is not apparent. This change is not considered to be biologically significant. 1,2-Dichlorobenzene did not affect the number of white cells, eosinophils, basophils, or monocytes.

1,2-Dichlorobenzene did not produce statistically significant increases in serum concentrations of SGPT (serum glutamic pyruvic transaminase), GGTP (gamma-glutamyl transpeptidase) or alkaline phosphatase (Appendix F, Tables F3 and F4). However, 1,2-dichlorobenzene produced slight dose-related increases in serum cholesterol at doses of 30, 125, 250, and 500 mg/kg (males) and 125-500 mg/kg (females), decreases in serum triglycerides at 500 mg/kg (males) and 250 mg/kg (females), and dose-related increases in total serum protein at 250-500 mg/kg (males) and at 30-500 mg/kg (females). All of these changes were relatively small; however, they may reflect hepatic effects

of the chemical at these doses. Minimal increases in serum glucose levels in female rats were observed at 30 mg/kg and 125 to 500 mg/kg.

Blood urea nitrogen was not affected in male or female rats receiving 500 mg/kg 1,2-dichlorobenzene (Tables F3 and F4). However, 24-hour urine volume was increased 57% over controls in male rats receiving 500 mg/kg 1,2-dichlorobenzene (Table F5).

The urinary concentration of uroporphyrin and coproporphyrin was three to five times higher in male and female rats receiving 500 mg/kg 1,2-dichlorobenzene than in controls (Table F5). However, this increase is not considered to be indicative of porphyria. The concentration of total porphyrins in the liver was not altered by 1,2-dichlorobenzene at any dose level (Table F5).

At necropsy, no consistent lesions were noted. The liver and kidneys from all rats (except for a few that died early in the study) were examined under long-range ultraviolet light. None had the positive reddish-brown pigmentation indicative of porphyria.

Microscopically, a number of lesions that appeared to be compound or dose related were observed. The two 500 mg/kg dose rats that died early had a moderate degree of centrolobular hepatocellular necrosis. Most of the surviving high dose rats (7/8 surviving females and 8/10 males) had liver lesions, either centrolobular degeneration or necrosis of individual hepatocytes. The necrosis of individual hepatocytes was characterized by randomly scattered hepatocytes that were pyknotic or karyolytic and had shrunken dark red cytoplasms. In addition, renal tubular degeneration was found in 6/10 high dose male rats and thymic lymphoid depletion was found in 4/10 high dose male rats.

The renal and thymic lesions were not present at the 250 mg/kg or 125 mg/kg doses. The individual hepatocellular necrosis persisted at the 250 mg/kg dose (4/9 males and 5/10 females). Individual hepatocellular necrosis was seen in one female rat at the 125 mg/kg dose. In addition, some focal hepatic necrosis was observed in one male rat at the 125 mg/kg dose that died early due to a ruptured esophagus and in two female rats at the 125 mg/kg dose; this was less pronounced than that observed at higher doses.

Yellow-green to gold pigment was observed in some of the livers at the 250 and 500 mg/kg doses. This pigment was periodic acid-Schiff (PAS) and Perls positive and was believed to be hemosiderin.

Because the liver lesions found in rats receiving 250 mg/kg were considered to be potentially life-shortening by the original pathologist, doses of 60 and 120 mg/kg 1,2-dichlorobenzene in corn oil were selected for rats in the 2-year study.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

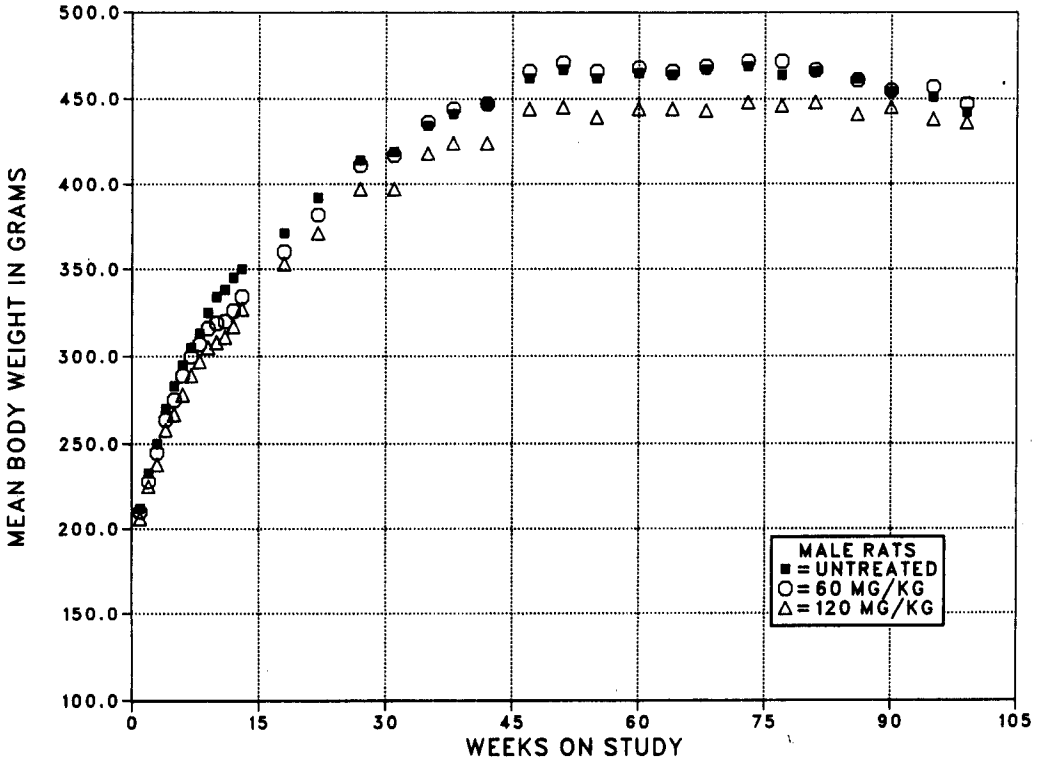
Throughout the 2-year studies, mean body weights of high dose male rats were slightly lower than those of the vehicle controls (Figure 1 and Table 4). Mean body weights of low dose and vehicle control male rats were comparable. After week 32, mean body weights of dosed female rats were higher than those of the controls.

Survival

Estimates of the probabilities of survival of vehicle control and dosed groups in these studies are shown by the Kaplan and Meier curves in Figure 2. The survival of high dose males was significantly reduced when compared with low dose ($P=0.014$) and control ($P<0.001$) groups. No other significant differences were observed. One high dose female, one vehicle control male, and five high dose male rats were accidentally killed as a result of gavage error. These animals were censored from the statistical analyses of survival at the date of death. In addition, small amounts of the dosing solution were found in the lungs of 3 control, 8 low dose, and 12 high dose male rats that died before the end of the study.

In the retrospective data audit (Appendix O) probable gavage-related deaths were reported in 1 high dose female, 1 vehicle control male, 1 low dose male, and 5 high dose males. Possible gavage-related deaths were also suggested in 3 vehicle control males, 4 low dose males, 12 high dose males, 2 low dose females, and 5 high dose females.

In male rats, 42/50 (84%) of the controls, 36/50 (72%) of the low dose, and 19/50 (38%) of the high dose group lived to the end of the study (104-105 weeks). In female rats, 31/50 (62%) of the controls, 33/50 (66%) of the low dose, and 32/50 (64%) of the high dose group lived to the end of the study (104-105 weeks). The survival incidences include one control male that died during the termination period of the study. For statistical purposes, this animal has been pooled with those killed at the end of the study.



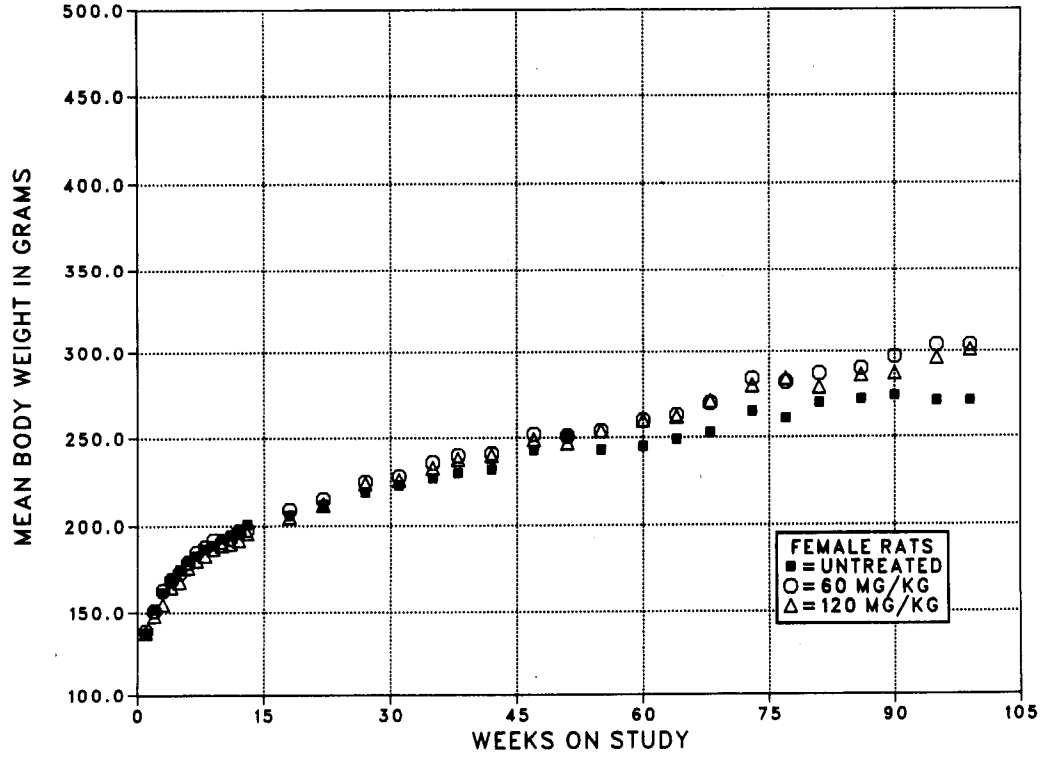


Figure 1. Growth Curves for Rats Administered 1,2-Dichlorobenzene in Corn Oil by Gavage

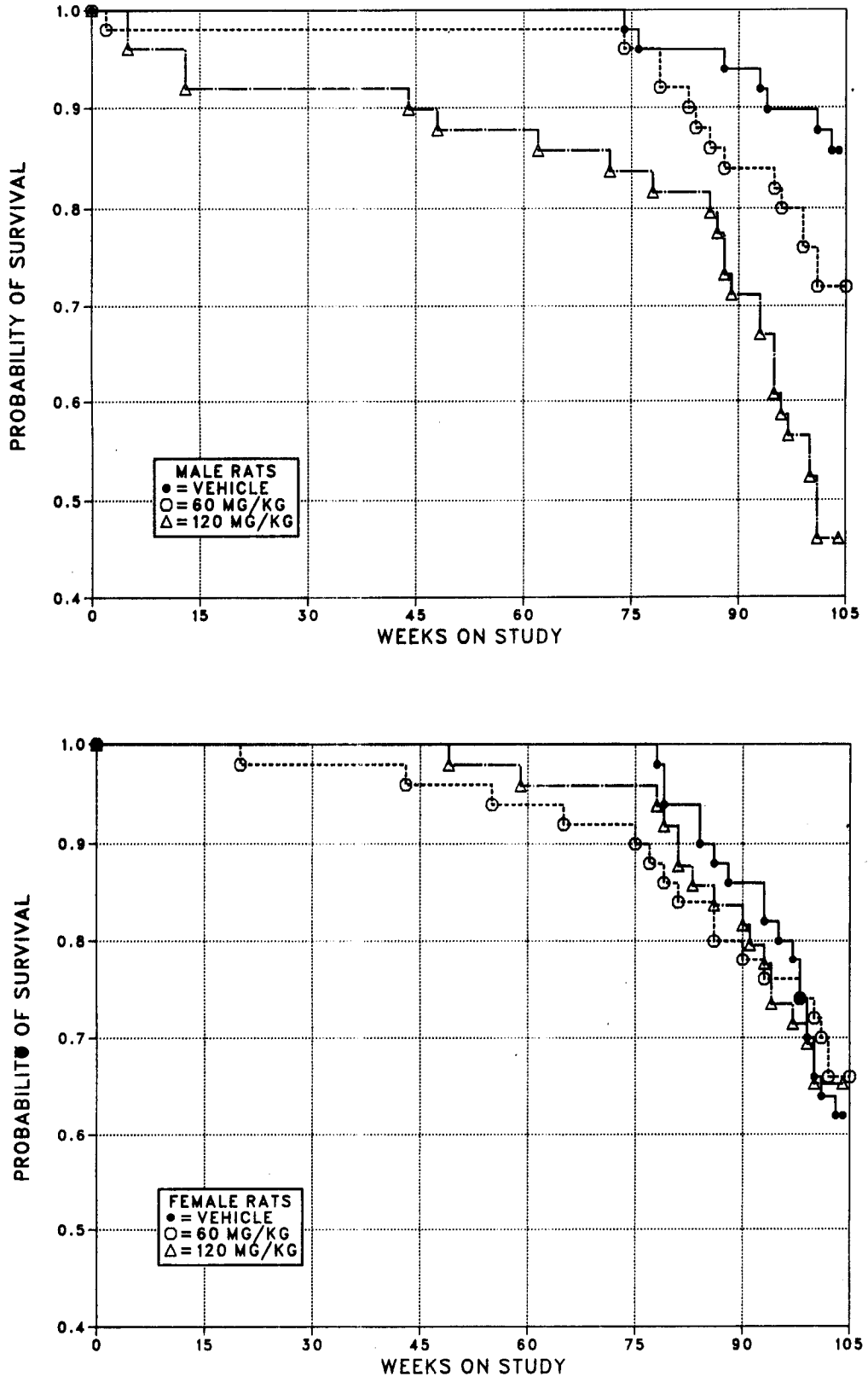


Figure 2. Kaplan-Meier Survival Curves for Rats Administered 1,2-Dichlorobenzene in Corn Oil by Gavage

TABLE 4. MEAN BODY WEIGHTS (RELATIVE TO CONTROLS) OF RATS ADMINISTERED 1,2-DICHLOROBENZENE BY GAVAGE FOR 2 YEARS

Week No.	Mean Body Weights (grams)			Body Weights Relative to Controls (percent) *(a)*	
	Control	Low Dose	High Dose	Low Dose	High Dose
Males					
1	212	210	206	- 1	- 3
22	392	382	371	- 3	- 5
42	447	447	424	0	- 5
60	465	468	444	+ 1	- 5
99	442	447	436	+ 1	- 1
Females					
1	138	139	138	+ 1	0
22	212	215	212	+ 1	0
42	232	241	240	+ 4	+ 3
60	245	260	260	+ 6	+ 6
99	271	304	301	+12	+11

(a) Weight Relative to Controls = $\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in rats in the 2-year studies are summarized in Appendix A, Tables A1 and A2; Tables A3 and A4 give the survival and tumor status for individual male and female rats. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2. Historical incidences of tumors in control animals are listed in Appendix G. Appendix H, Tables H1 and H2, contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Nonneoplastic lesions did not appear to be increased in the liver, kidney, bone marrow, spleen, thymus or other organs of male or female rats as a result of the administration of 1,2-dichlorobenzene in the two-year studies.

Adrenals: The incidence of pheochromocytomas in low dose male rats was increased when compared with controls (Table 5). This increase was significant by the life table test but not by the incidental tumor test. Since this tumor is not generally regarded as life-threatening, the most appropriate analysis for it is the incidental tumor test. The incidence of pheochromocytomas was not increased in high dose males and did not occur with a significant dose-response trend. Moreover, no malignant pheochromocytomas were observed in either of the dose groups.

Hematopoietic System: The incidence of undifferentiated leukemias was significantly lower in the low dose females than that in the controls (Table 6), but the incidence in the high dose females was the same as that in the controls. Moreover, there were no differences between the incidence of rats with all types of leukemia in the dosed versus control groups. No differences were observed between control and dosed male rats (10/50, 7/50, 5/50).

Testis: Interstitial-cell tumors occurred with a statistically significant positive trend in the life table test and with a significant negative trend by the Cochran-Armitage test (Table H1). No significant results were obtained by the incidental tumor test, which is the most appropriate test for the analysis of this generally nonfatal tumor.

Pancreatic Islets: The combined incidence of male rats with islet-cell adenomas or carcinomas occurred with a statistically significant negative trend by the Cochran-Armitage test (Table H1); however, when survival differences were taken into account, the trend was not significant. Results of pairwise comparisons between vehicle controls and dosed groups were not statistically significant.

TABLE 5. INCIDENCES OF MALE RATS WITH PHEOCHROMOCYTOMAS OF THE ADRENAL GLAND

	Vehicle Control	60 mg/kg	120 mg/kg
Overall Incidence	9/50 (18%)	16/50 (32%)	6/49 (12%)
Adjusted Incidence	20.9%	40.5%	21.7%
Terminal Incidence	8/42 (19%)	13/36 (36%)	2/18 (11%)
Life Table Test	P=0.201	P=0.039	P=0.380
Incidental Tumor Test	P=0.499N	P=0.070	P=0.420N
Cochran-Armitage Trend Test	P=0.285N		
Fisher Exact Test		P=0.083	P=0.303N

TABLE 6. INCIDENCES OF FEMALE RATS WITH LEUKEMIA

	Vehicle Control	60 mg/kg	120 mg/kg
Undifferentiated Leukemia			
Overall Incidence	12/50 (24%)	3/50 (6%)	12/50 (24%)
Adjusted Incidence	28.5%	7.0%	32.9%
Terminal Incidence	4/31 (13%)	0/33 (0%)	9/32 (28%)
Life Table Test	P=0.532	P=0.020N	P=0.570
Incidental Tumor Test	P=0.524	P=0.022N	P=0.567
Cochran-Armitage Trend	P=0.552		
Fisher Exact Test		P=0.011N	P=0.592N
All Leukemias			
Overall Incidence	13/50 (26%)	6/50 (12%)	12/50 (24%)
Adjusted Incidence	31.2%	14.7%	32.9%
Terminal Incidence	5/31 (19%)	2/33 (6%)	9/32 (28%)
Life Table Test	P=0.469N	P=0.083N	P=0.514N
Incidental Tumor Test	P=0.469N	P=0.104N	P=0.528N
Cochran-Armitage Trend Test	P=0.451N		
Fisher Exact Test		P=0.062N	P=0.500N

FOURTEEN-DAY STUDIES

Most dosed mice in the first 14-day study died (Table 7). Hepatic necrosis was observed in 3/3 males examined histologically at the 500 mg/kg dose level and in 1/3 females receiving 250 mg/kg. Hepatocellular degeneration was seen in 1/3 males receiving 250 mg/kg.

In the second study, one male receiving 500 mg/kg and one female receiving 125 mg/kg died. Tissues of four high dose males (500 mg/kg) and four high dose females (500 mg/kg) were examined histologically. Mild hepatocellular necrosis was observed in 2/4 males, but the livers of the other two males appeared normal at this dose. In high dose females, moderate focal hepatic necrosis was observed in 1/4 livers, mild multifocal hepatitis in 1/4, mild cytomegaly and karyomegaly in 2/4, and hepatocellular degeneration in 1/4. Mean body weights were comparable among groups (Table 7). No compound-related gross pathologic effects were observed in animals surviving to the end of the study. The reason for the discrepancy between the survival rate of male and female mice dosed with 250 and 500 mg/kg in the first study versus that in the second study is not known. However, the survival rates in the 13-week study are more consistent with the results of the second 14-day study than they are with with first.

THIRTEEN-WEEK STUDIES

Four of ten male mice and 3/10 female mice receiving 500 mg/kg died (Table 8). One male receiving 250 mg/kg died. Weight gains and final body weights relative to controls were depressed in male and female mice administered 1,2-dichlorobenzene at 500 mg/kg.

1,2-Dichlorobenzene caused significant increases in liver weight/body weight ratios in male and female mice receiving 500 mg/kg (Appendix F, Tables F12 and F13). The spleen weight/body weight at all doses decreased relative to controls in female mice given 1,2-dichlorobenzene for 13 weeks.

Only minor changes in hematology values were reported in the 13-week studies in mice. The apparent increase in white blood cell count, which occurred in males at all doses (Tables F8 and F9), seems to be the result of a low white blood cell count in control male mice ($3.4 \pm 0.8 \times 10^3/mm^3$). Previous studies from other NTP contract laboratories have reported white blood cell counts in control male mice of $4.3 \pm 1.8 \times 10^3/mm^3$ (N=10). Moreover, another study from Battelle Columbus Laboratories reported white blood cell counts of $8.5 \pm 1.8 \times 10^3/mm^3$ in control male mice. It is therefore unlikely that the increase in white blood cell count is biologically significant. A statistically significant increase in the relative number of lymphocytes occurred in males (from 67% ± 10% for controls to 78% ± 7% at 500 mg/kg), whereas a decrease in the relative number of lymphocytes occurred in females (from 87% ± 7% for controls to 74% ± 11% at the 250 mg/kg dose). Corresponding decreases (male mice) and increases (female mice) occurred in the relative number of neutrophils. These changes are probably not biologically significant. Mitruka and Rawnsley (1977) reported that the percentage of lymphocytes in the blood of the mouse varies from 60% to 90% while neutrophils range from 5% to 22%. A minimal increase in serum glutamic pyruvic transaminase (SGPT) was observed in male mice receiving 500 mg/kg 1,2-dichlorobenzene (Appendix F, Table F10). This increase was not statistically significant and was attributable to one male mouse in which hepatocellular necrosis was observed.

The urinary concentration of coproporphyrin was three times higher in female mice receiving 500 mg/kg 1,2-dichlorobenzene than in controls (Appendix F, Table F11). However, this moderate coproporphyrinuria was not considered to be indicative of porphyria. Moreover, the concentration of porphyrins in the liver of male mice was not altered by 1,2-dichlorobenzene, and only a twofold increase was observed in females that received 500 mg/kg (Appendix F, Table F11).

TABLE 7. SURVIVAL AND MEAN BODY WEIGHTS OF MICE ADMINISTERED 1, 2-DICHLOROBENZENE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)* (Day of Death)	Mean Body Weights (grams)			Final Body Weight Relative to Controls *(b)* (Percent)
		Initial	Final	Change	
		FIRST STUDY			
Males					
0	4/5 (4)	22.5	26.5	+4.0	—
250	1/5 (6,6,8,9)	22.5	26.0	+3.5	- 2
500	0/5 (4,5,6,8,8)	22.5	—	—	—
1,000	0/5 (3,3,4,8,11)	22.5	—	—	—
2,000	0/5 (2,2,2,2,3)	22.5	—	—	—
4,000	0/5 (2,2,2,2,3)	22.5	—	—	—
Females					
0	5/5	20.5	21.8	+1.3	—
250	1/5 (6,6,7,8)	20.5	21.0	+0.5	- 4
500	1/5 (7,8,8,9)	20.5	24.0	+3.5	+10
1,000	1/5 (3,3,3,5)	20.5	23.0	+2.5	+ 6
2,000	0/5 (2,2,3,3,3)	20.5	—	—	—
4,000	0/5 (2,2,2,2,2)	20.5	—	—	—
		SECOND STUDY			
Males					
0	5/5	21.4	24.6	+3.2	—
30	5/5	22.6	24.0	+1.4	- 2
60	5/5	23.2	24.6	+1.4	0
125	5/5	22.4	24.4	+2.0	- 1
250	5/5	22.4	24.6	+2.2	0
500	4/5 (3)	21.6	25.0	+3.4	+ 2
Females					
0	5/5	18.2	19.8	+1.6	—
30	5/5	18.6	19.4	+0.8	- 2
60	5/5	18.6	18.8	+0.2	- 5
125	4/5 (8)	18.4	19.0	+0.6	- 4
250	5/5	19.6	20.8	+1.2	+ 5
500	5/5	18.4	19.8	+1.4	0

(a) Number surviving/number per group

(b) Weight of the dosed group relative to that of the controls =

$$\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$$

TABLE 8. SURVIVAL AND MEAN BODY WEIGHTS OF MICE ADMINISTERED 1,2-DICHLOROBENZENE BY GAVAGE FOR 13 WEEKS

Dose (mg/kg)	Survival *(a)* (week of death)	Mean Body Weights (grams) Initial	Final	Change *(b)*	Final Body Weight Relative to Controls *(c)* (Percent)
Males					
0	10/10	24.3 ± 0.4	32.2 ± 0.9	+7.9 ± 0.7	—
30	10/10	23.2 ± 0.6	30.8 ± 0.6	+7.6 ± 0.4	- 4
60	10/10	24.8 ± 0.4	32.4 ± 1.1	+7.6 ± 0.9	+ 1
125	10/10	24.1 + 0.5	32.4 ± 0.6	+8.3 ± 0.8	+ 1
250	9/10 (13)	25.6 ± 0.3	32.1 ± 0.6	+6.5 ± 0.5	0
500	6/10 (6,6,6,13)	24.3 ± 0.6	28.5 ± 0.8	+4.2 ± 1.1	-11
Females					
0	10/10	19.5 ± 0.3	25.9 ± 0.5	+6.4 ± 0.3	—
30	10/10	18.2 ± 0.4	24.8 ± 0.6	+6.6 ± 0.5	- 4
60	10/10	19.6 ± 0.3	25.7 ± 0.7	+6.1 ± 0.4	- 1
125	10/10	18.8 ± 0.4	25.7 ± 0.5	+6.9 ± 0.5	- 1
250	10/10	18.3 ± 0.3	24.4 ± 0.6	+6.1 ± 0.5	- 6
500	7/10 (13,13,13)	18.9 ± 0.3	21.0 ± 1.2	+2.1 ± 1.1	-19

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study.

(b) Mean weight change of the survivors of the group ± standard error of the mean

(c) Weight of the dosed survivors relative to the survivors of the controls ◘

$$\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$$

No consistent lesions were noted in mice at necropsy. The liver and kidneys from all of the mice except a few that died early were examined under long-range ultraviolet light. There was no positive reddish-brown fluorescence in any of them.

Microscopically, a number of lesions were observed which appeared to be compound and dose related. In the livers of the 500 mg/kg group, centrolobular necrosis, necrosis of individual hepatocytes, or hepatocellular degeneration were observed in 9/10 male and 9/10 female mice. Many of the hearts had multiple foci of mineralization of myocardial fibers (3/10 males and 8/10 females) and some necrosis, myositis, and mineralization in skeletal muscle were observed as well. Lymphoid depletion was observed in the thymus (2/10 females and 2/10 male mice) and spleen (2/10 female and 4/10 male mice) at the 500 mg/kg dose. Necrosis of lymphocytes in the spleen was observed in one female mouse at 500 mg/kg. Yellow-green pigmentation was seen in the livers of 4/10 males and 2/10 females receiving 500 mg/kg. The pigment, which was PAS positive, iron positive, acid fast negative, and bilirubin negative, was considered to be hemosiderin.

At 250 mg/kg, the only compound-related lesions observed were necrosis of individual hepatocytes (2/10 males), hepatocellular degeneration (1/10 males) and pigment deposition (1/10 males). Livers of 4/10 males showed one of these changes. Myocardial dystrophic mineralization and lymphoid depletion of the thymus and spleen were not observed at this dose. No compound-related changes were observed in females at this dose.

No compound-related lesions were observed in livers or other organs of mice dosed with 125 mg/kg 1,2-dichlorobenzene.

Because compound-related histopathologic effects were observed in male mice receiving 250 mg/kg, doses of 60 and 120 mg/kg were selected for mice in the 2-year studies.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Throughout the 2-year studies, mean body weights of dosed and control male and female mice were comparable (Table 9 and Figure 3).

Survival

The probabilities of survival for control and dosed mice in these studies are shown by the Kaplan and Meier curves in Figure 4. One control female was accidentally killed and one high dose female was found to be missing; these animals were censored from the statistical analysis of survival at the time of death or disappearance. No significant differences in survival were observed between any groups of either sex. In male mice, 26/50 (52%) control, 32/50 (64%) low dose, and 35/50 (70%) high dose animals lived to the end of the study at 105 weeks. In female mice, 33/50 (66%) of the control, 40/50 (80%) of the low dose, and 38/50 (76%) of the high dose animals lived to the end of the study at 105 weeks.

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in mice in the 2-year studies are summarized in Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status for individual male and female mice. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2. Historical incidences of tumors in control animals are listed in Appendix G, Table G2. Tables 10 and 11 of the results and Appendix H (Tables H3 and H4) contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Data Recording and Statistical Methods) and Appendix H (footnotes).

Nonneoplastic lesions: There appeared to be a dose-related trend in tubular regeneration of the kidney in male mice (control, 17%; low dose, 24%; high dose, 35%). No other increases were observed in nonneoplastic lesions in the liver,

TABLE 9. MEAN BODY WEIGHTS (RELATIVE TO CONTROLS) OF MICE ADMINISTERED 1,2-DICHLOROBENZENE BY GAVAGE FOR 2 YEARS

Week No.	Mean Body Weights (grams)			Body Weights Relative to Controls *(a)* (percent)	
	Control	Low Dose	High Dose	Low Dose	High Dose
Males					
0	25	24	25	-4	0
20	38	38	38	0	0
42	39	40	38	+3	-3
59	41	43	42	+5	+2
102	39	38	40	-3	+3
Females					
0	19	19	19	0	0
20	27	27	30	0	+11
42	30	31	33	+3	+10
59	32	33	34	+3	+ 6
102	34	35	36	+3	+ 6

(a) Weight Relative to Controls = $\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$

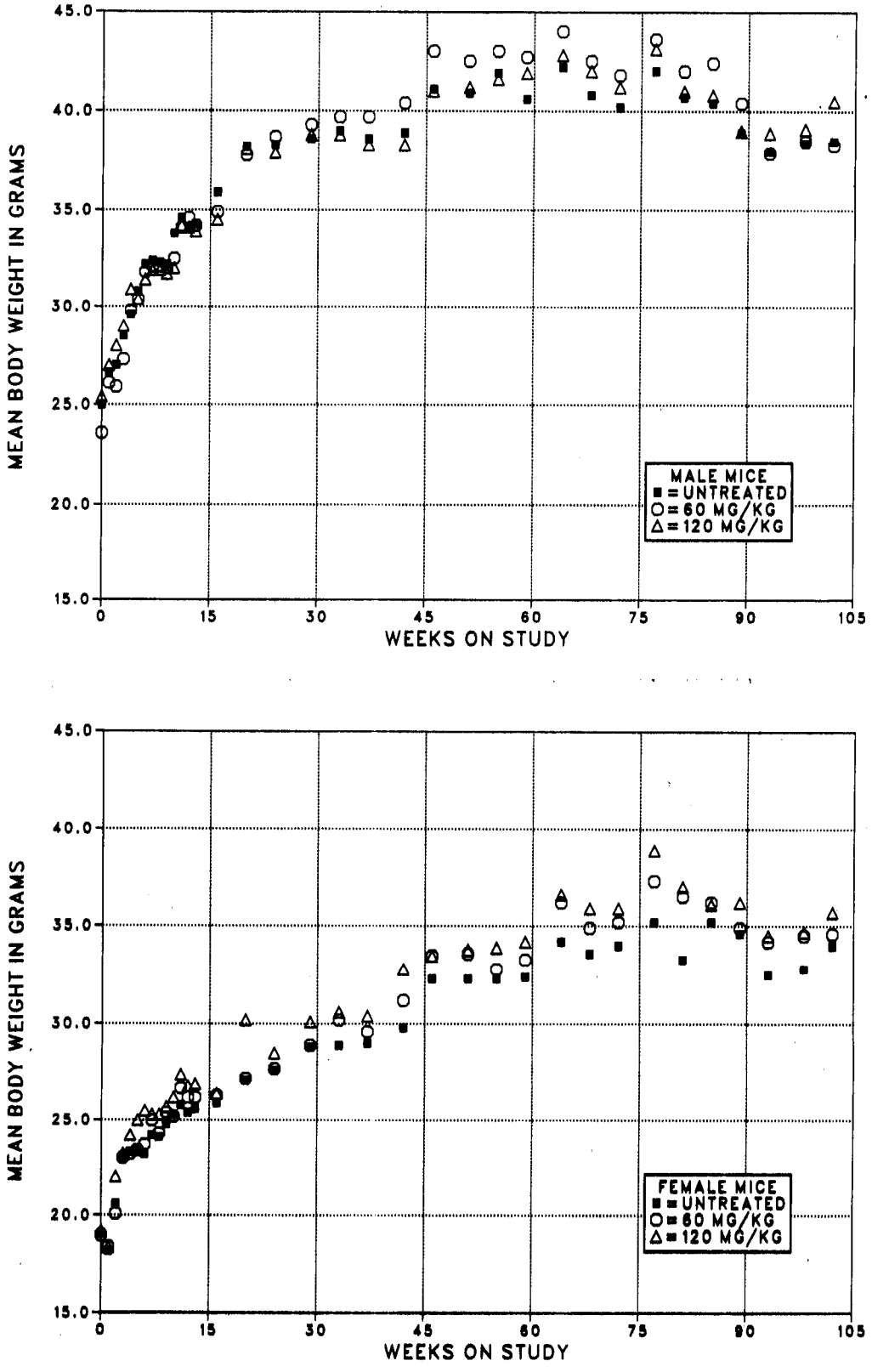
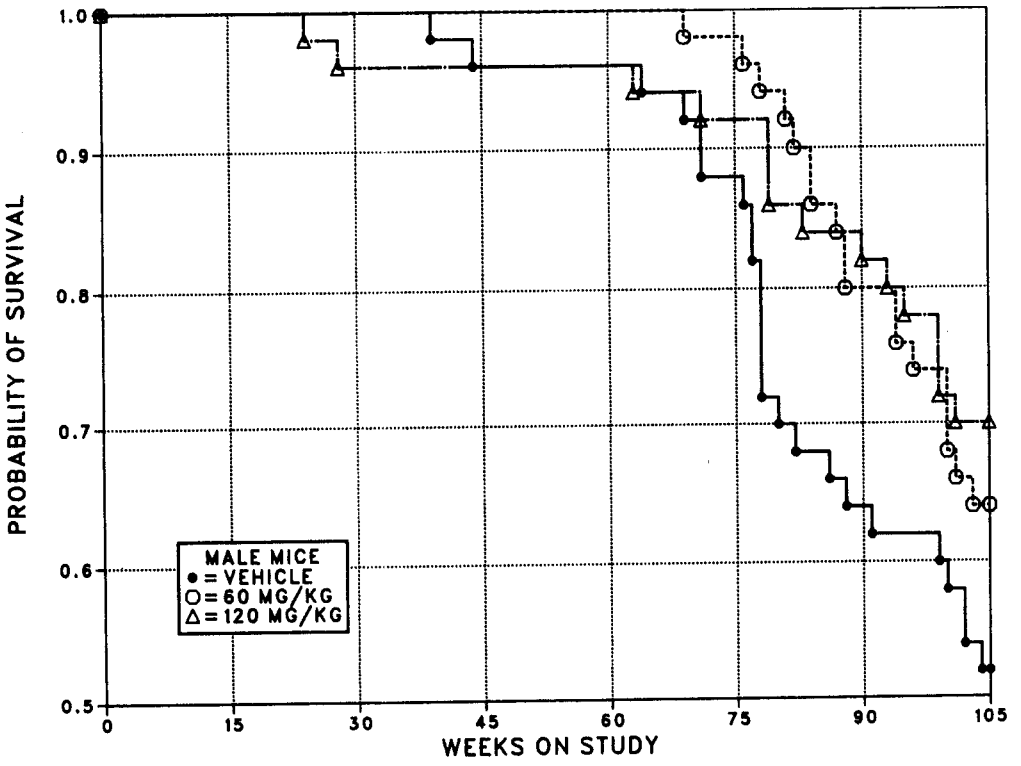


Figure 3. Growth Curves for Mice Administered 1,2-Dichlorobenzene in Corn Oil by Gavage



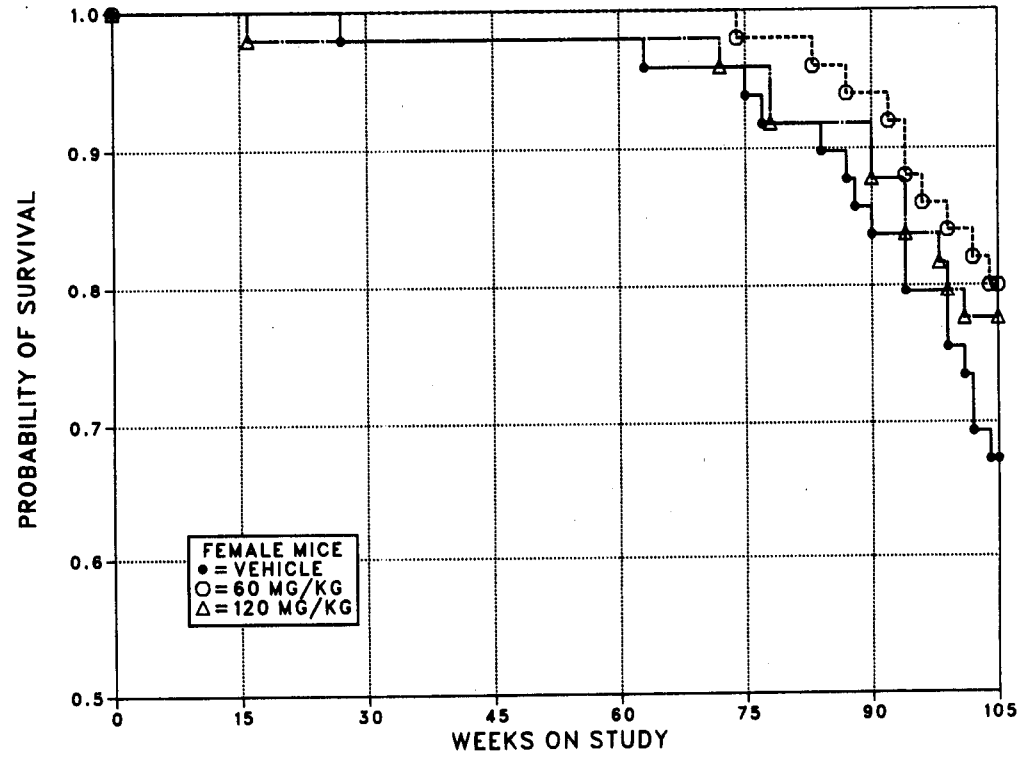


Figure 4. Kaplan-Meier Survival Curves for Mice Administered 1,2-Dichlorobenzene in Corn Oil by Gavage

bone marrow, spleen, or other organs as a result of administration of 1,2-dichlorobenzene in the 2-year study.

Hematopoietic system: Malignant histiocytic lymphomas occurred in male and female mice with statistically significant positive trends; however, malignant lymphocytic lymphomas were found in male mice with a statistically significant negative trend (Table 10). The combined incidence of all types of lymphomas was not significantly greater than that in controls for mice of either sex by any of the statistical tests.

Liver: The dose-related decrease in the incidence of hepatocellular adenomas in dosed male mice was significant (Table 11). The incidence of hepatocellular adenomas was significantly lower in the high dose group than in vehicle controls.

Lung: Alveolar/bronchiolar carcinomas occurred in male mice with a statistically significant positive trend (P = 0.037; 4/50, 2/50, 10/50, in the Cochran-Armitage test only), but the more appropriate combined incidence of male mice with alveolar/bronchiolar adenomas or carcinomas was not statistically significant in any of the tests (8/50, 8/50, 13/50).

TABLE 10. INCIDENCES OF MICE WITH MALIGNANT LYMPHOCYTIC OR HISTIOCYTIC LYMPHOMAS

	Vehicle Control	60 mg/kg	120 mg/kg
Males			
Malignant Lymphocytic Lymphoma			
Overall Incidence	7/50 (14%)	0/50 (0%)	0/50 (0%)
Adjusted Incidence	22.6%	0.0%	0.0%
Terminal Incidence	3/26 (12%)	0/32 (0%)	0/35 (0%)
Life Table Test	P<0.001N	P=0.005N	P=0.004N
Incidental Tumor Test	P<0.001N	P=0.002N	P=0.004N
Cochran-Armitage Trend Test	P=0.001N		
Fisher Exact Test		P=0.006N	P=0.006N
Malignant Histiocytic Lymphoma			
Overall Incidence	0/50 (0%)	1/50 (2%)	4/50 (8%)
Adjusted Incidence	0.0%	2.9%	10.1%
Terminal Incidence	0/26 (0%)	0/32 (0%)	2/35 (6%)
Life Table Test	P=0.043	P=0.532	P=0.107
Incidental Tumor Test	P=0.031	P=0.594	P=0.093
Cochran-Armitage Trend Test	P=0.026		
Fisher Exact Test		P=0.500	P=0.059
All Lymphoma			
Overall Incidence	8/50 (16%)	2/50 (4%)	4/50 (8%)
Adjusted Incidence	26.0%	5.4%	10.1%
Terminal Incidence	4/26 (15%)	0/32 (0%)	2/35 (6%)
Life Table Test	P=0.057N	P=0.027N	P=0.086N
Incidental Tumor Test	P=0.056N	P=0.011N	P=0.095N
Cochran-Armitage Trend Test	P=0.114N		
Fisher Exact Test		P=0.046N	P=0.178N
Females			
Malignant Lymphocytic Lymphoma			
Overall Incidence	7/49 (14%)	11/50 (22%)	8/49 (16%)
Adjusted Incidence	18.6 %	26.6%	18.1%
Terminal Incidence	4/33 (12%)	10/40 (25%)	3/38 (8%)
Life Table Test	P=0.542	P=0.358	P=0.572
Incidental Tumor Test	P=0.405	P=0.249	P=0.387
Cochran-Armitage Trend Test	P=0.447		
Fisher Exact Test		P=0.232	P=0.500
Malignant Histiocytic Lymphoma			
Overall Incidence	0/49 (0%)	0/50 (0%)	3/49 (6%)
Adjusted Incidence	0.0%	0.0%	7.9%
Terminal Incidence	0/33 (0%)	0/40 (0%)	3/38 (8%)
Life Table Test	P=0.042	*(a)*	P=0.147
Incidental Tumor Test	P=0.042	*(a)*	P=0.147
Cochran-Armitage Trend Test	P=0.037		
Fisher Exact Test		*(a)*	P=0.121
All Lymphomas			
Overall Incidence	11/49 (22%)	11/50 (22%)	13/49 (27%)
Adjusted Incidence	27.2.%	26.6%	29.8%
Terminal Incidence	5/33 (15%)	10/40 (25%)	8/38 (21%)
Life Table Test	P=0.475	P=0.424N	P=0.515
Incidental Tumor Test	P=0.302	P=0.588N	P=0.283
Cochran-Armitage Trend Test	P=0.361		
Fisher Exact Test		P=0.574N	P=0.407

(a) No tumors observed in control or dosed groups.

TABLE 11. INCIDENCES OF MALE MICE WITH LIVER TUMORS

	Vehicle Control	60 mg/kg	120 mg/kg
Adenoma			
Overall Incidence	8/50 (16%)	5/49 (10%)	2/46 (4%)
Adjusted Incidence	30.8%	13.4%	6.5%
Terminal Incidence	8/26 (31%)	3/32 (9%)	2/31 (6%)
Life Table Test	P=0.014N	P=0.152N	P=0.021N
Incidental Tumor Test	P=0.015N	P=0.145N	P=0.021N
Cochran-Armitage Trend Test	P=0.044N		
Fisher Exact Test		P=0.290N	P=0.060N
Carcinoma			
Overall Incidence	14/50 (28%)	10/49 (20%)	9/46 (20%)
Adjusted Incidence	39.5%	26.8%	24.9%
Terminal Incidence	7/26 (27%)	6/32 (19%)	6/31 (19%)
Life Table Test	P=0.073N	P=0.123N	P=0.099N
Incidental Tumor Test	P=0.220N	P=0.225N	P=0.312N
Cochran-Armitage Trend Test	P=0.191N		
Fisher Exact Test		P=0.259N	P=0.234N
Adenoma or Carcinoma			
Overall Incidence	19/50 (38%)	14/49 (29%)	11/46 (24%)
Adjusted Incidence	55.4%	35.5%	30.9%
Terminal Incidence	12/26 (46%)	8/32 (25%)	8/31 (26%)
Life Table Test	P=0.019N	P=0.076N	P=0.025N
Incidental Tumor Test	P=0.066N	P=0.130N	P=0.099N
Cochran-Armitage Trend Test	P=0.081N		
Fisher Exact Test		P=0.217N	P=0.102N

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

The liver has been reported to be the principal target organ for 1,2-dichlorobenzene-induced toxicity in rats and mice (Hollingsworth et al., 1958; Reid and Krishna, 1973). In the current 13-week studies, 1,2-dichlorobenzene produced centrolobular necrosis, hepatocellular necrosis, or hepatocellular degeneration in rats and mice at 500 mg/kg. Necrosis of individual hepatocytes or hepatocellular degeneration was also observed at 250 mg/kg in rats (4/9 males and 5/10 females) and in 3/10 male mice. Renal tubular degeneration (6/10 male rats) and lymphoid depletion of the thymus (4/10 male rats, 2/10 female mice, and 2/10 male mice) and of the spleen (4/10 male mice and 2/10 female mice) occurred at the 500 mg/kg dose, and multifocal mineralization of the myocardial fibers of the heart and skeletal muscle was seen in mice (3/10 males and 8/10 females) given 500 mg/kg.

1,2-Dichlorobenzene did not appear to cause hepatic porphyria in rats or mice at doses up to 500 mg/kg/day for 13 weeks. This finding is not altogether unexpected. Although there is clear-cut evidence that hexachlorobenzene produces porphyria (Cam and Nigogosyan, 1963; Ockner and Schmid, 1961; Carlson, 1977; Goldstein et al., 1978), several other chlorinated benzenes (1,4-dichlorobenzene, 1,2,4-trichlorobenzene, and pentachlorobenzene) do not appear to produce porphyria in rats or mice (Carlson, 1977; Linder et al., 1980). Chemically induced hepatic porphyria is an advanced disease state which is poorly reversible on removal of the chemical, and is characterized by approximately hundred-fold increases in hepatic and urinary porphyrins (Ockner and Schmid, 1961; Carlson, 1977). Small increases in urinary porphyrins were seen in the present study. However, changes of this magnitude are considered to be physiological rather than pathological. Such changes are generally termed as porphyrinuria. For comparison, when 300 ppm of hexachlorobenzene was administered in the diet to female Sprague-Dawley rats for 4 months, tissue porphyrins increased from 1.0 ± 0.1 to 385 ± 96 μg/g tissue and urinary uroporphyrin excretion from 1.4 ± 0.2 μg/24 hours to 383 ± 63 μg/24 hours (Goldstein et al., 1978).

The doses for animals in the 2-year studies (60 and 120 mg/kg) were selected because administration of 250 and 500 mg/kg of 1,2-dichlorobenzene for 13 weeks was associated with hepatic necrosis in rats and male mice. In the 2-year studies, survivals of the high dose female rats and high dose male and female mice were comparable with those of controls. Survival of high dose male rats was significantly shorter ($P<0.001$) than that of controls. However, there were 3 accidental deaths and 5 probable gavage-related deaths in this group; in addition several male rats that died before the end of the study had small amounts of corn oil or of the 1,2-dichlorobenzene/corn oil mixture in their lungs (3 control, 8 low dose, and 12 high dose). Therefore, gavage error may have contributed to their deaths. Thus, the lower survival of high dose male rats does not necessarily mean that the maximum tolerated dose was exceeded. A dose-related increase in tubular regeneration in the kidneys of male mice (control, 17%; low dose, 24%; high dose, 35%) was the only nonneoplastic change observed in the 2-year studies.

A few isolated reports have suggested that 1,2-dichlorobenzene might be associated with an increased incidence of blood dyscrasias and leukemia in humans (Gadrat et al., 1962; Girard et al., 1969). In the present study, doses of 1,2-dichlorobenzene which produced hepatotoxicity produced no hematological changes in rats or mice after 13 weeks of dosing. In the 2-year studies, statistically significant positive trends ($P<0.05$) occurred in the incidences of male and female mice with malignant histiocytic lymphomas. However, the incidences of male and female mice with all types of malignant lymphoma were not statistically different from those in the controls. Since histiocytic lymphoma is a controversial diagnosis among different pathologists and since all types of lymphomas have the same histogenesis, an increase in this specific type of lymphoma in the absence of an increase in the total incidence of all types of lymphomas is not considered to be biologically significant or to be related to 1,2-dichlorobenzene.

The incidence of adrenal pheochromocytomas was increased in low dose male rats only when compared with controls by life-table analysis ($P=0.039$, control, 9/50, low dose, 16/50, high dose, 6/49). Since adrenal pheochromocytoma is not generally regarded as life threatening and since there was no dose-response trend or high dose effect, the increase in the low dose group is not regarded as being related to the administration of 1,2-dichlorobenzene. Further, no malignant pheochromocytomas were observed in dosed male rats, and no increases in these tumors were found in female rats.

Interstitial-cell tumors of the testis in male rats occurred with a significant positive trend when

analyzed by the life-table test, but with a significant negative trend when analyzed by the Cochran-Armitage test. Since this tumor is not considered to be life threatening, the increase detected by the life-table test was discounted.

An increase in alveolar/bronchiolar carcinomas (control 4/50, 8%; low dose, 2/50, 4%; high dose, 10/50, 20%) in male mice (significant by the Cochran-Armitage test but not the life-table or incidental tumor test) was discounted because the combined incidence of male mice with alveolar/bronchiolar adenomas or carcinomas (control, 8/50, 16%; low dose, 8/50, 16%; high dose, 13/50, 26%) was not significantly greater than controls by any of the tests.

There was a significant decrease in hepatocellular adenomas in high dose male mice (control, 8/50, 16%; low dose, 5/49, 10%; high dose, 2/46, 4%). This decrease was accompanied by a negative dose-response trend using the Cochran-Armitage test. However, the combined incidence of male mice with liver adenoma or carcinoma (control, 19/50, 38%; low dose, 14/49, 29%; high dose, 11/46, 24%) was statistically significant only by the life table test.

1,2-Dichlorobenzene has been retested for mutagenic activity by the National Toxicology Program. 1,2-Dichlorobenzene did not produce a mutagenic response in *Salmonella typhimurium* tester strains TA98, 100, 1535, and 1537 (with or without metabolic activation by 9,000 x g liver supernatants from Aroclor-1254® induced male Sprague-Dawley rats or Syrian hamsters) at concentrations as high as 333 μg/plate.

Conclusions: Under the conditions of these two-year studies, there was no evidence of carcinogenicity of 1,2-dichlorobenzene for male or female F344/N rats or B6C3F$_1$ mice receiving 60 or 120 mg/kg per day.

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA			1 (2%)
BASAL-CELL CARCINOMA		1 (2%)	
TRICHOEPITHELIOMA	1 (2%)	1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
TRICHOEPITHELIOMA			1 (2%)
FIBROMA	1 (2%)	3 (6%)	
FIBROSARCOMA		2 (4%)	1 (2%)
LIPOMA			1 (2%)
NEUROFIBROMA			2 (4%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)		
ALVEOLAR/BRONCHIOLAR CARCINOMA		1 (2%)	2 (4%)
FIBROSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, UNDIFFER-TYPE	1 (2%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		
UNDIFFERENTIATED LEUKEMIA	9 (18%)	5 (10%)	5 (10%)
LYMPHOCYTIC LEUKEMIA		2 (4%)	
LEUKEMIA,MONONUCLEAR CELL	1 (2%)		
#PANCREATIC L.NODE	(45)	(40)	(40)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
HEMANGIOMA			1 (2%)
#HEART	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, INVASIV			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE		2 (4%)	1 (2%)
#PANCREAS	(50)	(50)	(49)
ACINAR-CELL ADENOMA		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
TRANSITIONAL-CELL PAPILLOMA	1 (2%)		
TUBULAR-CELL ADENOCARCINOMA			1 (2%)
FIBROSARCOMA, UNC PRIM OR META		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(49)	(49)
CARCINOMA,NOS	1 (2%)		
ADENOMA, NOS	14 (29%)	12 (24%)	11 (22%)
#ADRENAL	(50)	(50)	(49)
CORTICAL ADENOMA	1 (2%)	1 (2%)	
PHEOCHROMOCYTOMA	9 (18%)	16 (32%)	6 (12%)
#ZONA FASCICULATA	(50)	(50)	(49)
ADENOMA, NOS		1 (2%)	
#THYROID	(50)	(50)	(46)
C-CELL CARCINOMA	2 (4%)	2 (4%)	1 (2%)
PAPILLARY CYSTADENOMA, NOS			1 (2%)
#THYROID FOLLICLE	(50)	(50)	(46)
PAPILLARY ADENOCARCINOMA			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PARATHYROID	(42)	(34)	(38)
ADENOMA, NOS	1 (2%)	3 (9%)	1 (3%)
#PANCREATIC ISLETS	(50)	(50)	(49)
ISLET-CELL ADENOMA	2 (4%)		
ISLET-CELL CARCINOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA	1 (2%)	2 (4%)	2 (4%)
*PREPUTIAL GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS			1 (2%)
#PROSTATE	(50)	(48)	(49)
TUBULAR ADENOMA		1 (2%)	
#TESTIS	(50)	(50)	(50)
INTERSTITIAL-CELL TUMOR	47 (94%)	49 (98%)	41 (82%)
NERVOUS SYSTEM			
#CEREBRUM	(50)	(50)	(50)
ASTROCYTOMA	1 (2%)		
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*THORACIC CAVITY	(50)	(50)	(50)
MESOTHELIOMA, MALIGNANT		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*PERITONEUM	(50)	(50)	(50)
MESOTHELIOMA, NOS		2 (4%)	
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	3 (6%)	2 (4%)	2 (4%)
MESOTHELIOMA, MALIGNANT		1 (2%)	
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	1	8	14
MORIBUND SACRIFICE	7	6	12
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	41	36	19
ACCIDENTALLY KILLED, NOS	1		5
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	49	49	42
TOTAL PRIMARY TUMORS	101	112	84
TOTAL ANIMALS WITH BENIGN TUMORS	49	49	41
TOTAL BENIGN TUMORS	80	90	68
TOTAL ANIMALS WITH MALIGNANT TUMORS	16	14	13
TOTAL MALIGNANT TUMORS	18	15	13
TOTAL ANIMALS WITH SECONDARY TUMORS#		1	1
TOTAL SECONDARY TUMORS		1	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	3	5	3
TOTAL UNCERTAIN TUMORS	3	6	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC		1	
TOTAL UNCERTAIN TUMORS		1	

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SEBACEOUS ADENOMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
FIBROMA		1 (2%)	1 (2%)
FIBROSARCOMA	2 (4%)		1 (2%)
NEUROFIBROSARCOMA	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, UNDIFFER-TYPE	1 (2%)	2 (4%)	
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		
UNDIFFERENTIATED LEUKEMIA	12 (24%)	3 (6%)	12 (24%)
LYMPHOCYTIC LEUKEMIA		1 (2%)	
LEUKEMIA,MONONUCLEAR CELL	1 (2%)	2 (4%)	
#MANDIBULAR L. NODE	(46)	(44)	(45)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
#LUMBAR LYMPH NODE	(46)	(44)	(45)
ADENOCARCINOMA, NOS, METASTATIC	1 (2%)		
#MESENTERIC L. NODE	(46)	(44)	(45)
FIBROSARCOMA, METASTATIC			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#SPLEEN	(49)	(50)	(50)
HEMANGIOMA		1 (2%)	
*MESENTERY	(50)	(50)	(50)
HEMANGIOMA			1 (2%)
DIGESTIVE SYSTEM			
*DORSUM OF TONGUE	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
#LIVER	(49)	(49)	(50)
NEOPLASTIC NODULE	1 (2%)	1 (2%)	3 (6%)
#COLON	(48)	(47)	(48)
FIBROSARCOMA			1 (2%)
URINARY SYSTEM			
#URINARY BLADDER	(45)	(47)	(46)
PAPILLOMA, NOS	1 (2%)		
#U.BLADDER/MUSCULARIS	(45)	(47)	(46)
FIBROSARCOMA, METASTATIC			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(45)	(48)
ADENOMA, NOS	13 (28%)	16 (36%)	18 (38%)
#ANTERIOR PITUITARY	(46)	(45)	(48)
ADENOCARCINOMA, NOS	2 (4%)	1 (2%)	
#ADRENAL	(49)	(49)	(50)
PHEOCHROMOCYTOMA	5 (10%)	4 (8%)	3 (6%)
PHEOCHROMOCYTOMA, MALIGNANT		1 (2%)	
#ADRENAL CORTEX	(49)	(49)	(50)
ADENOCARCINOMA, NOS		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#ZONA FASCICULATA	(49)	(49)	(50)
ADENOMA, NOS	3 (6%)	1 (2%)	
#THYROID	(48)	(50)	(49)
ADENOCARCINOMA, NOS		1 (2%)	
C-CELL CARCINOMA	1 (2%)	3 (6%)	2 (4%)
CYSTADENOMA, NOS	1 (2%)	2 (4%)	1 (2%)
PAPILLARY CYSTADENOMA, NOS	2 (4%)		1 (2%)
#PANCREATIC ISLETS	(46)	(50)	(48)
ISLET-CELL ADENOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)		
ADENOCARCINOMA, NOS			1 (2%)
PAPILLARY ADENOMA		1 (2%)	
PAPILLARY CYSTADENOMA, NOS	1 (2%)		1 (2%)
PAPILLARY CYSTADENOCARCINOMA,NOS	1 (2%)		
FIBROADENOMA	6 (12%)	11 (22%)	7 (14%)
*CLITORAL GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA			1 (2%)
ADENOCARCINOMA, NOS	1 (2%)		1 (2%)
#UTERUS	(48)	(50)	(50)
FIBROSARCOMA			1 (2%)
LEIOMYOSARCOMA, INVASIVE		1 (2%)	
ENDOMETRIAL STROMAL POLYP	6 (13%)	9 (18%)	7 (14%)
ENDOMETRIAL STROMAL SARCOMA		1 (2%)	1 (2%)
#CERVIX UTERI	(48)	(50)	(50)
LEIOMYOSARCOMA		1 (2%)	
#ENDOMETRIAL GLAND	(48)	(50)	(50)
CARCINOMA,NOS		1 (2%)	
ADENOMA, NOS	1 (2%)		1 (2%)
#OVARY	(48)	(48)	(50)
CARCINOMA,NOS	1 (2%)		
THECOMA	1 (2%)		
LUTEOMA			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MESOTHELIOMA, NOS	1 (2%)		
#RIGHT OVARY	(48)	(48)	(50)
GRANULOSA-CELL TUMOR	1 (2%)		
NERVOUS SYSTEM			
#CEREBRUM	(49)	(50)	(50)
ADENOCARCINOMA, NOS, INVASIVE	1 (2%)		
ASTROCYTOMA	1 (2%)		
#BRAIN	(49)	(50)	(50)
ADENOCARCINOMA, NOS, INVASIVE	1 (2%)	1 (2%)	
ASTROCYTOMA			1 (2%)
OLIGODENDROGLIOMA		1 (2%)	
#MEDULLA OBLONGATA	(49)	(50)	(50)
ASTROCYTOMA	1 (2%)		
*SPINAL CORD	(50)	(50)	(50)
OSTEOSARCOMA	1 (2%)		
SPECIAL SENSE ORGANS			
*EAR CANAL	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA			1 (2%)
*ZYMBAL'S GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA			1 (2%)
ADENOCARCINOMA, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*VERTEBRAL COLUMN	(50)	(50)	(50)
OSTEOSARCOMA	1 (2%)		
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
NEOPLASM, NOS, UNC PRIM OR META	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
CARCINOMA, NOS, METASTATIC	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	9	9	6
MORIBUND SACRIFICE	10	8	11
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	31	33	32
ACCIDENTALLY KILLED, NOS			1

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	39	40	40
TOTAL PRIMARY TUMORS	76	66	71
TOTAL ANIMALS WITH BENIGN TUMORS	26	31	31
TOTAL BENIGN TUMORS	43	46	44
TOTAL ANIMALS WITH MALIGNANT TUMORS	23	17	20
TOTAL MALIGNANT TUMORS	29	19	24
TOTAL ANIMALS WITH SECONDARY TUMORS#	4	2	3
TOTAL SECONDARY TUMORS	4	2	5
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	1	3
TOTAL UNCERTAIN TUMORS	3	1	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC	1		
TOTAL UNCERTAIN TUMORS	1		

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	104	101	104	104	104	104	104	104	104	104	104	104	104	038	104	104	104	104	104	088	104	104	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRICHOEPITHELIOMA																						X			
SUBCUTANEOUS TISSUE	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																						X			
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA												X													
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	-	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	-	+
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE												X													
THYMUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL PAPILLOMA															X										
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS	X		X			X						X												X	X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA	X									X										X	X				
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA				X			X																		
PARATHYROID	-	+	+	+	+	+	+	-	+	+	+	+	-	+	+	-	+	-	+	-	+	+	+	+	+
ADENOMA, NOS						X																			
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA						X					X														
ISLET-CELL CARCINOMA																							X		
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	N	N	+	+	N	N	N	+	+	N	+	N	N	N	+	+	+	+	+	N	N	N
FIBROADENOMA																									
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																									
BODY CAVITIES																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS											X												X		
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, UNDIFFER-TYPE																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE				X																					
UNDIFFERENTIATED LEUKEMIA	X														X					X				X	
LEUKEMIA,MONONUCLEAR CELL																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
$: ANIMAL MIS-SEXED
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50M
TRICHOEPITHELIOMA	1
SUBCUTANEOUS TISSUE	50M
FIBROMA	1
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
ALVEOLAR/BRONCHIOLAR ADENOMA	2
TRACHEA	50
HEMATOPOIETIC SYSTEM	
BONE MARROW	49
SPLEEN	50
LYMPH NODES	49
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1
THYMUS	46
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	50
LIVER	50
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	50
ESOPHAGUS	50
STOMACH	50
SMALL INTESTINE	50
LARGE INTESTINE	50
URINARY SYSTEM	
KIDNEY	50
TRANSITIONAL-CELL PAPILLOMA	1
URINARY BLADDER	50
ENDOCRINE SYSTEM	
PITUITARY	49
CARCINOMA,NOS	1
ADENOMA, NOS	16
ADRENAL	50
CORTICAL ADENOMA	1
PHEOCHROMOCYTOMA	9
THYROID	50
C-CELL CARCINOMA	2
PARATHYROID	48
ADENOMA, NOS	1
PANCREATIC ISLETS	50
ISLET-CELL ADENOMA	2
ISLET-CELL CARCINOMA	1
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
FIBROADENOMA	1
TESTIS	50
INTERSTITIAL-CELL TUMOR	47
PROSTATE	50
NERVOUS SYSTEM	
BRAIN	50
ASTROCYTOMA	1
BODY CAVITIES	
TUNICA VAGINALIS	50M
MESOTHELIOMA, NOS	3
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
MALIG.LYMPHOMA, UNDIFFER-TYPE	1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1
UNDIFFERENTIATED LEUKEMIA	9
LEUKEMIA,MONONUCLEAR CELL	1

M ANIMALS NECROPSIED
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	091	086	104	104	084	104	104	104	096	104	104	104	086	079	104	074	104	086	104	104	104	104	084	104	104
INTEGUMENTARY SYSTEM																									
SKIN	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BASAL-CELL CARCINOMA															X										
TRICHOEPITHELIOMA		X																							
SUBCUTANEOUS TISSUE	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																X						X			
FIBROSARCOMA																								X	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA																			X						
FIBROSARCOMA, METASTATIC																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	+	-	+	-	-	-	-	-
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	-	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	-	+	-	-	+	+	+
THYMUS	-	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE										X		X													
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ACINAR-CELL ADENOMA																									
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA, UNC PRIM OR META												X													
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS									X		X				X				X						
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																								X	
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA	X				X	X		X					X		X				X	X				X	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA																					X				
PARATHYROID	+	+	+	-	-	-	-	+	-	-	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+
ADENOMA, NOS																								X	
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	+	+	+	N	+	+	N	+	+	+	+	N	N	+	+	+	N	+	+	N	N	N
FIBROADENOMA													X												
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
TUBULAR ADENOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
PLEURA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, MALIGNANT																									
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																									
MESOTHELIOMA, MALIGNANT																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
UNDIFFERENTIATED LEUKEMIA		X																		X					
LYMPHOCYTIC LEUKEMIA									X						X										

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50*
BASAL-CELL CARCINOMA	1
TRICHOEPITHELIOMA	1
SUBCUTANEOUS TISSUE	50*
FIBROMA	3
FIBROSARCOMA	2
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
ALVEOLAR/BRONCHIOLAR CARCINOMA	1
FIBROSARCOMA, METASTATIC	1
TRACHEA	50
HEMATOPOIETIC SYSTEM	
BONE MARROW	22
SPLEEN	49
LYMPH NODES	40
THYMUS	42
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	49
LIVER	50
NEOPLASTIC NODULE	2
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50*
PANCREAS	50
ACINAR-CELL ADENOMA	1
ESOPHAGUS	50
STOMACH	49
SMALL INTESTINE	48
LARGE INTESTINE	48
URINARY SYSTEM	
KIDNEY	50
FIBROSARCOMA, UNC PRIM OR META	1
URINARY BLADDER	50
ENDOCRINE SYSTEM	
PITUITARY	49
ADENOMA, NOS	12
ADRENAL	50
ADENOMA, NOS	1
CORTICAL ADENOMA	1
PHEOCHROMOCYTOMA	16
THYROID	50
C-CELL CARCINOMA	2
PARATHYROID	34
ADENOMA, NOS	3
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50*
FIBROADENOMA	2
TESTIS	50
INTERSTITIAL-CELL TUMOR	49
PROSTATE	48
TUBULAR ADENOMA	1
NERVOUS SYSTEM	
BRAIN	50
BODY CAVITIES	
PLEURA	50*
MESOTHELIOMA, MALIGNANT	1
PERITONEUM	50*
MESOTHELIOMA, NOS	2
TUNICA VAGINALIS	50*
MESOTHELIOMA, NOS	2
MESOTHELIOMA, MALIGNANT	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50*
UNDIFFERENTIATED LEUKEMIA	5
LYMPHOCYTIC LEUKEMIA	2

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
–: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

I: NO TISSUE INFORMATION SUBMITTED
C: *NECROPSY, NO HISTOLOGY DUE TO PROTOCOL*
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	062	089	101	104	105	096	078	104	104	100	104	104	104	093	104	104	104	104	104	072	104	101	093	095	048
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRICHOEPITHELIOMA						X																			
FIBROSARCOMA																									
LIPOMA																						X			
HEMANGIOMA																									
NEUROFIBROMA													X												
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA																				X					
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	-	-	+	+	+	-	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	-	+	+	-
THYMUS	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CA, INVASIVE																				X					
DIGESTIVE SYSTEM																									
SALIVARY GLAND	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE													X												
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA																X									
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS		X		X		X		X					X					X			X				
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA				X														X		X			X		
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
PAPILLARY ADENOCARCINOMA																					X				
C-CELL CARCINOMA															X										
PAPILLARY CYSTADENOMA, NOS				X																					
PARATHYROID	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
ADENOMA, NOS																				X					
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	N	+	N	N	N	N	N	+	+	N	+	N	N	N	N	N	+	N	+	+	+	N	+
FIBROADENOMA										X											X				
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR		X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS												X													
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																									
BODY CAVITIES																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS	X																								
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
UNDIFFERENTIATED LEUKEMIA										X								X	X				X		

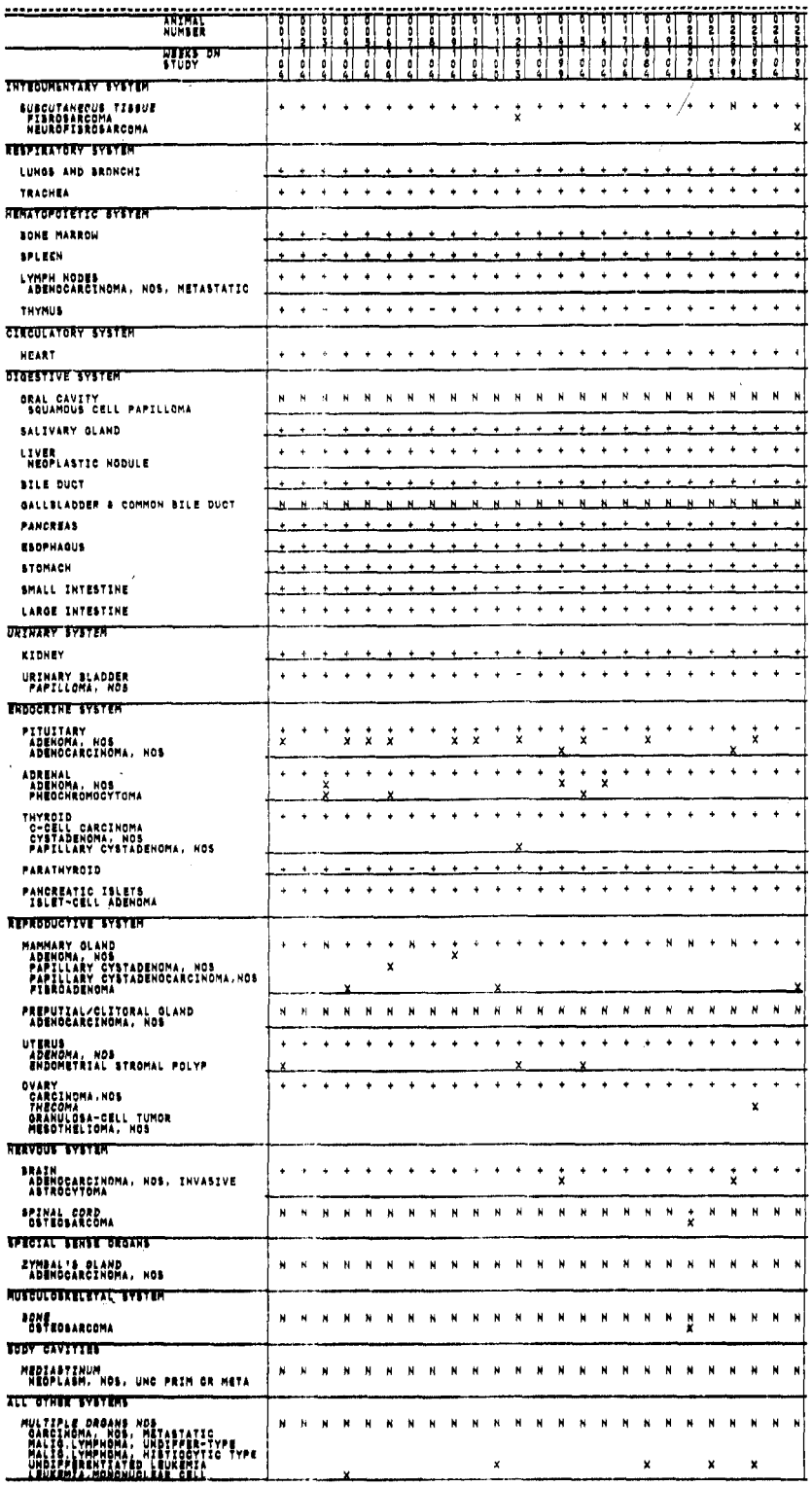
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50M
SQUAMOUS CELL PAPILLOMA	1
SUBCUTANEOUS TISSUE	50M
TRICHOEPITHELIOMA	1
FIBROSARCOMA	1
LIPOMA	1
HEMANGIOMA	1
NEUROFIBROMA	2
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
ALVEOLAR/BRONCHIOLAR CARCINOMA	2
TRACHEA	50
HEMATOPOIETIC SYSTEM	
BONE MARROW	50
SPLEEN	50
LYMPH NODES	49
THYMUS	47
CIRCULATORY SYSTEM	
HEART	50
ALVEOLAR/BRONCHIOLAR CA, INVASIVE	1
DIGESTIVE SYSTEM	
SALIVARY GLAND	48
LIVER	50
NEOPLASTIC NODULE	1
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	49
ESOPHAGUS	49
STOMACH	46
SMALL INTESTINE	46
LARGE INTESTINE	46
URINARY SYSTEM	
KIDNEY	49
TUBULAR-CELL ADENOCARCINOMA	1
URINARY BLADDER	46
ENDOCRINE SYSTEM	
PITUITARY	49
ADENOMA, NOS	11
ADRENAL	49
PHEOCHROMOCYTOMA	6
THYROID	46
PAPILLARY ADENOCARCINOMA	1
C-CELL CARCINOMA	1
PAPILLARY CYSTADENOMA, NOS	1
PARATHYROID	38
ADENOMA, NOS	1
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
FIBROADENOMA	2
TESTIS	50
INTERSTITIAL-CELL TUMOR	41
PROSTATE	49
PREPUTIAL/CLITORAL GLAND	50M
ADENOCARCINOMA, NOS	1
NERVOUS SYSTEM	
BRAIN	50
SPECIAL SENSE ORGANS	
ZYMBAL'S GLAND	50M
SQUAMOUS CELL CARCINOMA	1
BODY CAVITIES	
TUNICA VAGINALIS	50M
MESOTHELIOMA, NOS	2
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
UNDIFFERENTIATED LEUKEMIA	5

M ANIMALS NECROPSIED
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: VEHICLE CONTROL



+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHCLE CONTROL

ANIMAL NUMBER	0 2 1 1 0 4	0 2 2 6 8 8	0 2 3 1 0 4	0 2 3 8 0 7	0 3 1 1 0 9	0 3 1 2 0 4	0 3 1 5 0 4	0 3 1 6 0 4	0 3 1 6 0 7	0 3 1 6 0 9	0 3 1 7 0 1	0 3 1 7 0 6	0 3 1 8 0 4	0 3 1 9 0 4	0 4 0 4 0 4	0 4 0 4 0 8	0 4 0 4 1 0	0 4 0 4 2 0	0 4 0 4 3 0	0 4 0 4 4 5	0 4 0 4 5 0	0 4 0 4 6 6	0 4 0 4 7 0	0 4 0 4 7 9	0 4 0 4 8 9	0 4 0 4 9 8	0 4 0 5 1 0	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM																												
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROSARCOMA													X															2
NEUROFIBROSARCOMA																												1
RESPIRATORY SYSTEM																												
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																												
BONE MARROW	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	46
ADENOCARCINOMA, NOS, METASTATIC											X																	1
THYMUS	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	43
CIRCULATORY SYSTEM																												
HEART	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																												
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL PAPILLOMA																		X										1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASTIC NODULE														X														1
BILE DUCT	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	-	+	+	46
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
STOMACH	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																												
KIDNEY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	45
PAPILLOMA, NOS									X																			1
ENDOCRINE SYSTEM																												
PITUITARY	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ADENOMA, NOS				X		X					X																	13
ADENOCARCINOMA, NOS																												2
ADRENAL	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS								X										X										3
PHEOCHROMOCYTOMA																												5
THYROID	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	48
C-CELL CARCINOMA																									X			1
CYSTADENOMA, NOS																										X		1
PAPILLARY CYSTADENOMA, NOS						X																						2
PARATHYROID	-	+	-	-	+	+	+	+	+	-	+	-	+	-	-	-	+	-	+	-	-	-	-	-	+	33
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	-	+	+	46
ISLET-CELL ADENOMA							X																					1
REPRODUCTIVE SYSTEM																												
MAMMARY GLAND	+	+	+	+	+	+	N	N	N	N	+	N	+	+	N	N	+	+	+	+	N	+	N	+	+	+	+	50M
ADENOMA, NOS																												1
PAPILLARY CYSTADENOMA, NOS																												1
PAPILLARY CYSTADENOCARCINOMA,NOS																												1
FIBROADENOMA											X		X					X		X								6
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOCARCINOMA, NOS											X																	1
UTERUS	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS																			X									1
ENDOMETRIAL STROMAL POLYP							X	X																		X		6
OVARY	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CARCINOMA,NOS																										X		1
THECOMA																												1
GRANULOSA-CELL TUMOR																										X		1
MESOTHELIOMA, NOS																										X		1
NERVOUS SYSTEM																												
BRAIN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOCARCINOMA, NOS, INVASIVE																X												2
ASTROCYTOMA																							X					2
SPINAL CORD	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
OSTEOSARCOMA																												1
SPECIAL SENSE ORGANS																												
ZYMBAL'S GLAND	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOCARCINOMA, NOS		X																										1
MUSCULOSKELETAL SYSTEM																												
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
OSTEOSARCOMA																												1
BODY CAVITIES																												
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
NEOPLASM, NOS, UNC PRIM OR META																										X		1
ALL OTHER SYSTEMS																												
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
CARCINOMA, NOS, METASTATIC	X																									X		1
MALIG.LYMPHOMA, UNDIFFER-TYPE																												1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										X		1
UNDIFFERENTIATED LEUKEMIA			X		X	X						X	X		X			X						X				12
LEUKEMIA,MONONUCLEAR CELL																												1

* ANIMALS NECROPSIED
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	011	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	085	095	098	095	095	092	095	095	081	095	095	086	081	095	095	079	095	095	095	053	051	095	065	095	090
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA			X																						
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA																									
LYMPH NODES	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE										X															
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
LARGE INTESTINE	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-
ADENOMA, NOS		X		X		X	X				X		X	X							X				
ADENOCARCINOMA, NOS																									
ADRENAL	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
ADENOCARCINOMA, NOS																									X
PHEOCHROMOCYTOMA	X									X									X						
PHEOCHROMOCYTOMA, MALIGNANT																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																									
C-CELL CARCINOMA			X		X																				
CYSTADENOMA, NOS																									
PARATHYROID	+	+	-	-	-	+	+	+	+	+	-	+	+	+	+	+	-	+	-	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	N	N	N	+	+	+	+	+	N	N
PAPILLARY ADENOMA																									
FIBROADENOMA							X				X				X										
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
LEIOMYOSARCOMA																				X					
LEIOMYOSARCOMA, INVASIVE																				X					
ENDOMETRIAL STROMAL POLYP			X		X					X				X			X	X	X						
ENDOMETRIAL STROMAL SARCOMA																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, INVASIVE																									
OLIGODENDROGLIOMA																							X		
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, UNDIFFER-TYPE						X										X									
UNDIFFERENTIATED LEUKEMIA									X																
LYMPHOCYTIC LEUKEMIA												X													
LEUKEMIA,MONONUCLEAR CELL	X																								

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER / WEEKS ON STUDY	0207	0228	0229	0233	0310	0312	0313	0315	0318	0320	0321	0327	0328	0329	0330	0401	0405	0409	0412	0413	0416	0417	0418	0419	0420	0501	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM																											
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA																											1
RESPIRATORY SYSTEM																											
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																											
BONE MARROW	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOMA																	X										1
LYMPH NODES	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	44
THYMUS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	43
CIRCULATORY SYSTEM																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																											
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASTIC NODULE																											1
BILE DUCT	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																											
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																											
PITUITARY	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	45
ADENOMA, NOS			X		X				X	X						X					X		X		X	16
ADENOCARCINOMA, NOS																						X					1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS																						X					1
ADENOCARCINOMA, NOS																											1
PHEOCHROMOCYTOMA																		X									4
PHEOCHROMOCYTOMA, MALIGNANT											X																1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS											X																1
C-CELL CARCINOMA																X		X									3
CYSTADENOMA, NOS				X																							2
PARATHYROID	+	+	+	+	-	+	+	+	+	-	-	+	+	-	+	+	-	+	-	+	+	+	-	-	-		35
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND	+	+	+	+	+	N	N	+	+	+	N	+	+	N	+	N	N	+	N	+	+	+	+	+	+	+	50M
PAPILLARY ADENOMA																						X					1
FIBROADENOMA	X			X	X					X										X	X		X	X			11
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS																			X								1
LEIOMYOSARCOMA																											1
LEIOMYOSARCOMA, INVASIVE																											1
ENDOMETRIAL STROMAL POLYP										X											X						9
ENDOMETRIAL STROMAL SARCOMA																				X							1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																											
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, INVASIVE																						X					1
OLIGODENDROGLIOMA																											1
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIG.LYMPHOMA, UNDIFFER-TYPE																											2
UNDIFFERENTIATED LEUKEMIA			X			X																					3
LYMPHOCYTIC LEUKEMIA																											1
LEUKEMIA,MONONUCLEAR CELL																						X					2

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	100	100	104	104	104	109	104	104	093	100	078	101	104	086	041	109	104	097	104	104	081	104	090
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SEBACEOUS ADENOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA													X												
FIBROSARCOMA								X																	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																X									
ADENOCARCINOMA, NOS, METASTATIC																									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																X									
FIBROSARCOMA, METASTATIC																	X								
THYMUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE					X																				
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																	X								
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
FIBROSARCOMA, METASTATIC																		X							
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS			X				X					X					X	X	X					X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA		X				X																			
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA						X																			
CYSTADENOMA, NOS																									
PAPILLARY CYSTADENOMA, NOS																									
PARATHYROID	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	N	+	+	N	N	N	+	+	N	+	+
ADENOCARCINOMA, NOS																									
PAPILLARY CYSTADENOMA, NOS	X																								
FIBROADENOMA				X	X		X															X			
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																									
ADENOCARCINOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																			X						
FIBROSARCOMA																				X					
ENDOMETRIAL STROMAL POLYP																						X			
ENDOMETRIAL STROMAL SARCOMA																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LUTEOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																									
SPECIAL SENSE ORGANS																									
EAR	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA	X																								
ZYMBAL'S GLAND	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																X									
BODY CAVITIES																									
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEMANGIOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
UNDIFFERENTIATED LEUKEMIA	X	X															X			X	X		X		X

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: *ANIMAL MIS-SEXED*

I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	020	046	097	104	049	059	091	104	083	046	104	041	041	081	046	046	094	041	041	046	046	046	046	046	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
SEBACEOUS ADENOMA																								X		1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA																										1
FIBROSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA, METASTAT																										1
ADENOCARCINOMA, NOS, METASTATIC										X																1
ALVEOLAR/BRONCHIOLAR CARCINOMA																								X		1
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	46
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	45
SQUAMOUS CELL CARCINOMA, METASTAT																										1
FIBROSARCOMA, METASTATIC																										1
THYMUS	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE				X																					X	3
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	48
FIBROSARCOMA																										1
URINARY SYSTEM																										
KIDNEY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	46
FIBROSARCOMA, METASTATIC																										1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS					X				X		X	X	X			X			X		X		X	X	X	18
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA	X																									3
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	49
C-CELL CARCINOMA			X																							2
CYSTADENOMA, NOS																								X		1
PAPILLARY CYSTADENOMA, NOS												X														1
PARATHYROID	+	-	+	-	+	+	+	+	-	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	40
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	N	+	+	+	+	+	+	+	N	+	N	N	+	+	+	N	+	+	N	+	+	+	50M
ADENOCARCINOMA, NOS										X																1
PAPILLARY CYSTADENOMA, NOS																										1
FIBROADENOMA					X						X														X	7
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	50M
SQUAMOUS CELL CARCINOMA																										1
ADENOCARCINOMA, NOS																								X		1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	50
ADENOMA, NOS																										1
FIBROSARCOMA																										1
ENDOMETRIAL STROMAL POLYP			X						X				X							X	X					7
ENDOMETRIAL STROMAL SARCOMA			X																							1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LUTEOMA												X														1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA									X																	1
SPECIAL SENSE ORGANS																										
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL PAPILLOMA																										1
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL CARCINOMA																										1
BODY CAVITIES																										
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
HEMANGIOMA																							X			1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
UNDIFFERENTIATED LEUKEMIA									X							X	X					X	X			12

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SARCOMA, NOS	2 (4%)	1 (2%)	1 (2%)
FIBROMA	1 (2%)		
FIBROSARCOMA		2 (4%)	
NEUROFIBROSARCOMA	1 (2%)	2 (4%)	
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS	1 (2%)	1 (2%)	2 (4%)
FIBROMA			1 (2%)
FIBROSARCOMA	1 (2%)	1 (2%)	2 (4%)
LEIOMYOSARCOMA	1 (2%)		
RHABDOMYOSARCOMA			1 (2%)
NEUROFIBROSARCOMA	1 (2%)	2 (4%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
ADENOCARCINOMA, NOS, METASTATIC	1 (2%)		
HEPATOCELLULAR CARCINOMA, METAST	3 (6%)	4 (8%)	5 (10%)
ALVEOLAR/BRONCHIOLAR ADENOMA	4 (8%)	6 (12%)	4 (8%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	4 (8%)	2 (4%)	10 (20%)
FIBROSARCOMA, METASTATIC		1 (2%)	
LEIOMYOSARCOMA, METASTATIC		1 (2%)	
NEUROFIBROSARCOMA, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, UNDIFFER-TYPE		1 (2%)	
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	6 (12%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	3 (6%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
LYMPHOCYTIC LEUKEMIA		1 (2%)	
GRANULOCYTIC LEUKEMIA		1 (2%)	
#SPLEEN	(45)	(48)	(48)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
#MEDIASTINAL L.NODE	(33)	(38)	(40)
HEPATOCELLULAR CARCINOMA, METAST			1 (3%)
#LIVER	(50)	(49)	(46)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
#JEJUNUM	(39)	(40)	(43)
MALIGNANT LYMPHOMA, MIXED TYPE	1 (3%)		
CIRCULATORY SYSTEM			
#SPLEEN	(45)	(48)	(48)
HEMANGIOSARCOMA	2 (4%)	1 (2%)	1 (2%)
#SPLENIC RED PULP	(45)	(48)	(48)
HEMANGIOSARCOMA		1 (2%)	
#MYOCARDIUM OF RIGHT	(48)	(50)	(50)
HEMANGIOMA			1 (2%)
#LIVER	(50)	(49)	(46)
HEMANGIOSARCOMA	1 (2%)	2 (4%)	2 (4%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(46)
HEPATOCELLULAR ADENOMA	8 (16%)	5 (10%)	2 (4%)
HEPATOCELLULAR CARCINOMA	14 (28%)	10 (20%)	9 (20%)
#GASTRIC MUCOSA	(46)	(48)	(46)
ADENOCARCINOMA, NOS			1 (2%)
URINARY SYSTEM			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#ADRENAL	(50)	(47)	(48)
CORTICAL ADENOMA		3 (6%)	1 (2%)
PHEOCHROMOCYTOMA	4 (8%)	6 (13%)	2 (4%)
#ADRENAL/CAPSULE	(50)	(47)	(48)
ADENOMA, NOS	1 (2%)		
#ZONA GLOMERULOSA	(50)	(47)	(48)
ADENOMA, NOS			1 (2%)
#ZONA FASCICULATA	(50)	(47)	(48)
ADENOMA, NOS	1 (2%)		
#ZONA RETICULARIS	(50)	(47)	(48)
ADENOMA, NOS	1 (2%)		
#THYROID	(44)	(37)	(44)
PAPILLARY ADENOMA	1 (2%)		
FOLLICULAR-CELL ADENOMA	1 (2%)		
#PANCREATIC ISLETS	(48)	(49)	(45)
ISLET-CELL ADENOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
#TESTIS	(50)	(48)	(49)
INTERSTITIAL-CELL TUMOR			1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(50)	(50)	(50)
ADENOMA, NOS			1 (2%)
ADENOCARCINOMA, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			

\# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
LEIOMYOSARCOMA	1 (2%)		
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
SARCOMA, NOS, METASTATIC		1 (2%)	1 (2%)
LEIOMYOSARCOMA		1 (2%)	
LEIOMYOSARCOMA, METASTATIC	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	19	14	11
MORIBUND SACRIFICE	5	4	4
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	26	32	35
ACCIDENTALLY KILLED, NOS			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	38	32	36
TOTAL PRIMARY TUMORS	61	50	47
TOTAL ANIMALS WITH BENIGN TUMORS	17	16	14
TOTAL BENIGN TUMORS	23	20	14
TOTAL ANIMALS WITH MALIGNANT TUMORS	31	23	28
TOTAL MALIGNANT TUMORS	38	30	33
TOTAL ANIMALS WITH SECONDARY TUMORS#	6	6	6
TOTAL SECONDARY TUMORS	6	7	7
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING			1
ANIMALS NECROPSIED	49	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	48	49
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(49)	(50)	(49)
BASAL-CELL CARCINOMA		1 (2%)	
SARCOMA, NOS	2 (4%)		1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(47)	(48)	(48)
BASAL-CELL CARCINOMA, METASTATIC		1 (2%)	
HEPATOCELLULAR CARCINOMA, METAST			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	3 (6%)	4 (8%)	2 (4%)
ALVEOLAR/BRONCHIOLAR CARCINOMA			1 (2%)
SARCOMA, NOS, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
MALIG.LYMPHOMA, UNDIFFER-TYPE	3 (6%)		1 (2%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	7 (14%)	8 (16%)	8 (16%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			2 (4%)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
UNDIFFERENTIATED LEUKEMIA		1 (2%)	
LYMPHOCYTIC LEUKEMIA	2 (4%)	1 (2%)	1 (2%)
#SPLEEN	(45)	(46)	(47)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		1 (2%)	
#SPLENIC FOLLICLES	(45)	(46)	(47)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		2 (4%)	
#MESENTERIC L. NODE	(41)	(33)	(35)
SARCOMA, NOS, METASTATIC	1 (2%)		
MALIG.LYMPHOMA, UNDIFFER-TYPE			1 (3%)
#INGUINAL LYMPH NODE	(41)	(33)	(35)
SARCOMA, NOS, METASTATIC	1 (2%)		
#UTERUS	(48)	(47)	(49)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(49)
HEMANGIOSARCOMA			1 (2%)
#SPLEEN	(45)	(46)	(47)
HEMANGIOSARCOMA	2 (4%)		1 (2%)
#LIVER	(48)	(47)	(46)
HEMANGIOSARCOMA	1 (2%)		
*MESENTERY	(49)	(50)	(49)
HEMANGIOSARCOMA	1 (2%)		
#UTERUS	(48)	(47)	(49)
HEMANGIOMA			1 (2%)
HEMANGIOSARCOMA			1 (2%)
#UTERINE SEROSA	(48)	(47)	(49)
HEMANGIOMA		1 (2%)	
#OVARY	(47)	(44)	(43)
HEMANGIOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(48)	(47)	(46)
HEPATOCELLULAR ADENOMA	2 (4%)	4 (9%)	2 (4%)
HEPATOCELLULAR CARCINOMA	2 (4%)	1 (2%)	1 (2%)
*PERIRECTAL TISSUE	(49)	(50)	(49)
SQUAMOUS CELL CARCINOMA	1 (2%)		
URINARY SYSTEM			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(39)	(39)	(41)
CARCINOMA,NOS			1 (2%)
ADENOMA, NOS	7 (18%)	4 (10%)	3 (7%)
#ADRENAL	(48)	(48)	(46)
CORTICAL ADENOMA		1 (2%)	1 (2%)
PHEOCHROMOCYTOMA	1 (2%)		
#ADRENAL/CAPSULE	(48)	(48)	(46)
ADENOMA, NOS		1 (2%)	1 (2%)
SARCOMA, NOS, METASTATIC	1 (2%)		
#THYROID	(43)	(44)	(42)
PAPILLARY ADENOMA		1 (2%)	
FOLLICULAR-CELL ADENOMA			1 (2%)
PAPILLARY CYSTADENOMA, NOS	1 (2%)		
#PARATHYROID	(23)	(25)	(30)
ADENOMA, NOS	1 (4%)		
#PANCREATIC ISLETS	(46)	(47)	(47)
ISLET-CELL ADENOMA	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(49)
ADENOCARCINOMA, NOS		1 (2%)	
#UTERUS	(48)	(47)	(49)
ENDOMETRIAL STROMAL POLYP	2 (4%)		1 (2%)
#OVARY	(47)	(44)	(43)
CHORIOCARCINOMA			1 (2%)
NERVOUS SYSTEM			
#BRAIN/THALAMUS	(49)	(46)	(49)
CARCINOMA, NOS, INVASIVE			1 (2%)
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(49)	(50)	(49)
SQUAMOUS CELL CARCINOMA	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
PAPILLARY CYSTADENOMA, NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(50)	(49)
CARCINOMA, NOS, UNC PRIM OR META		1 (2%)	
SARCOMA, NOS, METASTATIC			1 (2%)
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	10	7	9
MORIBUND SACRIFICE	6	3	2
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	33	40	38
ACCIDENTALLY KILLED, NOS	1		
ANIMAL MISSING			1

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	32	28	29
TOTAL PRIMARY TUMORS	41	35	35
TOTAL ANIMALS WITH BENIGN TUMORS	17	14	11
TOTAL BENIGN TUMORS	18	18	12
TOTAL ANIMALS WITH MALIGNANT TUMORS	20	16	20
TOTAL MALIGNANT TUMORS	23	16	23
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	1	3
TOTAL SECONDARY TUMORS	4	1	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC		1	
TOTAL UNCERTAIN TUMORS		1	

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	076	105	105	105	102	105	105	105	105	104	082	077	105	077	078	091	078	071	064	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
SKIN	+	N	+	+	+	N	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	N	+
SARCOMA, NOS													X												X
FIBROMA																									
NEUROFIBROSARCOMA																									
SUBCUTANEOUS TISSUE	+	N	+	+	+	N	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	N	+
SARCOMA, NOS								X																	
FIBROSARCOMA										X															
LEIOMYOSARCOMA																									
NEUROFIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																									
HEPATOCELLULAR CARCINOMA, METASTA					X						X														
ALVEOLAR/BRONCHIOLAR ADENOMA							X	X												X					
ALVEOLAR/BRONCHIOLAR CARCINOMA																						X	X	X	
NEUROFIBROSARCOMA, METASTATIC																									
TRACHEA	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																					X				
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
LYMPH NODES	-	+	+	+	+	+	-	+	-	+	+	-	+	+	-	+	-	+	-	-	+	+	+	-	+
THYMUS	-	+	+	+	-	-	+	-	-	-	-	-	+	+	-	-	-	+	+	+	+	+	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA				X				X	X											X					X
HEPATOCELLULAR CARCINOMA	X			X	X						X						X			X					
HEMANGIOSARCOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	N	+	+	+	+	+	+	N	+	+	+	N	N	N	+	N	+	+	+	N	+	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ESOPHAGUS	+	-	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	-	+	-	+	+	+	+	+	+
MALIGNANT LYMPHOMA, MIXED TYPE							X																		
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	-	-	+	-	-	+	+	-	+	-	+	-	-	+	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS		X																		X					
PHEOCHROMOCYTOMA					X																				
THYROID	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-
PAPILLARY ADENOMA														X											
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	+	-	-	+	-	+	-	-	+	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-	-
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ISLET-CELL ADENO																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS																									
BODY CAVITIES																									
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEIOMYOSARCOMA											X														
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEIOMYOSARCOMA, METASTATIC																									
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE										v															

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	0202 0100	0202 0700	0202 0800	0202 0900	0313 0100	0313 0200	0313 0500	0313 0600	0313 0900	0313 1000	0313 1100	0313 1400	0313 1700	0313 1800	0313 1900	0401 0300	0401 0500	0401 1100	0401 1200	0401 1500	0401 1600	0401 1700	0401 1800	0401 1900	0401 2000	0401 2100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	0 3	0 7	0 7	0 5	0 7	0 8	0 7	0 5	0 9	0 9	0 5	0 5	0 4	0 5	0 5	0 3	0 5	0 5	0 2	0 5	0 5	0 5	0 8	0 5	0 6	0 8	1 0
INTEGUMENTARY SYSTEM																											
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS																			X								2
FIBROMA																											1
NEUROFIBROSARCOMA															X												1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS															X												1
FIBROSARCOMA																											1
LEIOMYOSARCOMA																											1
NEUROFIBROSARCOMA									X																		1
RESPIRATORY SYSTEM																											
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC															X												1
HEPATOCELLULAR CARCINOMA, METASTA										X																	3
ALVEOLAR/BRONCHIOLAR ADENOMA																						X					4
ALVEOLAR/BRONCHIOLAR CARCINOMA						X																					4
NEUROFIBROSARCOMA, METASTATIC									X																		1
TRACHEA	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																											
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	-	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
HEMANGIOSARCOMA																										X	2
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																											1
LYMPH NODES	+	-	+	+	-	+	+	-	-	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	-	+	33
THYMUS	+	-	-	+	-	-	-	+	-	+	-	+	-	-	+	+	-	+	+	+	-	+	-	+	+	+	26
CIRCULATORY SYSTEM																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	48
DIGESTIVE SYSTEM																											
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA								X			X											X					8
HEPATOCELLULAR CARCINOMA	X			X			X	X		X			X							X				X			14
HEMANGIOSARCOMA																											1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	+	N	N	+	N	N	+	N	N	+	+	N	N	+	+	+	+	N	N	+	N	+	N	N	+	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
STOMACH	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	46
SMALL INTESTINE	+	+	+	+	+	-	-	+	-	+	+	-	+	+	+	+	+	+	+	+	-	+	+	-	+		39
MALIGNANT LYMPHOMA, MIXED TYPE																											1
LARGE INTESTINE	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+		44
URINARY SYSTEM																											
KIDNEY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY BLADDER	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+		45
ENDOCRINE SYSTEM																											
PITUITARY	+	+	+	+	-	+	+	-	+	+	-	+	+	-	+	+	+	+	+	-	+	-	-	-	+	+	34
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS			X					X		X																	3
PHEOCHROMOCYTOMA																											4
THYROID	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
PAPILLARY ADENOMA																				X							1
FOLLICULAR-CELL ADENOMA																											1
PARATHYROID	+	-	-	+	-	-	-	+	-	+	-	-	+	+	+	+	+	-	-	+	-	-	+	-	-		17
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	48
ISLET-CELL ADENOMA																											1
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PROSTATE	+	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
NERVOUS SYSTEM																											
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																											
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOCARCINOMA, NOS														X													1
BODY CAVITIES																											
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
LEIOMYOSARCOMA																											1
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
LEIOMYOSARCOMA, METASTATIC																											1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE						X							X						X				X				6

* ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	096	087	105	105	109	108	103	105	105	101	105	082	084	105	105	103	105	105	105	105	105	105	084	105	105
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																							X		
FIBROSARCOMA																						X			
NEUROFIBROSARCOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
FIBROSARCOMA											X														
NEUROFIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									
ALVEOLAR/BRONCHIOLAR ADENOMA					X			X																	X
ALVEOLAR/BRONCHIOLAR CARCINOMA												X													
FIBROSARCOMA, METASTATIC																									
LEIOMYOSARCOMA, METASTATIC																									
TRACHEA	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																				X					
LYMPH NODES	+	-	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	-	+	-	+	+	-	-	+	-	-	+	+	+	+	+	+	+	+	-	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA		X				X						X													
HEPATOCELLULAR CARCINOMA														X										X	
HEMANGIOSARCOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	+	+	+	+	+	+	+	N	N	+	+	+	+	+	+	N	+	N	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
SMALL INTESTINE	+	-	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	-	-	+	-	-	+	+	+	+	+	+	+	+	-
ADRENAL	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
CORTICAL ADENOMA				X																					
PHEOCHROMOCYTOMA														X	X										
THYROID	+	-	-	+	+	+	+	+	+	-	-	-	+	-	+	-	+	-	+	+	+	+	-	+	+
PARATHYROID	-	-	-	+	-	+	+	-	+	-	+	-	+	-	+	-	+	-	+	-	-	+	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS, METASTATIC																									
LEIOMYOSARCOMA																									
MALIG.LYMPHOMA, UNDIFFER-TYPE											X														
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
LYMPHOCYTIC LEUKEMIA																									
GRANULOCYTIC LEUKEMIA																							X		

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50M
SARCOMA, NOS	1
FIBROSARCOMA	2
NEUROFIBROSARCOMA	2
SUBCUTANEOUS TISSUE	50M
SARCOMA, NOS	1
FIBROSARCOMA	1
NEUROFIBROSARCOMA	2
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
HEPATOCELLULAR CARCINOMA, METASTA	4
ALVEOLAR/BRONCHIOLAR ADENOMA	6
ALVEOLAR/BRONCHIOLAR CARCINOMA	2
FIBROSARCOMA, METASTATIC	1
LEIOMYOSARCOMA, METASTATIC	1
TRACHEA	44
HEMATOPOIETIC SYSTEM	
BONE MARROW	49
SPLEEN	48
HEMANGIOSARCOMA	2
LYMPH NODES	38
THYMUS	26
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	49
LIVER	49
HEPATOCELLULAR ADENOMA	5
HEPATOCELLULAR CARCINOMA	10
HEMANGIOSARCOMA	2
BILE DUCT	49
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	49
ESOPHAGUS	47
STOMACH	48
SMALL INTESTINE	40
LARGE INTESTINE	48
URINARY SYSTEM	
KIDNEY	50
URINARY BLADDER	46
ENDOCRINE SYSTEM	
PITUITARY	35
ADRENAL	47
CORTICAL ADENOMA	3
PHEOCHROMOCYTOMA	6
THYROID	37
PARATHYROID	18
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
TESTIS	48
PROSTATE	48
NERVOUS SYSTEM	
BRAIN	49
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
SARCOMA, NOS, METASTATIC	1
LEIOMYOSARCOMA	1
MALIG.LYMPHOMA, UNDIFFER-TYPE	1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1
LYMPHOCYTIC LEUKEMIA	1
GRANULOCYTIC LEUKEMIA	1

M ANIMALS NECROPSIED
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: HIGH DOSE

ANIMAL NUMBER	0 0 1	0 0 2	0 0 3	0 0 4	0 0 5	0 0 6	0 0 7	0 0 8	0 0 9	0 1 0	0 1 1	0 1 2	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 2 1	0 2 2	0 2 3	0 2 4	0 2 5
WEEKS ON STUDY	0 7 1	0 9 0	0 7 0	0 8 5	0 9 0	0 9 0	0 8 0	0 9 0	0 9 0	0 9 0	1 0 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 1	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
FIBROMA							X																		
FIBROSARCOMA					X																X				
RHABDOMYOSARCOMA																						X			
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA							X																	X	
ALVEOLAR/BRONCHIOLAR ADENOMA	X													X											
ALVEOLAR/BRONCHIOLAR CARCINOMA						X				X	X	X				X	X								X
TRACHEA	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA														X											
LYMPH NODES	+	-	+	+	+	-	+	-	-	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									
THYMUS	-	-	-	+	+	-	-	+	-	+	+	-	-	-	-	-	+	+	-	+	+	-	+	-	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA																									
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	-	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																					X				
HEPATOCELLULAR CARCINOMA							X								X				X					X	
HEMANGIOSARCOMA														X											
MALIG.LYMPHOMA, HISTIOCYTIC TYPE													X												
BILE DUCT	+	+	+	+	-	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	N	+	+	+	N	N	+	+	+	+	N	N	N	+	+	+	N	+	N	+	+	+	+
PANCREAS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ESOPHAGUS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS															X										
SMALL INTESTINE	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	+	-	-	+	-	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																		X							
CORTICAL ADENOMA																							X		
PHEOCHROMOCYTOMA																			X		X				
THYROID	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	-	-	+	+	-	+	-	+	-	+	-	+	+	+	-	-	-	-	+	-	+	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR																									
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS			X																						
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS, METASTATIC																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			X				X																		

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

I: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER / WEEKS ON STUDY	0226 0505	0227 0806	0228 0105	0229 0303	0230 0709	0231 0105	0232 0909	0233 0105	0234 0105	0235 0105	0236 0101	0237 0105	0238 0204	0239 0105	0240 0105	0241 0105	0242 0105	0243 0105	0244 0105	0245 0105	0246 0105	0247 0105	0248 0105	0249 0105	0250 0105	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	N	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS																					X					1
SUBCUTANEOUS TISSUE	+	+	+	+	N	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS																	X		X							2
FIBROMA																										1
FIBROSARCOMA																										2
RHABDOMYOSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA							X									X				X						5
ALVEOLAR/BRONCHIOLAR ADENOMA						X															X					4
ALVEOLAR/BRONCHIOLAR CARCINOMA						X											X						X			10
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
HEMANGIOSARCOMA																										1
LYMPH NODES	+	+	-	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	40
HEPATOCELLULAR CARCINOMA, METASTA							X																			1
THYMUS	+	+	+	-	-	+	-	+	+	-	+	+	+	+	-	+	+	-	-	-	+	-	+	-	-	25
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOMA			X																							1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	-	+	+	+	+	+	+	+	+	46
HEPATOCELLULAR ADENOMA																										2
HEPATOCELLULAR CARCINOMA	X						X									X			X	X						9
HEMANGIOSARCOMA										X																2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	46
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	+	N	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	50M
PANCREAS	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	45
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	46
ADENOCARCINOMA, NOS																										1
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	43
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	42
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	-	+	-	+	+	+	-	+	-	+	+	+	+	+	-	+	-	+	-	-	-	34
ADRENAL	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48
ADENOMA, NOS																										1
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA																										2
THYROID	+	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	44
PARATHYROID	+	-	+	-	-	-	+	+	+	-	-	+	+	-	+	+	+	-	-	-	-	+	-	-	+	25
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR																								X		1
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	50M
SARCOMA, NOS, METASTATIC																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									X	3

M ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: VEHICLE CONTROL

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0111	0112	0113	0114	0115	0116	0117	0118	0119	0120	0121	0122	0123	0124	0125
WEEKS ON STUDY	085	095	052	055	095	095	095	095	095	095	088	080	091	095	095	095	095	095	095	095	087	099	094	094	094
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE SARCOMA, NOS	+	+	N	+	+	+	+	N	N	+	+	+	+ X	+	+	N	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA SARCOMA, NOS, METASTATIC	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+ X	+	+	+	+	+	+	+ X	+	+	-
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
SPLEEN HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES SARCOMA, NOS, METASTATIC	-	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	-	+	+	+	+	+	+	+	+	+
THYMUS	+	+	-	+	+	+	+	+	+	+	-	-	-	-	-	+	+	+	+	+	+	-	-	+	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	N	N	+	N	N	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+
PANCREAS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
RECTUM SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	-	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS	+ X	+	+	-	+ X	+ X	-	+	+	+ X	+	+	+	+	+	+	+	+	+ X	+ X	-	+	+	+	+
ADRENAL PHEOCHROMOCYTOMA SARCOMA, NOS, METASTATIC	+	+	+	+	+	+	+ X	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
THYROID PAPILLARY CYSTADENOMA, NOS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	-
PARATHYROID ADENOMA, NOS	-	+	-	-	+	-	+	-	-	-	+	+	-	-	-	+	+	-	+	+	+	+	+	+	-
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	N	+	+	N	+	N	+	N	N	N	+	+	N	N	+	+	N	+	+	N	+	N	N
UTERUS ENDOMETRIAL STROMAL POLYP	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N
BODY CAVITIES																									
MESENTERY HEMANGIOSARCOMA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS MALIG.LYMPHOMA, UNDIFFER-TYPE MALIG.LYMPHOMA, LYMPHOCYTIC TYPE LYMPHOCYTIC LEUKEMIA	N	N	N X	N	N	N	N X	N	M	N X	N	N	N X	N	N	N	N X	N	N	N	N X	N	N	N	N X

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	0256	0257	0258	0259	0260	0351	0352	0353	0354	0355	0356	0357	0358	0359	0401	0402	0403	0404	0405	0406	0407	0408	0409	0450	TOTAL TISSUES TUMORS
WEEKS ON STUDY	0 8 4	1 0 5	0 6 3	1 0 5	1 0 5	1 0 5	1 0 4	1 0 9	1 0 5	1 0 5	0 0 6	1 0 2	1 0 5	1 0 5	1 0 5	1 0 7	1 0 7	0 2 7	1 0 5	1 0 5	1 0 5	1 1 1	1 0 5	1 0 7	0 5 8	
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE SARCOMA, NOS	+	+	+	+	+	N	+	+	+	+	B	+ X	+	+	+	+	N	+	+	+	+	N	+	+	49M 2
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA SARCOMA, NOS, METASTATIC	+	+	+	+	+	+	+	+	+	+	B	-	+	+	+	+	+	+	+ X	+	+	+	+	+	47 3 1
TRACHEA	+	+	+	+	+	-	+	+	+	+	B	+	+	+	-	+	-	+	+	+	+	+	+	+	45
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN HEMANGIOSARCOMA	+	+	+	+	+	+	+	+	+	+	B	+	+	+	-	-	+ X	+	+	+	-	+	+ X	+	-	45 2
LYMPH NODES SARCOMA, NOS, METASTATIC	-	-	-	-	+	+	+	+	-	+	B	+ X	+	+	+	+	+	+	+	+	+	+	+	+	-	41 2
THYMUS	-	+	-	+	+	-	-	-	+	+	B	+	+	+	-	+	-	+	+	-	+	-	+	+	+	31
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	-	+	+	+	+	48
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	+	+	-	-	44
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA HEMANGIOSARCOMA	+	+	+	+ X	+	+	+	+ X	+	+	B	+	+	+	+	+	+	+	+	+	+	-	+	+	+	48 2 2 1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	-	+	+	+	48
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	+	+	N	+	N	B	N	+	+	+	+	+	+	+	+	+	+	+	N	+	49M
PANCREAS	+	+	+	+	+	+	+	+	+	+	B	+	-	+	+	+	+	+	+	+	+	+	+	+	+	46
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	B	+	+	+	-	+	-	+	+	+	+	+	+	+	+	46
STOMACH	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	-	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	-	+	+	+	+	+	-	+	43
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
RECTUM SQUAMOUS CELL CARCINOMA	N	N	N	N	N	+ X	N	N	N	N	B	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M 1
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS	+	+	+	-	+	-	+	+	+	+ X	B	-	+	+	+	+	+	+	-	+	+	-	-	+	-	39 7
ADRENAL PHEOCHROMOCYTOMA SARCOMA, NOS, METASTATIC	+	+	+	+	+	+	+	+	+	+	B	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	48 1 1
THYROID PAPILLARY CYSTADENOMA, NOS	+	+	-	+	+	-	+	+	+	+	B	+	+	+	-	+	-	+	+	+	+	+	+	+	+	43 1
PARATHYROID ADENOMA, NOS	-	-	-	-	-	-	+	+	-	-	B	+	+	-	-	-	-	-	+	-	+	+	+	+	+ X	23 1
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	B	+	-	+	+	+	+	+	+	+	+	+ X	+	+	+	46 1
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	N	N	N	N	+	+	B	N	N	+	+	+	N	+	+	N	N	+	N	N	+		49M
UTERUS ENDOMETRIAL STROMAL POLYP	+	+	+	+	+	+	+ X	+	+	+	B	+	+	+	+	+	+	+	+	-	+	+	+	+	+	48 2
OVARY	+	+	+	+	+	+	+	+	+	+	B	-	+	+	+	+	+	+	+	+	+	+	+	+	+	47
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND SQUAMOUS CELL CARCINOMA	N	N	N	N	N	N	N	N	N	N	B	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M 1
BODY CAVITIES																									
MESENTERY HEMANGIOSARCOMA	N	N	N X	N	N	N	N	N	N	N	B	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49M 1
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS MALIG.LYMPHOMA, UNDIFFER-TYPE MALIG.LYMPHOMA, LYMPHOCYTIC TYPE LYMPHOCYTIC LEUKEMIA	N	N	N	N	N	N	N X	N X	N	N	B	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	49M 1 3 7 2

\# ANIMALS NECROPSIED

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
.: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: LOW DOSE

ANIMAL NUMBER	0011	0021	0031	0041	0051	0061	0071	0081	0091	0101	0111	0121	0131	0141	0151	0161	0171	0181	0191	0201	0211	0221	0231	0241	0251
WEEKS ON STUDY	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	087	094
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BASAL-CELL CARCINOMA																								X	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BASAL-CELL CARCINOMA, METASTATIC																								X	
ALVEOLAR/BRONCHIOLAR ADENOMA															X	X						X			
TRACHEA	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE												X													
LYMPH NODES	+	+	-	+	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	-	-	+	+	+
THYMUS	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA					X	X																X			
HEPATOCELLULAR CARCINOMA		X																							
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	+	-
ADENOMA, NOS			X												X										
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																						+			
CORTICAL ADENOMA																						X			
THYROID	-	+	+	+	-	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+
PAPILLARY ADENOMA														X											
PARATHYROID	+	-	-	+	-	+	-	-	-	+	+	-	-	-	-	+	+	-	+	-	+	+	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	+	+	+	+	+	N	N	N	+	N	N	N	N	+	N	+	+	+	N	+	N	N
ADENOCARCINOMA, NOS																	X								
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA												X													
OVARY	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
HEMANGIOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLARY CYSTADENOMA, NOS							X																		
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA, NOS, UNC PRIM OR META				X		X			X													X	X		X
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
UNDIFFERENTIATED LEUKEMIA																									
LYMPHOCYTIC LEUKEMIA																									

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES / TUMORS
INTEGUMENTARY SYSTEM	
SUBCUTANEOUS TISSUE	50M
BASAL-CELL CARCINOMA	1
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	48
BASAL-CELL CARCINOMA, METASTATIC	1
ALVEOLAR/BRONCHIOLAR ADENOMA	4
TRACHEA	44
HEMATOPOIETIC SYSTEM	
BONE MARROW	46
SPLEEN	46
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	3
LYMPH NODES	33
THYMUS	37
CIRCULATORY SYSTEM	
HEART	47
DIGESTIVE SYSTEM	
SALIVARY GLAND	47
LIVER	47
HEPATOCELLULAR ADENOMA	4
HEPATOCELLULAR CARCINOMA	1
BILE DUCT	47
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	47
ESOPHAGUS	48
STOMACH	46
SMALL INTESTINE	45
LARGE INTESTINE	46
URINARY SYSTEM	
KIDNEY	48
URINARY BLADDER	47
ENDOCRINE SYSTEM	
PITUITARY	39
ADENOMA, NOS	4
ADRENAL	48
ADENOMA, NOS	1
CORTICAL ADENOMA	1
THYROID	44
PAPILLARY ADENOMA	1
PARATHYROID	25
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
ADENOCARCINOMA, NOS	1
UTERUS	47
HEMANGIOMA	1
OVARY	44
HEMANGIOMA	1
NERVOUS SYSTEM	
BRAIN	44
SPECIAL SENSE ORGANS	
LACRIMAL GLAND	50M
PAPILLARY CYSTADENOMA, NOS	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
CARCINOMA, NOS, UNC PRIM OR META	1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	8
UNDIFFERENTIATED LEUKEMIA	1
LYMPHOCYTIC LEUKEMIA	1

M ANIMALS NECROPSIED
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF 1,2-DICHLOROBENZENE: HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	105	105	105	105	090	098	016	105	094	105	094	105	105	078	090	105	105	105	105	022	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	N	M	+	+	N	+	+
SARCOMA, NOS									X																
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA										X															
ALVEOLAR/BRONCHIOLAR ADENOMA																	X								
ALVEOLAR/BRONCHIOLAR CARCINOMA		X																							
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	M	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
HEMANGIOSARCOMA																		X							
LYMPH NODES	+	+	+	+	+	-	+	+	-	+	+	-	+	+	-	-	+	+	+	M	+	+	+	+	+
MALIG.LYMPHOMA, UNDIFFER-TYPE													X												
THYMUS	+	+	+	+	+	-	+	+	-	+	-	+	+	+	-	+	+	+	+	M	+	+	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	M	+	+	+	+	+
HEPATOCELLULAR ADENOMA																									
HEPATOCELLULAR CARCINOMA										X															
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	M	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	N	+	+	N	N	N	+	+	+	N	+	+	+	+	M	+	N	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	M	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	M	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	M	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	M	+	+	+	+	+
URINARY BLADDER	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	M	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	-	-	+	+	+	+	+	-	-	+	-	+	+	+	+	+	+	M	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS																									X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	-	+
ADENOMA, NOS				X																					
CORTICAL ADENOMA			X																						
THYROID	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	-	+	+	M	+	+	+	-	+
FOLLICULAR-CELL ADENOMA																X									
PARATHYROID	+	+	+	+	+	-	+	-	-	-	+	+	+	-	+	+	-	-	+	M	+	+	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	N	N	+	N	+	N	+	N	+	+	N	N	N	N	+	N	M	+	N	+	+	N
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP									X																
HEMANGIOMA																									
HEMANGIOSARCOMA												X													
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
OVARY	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	M	+	+	-	-	+
CHORIOCARCINOMA							X																		
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
CARCINOMA, NOS, INVASIVE																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	M	N	N	N	N	N
SARCOMA, NOS, METASTATIC									X																
HEMANGIOSARCOMA																								X	
MALIG.LYMPHOMA, UNDIFFER-TYPE																							X		
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE					X	X					X							X							X
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		X																							
MALIGNANT LYMPHOMA, MIXED TYPE																									
LYMPHOCYTIC LEUKEMIA															X										

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
S: ANIMAL MIS-SEXED

: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	101	105	105	105	105	105	099	078	105	105	072	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49*
SARCOMA, NOS																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	48
HEPATOCELLULAR CARCINOMA, METASTA																										1
ALVEOLAR/BRONCHIOLAR ADENOMA											X															2
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMANGIOSARCOMA																										1
LYMPH NODES	+	-	-	+	+	-	-	-	+	+	+	+	+	-	+	+	+	-	+	-	+	+	+	-	+	35
MALIG.LYMPHOMA, UNDIFFER-TYPE																										1
THYMUS	-	+	+	+	+	+	-	+	+	+	-	+	-	-	-	+	+	+	+	+	+	-	+	+	+	37
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	47
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	46
HEPATOCELLULAR ADENOMA						X				X																2
HEPATOCELLULAR CARCINOMA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	46
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	N	N	N	+	+	N	+	N	N	+	+	N	N	+	+	+	+	+	+	+	49*
PANCREAS	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
STOMACH	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	46
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	44
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY BLADDER	+	+	+	+	+	+	-	+	+	+	+	+	-	-	+	+	+	+	-	+	+	+	+	-	-	41
ENDOCRINE SYSTEM																										
PITUITARY	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	41
CARCINOMA,NOS		X																								1
ADENOMA, NOS									X									X								3
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	46
ADENOMA, NOS																										1
CORTICAL ADENOMA																										1
THYROID	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	42
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	+	-	-	+	-	+	+	-	+	+	+	+	+	-	+	+	+	-	-	-	+	-	-	-	+	30
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	N	+	N	+	N	+	N	N	N	N	N	N	N	+	+	N	N	N	N	N	N	N	N	49*
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOMETRIAL STROMAL POLYP																										1
HEMANGIOMA									X																	1
HEMANGIOSARCOMA																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE				X																						1
OVARY	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	43
CHORIOCARCINOMA																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA, NOS, INVASIVE		X																								1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
SARCOMA, NOS, METASTATIC																										1
HEMANGIOSARCOMA																										1
MALIG.LYMPHOMA, UNDIFFER-TYPE																										1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE				X									X	X												8
MALIG.LYMPHOMA, HISTIOCYTIC TYPE															X											2
MALIGNANT LYMPHOMA, MIXED TYPE																						X				1
LYMPHOCYTIC LEUKEMIA																										1

* ANIMALS NECROPSIED
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: NO TISSUE INFORMATION SUBMITTED
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
A: AUTOLYSIS
M: ANIMAL MISSING
B: NO NECROPSY PERFORMED

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
HYPERKERATOSIS			1 (2%)
ACANTHOSIS			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
INFLAMMATION, DIFFUSE			1 (2%)
INFLAMMATION ACTIVE CHRONIC			1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
RESPIRATORY SYSTEM			
#TRACHEA	(50)	(50)	(50)
INFLAMMATION, ACUTE FOCAL			1 (2%)
#TRACHEAL MUCOSA	(50)	(50)	(50)
HYPERPLASIA, FOCAL			2 (4%)
HYPERPLASIA, DIFFUSE	1 (2%)		
#TRACHEAL SUBMUCOSA	(50)	(50)	(50)
DILATATION, NOS	1 (2%)	1 (2%)	
#PERITRACHEAL TISSUE	(50)	(50)	(50)
FOREIGN BODY, NOS			1 (2%)
#LUNG	(50)	(50)	(50)
ASPIRATION, FOREIGN BODY	20 (40%)	27 (54%)	27 (54%)
EDEMA, NOS		1 (2%)	
HEMORRHAGE	1 (2%)		
INFLAMMATION, INTERSTITIAL			1 (2%)
PNEUMONIA, ASPIRATION			1 (2%)
INFLAMMATION, ACUTE FOCAL			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	9 (18%)	10 (20%)	8 (16%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
PNEUMONIA INTERSTITIAL CHRONIC		4 (8%)	
INFLAMMATION, GRANULOMATOUS	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOU	12 (24%)	5 (10%)	4 (8%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)	2 (4%)	1 (2%)
#LUNG/ALVEOLI	(50)	(50)	(50)
CONGESTION, NOS			5 (10%)
HEMORRHAGE		1 (2%)	
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(22)	(50)
HYPERPLASIA, GRANULOCYTIC		1 (5%)	2 (4%)
HYPERPLASIA, RETICULUM CELL	1 (2%)	1 (5%)	1 (2%)
HYPOPLASIA, HEMATOPOIETIC		1 (5%)	
#SPLEEN	(50)	(49)	(50)
LYMPHOID DEPLETION		1 (2%)	1 (2%)
HYPERPLASIA, LYMPHOID	2 (4%)	2 (4%)	
#SPLENIC FOLLICLES	(50)	(49)	(50)
NECROSIS, FOCAL		1 (2%)	
HYPERPLASIA, LYMPHOID	1 (2%)		
#SPLENIC RED PULP	(50)	(49)	(50)
CONGESTION, NOS	1 (2%)	1 (2%)	1 (2%)
PIGMENTATION, NOS	3 (6%)	3 (6%)	3 (6%)
HEMATOPOIESIS		4 (8%)	4 (8%)
#LYMPH NODE	(45)	(40)	(40)
HEMORRHAGE	1 (2%)		
PLASMACYTOSIS	1 (2%)		
#MANDIBULAR L. NODE	(45)	(40)	(40)
CYST, NOS	2 (4%)	2 (5%)	1 (3%)
HEMORRHAGE	2 (4%)	9 (23%)	5 (13%)
INFLAMMATION ACTIVE CHRONIC			1 (3%)
INFLAMMATION, ACUTE/CHRONIC			1 (3%)
INFLAMMATION, FOCAL GRANULOMATOU			1 (3%)
HISTIOCYTOSIS		1 (3%)	1 (3%)
PLASMACYTOSIS		2 (5%)	2 (5%)
HYPERPLASIA, LYMPHOID		2 (5%)	
#LYMPH NODE OF THORAX	(45)	(40)	(40)
CONGESTION, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEMORRHAGE		3 (8%)	1 (3%)
INFLAMMATION, ACUTE/CHRONIC			1 (3%)
INFLAMMATION, FOCAL GRANULOMATOU	2 (4%)	2 (5%)	4 (10%)
HISTIOCYTOSIS	1 (2%)		
PLASMACYTOSIS		1 (3%)	
#PANCREATIC L.NODE	(45)	(40)	(40)
INFLAMMATION, CHRONIC FOCAL		1 (3%)	
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
#MESENTERIC L. NODE	(45)	(40)	(40)
INFLAMMATION, ACUTE FOCAL			1 (3%)
#PEYER'S PATCH	(50)	(48)	(46)
HYPERPLASIA, LYMPHOID			1 (2%)
#KIDNEY/CORTEX	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID		1 (2%)	
#ADRENAL	(50)	(50)	(49)
HEMATOPOIESIS			1 (2%)
#THYMUS	(46)	(42)	(47)
THYROGLOSSAL DUCT CYST	1 (2%)		
HEMORRHAGE			2 (4%)
#THYMIC CORTEX	(46)	(42)	(47)
LYMPHOID DEPLETION	27 (59%)	19 (45%)	14 (30%)
CIRCULATORY SYSTEM			
#LUNG	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
#LEFT ATRIUM	(50)	(50)	(50)
THROMBUS, MURAL		1 (2%)	
#MYOCARDIUM	(50)	(50)	(50)
DEGENERATION, NOS	49 (98%)	45 (90%)	40 (80%)
#PANCREAS	(50)	(50)	(49)
PERIARTERITIS	4 (8%)		1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(49)	(48)
DILATATION/DUCTS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, FOCAL		1 (2%)	
#LIVER	(50)	(50)	(50)
CONGESTION, NOS	1 (2%)		
INFLAMMATION, ACUTE FOCAL		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOU	6 (12%)	1 (2%)	2 (4%)
DEGENERATION, CYSTIC	3 (6%)		
BASOPHILIC CYTO CHANGE	30 (60%)	7 (14%)	2 (4%)
EOSINOPHILIC CYTO CHANGE	1 (2%)		
CLEAR-CELL CHANGE	3 (6%)	3 (6%)	6 (12%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
CONGESTION, NOS			1 (2%)
DEGENERATION, NOS		1 (2%)	
NECROSIS, FOCAL	2 (4%)	6 (12%)	2 (4%)
NECROSIS, DIFFUSE		1 (2%)	
CYTOPLASMIC VACUOLIZATION			2 (4%)
#LIVER/PERIPORTAL	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION		2 (4%)	1 (2%)
#LIVER/HEPATOCYTES	(50)	(50)	(50)
NECROSIS, FOCAL			1 (2%)
CYTOPLASMIC VACUOLIZATION	5 (10%)	1 (2%)	
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, FOCAL	44 (88%)	43 (86%)	37 (74%)
#PANCREAS	(50)	(50)	(49)
DILATATION/DUCTS		2 (4%)	
FIBROSIS, DIFFUSE		1 (2%)	
#PANCREATIC ACINUS	(50)	(50)	(49)
ATROPHY, FOCAL	13 (26%)	13 (26%)	9 (18%)
ATROPHY, DIFFUSE		1 (2%)	1 (2%)
HYPERTROPHY, FOCAL		1 (2%)	
#ESOPHAGUS	(50)	(50)	(49)
NECROSIS, FOCAL			1 (2%)
FOREIGN MATERIAL, NOS			1 (2%)
#PERIESOPHAGEAL TISSU	(50)	(50)	(49)
INFLAMMATION, ACUTE	1 (2%)		
NECROSIS, FOCAL			3 (6%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOREIGN MATERIAL, NOS			1 (2%)
#GASTRIC MUCOSA	(50)	(49)	(46)
ULCERATION, DIFFUSE			2 (4%)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
ULCER, CHRONIC	1 (2%)	2 (4%)	
NECROSIS, FOCAL	1 (2%)		
HYPERKERATOSIS		2 (4%)	1 (2%)
ACANTHOSIS		2 (4%)	1 (2%)
#GASTRIC FUNDAL GLAND	(50)	(49)	(46)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
#GASTRIC PYLORIC GLAN	(50)	(49)	(46)
HYPERPLASIA, FOCAL		1 (2%)	
#GASTRIC SUBMUCOSA	(50)	(49)	(46)
INFLAMMATION, CHRONIC FOCAL		2 (4%)	
INFLAMMATION, CHRONIC SUPPURATIV			1 (2%)
#GASTRIC SEROSA	(50)	(49)	(46)
INFLAMMATION, CHRONIC DIFFUSE		1 (2%)	
#COLON	(50)	(48)	(46)
PARASITISM	2 (4%)	3 (6%)	1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
NEPHROPATHY	45 (90%)	46 (92%)	44 (90%)
HYPERPLASIA, TUBULAR CELL	1 (2%)		
#KIDNEY/CORTEX	(50)	(50)	(49)
NEPHROPATHY	1 (2%)		
#KIDNEY/MEDULLA	(50)	(50)	(49)
MINERALIZATION			2 (4%)
#KIDNEY/TUBULE	(50)	(50)	(49)
PIGMENTATION, NOS		3 (6%)	
REGENERATION, NOS			1 (2%)
#URINARY BLADDER	(50)	(50)	(46)
INFLAMMATION, ACUTE HEMORRHAGIC	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(49)	(49)
EMBRYONAL DUCT CYST	1 (2%)		
CONGESTION, NOS	1 (2%)		
#ANTERIOR PITUITARY	(49)	(49)	(49)
EMBRYONAL REST	1 (2%)		
EMBRYONAL DUCT CYST	1 (2%)		2 (4%)
HEMORRHAGE		2 (4%)	
CYTOPLASMIC CHANGE, NOS	1 (2%)		
#PITUITARY CELL	(49)	(49)	(49)
HYPERTROPHY, FOCAL	1 (2%)	1 (2%)	
HYPERPLASIA, FOCAL		1 (2%)	1 (2%)
#ADRENAL	(50)	(50)	(49)
CONGESTION, NOS			1 (2%)
PIGMENTATION, NOS			1 (2%)
#ADRENAL CORTEX	(50)	(50)	(49)
MULTIPLE CYSTS		1 (2%)	
CYTOPLASMIC VACUOLIZATION			1 (2%)
HYPERPLASIA, FOCAL	5 (10%)	2 (4%)	3 (6%)
#ZONA FASCICULATA	(50)	(50)	(49)
LIPOIDOSIS		4 (8%)	2 (4%)
CYTOPLASMIC VACUOLIZATION	1 (2%)		
HYPERPLASIA, FOCAL	2 (4%)	2 (4%)	1 (2%)
#ADRENAL MEDULLA	(50)	(50)	(49)
DEGENERATION, NOS			1 (2%)
HYPERPLASIA, FOCAL	4 (8%)	6 (12%)	5 (10%)
#THYROID	(50)	(50)	(46)
THYROGLOSSAL DUCT CYST			1 (2%)
FOLLICULAR CYST, NOS	1 (2%)		
HYPERPLASIA, C-CELL	23 (46%)	18 (36%)	14 (30%)
HYPERPLASIA, FOLLICULAR-CELL		2 (4%)	
#THYROID CAPSULE	(50)	(50)	(46)
INFLAMMATION, NECROTIZING		1 (2%)	
#THYROID FOLLICLE	(50)	(50)	(46)
MULTIPLE CYSTS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PARATHYROID	(42)	(34)	(38)
EMBRYONAL DUCT CYST		1 (3%)	
#PANCREATIC ISLETS	(50)	(50)	(49)
HYPERPLASIA, FOCAL		2 (4%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
DILATATION, NOS	2 (4%)		1 (2%)
GALACTOCELE		1 (2%)	
HYPERPLASIA, FOCAL	2 (4%)	4 (8%)	6 (12%)
HYPERPLASIA, CYSTIC	12 (24%)	2 (4%)	7 (14%)
*MAMMARY DUCT	(50)	(50)	(50)
MULTIPLE CYSTS	1 (2%)		
*PREPUCE	(50)	(50)	(50)
ULCER, NOS		2 (4%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION ACTIVE CHRONIC	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC FOCAL		2 (4%)	
ABSCESS, CHRONIC			1 (2%)
HYPERPLASIA, FOCAL		2 (4%)	
#PROSTATE	(50)	(48)	(49)
INFLAMMATION, ACUTE FOCAL			2 (4%)
INFLAMMATION, ACUTE DIFFUSE		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	6 (12%)	3 (6%)	5 (10%)
INFLAMMATION, CHRONIC FOCAL		5 (10%)	
FIBROSIS		1 (2%)	
NECROSIS, NOS			1 (2%)
NECROSIS, DIFFUSE			1 (2%)
#TESTIS	(50)	(50)	(50)
ASPERMATOGENESIS		1 (2%)	1 (2%)
HYPERPLASIA, INTERSTITIAL CELL	4 (8%)	4 (8%)	6 (12%)
#TESTIS/TUBULE	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
DEGENERATION, NOS	46 (92%)	45 (90%)	38 (76%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ATROPHY, FOCAL	1 (2%)		
*EPIDIDYMIS	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
DEGENERATION, NOS		1 (2%)	
NERVOUS SYSTEM			
#CEREBRUM	(50)	(50)	(50)
HEMORRHAGE			1 (2%)
ATROPHY, PRESSURE	3 (6%)	1 (2%)	1 (2%)
#BRAIN	(50)	(50)	(50)
HYDROCEPHALUS, NOS			1 (2%)
HEMORRHAGE	1 (2%)		
#CEREBRAL CORTEX	(50)	(50)	(50)
NECROSIS, ISCHEMIC	1 (2%)		
#MEDULLA OBLONGATA	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
*SPINAL CORD	(50)	(50)	(50)
HEMORRHAGE			1 (2%)
SPECIAL SENSE ORGANS			
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS	6 (12%)		1 (2%)
*EYE/CRYSTALLINE LENS	(50)	(50)	(50)
CATARACT	6 (12%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
FOREIGN BODY, NOS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC FOCAL			1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	1 (2%)	
#PERITONEUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#MEDIASTINAL PLEURA	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
#PERICARDIAL MESOTHEL	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
#MESENTERY	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU	4 (8%)	1 (2%)	
ALL OTHER SYSTEMS			
ADIPOSE TISSUE			
INFLAMMATION, FOCAL GRANULOMATOU			1
SPECIAL MORPHOLOGY SUMMARY			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
ABSCESS, NOS		1 (2%)	
FIBROSIS, FOCAL	1 (2%)		
RESPIRATORY SYSTEM			
#TRACHEA	(49)	(50)	(48)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
#LUNG	(50)	(50)	(50)
ASPIRATION, FOREIGN BODY	10 (20%)	11 (22%)	24 (48%)
EDEMA, NOS		2 (4%)	1 (2%)
INFLAMMATION, INTERSTITIAL		1 (2%)	4 (8%)
PNEUMONIA, ASPIRATION	2 (4%)		
INFLAMMATION, ACUTE FOCAL		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	10 (20%)	4 (8%)	
INFLAMMATION, GRANULOMATOUS		1 (2%)	
GRANULOMA, NOS		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU	17 (34%)	16 (32%)	13 (26%)
ALVEOLAR MACROPHAGES			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)		1 (2%)
#LUNG/ALVEOLI	(50)	(50)	(50)
CONGESTION, NOS	1 (2%)		
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(48)	(47)	(46)
FIBROUS OSTEODYSTROPHY	1 (2%)		
HYPERPLASIA, GRANULOCYTIC			1 (2%)
HYPERPLASIA, RETICULUM CELL	2 (4%)		1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPOPLASIA, HEMATOPOIETIC	1 (2%)		
#SPLEEN	(49)	(50)	(50)
LYMPHOID DEPLETION		1 (2%)	2 (4%)
#SPLENIC CAPSULE	(49)	(50)	(50)
HEMORRHAGE		1 (2%)	
#SPLENIC RED PULP	(49)	(50)	(50)
CONGESTION, NOS	1 (2%)		
PIGMENTATION, NOS		1 (2%)	1 (2%)
HEMATOPOIESIS	6 (12%)	4 (8%)	4 (8%)
#MANDIBULAR L. NODE	(46)	(44)	(45)
CYST, NOS		2 (5%)	4 (9%)
MULTIPLE CYSTS	1 (2%)		
CONGESTION, NOS	1 (2%)		1 (2%)
HEMORRHAGE	2 (4%)	12 (27%)	9 (20%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
LYMPHOID DEPLETION		1 (2%)	
HISTIOCYTOSIS	1 (2%)	1 (2%)	1 (2%)
ERYTHROPHAGOCYTOSIS	1 (2%)		1 (2%)
HYPERPLASIA, LYMPHOID	1 (2%)		
#LYMPH NODE OF THORAX	(46)	(44)	(45)
HEMORRHAGE		8 (18%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOU	2 (4%)	6 (14%)	4 (9%)
PIGMENTATION, NOS		2 (5%)	1 (2%)
#PANCREATIC L.NODE	(46)	(44)	(45)
INFLAMMATION, FOCAL GRANULOMATOU	2 (4%)		
#MESENTERIC L. NODE	(46)	(44)	(45)
CYST, NOS	1 (2%)		
MULTIPLE CYSTS		1 (2%)	
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU	4 (9%)	2 (5%)	
#LIVER	(49)	(49)	(50)
HEMATOPOIESIS			1 (2%)
#GASTRIC SUBMUCOSA	(49)	(48)	(48)
HYPERPLASIA, LYMPHOID			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#ZONA FASCICULATA	(49)	(49)	(50)
HEMATOPOIESIS			1 (2%)
#THYMUS	(43)	(45)	(45)
CONGESTION, NOS			1 (2%)
HEMORRHAGE			1 (2%)
NECROSIS, DIFFUSE		1 (2%)	
#THYMIC CORTEX	(43)	(45)	(45)
LYMPHOID DEPLETION	32 (74%)	23 (51%)	25 (56%)
#THYMIC MEDULLA	(43)	(45)	(45)
MULTIPLE CYSTS		1 (2%)	
#THYMIC LYMPHOCYTES	(43)	(45)	(45)
NECROSIS, NOS		1 (2%)	
CIRCULATORY SYSTEM			
#LUNG	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
#LEFT ATRIUM	(49)	(50)	(50)
FIBROSIS, DIFFUSE			1 (2%)
#MYOCARDIUM	(49)	(50)	(50)
INFLAMMATION, INTERSTITIAL			1 (2%)
DEGENERATION, NOS	44 (90%)	34 (68%)	39 (78%)
*CENTRAL VEINS/LIVER	(50)	(50)	(50)
THROMBUS, ORGANIZED	1 (2%)		
#HEPATIC SINUSOID	(49)	(49)	(50)
CONGESTION, NOS			1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(49)	(48)
RANULAR CYST		1 (2%)	
FOCAL CELLULAR CHANGE			1 (2%)
#LIVER	(49)	(49)	(50)
INFLAMMATION, FOCAL GRANULOMATOU	17 (35%)	7 (14%)	16 (32%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BASOPHILIC CYTO CHANGE	29 (59%)	34 (69%)	16 (32%)
CLEAR-CELL CHANGE			4 (8%)
#LIVER/CENTRILOBULAR	(49)	(49)	(50)
NECROSIS, NOS		1 (2%)	
NECROSIS, FOCAL	1 (2%)	1 (2%)	4 (8%)
HEMOSIDEROSIS		1 (2%)	
CYTOPLASMIC VACUOLIZATION		1 (2%)	
#LIVER/HEPATOCYTES	(49)	(49)	(50)
NECROSIS, FOCAL	1 (2%)		
CYTOPLASMIC VACUOLIZATION			1 (2%)
#BILE DUCT	(49)	(49)	(50)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL	26 (53%)	23 (47%)	11 (22%)
#PANCREATIC ACINUS	(46)	(50)	(48)
ATROPHY, FOCAL	9 (20%)	6 (12%)	13 (27%)
#ESOPHAGUS	(49)	(50)	(50)
DILATATION, NOS		1 (2%)	
INFLAMMATION ACTIVE CHRONIC			1 (2%)
#PERIESOPHAGEAL TISSU	(49)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
#GASTRIC MUCOSA	(49)	(48)	(48)
EMBRYONAL REST	1 (2%)		
ULCER, FOCAL		1 (2%)	
ULCER, CHRONIC	1 (2%)		
HYPERKERATOSIS	2 (4%)	1 (2%)	1 (2%)
ACANTHOSIS	2 (4%)	1 (2%)	1 (2%)
#GASTRIC SUBMUCOSA	(49)	(48)	(48)
INFLAMMATION, ACUTE FOCAL			1 (2%)
#JEJUNAL SUBMUCOSA	(48)	(48)	(47)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#COLON	(48)	(47)	(48)
PARASITISM		1 (2%)	1 (2%)
URINARY SYSTEM			
#KIDNEY	(49)	(50)	(49)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NEPHROPATHY	15 (31%)	21 (42%)	22 (45%)
PIGMENTATION, NOS		1 (2%)	
#KIDNEY/CORTEX	(49)	(50)	(49)
HEMORRHAGIC CYST	1 (2%)		
#KIDNEY/MEDULLA	(49)	(50)	(49)
MINERALIZATION	1 (2%)	2 (4%)	
#KIDNEY/GLOMERULUS	(49)	(50)	(49)
MINERALIZATION			1 (2%)
#KIDNEY/TUBULE	(49)	(50)	(49)
PIGMENTATION, NOS	1 (2%)		1 (2%)
REGENERATION, NOS			1 (2%)
#KIDNEY/PELVIS	(49)	(50)	(49)
MINERALIZATION	1 (2%)		3 (6%)
#URINARY BLADDER	(45)	(47)	(46)
INFLAMMATION, ACUTE DIFFUSE	1 (2%)		
HYPERPLASIA, EPITHELIAL	2 (4%)		
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(45)	(48)
EMBRYONAL DUCT CYST	2 (4%)		
CYST, NOS			1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		1 (2%)
#ANTERIOR PITUITARY	(46)	(45)	(48)
EMBRYONAL DUCT CYST	6 (13%)	1 (2%)	2 (4%)
MULTIPLE CYSTS		3 (7%)	
HEMORRHAGE			1 (2%)
HEMORRHAGE, CHRONIC		1 (2%)	
LIPOIDOSIS	1 (2%)		
HYPERPLASIA, CHROMOPHOBE-CELL			1 (2%)
#PITUITARY CELL	(46)	(45)	(48)
HYPERPLASIA, FOCAL	2 (4%)	5 (11%)	
#ADRENAL CORTEX	(49)	(49)	(50)
NECROSIS, FOCAL			1 (2%)
LIPOIDOSIS		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#ZONA FASCICULATA	(49)	(49)	(50)
NECROSIS, FOCAL			1 (2%)
NECROSIS, DIFFUSE		1 (2%)	
LIPOIDOSIS	5 (10%)	6 (12%)	3 (6%)
CYTOPLASMIC CHANGE, NOS			1 (2%)
EOSINOPHILIC CYTO CHANGE	1 (2%)		
HYPERPLASIA, FOCAL	1 (2%)	1 (2%)	1 (2%)
#ADRENAL MEDULLA	(49)	(49)	(50)
HYPERPLASIA, FOCAL		2 (4%)	
#THYROID	(48)	(50)	(49)
EMBRYONAL REST		1 (2%)	
EMBRYONAL DUCT CYST	1 (2%)		1 (2%)
HYPERPLASIA, C-CELL	19 (40%)	17 (34%)	16 (33%)
#PARATHYROID	(33)	(35)	(40)
HYPERPLASIA, FOCAL	1 (3%)		
#PANCREATIC ISLETS	(46)	(50)	(48)
HYPERPLASIA, FOCAL			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
DILATATION, NOS		1 (2%)	5 (10%)
MULTIPLE CYSTS	1 (2%)		
HYPERPLASIA, FOCAL	1 (2%)		
HYPERPLASIA, CYSTIC	7 (14%)	8 (16%)	8 (16%)
*CLITORAL GLAND	(50)	(50)	(50)
INFLAMMATION ACTIVE CHRONIC			1 (2%)
*VAGINAL MUCOSA	(50)	(50)	(50)
FIBROSIS		1 (2%)	
#UTERUS	(48)	(50)	(50)
DILATATION, NOS	1 (2%)	1 (2%)	5 (10%)
HEMORRHAGE	1 (2%)		
FIBROSIS, DIFFUSE	1 (2%)		
#UTERUS/ENDOMETRIUM	(48)	(50)	(50)
HYPERPLASIA, DIFFUSE			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#ENDOMETRIAL GLAND	(48)	(50)	(50)
CYST, NOS		4 (8%)	2 (4%)
MULTIPLE CYSTS		4 (8%)	2 (4%)
HYPERPLASIA, FOCAL		1 (2%)	
HYPERPLASIA, CYSTIC	20 (42%)	9 (18%)	16 (32%)
#ENDOMETRIAL STROMA	(48)	(50)	(50)
PIGMENTATION, NOS			1 (2%)
#OVARY	(48)	(48)	(50)
FOLLICULAR CYST, NOS			1 (2%)
CORPUS LUTEUM CYST		4 (8%)	1 (2%)
PAROVARIAN CYST	3 (6%)	3 (6%)	4 (8%)
ATROPHY, SENILE		1 (2%)	1 (2%)
NERVOUS SYSTEM			
#CEREBRUM	(49)	(50)	(50)
HEMORRHAGE	1 (2%)		
INFLAMMATION, CHRONIC FOCAL		1 (2%)	1 (2%)
ATROPHY, PRESSURE	5 (10%)	1 (2%)	1 (2%)
#BRAIN	(49)	(50)	(50)
HEMORRHAGE		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE/CORNEA	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS	7 (14%)	1 (2%)	2 (4%)
*EYE/CRYSTALLINE LENS	(50)	(50)	(50)
CATARACT	6 (12%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
*FEMUR	(50)	(50)	(50)
OSTEOSCLEROSIS	4 (8%)	8 (16%)	2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	2 (4%)
*MESENTERY	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	2 (4%)
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EDEMA, NOS		1 (2%)	
ULCER, FOCAL			1 (2%)
ULCER, ACUTE			1 (2%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
FIBROSIS, FOCAL		1 (2%)	1 (2%)
PARASITISM		1 (2%)	
ACANTHOSIS		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
RANULAR CYST		1 (2%)	
INFLAMMATION, ACUTE DIFFUSE		1 (2%)	
ABSCESS, CHRONIC		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
INFLAMMATION, INTERSTITIAL	1 (2%)		1 (2%)
INFLAMMATION, ACUTE FOCAL	1 (2%)	3 (6%)	
PNEUMONIA INTERSTITIAL CHRONIC			1 (2%)
INFLAMMATION, CHRONIC FOCAL			2 (4%)
NECROSIS, HEMORRHAGIC	1 (2%)		
FOREIGN MATERIAL, NOS	1 (2%)		
ALVEOLAR MACROPHAGES		2 (4%)	4 (8%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)	1 (2%)	2 (4%)
METAPLASIA, SQUAMOUS			1 (2%)
#LUNG/ALVEOLI	(50)	(50)	(50)
INFLAMMATION, INTERSTITIAL	1 (2%)		
FOREIGN MATERIAL, NOS	1 (2%)	3 (6%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
PIGMENTATION, NOS		2 (4%)	
HEMATOPOIETIC SYSTEM			
#SPLEEN	(45)	(48)	(48)
LYMPHOID DEPLETION	1 (2%)		
HEMATOPOIESIS	1 (2%)		
#SPLENIC FOLLICLES	(45)	(48)	(48)
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL			1 (2%)
LYMPHOID DEPLETION	1 (2%)		1 (2%)
HYPERPLASIA, LYMPHOID	2 (4%)		
#SPLENIC RED PULP	(45)	(48)	(48)
HEMATOPOIESIS	3 (7%)	5 (10%)	5 (10%)
#LYMPH NODE	(33)	(38)	(40)
INFLAMMATION, ACUTE/CHRONIC	1 (3%)		
#MANDIBULAR L. NODE	(33)	(38)	(40)
PLASMACYTOSIS			1 (3%)
HYPERPLASIA, LYMPHOID			1 (3%)
#MESENTERIC L. NODE	(33)	(38)	(40)
INFLAMMATION, ACUTE DIFFUSE			1 (3%)
GRANULOMA, NOS		1 (3%)	
HYPERPLASIA, RETICULUM CELL			2 (5%)
HYPERPLASIA, LYMPHOID	2 (6%)		
#LUNG	(50)	(50)	(50)
LEUKOCYTOSIS, NOS	1 (2%)	1 (2%)	1 (2%)
#PEYER'S PATCH	(39)	(40)	(43)
HYPERPLASIA, LYMPHOID	1 (3%)		
#THYMUS	(26)	(26)	(25)
LYMPHOID DEPLETION		2 (8%)	1 (4%)
#THYMIC CORTEX	(26)	(26)	(25)
NECROSIS, NOS	1 (4%)		
LYMPHOID DEPLETION		1 (4%)	
#THYMIC MEDULLA	(26)	(26)	(25)
HYPERPLASIA, EPITHELIAL		1 (4%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#THYMIC LYMPHOCYTES	(26)	(26)	(25)
NECROSIS, NOS			1 (4%)
CIRCULATORY SYSTEM			
#LUNG	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		
PERIVASCULITIS	1 (2%)		
#MYOCARDIUM	(48)	(50)	(50)
MINERALIZATION	1 (2%)		
INFLAMMATION, CHRONIC FOCAL			1 (2%)
PERIVASCULITIS			2 (4%)
DEGENERATION, NOS		2 (4%)	
NECROSIS, FOCAL			1 (2%)
*PULMONARY ARTERY	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
#KIDNEY	(48)	(50)	(49)
PERIARTERITIS	1 (2%)		
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(47)	(49)	(50)
NECROSIS, NOS	1 (2%)		
ATROPHY, FOCAL			1 (2%)
#LIVER	(50)	(49)	(46)
MINERALIZATION	1 (2%)		
GRANULOMA, NOS			1 (2%)
NECROSIS, FOCAL	2 (4%)		
NECROSIS, COAGULATIVE	3 (6%)		
N-C RATIO, ALTERATION	1 (2%)		
ANGIECTASIS	1 (2%)		1 (2%)
#LIVER/CENTRILOBULAR	(50)	(49)	(46)
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL		1 (2%)	
#LIVER/PERIPORTAL	(50)	(49)	(46)
CYTOPLASMIC VACUOLIZATION			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#LIVER/HEPATOCYTES	(50)	(49)	(46)
INFLAMMATION, ACUTE FOCAL			1 (2%)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
NECROSIS, FOCAL	2 (4%)	1 (2%)	2 (4%)
NECROSIS, DIFFUSE		1 (2%)	
NECROSIS, COAGULATIVE		3 (6%)	
NUCLEAR-SIZE ALTERATION			1 (2%)
CYTOPLASMIC VACUOLIZATION	1 (2%)		
CELL-SIZE, ALTERATION			1 (2%)
#PANCREAS	(48)	(49)	(45)
CYSTIC DUCTS		1 (2%)	
#PANCREATIC ACINUS	(48)	(49)	(45)
NECROSIS, FOCAL	1 (2%)		
ATROPHY, NOS		2 (4%)	
ATROPHY, FOCAL	1 (2%)		
#PANCREATIC INTERSTIT	(48)	(49)	(45)
INFLAMMATION, ACUTE DIFFUSE		1 (2%)	
#ESOPHAGUS	(47)	(47)	(49)
HYPERPLASIA, EPITHELIAL		1 (2%)	
#GASTRIC MUCOSA	(46)	(48)	(46)
MINERALIZATION	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL			1 (2%)
NECROSIS, FOCAL			1 (2%)
#CARDIAC STOMACH	(46)	(48)	(46)
HYPERPLASIA, EPITHELIAL			1 (2%)
#COLON	(44)	(48)	(45)
PARASITISM	2 (5%)	2 (4%)	
URINARY SYSTEM			
#KIDNEY	(48)	(50)	(49)
MINERALIZATION			1 (2%)
GLOMERULONEPHRITIS, MEMBRANOUS		1 (2%)	
GLOMERULONEPHRITIS, SUBACUTE			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
PYELONEPHRITIS, ACUTE/CHRONIC	1 (2%)		
GLOMERULONEPHRITIS, CHRONIC	1 (2%)		
METAPLASIA, OSSEOUS	3 (6%)	1 (2%)	1 (2%)
#KIDNEY/CAPSULE	(48)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
#KIDNEY/CORTEX	(48)	(50)	(49)
CYST, NOS	1 (2%)		1 (2%)
MULTIPLE CYSTS		2 (4%)	
GLOMERULONEPHRITIS, MEMBRANOUS	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	1 (2%)
METAPLASIA, OSSEOUS		1 (2%)	1 (2%)
#KIDNEY/TUBULE	(48)	(50)	(49)
MINERALIZATION	2 (4%)		2 (4%)
DILATATION, NOS	3 (6%)		
DEGENERATION, NOS		1 (2%)	
DEGENERATION, HYALINE	1 (2%)		
NECROSIS, FOCAL		2 (4%)	
NECROSIS, DIFFUSE	1 (2%)		
PIGMENTATION, NOS			1 (2%)
CYTOPLASMIC VACUOLIZATION			1 (2%)
REGENERATION, NOS	8 (17%)	12 (24%)	17 (35%)
#KIDNEY/PELVIS	(48)	(50)	(49)
DILATATION, NOS		1 (2%)	
INFLAMMATION, ACUTE FOCAL			1 (2%)
#URINARY BLADDER	(45)	(46)	(42)
ULCER, ACUTE	1 (2%)		
#U. BLADDER/MUCOSA	(45)	(46)	(42)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
*URETHRA	(50)	(50)	(50)
INFLAMMATION, ACUTE DIFFUSE			1 (2%)
INFLAMMATION, ACUTE NECROTIZING			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(34)	(35)	(34)
HYPERPLASIA, FOCAL	1 (3%)		
#ANTERIOR PITUITARY	(34)	(35)	(34)
HYPERPLASIA, CHROMOPHOBE-CELL	1 (3%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#ADRENAL/CAPSULE	(50)	(47)	(48)
HYPERPLASIA, NOS			1 (2%)
#ADRENAL CORTEX	(50)	(47)	(48)
NECROSIS, FOCAL	1 (2%)		
FOCAL CELLULAR CHANGE	3 (6%)	6 (13%)	4 (8%)
HYPERTROPHY, FOCAL	1 (2%)		
HYPERPLASIA, FOCAL		2 (4%)	4 (8%)
#ZONA GLOMERULOSA	(50)	(47)	(48)
HYPERPLASIA, FOCAL		1 (2%)	2 (4%)
#ZONA FASCICULATA	(50)	(47)	(48)
HYPERPLASIA, FOCAL	1 (2%)		1 (2%)
#ZONA RETICULARIS	(50)	(47)	(48)
HYPERPLASIA, FOCAL	1 (2%)		
#ADRENAL MEDULLA	(50)	(47)	(48)
HYPERPLASIA, NOS			2 (4%)
HYPERPLASIA, FOCAL	2 (4%)	1 (2%)	3 (6%)
#THYROID	(44)	(37)	(44)
HYPERPLASIA, FOLLICULAR-CELL	2 (5%)		1 (2%)
#THYROID FOLLICLE	(44)	(37)	(44)
DILATATION, NOS		1 (3%)	
HYPERPLASIA, PAPILLARY		1 (3%)	
REPRODUCTIVE SYSTEM			
*PENIS	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION, ACUTE DIFFUSE			1 (2%)
*PREPUCE	(50)	(50)	(50)
INFLAMMATION, ACUTE NECROTIZING	1 (2%)		
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		
ABSCESS, CHRONIC		1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PROSTATE	(46)	(48)	(49)
INFLAMMATION, ACUTE			1 (2%)
DEGENERATION, NOS		1 (2%)	
#TESTIS	(50)	(48)	(49)
HYPERPLASIA, INTERSTITIAL CELL	1 (2%)		
#TESTIS/TUBULE	(50)	(48)	(49)
MINERALIZATION	1 (2%)	1 (2%)	1 (2%)
#SPERMATOGENIC EPITHE	(50)	(48)	(49)
ATROPHY, DIFFUSE	1 (2%)	1 (2%)	1 (2%)
*EPIDIDYMIS	(50)	(50)	(50)
DILATATION, NOS	1 (2%)		
GRANULOMA, SPERMATIC			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(50)	(49)	(50)
PIGMENTATION, NOS		1 (2%)	
#HIPPOCAMPUS	(50)	(49)	(50)
NECROSIS, FOCAL			1 (2%)
#BRAIN/THALAMUS	(50)	(49)	(50)
MINERALIZATION	21 (42%)	16 (33%)	22 (44%)
#CEREBELLUM	(50)	(49)	(50)
MALACIA	1 (2%)		
SPECIAL SENSE ORGANS			
*EYE/CORNEA	(50)	(50)	(50)
ULCER, ACUTE		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*CORTEX OF BONE	(50)	(50)	(50)
FIBROUS OSTEODYSTROPHY	1 (2%)	1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, ACUTE FOCAL		1 (2%)	
*PERITONEAL CAVITY	(50)	(50)	(50)
NECROSIS, FAT			1 (2%)
*MEDIASTINAL PLEURA	(50)	(50)	(50)
INFLAMMATION, ACUTE NECROTIZING			1 (2%)
*MESENTERY	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
INFLAMMATION ACTIVE CHRONIC			1 (2%)
NECROSIS, FAT		1 (2%)	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	2	2	1

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING			1
ANIMALS NECROPSIED	49	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	48	49
INTEGUMENTARY SYSTEM			
*SKIN	(49)	(50)	(49)
METAPLASIA, OSSEOUS	1 (2%)		
*SUBCUT TISSUE	(49)	(50)	(49)
FIBROSIS, DIFFUSE		3 (6%)	
RESPIRATORY SYSTEM			
#LUNG	(47)	(48)	(48)
HEMORRHAGE		1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR	8 (17%)	10 (21%)	8 (17%)
INFLAMMATION, ACUTE DIFFUSE	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)	4 (8%)	2 (4%)
#LUNG/ALVEOLI	(47)	(48)	(48)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
FOREIGN MATERIAL, NOS	3 (6%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
#SPLEEN	(45)	(46)	(47)
INFARCT, FOCAL		1 (2%)	
HEMATOPOIESIS			1 (2%)
#SPLENIC FOLLICLES	(45)	(46)	(47)
HYPERPLASIA, LYMPHOID	1 (2%)	3 (7%)	4 (9%)
#SPLENIC RED PULP	(45)	(46)	(47)
HEMATOPOIESIS	2 (4%)	2 (4%)	1 (2%)
#MANDIBULAR L. NODE	(41)	(33)	(35)
PLASMACYTOSIS	2 (5%)	1 (3%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#MEDIASTINAL L.NODE	(41)	(33)	(35)
HYPERPLASIA, LYMPHOID			1 (3%)
#LUMBAR LYMPH NODE	(41)	(33)	(35)
PLASMACYTOSIS	1 (2%)		
#MESENTERIC L. NODE	(41)	(33)	(35)
ABSCESS, CHRONIC			1 (3%)
HYPERPLASIA, RETICULUM CELL	1 (2%)		
#RENAL LYMPH NODE	(41)	(33)	(35)
PLASMACYTOSIS	1 (2%)		
#LIVER	(48)	(47)	(46)
HEMATOPOIESIS		1 (2%)	
#HEPATIC SINUSOID	(48)	(47)	(46)
LEUKOCYTOSIS, NOS			1 (2%)
#PEYER'S PATCH	(43)	(45)	(44)
HYPERPLASIA, LYMPHOID	1 (2%)		
#U.BLADDER/SUBMUCOSA	(44)	(47)	(41)
HYPERPLASIA, LYMPHOID		1 (2%)	2 (5%)
#OVARY/PAROVARIAN	(47)	(44)	(43)
HYPERPLASIA, LYMPHOID			1 (2%)
#THYMUS	(31)	(37)	(37)
LYMPHOID DEPLETION	1 (3%)	1 (3%)	
#THYMIC CORTEX	(31)	(37)	(37)
LYMPHOID DEPLETION		1 (3%)	
#THYMIC MEDULLA	(31)	(37)	(37)
HYPERPLASIA, EPITHELIAL		1 (3%)	
HYPERPLASIA, LYMPHOID			1 (3%)
#THYMIC LYMPHOCYTES	(31)	(37)	(37)
NECROSIS, DIFFUSE	1 (3%)		
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
PERIARTERITIS			1 (2%)
*MEDIASTINUM	(49)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		
#MYOCARDIUM	(48)	(47)	(47)
MINERALIZATION	1 (2%)	1 (2%)	
INFLAMMATION, ACUTE FOCAL	1 (2%)		
DEGENERATION, NOS	1 (2%)		
*AORTA	(49)	(50)	(49)
PERIVASCULITIS			1 (2%)
#HEPATIC SINUSOID	(48)	(47)	(46)
DEPOSIT, NOS	1 (2%)		
#OVARY	(47)	(44)	(43)
THROMBOSIS, NOS	1 (2%)		
#ADRENAL MEDULLA	(48)	(48)	(46)
THROMBOSIS, NOS	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(48)	(47)	(46)
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
NECROSIS, FOCAL	1 (2%)		1 (2%)
BASOPHILIC CYTO CHANGE	1 (2%)		
#LIVER/CENTRILOBULAR	(48)	(47)	(46)
NECROSIS, DIFFUSE			1 (2%)
#LIVER/HEPATOCYTES	(48)	(47)	(46)
INFLAMMATION, ACUTE FOCAL		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
NECROSIS, FOCAL	4 (8%)	1 (2%)	3 (7%)
NECROSIS, COAGULATIVE		1 (2%)	1 (2%)
NUCLEAR-SIZE ALTERATION	1 (2%)		
#PANCREAS	(46)	(47)	(47)
DILATATION/DUCTS	1 (2%)		
CYSTIC DUCTS			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FIBROSIS, FOCAL		1 (2%)	
#PANCREATIC DUCT	(46)	(47)	(47)
INFLAMMATION, CHRONIC	1 (2%)		
#PANCREATIC ACINUS	(46)	(47)	(47)
ATROPHY, NOS	1 (2%)		2 (4%)
ATROPHY, FOCAL			1 (2%)
ATROPHY, DIFFUSE	1 (2%)		
#PANCREATIC INTERSTIT	(46)	(47)	(47)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
#PERIPANCREATIC TISSU	(46)	(47)	(47)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
ABSCESS, CHRONIC	1 (2%)		
#ESOPHAGUS	(46)	(48)	(47)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
#STOMACH	(49)	(46)	(46)
HYPERPLASIA, EPITHELIAL	1 (2%)		
#GASTRIC MUCOSA	(49)	(46)	(46)
MINERALIZATION	1 (2%)		
#CARDIAC STOMACH	(49)	(46)	(46)
HYPERPLASIA, EPITHELIAL		1 (2%)	
#COLON	(47)	(48)	(47)
PARASITISM	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(49)	(48)	(47)
LYMPHOCYTIC INFLAMMATORY INFILTR		2 (4%)	3 (6%)
GLOMERULONEPHRITIS, MEMBRANOUS		1 (2%)	
PYELONEPHRITIS, ACUTE/CHRONIC	1 (2%)		
METAPLASIA, OSSEOUS			1 (2%)
#KIDNEY/CAPSULE	(49)	(48)	(47)
INFLAMMATION, ACUTE FOCAL	1 (2%)	1 (2%)	
INFLAMMATION, CHRONIC FOCAL			1 (2%)
#KIDNEY/CORTEX	(49)	(48)	(47)
INFLAMMATION, CHRONIC FOCAL			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFARCT, FOCAL			2 (4%)
METAPLASIA, OSSEOUS			1 (2%)
#KIDNEY/GLOMERULUS	(49)	(48)	(47)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
INFLAMMATION, ACUTE DIFFUSE	1 (2%)		
#KIDNEY/TUBULE	(49)	(48)	(47)
MINERALIZATION	1 (2%)		
CAST, NOS	1 (2%)		
NECROSIS, FOCAL		1 (2%)	1 (2%)
REGENERATION, NOS		3 (6%)	
#KIDNEY/PELVIS	(49)	(48)	(47)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
#U.BLADDER/SUBMUCOSA	(44)	(47)	(41)
LYMPHOCYTIC INFLAMMATORY INFILTR	2 (5%)		
ENDOCRINE SYSTEM			
#PITUITARY	(39)	(39)	(41)
HYPERPLASIA, FOCAL			1 (2%)
HYPERPLASIA, CHROMOPHOBE-CELL			1 (2%)
#ANTERIOR PITUITARY	(39)	(39)	(41)
DILATATION, NOS		1 (3%)	
HYPERPLASIA, CHROMOPHOBE-CELL	1 (3%)		1 (2%)
ANGIECTASIS	1 (3%)		1 (2%)
#ADRENAL	(48)	(48)	(46)
FOCAL CELLULAR CHANGE			1 (2%)
#ADRENAL CORTEX	(48)	(48)	(46)
CYST, NOS	1 (2%)		1 (2%)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
FOCAL CELLULAR CHANGE	1 (2%)		
#ZONA RETICULARIS	(48)	(48)	(46)
HYPERPLASIA, FOCAL	1 (2%)		
#PERIADRENAL TISSUE	(48)	(48)	(46)
INFLAMMATION, CHRONIC	1 (2%)		
#THYROID	(43)	(44)	(42)
THYROGLOSSAL DUCT CYST		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOLLICULAR CYST, NOS		1 (2%)	
#THYROID FOLLICLE	(43)	(44)	(42)
HYPERPLASIA, EPITHELIAL	1 (2%)		
HYPERPLASIA, FOCAL	1 (2%)	1 (2%)	
HYPERPLASIA, PAPILLARY			2 (5%)
#PARATHYROID	(23)	(25)	(30)
THYROGLOSSAL DUCT CYST	1 (4%)		
REPRODUCTIVE SYSTEM			
*CLITORAL GLAND	(49)	(50)	(49)
ABSCESS, CHRONIC			1 (2%)
#UTERUS	(48)	(47)	(49)
DILATATION, NOS			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
ABSCESS, NOS	1 (2%)		
ABSCESS, CHRONIC			1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
#UTERUS/ENDOMETRIUM	(48)	(47)	(49)
INFLAMMATION, ACUTE FOCAL		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
#ENDOMETRIAL GLAND	(48)	(47)	(49)
MULTIPLE CYSTS	6 (13%)	4 (9%)	1 (2%)
HYPERPLASIA, CYSTIC	32 (67%)	38 (81%)	38 (78%)
#UTERUS/MYOMETRIUM	(48)	(47)	(49)
FIBROSIS, FOCAL		1 (2%)	
#OVARY/PAROVARIAN	(47)	(44)	(43)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
INFLAMMATION, ACUTE FOCAL		1 (2%)	
ABSCESS, CHRONIC	1 (2%)		
#OVARY	(47)	(44)	(43)
FOLLICULAR CYST, NOS	21 (45%)	17 (39%)	15 (35%)
MULTILOCULAR CYST	1 (2%)		
HEMORRHAGIC CYST	1 (2%)		1 (2%)
ABSCESS, CHRONIC		2 (5%)	2 (5%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN/MENINGES	(49)	(46)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
HEMOSIDEROSIS			1 (2%)
#BRAIN	(49)	(46)	(49)
NECROSIS, FOCAL	1 (2%)		
NECROSIS, HEMORRHAGIC			1 (2%)
#HIPPOCAMPUS	(49)	(46)	(49)
NECROSIS, FOCAL			1 (2%)
#BRAIN/THALAMUS	(49)	(46)	(49)
MINERALIZATION	20 (41%)	19 (41%)	17 (35%)
ATROPHY, PRESSURE	1 (2%)		
#CEREBELLAR WHITE MAT	(49)	(46)	(49)
MALACIA		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE/CORNEA	(49)	(50)	(49)
INFLAMMATION, ACUTE DIFFUSE		1 (2%)	
*EYE/LACRIMAL GLAND	(49)	(50)	(49)
INFLAMMATION, ACUTE	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*CORTEX OF BONE	(49)	(50)	(49)
FIBROUS OSTEODYSTROPHY	26 (53%)	23 (46%)	26 (53%)
*ABDOMINAL MUSCLE	(49)	(50)	(49)
INFLAMMATION ACTIVE CHRONIC	1 (2%)		
BODY CAVITIES			
*MEDIASTINUM	(49)	(50)	(49)
HEMORRHAGE, CHRONIC	1 (2%)		
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PERITONEUM	(49)	(50)	(49)
INFLAMMATION, ACUTE FOCAL	1 (2%)	1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		1 (2%)
ABSCESS, CHRONIC		1 (2%)	
#MESENTERY	(49)	(50)	(49)
NECROSIS, FAT			1 (2%)
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
ANIMAL MISSING/NO NECROPSY			1
ACCIDENTAL DEATH	1		
AUTO/NECROPSY/NO HISTO		2	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX E

METHODS USED IN HEMATOLOGIC ANALYSES

APPENDIX E

A. Hematocrit (HCT):

This volume was reported as a percentage of the whole blood volume (Lynch et al., 1969; Miale, 1967) on the Coulter (Coulter Electronics, 1970) flat pack accessory.

B. Hemoglobin (HGB):

The red cells in a specimen of blood were hemolyzed and the hemoglobin was converted into either oxy- or cyanmethemoglobin (Lynch et al., 1969; Miale, 1967). The optical density or percent transmittance of a dilute solution was measured and the hemoglobin concentration of the original sample was obtained automatically in grams percent on the Coulter Hemoglobinometer (Coulter Electronics, 1970).

C. Erythrocyte Count (RBC):

Whole blood was diluted with an isotonic solution and the number of red blood cells in a known volume was counted automatically on the Coulter Counter, Model FN (Coulter Electronics, 1970). RBC is expressed in $10^6/mm^3$ (Lynch et al., 1969; Miale, 1967).

D. Leukocyte Count (WBC):

Whole blood was diluted with an isotonic solution and the number of white cells in a known volume was counted automatically on a Coulter Counter, Model FN (Coulter Electronics, 1970). The WBC is expressed in $10^3/mm^3$ (Lynch et al., 1969; Miale, 1967).

E. Differential:

A count of 100 leukocytes was differentiated and reported in percent per type of cell. Slides were stained with May-Grunwald/Giemsa on the Ames automatic slide stainer (Ames Co., 1974).

F. Platelet:

The platelets in a diluted sample of blood were counted in a hemocytometer. This direct method of platelet determination was done with the Unopette disposable pipetting system (Becton-Dickinson Division, 1974).

G. MCV:

MCV was calculated on the Coulter FN (Coulter Electronics, 1970) flat pack accessory.

H. Reticulocytes:

Reticulocyte counts were performed by making a blood smear from a mixture of equal parts of fresh methylene blue and blood, and then counting from estimated fields containing 1,000 red blood cells.

APPENDIX F

BLOOD, CLINICAL CHEMISTRY, AND PORPHYRIN ANALYSES AND ORGAN WEIGHTS FOR RATS AND MICE ON THE 13-WEEK STUDIES

TABLE F1. RESULTS OF BLOOD ANALYSES IN MALE RATS ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

	Dose (mg/kg)					
	0	30	60	125	250	500
Hemoglobin (g/dl)	16.5 ± 0.9	16.9 ± 0.6	16.8 ± 0.9	16.6 ± 0.5	16.5 ± 1.1	15.0 ± 0.5 *(b,c)*
Hematocrit (percent)	51 ± 3	53 ± 1	51 ± 2	49 ± 2	50 ± 3	46 ± 1 *(b,c)*
White Blood Cells (10^3 cu mm)	6.7 ± 1.1	7.2 ± 0.8	7.0 ± 1.0	6.8 ± 1.1	7.0 ± 1.0	6.0 ± 1.4
Red Blood Cells (10^6 cu mm)	9.42 ± 0.53	9.70 ± 0.32	9.49 ± 0.48	9.46 ± 0.30	9.54 ± 0.63	8.57 ± 0.25 *(b,c)*
Mean Corpuscular volume (μ^3)	52 ± 1	53 ± 1	52 ± 1	50 ± 1 *(b)*	50 ± 1 *(b)*	51 ± 1 *(c)*
Bands (percent)	0	0	0	0	0	0
Segs (percent)	15 ± 4	19 ± 7	15 ± 3	16 ± 6	11 ± 4	22 ± 7 *(b)*
Eosinophils (percent)	0.3 ± 0.5	0.7 ± 1.1	1.3 ± 1.1	1.1 ± 1.1	0.7 ± 0.7	0.2 ± 0.4
Basophils (percent)	0	0	0	0	0	0
Lymphocytes (percent)	84 ± 4	80 ± 8	83 ± 4	83 ± 7	88 ± 5	78 ± 7 *(b)*
Monocytes (percent)	0	0	0.1 ± 0.3	0	0	0
Platelets x 10^5	4.46 ± 1.09	3.63 ± 1.07	4.23 ± 1.02	4.92 ± 0.95	5.26 ± 1.04	4.19 ± 1.51
Reticulocytes (percent)	2.4 ± 1.1	3.4 ± 1.2	3.0 ± 0.6	3.1 ± 1.0	2.8 ± 0.6	1.7 ± 0.9 *(c)*

(a) Groups contained 9 or 10 animals. Values presented represent the mean ± standard deviation.
(b) Dosed group significantly different from controls, $P<0.05$.
(c) Negative dose-response trend, $P<0.05$.

TABLE F2. RESULTS OF BLOOD ANALYSES IN FEMALE RATS ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

	Dose (mg/kg)					
	0	30	60	125	250	500
Hemoglobin (g/dl)	16.8 ± 0.6	17.0 ± 0.6	17.1 ± 1.0	17.0 ± 0.9	16.6 ± 0.4	15.9 ± 0.5 *(b,d)*
Hematocrit (percent)	48 ± 2	49 ± 2	48 ± 3	48 ± 3	48 ± 2	45 ± 2 *(b,d)*
White Blood Cells (10^3/cu mm)	8.2 ± 1.7	9.1 ± 0.9	9.1 ± 2.9	9.5 ± 1.6	8.1 ± 1.0	8.2 ± 0.7
Red Blood Cells (10^6/cu mm)	8.81 ± 0.31	8.90 ± 0.29	8.98 ± 0.47	8.86 ± 0.52	8.99 ± 0.27	8.42 ± 0.29
Mean Corpuscular volume (μ^3)	54 ± 2	54 ± 1	53 ± 1	54 ± 1	53 ± 0.4 *(b)*	53 ± 1 *(b,d)*
Bands (percent)	0	0	0	0	0	0
Segs (percent)	14 ± 5	13 ± 3	14 ± 6	15 ± 4	13 ± 4	13 ± 6
Eosinophils (percent)	0.8 ± 0.8	1.8 ± 1.6	1.2 ± 1.0	1.2 ± 0.9	0.6 ± 0.7	0.9 ± 0.6
Basophils (percent)	0	0	0	0	0	0
Lymphocytes (percent)	86 ± 5	85 ± 3	84 ± 7	84 ± 3	87 ± 4	86 ± 7
Monocytes (percent)	0	0	0	0	0	0
Platelets x 10^5	2.96 ± 0.39	4.09 ± 1.32	4.81 ± 0.63 *(b)*	5.85 ± 2.23 *(b)*	3.66 ± 0.63	5.24 ± 0.76 *(b,c)*
Reticulocytes (percent)	5.7 ± 2.2	4.7 ± 1.2	5.4 ± 0.7	5.8 ± 1.0	6.2 ± 1.2	8.2 ± 0.9 *(b,c)*

(a) Groups contained 7 to 10 animals. Values presented represent the mean ± standard deviation.
(b) Dosed group significantly different from controls, $P < 0.05$.
(c) Positive dose-response trend, $P < 0.05$.
(d) Negative dose-response trend, $P < 0.05$.

TABLE F3. RESULTS OF CLINICAL CHEMISTRY ANALYSES IN MALE RATS ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

	Dose (mg/kg)					
	0	30	60	125	250	500
Alkaline phosphatase (IU)	105 ± 8	97 ± 9	98 ± 9	80 ± 8 *(b)*	92 ± 16 *(b)*	106 ± 14
SGPT (IU)	62 ± 35	57 ± 21	65 ± 14	49 ± 13	83 ± 84	75 ± 31
GGTP (IU)	0	0	0	0	0	1 ± 1
Bilirubin (mg/dl)	0.29 ± 0.04	0.22 ± 0.04 *(b)*	0.24 ± 0.04	0.21 ± 0.04 *(b)*	0.27 ± 0.06	0.39 ± 0.09 *(b,c)*
Cholesterol (mg/dl)	34 ± 4	51 ± 9 *(b)*	40 ± 7	43 ± 5 *(b)*	58 ± 6 *(b)*	71 ± 8 *(b,c)*
Triglycerides (mg/dl)	242 ± 28	285 ± 50	264 ± 60	228 ± 56	236 ± 70	142 ± 75 *(b,d)*
Blood Urea Nitrogen (mg/dl)	21 ± 3	24 ± 4	23 ± 2	20 ± 2	21 ± 5	19 ± 3 *(d)*
Glucose (mg/dl)	214 ± 14	231 ± 26	224 ± 24	203 ± 23	203 ± 38	203 ± 17 *(d)*
Total Protein (g/dl)	7.0 ± 0.2	6.9 ± 0.4	7.1 ± 0.4	7.0 ± 0.2	7.5 ± 0.5*(b)*	7.5 ± 0.3 *(b,c)*
Albumin (g/dl)	4.9 ± 0.2	4.8 ± 0.4	4.9 ± 0.3	4.8 ± 0.2	5.1 ± 0.4	4.9 ± 0.2
Alpha-Globulin (g/dl)	0.74 ± 0.10	0.72 ± 0.11	0.77 ± 0.05	0.74 ± 0.09	0.83 ± 0.11	0.95 ± 0.19 *(b,c)*
Beta-Globulin (g/dl)	1.2 ± 0.1	1.2 ± 0.1	1.2 ± 0.04	1.2 ± 0.1	1.3 ± 0.1	1.4 ± 0.2 *(b,c)*
Gamma-Globulin (g/dl)	0.23 ± 0.05	0.20 ± 0.00	0.22 ± 0.04	0.26 ± 0.05	0.24 ± 0.10	0.19 ± 0.03

(a) Groups contained 9 or 10 animals. Values presented represent the mean ± standard deviation.
(b) Dosed group significantly different from controls, $P<0.05$.
(c) Positive dose-response trend, $P<0.05$.
(d) Negative dose-response trend, $P<0.05$.

TABLE F4. RESULTS OF CLINICAL CHEMISTRY ANALYSES IN FEMALE RATS ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

	Dose (mg/kg)					
	0	30	60	125	250	500
Alkaline phosphatase (IU)	69 ± 9	76 ± 6	77 ± 10	77 ± 12	72 ± 12	79 ± 10
SGPT (IU)	48 ± 30	53 ± 39	56 ± 53	63 ± 43	48 ± 32	52 ± 27
GGTP (IU)	1 ± 1	0.3 ± 0.5	0	0.1 ± 0.3	0	1 ± 1
Bilirubin (mg/dl)	0.21 ± 0.04	0.23 ± 0.08	0.22 ± 0.05	0.22 ± 0.03	0.22 ± 0.07	0.20 ± 0.07
Cholesterol (mg/dl)	49 ± 4	55 ± 7	55 ± 6	65 ± 4 *(b)*	62 ± 7 *(b)*	74 ± 7 *(b,c)*
Triglycerides (mg/dl)	180 ± 30	145 ± 33	172 ± 43	167 ± 32	141 ± 36 *(b)*	167 ± 17
Blood Urea Nitrogen (mg/dl)	23 ± 4	22 ± 2	24 ± 3	24 ± 4	21 ± 4	22 ± 4
Glucose (mg/dl)	176 ± 16	204 ± 12 *(b)*	195 ± 15	212 ± 16 *(b)*	206 ± 21 *(b)*	209 ± 17 *(b,c)*
Total Protein (g/dl)	6.4 ± 0.3	6.9 ± 0.1 *(b)*	6.7 ± 0.2 *(b)*	6.8 ± 0.2 *(b)*	6.8 ± 0.3 *(b)*	7.5 ± 0.3 *(b,c)*
Albumin (g/dl)	4.4 ± 0.3	4.6 ± 0.2	4.5 ± 0.2	4.6 ± 0.2	4.5 ± 0.2	5.1 ± 0.2 *(b,c)*
Alpha-Globulin (g/dl)	0.66 ± 0.07	0.74 ± 0.11	0.74 ± 0.08	0.75 ± 0.09	0.72 ± 0.06	0.80 ± 0.09 *(b,c)*
Beta-Globulin (g/dl)	1.1 ± 0.1	1.2 ± 0.1 *(b)*	1.2 ± 0.1 *(b)*	1.2 ± 0.1 *(b)*	1.2 ± 0.1 *(b)*	1.4 ± 0.1 *(b,c)*
Gamma-Globulin (g/dl)	0.27 ± 0.08	0.28 ± 0.07	0.32 ± 0.06	0.27 ± 0.05	0.30 ± 0.09	0.20 ± 0.05

(a) Groups contained 8 to 10 animals. Values presented represent the mean ± standard deviation.
(b) Dosed group significantly different from controls, $P<0.05$.
(c) Positive dose-response trend, $P<0.05$.

TABLE F5. RESULTS OF PORPHYRIN ANALYSES OF LIVER AND URINE IN RATS ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

Dose (mg/kg)	Liver	Urine		
	Total porphyrin (ng/g liver)	Coproporphyrin (μg/24 hours)	Uroporphyrin (μg/24 hours)	Volume (ml)
Males				
0	111.97 ± 28.15	0.51 ± 0.23	1.38 ± 0.42	5.6 ± 1.8
30	101.38 ± 11.16	—	—	
60	99.78 ± 23.92	—	—	
125	130.83 ± 32.41	—	—	
250	117.01 ± 16.57	—	—	
500	95.02 ± 13.51	4.99 ± 2.54 *(b)*	5.85 ± 2.78 *(b)*	8.8 ± 2.8 *(b)*
Females				
0	124.46 ± 30.18	0.46 ± 0.34	0.59 ± 0.14	3.1 ± 1.7
30	131.33 ± 21.57	—	—	—
60	150.21 ± 28.78	—	—	—
125	136.44 ± 16.13	—	—	—
250	147.45 ± 38.36	—	—	—
500	128.99 ± 14.89	2.53 ± 1.16 *(b)*	2.02 ± 0.88 *(b)*	5.3 ± 3.8

(a) Groups contain 6 to 10 animals. Values presented represent the mean ± standard deviation.
(b) Dosed group significantly different from controls, $P<0.05$.

TABLE F6. ORGAN WEIGHTS OF MALE RATS ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

Dose (mg/kg)	Body Weight (grams)	Lung	Heart	Liver	Spleen	Thymus	Right Kidney	Brain	Testicle
0									
Mean	274 ± 22	1.34 ± 0.18	0.98 ± 0.08	8.75 ± 1.15	0.54 ± 0.07	0.29 ± 0.09	0.97 ± 0.09	1.78 ± 0.08	2.16 ± 0.16
OW/BW *(b)*	—	0.49 ± 0.07	0.36 ± 0.02	3.18 ± 0.20	0.20 ± 0.02	0.11 ± 0.03	0.35 ± 0.01	0.65 ± 0.05	0.79 ± 0.08
30									
Mean	275 ± 2	1.44 ± 0.17	0.99 ± 0.08	9.00 ± 0.63	0.54 ± 0.04	0.27 ± 0.07	0.94 ± 0.07	1.77 ± 0.07	2.16 ± 0.16
OW/BW	—	0.52 ± 0.06	0.36 ± 0.03	3.28 ± 0.22	0.20 ± 0.01	0.10 ± 0.02	0.34 ± 0.02	0.64 ± 0.02	0.79 ± 0.06
60									
Mean	269 ± 17	1.46 ± 0.20	0.94 ± 0.08	8.34 ± 0.73	0.53 ± 0.05	0.28 ± 0.06	0.95 ± 0.10	1.80 ± 0.06	2.17 ± 0.32
OW/BW	—	0.54 ± 0.08	0.35 ± 0.02	3.10 ± 0.15	0.20 ± 0.01	0.10 ± 0.02	0.35 ± 0.03	0.67 ± 0.04	0.81 ± 0.08
125									
Mean	261 ± 15	1.32 ± 0.14	1.02 ± 0.21	8.98 ± 0.95	0.52 ± 0.06	0.25 ± 0.02	1.02 ± 0.15	1.82 ± 0.07	1.95 ± 0.09
OW/BW	—	0.51 ± 0.07	0.39 ± 0.07	3.43 ± 0.22 *(c)*	0.20 ± 0.01	0.10 ± 0.01	0.39 ± 0.06	0.70 ± 0.05	0.75 ± 0.03
250									
Mean	258 ± 25	1.36 ± 0.15	0.89 ± 0.04	9.62 ± 1.28	0.49 ± 0.08	0.23 ± 0.08	0.95 ± 0.06	1.77 ± 0.09	1.91 ± 0.17
OW/BW	—	0.53 ± 0.05	0.35 ± 0.03	3.72 ± 0.29 *(c)*	0.19 ± 0.02	0.09 ± 0.04	0.37 ± 0.03	0.69 ± 0.05	0.74 ± 0.07
500									
Mean	224 ± 27	1.46 ± 0.69	0.82 ± 0.12 *(c,e)*	10.27 ± 1.04 *(c,d)*	0.44 ± 0.06 *(c,e)*	0.17 ± 0.11 *(c,e)*	0.91 ± 0.10	1.73 ± 0.08	1.76 ± 0.29 *(c,e)*
OW/BW	*(c,e)*	0.66 ± 0.34 *(c,d)*	0.37 ± 0.04	4.61 ± 0.47 *(c,d)*	0.19 ± 0.01	0.07 ± 0.05 *(c,e)*	0.40 ± 0.02 *(c,d)*	0.78 ± 0.07 *(c,d)*	0.78 ± 0.06

(a) Groups contained 9 or 10 animals.
(b) Organ weight/body weight x 100 (percent).
(c) Dosed group significantly different from controls, $P<0.05$.
(d) Positive dose-response trend, $P<0.05$
(e) Negative dose-response trend, $P<0.05$.

TABLE F7. ORGAN WEIGHTS OF FEMALE RATS ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

Dose (mg/kg)	Body Weight (grams)	Lung	Heart	Liver	Spleen	Thymus	Right Kidney	Brain	Right Ovary	Uterus
0										
Mean	169 ± 13	1.13 ± 0.22	0.62 ± 0.07	4.87 ± 0.24	0.42 ± 0.04	0.25 ± 0.06	0.58 ± 0.03	1.67 ± 0.12	0.11 ± 0.15	0.61 ± 0.20
OW/BW *(b)*	—	0.67 ± 0.09	0.37 ± 0.02	2.90 ± 0.20	0.25 ± 0.03	0.15 ± 0.03	0.35 ± 0.03	1.00 ± 0.11	0.06 ± 0.09	0.48 ± 0.10
30										
Mean	166 ± 13	1.13 ± 0.18	0.62 ± 0.07	4.95 ± 0.53	0.39 ± 0.05	0.22 ± 0.06	0.58 ± 0.06	1.70 ± 0.10	0.06 ± 0.01	0.48 ± 0.10
OW/BW	—	0.68 ± 0.11	0.37 ± 0.03	2.98 ± 0.15	0.23 ± 0.01	0.13 ± 0.03	0.35 ± 0.02	1.03 ± 0.08	0.04 ± 0.01	0.29 ± 0.07
60										
Mean	166 ± 16	1.05 ± 0.14	0.62 ± 0.06	4.84 ± 0.44	0.40 ± 0.04	0.26 ± 0.05	0.57 ± 0.06	1.73 ± 0.08	0.06 ± 0.02	0.53 ± 0.25
OW/BW	—	0.63 ± 0.07	0.37 ± 0.03	2.92 ± 0.16	0.24 ± 0.03	0.16 ± 0.03	0.34 ± 0.02	1.05 ± 0.07	0.04 ± 0.01	0.31 ± 0.12
125										
Mean	164 ± 10	1.08 ± 0.23	0.63 ± 0.07	5.13 ± 0.53	0.39 ± 0.03	0.23 ± 0.06	0.60 ± 0.06	1.69 ± 0.08	0.07 ± 0.01	0.58 ± 0.17
OW/BW	—	0.66 ± 0.14	0.39 ± 0.05	3.13 ± 0.20 *(c)*	0.24 ± 0.01	0.14 ± 0.03	0.37 ± 0.03	1.04 ± 0.07	0.04 ± 0.01	0.35 ± 0.10
250										
Mean	160 ± 13	1.04 ± 0.09	0.61 ± 0.07	5.33 ± 0.51	0.42 ± 0.17	0.24 ± 0.05	0.59 ± 0.06	1.69 ± 0.10	0.07 ± 0.04	0.60 ± 0.18
OW/BW	—	0.65 ± 0.07	0.38 ± 0.03	3.33 ± 0.18 *(c)*	0.26 ± 0.10	0.15 ± 0.03	0.37 ± 0.02	1.06 ± 0.06	0.04 ± 0.02	0.38 ± 0.11
500										
Mean	165 ± 14	1.19 ± 0.16	0.61 ± 0.11	6.03 ± 0.54 *(c,d)*	0.38 ± 0.03	0.20 ± 0.09	0.59 ± 0.04	1.68 ± 0.07	0.06 ± 0.03	0.37 ± 0.10 *(c)*
OW/BW		0.74 ± 0.08	0.38 ± 0.05	3.78 ± 0.30 *(c,d)*	0.24 ± 0.02	0.12 ± 0.05	0.37 ± 0.03 *(d)*	1.06 ± 0.08	0.04 ± 0.01	0.23 ± 0.07 *(c)*

(a) Groups contained 8 to 10 animals.
(b) Organ weight/body weight x 100 (percent).
(c) Dosed group significantly different from controls, $P<0.05$.
(d) Positive dose-response trend, $P<0.05$.

TABLE F8. RESULTS OF BLOOD ANALYSES IN MALE MICE ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

	Dose (mg/kg)					
	0	30	60	125	250	500
Hemoglobin (g/dl)	15.8 ± 0.8	16.3 ± 0.5	16.0 ± 0.7	16.6 ± 0.5 *(b)*	15.6 ± 0.6	15.4 ± 0.7
Hematocrit (percent)	50 ± 2	52 ± 2	51 ± 1	53 ± 1 *(b)*	51 ± 2	51 ± 2
White Blood Cells (10^3 cu mm)	3.4 ± 0.8	6.6 ± 1.1 *(b)*	7.2 ± 1.3 *(b)*	5.7 ± 1.2 *(b)*	5.4 ± 1.0 *(b)*	6.5 ± 1.3 *(b,c)*
Red Blood Cells (10^6 cu mm)	9.82 ± 0.47	10.21 ± 0.36	10.07 ± 0.39	10.33 ± 0.31 *(b)*	9.86 ± 0.40	9.72 ± 0.54
Mean Corpuscular volume (μ^3)	51 ± 1	51 ± 1	51 ± 1	52 ± 1	52 ± 1	52 ± 1 *(c)*
Bands (percent)	0	0	0	0	0	0
Segs (percent)	33 ± 10	17 ± 4 *(b)*	24 ± 7 *(b)*	17 ± 9 *(b)*	27 ± 4	22 ± 8 *(b)*
Eosinophils (percent)	0.5 ± 0.7	0.7 ± 1.0	1.8 ± 1.9 *(b)*	0.1 ± 0.3	0.3 ± 0.7	0.5 ± 0.6
Basophils (percent)	0	0	0	0	0	0
Lymphocytes (percent)	67 ± 10	82 ± 3 *(b)*	75 ± 7	83 ± 9 *(b)*	73 ± 4	78 ± 7 *(b)*
Monocytes (percent)	0	0	0	0	0.1 ± 0.3	0
Platelets x 10^5	6.66 ± 1.32	5.10 ± 0.90 *(b)*	5.53 ± 0.62	6.15 ± 1.71	7.11 ± 1.04	5.82 ± 1.65
Reticulocytes (percent)	2.2 ± 0.6	2.0 ± 0.3	2.4 ± 0.7	2.3 ± 0.6	2.3 ± 0.4	2.0 ± 0.8

(a) Groups contained 6 to 10 animals. Values presented represent the mean ± standard deviation.
(b) Dosed group significantly different from controls, $P<0.05$.
(c) Positive dose-response trend, $P<0.05$

TABLE F9. RESULTS OF BLOOD ANALYSES IN FEMALE MICE ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

	Dose (mg/kg)					
	0	30	60	125	250	500
Hemoglobin (g/dl)	16.0 ± 1.1	16.3 ± 0.5	16.0 ± 0.5	16.1 ± 0.3	15.7 ± 0.4	15.9 ± 1.0
Hematocrit (percent)	51 ± 4	52 ± 1	51 ± 2	51 ± 1	50 ± 1	50 ± 2
White Blood Cells (10^3 cu mm)	4.8 ± 1.3	6.7 ± 1.0 *(b)*	5.2 ± 1.2	5.1 ± 0.9	4.4 ± 1.3	5.4 ± 0.9
Red Blood Cells (10^6 cu mm)	9.81 ± 0.90	10.02 ± 0.28	9.92 ± 0.33	9.86 ± 0.18	9.59 ± 0.18	10.18 ± 0.65
Mean Corpuscular volume (μ^3)	53 ± 1	52 ± 1	52 ± 1	51 ± 0.4 *(b)*	52 ± 1	51 ± 1 *(b,d)*
Bands (percent)	0	0	0	0	0	0
Segs (percent)	12 ± 7	17 ± 5	14 ± 3	20 ± 5 *(b)*	22 ± 5 *(b)*	19 ± 8 *(b)*
Eosinophils (percent)	0.4 ± 0.5	0.5 ± 0.7	0.7 ± 0.8	0.6 ± 0.7	0.9 ± 1.1	0.2 ± 0.4
Basophils (percent)	0	0	0	0	0	0
Lymphocytes (percent)	87 ± 7	83 ± 5	85 ± 3	80 ± 5 *(b)*	77 ± 11 *(b)*	81 ± 8 *(d)*
Monocytes (percent)	0	0.1 ± 0.30	0	0	0	0
Platelets x 10^5	5.43 ± 0.86	4.49 ± 1.01	6.04 ± 1.11	6.94 ± 1.67 *(b)*	6.00 ± 0.73	5.96 ± 0.92 *(c)*
Reticulocytes (percent)	2.5 ± 1.1	2.7 ± 0.9	2.7 ± 0.6	3.1 ± 0.6	2.9 ± 0.9	1.9 ± 1.0

(a) Groups contained 6 to 10 animals. Values presented represent the mean ± standard deviation.
(b) Dosed group significantly different from controls $P<0.05$.
(c) Positive dose-response trend, $P<0.05$.
(d) Negative dose-response trend, $P<0.05$.

TABLE F10. RESULTS OF CLINICAL CHEMISTRY ANALYSES IN MICE ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

	Dose (mg/kg)					
	0	**30**	**60**	**125**	**250**	**500**
MALES						
Alkaline Phosphatase (IU)	25 ± 6 (8)	33 ± 13 (7)	36 ± 12 (9)	39 ± 8 (10) *(b)*	37 ± 4 (9) *(b)*	36 ± 17 (4)
SGPT (IU)	22 ± 6 (8)	-	-	21 (1)	35 ± 16 (9) *(b)*	64 ± 45 (2)
GGPT (IU)	0 (8)	-	-	0 (1)	0 (8)	0 (2)
FEMALES						
Alkaline Phosphatase (IU)	62 ± 12 (7)	49 ± 10 (5)	64 ± 8 (5)	54 ± 11 (6)	47 ± 4 (6)	62 ± 4 (6)
SGPT (IU)	-	14 ± 4 (2)	-	-	-	-
GGTP (IU)	-	-	-	-	-	-

(a) Values presented represent the mean ± standard deviation, followed parenthetically by the number of samples taken. When no values are given, the quantity of samples was not sufficient for analyses.

(b) Dosed group was significantly different from controls, $P < 0.05$.

TABLE F11. RESULTS OF PORPHYRIN ANALYSES IN MICE ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

Dose (mg/kg)	Liver	Urine	
	Total porphyrin (ng/g liver)	Coproporphyrin (μg/24 hours)	Uroporphyrin (μg/24 hours)
Males			
0	77.88 ± 22.95 (10)	0.13 ± 0.10 (2)	0.42 ± 0.01 (2)
30	104.64 ± 20.83 (10)	—	—
60	64.57 ± 11.59 (10)	—	—
125	88.46 ± 35.76 (10)	—	—
250	64.08 ± 21.47 (9)	—	—
500	70.07 ± 29.45 (6)	0.19 ± 0.13 (2)	2.51 ± 1.30 (2) *(b)*
Females			
0	103.23 ± 39.11 (10)	0.30 ± 0.34 (2)	0.74 ± 0.17 (2)
30	140.76 ± 37.51 (10)	—	—
60	140.07 ± 37.83 (9)	—	—
125	145.67 ± 37.05 (10)	—	—
250	175.48 ± 49.31 (10) *(b)*	—	—
500	193.33 ± 28.39 (7) *(b,c)*	0.86 ± 0.23 (2)	0.80 ± 0.09 (2)

(a) Values presented represent the mean ± standard deviation, followed parenthetically by the number of samples in each group.
(b) Dosed group significantly different from controls, $P<0.05$.
(c) Positive dose-response trend, $P<0.05$.

TABLE F12. ORGAN WEIGHTS OF MALE MICE ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

Dose (mg/kg)	Body Weight (grams)	Lung	Heart	Liver	Spleen	Thymus	Right Kidney	Brain	Right Testicle
0									
Mean	29 ± 3	0.20 ± 0.06	0.16 ± 0.02	1.31 ± 0.20	0.09 ± 0.03	0.03 ± 0.01	0.25 ± 0.04	0.46 ± 0.02	0.22 ± 0.05
OW/BW *(b)*	-	0.69 ± 0.15	0.56 ± 0.07	4.46 ± 0.45	0.29 ± 0.09	0.11 ± 0.04	0.86 ± 0.07	1.56 ± 0.08	0.77 ± 0.16
30									
Mean	28 ± 2	0.22 ± 0.04	0.14 ± 0.02	1.10 ± 0.07 *(c)*	0.06 ± 0.01 *(c)*	0.04 ± 0.01	0.23 ± 0.03	0.46 ± 0.03	0.22 ± 0.01
OW/BW	-	0.76 ± 0.11	0.50 ± 0.06	3.87 ± 0.27 *(c)*	0.21 ± 0.02 *(c)*	0.13 ± 0.03	0.80 ± 0.05	1.62 ± 0.16	0.79 ± 0.06
60									
Mean	30 ± 3	0.21 ± 0.04	0.16 ± 0.04	1.28 ± 0.18	0.07 ± 0.02	0.03 ± 0.01	0.25 ± 0.02	0.45 ± 0.02	0.22 ± 0.03
OW/BW	-	0.70 ± 0.09	0.55 ± 0.11	4.31 ± 0.36	0.25 ± 0.07	0.12 ± 0.03	0.86 ± 0.07	1.54 ± 0.11	0.76 ± 0.13
125									
Mean	30 ± 2	0.20 ± 0.03	0.19 ± 0.18	1.17 ± 0.08	0.07 ± 0.04	0.04 ± 0.01	0.22 ± 0.02 *(c)*	0.45 ± 0.02	0.24 ± 0.04
OW/BW	-	0.65 ± 0.08	0.63 ± 0.55	3.91 ± 0.19 *(c)*	0.24 ± 0.12	0.12 ± 0.03	0.73 ± 0.08 *(c)*	1.49 ± 0.08	0.80 ± 0.12
250									
Mean	30 ± 2	0.24 ± 0.11	0.14 ± 0.02	1.36 ± 0.07	0.07 ± 0.01	0.03 ± 0.01	0.24 ± 0.02	0.43 ± 0.04	0.22 ± 0.04
OW/BW	-	0.77 ± 0.31	0.47 ± 0.06	4.47 ± 0.32	0.22 ± 0.03	0.10 ± 0.02	0.80 ± 0.06	1.41 ± 0.13 *(c)*	0.72 ± 0.11
500									
Mean	27 ± 3 *(e)*	0.18 ± 0.03	0.13 ± 0.02	1.52 ± 0.11 *(c,d)*	0.06 ± 0.01 *(e)*	0.03 ± 0.01	0.23 ± 0.02	0.43 ± 0.01 *(e)*	0.19 ± 0.03
OW/BW	-	0.67 ± 0.10	0.48 ± 0.05	5.59 ± 0.54 *(c,d)*	0.22 ± 0.04	0.12 ± 0.04	0.85 ± 0.05	1.58 ± 0.11 *(e)*	0.70 ± 0.12

(a) Values presented represent the mean ± standard deviation; groups contained 7 to 10 mice.
(b) Organ weight/body weight x 100 (percent).
(c) Dosed group significantly different from controls, $P<0.05$.
(d) Positive dose-response trend, $P<0.05$.
(e) Negative dose-response trend, $P<0.05$.

TABLE F13. ORGAN WEIGHTS OF FEMALE MICE ADMINISTERED 1,2-DICHLOROBENZENE FOR 13 WEEKS *(a)*

Dose (mg/kg)	Body Weight (grams)	Lung	Heart	Liver	Spleen	Thymus	Right Kidney	Brain	Right Ovary	Uterus
0										
Mean	23 ± 1	0.20 ± 0.03	0.12 ± 0.02	0.97 ± 0.06	0.09 ± 0.04	0.04 ± 0.01	0.17 ± 0.02	0.44 ± 0.07	0.05 ± 0.09	0.11 ± 0.05
OW/BW *(b)*	-	0.85 ± 0.12	0.53 ± 0.07	4.20 ± 0.23	0.40 ± 0.14	0.15 ± 0.05	0.74 ± 0.09	1.91 ± 0.36	0.21 ± 0.37	0.51 ± 0.16
30										
Mean	22 ± 1	0.20 ± 0.03	0.11 ± 0.01	0.91 ± 0.07	0.07 ± 0.01	0.04 ± 0.01	0.16 ± 0.02	0.47 ± 0.05	0.02 ± 0.01	0.12 ± 0.02
OW/BW	-	0.95 ± 0.14	0.51 ± 0.05	4.21 ± 0.30	0.31 ± 0.03 *(c)*	0.19 ± 0.05	0.75 ± 0.07	2.17 ± 0.27	0.08 ± 0.03	0.54 ± 0.10
60										
Mean	23 ± 2	0.18 ± 0.04	0.13 ± 0.04	0.95 ± 0.09	0.07 ± 0.01	0.04 ± 0.02	0.17 ± 0.02	0.46 ± 0.03	0.02 ± 0.01	0.12 ± 0.03
OW/BW	-	0.79 ± 0.19	0.57 ± 0.23	4.12 ± 0.22	0.29 ± 0.05 *(c)*	0.18 ± 0.06	0.73 ± 0.06	2.03 ± 0.23	0.08 ± 0.04	0.53 ± 0.13
125										
Mean	23 ± 1	0.22 ± 0.08	0.12 ± 0.02	0.94 ± 0.08	0.06 ± 0.01	0.03 ± 0.01	0.16 ± 0.01	0.45 ± 0.01	0.02 ± 0.01	0.11 ± 0.02
OW/BW	-	0.98 ± 0.39	0.52 ± 0.08	4.12 ± 0.31	0.28 ± 0.03 *(c)*	0.15 ± 0.06	0.69 ± 0.06	1.98 ± 0.11	0.11 ± 0.04	0.48 ± 0.07
250										
Mean	21 ± 1	0.19 ± 0.03	0.11 ± 0.01	0.94 ± 0.08	0.06 ± 0.01 *(c)*	0.04 ± 0.02	0.16 ± 0.02	0.45 ± 0.08	0.02 ± 0.01	0.12 ± 0.04
OW/BW	-	0.91 ± 0.14	0.52 ± 0.05	4.44 ± 0.29	0.28 ± 0.05 *(c)*	0.20 ± 0.11	0.75 ± 0.08	2.13 ± 0.38	0.10 ± 0.05	0.56 ± 0.17
500										
Mean	20 ± 3 *(c,e)*	0.20 ± 0.02	0.11 ± 0.02	1.02 ± 0.14	0.05 ± 0.02 *(c)*	0.02 ± 0.01	0.17 ± 0.03	0.43 ± 0.02	0.01 ± 0.01	0.08 ± 0.03
OW/BW	-	1.08 ± 0.28	0.57 ± 0.05	5.53 ± 0.36 *(c,d)*	0.28 ± 0.06 *(c,e)*	0.09 ± 0.05	0.91 ± 0.05 *(d)*	2.37 ± 0.27 *(c,d)*	0.06 ± 0.04	0.41 ± 0.09

(a) Values represent the mean ± standard deviation; groups contained 8 to 10 mice.
(b) Organ weight/body weight x 100 (percent).
(c) Dosed group significantly different from controls, $P<0.05$.
(d) Positive dose-response trend, $P<0.05$.
(e) Negative dose-response trend, $P<0.05$

APPENDIX G

HISTORICAL INCIDENCES OF TUMORS IN MALE F344/N RATS AND B6C3F$_1$ MICE

TABLE G1. HISTORICAL INCIDENCE OF ADRENAL TUMORS IN MALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Pheochromocytoma
Battelle	14/99 (14.1%)
Gulf South	24/289 (8.3%)
Hazleton	8/50 (16.0%)
Litton	19/128 (14.8%)
Mason	25/125 (20.0%)
Papanicolaou	3/45 (6.7%)
Southern	60/250 (24.0%)
Total	153/986 (15.5%)
SD *(b)*	8.74%
Overall Historical Range	
High	16/50
Low	2/46

(a) Data as of November 30, 1981 for studies of at least 104 weeks.
(b) Standard deviation. Range and SD are presented for groups of 35 or more animals.

TABLE G2. HISTORICAL INCIDENCE OF LUNG TUMORS IN MALE B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Alveolar/ Bronchiolar Adenoma	Alveolar/ Bronchiolar Carcinoma	Alveolar/ Bronchiolar Adenoma or Carcinoma
Battelle	8/100 (8.0%)	6/100 (6.0%)	14/100 (14.0%)
Gulf South	12/235 (5.1%)	17/235 (7.2%)	29/235 (12.3%)
Litton	5/120 (4.2%)	3/120 (2.5%)	8/120 (6.7%)
Mason	19/150 (12.7%)	4/150 (2.7%)	22/150 (14.7%)
Papanicolaou	4/49 (8.2%)	3/49 (6.1%)	7/49 (14.3%)
Southern	32/248 (12.9%)	11/248 (4.4%)	43/248 (17.3%)
Total	80/902 (8.9%)	44/902 (4.9%)	123/902 (13.6%)
SD *(b)*	5.00%	3.74%	5.45%
Overall Historical Range			
High	10/50	7/50	13/50
Low	0/47	0/50	2/50

(a) Data as of November 30, 1981 for studies of at least 104 weeks.
(b) Standard deviation. Range and standard deviation are presented for groups of 35 or more animals.

APPENDIX H

ANALYSIS OF PRIMARY TUMORS IN RATS AND MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

TABLE H1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	60 mg/kg	120 mg/kg
Subcutaneous Tissue: Fibroma			
Tumor Rates			
Overall *(a)*	1/50 (2%)	3/50 (6%)	0/50 (0%)
Adjusted *(b)*	2.1%	7.5%	0.0%
Terminal *(c)*	0/42 (0%)	2/36 (6%)	0/19 (0%)
Statistical Tests *(d)*			
Life Table	P=0.528N	P=0.274	P=0.548N
Incidental Tumor Test	P=0.335N	P=0.336	P=0.186N
Cochran-Armitage Trend Test	P=0.378N		
Fisher Exact Test		P=0.309	P=0.500N
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(a)*	9/50 (18%)	5/50 (10%)	5/50 (10%)
Adjusted *(b)*	20.3%	12.1%	20.4%
Terminal *(c)*	7/42 (17%)	2/36 (6%)	3/19 (16%)
Statistical Tests *(d)*			
Life Table	P=0.513N	P=0.280N	P=0.561
Incidental Tumor Test	P=0.143N	P=0.130N	P=0.330N
Cochran-Armitage Trend Test	P=0.146N		
Fisher Exact Test		P=0.194N	P=0.194N
Hematopoietic System: All Leukemias			
Tumor Rates			
Overall *(a)*	10/50 (20%)	7/50 (14%)	5/50 (10%)
Adjusted *(b)*	22.6%	16.7%	20.4%
Terminal *(c)*	8/42 (19%)	3/36 (8%)	3/19 (16%)
Statistical Tests *(d)*			
Life Table	P=0.467N	P=0.408N	P=0.600N
Incidental Tumor Test	P=0.098N	P=0.219N	P=0.268N
Cochran-Armitage Trend Test	P=0.102N		
Fisher Exact Test		P=0.298N	P=0.131N
Hematopoietic System: All Lymphomas			
Tumor Rates			
Overall *(a)*	3/50 (6%)	0/50 (0%)	0/50 (0%)
Adjusted *(b)*	6.6%	0.0%	0.0%%
Terminal *(c)*	1/42 (2%)	0/36 (0%)	0/19 (0%)
Statistical Tests *(d)*			
Life Table	P=0.067N	P=0.142N	P=0.225N
Incidental Tumor Test	P=0.015N	P=0.144N	P=0.051N
Cochran-Armitage Trend Test	P=0.037N		
Fisher Exact Test		P=0.122N	P=0.122N
Pituitary: Adenoma			
Tumor Rates			
Overall *(a)*	14/49 (29%)	12/49 (24%)	11/49 (22%)
Adjusted *(b)*	31.7%	31.0%	46.9%
Terminal *(c)*	12/42 (29%)	9/35 (26%)	7/18 (39%)
Statistical Tests *(d)*			
Life Table	P=0.127	P=0.576	P=0.123
Incidental Tumor Test	P=0.542N	P=0.394N	P=0.543
Cochran-Armitage Trend Test	P=0.280N		
Fisher Exact Test		P=0.410N	P=0.322N

TABLE H1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	15/49 (31%)	12/49 (24%)	11/49 (22%)
Adjusted *(b)*	34.0%	31.0%	46.9%
Terminal *(c)*	13/42 (31%)	9/35 (26%)	7/18 (39%)
Statistical Tests *(d)*			
Life Table	P=0.171	P=0.519N	P=0.158
Incidental Tumor Test	P=0.465N	P=0.317N	P=0.605
Cochran-Armitage Trend Test	P=0.210N		
Fisher Exact Test		P=0.326N	P=0.246N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(a)*	9/50 (18%)	16/50 (32%)	6/49 (12%)
Adjusted *(b)*	20.9%	40.5%	21.7%
Terminal *(c)*	8/42 (19%)	13/36 (36%)	2/18 (11%)
Statistical Tests *(d)*			
Life Table	P=0.201	P=0.039	P=0.380
Incidental Tumor Test	P=0.499N	P=0.070	P=0.420N
Cochran-Armitage Trend Test	P=0.285N		
Fisher Exact Test		P=0.083	P=0.303N
Parathyroid: Adenoma			
Tumor Rates			
Overall *(a)*	1/42 (2%)	3/34 (9%)	1/38 (3%)
Adjusted *(b)*	2.9%	10.2%	6.7%
Terminal *(c)*	1/35 (3%)	2/24 (8%)	1/15 (7%)
Statistical Tests *(d)*			
Life Table	P=0.355	P=0.213	P=0.562
Incidental Tumor Test	P=0.425	P=0.321	P=0.562
Cochran-Armitage Trend Test	P=0.570		
Fisher Exact Test		P=0.232	P=0.728
Pancreatic Islets: Islet Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	0/50 (0%)	0/49 (0%)
Adjusted *(b)*	7.1%	0.0%	0.0%
Terminal *(c)*	3/42 (7%)	0/36 (0%)	0/19 (0%)
Statistical Tests *(d)*			
Life Table	P=0.084N	P=0.150N	P=0.291N
Incidental Tumor Test	P=0.084N	P=0.150N	P=0.291N
Cochran-Armitage Trend Test	P=0.038N		
Fisher Exact Test		P=0.121N	P=0.125N
Testis: Interstitial Cell Tumor *(e)*			
Tumor Rates			
Overall *(a)*	47/50 (94%)	49/50 (98%)	41/50 (82%)
Adjusted *(b)*	100.0%	100.0%	100.0%
Terminal *(c)*	42/42 (100%)	36/36 (100%)	19/19 (100%)
Statistical Tests *(d)*			
Life Table	P<0.001	P=0.036	P<0.001
Incidental Tumor Test	P=0.235	P=0.142	P=0.256
Cochran-Armitage Trend Test	P=0.025N		
Fisher Exact Test		P=0.309	P=0.061N

TABLE H1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Tunica Vaginalis: Mesothelioma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	3/50 (6%)	2/50 (4%)
Adjusted *(b)*	7.1%	8.3%	5.0%
Terminal *(c)*	3/42 (7%)	3/36 (8%)	0/19 (0%)
Statistical Tests *(d)*			
Life Table	P=0.492	P=0.590	P=0.627
Incidental Tumor Test	P=0.557N	P=0.590	P=0.526N
Cochran-Armitage Trend Test	P=0.412N		
Fisher Exact Test		P=0.661	P=0.500N
All Sites: Mesothelioma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	4/50 (8%)	2/50 (4%)
Adjusted *(b)*	7.1%	10.2%	5.0%
Terminal *(c)*	3/42 (7%)	3/36 (8%)	0/19 (0%)
Statistical Tests *(d)*			
Life Table	P=0.482	P=0.430	P=0.627
Incidental Tumor Test	P=0.495N	P=0.541	P=0.526N
Cochran-Armitage Trend Test	P=0.417N		
Fisher Exact Test		P=0.500	P=0.500N

(a) Number of tumor bearing animals/number of animals examined at the site.
(b) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(c) Observed tumor incidence at terminal kill.
(d) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in the dosed group is indicated by (N).
(e) Because this tumor is not generally regarded as life threatening, and significant differences in survival occurred among groups, the incidental tumor test is most appropriate for this particular lesion.

TABLE H2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	60 mg/kg	120 mg/kg
Subcutaneous Tissue: Sarcoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	0/50 (0%)	1/50 (2%)
Adjusted *(b)*	7.7%	0.0%	2.9%
Terminal *(c)*	1/31 (3%)	0/33 (0%)	0/32 (0%)
Statistical Tests *(d)*			
Life Table	P=0.191N	P=0.131N	P=0.327N
Incidental Tumor Test	P=0.287N	P=0.202N	P=0.452N
Cochran-Armitage Trend Test	P=0.176N		
Fisher Exact Test		P=0.121N	P=0.309N
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(a)*	12/50 (24%)	3/50 (6%)	12/50 (24%)
Adjusted *(b)*	28.5%	7.0%	32.9%
Terminal *(c)*	4/31 (13%)	0/33 (0%)	9/32 (28%)
Statistical Tests *(d)*			
Life Table	P=0.532	P=0.020N	P=0.570
Incidental Tumor Test	P=0.524	P=0.022N	P=0.567
Cochran-Armitage Trend Test	P=0.552		
Fisher Exact Test		P=0.011N	P=0.592
Hematopoietic System: All Leukemias			
Tumor Rates			
Overall *(a)*	13/50 (26%)	6/50 (12%)	12/50 (24%)
Adjusted *(b)*	31.2%	14.7%	32.9%
Terminal *(c)*	5/31 (16%)	2/33 (6%)	9/32 (28%)
Statistical Tests *(d)*			
Life Table	P=0.469N	P=0.083N	P=0.514N
Incidental Tumor Test	P=0.469N	P=0.104N	P=0.528N
Cochran-Armitage Trend Test	P=0.451N		
Fisher Exact Test		P=0.062N	P=0.500N
Liver: Neoplastic Nodule			
Tumor Rates			
Overall *(a)*	1/49 (2%)	1/49 (2%)	3/50 (6%)
Adjusted *(b)*	3.2%	3.0%	8.9%
Terminal *(c)*	1/31 (3%)	1/33 (3%)	2/32 (6%)
Statistical Tests *(d)*			
Life Table	P=0.202	P=0.748N	P=0.305
Incidental Tumor Test	P=0.179	P=0.748N	P=0.267
Cochran-Armitage Trend Test	P=0.207		
Fisher Exact Test		P=0.753N	P=0.316
Pituitary: Adenoma			
Tumor Rates			
Overall *(a)*	13/46 (28%)	16/45 (36%)	18/48 (38%)
Adjusted *(b)*	35.1%	46.5%	55.9%
Terminal *(c)*	7/29 (24%)	13/31 (42%)	16/30 (53%)
Statistical Tests *(d)*			
Life Table	P=0.176	P=0.384	P=0.204
Incidental Tumor Test	P=0.110	P=0.130	P=0.129
Cochran-Armitage Trend Test	P=0.202		
Fisher Exact Test		P=0.301	P=0.232

TABLE H2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Pituitary: Adenoma or Adenocarcinoma			
Tumor Rates			
Overall *(a)*	15/46 (33%)	17/45 (38%)	18/48 (38%)
Adjusted *(b)*	38.6%	49.4%	55.9%
Terminal *(c)*	7/29 (24%)	14/31 (45%)	16/30 (53%)
Statistical Tests *(d)*			
Life Table	P=0.312	P=0.471	P=0.345
Incidental Tumor Test	P=0.197	P=0.137	P=0.219
Cochran-Armitage Trend Test	P=0.351		
Fisher Exact Test		P=0.383	P=0.390
Adrenal: Cortical Adenoma			
Tumor Rates			
Overall *(a)*	3/49 (6%)	1/49 (2%)	0/50 (0%)
Adjusted *(b)*	9.0%	3.1%	0.0%
Terminal *(c)*	2/31 (6%)	1/32 (3%)	0/32 (0%)
Statistical Tests *(d)*			
Life Table	P=0.060N	P=0.298N	P=0.122N
Incidental Tumor Test	P=0.077N	P=0.357N	P=0.149N
Cochran-Armitage Trend Test	P=0.059N		
Fisher Exact Test		P=0.309N	P=0.117N
Adrenal: Cortical Adenoma or Adenocarcinoma			
Tumor Rates			
Overall *(a)*	3/49 (6%)	2/49 (4%)	0/50 (0%)
Adjusted *(b)*	9.0%	5.5%	0.0%
Terminal *(c)*	2/31 (6%)	1/32 (3%)	0/32 (0%)
Statistical Tests *(d)*			
Life Table	P=0.084N	P=0.498N	P=0.122N
Incidental Tumor Test	P=0.091N	P=0.552N	P=0.149N
Cochran-Armitage Trend Test	P=0.079N		
Fisher Exact Test		P=0.500N	P=0.117N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(a)*	5/49 (10%)	4/49 (8%)	3/50 (6%)
Adjusted *(b)*	16.1%	12.0%	9.4%
Terminal *(c)*	5/31 (16%)	3/32 (9%)	3/32 (9%)
Statistical Tests *(d)*			
Life Table	P=0.273N	P=0.476N	P=0.336N
Incidental Tumor Test	P=0.299N	P=0.529N	P=0.336N
Cochran-Armitage Trend Test	P=0.280N		
Fisher Exact Test		P=0.500N	P=0.346N
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant			
Tumor Rates			
Overall *(a)*	5/49 (10%)	5/49 (10%)	3/50 (6%)
Adjusted *(b)*	16.1%	14.4%	9.4%
Terminal *(c)*	5/31 (16%)	3/32 (9%)	3/32 (9%)
Statistical Tests *(d)*			
Life Table	P=0.283N	P=0.603N	P=0.336N
Incidental Tumor Test	P=0.333N	P=0.562	P=0.336N
Cochran-Armitage Trend Test	P=0.286N		
Fisher Exact Test		P=0.630	P=0.346N

TABLE H2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Thyroid: Adenoma *(e)*			
Tumor Rates			
Overall *(a)*	3/48 (6%)	2/50 (4%)	2/49 (4%)
Adjusted *(b)*	7.9%	5.6%	6.3%
Terminal *(c)*	1/31 (3%)	1/33 (3%)	2/32 (6%)
Statistical Tests *(d)*			
Life Table	P=0.419N	P=0.502N	P=0.510N
Incidental Tumor Test	P=0.539N	P=0.674N	P=0.614N
Cochran-Armitage Trend Test	P=0.397N		
Fisher Exact Test		P=0.480N	P=0.490N
Thyroid: C-Cell Carcinoma			
Tumor Rates			
Overall *(a)*	1/48 (2%)	3/50 (6%)	2/49 (4%)
Adjusted *(b)*	2.6%	8.7%	6.3%
Terminal *(c)*	0/31 (0%)	2/33 (6%)	2/32 (6%)
Statistical Tests *(d)*			
Life Table	P=0.401	P=0.325	P=0.495
Incidental Tumor Test	P=0.313	P=0.200	P=0.429
Cochran-Armitage Trend Test	P=0.407		
Fisher Exact Test		P=0.324	P=0.508
Thyroid: Adenoma or Adenocarcinoma *(e)*			
Tumor Rates			
Overall *(a)*	3/48 (6%)	3/50 (6%)	2/49 (4%)
Adjusted *(b)*	7.9%	8.2%	6.3%
Terminal *(c)*	1/31 (3%)	1/33 (3%)	2/32 (6%)
Statistical Tests *(d)*			
Life Table	P=0.425N	P=0.655N	P=0.510N
Incidental Tumor Test	P=0.582N	P=0.451	P=0.614N
Cochran-Armitage Trend Test	P=0.402N		
Fisher Exact Test		P=0.641N	P=0.490N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(a)*	6/50 (12%)	11/50 (22%)	7/50 (14%)
Adjusted *(b)*	17.4%	30.6%	21.1%
Terminal *(c)*	4/31 (13%)	9/33 (27%)	6/32 (19%)
Statistical Tests *(d)*			
Life Table	P=0.457	P=0.166	P=0.510
Incidental Tumor Test	P=0.423	P=0.156	P=0.425
Cochran-Armitage Trend Test	P=0.446		
Fisher Exact Test		P=0.143	P=0.500
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(a)*	6/48 (13%)	9/50 (18%)	7/50 (14%)
Adjusted *(b)*	18.1%	26.2%	21.9%
Terminal *(c)*	5/31 (16%)	8/33 (24%)	7/32 (22%)
Statistical Tests *(d)*			
Life Table	P=0.458	P=0.320	P=0.517
Incidental Tumor Test	P=0.420	P=0.259	P=0.491
Cochran-Armitage Trend Test	P=0.477		
Fisher Exact Test		P=0.318	P=0.532

TABLE H2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Uterus: Endometrial Stromal Polyp or Sarcoma			
Tumor Rates			
Overall *(a)*	6/48 (13%)	10/50 (20%)	7/50 (14%)
Adjusted *(b)*	18.1%	28.1%	21.9%
Terminal *(c)*	5/31 (16%)	8/33 (24%)	7/32 (22%)
Statistical Tests *(d)*			
Life Table	P=0.456	P=0.231	P=0.517
Incidental Tumor Test	P=0.400	P=0.158	P=0.491
Cochran-Armitage Trend Test	P=0.479		
Fisher Exact Test		P=0.233	P=0.532

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

TABLE H3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	60 mg/kg	120 mg/kg
Epithelium: Fibrosarcoma			
Tumor Rates			
Overall *(a)*	1/50 (2%)	3/50 (6%)	2/50 (4%)
Adjusted *(b)*	3.8%	8.5%	5.7%
Terminal *(c)*	1/26 (4%)	2/32 (6%)	2/35 (6%)
Statistical Tests *(d)*			
Life Table	P=0.513	P=0.386	P=0.604
Incidental Tumor Test	P=0.497	P=0.395	P=0.604
Cochran-Armitage Trend Test	P=0.399		
Fisher Exact Test		P=0.309	P=0.500
Epithelium: Neurofibrosarcoma			
Tumor Rates			
Overall *(a)*	2/50 (4%)	4/50 (8%)	0/50 (0%)
Adjusted *(b)*	6.9%	10.3%	0.0%
Terminal *(c)*	1/26 (4%)	1/32 (3%)	0/35 (0%)
Statistical Tests *(d)*			
Life Table	P=0.155N	P=0.442	P=0.184N
Incidental Tumor Test	P=0.158N	P=0.511	P=0.189N
Cochran-Armitage Trend Test	P=0.222N		
Fisher Exact Test		P=0.339	P=0.247N
Epithelium: All Sarcomas			
Tumor Rates			
Overall *(a)*	7/50 (14%)	9/50 (18%)	6/50 (12%)
Adjusted *(b)*	22.5%	21.5%	16.1%
Terminal *(c)*	4/26 (15%)	3/32 (9%)	5/35 (14%)
Statistical Tests *(d)*			
Life Table	P=0.269N	P=0.561	P=0.315N
Incidental Tumor Test	P=0.356N	P=0.448	P=0.327N
Cochran-Armitage Trend Test	P=0.444N		
Fisher Exact Test		P=0.393	P=0.500N
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(a)*	4/50 (8%)	6/50 (12%)	4/50 (8%)
Adjusted *(b)*	14.2%	18.8%	10.5%
Terminal *(c)*	3/26 (12%)	6/32 (19%)	3/35 (9%)
Statistical Tests *(d)*			
Life Table	P=0.397N	P=0.507	P=0.498N
Incidental Tumor Test	P=0.490N	P=0.513	P=0.624N
Cochran-Armitage Trend Test	P=0.568		
Fisher Exact Test		P=0.370	P=0.643
Lung: Alveolar/Bronchiolar Carcinoma			
Tumor Rates			
Overall *(a)*	4/50 (8%)	2/50 (4%)	10/50 (20%)
Adjusted *(b)*	14.1%	4.5%	26.6%
Terminal *(c)*	3/26 (12%)	0/32 (0%)	8/35 (23%)
Statistical Tests *(d)*			
Life Table	P=0.094	P=0.243N	P=0.191
Incidental Tumor Test	P=0.070	P=0.215N	P=0.169
Cochran-Armitage Trend Test	P=0.037		
Fisher Exact Test		P=0.339N	P=0.074

TABLE H3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	8/50 (16%)	8/50 (16%)	13/50 (26%)
Adjusted *(b)*	27.6%	22.4%	33.5%
Terminal *(c)*	6/26 (23%)	6/32 (19%)	10/35 (29%)
Statistical Tests *(d)*			
Life Table	P=0.313	P=0.421N	P=0.389
Incidental Tumor Test	P=0.221	P=0.398N	P=0.283
Cochran-Armitage Trend Test	P=0.127		
Fisher Exact Test		P=0.607	P=0.163
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Tumor Rates			
Overall *(a)*	7/50 (14%)	0/50 (0%)	0/50 (0%)
Adjusted *(b)*	22.6%	0.0%	0.0%
Terminal *(c)*	3/26 (12%)	0/32 (0%)	0/35 (0%)
Statistical Tests *(d)*			
Life Table	P<0.001N	P=0.005N	P=0.004N
Incidental Tumor Test	P<0.001N	P=0.002N	P=0.004N
Cochran-Armitage Trend Test	P=0.001N		
Fisher Exact Test		P=0.006N	P=0.006N
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Tumor Rates			
Overall *(a)*	0/50 (0%)	1/50 (2%)	4/50 (8%)
Adjusted *(b)*	0.0%	2.9%	10.1%
Terminal *(c)*	0/26 (0%)	0/32 (0%)	2/35 (6%)
Statistical Tests *(d)*			
Life Table	P=0.043	P=0.532	P=0.107
Incidental Tumor Test	P=0.031	P=0.594	P=0.093
Cochran-Armitage Trend Test	P=0.026		
Fisher Exact Test		P=0.500	P=0.059
Hematopoietic System: Lymphoma, All Malignant			
Tumor Rates			
Overall *(a)*	8/50 (16%)	2/50 (4%)	4/50 (8%)
Adjusted *(b)*	26.0%	5.4%	10.1%
Terminal *(c)*	4/26 (15%)	0/32 (0%)	2/35 (6%)
Statistical Tests *(d)*			
Life Table	P=0.057N	P=0.027N	P=0.086N
Incidental Tumor Test	P=0.056N	P=0.011N	P=0.095N
Cochran-Armitage Trend Test	P=0.114N		
Fisher Exact Test		P=0.046N	P=0.178N
Circulatory System: Hemangiosarcoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	4/50 (8%)	2/50 (4%)
Adjusted *(b)*	10.6%	10.3%	5.6%
Terminal *(c)*	2/26 (8%)	2/32 (6%)	1/35 (3%)
Statistical Tests *(d)*			
Life Table	P=0.306N	P=0.603	P=0.379N
Incidental Tumor Test	P=0.422N	P=0.524	P=0.404N
Cochran-Armitage Trend Test	P=0.417N		
Fisher Exact Test		P=0.500	P=0.500N

TABLE H3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Circulatory System: Hemangioma or Hemangiosarcoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	4/50 (8%)	3/50 (6%)
Adjusted *(b)*	10.6%	10.3%	8.3%
Terminal *(c)*	2/26 (8%)	2/32 (6%)	2/35 (6%)
Statistical Tests *(d)*			
Life Table	P=0.451N	P=0.603	P=0.530N
Incidental Tumor Test	P=0.575N	P=0.524	P=0.553N
Cochran-Armitage Trend Test	P=0.579		
Fisher Exact Test		P=0.500	P=0.661
Liver: Adenoma			
Tumor Rates			
Overall *(a)*	8/50 (16%)	5/49 (10%)	2/46 (4%)
Adjusted *(b)*	30.8%	13.4%	6.5%
Terminal *(c)*	8/26 (31%)	3/32 (9%)	2/31 (6%)
Statistical Tests *(d)*			
Life Table	P=0.014N	P=0.152N	P=0.021N
Incidental Tumor Test	P=0.015N	P=0.145N	P=0.021N
Cochran-Armitage Trend Test	P=0.044N		
Fisher Exact Test		P=0.290N	P=0.060N
Liver: Carcinoma			
Tumor Rates			
Overall *(a)*	14/50 (28%)	10/49 (20%)	9/46 (20%)
Adjusted *(b)*	39.5%	26.8%	24.9%
Terminal *(c)*	7/26 (27%)	6/32 (19%)	6/31 (19%)
Statistical Tests *(d)*			
Life Table	P=0.073N	P=0.123N	P=0.099N
Incidental Tumor Test	P=0.220N	P=0.225N	P=0.312N
Cochran-Armitage Trend Test	P=0.191N		
Fisher Exact Test		P=0.259N	P=0.234N
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	19/50 (38%)	14/49 (29%)	11/46 (24%)
Adjusted *(b)*	55.4%	35.5%	30.9%
Terminal *(c)*	12/26 (46%)	8/32 (25%)	8/31 (26%)
Statistical Tests *(d)*			
Life Table	P=0.019N	P=0.076N	P=0.025N
Incidental Tumor Test	P=0.066N	P=0.130N	P=0.099N
Cochran-Armitage Trend Test	P=0.081N		
Fisher Exact Test		P=0.217N	P=0.102N
Adrenal: Cortical Adenoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	3/47 (6%)	2/48 (4%)
Adjusted *(b)*	11.5%	8.2%	5.7%
Terminal *(c)*	3/26 (12%)	1/31 (3%)	2/35 (6%)
Statistical Tests *(d)*			
Life Table	P=0.291N	P=0.569N	P=0.365N
Incidental Tumor Test	P=0.327N	P=0.532N	P=0.365N
Cochran-Armitage Trend Test	P=0.432N		
Fisher Exact Test		P=0.631	P=0.520N

TABLE H3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(a)*	4/50 (8%)	6/47 (13%)	2/48 (4%)
Adjusted *(b)*	13.0%	18.2%	5.7%
Terminal *(c)*	2/26 (8%)	5/31 (16%)	2/35 (6%)
Statistical Tests *(d)*			
Life Table	P=0.172N	P=0.485	P=0.233N
Incidental Tumor Test	P=0.266N	P=0.413	P=0.369N
Cochran-Armitage Trend Test	P=0.312N		
Fisher Exact Test		P=0.331	P=0.359N

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

TABLE H4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE ADMINISTERED 1,2-DICHLOROBENZENE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	60 mg/kg	120 mg/kg
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(a)*	3/47 (6%)	4/48 (8%)	2/48 (4%)
Adjusted *(b)*	8.5%	10.0%	5.3%
Terminal *(c)*	2/33 (6%)	4/40 (10%)	2/38 (5%)
Statistical Tests *(d)*			
Life Table	P=0.356N	P=0.596	P=0.449N
Incidental Tumor Test	P=0.378N	P=0.575	P=0.485N
Cochran-Armitage Trend Test	P=0.406N		
Fisher Exact Test		P=0.512	P=0.490N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	3/47 (6%)	4/48 (8%)	3/48 (6%)
Adjusted *(b)*	8.5%	10.0%	7.9%
Terminal *(c)*	2/33 (6%)	4/40 (10%)	3/38 (8%)
Statistical Tests *(d)*			
Life Table	P=0.515N	P=0.596	P=0.607N
Incidental Tumor Test	P=0.537N	P=0.575	P=0.639N
Cochran-Armitage Trend Test	P=0.569		
Fisher Exact Test		P=0.512	P=0.651
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Tumor Rates			
Overall *(a)*	7/49 (14%)	11/50 (22%)	8/49 (16%)
Adjusted *(b)*	18.6%	26.6%	18.1%
Terminal *(c)*	4/33 (12%)	10/40 (25%)	3/38 (8%)
Statistical Tests *(d)*			
Life Table	P=0.542	P=0.358	P=0.572
Incidental Tumor Test	P=0.405	P=0.249	P=0.387
Cochran-Armitage Trend Test	P=0.447		
Fisher Exact Test		P=0.232	P=0.500
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Tumor Rates			
Overall *(a)*	0/49 (0%)	0/50 (0%)	3/49 (6%)
Adjusted *(b)*	0.0%	0.0%	7.9%
Terminal *(c)*	0/33 (0%)	0/40 (0%)	3/38 (8%)
Statistical Tests *(d)*			
Life Table	P=0.042	*(e)*	P=0.147
Incidental Tumor Test	P=0.042	*(e)*	P=0.147
Cochran-Armitage Trend Test	P=0.037		
Fisher Exact Test		*(e)*	P=0.121
Hematopoietic System: Malignant Lymphoma, Undifferentiated Type			
Tumor Rates			
Overall *(a)*	3/49 (6%)	0/50 (0%)	2/49 (4%)
Adjusted *(b)*	7.7%	0.0%	5.3%
Terminal *(c)*	1/33 (3%)	0/40 (0%)	2/38 (5%)
Statistical Tests *(d)*			
Life Table	P=0.356N	P=0.103N	P=0.456N
Incidental Tumor Test	P=0.443N	P=0.146N	P=0.564N
Cochran-Armitage Trend Test	P=0.390N		
Fisher Exact Test		P=0.117N	P=0.500N

TABLE H4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Hematopoietic System: Lymphoma, All Malignant			
Tumor Rates			
Overall *(a)*	11/49 (22%)	11/50 (22%)	13/49 (27%)
Adjusted *(b)*	27.2%	26.6%	29.8%
Terminal *(c)*	5/33 (15%)	10/40 (25%)	8/38 (21%)
Statistical Tests *(d)*			
Life Table	P=0.475	P=0.424N	P=0.515
Incidental Tumor Test	P=0.302	P=0.588N	P=0.283
Cochran-Armitage Trend Test	P=0.361		
Fisher Exact Test		P=0.574N	P=0.407
Circulatory System: Hemangiosarcoma			
Tumor Rates			
Overall *(a)*	3/49 (6%)	0/50 (0%)	3/49 (6%)
Adjusted *(b)*	7.1%	0.0%	7.9%
Terminal *(c)*	1/33 (3%)	0/40 (0%)	3/38 (8%)
Statistical Tests *(d)*			
Life Table	P=0.564N	P=0.107N	P=0.615N
Incidental Tumor Test	P=0.564N	P=0.219N	P=0.621N
Cochran-Armitage Trend Test	P=0.601		
Fisher Exact Test		P=0.117N	P=0.661
Circulatory System: Hemangioma or Hemangiosarcoma			
Tumor Rates			
Overall *(a)*	3/49 (6%)	2/50 (4%)	4/49 (8%)
Adjusted *(b)*	7.1%	4.8%	10.5%
Terminal *(c)*	1/33 (3%)	1/40 (3%)	4/38 (11%)
Statistical Tests *(d)*			
Life Table	P=0.464	P=0.448N	P=0.556
Incidental Tumor Test	P=0.436	P=0.684N	P=0.556
Cochran-Armitage Trend Test	P=0.416		
Fisher Exact Test		P=0.490N	P=0.500
Liver: Adenoma			
Tumor Rates			
Overall *(a)*	2/48 (4%)	4/47 (9%)	2/46 (4%)
Adjusted *(b)*	6.1%	10.3%	5.6%
Terminal *(c)*	2/33 (6%)	4/39 (10%)	2/36 (6%)
Statistical Tests *(d)*			
Life Table	P=0.551N	P=0.416	P=0.664N
Incidental Tumor Test	P=0.551N	P=0.416	P=0.664N
Cochran-Armitage Trend Test	P=0.568		
Fisher Exact Test		P=0.329	P=0.675
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	4/48 (8%)	5/47 (11%)	3/46 (7%)
Adjusted *(b)*	11.4%	12.8%	8.3%
Terminal *(c)*	3/33 (9%)	5/39 (13%)	3/36 (8%)
Statistical Tests *(d)*			
Life Table	P=0.380N	P=0.599	P=0.459N
Incidental Tumor Test	P=0.408N	P=0.570	P=0.502N
Cochran-Armitage Trend Test	P=0.451N		
Fisher Exact Test		P=0.486	P=0.524N

TABLE H4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE (Continued)

	Vehicle Control	60 mg/kg	120 mg/kg
Pituitary: Adenoma			
Tumor Rates			
Overall *(a)*	7/39 (18%)	4/39 (10%)	3/41 (7%)
Adjusted *(b)*	26.9%	10.9%	9.4%
Terminal *(c)*	7/26 (27%)	3/34 (9%)	3/32 (9%)
Statistical Tests *(d)*			
Life Table	P=0.059N	P=0.134N	P=0.081N
Incidental Tumor Test	P=0.071N	P=0.161N	P=0.081N
Cochran-Armitage Trend Test	P=0.097N		
Fisher Exact Test		P=0.259N	P=0.136N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	7/39 (18%)	4/39 (10%)	4/41 (10%)
Adjusted *(b)*	26.9%	10.9%	12.5%
Terminal *(c)*	7/26 (27%)	3/34 (9%)	4/32 (13%)
Statistical Tests *(d)*			
Life Table	P=0.116N	P=0.134N	P=0.147N
Incidental Tumor Test	P=0.135N	P=0.161N	P=0.147N
Cochran-Armitage Trend Test	P=0.177N		
Fisher Exact Test		P=0.259N	P=0.230N

(a) Number of tumor bearing animals/number of animals examined at the site.
(b) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(c) Observed tumor incidence at terminal kill.
(d) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in the dosed group is indicated by (N).
(e) No tumors observed in dosed or control groups.

APPENDIX I

MUTAGENESIS RESULTS FOR 1,2-DICHLOROBENZENE IN *SALMONELLA TYPHIMURIUM*

APPENDIX I

A. METHODS FOR SALMONELLA/MICROSOME MUTAGENICITY TEST SYSTEM *(a)*

1,2-Dichlorobenzene *(b)* was tested and evaluated in the blind in each of four tester strains of *Salmonella typhimurium,* using a preincubation modification (Yahagi et al., 1975) of the *Salmonella* assay (Ames et al., 1975). Strains of TA98 and TA1537 are more sensitive to chemicals that express frameshift mutagenic activity; strains TA100 and TA1535 are more sensitive to chemicals that cause base-pair substitutions.

1,2-Dichlorobenzene was dissolved in dimethyl sulfoxide (DMSO) and added to the suspension culture. This mixture was incubated with the tester strains in suspension culture (20 min at 37° C) prior to adding soft agar and plating for detection of induced mutants. Exogenous metabolic activation was provided by liver S-9 preparations from Aroclor-1254® induced rats and hamsters. Coded chemicals were tested at five doses (μg/plate) in triplicate (A, B, and C) in each strain and were retested two weeks later.

B. RESULTS

See Tables I1-I4.

(a) Conducted under NTP contract N0l-ES-92136 at Case Western University during 1979 (William Speck, Principal Investigator)

(b) Lot No Dll-H18 obtained from Matheson, Coleman, and Bell (Cincinnati, Ohio); stated to be 95% pure by the manufacturer.

TABLE I1. RESULTS OF MUTAGENICITY TESTS OF 1,2-DICHLOROBENZENE IN *SALMONELLA TYPHIMURIUM* TA98

Dose (μg/plate)	Number of Revertants per Plate *(a)* Initial Test A	B	C	Mean ± SE	Dose (μg/plate)	Retest *(b)* A	B	C	Mean ± SE
A. No Activation									
0.0 *(c)*	13	*(d)*	8	10 ± 2.5	0.0	8	11	15	11 ± 2.0
3.3	5	10	11	9 ± 1.9	1.0	9	10	8	9 ± 0.6
10.0	6	14	13	11 ± 2.5	3.3	9	6	12	9 ± 1.7
33.0	11	1	9	7 ± 3.1	10.0	11	6	13	10 ± 2.1
100.0	6 *(e)*	0	10	5 ± 5.0	33.0	7	2	14	8 ± 3.5
333.0	0	0	0	0 ± 0.0	100.0	5	13	0 *(e)*	9 ± 4.0
B. Preincubation with Arochlor-1254® Induced Sprague-Dawley Rat Liver S-9 Preparation									
0.0 *(c)*	23	13	15	17 ± 3.1	0.0	15	17	19	17 ± 1.2
3.3	11	15	17	14 ± 1.8	1.0	15	17	15	16 ± 0.7
10.0	22	15	23	20 ± 2.5	3.3	14	13	18	15 ± 1.5
33.0	11	11	15	12 ± 1.3	10.0	20	13	19	17 ± 2.2
100.0	11	12	14	12 ± 0.9	33.0	12	16	16	15 ± 1.3
333.0	0	0	0	0 ± 0.0	100.0	12	16	16	15 ± 1.3
C. Preincubation with Arochlor-1254® Induced Syrian Hamster Liver S-9 Preparation									
0.0 *(c)*	13	15	11	13 ± 1.2	0.0	13	19	21	18 ± 2.4
3.3	13	17	19	16 ± 1.8	1.0	17	21	32	23 ± 4.5
10.0	9	11	14	11 ± 1.5	3.3	18	24	26	23 ± 2.4
33.0	10	20	19	16 ± 3.2	10.0	12	15	19	15 ± 2.0
100.0	24	15	23	21 ± 2.8	33.0	14	28	26	23 ± 4.4
333.0	0	0	0	0 ± 0.0	100.0	33	21	32	29 ± 3.8

(a) Retest performed 2 weeks after initial test
(b) Measured in triplicate (A, B, C)
(c) DMSO used as solvent control
(d) Plate was contaminated
(e) Chemical was toxic

TABLE 12. RESULTS OF MUTAGENICITY TESTS OF 1,2-DICHLOROBENZENE IN *SALMONELLA TYPHIMURIUM* TA100

Dose (μg/plate)	Number of Revertants per Plate (a) Initial Test A	B	C	Mean ± SE	Dose (μg/plate)	First Retest (b) A	B	C	Mean ± SE	Dose (μg/plate)	Second Retest (b) A	B	C	Mean ± SE
A. No Activation														
0.0 (d)	187	125		156 ± 31.0	0.0 (d)	116	110	109	112 ± 2.2	0.0 (d)	112	109	146	112 ± 11.9
100.0	77	84		80 ± 3.5	3.3	106	102	115	108 ± 3.8	1.0	125	175	166	155 ± 15.4
1000.0	0	0		0 + 0.0	10.0	144	149	157	150 ± 3.8	3.3	118	111	115	115 ± 2.0
10000.0	0	0		0 ± 0.0	33.0	114	132	149	142 ± 5.0	10.0	163	157	162	161 + 1.9
13000.0	0	0		0 + 0.0	100.0	136	120	139	132 + 5.9	33.0	155	144	157	152 ± 4.0
					333.0	150	76	124	117 ± 21.7	100.0	144	131	148	141 ± 5.1
B. Preincubation with Arochlor-1254® Induced Sprague-Dawley Rat Liver S-9 Preparation														
0.0 (d)	155	157	168	160 ± 4.0	0.0 (d)	160	240	146	182 ± 29.3					
3.3	137	166	164	156 ± 9 4	1.0	197	221	218	212 ± 7.5					
10.0	173	164	181	173 ± 4.9	3.3	177	156	187	173 ± 9.1					
33.0	161	174	180	172 ± 5.6	10.0	197	187	197	194 ± 3.3					
100.0	150	129	152	144 ± 7.4	33.0	196	183	198	192 ± 4.7					
333.0	3T	0	0	0 ± 0.0	100.0	164	151	146	154 ± 5.4					
C. Preincubation with Arochlor-1254® Induced Syrian Hamster Liver S-9 Preparation														
0.0 (d)	176	181	192	183 ± 4.7	0.0 (d)	183	156	159	166 ± 8.5					
3.3	140	178	173	164 ± 11.9	1.0	159	147	150	152 ± 3.6					
10.0	172	143	171	162 ± 9.5	3.3	149	127	157	144 ± 9.0					
33.0	141	150	159	150 ± 5.2	10.0	147	130	155	144 ± 7.4					
100.0	166	140	167	158 ± 8.8	33.0	136	128	136	133 ± 2.7					
333.0	0	0	0	0 ± 0.0	100.0	143	137	127	136 ± 4.7					

(a) Measured in triplicate (A,B,C)
(b) Retest was done 7 weeks after initial test
(c) Retest was done 2 weeks after first retest
(d) DMSO used as solvent control

TABLE I3. RESULTS OF MUTAGENICITY TESTS OF 1,2-DICHLOROBENZENE IN *SALMONELLA TYPHIMURIUM* TA1535

Dose (μg/plate)	Number of Revertants per Plate *(a)* Initial Test A	B	C	Mean ± SE	Dose (μg/plate)	Retest *(b)* A	B	C	Mean ± SE
A. No Activation									
0.0 *(c)*	9	6	12	9 ± 1.7	0.0 *(c)*	9	9	12	10 ± 1.0
3.3	4	8	8	7 ± 1.3	1.0	10	12	7	10 ± 1.5
10.0	11	10	9	10 ± 0.6	3.3	10	9	9	9 ± 0.3
33.0	10	6	3	6 ± 2.0	10.0	11	10	11	11 + 0.3
100.0	10	4 *(d)*		0	33.0	7	3	7	6 ± 1.3
333.0	0	0	0	0 ± 0.0	100.0	11		0 *(d)*	11
B. Preincubation with Arochlor-1254® Induced Sprague-Dawley Rat Liver S-9 Preparation									
0.0 *(c)*	9	3	9	7 ± 2.0	0.0 *(c)*	7	13	10	10 ± 1.7
3.3	4	8	8	7 ±1.3	1.0	13	10	13	12 ± 1.0
10.0	2	9	7	6 ± 2.1	3.3	10	6	11	9 ± 1.5
33.0	2	9	9	7 ± 2.3	10.0	9	3	10	7 ± 2.2
100.0	4	17 *(d)*	20 *(d)*	4 ± 0.0	33.0	10	13	3	9 ± 3.0
333.0	1T	0	0	0 ± 0.0	100.0	20	13	6	13 ± 4.0
C. Preincubation with Arochlor-1254® Induced Syrian Hamster Liver S-9 Preparation									
0.0 *(c)*	10	8	12	10 ± 1.2	0.0 *(c)*	10	12	13	12 ± 0.9
3.3	4	5	6	5 ± 0.6	1.0	7	10	7	8 ± 1.0
10.0	4	9	8	7 ± 1.5	3.3	6	5	6	6 ± 0.3
33.0	6	1	3	3 ± 1.5	10.0	8	5	10	8 ± 1.5
100.0	2	2	3	2 ± 0.3	33.0	4	1	4	3 ± 1.0
333.0	0	0	0	0 ± 0.0	100.0	2	15	2	6 ± 4.3

(a) Measured in triplicate (A,B,C)
(b) Retest was done 7 weeks after initial test
(c) Retest was done 2 weeks after first retest
(d) DMSO used as solvent control

TABLE I4. RESULTS OF MUTAGENICITY TESTS OF 1,2-DICHLOROBENZENE IN *SALMONELLA TYPHIMURIUM* TA1537

Dose (μg/plate)	Number of Revertants per Plate *(a)* Initial Test A	B	C	Mean ± SE	Dose (μg/plate)	Retest *(b)* A	B	C	Mean ± SE
A. No Activation									
0.0 *(c)*	9	8	6	8 ± 0.9	0.0 *(c)*	8	6	7	7 ± 0.6
3.3	9	3	9	7 ± 2.0	1.0	6	5	4	5 ± 0.6
10.0	5	2	6	4 ± 1.2	3.0	6	4	11	7 ± 2.1
33.0	1	3	5	3 ± 1.2	10.0	4	4	9	6 ± 1.7
100.0	0 *(d)*	0	9	4 + 4.5	33.0	3	2	7	4 ± 1.5
333.0	0	0	0	0 ± 0.0	100.0	4	8	0 *(d)*	6 ± 2.0
B. Preincubation with Arochlor-1254® Induced Sprague-Dawley Rat Liver S-9 Preparation									
0.0 *(c)*	12	13	12	12 ± 0.3	0.0 *(c)*	12	12	9	11 ± 1.0
3.3	8	4	9	7 ± 1.5	1.0	8	7	8	8 ± 0.3
10.0	6	7	10	8 ± 1.2	3.3	6	7	15	9 ± 2.8
33.0	9	0 *(d)*	8	8 ± 0.5	10.0	7	8	10	8 ± 0.9
100.0	5	6	6	6 ± 0.3	33.0	8	6	10	8 ± 1.2
333.0	0	0	0	0 ± 0.0	100.0	6	0 *(d)*	9	8 ± 1.5
C. Preincubation with Arochlor-1254® Induced Sprague-Dawley Rat Liver S-9 Preparation									
0.0 *(c)*	6	12	19	12 ± 3.8	0.0 *(c)*	12	19	9	13 ± 3.0
3.3	11	11	14	12 ±	1.0	13	10	12	12 ± 0.9
10.0	7	5	9	7 ± 1.2	3.3	13	11	11	12 ± 0.7
33.0	11	8	13	11 ± 1.5	10.0	9	7	10	9 ± 0.9
100.0	5 *(d)*	3 *(d)*	10	10 ±	33.0	12	9	12	11 ± 1.0
333.0	0	0	0	0 ± 0.0	100.0	11	11	0 *(d)*	11 ± 0.0

(a) Measured in triplicate (A,B,C)
(b) Retest was 2 weeks after initial test
(c) DMSO solvent control
(d) Chemical was toxic

APPENDIX J

METHODS USED IN CLINICAL CHEMISTRY ANALYSES

APPENDIX J

Alkaline Phosphatase analysis was performed on a Gemsaec Centrifugal Analyzer using Spin Chem® reagents. Phosphatase activity at pH 10.2 is determined by kinetic measurement of the conversion of p-nitrophenyl phosphate to p-nitrophenol (Wilkinson et al., 1969).

Serum Glutamic Pyruvic Transaminase (SGPT) activity was determined on a Gemsaec Centrifugal Analyzer using Worthington Statzyme® reagents. The procedure is based on the method of Henry et al. (1960) in which SGPT catalyzes the conversion of L-alanine to pyruvate. Pyruvate is then converted to lactate by an excess of lactate dehydrogenase in the reagent. This latter reaction is accompanied by the conversion of NADH to NAD. The formation of NAD is proportional to SGPT activity and can be measured as a decreased absorption at 340 nm.

Gamma Glutamyl Transpeptidase (GGTP). Assays were performed on a Gemsaec Centrifugal Analyzer using Worthington Statzyme® reagents. The procedure is based on the method of Szasz (1969) in which GGTP catalyzes the conversion of gamma-glutamyl-p-nitroanilide to p-nitroanaline which absorbs at 405 nm. Enzyme activity is proportional to the rate of increased absorbance at this wavelength.

Bilirubin was determined on a Gemsaec Centrifugal Analyzer using a modification of the method of Malloy and Evelyn (1937). Bilirubin reacts with diazotized sulfanilic acid to form the chromagen azobilirubin which absorbs light at 560 nm.

Chloresterol analysis was performed by the method of Wybenga et al. (1970) using reagent commercially prepared by Dow Diagnostics (Diagnostest® Cholesterol Reagent). In this procedure, cholesterol reacts with the reagent composed of ethylacetate, sulfuric acid, and ferric perchlorate to form a purple chromophore which is measured spectrophotometrically at 595 nm.

Triglyceride was determined enzymatically on a Gemsaec Centrifugal analyzer using the method of Pinter et al. (1967) as modified by Bucolo and David (1973).

Urea Nitrogen (BUN) was determined using diacetylmonoxine thiosemicarbazide reagent (Wybenga et al., 1971). Color development, which is proportional to the amount of urea in the serum, was measured on a Coleman Jr.II spectrophotometer.

Glucose was determined by a hexokinase method (Barthelmai and Czok, 1962) on a Gemsaec Centrifugal Analyzer. Spin Chem® reagent (Smith Kline, Inc.) was used for the analyses.

Total Protein was determined by the biuret color reaction (Weichselbaum, 1946) on a Gemsaec Centrifugal Analyzer.

Globulin was determined by the glyoxylic acid reaction (Hopkins and Cole, 1901) as modified by Goldenberg and Drews (1971). Reagents were purchased from Dow Diagnostics. Color development was measured on a Coleman Jr.II spectrophotometer.

APPENDIX K

ANALYSIS OF 1,2-DICHLOROBENZENE

APPENDIX K

A. ELEMENTAL ANALYSIS

Element	C	H	Cl
Theory	49.02	2.74	48.24
Determined	49.30	2.57	48.26
	49.31	2.71	48.10

B. WATER ANALYSIS (Karl Fischer)

0.016 ± 0.001 (δ)%

C. ANALYSIS OF ACIDIC COMPONENTS

Titration with sodium hydroxide
10.8 ± 0.2(δ) ppm (assumed to be HCl)

D. BOILING POINT

Determined
178.5°C ± 0.3°C
at 729 mm Hg (visual,
microboiling point)

Literature Value
180.5 (Merck Index, 1976)

E. INDEX OF REFRACTION

Determined

n_D^{20} : 1.5496 ± 0.0001 (δ)

Literature Values

n_D^{20} : 1.5515;

n_D^{25} : 1.5491 (Merck Index, 1976)

F. DENSITY

Determined

d_{24}^{24} : 1.2994 ± 0.001(δ) g/ml

Literature Values

d_4^{20}: 1.3059;

d_4^{25}: 1.3003 (Merck Index, 1976)

G. GAS-LIQUID CHROMATOGRAPHY

(1) System 1

Instrument: Varian Aerograph 2440 Series
Detector: Flame ionization
Inlet temperature: 160°C
Detector temperature: 220°C
Carrier gas: Nitrogen
Carrier flow rate: 42 cc/min

Column: 3% SP 2250 on 80/100 Supelcoport, 1.8 m x 4 mm I.D. glass
Oven temperature program: 5 min at 50°C, then 50° to 250°C at 10°C/min
Sample injected: (7μl) neat liquid, and 1.0% and 0.5% in hexane to check for overloading and quantitate major peak
Results: Major peak and seven impurities. The total area of the seven impurities was less than 0.07% of the major peak area

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dichlorobenzene)	Area (Percent of 1,2-Dichlorobenzene)
1	1.4	0.10	0.0001
2	7.3	0.56	0.0002
3	9.6	0.74	0.0002
4	10.2	0.79	0.0003
5	11.9	0.92	0.06
6	12.9	1.00	100
7	14.2	1.10	0.002
8	15.1	1.17	0.0002

(2) System 2

Instrument: Varian Aerograph 2440
Detector: Flame ionization
Inlet temperature: 180°C
Detector temperature: 207°C
Carrier gas: Nitrogen
Carrier flow rate: 40 cc/min
Column: 3% OV 225 on 80/100 Supelcoport, 1.8 m x 4 mm I.D., glass
Oven temperature program: 5 min at 70°C, then 70° to 250°C at 10°C/min
Sample injected: (7 μl) 10.0% in petroleum ether, and 1.0% and 0.5% in petroleum ether to check for overloading and quantitate major peak.
Results: Major peak and one impurity

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dichlorobenzene)	Area (Percent of 1,2-Dichlorobenzene)
1	9.3	0.90	0.66
2	10.4	1.00	100

(3) System 3 (Quantitation of the amount of m-dichlorobenzene and p-dichlorobenzene in o-dichlorobenzene)

Instrument: Varian 2400
Column: 3% OV-225 on 80/100 Supelcoport, 1.8 m x 4 mm I.D., glass
Detector: Flame ionization
Carrier gas: Nitrogen
Carrier gas flow rate: 40 cc/min
Oven temperature program: 100°C isothermal
Inlet temperature: 180°C
Detector temperature: 210°C
Retention times: o-dichlorobenzene 5.7 min; p-dichlorobenzene 4.5 min; m-dichlorobenzene 4.1 min

When a solution of o-dichlorobenzene (1% v/v in petroleum ether) was injected on the system described above, one major peak and one impurity peak were seen.

Peak	Retention Time (min.)	Retention Time (Relative to Major Peak)
1	4.5	0.79
2	5.7	1.00

Enhancement and Quantitation Data

When a solution of o-dichlorobenzene in petroleum ether (1.0% v/v) was injected on the system given above, an impurity peak with a retention time of 4.5 min was seen. This peak was enhanced when a solution of o-dichlorobenzene spiked with authentic p-dichlorobenzene was injected. The amount of p-chlorobenzene present was quantitated by comparing the peak area provided by a standard solution of p-dichlorobenzene (0.01% v/v in petroleum ether) with the peak area of the p-dichlorobenzene in a solution of the sample (1.0% v/v in petroleum ether). p-Dichlorobenzene was found to be present in the sample at a level of 0.84 ± 0.05 (δ)% v/v. When the enhancement data from spikes were used, m-dichlorobenzene was not found to be present in the sample at a level 0.1% v/v.

APPENDIX K

H. CONFIRMATION OF THE IDENTITY OF p-DICHLOROBENZENE BY GAS CHROMATOGRAPHY/MASS SPECTROMETRY

1. System

Instrument: Varian MAT CH4-B mass spectrometer interfaced via a Watson-Biemann helium separator to a Tracor MT-2000R gas chromatograph. Data handled by a Varian 620/i data system.
Column: 3% OV-225 on 100/120 Supelcoport; 1.8 m x 2 mm I.D.; glass
Oven temperature program: 75°C, isothermal
Carrier gas: Helium
Carrier gas flow rate: 30 cc/min
Inlet temperature: 170°C
Transfer temperature: 210°C
Electron energy: 70 eV
Sample injected: 0.5 μl of a 10% v/v solution of 1,2-dichlorobenzene in hexane

2. Results

a. Reconstructed Ion Chromatogram

The reconstructed ion chromatogram indicated the presence of one major peak and one impurity peak.

Peak	Retention Time (min.)	Retention Time (Relative to Major Peak)
1	3.1	0.78
2	4.0	1.0

b. Spectra Obtained

(1) Peak 1

Spectrum Obtained From Peak 1		Literature Spectrum of p-Dichlorobenzene (Eight Peak Index, 1970)	
m/e	Relative Abundance (Percent of m/e 146)	m/e	Relative Abundance (Percent of m/e 146)
146	100	146	100
148	64	148	65
111	35	111	32
75	23	75	19
50	16	74	12
74	12	150	11
150	11	113	10
113	9	73	8
73	9		

APPENDIX K

This spectrum is consistent with the expected fragmentation and with a literature spectrum of p-dichlorobenzene. Although the isomers of dichlorobenzene produce mass spectra which are indistinguishable, peak 1 has been shown to be the p-isomer from retention and enhancement data (see system 4, enhancement and quantitation data).

(2) Peak 2 (Major Component)

Although spectra obtained from the major component are saturated, the ions produced confirm the identity of this peak as 1,2-dichlorobenzene.

3. Conclusions

m-Dichlorobenzene was not found to be present in 1,2-dichlorobenzene at a level greater than or equal to 0.1% v/v. p-Dichlorobenzene was found to be present by mass spectrometry and GC peak enhancement data; and was quantitated against standards as being present at a level of $0.84 \pm 0.05(\delta)\%$ v/v in the 1,2-dichlorobenzene.

I. SPECTRAL DATA

1. Infrared

Instrument: Beckman IR-12
Cell: Liquid Cell NaCl plates, 25 μ path
Results: See Figure 5

Sample peaks at 1083 cm^{-1} and 1015 cm^{-1} smaller than corresponding peaks in the literature spectrum (Sadtler Standard Spectra. Otherwise, sample spectrum consistent with literature.

2. Ultraviolet/Visible

Instrument: Cary 118

Determined		Literature Values (Sadtler Standard Spectra)	
λ max (nm)	ε	λ max (nm)	ε
277.5	337.7 ± 3.4	276	305
270.2	357.1 ± 1.6	269	331
267.7 (shoulder)	209.2 ± 1.3	262	245
262.0	231.9 ± 2.3	255	155
260.0 (shoulder)	151.8 ± 1.8	248 (shoulder)	97
256.2	134.7 ± 0.8		
249.6	73.9 ± 0.4		
242.9	47.4 ± 0.4		

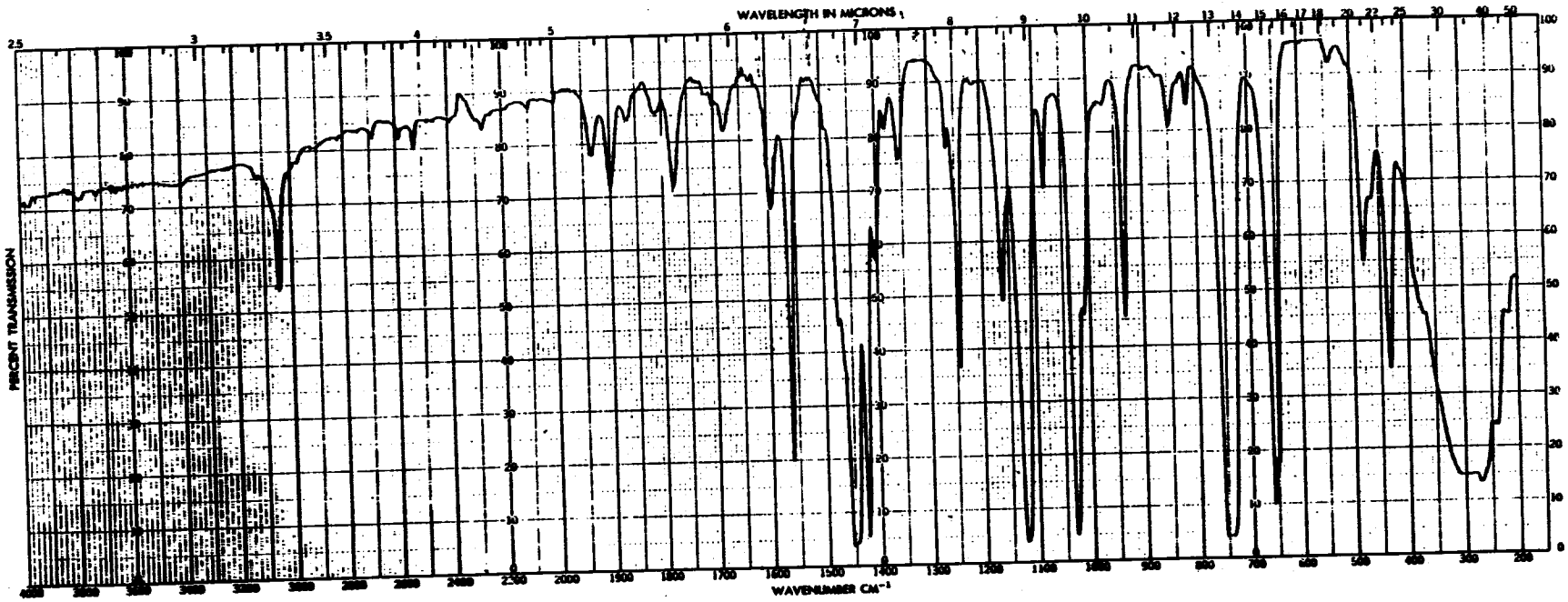


Figure 5. Infrared Absorption Spectrum of 1,2-Dichlorobenzene (Lot No. SC81377)

APPENDIX K

No absorbance between 350 and 800 nm (visible range) at a concentration of 0.03% (w/v)

Solvent: Petroleum ether	Solvent: Isooctane

3. Nuclear Magnetic Resonance

Instrument: Varian HA-100 Solvent: Neat, tetramethylsilane added Assignments: See Figure 6 (a) m, δ, 6.76-7.24 ppm Characteristic symmetrical ABCD splitting pattern for ortho disubstituted benzene Integration ratios: (a) 4.00	Consistent with literature spectrum (Sadtler Standard Spectra)

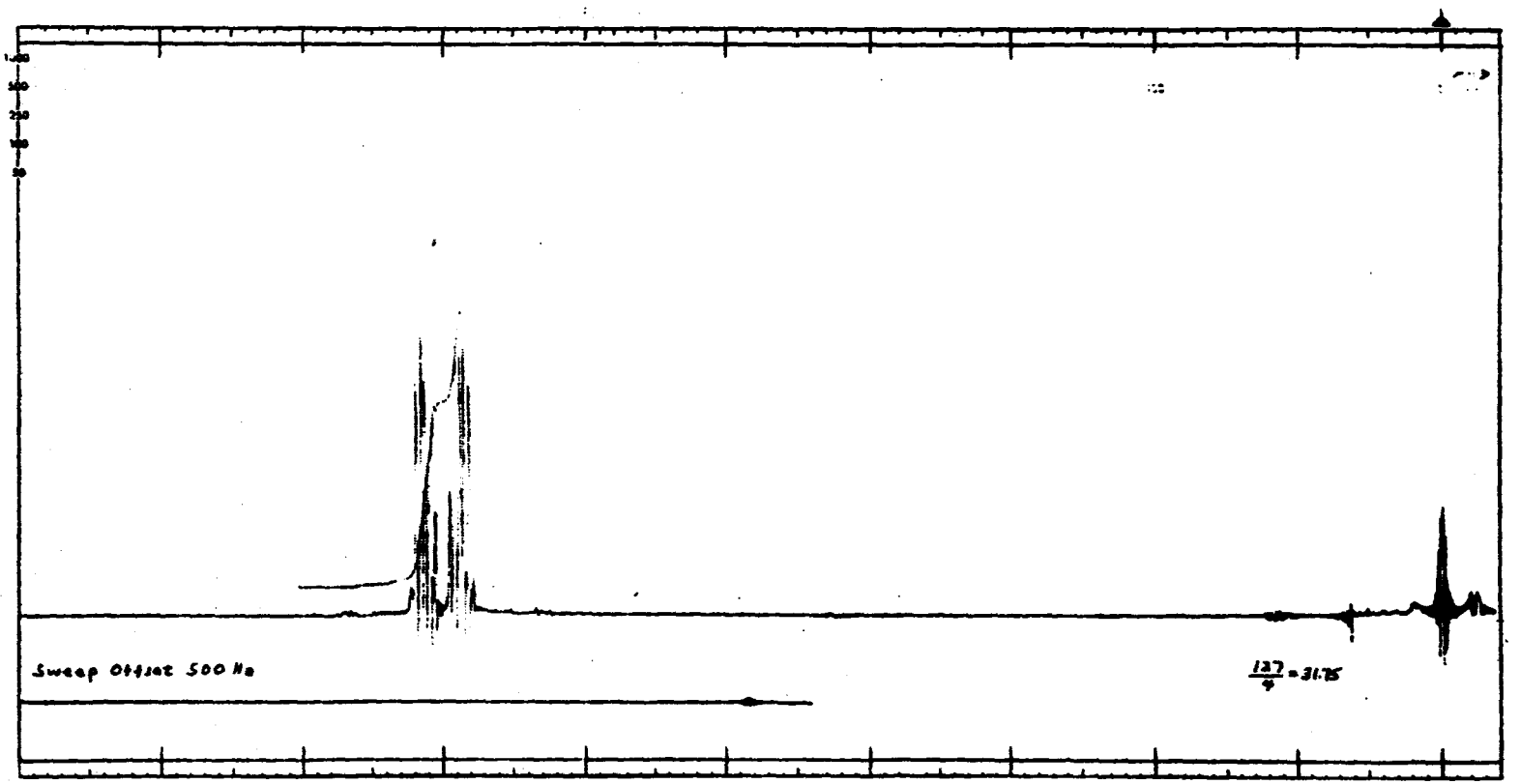


Figure 6. Nuclear Magnetic Resonance Spectrum of 1,2-Dichlorobenzene (Lot No. SC61377)

APPENDIX L

ANALYSIS OF 1,2-DICHLOROBENZENE IN CORN OIL FOR STABILITY OF 1,2-DICHLOROBENZENE

APPENDIX L

A. PREPARATION OF SAMPLE AND STORAGE

A 4% (w/v) (3% v/v) solution of 1,2-dichlorobenzene was prepared by pipetting a 3-ml aliquot of 1,2-dichlorobenzene into a 100-ml volumetric flask and diluting to 100 ml with corn oil, with occasional swirling of the flask. The contents were then agitated manually for 30 seconds. A 1.84-ml aliquot of this solution was pipetted into each of eight small septum vials and the vials quickly sealed. These vials were stored at room temperature for the appropriate time period. No attempt was made to protect the samples from light.

B. EXTRACTION AND ANALYSIS

1. Procedure

The 1.84-ml aliquot of the above stock solution (3% v/v, 1,2-dichlorobenzene in corn oil) was extracted with 2 ml methanol which was injected into the septum vial with a 2-ml syringe. The solution was agitated on a vortex mixer for 1 minute and placed in an ultrasonic vibrator bath for 2 minutes. Aliquots for analysis were removed directly from the methanol (top) layer of each sample with a microliter syringe and analyzed by vapor-phase chromatography.

2. Instrumental Parameters

Instrument: Varian 2400 with Heath chart/recorder
Detector: Flame ionization
Column: 3% OV-255 on 80/100 mesh Supelcoport, 1.8 m x 2 mm I.D. glass
Oven temperature: 75°C, isothermal
Inlet temperature: 160°C
Detector temperature: 210°C
Carrier gas: Nitrogen
Carrier flow rate: 50 cc/min
Sample injected: 5 μ l

C. QUALITY ASSURANCE PROCEDURES

Each analysis was performed in duplicate. Recovery of 1,2-dichlorobenzene from corn oil was determined twice during the 7-day study, in duplicate at a 3% (v/v) 1,2-dichlorobenzene in corn oil concentration level. Linearity studies were done at three concentration levels: 0.4%, 0.8%, and 1.2%, v/v.

D. RESULTS

Day	Theoretical Percent (v/v) Chemical/Vehicle	Determined Percent (v/v) Chemical/Vehicle	Corrected *(a)* Percent (v/v) Chemical/Vehicle
0	3.00	1.16 ± 0.02	3.2 ± 0.2
2	3.00	1.16 ± 0.02	3.2 ± 0.2
4	3.00	1.15 ± 0.02	3.2 ± 0.2
7	3.00	1.17 ± 0.02	3.2 ± 0.2

(a) Corrected for recovery of 36.3% ± 3.5%

Retention time of 1,2-dichlorobenzene: 2.2 min
Recovery: 36.3% ± 3.5%
Linearity: 0.999 correlation coefficient

E. CONCLUSION

1,2-Dichlorobenzene in corn oil is stable during storage at room temperature for a 7-day period.

APPENDIX M

ANALYSIS OF 1,2-DICHLOROBENZENE IN CORN OIL FOR CONCENTRATION OF 1,2-DICHLOROBENZENE

APPENDIX M

Standards were prepared by weighing out appropriate amounts at 480.0 mg, 360.0 mg, 240.0 mg, 120.0 mg, and 60.0 mg in 10 ml corn oil. Mixtures were shaken until a clear solution was observed. Standards and test samples were then treated in the same manner. One-milliliter aliquots of standards and test samples were extracted with 9.0 ml methanol, vortexed, and then centrifuged. An aliquot of the clear methanol layer was analyzed by gas chromatography. Analyses were done in duplicate and concentrations determined by linear regression analysis of the data.

Instrument: Varian Aerograph 2100 -Gas Chromatograph with CDS lllL
Data System
Column: Three percent OV-1
Temperatures: Detector, 230°C; injector, 170°C
Temperature program: 75°C
Sample injected: 2 microliters
Chart speed: 6 min/inch
Flow rate: 30 ml/min
Carrier gas: Nitrogen
Flow rate: 30 ml/min

TABLE M1. ANALYSES OF CORN OIL MIXTURES

Date Mixed *(a)*	Date Used	Concentration *(a)* of 1,2-Dichlorobenzene in Corn Oil for Target Concentration	
		12 mg/ml	24 mg/ml
07/27/79	07/31/79		24.9
08/24/79	08/28/79	11.4	24.1
10/17/79	10/24/79	12.2	23.1
			(24.5) *(b)*
12/13/79	12/17/79	11.4	22.7
02/21/80	02/25/80	11.9	23.1
04/ 3/80	04/ 7/80	12.1	23.4
		(11.7) *(b)*	
06/ 6/80	06/10/80	12.5	22.1
08/14/80	08/18/80	12.9	24.7
09/18/80	09/19/80	11.7	24.7
			(23.9) *(b)*
11/13/80	11/17/80	11.5	23.3
01/14/81	01/17/81	11.1	24.9
Mean (mg/ml)		11.9	23.7
Standard deviation		0.5	1.0
oefficient of variation (%)		4.2	4.2
Range (mg/ml)		11.1-12.9	22.1-24.9
Number of samples		10	11

(a) The data presented are the average of the results of duplicate analyses. Values were corrected for recovery.
(b) Results of referee analyses at Midwest Research Institute.

APPENDIX N

SEPARATION AND QUANTITATION OF COPROPORPHYRIN AND UROPORPHYRIN IN URINE

APPENDIX N

A. APPARATUS

Glass Column: 1 cm I.D. and 30 cm long
Spectrophotometer: Aminco-Bowman Spectrophotofluorometer (American Instrument Company, Silver Spring, MD)
Disposable Micropipets: Used to measure the standard porphyrin solution.

B. REAGENTS

Anion-Exchanged resin chloride form (Bio-Rad 1x2 200-400 mesh, Bio-Rad Labs., Richmond, CA)

This resin was used as received without further treatment. The resin was allowed to swell in distilled water and was then transferred to columns (containing a small glass-wool plug at the bottom) as a measured volume of slurry, in amount sufficient to give a resin bed that is 10 cm high.

Wash Solvent. This solution contained ethanol:water (15:85 by volume) and 1.0 mol of acetic acid per liter. About 500 ml distilled water, 150 ml of absolute ethanol, and 57 ml of glacial acetic acid, were added to a one-liter volumetric flask and mixed. The mixture was diluted to 1.0 liter with distilled water and stirred.

Coproporphyrin Elution Solvent. To a one-liter volumetric flask were added about 500 ml of distilled water and 8.3 ml (0.1 mol) of concentrated hydrochloric acid. After mixing, 250 ml isopropanol (analytical grade) and 100 ml of absolute ethanol were added and mixed. After being diluted to the mark with distilled water, the solution was mixed.

Uroporphyrin Elution Solvent. To a one-liter volumetric flask, about 500 ml of distilled 83 ml (10 mol) concentrated hydrochloric acid was added, and the solution was mixed. Two hundred and fifty milliliters of n-propanol (spectro-quality) was added. After mixing, the solution was diluted to the mark with distilled water and mixed.

Standard Porphyrins. The following prophyrins were used: coproporphyrin-I and uroporphyrin-I (Sigma Chemical Company, St. Louis, MO).

C. PROCEDURE (Sobel et al., 1974; Lavallee and Novellus, 1977)

Before analysis, the column was washed with 20 ml wash solvent and 20 ml distilled water. Three milliliters of urine (taken from 24-hour collection) were added to a column anion-exchange resin (15 ml slurry volume 10 cm high). The fluid was eluted slowly from the column until the urine level receded to the resin surface. Twenty milliliters distilled water was added and allowed to drain. Ten milliliters of coproporphyrin eluent was added. The coproporphyrin fraction was collected. When the eluent reached the resin surface, 5 ml of water was added and collection was stopped. Then, the column was rinsed with 20 ml of distilled water and the same procedure was repeated using uroporphyrin eluent.

Aliquots (5 ml) of each fraction were pipetted into a test tube. The solution was diluted to 10 ml with respective eluent and the fluorescence of the porphyrin was recorded. The excitation wavelengths were 404 nm for the coproporphyrin and 410 nm for the uroporphyrin. The fluorescence emission for both porphyrins used was 650 nm.

APPENDIX O

DATA AUDIT SUMMARY

DATA AUDIT SUMMARY

An audit was conducted on the archival data and pathology materials for the two-year toxicology and carcinogenesis studies of 1,2-dichlorobenzene in rats and mice. The studies were performed at Battelle Columbus Laboratory, Columbus, OH, under a subcontract with Tracor Jitco for the National Toxicology Program, from February 1979 to March 1981 and were initiated prior to the requirement of compliance to Good Laboratory Practice standards by NTP in October 1981. The audit was conducted at the NTP Archives in Rockville, MD by the following Dynamac Corporation personnel: Henry Appleton, Ph.D., Chris Dippel, M.S., Curt Lunchick, M.S., James Plautz, M.S., Floris Garner, D.V.M., and Cynthia Sunier. NTP participants were Amelia Grant, Gloria Heuckeroth, Carolyn Lingeman, M.D., Mark Pielmeier, and Joyce Goldstein, Ph.D. The audit report has been reviewed and approved by NTP personnel and is on file at the NTP, Research Triangle Park, NC.

The audit consisted of a review of the data and pathology materials collected during the conduct of the study as well as review of the correspondence and the Technical Report. For the inlife toxicology data, this review involved examination of 100% of the records on animal receipt and husbandry, mortality, and examination of body weight and clinical observation data for selected animals. In the review of the chemistry data associated with the study, all of the records were examined pertaining to receipt and use of the test chemical, analysis of the bulk chemical and dosed diets by the contract laboratory, and characterization of the bulk chemical and analysis of the dosed diets by the reference laboratory. The audit of the pathology materials included review of 100% of the Individual Animal Data Records (IADRs) for correlation between gross and microscopic diagnoses, clerical errors, examination of the wet tissues of 51 animals for unidentified lesions and correct identification, correlation of slides and tissue blocks for all control and high dose groups, and verification of the reported pathology on a 10% sample of the animals.

Review of the toxicology data found that records of the quarantine of animals were not available for review and clinical observation data were limited by infrequent and nondetailed entries. Comparison of the available inlife mortality records with the IADRs found several discrepancies in dates and modes of death. Instances of a watering system problem were reported which resulted in animal dehydration and cage flooding; 3 high dose male rats were drowned. Clinical observation discrepancies included the location of masses and the failure to report masses inlife that were seen at necropsy.

A review of the available chemistry data showed that all of the required information was present. Records indicated the test material was received, dosing solution concentrations were properly prepared, and chemical analyses on the bulk chemical and chemical/vehicle mixtures were performed as required. Data were not present for corn oil analysis from 2/79 to 8/79.

Discrepancies noted during the audit of the pathology materials included some discrepancies between gross and microscopic diagnoses in both the rats and mice, and several possible disposition code discrepancies. Several rats were believed to have died as a result of gavage error: 1 vehicle control male, 1 low dose male, 5 high dose males, and 1 high dose female. In addition, possible gavage-related deaths were suggested for 3 vehicle control males, 4 low dose males, 12 high dose males, 2 low dose females, and 5 high dose females. None of the wet tissues were positively identifiable because neither feet nor ears were retained. These were not required to be saved under the protocol used at the time.

Overall, although some problems and discrepancies were identified, these were adequately resolved or were determined not to affect the outcome of the studies. In conclusion, the data examined in this audit are considered adequate to meet the objectives of the study.

U.S. GOVERNMENT PRINTING OFFICE: 1985 491 292 21273