NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 237

CARCINOGENESIS STUDIES OF 1,1,1,2-TETRACHLOROETHANE

(CAS NO. 630-20-6)

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

CARCINOGENESIS STUDIES OF 1,1,1,2-TETRACHLOROETHANE

(CAS NO. 630-20-6)

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

NATIONAL TOXICOLOGY PROGRAM
Box 12233
Research Triangle Park
North Carolina 27709

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

NOTE TO THE READER

This is one in a series of experiments designed to determine whether selected chemicals produce cancer in animals. Chemicals selected for testing in the NTP carcinogenesis bioassay program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical has the potential for hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

This study was initiated by the National Cancer Institute's Carcinogenesis Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program.

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room 835B, Westwood Towers, 5401 Westbard Ave., Bethesda, MD 20205 (301-496-1152) or at Research Triangle Park, NC 27709 (919-541-3991).

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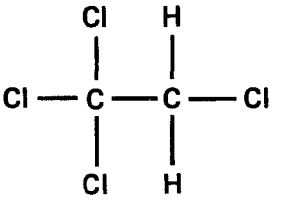
CARCINOGENESIS
STUDIES OF 1,1,1,2-TETRACHOLOROETHANE



1,1,1,2–TETRACHLOROETHANE

CAS NO. 630-20-6
$C_2H_2Cl_4$ Mol. Wt. 167.83

ABSTRACT

Carcinogenesis studies of technical grade 1,1,1,2-tetrachloroethane (>99% pure) were conducted by administering the test chemical in corn oil by gavage to groups of 50 male and 50 female F344/N rats at doses of 125 or 250 mg/kg body weight and to groups of 50 male and 50 female $B6C3F_1$ mice at doses of 250 or 500 mg/kg. Doses were administered five times per week for 103 weeks. Due to chemically-induced toxicity, high-dose mice received the chemical for only 65 weeks. Groups of 50 rats and 50 mice of each sex received corn oil by gavage on the same dosing schedule and served as vehicle controls.

The chemical produced cumulative toxic effects with signs of central nervous system involvement from week 44 forward in the chronic study, resulting in significantly lower survival of high-dose male rats (P=0.001), and possibly decreasing the incidence of late-developing tumors in this group. Mean body weights of dosed and control rats of each sex were similar. Fourteen control, 10 low-dose, and 3 high-dose male rats and 2 control, 5 low-dose, and 8 high-dose female rats were killed accidentally during the study; of these, 11 control and 7 low-dose males died apparently from heat stress during week 62 as a result of a 6-hour elevated temperature (>34°C) in the animal room.

Neither hepatocellular neoplastic nodules alone nor hepatocellular carcinomas alone occurred in statistically significant incidences in male rats, but the combined incidence of male rats with either hepatocellular neoplastic nodules or carcinomas occurred with a statistically significant positive trend ($P<0.05$) in the life table test (controls, 0/49, 0%; low-dose, 1/49, 2%; high-dose, 3/48, 6%). A single hepatocellular carcinoma occurred in the high-dose group. The combined incidence of liver tumors in the high-dose males (3/48, 6%) did not greatly exceed the historical incidences of liver tumors in groups of vehicle controls in other studies at this laboratory (5/243, 2.1%; range 0%-4%). However, reduced survival of the high-dose group in the present study may have reduced the sensitivity of this bioassay for detecting liver tumors. Mineralization of the kidney increased in a dose-related fashion in the male rats (12/48, 19/50, 26/48).

Fibroadenomas in the mammary gland of female rats occurred with a statistically significant ($P<0.05$) increased incidence in the low-dose group as compared with the controls (6/49, 15/49, 7/46). The incidence in the high-dose group was not different than that in the controls.

The combined incidence of adenomas, adenocarcinomas, and carcinomas in the pituitary gland of female rats showed a statistically significant ($P<0.05$) negative trend and the incidence in the high-dose group was significantly ($P<0.05$) less than that in the controls (18/39, 16/45, 7/42).

Mean body weight of high-dose mice was less than that of controls after week 20 in males and after week 40 in females. Clinical signs of central nervous system toxicity occurred at week 51 in both sexes of high-dose mice and by week 66 they were dead or moribund and were killed. Survival of low-dose females was also significantly ($P<0.05$) less than that of controls.

The maximum tolerated dose was exceeded in high-dose mice. Inflammation, necrosis, fatty metamorphosis, and hepatocytomegaly were observed in increased incidences in the livers of high-dose male and female mice. The major neoplastic histopathological effects occurred in the liver, where dose-related statistically significant ($P<0.05$) increases in the incidence of hepatocellular adenomas occurred in both male and female mice: vehicle controls, low-, and high-dose male mice had rates of 13% (6/48), 30% (14/46), and 42% (21/50); corresponding percentages in female mice were 8% (4/49), 17% (8/46), and 50% (24/48). Evidence for the association between 1,1,1,2-tetrachloroethane and development of hepatocellular carcinomas in mice was limited because of poor survival in the high-dose groups. Nevertheless, there was an increased incidence of hepatocellular carcinomas in female mice despite the reduced survival in the dosed groups (controls, 1/49, 2%; low-dose, 5/46, 11%; high-dose, 6/48, 13%). There was no clear effect in male mice.

Under the conditions of these studies, 1,1,1,2-tetracholoroethane was not demonstrated to be carcinogenic in F344/N rats, although the observed increase in the proportion of male rats with liver tumors may have been associated with the administration of 1,1,1,2-tetrachloroethane; accidental killing of 27 male and 15 female rats reduced the sensitivity of this bioassay for detecting a carcinogenic response. 1,1,1,2-Tetrachloroethane was carcinogenic for $B6C3F_1$ mice, causing an increased proportion of female mice with hepatocellular carcinomas and an increased proportion of male and female mice with hepatocellular adenomas; the decreased survival in high-dose male and female mice compromised the ability of this bioassay to further determine the presence or absence of a carcinogenic effect and gave clear evidence that these doses were toxic.

CONTRIBUTORS

The carcinogenesis studies of 1,1,1,2-tetrachloroethane were conducted at Gulf South Research Institute under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The chronic study was begun in November 1977 and completed in December 1979.

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SUMMARY OF PEER REVIEW COMMENTS ON THE CARCINOGENESIS STUDIES OF 1,1,1,2-TETRACHLOROETHANE

On 16 December 1981 this report underwent peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9:00 a.m. in Conference Room A, Landow Building, 7910 Woodmont Avenue, Bethesda, Maryland.

Dr. Harper, a principal reviewer for the technical report on 1,1,1,2-tetrachloroethane, stated that the conduct of the studies in rats was less than adequate due to the deaths of 42 rats either from elevated room temperature or by gavage error. However, considering the positive trend for the combined incidences of hepatocellular nodules and carcinomas in male rats, he thought the evidence did not support the conclusion that 1,1,1,2-tetrachloroethane was not carcinogenic. The experimental design in mice was considered questionable because the maximum tolerated dose (MTD) was exceeded and none of the high-dose mice survived beyond 65 weeks. Nonetheless, he agreed with the report conclusion that 1,1,1,2-tetrachloroethane was carcinogenic for mice. Dr. Harper also noted an increased incidence of mineralization of the kidney in rats which should be highlighted.

As a second principal reviewer, Dr. Vesselinovitch commented on the high dose levels being in excess of the MTD as evidenced by reduction of survival in male rats and in mice of both sexes; a situation he felt might preclude the use of high-dose endpoints in assessing potential carcinogenicity. Because of possible 'metabolic overload,' it was difficult to say whether or not observed tumor responses were factual or spurious. However, he generally agreed that there was an apparent enhancing effect of the chemical upon development of neoplastic nodules of the liver in male rats and fibroadenomas of the mammary gland in female rats, an effect he described as being "tumorigenic," i.e., indirect evidence of carcinogenicity. He concluded that 1,1,1,2-tetrachloroethane was causally associated with development of hepatocellular carcinomas in female mice and of hepatocellular adenomas in male and female mice.

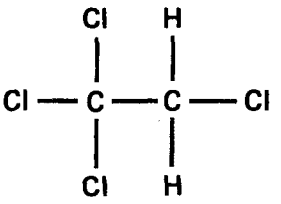
Dr. Swenberg stated that in a study in which the high dose clearly exceeds the MTD, the low dose becomes essentially an MTD, and a negative result for this one dose should mean a negative study since extrapolations above this dose are inappropriate. Because central nervous system toxicity was an apparent major cause of death in both species, more discussion of this toxicity should be considered, especially in the pathology section. There was discussion about the appropriateness of life table analysis for assessing significance of liver tumors in mice since the tumors apparently are not the cause of death.

As a third principal reviewer, Dr. Breslow voiced two major criticisms: the statistical power of the bioassay in rats was reduced to an unspecified degree by the high rates of accidental and toxic deaths to the extent that fewer than 60 percent of the animals in any dose group were available for terminal sacrifice. This renders the possibility that the assay in rats may have been inadequate to determine the presence or absence of a carcinogenic response. Secondly, there was nonuniform distribution among rat groups of deaths from "heat stress," which seemed to relate to cage position in the animal room. This raises a general question of how to measure and adequately account for cage and position effects in NTP carcinogenesis studies. With regard to the conclusions, Dr. Breslow said that in spite of reduced survival in the high-dose group, female mice displayed clear evidence of a dose-related increase in hepatocellular carcinoma.

Dr. Harper moved that the technical report on 1,1,1,2-tetrachloroethane be accepted with the agreed upon modifications. Dr. Swenberg seconded the motion and the report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION



1,1,1,2–TETRACHLOROETHANE

CAS NO. 630-20-6
$C_2H_2Cl_4$ Mol. Wt. 167.83

1,1,1,2-Tetrachloroethane is used as a chemical intermediate in the production of trichloroethylene and tetrachloroethylene. It has been found as a trace contaminant in these two compounds and has been identified in drinking water (Kirk-Othmer, 1979; NCI, 1976; Truhaut et al., 1974). Specific production figures for 1,1,1,2-tetrachloroethane are not available (USITC, 1980).

The following oral LD_{50} values have been reported (Truhaut et al., 1974) for rats and mice: male Wistar rats, 670±70 mg/kg; female Wistar rats, 780±100 mg/kg; male Swiss-Webster mice, 1,500±80 mg/kg.

Hepatotoxic effects such as microvacuolization and centrilobular necrosis have been observed in Wistar rats administered 0.3 g/kg 1,1,1,2-tetrachloroethane by gavage, five times per week, for 10 months (Truhaut et al., 1974). Sixty percent of the dose administered was expired unchanged, and the rest was primarily metabolized to a conjugated glucuronic acid derivative of trichloroethanol (21%) or trichloroacetic acid (10%) and excreted in the urine. In parallel studies in rabbits, 22% of orally administered 1,1,1,2-tetrachloroethane (0.5 g/kg) was excreted in the urine as a trichloroethanol derivative and less than 1% as trichloroacetic acid. In guinea pigs, 30% of a 0.3 g/kg dose was excreted in the urine as a derivative of trichloroethanol and 0.4% as trichloroacetic acid (Truhaut and Lich, 1973). When 1.2-2.0 g/kg 1,1,1,2-tetrachloroethane was administered to female NMRI mice by subcutaneous injection, 21%-62% was expired unchanged, 17%-49% was excreted as trichloroethanol or its glucuronide conjugate, and 1%-7% was excreted as trichloroacetic acid (Yllner, 1971a). Trichloroethanol and trichloroacetic acid were also identified as urinary metabolites when Wistar rats were administered 1,1,1,2-tetrachloroethane by inhalation or subcutaneous injection (Ikeda and Ohtsuji, 1972).

1,1,1,2-Tetrachloroethane was not mutagenic, with or without exogenous metabolic activation provided by liver S-9 preparations, in *Salmonella typhimurium* TA 98, TA 100, TA 1535, TA 1537, or TA 1538 (Simmon et al., 1977).

A related chemical (1,1,2,2-tetrachloroethane) caused hepatocellular carcinomas in B6C3F$_1$ mice (NCI, 1978b; IARC, 1979).

1,1,1,2-Tetrachloroethane was tested by the carcinogenesis bioassay program as one of a series of chlorinated ethanes and because of its identification in drinking water in the United States and the lack of data on its long-term effects.

II. MATERIALS AND METHODS

CHEMICAL ANALYSES

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Clinical Examinations and Pathology

Data Recording and Statistical Methods

CHEMICAL ANALYSES

The 1,1,1,2-tetrachloroethane used in these studies was obtained from Aldrich Chemical Company (Milwaukee, WI) in two lots: Lot No. 102957 (used for prechronic studies and the first 4 months of the chronic studies) and Lot No. KB081977 (used for the final 20 months of the chronic studies). Both lots were stored at -20° C.

Results of elemental analyses of both lots agreed with the theoretical values, and infrared and nuclear magnetic resonance spectra were consistent with the spectra in the literature (Appendixes E and F) and with the structure. Analysis by vapor-phase chromatography revealed impurities totaling <0.6% of the area of the major peak in Lot No. 102957 in one system and 12 impurities totaling less than 0.3% of the area of the major peak in a second system. Four of these impurities were identified by gas chromatography/mass spectrometry and quantitated by gas chromatography against standard solutions: acetone (0.05%), tetrachloroethylene (0.04%), trichloroethylene (0.06%), and pentachloroethane (0.15%). 1,2-Dichloroethane, 1,1,2-trichloroethane, and 1,1,2,2-tetrachloroethane were each not present at concentrations greater than 0.01%.

In Lot No. KB081977 only, two impurities totaling 0.07% of the area of the major peak were detected by system 1 (vapor-phase chromatography). In the second vapor-phase chromatography system, only two impurities totaling 0.08% of the area of the major peak were detected. The following impurites were identified through vapor-phase chromatography/mass spectrometry and then quantitated by vapor-phase chromatography against standard solutions: trichloroethylene and a hydrocarbon similar in structure to 2,6-dimethylundecane (not quantitated), tetrachloroethylene (0.06%), 1,1,2,2-tetrachloroethane (<0.01%), and pentachloroethane (0.05%). Lot No. KB081977 did not contain acetone, 1,2-dichloroethane, or 1,1,2-trichloroethane at levels greater than 0.01%.

Each lot of the bulk chemical at Gulf South Research Institute was stored at -20° C to ensure stability. To determine if degradation was taking place, Gulf South Research Institute reanalyzed each batch periodically throughout the study by infrared spectroscopy and vapor-phase chromatography (Appendix E, System 2) and by titration for acidic components. No evidence of degradation was found. Levels of acidic components, pentachloroethane, and tetrachloroethylene remained the same throughout the study.

The chemicals used in these studies were analyzed by the Midwest Research Institute, 425 Volker Blvd., Kansas City, Missouri 64110. Reanalysis of the bulk chemical and analysis of chemical/vehicle mixtures were conducted at South Research Institute.

Midwest Research Institute determined that 1,1,1,2-tetrachloroethane/corn oil solutions were stable for at least 7 days at room temperature (Appendix G). Once formulated, solutions were stored for only 7 days at 4° C. Results of analysis of the 50 mg/ml level, which was used to prepare the other dose levels, indicate that all formulations analyzed conformed to specifications (Appendix H).

PRECHRONIC STUDIES

Single-Dose Study

Groups of five F344/N rats and B6C3F$_1$ mice of each sex were administered single doses of 1,1,1,2-tetrachloroethane (0, 10, 100, 500, 1,000, or 5,000 mg/kg) in corn oil by gavage. Animals were observed daily for mortality. Necropsies were performed on all animals. Further details of the study are presented in Table 1.

Fourteen-Day Study

Groups of five rats and mice of each sex were administered 1,1,1,2-tetrachloroethane (0, 10, 50, 100, 500, or 1,000 mg/kg) in corn oil by gavage for 14 consecutive days (Table 1). Animals were observed daily for mortality and were weighed on the first day of the study and on day 14. Necropsies were performed on all animals.

Thirteen-Week Study

Thirteen-week studies were conducted to evaluate the cumulative toxicity of 1,1,1,2-tetrachloroethane and to determine the doses to be used in the chronic studies.

Groups of 10 rats and mice of each sex were administered 1,1,1,2-tetrachloroethane (0, 5, 10, 50, 100, or 500 mg/kg) in corn oil by gavage 5 days per week for 13 weeks. Animals were checked daily for mortality and signs of morbidity. Those animals judged moribund were killed and necropsied. Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling. Body weight data were collected weekly by cage. At the end of the 91-day study, survivors were killed with carbon dioxide. Necropsies were performed on all animals not autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group. The following specimens were examined for control and high-dose groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland (female mice), salivary gland, bone marrow, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/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.

CHRONIC STUDY

Groups of 50 rats of each sex were administered 125 or 250 mg/kg 1,1,1,2-tetrachloroethane in corn oil by gavage 5 days per week for 103 weeks. Groups of 50 mice of each sex received 250 or 500 mg/kg 1,1,1,2-tetrachloroethane on the same schedule. Groups of 50 rats and 50 mice of each sex received corn oil only and served as vehicle controls (Table 1).

Control and dosed groups were of the same strain, sex, and age range and were from the same source and shipment. All animals were housed in the same room, and no other chemicals were on test in that room. All aspects of animal care and maintenance were similar. Animals were randomized to control and dosed groups as described in Table 1. Chronic studies for rats and mice began in November 1977.

Clinical Examinations and Pathology

All animals were observed twice daily for signs of morbidity and mortality. Clinical signs and body weights by cage were recorded every 4 weeks. The mean body weight of each group was calculated by dividing the total weight of 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 necropsied.

Necropsies were performed on all animals not autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

Examinations for grossly visible lesions were performed on major tissues and 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 lymph nodes, mammary gland, salivary gland, thigh muscle, bone marrow, femur, thymus, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesentric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, and pituitary.

The classification of neoplastic nodules was done 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 percent of the animals were evaluated by an experienced pathologist of rodents. Slides of all target tissues and those on 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 in the blind by the PWG's members, expert in rodent pathology, 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, R.R. and Boorman, G.A., in press). The final diagnosis represents a consensus of contractor pathologists and the NTP Pathology Working Group.

Data Recording and Statistical Methods

Data on 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).

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 of 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.

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 macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

For the statistical analysis of tumor incidence data, two different methods of adjusting for intercurrent mortality were employed. Each used the classical methods 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 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 Tarone (1975).

The second method of analysis 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, 79-92 weeks, week 93 to the week before the terminal kill, and the terminal kill period. The denominator of these proportions was the number of animals actually autopsied 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 for 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 the Cochran-Armitage linear trend test for dose-response trends (Armitage, 1971; Gart et al., 1979). The tests were based on the overall proportion of tumor-bearing animals. All reported P values 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 AND MATERIALS AND METHODS

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study *(a)*
Experimental Design				
Size of Test Groups	5 males and 5 females of each species	Same as single-dose study each species	10 males and 10 females of each species	50 males and 50 females of each species
Doses	0, 10, 100, 500, 1,000, or 5,000 mg/kg 1,1,1,2-Tetrachloroethane in corn oil (LouAna Brand, LouAna Co., Opelousas, LA) by gavage	0, 10, 50, 100, 500, or 1,000 mg/kg 1,1,1,2-Tetrachloroethane in corn oil (LouAna Brand, LouAna Co., Opelousas, LA) by gavage	0, 5, 10, 50, 100, or 500 mg/kg 1,1,1,2-Tetrachloroethane in corn oil (LouAna Brand, LouAna Co., Opelousas, LA) by gavage	Rats: 0, 125, or 250 mg/kg 1,1,1,2-Tetrachloroethane in corn oil (LouAna Brand, LouAna Co., Opelousas, LA) by gavage (5 ml/kg) Mice: 0, 250, or 500 mg/kg 1,1,1,2-Tetrachloroethane in corn oil (LouAna Brand, LouAna Co., Opelousas, LA) by gavage (10 ml/kg)
Duration of Dosing	Single Dose	14 consecutive days	5 days per week for 13 weeks	5 days per week for 103 weeks (high-dose mice, 65 weeks)
Type and Frequency of Observation	Observed daily for mortality; weighed at days 1 and 14	Same as single-dose study	Observed daily, weighed weekly	Observed twice daily, weighed monthly
Necropsy and Histological Examination	Necropsy of all animals	Same as single-dose study	Same as single-dose study *(b)*	All animals were examined histologically
Animals and Animal Maintenance				
Species	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice
Animal Source	Frederick Cancer Research Center, Frederick, MD	Same as single-dose study	Same as single-dose study	Charles River Breeding Laboratories, Wilmington, MA
Time Held Before Start of Test	7 days	Rats: 9 days; mice: 26 days	14 days	19 days

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS (Continued)

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study *(a)*
Age When Placed On Study	4-5 weeks	Rats: 5 weeks; mice: 7 weeks	5-6 weeks	Rats: 49 days old; mice: 55 days old
Method of Animal Distribution	Randomized using a table of random numbers	Animals weighed and distributed so that each dose group had animals of approximately the same average weight	Animals were assigned to cages using a table of random numbers. Cages were then assigned to control and dosed groups using another table of random numbers	Same as 13-week study
Feed	Wayne Lab Chow®, Allied Mills, (Chicago, IL) available *ad libitum*	Same as single-dose study	Same as single-dose study	Same as single-dose study
Bedding	Absorb-Dri® heat-treated hardwood chips, Lab Products, Inc., Garfield, NJ	Same as single-dose study	Same as single-dose study	Same as single-dose study
Water	City tap water in bottles	Same as single-dose study	Same as single-dose study	Tap water, automatic system, Edstrom Industries, Waterford, WI
Cages	Rats: wire mesh, Hoeltge Co., Cincinnati, OH Mice: polypropylene, Lab Products, Inc., Garfield, NJ	Same as single-dose study	Same as single-dose study	Polycarbonate suspended, Lab Products, Inc., Garfield, NJ
Animals Per Cage	Rats: 1 per cage; mice: 5 per cage	Same as single-dose study	Same as single-dose study	5 per cage
Cage Filters	Polyester filter bonnet, Lab Products, Inc., Garfield, NJ	—	—	Bonded spun fiberglass, Lab Products, Inc. Garfield, NJ
Animal Room Environment	21°C ± 2°; humidity uncontrolled; 13 changes of room air per hour; 10 hours of fluorescent light	Same as single-dose study	Same as single-dose study	21°C ± 2° *(c)*; humidity, 40%-70%; 10-12 changes of room air per hour; 12 hours of fluorescent light

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS (Continued)

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study *(a)*
Chemical/Vehicle Mixture				
Preparation	1,1,1,2-tetrachloroethane was added to corn oil on a weight per volume basis	Same as single-dose study	Same as single-dose study	High-dose prepared by adding 1,1,1,2-tetrachloroethane to corn oil on a weight per volume basis; low dose prepared by diluting high-dose mixture with corn oil
Maximum Storage Time	—	—	7 days	7 days
Storage Conditions	—	—	4°C	4°C

(a) Control and dosed animals were of the same strain, sex, and age range, and from the same source and shipment. All animals shared the same room, and all aspects of animal care and maintenance were similar.

(b) The following tissues from animals receiving 500 mg/kg and animals in the vehicle control groups were evaluated microscopically: brain, adrenal, pituitary, thyroid, parathyroid, esophagus, trachea, lymph node, liver, lung, kidney, spleen, salivary gland, heart, pancreas, testis/prostate, ovary/uterus, urinary bladder, stomach, duodenum, colon, skin, bone marrow, gallbladder (mice), mammary tissue (female mice), and gross lesions, when observed.

(c) The air conditioning system failed once for 6 hours causing temperatures temporarily to exceed 34°C.

III. RESULTS

RATS

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

PRECHRONIC STUDIES

Single-Dose Study

All rats administered 5,000 mg/kg 1,1,1,2-tetrachloroethane died (Table 2). One of five males and 3/5 females administered 1,000 mg/kg died. No compound-related, gross pathologic effects were observed.

TABLE 2. SURVIVAL OF RATS ADMINISTERED A SINGLE DOSE OF 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

Dose (mg/kg)	Survival	
	Males	Females
0	5/5	5/5
10	5/5	5/5
100	5/5	5/5
500	5/5	5/5
1,000	4/5 *(a)*	2/5 *(b)*
5,000	0/5 *(a)*	0/5 *(c)*

(a) Deaths occurred on day 1.
(b) Deaths occurred on days 1, 2, and 4.
(c) Four animals died on day 1 and one animal died on day 6.

Fourteen-Day Study

Three of five males and 1/5 females administered 1,000 mg/kg and 1/5 females receiving 500 mg/kg died (Table 3). Final body weight compared to controls was depressed 5-10% in males and females administered 1000 mg/kg. No compound-related effects were observed at necropsy.

TABLE 3. SURVIVAL AND MEAN BODY WEIGHTS OF RATS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE FOR 14 DAYS

Dose mg/kg	Survival (a)	Mean Body Weight (grams)			Final Body Weight Relative to Controls (c) (Percent)
		Initial	Final	Change (b)	
Males					
0	5/5	84.6 ± 2.4	147.4 ± 5.0	+62.8 ± 4.0	
10	5/5	82.4 ± 2.6	144.6 ± 3.8	+62.2 ± 3.7	-2
50	5/5	82.0 ± 2.8	143.2 ± 5.8	+61.2 ± 3.7	-3
100	5/5	87.0 ± 3.1	141.8 ± 5.1	+54.8 ± 5.3	-4
500	5/5	85.6 ± 2.5	146.2 ± 4.6	+60.6 ± 3.0	-1
1,000	2/5	86.0 ± 1.0	134.0 ± 4.0	+48.0 ± 5.0	-9
Females					
0	5/5	75.0 ± 0.8	112.4 ± 3.6	+37.4 ± 3.3	
10	5/5	75.4 ± 0.9	117.6 ± 2.2	+42.2 ± 2.9	+5
50	5/5	76.2 ± 1.0	112.0 ± 2.5	+35.8 ± 1.7	0
100	5/5	77.0 ± 0.6	114.8 ± 1.4	+37.8 ± 1.0	+2
500	4/5	76.0 ± 0.9	116.0 ± 3.3	+40.0 ± 3.4	+3
1,000	4/5	76.0 ± 0.7	105.5 ± 4.4	+29.5 ± 4.8	+6

(a) Number surviving/number initially in the group.
(b) Mean body weight changes of the survivors of the group ± standard error of the mean.
(c) Weight of the dosed group relative to that of the controls =

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

Thirteen-Week Study

Four rats died: one male and one female administered 500 mg/kg, one female administered 100 mg/kg, and one male vehicle control (Table 4). Final body weight gain for males and females receiving 500 mg/kg was depressed 7-8% compared to controls. Females administered 500 mg/kg also exhibited loss of equilibrium. No compound-related histopathologic effects were detected.

Doses of 125 and 250 mg/kg 1,1,1,2-tetrachloroethane, administered in corn oil by gavage five times per week, were selected for rats on the chronic study.

TABLE 4. SURVIVAL AND MEAN BODY WEIGHTS OF RATS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE FOR 13 WEEKS

Dose mg/kg	Survival (a)	Mean Body Weight (grams) (b)			Final Body Weight Relative to Controls (c) (Percent)
		Initial	Final	Change	
Males					
0	9/10 (d)	122	314	+192	
5	10/10	117	308	+191	-2
10	10/10	120	325	+205	+4
50	10/10	120	323	+203	+3
100	10/10	118	318	+200	+1
500	9/10 (e)	115	292	+177	-7
Females					
0	10/10	102	199	+ 97	
5	10/10	98	190	+ 92	-5
10	10/10	93	188	+ 95	-6
50	10/10	100	193	+ 93	-3
100	9/10 (d)	97	186	+ 89	-7
500	9/10 (f)	97	183	+ 86	-8

(a) Number surviving/number per group.
(b) Measured as cage weights.
(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) Death occurred at week 2.
(e) Death occurred at week 10.
(f) Death occurred at week 11.

CHRONIC STUDY

Body Weights and Clinical Signs

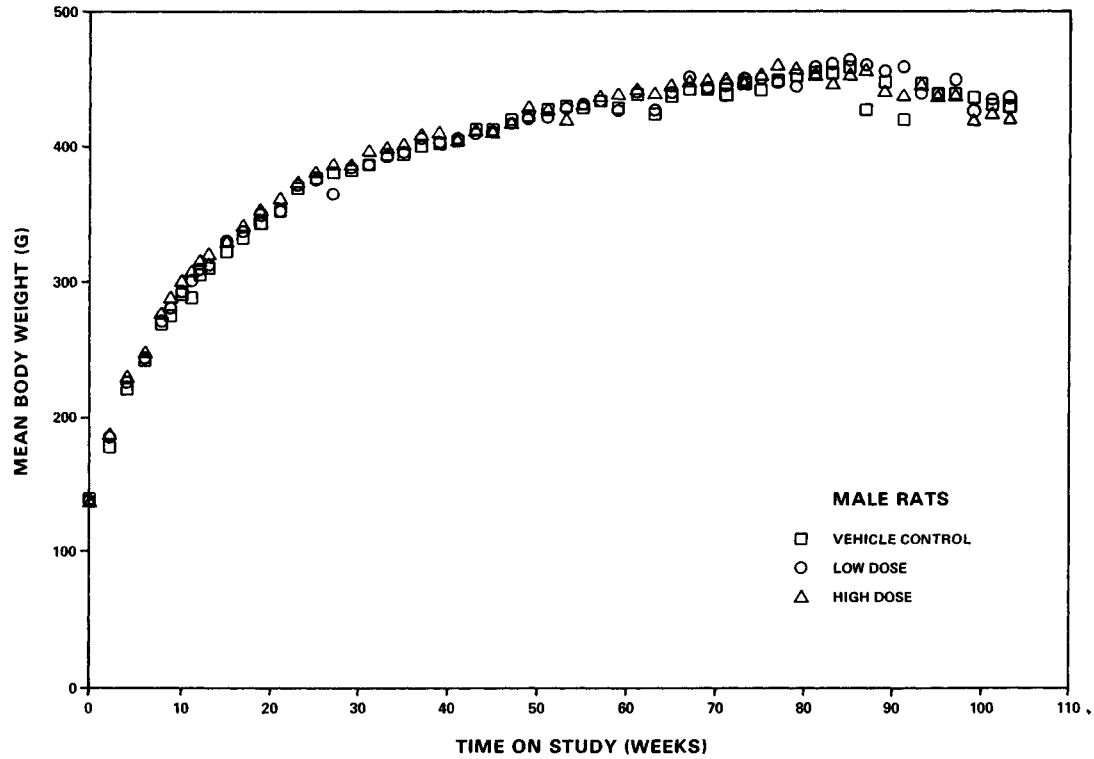
Mean body weights of dosed and control rats were comparable throughout the study (Figure 1 and Appendix I, Table I1). High-dose males and females were often weak, inactive, and uncoordinated following dosing during weeks 44-103.

Survival

Estimates of the probabilities of survival of male and female rats administered 1,1,1,2-tetrachloroethane at the doses used in this bioassay, and those of the control groups, are shown by the Kaplan and Meier curves in Figure 2. Survival of male rats in the high-dose group was significantly reduced (P=0.001) when compared with that for controls. No other significant differences in survival were observed between any groups of either sex.

In male rats, 29/50 (58%) of the controls, 25/50 (50%) of the low-dose group, and 21/50 (42%) of the high-dose group lived to the termination period of the study at 104 weeks. In female rats, 29/50 (58%) of the controls, 27/50 (54%) of the low-dose group, and 24/50 (48%) of the high-dose group lived to the termination period of the study at 104 weeks. Fourteen control, 10 low-dose, and 3 high-dose males and 2 control, 5 low-dose, and 8 high-dose females were accidentally killed during the study and were censored from the statistical comparison of survival (Figure 2). Of these animals, 11 control males and 7 low-dose males died from heat stress during week 62 of the study as a result of elevated (>34° C) temperatures in the animal room. Gross examination showed that the other animals that died had the dose mixture in their lungs, indicating gavage error.

The terminal survival data given above include one control female that died during the termination period. For statistical purposes, this animal was considered to have been killed at the end of the study.



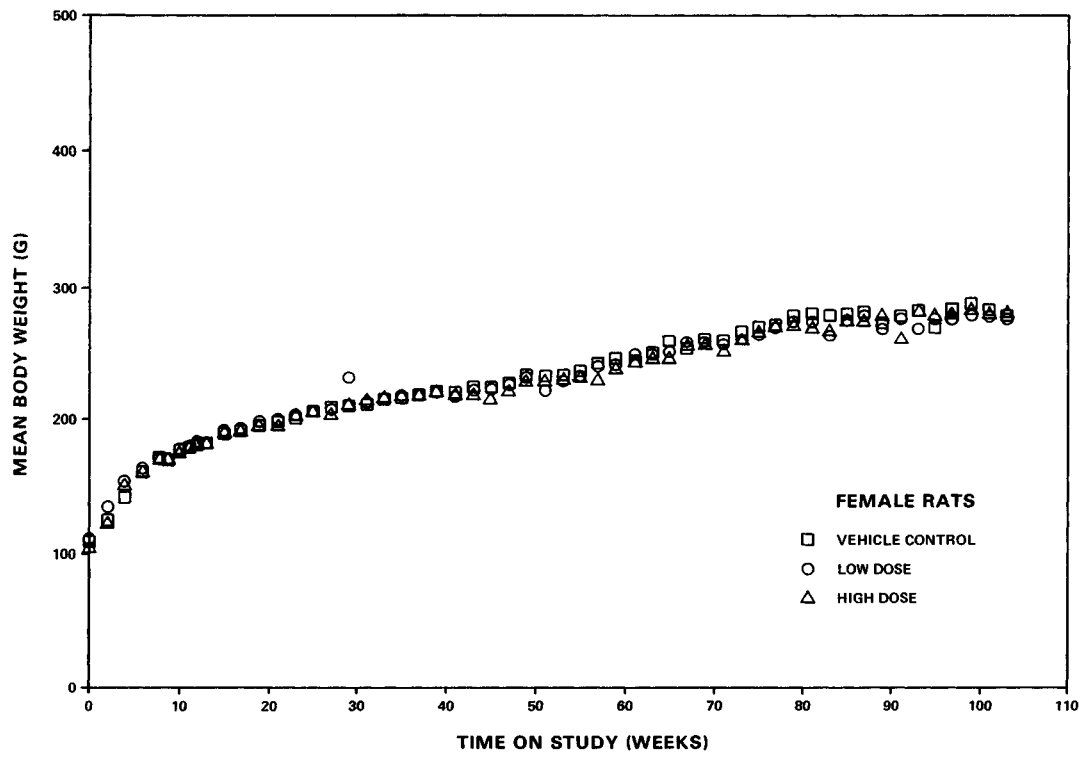
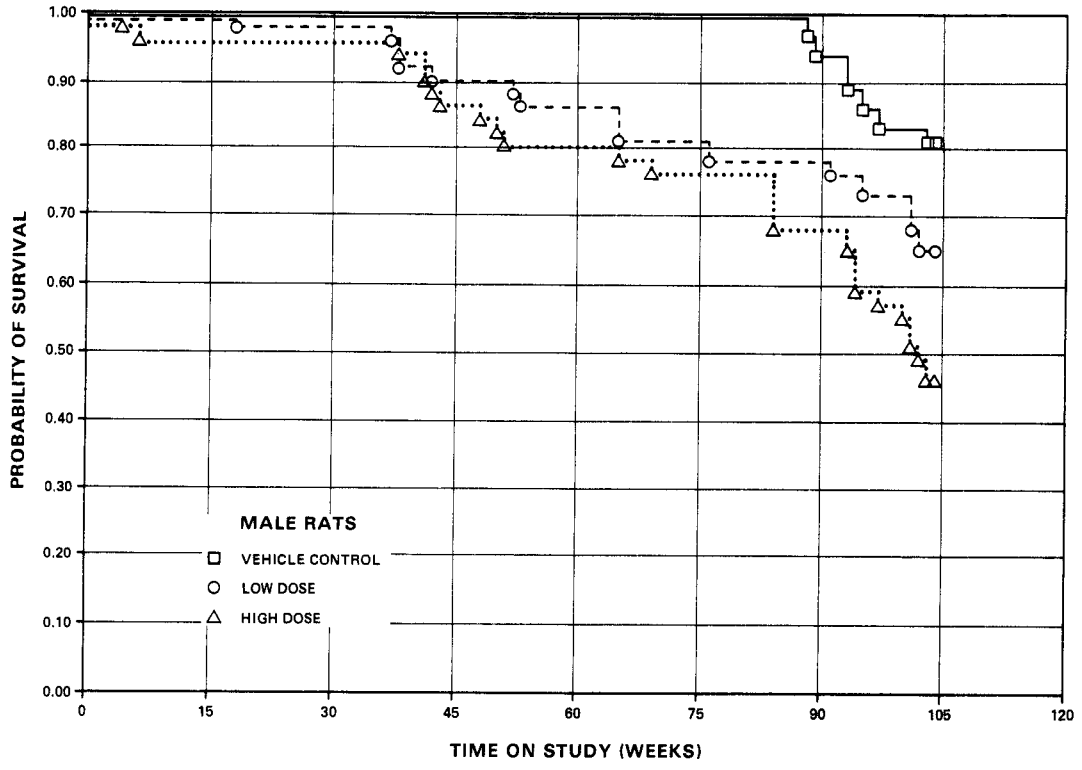


Figure 1. Growth Curves for Rats Administered 1,1,1,2-Tetrachloroethane by Gavage



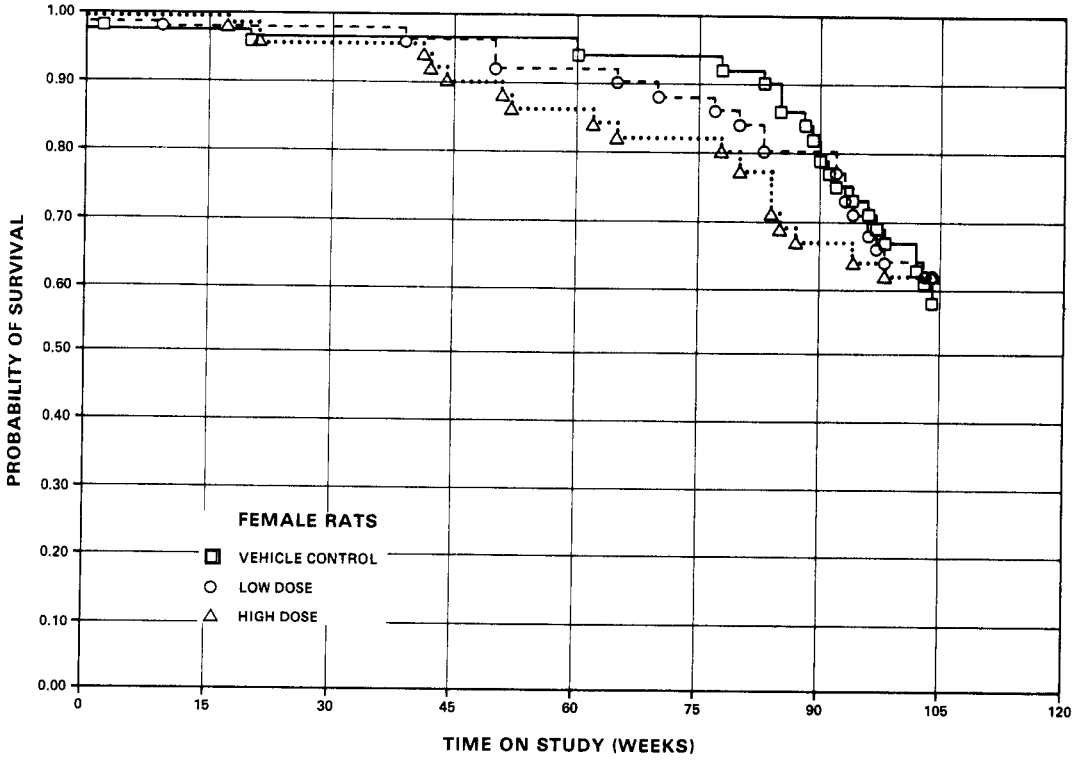


Figure 2. Survival Curves for Rats Administered 1,1,1,2-Tetrachloroethane by Gavage

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; Tables A3 and A4 give the survival and tumor status for each individual animal in the male rat and female rat studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2. Tables 5 and 6 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Liver: Neither neoplastic nodules alone nor carcinomas alone occurred at statistically significant incidences in male rats. The combined incidence of neoplastic nodules and carcinomas in male rats increased in relation to the dose (control, 0/49; low-dose, 1/49, 2%; high-dose, 3/48, 6%), but the results were statistically significant only by the life table trend test (P=0.044). Neoplastic nodules did not appear in statistically significant proportions in female rats (control, 1/48, 2%; low-dose, 0/49; high-dose, 2/44, 5%). The nodules were composed of basophilic or eosinophilic hepatocytes.

Pituitary: A significant ($P<0.05$) negative trend was observed in the combined incidence of adenomas, adenocarcinomas, or carcinomas in female rats (control, 18/39, 46%; low-dose, 16/45, 36%; high-dose, 7/42, 17%). The incidence in the high-dose group was significantly less ($P<0.05$) than that in the control group. The incidences of male rats with adenomas of the pituitary were lower in the dosed groups than in the controls. The incidence in the low-dose group was significantly less ($P\leq0.05$) than that in the controls.

Mammary Gland: The incidence of fibroadenomas in female rats was significantly increased ($P<0.05$) in the low-dose group (15/49, 31%), but the incidence in the high-dose group (7/46, 15%) was not significantly different from that in the controls (6/49, 12%).

Kidney: Mineralization of the kidney occurred in 12/48 (25%) of the control males, 19/50 (38%) of the low-dose males, and 26/48 (54%) of the high-dose males. The lesion was characterized by multifocal deposits of basophilic material (probably calcium) and crystals in the tubules of the papilla.

Lung: Pulmonary alveolar emphysema was observed at the following incidences—control males, 3/49 (6%); low-dose males, 11/50 (22%); high-dose males, 6/46 (13%); control females, 5/49 (10%); low-dose females, 9/47 (19%); high-dose females, 12/46 (26%).

TABLE 5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	3/49 (6%)	2/50 (4%)	3/46 (7%)
Adjusted *(c)*	10.3%	8.0%	12.2%
Terminal *(d)*	3/29 (10%)	2/25 (8%)	2/21 (10%)
Statistical Tests *(e)*			
Life Table	P=0.452	P=0.568N	P=0.529
Incidental Tumor Test	P=0.456	P=0.568N	P=0.534
Cochran-Armitage Trend, Fisher Exact Tests	P=0.559	P=0.490N	P=0.631
Hematopoietic System: Leukemia			
Tumor Rates			
Overall	2/49 (4%)	3/50 (6%)	5/48 (10%)
Adjusted *(c)*	5.9%	10.5%	13.9%
Terminal *(d)*	0/29 (0%)	1/25 (4%)	0/21 (0%)
Statistical Tests *(e)*			
Life Table	P=0.132	P=0.449	P=0.188
Incidental Tumor Test	P=0.308	P=0.474	P=0.306
Cochran-Armitage Trend, Fisher Exact Tests	P=0.151	P=0.510	P=0.209
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	2/49 (4%)	4/50 (8%)	5/48 (10%)
Adjusted *(c)*	5.9%	14.0%	13.9%
Terminal *(d)*	0/29 (0%)	1/25 (4%)	0/21 (0%)
Statistical Tests *(e)*			
Life Table	P=0.137	P=0.289	P=0.188
Incidental Tumor Test	P=0.359	P=0.314	P=0.306
Cochran-Armitage Trend, Fisher Exact Tests	P=0.161	P=0.349	P=0.209
Liver: Neoplastic Nodule or Carcinoma			
Tumor Rates			
Overall *(b)*	0/49 (0%)	1/49 (2%)	3/48 (6%)
Adjusted *(c)*	0.0%	3.3%	12.6%
Terminal *(d)*	0/29 (0%)	0/25 (0%)	2/21 (10%)
Statistical Tests *(e)*			
Life Table	P=0.044	P=0.494	P=0.084
Incidental Tumor Test	P=0.093	P=0.536	P=0.125
Cochran-Armitage Trend, Fisher Exact Tests	P=0.058	P=0.500	P=0.117
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	14/44 (32%)	6/49 (12%)	8/45 (18%)
Adjusted *(c)*	46.0%	21.7%	29.6%
Terminal *(d)*	10/25 (40%)	5/25 (20%)	4/21 (19%)
Statistical Tests *(e)*			
Life Table	P=0.144N	P=0.045N	P=0.212N
Incidental Tumor Test	P=0.062N	P=0.019N	P=0.122N
Cochran Armitage Trend, Fisher Exact Tests	P=0.066N	P=0.020N	P=0.099N

TABLE 5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	2/46 (4%)	3/50 (6%)	0/47 (0%)
Adjusted *(c)*	7.7%	12.0%	0.0%
Terminal *(d)*	2/26 (8%)	3/25 (12%)	0/20 (0%)
Statistical Tests *(e)*			
Life Table	P=0.267N	P=0.482	P=0.297N
Incidental Tumor Test	P=0.267N	P=0.482	P=0.297N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.194N	P=0.540	P=0.242N
Adrenal: Pheochromocytoma or Malignant Pheochromocytoma			
Tumor Rates			
Overall *(b)*	3/46 (7%)	3/50 (6%)	0/47 (0%)
Adjusted *(c)*	11.5%	12.0%	0.0%
Terminal *(d)*	3/26 (12%)	3/25 (12%)	0/20 (0%)
Statistical Tests *(e)*			
Life Table	P=0.146N	P=0.648	P=0.169N
Incidental Tumor Test	P=0.146N	P=0.648	P=0.169N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.095N	P=0.621N	P=0.117N
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	3/42 (7%)	2/48 (4%)	3/44 (7%)
Adjusted *(c)*	11.5%	8.0%	14.3%
Terminal *(d)*	3/26 (12%)	2/25 (8%)	3/21 (14%)
Statistical Tests *(e)*			
Life Table	P=0.490	P=0.518N	P=0.562
Incidental Tumor Test	P=0.490	P=0.518N	P=0.562
Cochran-Armitage Trend, Fisher Exact Tests	P=0.568N	P=0.436N	P=0.639N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/42 (10%)	3/48 (6%)	3/44 (7%)
Adjusted *(c)*	15.4%	12.0%	14.3%
Terminal *(d)*	4/26 (15%)	3/25 (12%)	3/21 (14%)
Statistical Tests *(e)*			
Life Table	P=0.532N	P=0.522N	P=0.619N
Incidental Tumor Test	P=0.532N	P=0.522N	P=0.619N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.395N	P=0.425N	P=0.474N
Pancreatic Islets: Islet-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	1/47 (2%)	3/50 (6%)	0/46 (0%)
Adjusted *(c)*	3.6%	11.2%	0.0%
Terminal *(d)*	1/28 (4%)	2/25 (8%)	0/21 (0%)
Statistical Tests *(e)*			
Life Table	P=0.452N	P=0.276	P=0.557N
Incidental Tumor Test	P=0.372N	P=0.291	P=0.557N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.384N	P=0.332	P=0.505N

TABLE 5. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Prostate: Adenoma			
Tumor Rates			
Overall *(b)*	0/40 (0%)	3/40 (7%)	0/34 (0%)
Adjusted *(c)*	0.0%	12.6%	0.0%
Terminal *(d)*	0/22 (0%)	2/21 (10%)	0/14 (0%)
Statistical Tests *(e)*			
Life Table	P=0.554	P=0.115	*(f)*
Incidental Tumor Test	P=0.635N	P=0.117	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.598	P=0.120	*(f)*
Testis: Interstitial-Cell Tumor			
Tumor Rates			
Overall *(b)*	37/49 (76%)	37/49 (76%)	37/48 (77%)
Adjusted *(c)*	94.8%	97.3%	100.0%
Terminal *(d)*	27/29 (93%)	24/25 (96%)	21/21(100%)
Statistical Tests *(e)*			
Life Table	P=0.052	P=0.208	P=0.062
Incidental Tumor Test	P=0.093	P=0.078	P=0.169
Cochran-Armitage Trend, Fisher Exact Tests	P=0.476	P=0.593	P=0.523
Multiple Sites, Peritoneum, Tunica Vaginalis: Mesothelioma			
Tumor Rates			
Overall *(b)*	0/49 (0%)	3/50 (6%)	3/48 (6%)
Adjusted *(c)*	0.0%	10.7%	9.3%
Terminal *(d)*	0/29 (0%)	2/25 (8%)	0/21 (0%)
Statistical Tests *(e)*			
Life Table	P=0.085	P=0.100	P=0.118
Incidental Tumor Test	P=0.108	P=0.106	P=0.252
Cochran-Armitage Trend, Fisher Exact Tests	P=0.097	P=0.125	P=0.117

(a) Dosed groups received doses of 125 or 250 mg/kg of 1,1,1,2-tetrachloroethane by gavage.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(e) 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 is indicated by (N).
(f) No statistical test was performed because there was no tumor incidence in the high-dose or vehicle control groups.

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Hematopoietic System: Leukemia			
Tumor Rates			
Overall *(b)*	5/49 (10%)	2/49 (4%)	3/46 (7%)
Adjusted *(c)*	12.9%	4.6%	8.7%
Terminal *(d)*	2/29 (7%)	0/27 (0%)	0/24 (0%)
Statistical Tests *(e)*			
Life Table	P=0.380N	P=0.251N	P=0.486N
Incidental Tumor Test	P=0.269N	P=0.158N	P=0.381N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.301N	P=0.218N	P=0.393N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	6/49 (12%)	2/49 (4%)	5/46 (11%)
Adjusted *(c)*	15.2%	4.6%	15.8%
Terminal *(d)*	2/29 (7%)	0/27 (0%)	1/24 (4%)
Statistical Tests *(e)*			
Life Table	P=0.559N	P=0.162N	P=0.593
Incidental Tumor Test	P=0.477N	P=0.096N	P=0.588N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.468N	P=0.134N	P=0.545N
Liver: Neoplastic Nodule			
Tumor Rates			
Overall *(b)*	1/48 (2%)	0/49 (0%)	2/44 (5%)
Adjusted *(c)*	3.6%	0.0%	9.1%
Terminal *(d)*	1/28 (4%)	0/27 (0%)	2/22 (9%)
Statistical Tests *(e)*			
Life Table	P=0.296	P=0.507N	P=0.415
Incidental Tumor Test	P=0.296	P=0.507N	P=0.415
Cochran-Armtage Trend, Fisher Exact Tests	P=0.336	P=0.495N	P=0.467
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	16/39 (41%)	16/45 (36%)	7/42 (17%)
Adjusted *(c)*	54.6%	44.0%	24.3%
Terminal *(d)*	11/23 (48%)	7/25 (28%)	3/21 (14%)
Statistical Tests *(e)*			
Life Table	P=0.078N	P=0.549N	P=0.072N
Incidental Tumor Test	P=0.038N	P=0.469N	P=0.043N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.012N	P=0.386N	P=0.014N
Pituitary: Adenoma, Adenocarcinoma, or Carcinoma			
Tumor Rates			
Overall *(b)*	18/39 (46%)	16/45 (36%)	7/42 (17%)
Adjusted *(c)*	59.7%	44.0%	24.3%
Terminal *(d)*	12/23 (52%)	7/25 (28%)	3/21 (14%)
Statistical Tests *(e)*			
Life Table	P=0.037N	P=0.394N	P=0.035N
Incidental Tumor Test	P=0.013N	P=0.293N	P=0.017N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.004N	P=0.222N	P=0.004N

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	1/41 (2%)	3/44 (7%)	1/42 (2%)
Adjusted *(c)*	3.7%	9.6%	4.5%
Terminal *(d)*	1/27 (4%)	1/25 (4%)	1/22 (5%)
Statistical Tests *(e)*			
Life Table	P=0.532	P=0.289	P=0.716
Incidental Tumor Test	P=0.554	P=0.319	P=0.716
Cochran-Armitage Trend, Fisher Exact Tests	P=0.603N	P=0.335	P=0.747N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	6/49 (12%)	15/49 (31%)	7/46 (15%)
Adjusted *(c)*	17.7%	45.6%	24.7%
Terminal *(d)*	3/29 (10%)	10/27 (37%)	4/24 (17%)
Statistical Tests *(e)*			
Life Table	P=0.273	P=0.021	P=0.345
Incidental Tumor Test	P=0.230	P=0.014	P=0.304
Cochran-Armitage Trend, Fisher Exact Tests	P=0.390	P=0.024	P=0.451
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(b)*	6/44 (14%)	4/47 (9%)	3/42 (7%)
Adjusted *(c)*	18.3%	11.6%	12.1%
Terminal *(d)*	3/26 (12%)	1/26 (4%)	2/22 (9%)
Statistical Tests *(e)*			
Life Table	P=0.280N	P=0.391N	P=0.350N
Incidental Tumor Test	P=0.270N	P=0.353N	P=0.295N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.202N	P=0.328N	P=0.266N

(a) Dosed groups received doses of 125 or 250 mg/kg of 1,1,1,2-tetrachloroethane by gavage.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(e) 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 is indicated by (N).

PRECHRONIC STUDIES

Single-Dose Study

All mice receiving 5,000 mg/kg 1,1,1,2-tetrachloroethane died within 24 hours of dosing. All other mice survived to the end of the 14-day observation period. No compound-related gross pathologic effects were observed.

Fourteen-Day Study

One of five males and 2/5 females receiving 1,000 mg/kg died. Final weights of dosed and control female mice were comparable (Table 7). No compound-related gross pathologic effects were observed.

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

Dose (mg/kg)	Survival *(a)*	Mean Body Weight (grams)			Final Body Weight Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
Males					
0	5/5	27.4 ± 0.2	27.0 ± 0.7	- 0.4 ± 0.5	
10	5/5	27.2 ± 0.6	27.0 ± 0.7	- 0.2 ± 0.6	*(e)*
50	5/5	26.6 ± 0.4	27.0 ± 0.7	+ 0.4 ± 0.5	*(e)*
100	5/5	28.4 ± 0.7	28.6 ± 0.9	+ 0.2 ± 0.4	*(e)*
500	5/5	28.2 ± 0.5	29.0 ± 0.3	+ 0.8 ± 0.4	*(e)*
1,000	4/5(d)	27.8 ± 1.0	27.8 ± 1.5	+ 0.0 ± 0.7	*(e)*
Females					
0	5/5	20.0 ± 0.3	22.0 ± 0.3	+ 2.0 ± 0.3	
10	5/5	21.4 ± 0.4	22.6 ± 0.6	+ 1.2 ± 0.4	+3
50	5/5	20.0 ± 0.3	21.4 ± 0.2	+ 1.4 ± 0.2	-3
100	5/5	20.8 ± 0.6	22.0 ± 0.5	+ 1.2 ± 0.4	0
500	5/5	20.8 ± 0.4	22.4 ± 0.2	+ 1.6 ± 0.2	+2
1,000	3/5(f)	21.3 ± 0.3	22.3 ± 0.3	+ 1.0 ± 0.0	+1

(a) Number surviving/number initially in the group.
(b) Mean weight change of the survivors of the group ± standard error of the mean.
(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) Death occurred on day 3.
(e) The relative weight was not determined due to the failure of the controls to gain weight.
(f) Deaths occurred on days 1 and 4.

Thirteen-Week Study

One male administered 500 mg/kg died. No compound-related histopathologic effects were observed. Mean body weights of dosed and control mice were comparable (Table 8).

Doses of 250 and 500 mg/kg 1,1,1,2-tetrachloroethane in corn oil, administered by gavage five times per week, were selected for mice in the chronic study.

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

Dose (mg/kg) *(a)*	Survival *(b)*	Mean Body Weight (grams) *(b)*			Final Body Weight Relative to Controls *(c)* (Percent)
		Initial	Final	Change	
Males					
0	10/10	21	34	+13	
5	10/10	22	35	+13	+ 3
10	10/10	22	36	+14	+ 6
50	10/10	21	30	+ 9	-12
100	10/10	21	34	+13	0
500	9/10 *(d)*	22	33	+11	- 3
Females					
0	10/10	19	25	+ 6	
5	10/10	18	27	+ 9	+ 8
10	10/10	18	27	+ 9	+ 8
50	10/10	18	28	+10	+12
100	10/10	18	26	+ 8	+ 4
500	10/10	18	27	+ 9	+ 8

(a) Number surviving/number per group

(b) Weight recorded by cage.

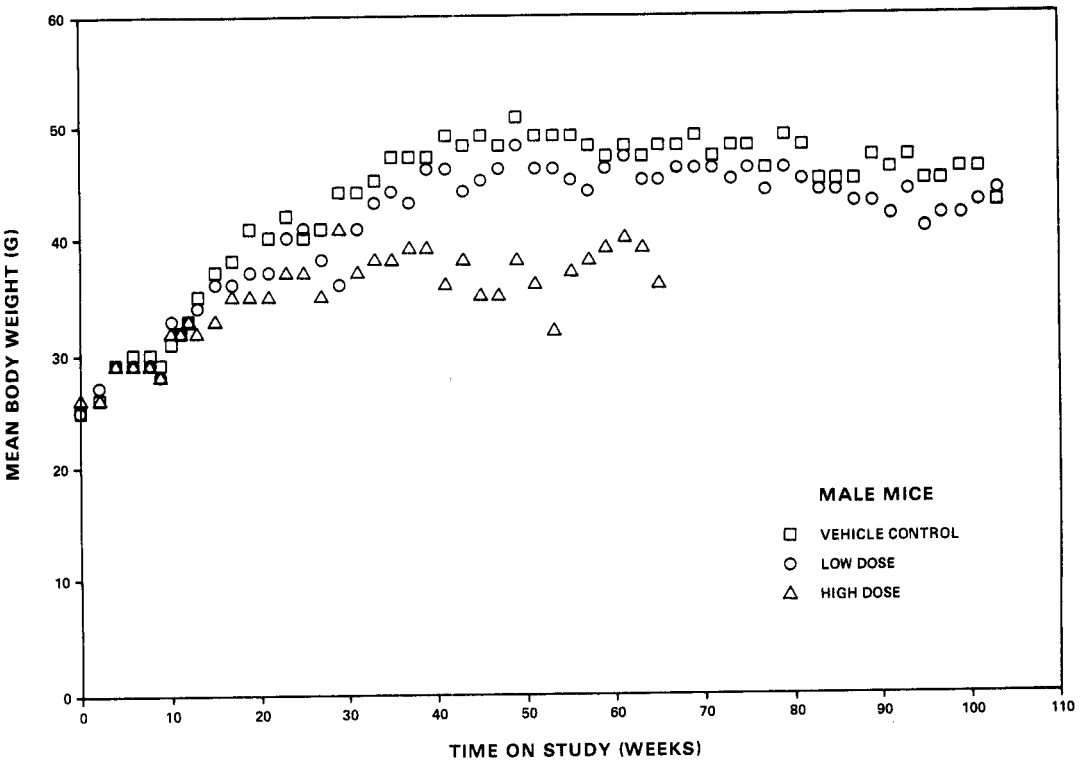
(c) Weight of the dosed group relative to that of the controls = $\frac{\text{Weight (Dosed Group)} - \text{Weight (Control Group)}}{\text{Weight (Control Group)}} \times 100$

(d) Animal died during week 3.

CHRONIC STUDY

Body Weights and Clinical Signs

The mean body weights of high-dose mice of each sex were lower than those of the corresponding controls (Figure 3 and Appendix I, Table I2). Beginning with week 34, all high-dose animals were sluggish after dosing. By week 51, high-dose animals were uncoordinated and weak and were breathing rapidly after dosing.



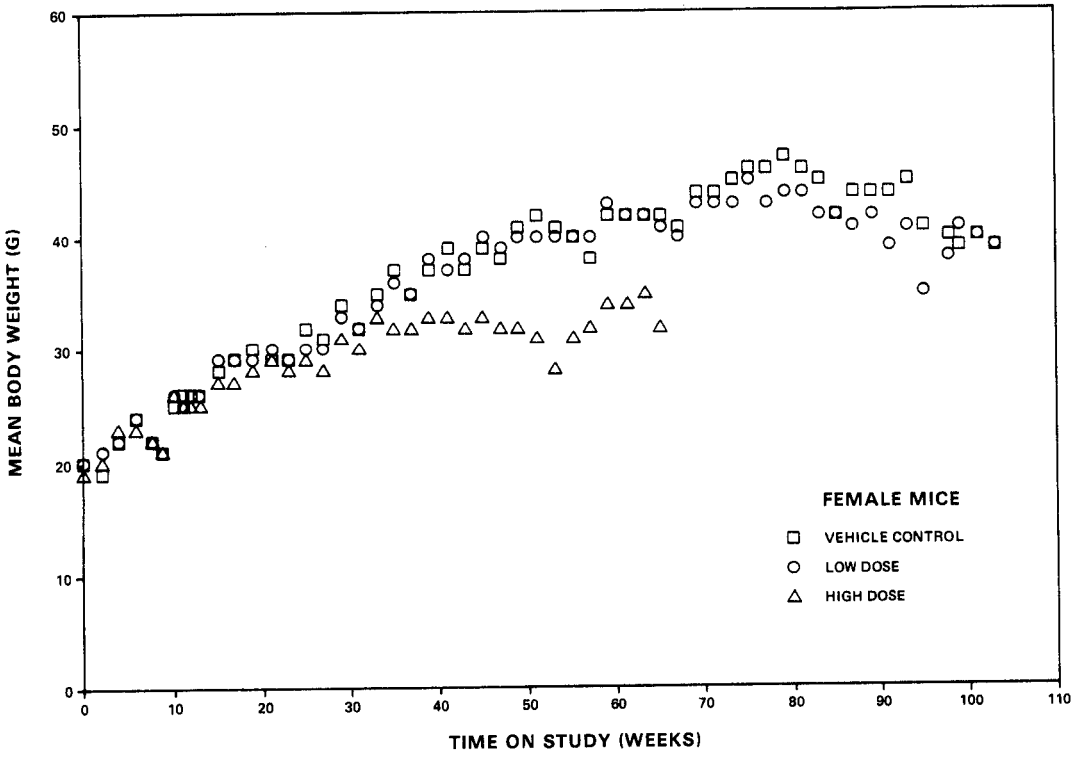


Figure 3. Growth Curves for Mice Administered 1,1,1,2-Tetrachloroethane by Gavage

Survival

Estimates of the probabilities of survival of male and female mice administered 1,1,1,2-tetrachloroethane by gavage at the doses used in this bioassay, and for the control groups, are shown by the Kaplan and Meier curves in Figure 4. Survival in the group of high-dose male mice was significantly reduced when compared with that of the other two groups ($P<0.001$). All surviving high-dose mice were killed after 65 weeks because of their moribund condition. In female mice, survival of both dosed groups was significantly reduced when compared with that of controls ($P=0.039$ for the low-dose group, $P<0.001$ for the high-dose group), and survival in the high-dose group was significantly less than that for the low-dose group ($P<0.001$). No significant difference was observed between the survival of control and low-dose male mice.

In male mice, 38/50 (76%) of the controls, 34/50 (68%) of the low-dose group, and none of the high-dose group lived to the termination period of the study at 104 weeks. In female mice, 41/50 (82%) of the controls, 31/50 (62%) of the low-dose group, and none of the high-dose group lived to the end of the termination period of the study at 104 weeks.

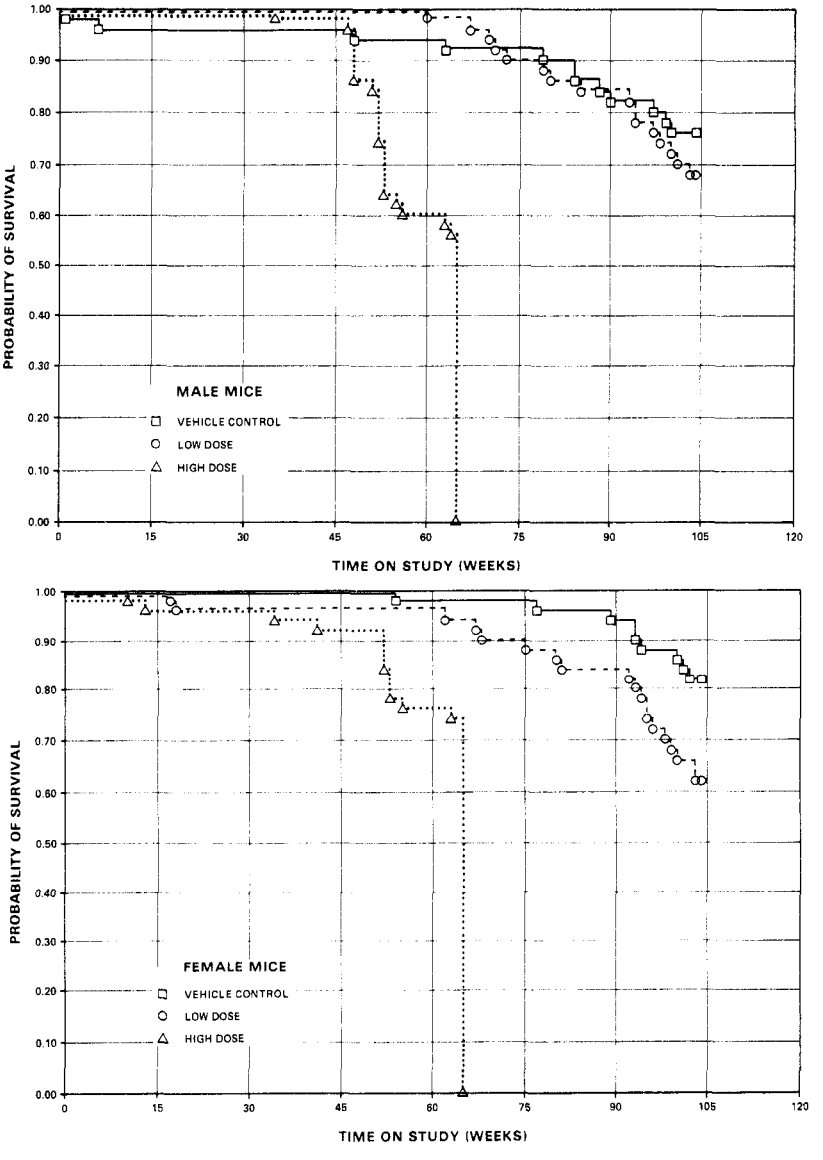


Figure 4. Survival Curves for Mice Administered 1,1,1,2-Tetrachloroethane by Gavage

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in mice are summarized in Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status for each individual animal in the male and female mouse studies, respectively. Findings on nonneoplastic lesions are summarized in Table 9 and Appendix D, Tables D1 and D2. Tables 10 and 11 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Liver: Life table analyses indicated significant ($P<0.05$) increases in both hepatocellular adenomas and carcinomas (considered separately) in high-dose male and female mice. The increased incidence of hepatocellular adenoma in low-dose male mice was also significant ($P<0.05$).

The combined incidence of hepatocellular adenomas and carcinomas exhibited a statistically significant, positive, dose-related trend among both male and female mice. Life table tests for trend were significant ($P<0.001$) for males and females. Statistical tests between the high-dose groups and the corresponding controls were significant even though animals in the high-dose groups were killed at 65 weeks and controls were killed at weeks 104-105. For females, the Fisher exact test and the life table test using the high-dose and control groups had probability levels of $P<0.001$, and the increases seen at the low dose were also significant ($P<0.05$) for both sexes. The incidental tumor test was not performed for high-dose male or female mice because all high-dose animals died or were killed before any control animals (except for two males and one female) died.

Inflammation, fatty metamorphosis, necrosis, and hepatocytomegaly occurred in high-dose mice at incidences much higher than those seen in the controls (Table 9).

Reproductive System: A decrease in cystic hyperplasia of the uterus was observed in female mice administered high doses of 1,1,1,2-tetrachloroethane (controls, 36/50, 72%; low-dose, 26/43, 60%; high-dose, 4/41, 10%; Appendix D, Table D2).

TABLE 9. INCIDENCE OF NONNEOPLASTIC LESIONS OF THE LIVER IN MICE ADMINISTERED 1,1,1,2-TETRACHLOROETHANE IN THE CHRONIC STUDY

	Males			Females		
	Controls	Low Dose	High Dose	Controls	Low Dose	High Dose
Number of Livers Examined Microscopically	48	46	50	49	46	48
Incidence of:						
Inflammation	5(10%)	2(4%)	15(30%)	2(4%)	1(2%)	18(37%)
Necrosis	8(17%)	3(7%)	40(80%)	1(2%)	0(0%)	35(73%)
Fatty Metamorphosis	4(8%)	2(4%)	33(66%)	1(2%)	3(7%)	25(52%)
Hepatocytomegaly	1(2%)	2(4%)	17(34%)	0(0%)	0(0%)	22(46%)

TABLE 10. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(b)*	5/45 (11%)	5/45 (11%)	3/50 (6%)
Adjusted *(c)*	13.9%	14.0%	10.7%
Terminal *(d)*	5/36 (14%)	4/34 (12%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.061	P=0.595	P=0.050
Incidental Tumor Test	P=0.532	P=0.631	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.244N	P=0.630	P=0.300N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	6/45 (13%)	5/45 (11%)	3/50 (6%)
Adjusted *(c)*	16.7%	14.0%	10.7%
Terminal *(d)*	6/36 (17%)	4/34 (12%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.101	P=0.540N	P=0.050
Incidental Tumor Test	P=0.590N	P=0.505N	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.153N	P=0.500N	P=0.193N
Hematopoietic System: Malignant Lymphoma			
Tumor Rates			
Overall *(b)*	2/48 (4%)	3/46 (7%)	0/50 (0%)
Adjusted *(c)*	5.3%	8.1%	0.0%
Terminal *(d)*	2/38 (5%)	2/34 (6%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.460	P=0.460	*(g)*
Incidental Tumor Test	P=0.434	P=0.434	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.194N	P=0.480	P=0.237N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	3/48 (6%)	4/46 (9%)	0/50 (0%)
Adjusted *(c)*	7.3%	10.1%	0.0%
Terminal *(d)*	2/38 (5%)	2/34 (6%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.463	P=0.463	*(g)*
Incidental Tumor Test	P=0.393	P=0.393	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.112N	P=0.476	P=0.114N
Circulatory System: Hemangioma			
Tumor Rates			
Overall *(b)*	3/48 (6%)	1/46 (2%)	0/50 (0%)
Adjusted *(c)*	7.9%	2.1%	0.0%
Terminal *(d)*	3/38 (8%)	0/34 (0%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.333N	P=0.333N	*(g)*
Incidental Tumor Test	P=0.030N	P=0.223N	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.059N	P=0.325N	P=0.114N

TABLE 10. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Circulatory System: Hemangiosarcoma			
Tumor Rates			
Overall *(b)*	0/48 (0%)	3/46 (7%)	0/50 (0%)
Adjusted *(c)*	0.0%	7.7%	0.0%
Terminal *(d)*	0/38 (0%)	1/34 (3%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.116	P=0.116	*(h)*
Incidental Tumor Test	P=0.168	P=0.168	*(h)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.627N	P=0.113	*(h)*
Liver: Adenoma			
Tumor Rates			
Overall *(b)*	6/48 (13%)	14/46 (30%)	21/50 (42%)
Adjusted *(c)*	15.8%	38.4%	64.7%
Terminal *(d)*	6/38 (16%)	12/34 (35%)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P=0.021	P<0.001
Incidental Tumor Test	P=0.010	P=0.033	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.001	P=0.030	P=0.001
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	12/48 (25%)	13/46 (28%)	6/50 (12%)
Adjusted *(c)*	27.6%	31.8%	15.2%
Terminal *(d)*	7/38 (18%)	8/34 (24%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.012	P=0.423	P=0.010
Incidental Tumor Test	P=0.454N	P=0.576	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.073N	P=0.450	P=0.080N
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	18/48 (38%)	27/46 (59%)	27/50 (54%)
Adjusted *(c)*	41.6%	65.0%	71.8%
Terminal *(d)*	13/38 (34%)	20/34 (59%)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P=0.035	P<0.001
Incidental Tumor Test	P=0.049	P=0.062	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.065	P=0.032	P=0.075

(a) Dosed groups received doses of 250 or 500 mg/kg of 1,1,1,2-tetrachloroethane by gavage.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(e) 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's exact tests compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).
(f) The incidental tumor test was not used because there was markedly reduced survival in the high-dose group.
(g) The life table analysis was not done because the tumors observed in control animals were found only after the death of the last high-dose animal.
(h) No statistical test was performed because there was no tumor incidence in the high-dose or vehicle control group.

TABLE 11. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Hematopoietic System: Malignant Lymphoma			
Tumor Rates			
Overall *(b)*	8/50 (16%)	6/47 (13%)	0/48 (0%)
Adjusted *(c)*	18.5%	16.2%	0.0%
Terminal *(d)*	6/41 (15%)	3/31 (10%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.478N	P=0.570N	*(f)*
Incidental Tumor Test	P=0.171N	P=0.414N	*(g)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.006N	P=0.436N	P=0.003N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall (b)	9/50 (18%)	7/47 (15%)	0/48 (0%)
Adjusted (c)	20.2%	19.2%	0.0%
Terminal (d)	6/41 (15%)	4/31 (13%)	0/0
Statistical Tests (e)			
Life Table	P=0.498N	P=0.586N	*(f)*
Incidental Tumor Test	P=0.055N	P=0.411N	*(g)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.004N	P=0.446N	P=0.002N
Circulatory System: Hemangioma, Hemangiosarcoma, or Angiosarcoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	1/47 (2%)	0/48 (0%)
Adjusted *(c)*	6.9%	3.2%	0.0%
Terminal *(d)*	2/41 (5%)	1/31 (3%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.396N	P=0.396N	*(f)*
Incidental Tumor Test	P=0.284N	P=0.284N	*(g)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.066N	P=0.332N	P=0.129N
Liver: Adenoma			
Tumor Rates			
Overall *(b)*	4/49 (8%)	8/46 (17%)	24/48 (50%)
Adjusted *(c)*	9.5%	23.9%	59.7%
Terminal *(d)*	3/40 (7%)	6/30 (20%)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P=0.086	P<0.001
Incidental Tumor Test	P=0.033	P=0.128	*(g)*
Cochran-Armitage Trend, Fisher Exact Tests	P<0.001	P=0.148	P<0.001
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	1/49 (2%)	5/46 (11%)	6/48 (13%)
Adjusted *(c)*	2.5%	13.9%	15.2%
Terminal *(d)*	1/40 (3%)	2/30 (7%)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P=0.065	P=0.008
Incidental Tumor Test	P=0.071	P=0.110	*(g)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.047	P=0.088	P=0.053

TABLE 11. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	5/49 (10%)	13/46 (28%)	30/48 (63%)
Adjusted *(c)*	11.9%	35.6%	71.3%
Terminal *(d)*	4/40 (10%)	8/30 (27%)	0/0
Statistical Tests *(e)*			
Life Table	P<0.001	P=0.011	P<0.001
Incidental Tumor Test	P=0.002	P=0.023	*(g)*
Cochran-Armitage Trend, Fisher Exact Tests	P<0.001	P=0.023	P<0.001
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	4/43 (9%)	8/41 (20%)	0/40 (0%)
Adjusted *(c)*	11.8%	26.9%	0.0%
Terminal *(d)*	4/34 (12%)	6/26 (23%)	0/0
Statistical Tests *(e)*			
Life Table	P=0.082	P=0.082	*(f)*
Incidental Tumor Test	P=0.102	P=0.102	*(g)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.118N	P=0.153	P=0.067N

(a) Dosed groups received doses of 250 or 500 mg/kg of 1,1,1,2-tetrachloroethane by gavage.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(e) 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's exact tests compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).
(f) The life table analysis was not done because the tumors observed in control animals were found only after the death of the last high-dose animal.
(g) The incidental tumor test was not used because there was markedly reduced survival in the high-dose group.

IV. DISCUSSION AND CONCLUSIONS

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Based on the results of the prechronic studies, doses of 125 and 250 mg/kg were selected for rats in the chronic study. During the two-year study, mean body weights of dosed and control rats were comparable; however, survival of high-dose males was significantly less (P=0.001) than that of the controls. The chemical produced cumulative toxicity from week 44 forward, as evidenced by weakness, inactivity, and loss of coordination after dosing. Based on present cumulative toxicity data and the findings from previous rodent bioassays of other short-chain chlorinated ethanes (NCI, 1978a, b, and c; NTP, 1982a), the high dose selected in this experiment exceeded the estimated maximum tolerated dose. The resultant increased mortality in the high-dose males likely reduced the sensitivity of this study for detecting a carcinogenic response and certainly made the interpretation of data for hepatic carcinogenesis difficult.

Analyzed separately, neither hepatocellular neoplastic nodules nor carcinomas occurred with a statistically significant incidence in male rats; when the combined incidences of these lesions were analyzed, a positive trend was observed (P=0.044, life table test). The combined incidence of these liver tumors in the high-dose males (3/48, 6%) was not significant (P=0.13) relative to their combined incidence in male vehicle control rats as observed in previous bioassays in this laboratory, (5/243, 2.1%, range 0%-4%). Thus, clear evidence for the association between liver tumors in male rats and the administration of 1,1,1,2-tetrachloroethane was not found. However, the positive trend, considered together with the cumulative toxicity and accidental deaths, suggests that the administration of 1,1,1,2-tetrachloroethane may have been associated with the increased incidence of liver tumors.

Fibroadenomas of the mammary gland occurred in low-dose female rats at an increased ($P<0.05$) incidence when compared with the concurrent controls. The incidence in the high-dose group was not significantly higher than that in the controls. The incidence of fibroadenomas of the mammary gland in low-dose females (15/49, 31%) is higher than that seen in female vehicle control groups at the same laboratory (42/245, 17.1%; range 2% to 28%), suggesting a tumorigenic effect. The number of female rats in the high-dose group surviving to the end of the experiment (24/50) was below average for this strain.

Adenomas, adenocarcinomas, or carcinomas (combined) of the pituitary gland occurred in female rats with a negative trend ($P<0.05$), and the incidence in the high-dose group was less ($P<0.05$) than that in the controls (18/39, 46%; 16/45, 36%; 7/42, 17%). The combined incidence of these lesions in previous bioassays for this laboratory was 103/228 (45.2%) with a range of 33% to 53%. These lesions were not considered to be associated with 1,1,1,2-tetrachloroethane.

Nonneoplastic renal lesions were observed in male rats. Mineralization of the kidney, characterized by multifocal deposits of basophilic material and crystals in the tubules of the papilla, was increased in dosed male rats (control, 12/48, 25%; low-dose, 19/50, 38%; high-dose, 26/48, 54%) and was considered to be related to administration of 1,1,1,2-tetrachloroethane.

Pulmonary alveolar emphysema also occurred at a higher incidence in male and female dosed rats than in controls, but its frequent association with pulmonary hemorrhage and focal granulomatous inflammation suggests that a mechanical lesion was produced, probably during gastric intubation. Furthermore, all the affected animals died or were killed in a moribund state before the end of the study. Alveolar emphysema was not observed in those animals killed at the end of the study.

The doses of 250 and 500 mg/kg selected for mice in the 2-year study were consistent with the lack of observed toxicity in the 91-day study, yet these clearly caused toxicity during the chronic exposure. By week 34 high-dose mice were sluggish, and by week 51 other symptoms of central nervous system toxicity were evident, including incoordination, weakness, and rapid breathing. After week 20 for males and after week 40 for females, mean body weights of high-dose mice relative to controls were depressed 12% or more. By week 66 all high-dose mice were dead or moribund and had to be killed; survival of high-dose male mice and both high- and low-dose female mice was significantly less ($P<0.05$) than that of corresponding controls. These data clearly indicate that the estimated maximum tolerated dose for high-dose mice was exceeded.

Histopathological examination identified the liver as the major target organ in mice for 1,1,1,2-tetrachloroethane-induced tumorigenicity. The comparative incidences of liver tumors for control mice in the present study, previous studies from this laboratory, and the incidences at all testing laboratories in the program are shown in Table 12. The association between hepatocellular adenomas and chronic exposure

TABLE 12. INCIDENCE OF LIVER TUMORS IN CONTROL MICE

Tumor Type	Present Study	Other Studies at Same Laboratory	Range		Incidence at All Laboratories
			Low	High	
Adenoma					
Males	6/48(13%)	27/190(14%)	8%	21%	99/904(11%)
Females	4/49(8%)	13/285(5%)	3%	8%	38/996(4%)
Carcinoma					
Males	12/48(25%)	32/190(17%)	8%	25%	187/904(21%)
Females	1/49(2%)	8/285(3%)	0%	4%	30/996(3%)
Adenoma or Carcinoma					
Males	18/48(38%)	59/190(31%)	25%	38%	276/904(31%)
Females	5/49(10%)	21/285(7%)	4%	10%	67/996(7%)

to 1,1,1,2-tetrachloroethane was evident in both male and female mice, with dose-related increases that were statistically significant by all three trend tests. There was also evidence of an increased incidence of hepatocellular carcinoma in female mice. The tumor incidences in the low- and high-dose groups (5/46, 11% and 6/48, 13%, respectively) exceeded the historical control rate at this laboratory (8/285, 3%; range 0%-4%; see Table 12) despite the decreased survival in both dosed groups. Clear evidence of an increased incidence of hepatocellular carcinomas in male mice was not found. The incidence of these tumors in the high-dose group was actually less than that observed in the controls, and a significant positive effect was found only by a life table test, which presumes these carcinomas to be the cause of death. However, the evidence suggests that mortality was caused by toxicity and not due to the hepatocellular carcinomas. In this instance, therefore, adjustment for intercurrent mortality by life table analysis is questionable. Retrospectively, it might have been preferable to kill some control animals by week 66 concurrently with the high-dose animals to enable direct comparisons to be made of tumor incidences.

Nonneoplastic liver lesions, such as inflammation, necrosis, fatty metamorphosis, and hepatomegaly, were also observed at increased incidences in high-dose male and female mice in the present study (Table 9). Since overt signs of clinical toxicity did not appear until week 51 of dosing and no toxic effects on the liver were observed in the 13-week study, the toxicity of 1,1,1,2-tetrachloroethane appears to be cumulative.

The reduced survival of high-dose female mice as compared with controls may have been responsible for the decreased incidence of uterine cystic hyperplasia in the high-dose female as compared with controls (Appendix D, Table D2).

Although several minor impurities in the technical grade 1,1,1,2-tetrachloroethane (i.e., trichloroethylene, tetrachloroethylene, and pentachloroethane) are known hepatocarcinogens in B6C3F$_1$ mice (NCI, 1976, 1977; NTP, 1983a and 1983b; IARC, 1979), the amounts of these compounds present are considered to be insufficient to account for the tumorigenic effects of 1,1,1,2-tetrachloroethane (Appendixes E and F). The 1,1,1,2-isomer used in this bioassay was >99% pure.

The structurally related compound 1,1,2,2-tetrachloroethane was tested previously in B6C3F$_1$ mice in the Bioassay Program, using a high dose that was roughly equivalent to the low dose in the present study. At these nearly equivalent doses, the incidence of hepatocellular carcinomas in the high-dose mice administered 1,1,2,2-tetrachloroethane was ≥90% and considerably higher than that in the mice administered 1,1,1,2-tetrachloethane in the current study (Table 13). Differences in the metabolism and fate of 1,1,1,2- and 1,1,2,2-tetrachloroethane have been reported in female NMRI mice (Yllner, 1971a, 1971b) (Table 14), in female DD mice (Ikeda and Ohtsuji, 1972) and in male and female Wistar rats (Ikeda and Ohtsuji, 1972; Yllner, 1971b). Both compounds yielded substantial amounts of trichloroethanol and trichloroacetic acid, but the asymmetric isomer (1,1,1,2-tetrachloroethane) was more readily metabolized to these products than was the symmetric one (1,1,2,2-tetrachloroethane). Although trichloroethanol and trichloroacetic acid are also metabolites of trichloroethylene (a hepatocarcinogen in B6C3F$_1$ mice) (NCI, 1976; NTP, 1983b), trichloroethylene does not appear to be an intermediate in the metabolism of

TABLE 13. INCIDENCE OF LIVER TUMORS IN B6C3F$_1$ MICE IN NCI/NTP BIOASSAYS OF CHLORINATED ETHANES ADMINISTERED BY GAVAGE

Chemical	Dose (mg/kg) Low	Dose (mg/kg) High	Sex	Incidence of Hepatocellular Adenomas: Vehicle Control	Low Dose	High Dose	Incidence of Hepatocellular Carcinomas: Vehicle Control	Low Dose	High Dose	Reference
Hexachloroethane	590	1,179	M	0/20	0/50	0/49	3/20	15/50	31/49(a)	(NCI,
			F	0/20	0/50	0/49	2/20	20/50 *(c)*	15/49	1978a)
Pentachloroethane	250	500 *(b)*	M	10/48	4/44	7/45	4/48	26/44 *(a)*	7/45 *(c)*	(NTP,
			F	2/46	8/42 *(c)*	19/45 *(a)*	1/46	28/42 *(a)*	13/45 *(a)*	1983a)
1,1,1,2-Tetrachloroethane	250	500 *(d)*	M	6/48	14/46 *(c)*	21/50 *(a)*	12/48	13/46	6/50	Current
			F	4/49	8/46	24/48 *(a)*	1/49	5/46	6/48 *(c)*	Study
1,1,2,2-Tetrachloroethane	142	284	M	0/18	0/50	0/49	1/18	13/50	44/49 *(a)*	(NCI,
			F	0/20	0/48	0/47	0/20	30/48 *(a)*	43/47 *(a)*	1978b)
1,1,2-Trichloroethane	195	390	M	0/20	0/49	0/49	2/20	18/49 *(c)*	37/49 *(a)*	(NCI,
			F	0/20	0/48	0/45	0/20	16/48 *(c)*	40/45 *(a)*	1978c)

(a) Significantly ($P<0.001$) greater than controls.
(b) All high dose mice had died or were killed by week 41 (males) or week 74 (females).
(c) Significantly (≤ 0.05) greater than controls.
(d) All high dose mice had died or were killed by week 66.

TABLE 14. COMPARATIVE FATE OF 1,1,1,2-TETRACHLOROETHANE AND 1,1,2,2-TETRACHLOROETHANE IN MICE

	^{14}C-1,1,1,2-Tetrachloroethane *(a)*	^{14}C-1,1,2,2-Tetrachloroethane
Expired unchanged (%)	21-62	<4 *(b)*
Carbon dioxide	-	45-61 *(b)*
Total in urine and feces (%)	at least 20	28 *(b)*
Not excreted	-	16 *(b)*
Urinary and fecal metabolites (% of total dose)		
Trichloroethanol	17-49	1-5 *(c)*
Dichloroacetic acid	-	6.6-12*(c)*
Trichloroacetic acid	1-7	0.6-2.2 *(c)*
Urea	-	0.6-0.8 *(c)*
Oxalic acid	-	1.4-2.8 *(c)*
Glyoxylic acid	-	0.1-0.4 *(c)*

(a) 1.2-2.0 g/kg administered subcutaneously; animals observed for 3 days (Yllner, 1971a)
(b) 0.1-0.32 g/kg administered intraperitoneally; animals observed for 3 days (Yllner, 1971b)
(c) After 24 hours

of 1,1,1,2-tetrachloroethane as it is for 1,1,2,2-tetrachloroethane. The trichloroethanol is formed by hydrolytic dehalogenation of 1,1,1,2-tetrachloroethane (Truhaut and Lich, 1973; Yllner, 1971a) and trichloroacetic acid by oxidation of 1,1,1-trichloroethane. Administration of other chlorinated ethanes has also been associated with liver tumors in B6C3F$_1$ mice (Table 13).

IV. DISCUSSION AND CONCLUSIONS

Conclusions: Under the conditions of these studies, 1,1,1,2-tetrachloroethane was not demonstrated to be carcinogenic in F344/N rats, although the observed increase in the proportion of male rats with liver tumors may have been associated with the administration of 1,1,1,2-tetrachloroethane; accidental killing of 27 male and 15 female rats reduced the sensitivity of this bioassay for detecting a carcinogenic response. 1,1,1,2-Tetrachloroethane was carcinogenic for B6C3F$_1$ mice, causing an increased proportion of female mice with hepatocellular carcinomas and an increased proportion of male and female mice with hepatocellular adenomas; the decreased survival in high-dose male and female mice compromised the ability of this bioassay to further determine the presence or absence of a carcinogenic effect and gave clear evidence that these doses were toxic.

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	48
INTEGUMENTARY SYSTEM			
*SKIN	(49)	(50)	(48)
ADENOMA, NOS			1 (2%)
*SUBCUT TISSUE	(49)	(50)	(48)
FIBROMA	2 (4%)	1 (2%)	1 (2%)
FIBROUS HISTIOCYTOMA, MALIGNANT	2 (4%)		1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(46)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	2 (4%)	2 (4%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(48)
LEUKEMIA,NOS	1 (2%)	2 (4%)	4 (8%)
MONOCYTIC LEUKEMIA	1 (2%)	1 (2%)	
*SUBCUT TISSUE	(49)	(50)	(48)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
#LIVER	(49)	(49)	(48)
LEUKEMIA,NOS			1 (2%)
CIRCULATORY SYSTEM			
#SPLEEN	(47)	(50)	(46)
HEMANGIOMA		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
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(48)
NEOPLASTIC NODULE		1 (2%)	2 (4%)
HEPATOCELLULAR CARCINOMA			1 (2%)
FIBROUS HISTIOCYTOMA, METASTATIC			1 (2%)
#PANCREAS	(47)	(50)	(46)
ADENOMA, NOS			1 (2%)
ADENOCARCINOMA, NOS			1 (2%)
ACINAR-CELL ADENOMA			1 (2%)
#STOMACH	(45)	(48)	(42)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
#COLON	(39)	(43)	(40)
ADENOMATOUS POLYP, NOS		1 (2%)	
LIPOMA	1 (3%)		
URINARY SYSTEM			
#KIDNEY	(48)	(50)	(48)
TUBULAR-CELL ADENOMA			1 (2%)
#URINARY BLADDER	(35)	(41)	(41)
TRANSITIONAL-CELL PAPILLOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(44)	(49)	(45)
ADENOMA, NOS	14 (32%)	6 (12%)	8 (18%)
#ADRENAL	(46)	(50)	(47)
PHEOCHROMOCYTOMA	2 (4%)	3 (6%)	
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)		
#THYROID	(42)	(48)	(44)
FOLLICULAR-CELL ADENOMA		1 (2%)	1 (2%)
C-CELL ADENOMA	3 (7%)	2 (4%)	3 (7%)
C-CELL CARCINOMA	1 (2%)	1 (2%)	
#PANCREATIC ISLETS	(47)	(50)	(46)
ISLET-CELL ADENOMA	1 (2%)	2 (4%)	

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ISLET-CELL CARCINOMA		1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(48)
FIBROMA		1 (2%)	
FIBROADENOMA		1 (2%)	
#PROSTATE	(40)	(40)	(34)
ADENOMA, NOS		3 (8%)	
#TESTIS	(49)	(49)	(48)
INTERSTITIAL-CELL TUMOR	37 (76%)	37 (76%)	37 (77%)
MESOTHELIOMA, NOS	1 (2%)		
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERITONEUM	(49)	(50)	(48)
MESOTHELIOMA, NOS		2 (4%)	2 (4%)
*TUNICA VAGINALIS	(49)	(50)	(48)
MESOTHELIOMA, NOS		1 (2%)	1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(50)	(48)
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
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	10	19
MORIBUND SACRIFICE	2	5	7
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED	14	10	3
TERMINAL SACRIFICE	29	25	21
ANIMAL MISSING			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	41	38	40
TOTAL PRIMARY TUMORS	71	71	72
TOTAL ANIMALS WITH BENIGN TUMORS	41	38	38
TOTAL BENIGN TUMORS	63	62	57
TOTAL ANIMALS WITH MALIGNANT TUMORS	7	6	10
TOTAL MALIGNANT TUMORS	7	6	10
TOTAL ANIMALS WITH SECONDARY TUMORS#			1
TOTAL SECONDARY TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	3	4
TOTAL UNCERTAIN TUMORS	1	3	5
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

* 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 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	49	46
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	49	46
INTEGUMENTARY SYSTEM			
*SKIN	(49)	(49)	(46)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
SQUAMOUS CELL CARCINOMA		2 (4%)	
*SUBCUT TISSUE	(49)	(49)	(46)
FIBROMA	1 (2%)	1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(47)	(46)
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)		
ALVEOLAR/BRONCHIOLAR CARCINOMA		1 (2%)	
FIBROSARCOMA	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(49)	(46)
MALIGNANT LYMPHOMA, NOS	1 (2%)		1 (2%)
LEUKEMIA,NOS	3 (6%)		
MYELOMONOCYTIC LEUKEMIA		1 (2%)	
LYMPHOCYTIC LEUKEMIA			2 (4%)
MONOCYTIC LEUKEMIA	2 (4%)	1 (2%)	1 (2%)
#LYMPH NODE	(35)	(38)	(27)
MALIGNANT LYMPHOMA, NOS			1 (4%)
#THYMUS	(2)	(8)	(5)
OSTEOSARCOMA		1 (13%)	
CIRCULATORY SYSTEM			
NONE			

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
#LIVER	(48)	(49)	(44)
NEOPLASTIC NODULE	1 (2%)		2 (5%)
#ESOPHAGUS	(42)	(45)	(42)
SQUAMOUS CELL CARCINOMA			1 (2%)
URINARY SYSTEM			
#KIDNEY	(49)	(47)	(46)
TUBULAR-CELL ADENOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(39)	(45)	(42)
CARCINOMA,NOS	1 (3%)		
ADENOMA, NOS	16 (41%)	16 (36%)	7 (17%)
ADENOCARCINOMA, NOS	1 (3%)		
#ADRENAL	(45)	(46)	(44)
CORTICAL ADENOMA		1 (2%)	1 (2%)
PHEOCHROMOCYTOMA	1 (2%)	1 (2%)	
#THYROID	(41)	(44)	(42)
FOLLICULAR-CELL ADENOMA		1 (2%)	1 (2%)
C-CELL ADENOMA	1 (2%)	3 (7%)	1 (2%)
#PARATHYROID	(31)	(26)	(29)
ADENOMA, NOS			1 (3%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(49)	(46)
ADENOMA, NOS	1 (2%)	1 (2%)	1 (2%)
ADENOCARCINOMA, NOS		1 (2%)	
FIBROMA	1 (2%)		
FIBROADENOMA	6 (12%)	15 (31%)	7 (15%)
CYSTFIBROADENOMA		1 (2%)	
*CLITORAL GLAND	(49)	(49)	(46)
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
#UTERUS	(44)	(47)	(42)
ADENOCARCINOMA, NOS			1 (2%)
LEIOMYOMA		1 (2%)	
LEIOMYOSARCOMA	1 (2%)		
ENDOMETRIAL STROMAL POLYP	6 (14%)	4 (9%)	3 (7%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(49)	(46)
SARCOMA, NOS	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	13	11	13
MORIBUND SACRIFICE	7	7	5
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED	2	5	8
TERMINAL SACRIFICE	28	27	24
ANIMAL MISSING			

@ 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*	33	31	21
TOTAL PRIMARY TUMORS	48	52	32
TOTAL ANIMALS WITH BENIGN TUMORS	27	29	16
TOTAL BENIGN TUMORS	35	44	23
TOTAL ANIMALS WITH MALIGNANT TUMORS	11	7	7
TOTAL MALIGNANT TUMORS	12	7	7
TOTAL ANIMALS WITH SECONDARY TUMORS#			
TOTAL SECONDARY TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	1	2
TOTAL UNCERTAIN TUMORS	1	1	2
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 A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

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	090	041	041	044	041	095	044	044	041	033	093	044	041	041	041	062	044	044	062	041	041	044	044	062
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	N	+	+	+	+	+	A	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+
FIBROMA				X										X											
FIBROUS HISTIOCYTOMA, MALIGNANT																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA				X												X									
ALVEOLAR/BRONCHIOLAR CARCINOMA					X																				
TRACHEA	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	-	+	+	A	+	+	-	+	+	+	+	+	+	+	-	-	-	+	+	+	+
THYMUS	-	-	-	-	-	-	+	A	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	-	+	+	A	+	+	+	+	+	-	+	+	+	-	+	-	+	+	-	+	-	+
STOMACH	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA														X											
SMALL INTESTINE	+	+	+	+	+	+	+	A	+	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	A	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+
LIPOMA																X									
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	-	-	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	-	-	+	-	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	A	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
ADENOMA, NOS	X			X	X	X										X	X						X	X	
ADRENAL	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+
PHEOCHROMOCYTOMA																									
PHEOCHROMOCYTOMA, MALIGNANT																X									
THYROID	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+
C-CELL ADENOMA									X										X						
C-CELL CARCINOMA																									
PARATHYROID	+	+	-	+	+	-	+	A	+	-	+	+	-	+	-	+	-	-	+	-	-	-	+	+	-	-
PANCREATIC ISLETS	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X		X	X			X	X	X	X	X	X	X	X	X				X		X	X	X	
MESOTHELIOMA, NOS																									
PROSTATE	-	+	+	-	+	+	+	A	+	+	+	+	-	+	+	+	+	-	+	-	+	+	+	-	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS												X													
MONOCYTIC LEUKEMIA																									

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

ANIMAL NUMBER	0212	0217	0228	0229	0301	0311	0312	0333	0334	0335	0336	0337	0338	0339	0401	0411	0412	0413	0414	0415	0416	0417	0418	0419	0501	TOTAL
WEEKS ON STUDY	1104	0891	1014	0907	0931	1004	0933	1004	1104	1004	0922	1004	0622	1004	1004	1004	0622	0622	1004	0622	0622	0622	1004	0888	0622	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	N	+	+	+	+	+	+	N	+	+	N	+	N	+	+	+	+	+	+	N	+	+	49*
FIBROMA																									2
FIBROUS HISTIOCYTOMA, MALIGNANT											X													X	2
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	•	49
ALVEOLAR/BRONCHIOLAR ADENOMA																									2
ALVEOLAR/BRONCHIOLAR CARCINOMA																									1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	47
LYMPH NODES	–	–	–	+	–	+	–	–	–	+	+	+	–	+	+	–	+	+	+	+	+	–	+	+	34
THYMUS	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	48
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
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	49*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	40
STOMACH	+	+	+	+	+	+	–	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	45
SQUAMOUS CELL PAPILLOMA																									1
SMALL INTESTINE	+	–	+	+	+	+	–	–	+	+	–	+	+	+	+	+	–	+	+	–	–	–	+	–	36
LARGE INTESTINE	+	–	+	+	+	–	–	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	–	39
LIPOMA																									1
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY BLADDER	+	–	+	–	+	+	–	–	–	+	+	+	+	+	–	+	•	+	–	+	+	+	+	–	35
ENDOCRINE SYSTEM																									
PITUITARY	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	44
ADENOMA, NOS		X			X		X		X						X					X					14
ADRENAL	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
PHEOCHROMOCYTOMA												X			X										2
PHEOCHROMOCYTOMA, MALIGNANT																									1
THYROID	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	42
C-CELL ADENOMA			X																						3
C-CELL CARCINOMA														X											1
PARATHYROID	–	–	–	+	–	+	–	–	–	–	+	+	+	+	+	–	–	–	+	+	+	–	+	+	24
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	47
ISLET-CELL ADENOMA			X																						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	49*
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X			X			X	X	X	37
MESOTHELIOMA, NOS		X																							1
PROSTATE	+	+	+	•	+	+	–	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	40
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
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	49*
LEUKEMIA,NOS																									1
MONOCYTIC LEUKEMIA		X																							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 A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

LOW DOSE

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	104	104	104	052	038	104	098	104	118	104	104	104	104	104	076	104	104	104	062	104	062	062	062	104	065
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+
FIBROMA															X										
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA	X					X																			
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA																									
LYMPH NODES	+	-	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
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	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-
ADENOMATOUS POLYP, NOS																								X	
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS						X										X								X	X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA											X							X						X	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
C-CELL ADENOMA			X								X														
C-CELL CARCINOMA																									
PARATHYROID	-	-	-	-	-	-	-	-	-	+	-	-	+	+	+	+	+	-	+	-	+	+	+	+	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA							X																		
ISLET-CELL CARCINOMA						X																			
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
FIBROMA																X									
FIBROADENOMA																									
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X			X	X	X			X	X	X	X	X	X	X	X		X	X		X		
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	
ADENOMA, NOS							X				X					X									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
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	X														X										
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS																									
MONOCYTIC LEUKEMIA																									

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

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 01	03 11	03 12	03 13	03 14	03 15	03 16	03 17	03 18	03 19	04 01	04 11	04 21	04 31	04 41	04 51	04 61	04 71	04 81	04 91	05 01	TOTAL
WEEKS ON STUDY	10 12	09 10	05 13	11 01	04 02	01 04	09 11	03 18	01 01	01 04	04 04	01 04	04 04	04 04	01 04	01 04	06 22	06 22	01 04	06 22	06 22	06 51	09 41	09 15	10 04	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	N	N	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	50M
FIBROMA																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	X																									1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																										2
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	•	+	+	•	+	+	•	+	−	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOMA																								X		1
LYMPH NODES	−	+	−	+	+	−	−	+	−	−	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	39
THYMUS	−	−	−	+	+	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	+		5
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
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	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	44
STOMACH	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	−	+	+	+	−	+	+	+	+	43
LARGE INTESTINE	+	+	+	+	+	+	−	+	+	+	+	•	+	+	+	+	−	+	+	+	−	+	+	+	+	43
ADENOMATOUS POLYP, NOS																										1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	−	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	−	+	41
ENDOCRINE SYSTEM																										
PITUITARY	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS											X				X											6
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA																										3
THYROID	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	48
FOLLICULAR-CELL ADENOMA				X																						1
C-CELL ADENOMA																										2
C-CELL CARCINOMA												X														1
PARATHYROID	−	+	+	−	+	+	−	−	+	−	+	−	+	−	+	−	−	+	+	−	−	+	+	−	+	25
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA						X																				2
ISLET-CELL CARCINOMA																										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	50M
FIBROMA		X																								1
FIBROADENOMA																										1
TESTIS	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR	X	X		X		X	X		X	X	X	X	X	X	X	X	X	X	X			X	X	X	X	37
PROSTATE	−	+	−	−	+	+	−	+	−	+	+	+	+	−	+	−	+	+	−	+	+	+	+	+	+	40
ADENOMA, NOS																										3
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BODY CAVITIES																										
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	50M
MESOTHELIOMA, NOS																										2
TUNICA VAGINALIS	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
MESOTHELIOMA, NOS														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
LEUKEMIA,NOS				X																				X		2
MONOCYTIC LEUKEMIA						X																				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 A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

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	110	051	104	069	081	041	097	091	121	041	041	041	381	041	041	001	041	091	041	050	041	097	091	061	104
INTEGUMENTARY SYSTEM																									
SKIN	+	A	+	+	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+
ADENOMA, NOS																									
SUBCUTANEOUS TISSUE	+	A	+	+	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+
FIBROMA														X											
FIBROUS HISTIOCYTOMA, MALIGNANT																X									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA						X		X																	
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	-	A	+	+	-	+	+	-	-	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	-
THYMUS	-	A	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	+	-
CIRCULATORY SYSTEM																									
HEART	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE			X																						
HEPATOCELLULAR CARCINOMA							X																		
FIBROUS HISTIOCYTOMA, METASTATIC																X									
LEUKEMIA,NOS																									
BILE DUCT	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
ADENOCARCINOMA, NOS																									
ACINAR-CELL ADENOMA																									
ESOPHAGUS	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+
STOMACH	+	A	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+
SMALL INTESTINE	+	A	+	+	+	+	-	+	+	+	+	-	-	+	+	+	-	+	+	-	+	+	+	+	+
LARGE INTESTINE	+	A	+	+	+	+	-	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA																									
URINARY BLADDER	-	A	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL PAPILLOMA							X																		
ENDOCRINE SYSTEM																									
PITUITARY	+	A	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS										X													X		
ADRENAL	+	A	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																					X				
C-CELL ADENOMA										X					X										
PARATHYROID	-	A	+	-	+	+	+	+	+	-	+	+	-	+	+	+	+	-	-	+	-	+	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	A	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	+	+	N	N
TESTIS	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X		X	X	X	X	X	X	X	X	X	X		X	X	X	X	X		X	X	X	X		X
PROSTATE	-	A	+	+	+	-	-	+	-	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
PERITONEUM	N	A	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	X											X													
TUNICA VAGINALIS	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS	X																								
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, MALIGNANT																			X						
LEUKEMIA,NOS				X	X																				

+: 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 A3. MALE 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
WEEKS ON STUDY	104	102	084	104	104	104	042	051	104	093	048	101	104	104	103	104	104	041	104	104	104	104	084	094	065	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	N	+	N	+	+	+	+	+	N	+	A	N	+	+	+	+	+	+	+	+	+	+	+	+	+	48*
ADENOMA, NOS						X																				1
SUBCUTANEOUS TISSUE	N	+	N	+	+	+	+	+	N	+	A	N	+	+	+	+	+	+	+	+	+	+	+	+	+	48*
FIBROMA																										1
FIBROUS HISTIOCYTOMA, MALIGNANT																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	46
ALVEOLAR/BRONCHIOLAR ADENOMA																X										2
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	-	+	+		45
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
LYMPH NODES	+	-	-	+	+	+	+	+	-	+	A	-	+	+	+	+	+	+	+	+	+	-	-	-	+	34
THYMUS	-	-	-	-	-	-	-	+	-	-	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NEOPLASTIC NODULE									X																	2
HEPATOCELLULAR CARCINOMA																										1
FIBROUS HISTIOCYTOMA, METASTATIC																										1
LEUKEMIA,NOS												X														1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	+	N			48*
PANCREAS	+	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ADENOMA, NOS																X										1
ADENOCARCINOMA, NOS																				X						1
ACINAR-CELL ADENOMA									X																	1
ESOPHAGUS	+	+	+	+	-	+	+	+	+	-	A	+	+	-	+	+	+	-	+	+	+	+	-	+	+	41
STOMACH	+	-	+	+	+	+	-	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	42
SMALL INTESTINE	+	-	+	+	+	+	-	+	+	-	A	+	+	+	-	+	+	-	+	+	+	+	+	+	+	38
LARGE INTESTINE	+	-	+	+	+	+	-	+	+	-	A	+	+	+	-	+	+	+	+	+	+	-	+	+	+	40
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
TUBULAR-CELL ADENOMA									X																	1
URINARY BLADDER	+	+	+	+	+	+	-	-	+	-	A	+	+	+	+	+	+	+	+	+	+	+	-	+		41
TRANSITIONAL-CELL PAPILLOMA																										1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	-	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
ADENOMA, NOS						X						X		X					X		X	X				8
ADRENAL	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
THYROID	+	+	+	+	+	+	-	+	+	-	A	+	+	+	+	+	+	-	+	+	+	+	+	+	+	44
FOLLICULAR-CELL ADENOMA																										1
C-CELL ADENOMA																				X						3
PARATHYROID	+	+	+	+	+	+	-	+	+	-	A	-	-	-	+	+	+	-	+	-	+	+	-	+	+	29
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	N	N	N	N	N	N	N	A	+	N	N	N	N	N	N	+	N	N	N	+	N	N	48*
TESTIS	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
INTERSTITIAL-CELL TUMOR	X	X		X	X	X			X			X	X	X	X	X	X		X	X			X	X	X	37
PROSTATE	+	+	+	-	+	+	+	+	+	-	A	+	+	+	+	+	-	+	-	-	+	-	+	+	-	34
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
MESOTHELIOMA, NOS																										2
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48*
MESOTHELIOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
MESOTHELIOMA, MALIGNANT																										1
LEUKEMIA,NOS			X							X																4

* 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 1,1,1,2–TETRACHLOROETHANE

VEHICLE CONTROL

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	101	090	104	088	078	104	085	101	101	104	104	101	102	104	097	021	104	104	102	098	060	104	091	104	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	I	+
SQUAMOUS CELL PAPILLOMA									X																
SUBCUTANEOUS TISSUE	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	I	+
FIBROMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	I	+
ALVEOLAR/BRONCHIOLAR ADENOMA										X															
FIBROSARCOMA													X												
TRACHEA	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	+	+	A	+	+	+	+	I	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	+	+	-
LYMPH NODES	+	+	-	+	+	-	+	+	+	+	+	-	+	-	+	+	+	A	+	+	-	-	+	+	-
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	-	+	-	-	
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
NEOPLASTIC NODULE	X																								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N
PANCREAS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	-
ESOPHAGUS	+	-	+	-	+	+	+	+	+	-	+	+	+	+	+	-	+	+	A	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	A	+	+	+	-	+	-
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	-	+	-	+	-
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	-	+	-	-	+	+	A	+	-	+	-	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	-	-	+	+	-	+	+	+	+	-	+	-	+	A	+	-	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	-	+	A	+	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS		X	X		X					X	X	X	X	X									X		
ADENOCARCINOMA, NOS																				X					
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	-	-
PHEOCHROMOCYTOMA						X																			
THYROID	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	+	+	A	+	-	+	+	+	+
C-CELL ADENOMA																									
PARATHYROID	+	+	+	-	+	+	+	+	+	-	-	-	-	+	+	-	-	+	A	+	-	+	-	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	N	N	N	+	+	+	N	+	+	+	N	N	N	+	N	A	N	N	+	+	N	+
ADENOMA, NOS																				X					
FIBROMA																									
FIBROADENOMA								X															X		X
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N
ADENOCARCINOMA, NOS																				X					
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	
LEIOMYOSARCOMA																									
ENDOMETRIAL STROMAL POLYP	X				X																				
OVARY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	-
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N
SARCOMA, NOS							X																		
MALIGNANT LYMPHOMA, NOS																									
LEUKEMIA,NOS					X																X				
MONOCYTIC LEUKEMIA																									

+: 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. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	104	083	103	089	085	089	096	104	104	104	104	104	092	104	106	104	104	104	102	090	104	104	091	104	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	N	+	+	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	49*
SQUAMOUS CELL PAPILLOMA																										1
SUBCUTANEOUS TISSUE	+	+	N	+	+	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	49*
FIBROMA																									X	1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
FIBROSARCOMA																										1
TRACHEA	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	-	+	+	42
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	45
LYMPH NODES	+	+	-	+	+	+	-	-	+	-	+	+	+	+	+	-	+	+	+	-	+	+	-	+	+	35
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	2
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	48
NEOPLASTIC NODULE																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	48
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	49*
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	45
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	-	+	+	42
STOMACH	+	+	-	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	41
SMALL INTESTINE	+	+	-	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	41
LARGE INTESTINE	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	38
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	40
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	-	+	-	+	+	+	+	-	+	+	+	-	-	+	+	+	+	-	+	+	+	+	39
CARCINOMA,NOS		X																								1
ADENOMA, NOS	X											X					X	X	X	X					X	16
ADENOCARCINOMA, NOS																										1
ADRENAL	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	45
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	-	+	41
C-CELL ADENOMA																									X	1
PARATHYROID	+	+	-	+	+	+	+	-	+	+	-	+	+	+	-	-	+	-	+	-	-	+	+	-	+	31
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	+	+	+	+	N	+	+	N	N	N	N	+	N	N	N	+	+	+	+	N	N	+	49*
ADENOMA, NOS																										1
FIBROMA				X																						1
FIBROADENOMA											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	49*
ADENOCARCINOMA, NOS																										1
UTERUS	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	-	+	+	44
LEIOMYOSARCOMA			X																							1
ENDOMETRIAL STROMAL POLYP				X			X						X						X							6
OVARY	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	44
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
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																										1
MALIGNANT LYMPHOMA, NOS																								X		1
LEUKEMIA,NOS																	X									3
MONOCYTIC LEUKEMIA					X							X														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 A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

LOW DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	076	075
WEEKS ON STUDY	104	104	091	102	091	104	104	104	090	104	104	050	104	104	104	092	097	104	050	091	083	077	104	080	098
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																	X								
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	-	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	-	-	+	+	+	-	+	-	+	+	+	+	-	+	+	+	+	+	-	+	-	-
THYMUS	-	+	-	-	-	-	-	-	+	-	-	+	-	-	-	+	-	-	-	-	-	-	+	-	-
OSTEOSARCOMA																							X		
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
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
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																					X				
C-CELL ADENOMA				X					X																
PARATHYROID	+	-	+	+	-	+	-	-	+	-	-	+	-	-	+	+	+	+	+	-	-	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+
ADENOMA, NOS																									
ADENOCARCINOMA, NOS	X	X				X				X	X					X								X	X
FIBROADENOMA		X																							
CYSTFIBROADENOMA																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
LEIOMYOMA							X																		
ENDOMETRIAL STROMAL POLYP					X											X									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MYELOMONOCYTIC LEUKEMIA																					X				
MONOCYTIC LEUKEMIA																									

+: 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. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	065	104	093	104	104	104	093	103	104	104	092	104	104	104	094	009	104	083	096	070	104	104	104	104	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49*
SQUAMOUS CELL CARCINOMA						X																				2
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49*
FIBROMA							X																			1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ALVEOLAR/BRONCHIOLAR CARCINOMA	X																									1
TRACHEA	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	45
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	-	+	+	+	+	A	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	46
SPLEEN	+	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LYMPH NODES	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	-	38
THYMUS	-	-	-	-	+	+	-	-	A	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	8
OSTEOSARCOMA																										1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
BILE DUCT	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
PANCREAS	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	47
ESOPHAGUS	-	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
STOMACH	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																										
KIDNEY	-	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY BLADDER	+	+	+	+	+	+	-	+	A	+	+	-	-	+	-	+	+	+	+	+	-	+	+	+	+	41
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	45
ADENOMA, NOS	X			X				X				X							X			X	X	X		16
ADRENAL	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	46
CORTICAL ADENOMA															X											1
PHEOCHROMOCYTOMA			X																							1
THYROID	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	44
FOLLICULAR-CELL ADENOMA																										1
C-CELL ADENOMA	X																									3
PARATHYROID	+	+	+	-	-	+	-	+	A	+	-	+	-	-	+	+	-	-	+	-	-	+	+	-	-	26
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	+	N	+	+	+	A	+	N	N	+	N	+	N	N	+	+	+	N	+	+	+	+	49*
ADENOMA, NOS				X																						1
ADENOCARCINOMA, NOS				X																						1
FIBROADENOMA	X					X	X	X												X		X		X		15
CYSTFIBROADENOMA																										1
UTERUS	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	47
LEIOMYOMA																										1
ENDOMETRIAL STROMAL POLYP																X								X		4
OVARY	+	+	+	+	+	+	+	+	A	+	●	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
MYELOMONOCYTIC LEUKEMIA																										1
MONOCYTIC LEUKEMIA																					X					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 1,1,1,2–TETRACHLOROETHANE

HIGH DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	091	101	084	041	104	062	078	096	104	044	104	104	021	104	104	094	041	085	052	097	104	104	097	104	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	A	A	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	–	+	–	+	+	A	A	–	+	–	–	+	+	–	–	–	+	+	+	–	+	–	+	–	+
MALIGNANT LYMPHOMA, NOS																							X		
THYMUS	–	–	–	–	–	A	A	–	–	+	–	–	+	–	–	–	–	+	+	–	–	–	–	–	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	A	A	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	–	A	A	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
BILE DUCT	+	+	+	+	–	A	A	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	A	A	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	A	A	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
STOMACH	+	+	+	+	+	A	A	–	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	A	A	–	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	A	A	–	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA																					X				
URINARY BLADDER	+	+	+	+	+	A	A	–	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	–	A	A	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
ADENOMA, NOS			X																	X	X	X			X
ADRENAL	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+
CORTICAL ADENOMA					X																				
THYROID	+	+	+	+	+	A	A	+	+	–	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+
FOLLICULAR-CELL ADENOMA																				X					
C-CELL ADENOMA																									
PARATHYROID	–	+	+	+	–	A	A	+	+	–	–	–	–	–	+	+	+	+	+	+	–	+	+	–	+
ADENOMA, NOS																				X					
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	+	+	+	A	A	N	N	N	N	N	N	+	+	+	+	+	N	+	+	+	N	N	N
ADENOMA, NOS					X																				
FIBROADENOMA																X	X			X					
UTERUS	+	+	+	+	+	A	A	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS															X										
ENDOMETRIAL STROMAL POLYP	X																								
OVARY	+	+	+	+	+	A	A	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	A	A	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	A	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																									X
LYMPHOCYTIC LEUKEMIA																		X							
MONOCYTIC LEUKEMIA																									

+: 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. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	0076	0077	0078	0079	0081	0082	0083	0084	0085	0086	0087	0088	0089	0090	0091	0092	0093	0094	0095	0096	0097	0098	0099	0100	TOTAL
WEEKS ON STUDY	1041	1044	0844	1040	0901	1041	1041	0841	0412	1041	0857	0151	0651	1041	0708	1041	1041	0981	0941	0717	1080	1041	1041	0718	0017	TISSUES TUMORS
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 46
TRACHEA	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 44
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 45
SPLEEN	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 45
LYMPH NODES	+	-	+	+	-	-	-	A	+	-	+	+	+	-	+	+	+	+	+	A	-	+	+	+	- 27
MALIGNANT LYMPHOMA, NOS																									1
THYMUS	-	-	-	-	-	-	-	A	-	-	-	-	-	-	-	-	-	-	-	A	-	-	-	-	- 5
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 46
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	+	+ 43
LIVER	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 44
NEOPLASTIC NODULE		X														X									2
BILE DUCT	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 44
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N 46*
PANCREAS	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 44
ESOPHAGUS	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	-	+	A	+	+	+	+	+ 42
SQUAMOUS CELL CARCINOMA		X																							1
STOMACH	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 43
SMALL INTESTINE	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 42
LARGE INTESTINE	+	+	+	+	+	+	+	A	+	+	+	+	+	-	+	+	+	+	+	A	+	+	+	+	+ 42
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 46
TUBULAR-CELL ADENOMA																									1
URINARY BLADDER	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	+	+ 42
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+	+	-	+	A	+	+	+	+	+ 42
ADENOMA, NOS			X																		X				7
ADRENAL	+	+	+	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	+	A	+	+	+	+	+ 44
CORTICAL ADENOMA																									1
THYROID	+	+	+	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	+	A	+	+	+	+	+ 42
FOLLICULAR-CELL ADENOMA																									1
C-CELL ADENOMA																						X			1
PARATHYROID	+	+	+	+	-	+	+	A	-	+	-	+	-	-	-	+	+	-	+	A	+	+	+	-	+ 29
ADENOMA, NOS																									1
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	N	A	+	N	+	+	+	+	+	+	+	+	N	A	+	+	N	N	N 46*
ADENOMA, NOS																									1
FIBROADENOMA	X	X	X			X																			7
UTERUS	+	+	-	+	+	+	-	A	+	+	+	+	+	-	+	+	+	+	+	A	+	+	+	+	+ 42
ADENOCARCINOMA, NOS																									1
ENDOMETRIAL STROMAL POLYP	X			X																					3
OVARY	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+ 44
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	A	+	+	*	+	+ 45
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N 46*
MALIGNANT LYMPHOMA, NOS																									1
LYMPHOCYTIC LEUKEMIA			X																						2
MONOCYTIC LEUKEMIA											X														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 B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	46	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	46	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(48)	(46)	(50)
SARCOMA, NOS	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(45)	(45)	(50)
HEPATOCELLULAR CARCINOMA, METAST	2 (4%)	1 (2%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	5 (11%)	5 (11%)	3 (6%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		
PAPILLARY ADENOCARCINOMA, METAST		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(48)	(46)	(50)
MALIGNANT LYMPHOMA, NOS	2 (4%)	2 (4%)	
LEUKEMIA,NOS	1 (2%)	1 (2%)	
#LYMPH NODE	(41)	(38)	(41)
MALIGNANT LYMPHOMA, NOS		1 (3%)	
MAST-CELL TUMOR	1 (2%)		
CIRCULATORY SYSTEM			
#SPLEEN	(45)	(42)	(48)
HEMANGIOMA	2 (4%)	1 (2%)	
HEMANGIOSARCOMA		1 (2%)	
#LIVER	(48)	(46)	(50)
HEMANGIOMA	1 (2%)		
HEMANGIOSARCOMA		2 (4%)	

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
#LIVER	(48)	(46)	(50)
HEPATOCELLULAR ADENOMA	6 (13%)	14 (30%)	21 (42%)
HEPATOCELLULAR CARCINOMA	12 (25%)	13 (28%)	6 (12%)
HEPATOBLASTOMA		1 (2%)	
#JEJUNUM	(39)	(36)	(38)
ADENOMATOUS POLYP, NOS		1 (3%)	
#COLON	(37)	(38)	(35)
LEIOMYOMA		1 (3%)	
URINARY SYSTEM			
#KIDNEY	(48)	(44)	(50)
TUBULAR-CELL ADENOMA	2 (4%)		
ENDOCRINE SYSTEM			
#ADRENAL	(45)	(43)	(50)
CORTICAL ADENOMA	1 (2%)	2 (5%)	
#THYROID	(32)	(35)	(47)
FOLLICULAR-CELL ADENOMA	1 (3%)	1 (3%)	
REPRODUCTIVE SYSTEM			
NONE			
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(48)	(46)	(50)
ADENOMA, NOS	1 (2%)		
PAPILLARY ADENOMA		1 (2%)	

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
PAPILLARY ADENOCARCINOMA		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*CRANIAL AND FACIAL B	(48)	(46)	(50)
OSTEOMA		1 (2%)	
BODY CAVITIES			
*PLEURA	(48)	(46)	(50)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	11	13	19
MORIBUND SACRIFICE	1	3	30
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	38	34	1
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	28	36	27
TOTAL PRIMARY TUMORS	37	49	30
TOTAL ANIMALS WITH BENIGN TUMORS	16	24	22
TOTAL BENIGN TUMORS	19	27	24
TOTAL ANIMALS WITH MALIGNANT TUMORS	14	18	6
TOTAL MALIGNANT TUMORS	17	22	6
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	2	
TOTAL SECONDARY TUMORS	3	2	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1		
TOTAL UNCERTAIN TUMORS	1		
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 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	47	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	47	48
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(47)	(48)
SARCOMA, NOS	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(46)	(48)
ALVEOLAR/BRONCHIOLAR ADENOMA		2 (4%)	
SARCOMA, NOS, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(47)	(48)
MALIGNANT LYMPHOMA, NOS	7 (14%)	4 (9%)	
LEUKEMIA,NOS		1 (2%)	
LYMPHOCYTIC LEUKEMIA	1 (2%)		
#SPLEEN	(49)	(44)	(47)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
#LIVER	(49)	(46)	(48)
MALIGNANT LYMPHOMA, NOS		2 (4%)	
CIRCULATORY SYSTEM			
*SUBCUT TISSUE	(50)	(47)	(48)
HEMANGIOSARCOMA	1 (2%)		
#SPLEEN	(49)	(44)	(47)
HEMANGIOMA	1 (2%)		
#LIVER	(49)	(46)	(48)
HEMANGIOMA	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
#OVARY	(49)	(42)	(42)
ANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(44)	(47)
ADENOMA, NOS	1 (2%)		
#LIVER	(49)	(46)	(48)
HEPATOCELLULAR ADENOMA	4 (8%)	8 (17%)	24 (50%)
HEPATOCELLULAR CARCINOMA	1 (2%)	5 (11%)	6 (13%)
#STOMACH	(45)	(41)	(44)
PAPILLOMA, NOS			1 (2%)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(49)	(46)	(48)
HEPATOCELLULAR CARCINOMA, METAST		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(43)	(41)	(40)
ADENOMA, NOS	4 (9%)	8 (20%)	
#THYROID	(41)	(40)	(42)
FOLLICULAR-CELL ADENOMA	1 (2%)	1 (3%)	
#PANCREATIC ISLETS	(47)	(46)	(47)
ISLET-CELL CARCINOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(47)	(48)
CARCINOMA,NOS	1 (2%)		
ADENOMA, NOS	1 (2%)		
#UTERUS	(50)	(43)	(41)
ENDOMETRIAL STROMAL POLYP	1 (2%)	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
#OVARY	(49)	(42)	(42)
GRANULOSA-CELL CARCINOMA	1 (2%)		
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(47)	(48)
SARCOMA, NOS		1 (2%)	
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(47)	(48)
SARCOMA, NOS	2 (4%)	2 (4%)	
LEIOMYOSARCOMA		1 (2%)	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	7	13	20
MORIBUND SACRIFICE	2	6	30
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	41	31	
ANIMAL MISSING			

@ 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*	25	31	30
TOTAL PRIMARY TUMORS	31	38	31
TOTAL ANIMALS WITH BENIGN TUMORS	12	18	24
TOTAL BENIGN TUMORS	14	21	25
TOTAL ANIMALS WITH MALIGNANT TUMORS	16	17	6
TOTAL MALIGNANT TUMORS	17	17	6
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	1	
TOTAL SECONDARY TUMORS	1	1	
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 B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

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	100	104	101	104	086	104	104	104	104	104	104	104	104	090	104	097	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE SARCOMA, NOS	+	+	+	+	+	N	+	+	+	+	+	+ X	+	+	+	+	N	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI HEPATOCELLULAR CARCINOMA, METASTA ALVEOLAR/BRONCHIOLAR ADENOMA ALVEOLAR/BRONCHIOLAR CARCINOMA	+	+	+ X	+	+	+	+	−	+ X	−	+	+	+	+	+ X	+	+	+	+ X	+	+	+	+ X	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	−	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+
SPLEEN HEMANGIOMA	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+
LYMPH NODES MAST-CELL TUMOR	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	−	+	+	+	+
THYMUS	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA HEMANGIOMA	+	+ X	+	+ X	+	+	+	+	+ X	+	+ X	+ X	+	+	+ X	+	+	+	+	+	+	+	+ X	+	+ X
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	+	+	+	+	+	+	N	N	+	+	N	+	+	N	+	+	+	N	N	N	N	+	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	
ESOPHAGUS	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	−	+	
STOMACH	+	+	+	+	+	−	+	+	+	+	+	+	+	+	−	+	−	+	+	+	−	+	+	+	
SMALL INTESTINE	+	+	+	+	+	−	+	+	+	+	+	+	+	+	−	+	−	+	−	+	−	+	+	+	
LARGE INTESTINE	+	+	+	+	+	−	+	+	+	+	+	−	+	+	−	+	−	+	−	−	+	+	+	+	
URINARY SYSTEM																									
KIDNEY TUBULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	−	+	+	+	+	−	+	+	−	+	+	+	−	+	+	−	−
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	−	−	−	+	+	−	+	+	+	−	+	+	+	−	+	+	+	
ADRENAL CORTICAL ADENOMA	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID FOLLICULAR-CELL ADENOMA	+	−	+	+	−	+	+	+	−	+	+	+	+	−	+	+	+	+	−	+	−	+ X	+	+	+
PARATHYROID	−	−	−	−	−	+	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	+	−	+	−
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	−	−	+	+	+	+	−	+	+	+	+	+	−	+	−	+	+	+	−	+	+	+	−
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND ADENOMA, 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
BODY CAVITIES																									
PLEURA HEPATOCELLULAR CARCINOMA, METASTA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS LEUKEMIA,NOS	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N

+: 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. MALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 30	03 31	03 32	03 33	03 34	03 35	03 36	03 37	03 38	03 39	04 40	04 41	04 42	04 43	04 44	04 45	04 46	04 47	04 48	04 49	05 01	TOTAL
WEEKS ON STUDY	10 4	10 4	10 4	10 4	10 4	09 9	10 4	08 8	10 4	08 4	08 4	10 4	07 9	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	10 4	06 3	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE SARCOMA, NOS	+	+	+	+	+	N	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	48* 1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI HEPATOCELLULAR CARCINOMA, METASTA ALVEOLAR/BRONCHIOLAR ADENOMA ALVEOLAR/BRONCHIOLAR CARCINOMA	+	+	+	+	+	+	+	A	+	+	+ X	+	+	+	+	+	+	+ X	+	+ X	+	−	A	+	+	45 2 5 1
TRACHEA	+	+	−	+	+	+	+	A	+	+	+	+	+	+	+	−	+	−	+	+	+	−	A	+	+	44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	−	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	46
SPLEEN HEMANGIOMA	+	+	+	+	+	+	+	A	+ X	+	+	+	+	+	+	+	+	+	−	+	+	+	A	+	+	45 2
LYMPH NODES MAST-CELL TUMOR	+	+	+	+	+	+	+	A	+	+	−	+	+	−	+	+	+	+	−	+	+	A	−	−		41 1
THYMUS	−	−	−	−	−	−	−	A	−	−	−	−	−	−	−	−	−	−	−	−	−	−	A	−	−	0
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	47
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	48
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA HEMANGIOMA	+ X	+	+ X	+ X	+	+	+ X	A	+	+ X X	+ X	+	+ X	+	+	+	+	+ X	+	+	+ X	+	A	+	+	48 6 12 1
BILE DUCT	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	48
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	+	+	A	+	+	N	+	N	+	N	+	+	+	+	+	+	+	A	+	+	48*
PANCREAS	+	+	+	+	+	+	+	A	+	+	+	+	−	+	+	+	+	+	+	+	+	+	A	+	+	45
ESOPHAGUS	+	+	−	+	−	+	+	A	+	+	+	+	+	+	+	−	−	−	+	+	+	−	A	+	+	39
STOMACH	+	+	+	+	+	+	+	A	+	+	+	+	−	+	+	+	+	+	+	+	+	−	A	+	−	41
SMALL INTESTINE	+	+	+	+	+	+	+	A	+	+	+	+	−	+	+	+	+	+	+	−	+	−	A	+	−	39
LARGE INTESTINE	+	+	+	+	+	+	+	A	−	+	+	+	−	+	+	+	+	+	+	+	−	A	+	−		37
URINARY SYSTEM																										
KIDNEY TUBULAR-CELL ADENOMA	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+ X	+	+	+ X	+	+	+	+	A	+	+	48 2
URINARY BLADDER	+	+	+	+	+	+	+	A	+	+	+	+	+	+	−	+	+	+	+	+	+	+	A	+	+	41
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	−	+	−	+	A	−	+	+	−	+	+	+	+	+	+	+	−	+	+	A	+	−	36
ADRENAL CORTICAL ADENOMA	+	+	+	+	+	+	+	A	+	+	+	+	+	+	−	+	+	+	+ X	+	+	+	A	+	+	45 1
THYROID FOLLICULAR-CELL ADENOMA	−	+	−	+	+	+	−	A	+	+	+	+	+	−	+	−	−	−	−	−	−	+	A	+	+	32 1
PARATHYROID	−	+	−	−	+	+	−	A	+	+	−	−	+	−	−	−	−	−	−	−	−	−	A	−	+	11
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	48*
TESTIS	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	48
PROSTATE	−	+	+	−	+	+	+	A	+	+	+	+	+	+	+	+	+	−	+	+	−	+	A	+	+	37
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	A	+	+	+	+	−	+	+	+	+	+	+	+	+	+	A	+	+	45
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND *ADENOMA, NOS*	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N X	N	48* 1
BODY CAVITIES																										
PLEURA HEPATOCELLULAR CARCINOMA, METASTA	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	48* 1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS LEUKEMIA,NOS	N	N	N	N	N	N	N	A	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	A	N	N	48* 2 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 B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

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	104	101	060	104	104	104	104	071	098	097	104	104	104	104	104	104	104	104	073	104	104	104	104	104	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									
ALVEOLAR/BRONCHIOLAR ADENOMA				X						X								X						
PAPILLARY ADENOCARCINOMA, METASTA										X															
TRACHEA	+	-	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	A	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	-	+
SPLEEN	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
HEMANGIOMA																									
HEMANGIOSARCOMA																									
LYMPH NODES	+	+	A	+	+	+	+	-	A	+	-	-	+	+	-	+	+	+	A	+	+	+	+	+	-
MALIGNANT LYMPHOMA, NOS																									
THYMUS	-	-	A	-	-	-	-	-	A	-	-	-	-	-	-	-	-	-	A	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
LIVER	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA	X						X				X	X		X	X							X			X
HEPATOCELLULAR CARCINOMA						X		X		X						X	X	X					X	X	
HEPATOBLASTOMA																									
HEMANGIOSARCOMA										X														X	
BILE DUCT	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	A	+	+	+	+	N	A	+	+	+	+	+	N	+	N	+	N	N	+	+	+	+	+
PANCREAS	+	+	A	-	+	+	+	+	A	+	+	+	-	+	+	+	+	+	A	+	+	+	+	+	+
ESOPHAGUS	+	-	A	+	+	+	+	+	A	+	+	+	-	+	-	+	+	+	A	+	+	+	+	+	+
STOMACH	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
SMALL INTESTINE	+	+	A	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
ADENOMATOUS POLYP, NOS																									
LARGE INTESTINE	+	+	A	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	A	+	+	+	+	+	+
LEIOMYOMA					X																				
URINARY SYSTEM																									
KIDNEY	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
URINARY BLADDER	+	+	A	+	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	A	+	-	+	+	-	A	+	+	+	+	+	+	+	+	-	A	+	+	+	-	+	+
ADRENAL	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	-	+	+	+	+	+
CORTICAL ADENOMA																X									
THYROID	+	-	A	+	+	-	-	-	A	+	+	+	+	-	+	+	+	+	A	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	-	-	A	-	-	-	-	-	A	-	-	+	-	-	-	-	+	-	A	-	-	-	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	A	N	N	N	N	N	A	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	A	+	+	+	+	-	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	A	+	+	+	+	-	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
NERVOUS SYSTEM																									
BRAIN	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLARY ADENOMA																				X					
PAPILLARY ADENOCARCINOMA										X															
MUSCULOSKELETAL SYSTEM																									
BONE	N	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOMA																					X				
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS							X																		
LEUKEMIA,NOS																									

+: 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. MALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 01	03 11	03 12	03 33	03 34	03 35	03 36	03 37	03 38	03 39	04 01	04 11	04 12	04 13	04 45	04 45	04 46	04 47	04 48	04 49	05 00	TOTAL TISSUES TUMORS
WEEKS ON STUDY	07 00	07 09	10 41	10 41	10 41	10 41	10 41	10 41	10 41	10 41	10 41	10 41	06 07	09 33	10 41	10 41	10 41	09 44	08 00	10 41	09 41	10 33	10 41	08 52	10 49	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	45
HEPATOCELLULAR CARCINOMA, METASTA										X										X						1
ALVEOLAR/BRONCHIOLAR ADENOMA																										5
PAPILLARY ADENOCARCINOMA, METASTA																										1
TRACHEA	+	-	+	-	+	+	+	+	+	+	+	-	+	-	+	+	+	A	-	+	A	+	+	-	+	38
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	43
SPLEEN	+	-	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	42
HEMANGIOMA	X																									1
HEMANGIOSARCOMA														X												1
LYMPH NODES	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	-	+	+	38
MALIGNANT LYMPHOMA, NOS																				X						1
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	A	-	-	-	-	0
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+	A	+	+	+	+	45
DIGESTIVE SYSTEM																										
SALIVARY GLAND	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	44
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	46
HEPATOCELLULAR ADENOMA	X		X		X				X		X						X									14
HEPATOCELLULAR CARCINOMA				X						X			X	X					X							13
HEPATOBLASTOMA															X											1
HEMANGIOSARCOMA																										2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	46
GALLBLADDER & COMMON BILE DUCT	N	N	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	A	+	+	A	N	+	N	N	46*
PANCREAS	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	A	+	+	+	+	41
ESOPHAGUS	+	+	+	-	+	+	-	+	+	+	+	-	+	-	+	+	+	A	-	+	A	+	+	+	+	37
STOMACH	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	-	+	-	+	42
SMALL INTESTINE	-	-	+	+	+	+	+	-	+	+	+	+	-	-	+	+	-	A	+	+	A	-	+	-	+	36
ADENOMATOUS POLYP, NOS											X															1
LARGE INTESTINE	-	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	A	-	+	A	-	+	-	+	38
LEIOMYOMA																										1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	44
URINARY BLADDER	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	44
ENDOCRINE SYSTEM																										
PITUITARY	+	-	-	-	+	-	+	-	+	+	+	+	+	+	+	+	+	A	+	-	A	+	-	-	-	32
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	-	+	+	+	43
CORTICAL ADENOMA							X																			2
THYROID	+	+	+	-	-	+	+	+	+	+	+	-	+	-	+	+	+	A	+	-	A	+	+	+	+	35
FOLLICULAR-CELL ADENOMA																			X							1
PARATHYROID	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	A	+	-	A	-	-	-	+	7
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	A	+	N	A	N	N	+	N	46*
TESTIS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	43
PROSTATE	-	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	A	+	+	A	+	+	-	+	39
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	-	+	44
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	A	N	N	N	N	46*
PAPILLARY ADENOMA																										1
PAPILLARY ADENOCARCINOMA																										1
MUSCULOSKELETAL SYSTEM																										
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	A	N	N	N	N	46*
OSTEOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	A	N	N	N	N	46*
MALIGNANT LYMPHOMA, NOS																								X		2
LEUKEMIA,NOS		X																								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 B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

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	052	065	065	053	035	065	065	052	065	052	053	065	065	065	065	065	065	064	065	065	065	065	065	048	065
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																				X					
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+
THYMUS	-	-	-	-	-	-	-	-	+	-	-	+	+	-	-	-	+	-	-	-	+	-	+	-	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA		X				X	X		X			X			X		X		X	X		X	X		
HEPATOCELLULAR CARCINOMA																		X							
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	N	+	+	+	+	N	+	+	N	+	+	N	+	N	N	+	+	+	+	+
PANCREAS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	-	-	+	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	-	-	+	+	+	+	-	-	+	-	+	+	+	+	-	-	+	+	+	+	-	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	-	+	+	+	-	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	+	-	-	-	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	-	+	-	-	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
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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. MALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	0262	0277	0288	0299	0310	0311	0323	0334	0345	0356	0367	0378	0391	0400	0411	0423	0434	0445	0456	0467	0478	0489	0501	TOTAL
WEEKS ON STUDY	0512	0591	0665	0665	0665	0665	0665	0448	0418	0486	0665	0633	0655	0552	0665	0665	0665	0653	0473	0448	0556	0513	0555	TISSUES TUMORS
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA				X															X					3
TRACHEA	+	+	+	●	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	48
LYMPH NODES	-	+	-	+	+	+	+	-	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	41
THYMUS	-	+	-	-	+	+	-	-	-	-	-	-	+	-	+	-	-	-	-	-	+	-	-	14
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA	X			X		X	X		X		X	X			X		X		X		X			21
HEPATOCELLULAR CARCINOMA														X				X		X	X		X	6
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	+	+	N	N	N	+	+	+	N	+	N	+	N	+	+	N	+	+	N	N	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	48
ESOPHAGUS	+	-	+	+	+	+	+	+	+	-	+	+	+	-	+	-	-	+	+	+	+	+	+	42
STOMACH	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	-	44
SMALL INTESTINE	+	-	+	+	+	+	+	+	+	+	-	-	+	-	-	+	+	-	+	+	+	+	-	38
LARGE INTESTINE	+	-	+	+	+	+	+	●	+	+	+	-	+	-	-	+	+	-	+	+	+	-	+	35
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	+	+	+	+	43
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	-	-	+	+	-	40
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	47
PARATHYROID	-	+	-	-	-	+	-	-	-	+	-	-	-	+	-	+	-	-	-	+	+	-	-	14
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
TESTIS	+	+	+	●	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PROSTATE	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	-	+	+	+	+	+	-	40
NERVOUS SYSTEM																								
BRAIN	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	47

* 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 1,1,1,2–TETRACHLOROETHANE

VEHICLE CONTROL

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	104	104	104	077	104	104	093	093	104	104	104	094	104	104	104	104	104	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+
SARCOMA, NOS																									
HEMANGIOSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS, METASTATIC																									
TRACHEA	+	+	+	+	+	+	−	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA																						X			
MALIGNANT LYMPHOMA, NOS																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	−	+	−	+	−	+	+	−	−
THYMUS	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+
ADENOMA, NOS																X									
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA							X												X						
HEPATOCELLULAR CARCINOMA		X																							
HEMANGIOMA																									
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	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	−
ADENOMA, NOS															X										
ADRENAL	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	−	+	+	+	+	+	−	+	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+	−	+
FOLLICULAR-CELL ADENOMA																X									
PARATHYROID	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−	−	−	−	−	−	−	−	+	−	−
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	N	+	+	+	+	+	N	N	+	N	+	+	N	+	+	+	+	N	N	N	N	N
CARCINOMA,NOS									X																
ADENOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
GRANULOSA-CELL CARCINOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS						X				X		X				X									
MALIGNANT LYMPHOMA, NOS																									
LYMPHOCYTIC LEUKEMIA				X																					

+: 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. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	07 16	07 17	07 18	07 19	08 01	08 11	08 12	08 13	08 14	08 15	08 16	08 17	08 18	08 19	09 01	09 11	09 23	09 34	09 45	09 56	09 67	09 78	09 91	10 02	TOTAL TISSUES TUMORS
WEEKS ON STUDY	11 00	10 04	10 04	10 04	10 04	10 04	11 01	08 89	10 04	10 04	10 04	10 04	10 04	10 04	10 04	10 04	10 04	10 04	05 04	10 04	10 04	10 04	10 04	10 04	
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS	X																								1
HEMANGIOSARCOMA								X																	1
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SARCOMA, NOS, METASTATIC	X																								1
TRACHEA	+	+	+	-	-	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	42
HEMATOPOIETIC SYSTEM																									
BONE MARROW	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMANGIOMA																									1
MALIGNANT LYMPHOMA, NOS																								X	1
LYMPH NODES	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	+	+	+	-	+	+	+	41
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS																									1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
HEPATOCELLULAR ADENOMA											X				X										4
HEPATOCELLULAR CARCINOMA																	X								1
HEMANGIOMA																									1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	N	N	+	N	+	+	+	+	+	+	+	N	N	+	+	+	+	+	50M
PANCREAS	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	44
STOMACH	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
SMALL INTESTINE	+	-	+	+	-	+	-	-	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	41
LARGE INTESTINE	+	+	+	+	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	42
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	-	+	+	+	-	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	40
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	-	-	+	+	43
ADENOMA, NOS											X	X						X							4
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	47
THYROID	+	-	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	41
FOLLICULAR-CELL ADENOMA																									1
PARATHYROID	-	-	+	-	-	-	-	+	-	+	-	-	-	-	+	-	-	+	-	-	-	-	-	+	8
PANCREATIC ISLETS	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ISLET-CELL CARCINOMA		X																							1
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	N	+	N	50M
CARCINOMA,NOS					X																				1
ADENOMA, NOS																									1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP																						X			1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GRANULOSA-CELL CARCINOMA												X													1
NERVOUS SYSTEM																									
BRAIN	-	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	46
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	50M
SARCOMA, NOS							X	X																X	2
MALIGNANT LYMPHOMA, NOS						X									X								X		7
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 1,1,1,2–TETRACHLOROETHANE

LOW DOSE

ANIMAL NUMBER	0511	0512	0513	0514	0515	0516	0517	0518	0519	0601	0611	0612	0613	0614	0615	0616	0617	0618	0619	0701	0711	0712	0713	0714	0715
WEEKS ON STUDY	1104	1104	0909	1103	1104	1104	0904	0905	1104	0902	0904	0602	0401	0801	1004	0904	0905	0104	1004	1004	0608	1103	0804	1104	1004
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA	+	+	+	A	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	A	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	–	–	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
SPLEEN	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	–
LYMPH NODES	+	+	+	A	+	–	+	+	–	+	–	+	+	+	+	+	+	+	+	+	–	+	–	+	
THYMUS	–	–	–	A	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	+	–	–	–	–	–
CIRCULATORY SYSTEM																									
HEART	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	A	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA MALIGNANT LYMPHOMA, NOS	+	+ X	+ X	A	+	+ X	+ X	+ X	+	+	+	+	+	+	+	+ X	+	+ X	+ X	+	+ X	+	+	+	+
BILE DUCT	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+
PANCREAS	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
ESOPHAGUS	+	+	+	A	+	–	–	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	–	–
STOMACH SQUAMOUS CELL PAPILLOMA	+	+	+	A	+	+	+	+	+	+	–	+ X	–	+	+	+	+	+	+	–	–	+	+	+	+
SMALL INTESTINE	+	+	+	A	+	+	+	–	+	–	+	–	+	–	+	+	+	+	–	+	–	–	+	+	+
LARGE INTESTINE	+	+	+	A	+	+	+	+	+	–	+	–	+	–	+	–	+	+	+	+	–	–	–	+	+
URINARY SYSTEM																									
KIDNEY HEPATOCELLULAR CARCINOMA, METASTA	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS	+ X	+	+	A	+	+	+ X	+	–	+	+	+	–	+	+ X	+	+ X	–	+	+	+	+	+	+ X	+
ADRENAL	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID FOLLICULAR-CELL ADENOMA	+	+	+	A	+	+	–	+	+	+	+	+	+	+ X	–	+	+	+	+	–	+	+	–	+	
PARATHYROID	–	–	+	A	–	–	–	–	–	+	–	–	–	+	–	+	–	–	–	+	–	–	–	–	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	A	+	+	N	N	N	+	+	N	+	N	N	N	+	+	N	N	+	N	N	+	N
UTERUS ENDOMETRIAL STROMAL POLYP	+	+	+	A	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	–	–	+	+	+
OVARY ANGIOSARCOMA	+ X	+	–	A	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	–
NERVOUS SYSTEM																									
BRAIN	+	+	+	A	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
MUSCLE SARCOMA, NOS	N	N	N	A	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 SARCOMA, NOS LEIOMYOSARCOMA MALIGNANT LYMPHOMA, NOS LEUKEMIA,NOS	N	N	N	A	N X	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N X	N	N	N

+: 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. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	0176	0778	0791	0801	0811	0821	0834	0844	0855	0866	0878	0881	0894	0901	0911	0922	0933	0944	0955	0966	0977	0988	0991	1000	TOTAL
WEEKS ON STUDY	1004	1018	1044	0996	1004	0675	1041	1004	1004	0903	1081	1046	1044	1041	1041	1044	1044	1044	1044	1044	1010	0717	1044	0984	1014	TISSUES TUMORS
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	A	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ALVEOLAR/BRONCHIOLAR ADENOMA									X																2
TRACHEA	+	A	+	+	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	39
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	A	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
SPLEEN	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
LYMPH NODES	+	A	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	40
THYMUS	-	A	-	-	-	-	A	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	2
CIRCULATORY SYSTEM																									
HEART	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
DIGESTIVE SYSTEM																									
SALIVARY GLAND	-	A	+	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	44
LIVER	+	A	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	46
HEPATOCELLULAR ADENOMA									X																8
HEPATOCELLULAR CARCINOMA																			X				X	X	5
MALIGNANT LYMPHOMA, NOS																X								X	2
BILE DUCT	+	A	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	46
GALLBLADDER & COMMON BILE DUCT	+	A	N	N	+	+	A	+	+	+	+	+	+	+	N	N	+	+	+	N	N	N	+	+	47*
PANCREAS	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ESOPHAGUS	+	A	-	+	+	+	A	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	38
STOMACH	+	A	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
SQUAMOUS CELL PAPILLOMA																									1
SMALL INTESTINE	+	A	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
LARGE INTESTINE	+	A	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
URINARY SYSTEM																									
KIDNEY	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	46
HEPATOCELLULAR CARCINOMA, METASTA																									1
URINARY BLADDER	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
ENDOCRINE SYSTEM																									
PITUITARY	+	A	+	-	+	+	A	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	41
ADENOMA, NOS										X							X		X						8
ADRENAL	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
THYROID	+	A	+	-	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	40
FOLLICULAR-CELL ADENOMA																									1
PARATHYROID	-	A	-	-	-	+	A	-	-	+	-	+	+	+	-	-	+	-	+	+	-	+	-	+	16
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	A	N	N	+	N	A	+	N	+	+	N	N	N	N	+	N	+	+	N	N	+	N	+	47*
UTERUS	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
ENDOMETRIAL STROMAL POLYP														X											1
OVARY	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
ANGIOSARCOMA																									1
NERVOUS SYSTEM																									
BRAIN	+	A	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
MUSCULOSKELETAL SYSTEM																									
MUSCLE	N	A	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	47*
SARCOMA, NOS																							X		1
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	A	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	47*
SARCOMA, NOS																				X					2
LEIOMYOSARCOMA												X													1
MALIGNANT LYMPHOMA, NOS	X									X											X				4
LEUKEMIA,NOS																									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 B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF 1,1,1,2–TETRACHLOROETHANE

HIGH DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	065	065	061	061	065	065	061	061	052	065	065	065	034	053	061	065	010	065	041	061	065	065	065	063	065
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
TRACHEA	+	-	+	+	+	+	+	+	-	+	+	+	-	+	+	+	A	+	+	+	+	-	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+
LYMPH NODES	+	-	+	+	+	+	+	+	-	+	-	+	+	-	+	+	A	+	+	+	+	+	-	+	+
THYMUS	-	-	+	+	-	+	+	-	-	-	-	-	-	-	-	-	A	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA	X	X		X	X			X	X	X	X				X	X		X			X	X	X		
HEPATOCELLULAR CARCINOMA																									X
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	+	+	+	+	N	+	N	N	N	N	N	N	N	N	A	+	+	+	+	+	+	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+
ESOPHAGUS	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	-
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	A	+	-	+	+	+	+	+	+
PAPILLOMA, NOS																									
SMALL INTESTINE	+	+	-	+	+	+	+	+	-	+	-	-	-	-	-	-	A	+	-	+	-	-	+	-	+
LARGE INTESTINE	+	+	-	+	+	+	+	+	-	+	-	+	-	-	+	-	A	+	-	-	+	+	+	-	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	A	+	+	+	+	-	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	-	-	-	+	+	A	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	A	+	+	+	+	+	+	-	+
THYROID	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+
PARATHYROID	-	-	+	+	+	-	+	-	+	+	-	+	-	-	+	-	A	+	+	-	-	-	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	+	+	+	+	+	N	N	+	N	N	N	N	N	A	+	+	+	+	N	+	N	+
UTERUS	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	A	+	-	+	+	+	+	+	+
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	A	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	A	+	+	+	+	+	+	+	+

+: 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. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	065	052	065	065	052	051	013	065	053	053	065	065	065	051	065	065	065	052	065	065	065	065	065	051	065	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
TRACHEA	+	+	+	+	+	+	A	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	-	+	+	41
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	-	+	+	+	+	-	A	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	-	+	38
THYMUS	-	-	-	+	-	-	A	-	-	-	-	-	-	+	+	+	-	-	+	-	+	-	-	-	-	10
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	A	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEPATOCELLULAR ADENOMA				X	X	X		X			X						X	X				X	X		X	24
HEPATOCELLULAR CARCINOMA									X			X	X								X			X		6
BILE DUCT	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
GALLBLADDER & COMMON BILE DUCT	N	N	N	+	+	+	A	+	+	+	N	+	N	+	+	N	+	+	+	+	+	+	+	+	N	48*
PANCREAS	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	A	+	+	+	+	-	+	+	+	-	+	+	+	+	+	-	+	-	-	40
STOMACH	-	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
PAPILLOMA, NOS						X																				1
SMALL INTESTINE	-	+	+	-	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	32
LARGE INTESTINE	-	+	+	-	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	36
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY BLADDER	-	+	+	+	+	+	A	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	42
ENDOCRINE SYSTEM																										
PITUITARY	+	-	-	+	+	-	A	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	40
ADRENAL	+	+	+	+	+	+	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	45
THYROID	+	+	+	+	+	+	A	+	+	+	+	-	+	+	+	-	+	+	-	+	+	-	+	+	+	42
PARATHYROID	+	+	-	-	-	-	A	-	-	+	+	-	-	+	+	-	+	-	-	+	-	-	-	-	-	20
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	+	+	N	+	A	+	+	N	N	N	+	N	N	N	+	N	+	N	N	N	+	N	+	48*
UTERUS	+	+	+	+	+	+	A	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	-	+	+	41
OVARY	+	+	+	+	+	+	A	+	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	-	+	42
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46

* 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 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	48
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
#TRACHEA	(47)	(48)	(45)
INFLAMMATION, CHRONIC			1 (2%)
#LUNG/BRONCHUS	(49)	(50)	(46)
BRONCHIECTASIS		1 (2%)	
#LUNG	(49)	(50)	(46)
EMPHYSEMA, NOS	1 (2%)		
EMPHYSEMA, ALVEOLAR	2 (4%)	11 (22%)	6 (13%)
CONGESTION, NOS	1 (2%)		
HEMORRHAGE	2 (4%)	2 (4%)	
INFLAMMATION, INTERSTITIAL	1 (2%)	3 (6%)	1 (2%)
PNEUMONIA INTERSTITIAL CHRONIC		1 (2%)	
INFLAMMATION, GRANULOMATOUS	2 (4%)		
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM			1 (2%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(47)	(50)	(46)
CONGESTION, NOS		3 (6%)	1 (2%)
INFARCT, NOS	1 (2%)		
HYPERPLASIA, LYMPHOID		1 (2%)	1 (2%)
CIRCULATORY SYSTEM			
#HEART	(48)	(50)	(48)
INFLAMMATION, INTERSTITIAL			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
FIBROSIS, FOCAL		1 (2%)	
PERIARTERITIS	1 (2%)		
#HEART/ATRIUM	(48)	(50)	(48)
INFLAMMATION, FOCAL		1 (2%)	
#MYOCARDIUM	(48)	(50)	(48)
INFLAMMATION, INTERSTITIAL			1 (2%)
#PANCREAS	(47)	(50)	(46)
PERIARTERITIS		1 (2%)	
ARTERIOSCLEROSIS, NOS			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(48)
INFLAMMATION, MULTIFOCAL		1 (2%)	
INFLAMMATION, DIFFUSE		1 (2%)	
NECROSIS, NOS		1 (2%)	
NECROSIS, FOCAL		2 (4%)	
METAMORPHOSIS FATTY	5 (10%)	6 (12%)	10 (21%)
CYTOPLASMIC CHANGE, NOS			2 (4%)
BASOPHILIC CYTO CHANGE			1 (2%)
CLEAR-CELL CHANGE		6 (12%)	2 (4%)
HEPATOCYTOMEGALY			1 (2%)
#BILE DUCT	(49)	(49)	(48)
HYPERPLASIA, NOS	19 (39%)	4 (8%)	8 (17%)
HYPERPLASIA, FOCAL			1 (2%)
#PANCREATIC ACINUS	(47)	(50)	(46)
ATROPHY, FOCAL	1 (2%)	4 (8%)	5 (11%)
HYPERPLASIA, FOCAL			1 (2%)
#ESOPHAGUS	(40)	(44)	(41)
DISTENTION			1 (2%)
#STOMACH	(45)	(48)	(42)
ULCER, NOS			1 (2%)
EROSION		1 (2%)	
HYPERPLASIA, EPITHELIAL	1 (2%)		
HYPERPLASIA, BASAL CELL		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(48)	(50)	(48)
MINERALIZATION	12 (25%)	19 (38%)	26 (54%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CAST, NOS		6 (12%)	1 (2%)
PYELONEPHRITIS, NOS		1 (2%)	
INFLAMMATION, CHRONIC	12 (25%)	7 (14%)	20 (42%)
NEPHROSIS, NOS		1 (2%)	
HEMOSIDEROSIS			1 (2%)
#KIDNEY/PELVIS	(48)	(50)	(48)
INFLAMMATION, CHRONIC		1 (2%)	
• HYPERPLASIA, EPITHELIAL		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(44)	(49)	(45)
CYST, NOS	1 (2%)	5 (10%)	1 (2%)
HYPERPLASIA, CHROMOPHOBE-CELL		1 (2%)	
ANGIECTASIS		2 (4%)	4 (9%)
#ADRENAL	(46)	(50)	(47)
ANGIECTASIS		2 (4%)	
#ADRENAL MEDULLA	(46)	(50)	(47)
HYPERPLASIA, NOS		1 (2%)	
#THYROID	(42)	(48)	(44)
FOLLICULAR CYST, NOS		1 (2%)	
HYPERPLASIA, C-CELL	2 (5%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(48)
HYPERPLASIA, NOS			3 (6%)
LACTATION			1 (2%)
#PROSTATE	(40)	(40)	(34)
INFLAMMATION, ACUTE			1 (3%)
INFLAMMATION, CHRONIC	1 (3%)		
ATROPHY, NOS			1 (3%)
#TESTIS	(49)	(49)	(48)
ATROPHY, NOS	5 (10%)	2 (4%)	3 (6%)
NERVOUS SYSTEM			
#BRAIN	(48)	(50)	(48)
HEMORRHAGE		1 (2%)	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
NECROSIS, FOCAL		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE/CRYSTALLINE LENS	(49)	(50)	(48)
MINERALIZATION	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*THORACIC CAVITY	(49)	(50)	(48)
INFLAMMATION, CHRONIC	1 (2%)		
*ABDOMINAL CAVITY	(49)	(50)	(48)
LIPOGRANULOMA		1 (2%)	
*DIAPHRAGMATIC PLEURA	(49)	(50)	(48)
INFLAMMATION, NOS	1 (2%)		
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	6	3	3
AUTOLYSIS/NO NECROPSY	1		2

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

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	49	46
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	49	46
INTEGUMENTARY SYSTEM			
*SKIN	(49)	(49)	(46)
ABSCESS, NOS			1 (2%)
RESPIRATORY SYSTEM			
#TRACHEA	(42)	(45)	(44)
HEMORRHAGE		1 (2%)	
INFLAMMATION, CHRONIC			1 (2%)
#LUNG	(49)	(47)	(46)
EMPHYSEMA, ALVEOLAR	5 (10%)	9 (19%)	12 (26%)
HEMORRHAGE	2 (4%)	4 (9%)	
INFLAMMATION, NOS	1 (2%)	2 (4%)	
INFLAMMATION, FOCAL	1 (2%)	2 (4%)	1 (2%)
INFLAMMATION, INTERSTITIAL	1 (2%)	2 (4%)	
INFLAMMATION, ACUTE FOCAL			1 (2%)
ABSCESS, NOS	1 (2%)		
INFLAMMATION, GRANULOMATOUS	3 (6%)		
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(45)	(48)	(45)
CONGESTION, NOS	1 (2%)		1 (2%)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, LYMPHOID		1 (2%)	
#LIVER	(48)	(49)	(44)
HEMATOPOIESIS	1 (2%)		
CIRCULATORY SYSTEM			
#MYOCARDIUM	(48)	(49)	(46)
DEGENERATION, NOS	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
DIGESTIVE SYSTEM			
#LIVER	(48)	(49)	(44)
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, GRANULOMATOUS			1 (2%)
NECROSIS, NOS		1 (2%)	
NECROSIS, FOCAL	1 (2%)	1 (2%)	1 (2%)
METAMORPHOSIS FATTY	3 (6%)	1 (2%)	7 (16%)
BASOPHILIC CYTO CHANGE		1 (2%)	1 (2%)
CLEAR-CELL CHANGE		3 (6%)	9 (20%)
CYTOLOGIC ALTERATION, NOS			2 (5%)
ANGIECTASIS	1 (2%)		
#BILE DUCT	(48)	(49)	(44)
FIBROSIS	1 (2%)		
HYPERPLASIA, NOS	6 (13%)	3 (6%)	5 (11%)
#PANCREAS	(45)	(47)	(44)
FIBROSIS			1 (2%)
#PANCREATIC ACINUS	(45)	(47)	(44)
ATROPHY, NOS			1 (2%)
ATROPHY, FOCAL	1 (2%)		
#STOMACH	(41)	(48)	(43)
ULCER, NOS	1 (2%)	1 (2%)	
#GASTRIC SUBMUCOSA	(41)	(48)	(43)
EDEMA, NOS			1 (2%)
URINARY SYSTEM			
#KIDNEY	(49)	(47)	(46)
HAMARTOMA			1 (2%)
PYELONEPHRITIS, ACUTE	1 (2%)		
INFLAMMATION, CHRONIC		1 (2%)	
INFARCT, NOS			1 (2%)
HEMOSIDEROSIS		1 (2%)	
#KIDNEY/PELVIS	(49)	(47)	(46)
HYPERPLASIA, EPITHELIAL	1 (2%)		
METAPLASIA, NOS		1 (2%)	
#URINARY BLADDER	(40)	(41)	(42)
INFLAMMATION, NOS	1 (3%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, EPITHELIAL	1 (3%)		
ENDOCRINE SYSTEM			
#PITUITARY	(39)	(45)	(42)
CYST, NOS	1 (3%)	1 (2%)	1 (2%)
MULTIPLE CYSTS		1 (2%)	1 (2%)
ANGIECTASIS	3 (8%)	2 (4%)	5 (12%)
#ADRENAL	(45)	(46)	(44)
METAMORPHOSIS FATTY	1 (2%)		
ANGIECTASIS		1 (2%)	1 (2%)
#THYROID	(41)	(44)	(42)
FOLLICULAR CYST, NOS			1 (2%)
HYPERPLASIA, C-CELL		3 (7%)	
#PANCREATIC ISLETS	(45)	(47)	(44)
ATROPHY, NOS			1 (2%)
HYPERPLASIA, FOCAL		1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(49)	(46)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, CYSTIC	4 (8%)	1 (2%)	4 (9%)
LACTATION	7 (14%)	14 (29%)	2 (4%)
#UTERUS	(44)	(47)	(42)
HYDROMETRA	2 (5%)	3 (6%)	1 (2%)
CYST, NOS			1 (2%)
#UTERUS/ENDOMETRIUM	(44)	(47)	(42)
INFLAMMATION, NOS		1 (2%)	
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, CYSTIC		5 (11%)	1 (2%)
#OVARY	(44)	(48)	(44)
CYST, NOS		1 (2%)	
NERVOUS SYSTEM			
#CEREBRAL VENTRICLE	(48)	(49)	(45)
HEMORRHAGE		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
INFLAMMATION, NOS	1 (2%)		
#BRAIN	(48)	(49)	(45)
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, CHRONIC DIFFUSE	1 (2%)		
NECROSIS, NOS		1 (2%)	
INFARCT HEMORRHAGIC	1 (2%)		
*SPINAL CORD	(49)	(49)	(46)
HEMORRHAGE		1 (2%)	
NECROSIS, NOS		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE/CORNEA	(49)	(49)	(46)
DEGENERATION, NOS			1 (2%)
*EYE/CRYSTALLINE LENS	(49)	(49)	(46)
MINERALIZATION	1 (2%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
*ABDOMINAL MUSCLE	(49)	(49)	(46)
HEMORRHAGE			1 (2%)
BODY CAVITIES			
*PLEURA	(49)	(49)	(46)
INFLAMMATION, FOCAL		1 (2%)	
INFLAMMATION, CHRONIC		1 (2%)	1 (2%)
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	6	1	2
AUTOLYSIS/NO NECROPSY	1	1	4

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

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	46	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	46	50
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
#TRACHEA	(44)	(38)	(49)
HEMORRHAGE			1 (2%)
INFLAMMATION, NOS			1 (2%)
#LUNG	(45)	(45)	(50)
BRONCHOPNEUMONIA, NOS			1 (2%)
INFLAMMATION, NOS	2 (4%)		
HEMATOPOIETIC SYSTEM			
#SPLEEN	(45)	(42)	(48)
CONGESTION, NOS		1 (2%)	
INFLAMMATION, ACUTE	1 (2%)		
HYPERPLASIA, LYMPHOID	1 (2%)		
#LYMPH NODE	(41)	(38)	(41)
NECROSIS, NOS		1 (3%)	
HYPERPLASIA, LYMPHOID		2 (5%)	
#MANDIBULAR L. NODE	(41)	(38)	(41)
NECROSIS, FOCAL	1 (2%)		
#MESENTERIC L. NODE	(41)	(38)	(41)
HEMORRHAGE	1 (2%)		
HYPOPLASIA, LYMPHOID	1 (2%)		
#LIVER	(48)	(46)	(50)
HYPERPLASIA, LYMPHOID	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
#SMALL INTESTINE	(39)	(36)	(38)
HYPERPLASIA, LYMPHOID	1 (3%)		
CIRCULATORY SYSTEM			
#HEART	(47)	(45)	(50)
MINERALIZATION		1 (2%)	
INFLAMMATION, FOCAL	1 (2%)		
#MYOCARDIUM	(47)	(45)	(50)
INFLAMMATION, MULTIFOCAL			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(48)	(46)	(50)
HEMORRHAGE			3 (6%)
INFLAMMATION, NOS		1 (2%)	8 (16%)
INFLAMMATION, FOCAL	1 (2%)	1 (2%)	
INFLAMMATION, MULTIFOCAL			4 (8%)
INFLAMMATION, DIFFUSE			1 (2%)
INFLAMMATION, NECROTIZING			1 (2%)
INFLAMMATION, ACUTE	1 (2%)		
ABSCESS, NOS	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
INFLAMMATION, GRANULOMATOUS	2 (4%)		1 (2%)
CIRRHOSIS, NOS			3 (6%)
NECROSIS, NOS	6 (13%)	2 (4%)	7 (14%)
NECROSIS, FOCAL	1 (2%)	1 (2%)	22 (44%)
NECROSIS, DIFFUSE	1 (2%)		11 (22%)
METAMORPHOSIS FATTY	4 (8%)	2 (4%)	33 (66%)
HEMOSIDEROSIS	1 (2%)		
BASOPHILIC CYTO CHANGE			1 (2%)
FOCAL CELLULAR CHANGE	1 (2%)	3 (7%)	
EOSINOPHILIC CYTO CHANGE		2 (4%)	
CLEAR-CELL CHANGE		2 (4%)	1 (2%)
HEPATOCYTOMEGALY	1 (2%)	2 (4%)	17 (34%)
ANGIECTASIS			1 (2%)
#LIVER/CENTRILOBULAR	(48)	(46)	(50)
METAMORPHOSIS FATTY			2 (4%)
*GALLBLADDER	(48)	(46)	(50)
INFLAMMATION, NOS	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
#BILE DUCT	(48)	(46)	(50)
DILATATION, NOS	1 (2%)		
#PANCREAS	(45)	(41)	(48)
INFLAMMATION, ACUTE	1 (2%)		
NECROSIS, NOS			1 (2%)
#PANCREATIC ACINUS	(45)	(41)	(48)
ATROPHY, DIFFUSE		1 (2%)	
#STOMACH	(41)	(42)	(44)
ULCER, NOS	1 (2%)		1 (2%)
HYPERPLASIA, FOCAL		1 (2%)	
#JEJUNUM	(39)	(36)	(38)
CYST, NOS		1 (3%)	
URINARY SYSTEM			
#KIDNEY	(48)	(44)	(50)
CAST, NOS			1 (2%)
INFLAMMATION, FOCAL	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)	2 (5%)	1 (2%)
#KIDNEY/TUBULE	(48)	(44)	(50)
ATROPHY, NOS	1 (2%)		
#KIDNEY/PELVIS	(48)	(44)	(50)
INFLAMMATION, NOS			1 (2%)
#URINARY BLADDER	(41)	(44)	(43)
INFLAMMATION, ACUTE	1 (2%)		1 (2%)
ENDOCRINE SYSTEM			
#ADRENAL	(45)	(43)	(50)
ANGIECTASIS		1 (2%)	
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(48)	(46)	(50)
CYST, NOS		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
EPIDERMAL INCLUSION CYST		1 (2%)	
INFLAMMATION, NOS		2 (4%)	
ABSCESS, NOS	2 (4%)		
DEGENERATION, CYSTIC		1 (2%)	
#PROSTATE	(37)	(39)	(40)
INFLAMMATION, NOS	2 (5%)		
*SEMINAL VESICLE	(48)	(46)	(50)
CYST, NOS		1 (2%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE	(48)	(46)	(50)
INFLAMMATION, NOS		1 (2%)	
*EYE/LACRIMAL GLAND	(48)	(46)	(50)
DEGENERATION, CYSTIC		1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(48)	(46)	(50)
INFLAMMATION, NOS	1 (2%)		
ALL OTHER SYSTEMS			
ADIPOSE TISSUE			
STEATITIS		1	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	12	3	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
AUTO/NECROPSY/HISTO PERF		1	
AUTOLYSIS/NO NECROPSY	2	4	

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

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	47	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	47	48
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
#LUNG	(50)	(46)	(48)
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, FOCAL		3 (7%)	
INFLAMMATION, SUPPURATIVE			1 (2%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(49)	(44)	(47)
HYPERPLASIA, RETICULUM CELL	1 (2%)	1 (2%)	
HYPERPLASIA, LYMPHOID	3 (6%)	1 (2%)	
#LYMPH NODE	(41)	(40)	(38)
HYPERPLASIA, RETICULUM CELL		1 (3%)	
#KIDNEY	(49)	(46)	(48)
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	1 (2%)
CIRCULATORY SYSTEM			
#HEART	(50)	(47)	(48)
EMBOLUS, SEPTIC	1 (2%)		
PERIVASCULITIS		1 (2%)	
#LIVER	(49)	(46)	(48)
PERIVASCULITIS	1 (2%)		
#UTERUS	(50)	(43)	(41)
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
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(44)	(47)
INFLAMMATION, FOCAL	2 (4%)		2 (4%)
#LIVER	(49)	(46)	(48)
HEMORRHAGE			2 (4%)
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, FOCAL	2 (4%)		
INFLAMMATION, MULTIFOCAL			13 (27%)
INFLAMMATION, DIFFUSE			5 (10%)
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL	1 (2%)		22 (46%)
NECROSIS, DIFFUSE			12 (25%)
METAMORPHOSIS FATTY	1 (2%)	3 (7%)	25 (52%)
CLEAR-CELL CHANGE			1 (2%)
CYTOLOGIC ALTERATION, NOS			1 (2%)
HEPATOCYTOMEGALY			22 (46%)
ANGIECTASIS			1 (2%)
#LIVER/CENTRILOBULAR	(49)	(46)	(48)
NECROSIS, DIFFUSE		1 (2%)	
#PANCREAS	(47)	(46)	(47)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
#STOMACH	(45)	(41)	(44)
ULCER, NOS			1 (2%)
HYPERPLASIA, EPITHELIAL			1 (2%)
HYPERKERATOSIS			1 (2%)
#JEJUNUM	(41)	(39)	(32)
INTUSSUSCEPTION	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(49)	(46)	(48)
CAST, NOS			2 (4%)
CYST, NOS	1 (2%)		
INFLAMMATION, NOS	1 (2%)	1 (2%)	
INFLAMMATION, FOCAL		1 (2%)	
INFLAMMATION, CHRONIC		2 (4%)	
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, NOS		1 (2%)	
#URINARY BLADDER	(40)	(45)	(42)
INFLAMMATION, FOCAL	1 (3%)		
ENDOCRINE SYSTEM			
#PITUITARY	(43)	(41)	(40)
HYPERPLASIA, FOCAL		1 (2%)	
ANGIECTASIS		2 (5%)	
#ADRENAL	(47)	(47)	(45)
CYST, NOS	1 (2%)		
INFLAMMATION, GRANULOMATOUS		1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(47)	(48)
HYPERPLASIA, NOS		1 (2%)	
LACTATION	3 (6%)	3 (6%)	
#UTERUS	(50)	(43)	(41)
HYDROMETRA	2 (4%)	1 (2%)	2 (5%)
INFLAMMATION, ACUTE			1 (2%)
ABSCESS, NOS	1 (2%)		
#UTERUS/ENDOMETRIUM	(50)	(43)	(41)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, CYSTIC	36 (72%)	26 (60%)	4 (10%)
#OVARY	(49)	(42)	(42)
CYST, NOS	8 (16%)	6 (14%)	
HEMORRHAGIC CYST		1 (2%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE	(50)	(47)	(48)
DEGENERATION, CYSTIC		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
*EYE/LACRIMAL GLAND	(50)	(47)	(48)
DEGENERATION, CYSTIC		1 (2%)	
METAMORPHOSIS FATTY		1 (2%)	
HEMOSIDEROSIS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERICARDIUM	(50)	(47)	(48)
INFLAMMATION, CHRONIC		1 (2%)	
*MESENTERY	(50)	(47)	(48)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED		1	1
AUTOLYSIS/NO NECROPSY		3	2

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

APPENDIX E

ANALYSIS OF 1,1,1,2-TETRACHLOROETHANE
(LOT NO. 102957)
MIDWEST RESEARCH INSTITUTE

APPENDIX E

A. ELEMENTAL ANALYSIS

Element	C	H	Cl
Theory	14.31	1.20	84.49
Determined	14.42	1.19	84.55
	14.54	1.26	84.38

B. BOILING POINT

Determined	Literature Values
128°C at 742 mm (visual, micro boiling point)	130.20°C at 760 mm (Dreisbach and Martin, 1949)

C. DENSITY

d_{23}^{27}: 1.547 ± 0.004 ± d	d_4^{25}: 1.53281

D. REFRACTIVE INDEX

n_D^{20}: 1.4816	1.48206

E. WATER ANALYSIS (Karl Fisher)

0.028 ± 0.001 (δ)%

F. TITRATION FOR ACIDIC COMPONENTS

Determined

Titration with sodium hydroxide,
56 ± 1 ppm (assumed to be HCl)

G. VAPOR-PHASE CHROMATOGRAPHY

1. Impurity Detection

Instrument: Tracor MT-220
Detector: Flame ionization
Carrier gas: Nitrogen

a. System 1
Inlet temperature: 195°C
Detector temperature: 210°C
Carrier flow rate: 44 cc/min.
Column: 10% Carbowax 20M-TPA on 80/100 Chromosorb W(AW), 1.7 m x 4 mm, glass
Oven temperature program: 50°C, 5 min.; 50° to 200°C, 10°C/min.
Sample injected: 3.5 μl neat liquid, diluted to 0.50% and 0.25% in hexane to quantitate major peak and check for overloading
Results: Major peak and nine impurities. The areas of the nine impurities total<0.6% of the area of the major peak.

APPENDIX E

Peak	Retention Time (min.)	Retention Time (Relative to 1,1,1,2-Tetrachloroethane)	Area (Relative to 1,1,1,2-Tetrachloroethane)
1	0.7	0.06	0.0004
2	1.6	0.14	0.08
3	5.9	0.51	0.09
4	8.8	0.77	0.06
5	10.6	0.93	0.06
6	11.4	1.00	100
7	12.0	1.04	0.07
8	12.8	1.12	0.07
9	13.5	1.18	0.09
10	14.1	1.23	0.02

b. System 2

Inlet temperature: 200°C
Detector temperature: 225°C
Carrier flow rate: 70 cc/min.
Column: GP 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm, glass
Oven temperature program: 50°C, 5 min; 50° to 150°C, 10°C/min.
Sample injected: 6.2 μl neat liquid, diluted to 1.0% and 0.5% to quantitate major peak and check for overloading
Results: Major peak and 12 impurities. Areas of impurity peaks total $<0.3\%$ of the area of the major peaks.

Peak	Retention Time (min.)	Retention Time (Relative to 1,1,1,2-Tetrachloroethane)	Area (Relative to 1,1,1,2-Tetrachloroethane)
1	0.7	0.07	0.0002
2	0.9	0.10	0.04
3	2.2	0.24	0.0001
4	2.6	0.28	0.00005
5	2.8	0.31	0.0002
6	4.0	0.44	0.05
7	8.3	0.91	0.02
8	9.1	1.00	100
9	10.3	1.13	0.03
10	10.8	1.18	0.0003 (shoulder)
11	11.0	1.20	0.00003 (shoulder)
12	11.5	1.26	0.09
13	11.9	1.30	0.002

2. Identification and Quantitation of Impurities

Instrument: Varian Aerograph 2400
Detector: Flame ionization
Inlet temperature: 150°C
Detector temperature: 220°C
Carrier gas: Nitrogen
Carrier flow rate: 70 cc/min.
Column: 20% SP-2100/0.1% Carbowax 1500 on 100/120
Supelcoport, 1.8 m x 4 mm, glass

Note: Some impurities are reported not to be present at a concentration of >0.01%. This does not necessarily represent the limit of detection for these compounds.

a. System 1 (1,2-Dichloroethane)

Oven temperature program: 60°C isothermal
Standards (3 μl) were injected containing 1.0% 1,2-dichloroethane in xylene. 1,2-Dichloroethane had a retention time of 3.6 minutes. A spike of 0.01% 1,2-dichloroethane in xylene, in neat 1,1,1,2-tetrachloroethane (1:1, v:v) at 3.6 minutes gave a peak larger than any peak in the same region when 1,1,1,2-tetrachloroethane was injected neat under the same conditions.

Conclusions: The sample did not contain 1,2-dichloroethane at a level >0.01%.

b. System 2 (1,1,2-Trichloroethane)

Oven temperature program: 80°C isothermal
Standards (4 μl) were injected containing 0.01% 1,1,2-trichloroethane in pentane. 1,1,2-Trichloroethane had a retention time of 6.2 minutes. A spike of 0.01% 1,1,2-trichloroethane in pentane, in neat 1,1,1,2-tetrachloroethane (1:1, v:v) at 6.2 minutes retention time gave a peak larger than any peak in the same region when 1,1,1,2-tetrachloroethane was injected neat under the same conditions.

Conlusions: The sample did not contain 1,1,2-trichloroethane at a level >0.01%.

c. System 3 (1,1,2,2-Tetrachloroethane)

Oven temperature program: 120°C isothermal
Standards (4 μl) were injected containing 0.01% 1,1,2,2-tetrachloroethane in pentane. 1,1,2,2-Tetrachloroethane had a retention time of 4.9 minutes. A spike of 0.01% 1,1,2,2-tetrachloroethane in pentane, in neat 1,1,2,2-tetrachloroethane (1:1, v:v) at 4.9 minutes retention time, gave a peak larger than any peak in the same region when 1,1,1,2-tetrachloroethane was injected neat under the same conditions.

Conclusions: The sample did not contain 1,1,2,2-tetrachloroethane at a level >0.01%.

Instrument: Tracor MT-200
Detector: Flame ionization
Carrier gas: Nitrogen
Column: 20% SP-2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm, glass

d. System 4 (Acetone)

Inlet temperature: 130° C
Detector temperature: 195° C
Carrier flow rate: 70 cc/min.
Oven temperature program: 50° C isothermal
Standards (6 μl) were injected containing 0.04% acetone in o-dichlorobenzene. Acetone had a retention time of 1.4 minutes. When injected under the same conditions, at 1.4 minutes neat 1,1,1,2-tetrachloroethane had a peak which was enhanced with the addition of acetone. Acetone in the sample was quantitated against a 0.04% standard of acetone in o-dichlorobenzene.

Conclusions: Sample contained 0.05% ± 0.01% (δ) acetone.

e. System 5 (Tetrachloroethylene)

Inlet temperature: 130° C
Detector temperature: 195° C
Carrier flow rate: 70 cc/min.
Oven temperature program: 55° C isothermal
Standards (8 μl) were injected containing 0.02% tetrachloroethylene in pentane. Tetrachloroethylene had a retention time of 9.5 minutes. When injected under the same conditions, neat 1,1,1,2-tetrachloroethane had a peak of 9.5 minutes which was enhanced by the addition of tetrachloroethylene. Tetrachloroethylene in the sample was quantitated against a 0.02% tetrachloroethylene standard in pentane.

Conclusions: Sample contained 0.04% ± 0.01 (δ)% tetrachloroethylene.

f. System 6 (Trichloroethylene)

Inlet temperature: 130°, 165°, and 200° C. (The sample was injected at three different inlet temperatures to check for inlet decomposition. The area of the trichloroethylene peak remained constant when the inlet temperature was changed.)
Detector temperature: 220° C
Carrier flow rate: 60 cc/min.
Oven temperature program: 60° C isothermal
Standards (4 μl) were injected containing 1.0% trichloroethylene in o-dichlorobenzene. Trichloroethylene had a retention time of 3.8 minutes. 1,1,1,2-Tetrachloroethylene had a peak at the same retention time when injected neat under the same conditions. The peak was enhanced by the addition of trichloroethylene. The trichloroethane in the sample was quantitated against a 0.05% standard in o-dichlorobenzene.

Conclusions: Sample contained 0.06% ± 0.01 (δ)% trichloroethylene.

g. System 7 (Pentachloroethane)

Inlet temperatures: 125°, 160°, and 200°C (as in System 6 above, the sample was injected at three different inlet temperatures to check for inlet decomposition. Trichloroethylene was found as a decomposition product under the pentachloroethane peak by vapor-phase chromatography/mass spectrometry. The area of the pentachloroethane peak remained constant as the inlet temperature was changed.)
Detector temperature: 210°C
Carrier flow rate: 60 cc/min.
Oven temperature program: 100°C isothermal
Standards (5 μl) were injected containing 0.05% pentachloroethane in pentane. Pentachloroethane had a retention time of 5.8 minutes. When injected neat under the same conditions, 1,1,1,2-tetrachloroethane at 5.8 minutes had a peak which was enhanced by the addition of pentachloroethane. Pentachloroethane in the sample was quantitated against a 0.1% standard of pentachloroethane in pentane.
Conclusions: The sample contained 0.15% ± 0.01 (δ)% pentachloroethane.

H. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY

Instrument: Varian MAT CH4B mass spectrometer interfaced via a Watson-Biemann helium separator to a Tracor MT 2000 MF vapor-phase chromatograph. Data processed by a Varian 620/i computer.
Vapor-phase chromatograph column: 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.6 m x 4 mm I.D., glass
Inlet temperature: 165°C
Oven temperature program: 50°C, 5 min.; 50° to 160°C at 10°C/min.
Sample injected: 1 μl neat liquid
Carrier gas: Helium
Carrier flow rate: 70 cc/min.

Results: Major peak and 4 impurities (Table E1). A fifth impurity was detected on the falling edge of the major peak by the total ion current monitor, but it was not sufficiently resolved from the major peak to obtain a spectrum, and it has not been included in the tabulated data.

TABLE E1. CHROMATOGRAPHIC DATA

Peak	Retention Time (min.)	Retention Time (Relative to 1,1,1,2-Tetrachloroethane)	Corresponding Peak by FID in Section G-1-b
1	3.6	0.27	2
2	9.8	0.74	6
3	12.8	0.96	7
4	13.3	1.00	8
5	15.7	1.18	12

Conclusions: Comparison with literature spectra (Tables E2 and E3) indicated the following possible impurities.

Peak No. 1	Acetone
Peak No. 2	Trichloroethylene
Peak No. 3	Tetrachloroethane
Peak No. 4	1,1,1,2-Tetrachloroethylene
Peak No. 5	Pentachloroethane and trichloroethylene from decomposition of the major component.

Specific ion searches were also done for masses 62, 64 characteristic of 1,2-dichloroethane, for masses 83, 97 characteristic of 1,1,2-trichloroethane, and for masses 83, 168 characteristic of 1,1,2,2-tetrachloroethane. Masses 62, 64 were observed only under the major peak. Masses 83, 97, and 168 were observed under the major peak and under peak No. 5, identified as pentachloroethane with trichloroethylene formed by decomposition of the major peak.

1,2-Dichloroethane, 1,1,2-trichloroethane, and 1,1,2,2-tetrachloroethane were not in the sample at concentrations greater than 0.01%. Acetone, trichloroethylene, tetrachloroethylene, and pentachloroethane were present as impurities.

TABLE E2. MASS SPECTRAL DATA

Peak	Mass	Percent of Base Peak
1	58	74
	43	100
	42	9
	39	4
	29	31
	27	7
	26	7
	15	37
2	134	32
	132	92
	130	100
	99	8
	97	59
	95	85
	62	6
	60	24
3	168	47
	166	100
	164	78
	133	18
	131	61
	129	62
	96	12
	94	18
4	135	40
	133	100 saturated
	131	100 saturated
	121	39
	119	100 saturated
	117	100 saturated
	97	28
	95	39
5	169	22 (46)*(a)*
	167	48 (100)
	166	12 (26)
	165	38 (79)
	164	9 (20)
	134	32
	132	91
	130	100
	119	47 (99)
	117	47 (98)
	99	9
	97	52
	95	88
	82	3 (7)
	62	9
	60	29

(a) The numbers in parentheses are calculated based on the mass 167 peak of pentachloroethane being the base peak.

TABLE E3. LITERATURE SPECTRA OF IMPURITIES

Compound	Literature Spectrum *(a)*	
	Mass	Percent of Base Peak
Acetone	58	42
	43	100
	42	7
	39	3
	29	2
	27	4
	26	3
	15	14
Trichloroethylene	134	30
	132	94
	130	98
	99	11
	97	64
	95	100
	62	10
	60	31
Tetrachloroethylene	168	48
	166	100
	164	78
	133	20
	131	62
	129	64
	96	14
	94	21
1,1,1,2-Tetrachloroethane	135	32
	133	96
	131	100
	121	26
	119	78
	117	82
	97	20
	95	28
Pentachloroethane	169	48
	167	100
	166	60
	165	78
	164	46
	119	97
	117	99
	82	61

(a) Eight peak index

APPENDIX E

I. SPECTRAL DATA

Determined	Literature Values
1. Infrared	
Instrument: Beckman, IR-12 Cell: 0.025 mm liquid cell, sodium chloride windows Results: See Figure 5	Consistent with a literature spectrum which was recorded from 400 to 1,200 cm^{-1} (Bernstein, 1950)
2. Nuclear Magnetic Resonance	
Instrument: Varian HA-100 Solvent: Neat Assignments: See Figure 6 (a) s, δ 4.20 ppm	ν □ 258.5 cps at 60 MHz = 4.31 ppm (McClellan and Nicksic, 1965,)
Integration ratios: (a) 2.00	

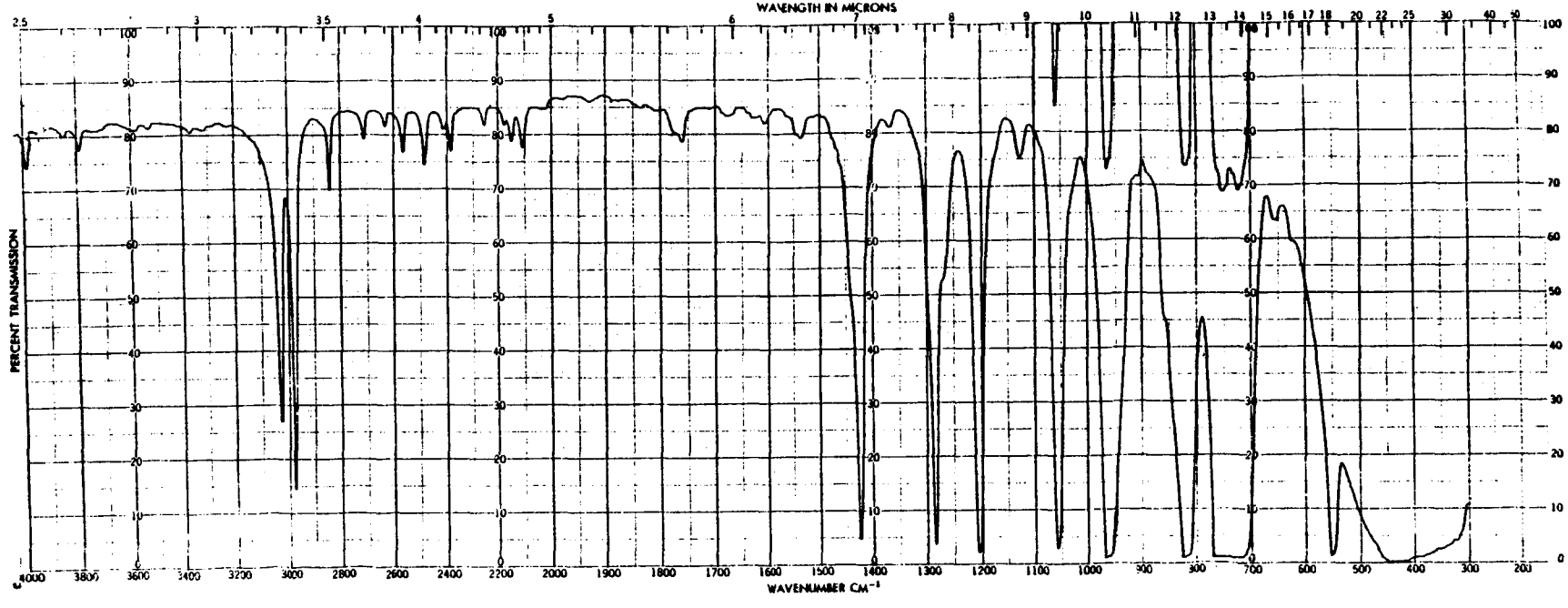

Figure 5. Infrared Absorption Spectrum of 1,1,1,2-Tetrachloroethane (Lot No. 102957)

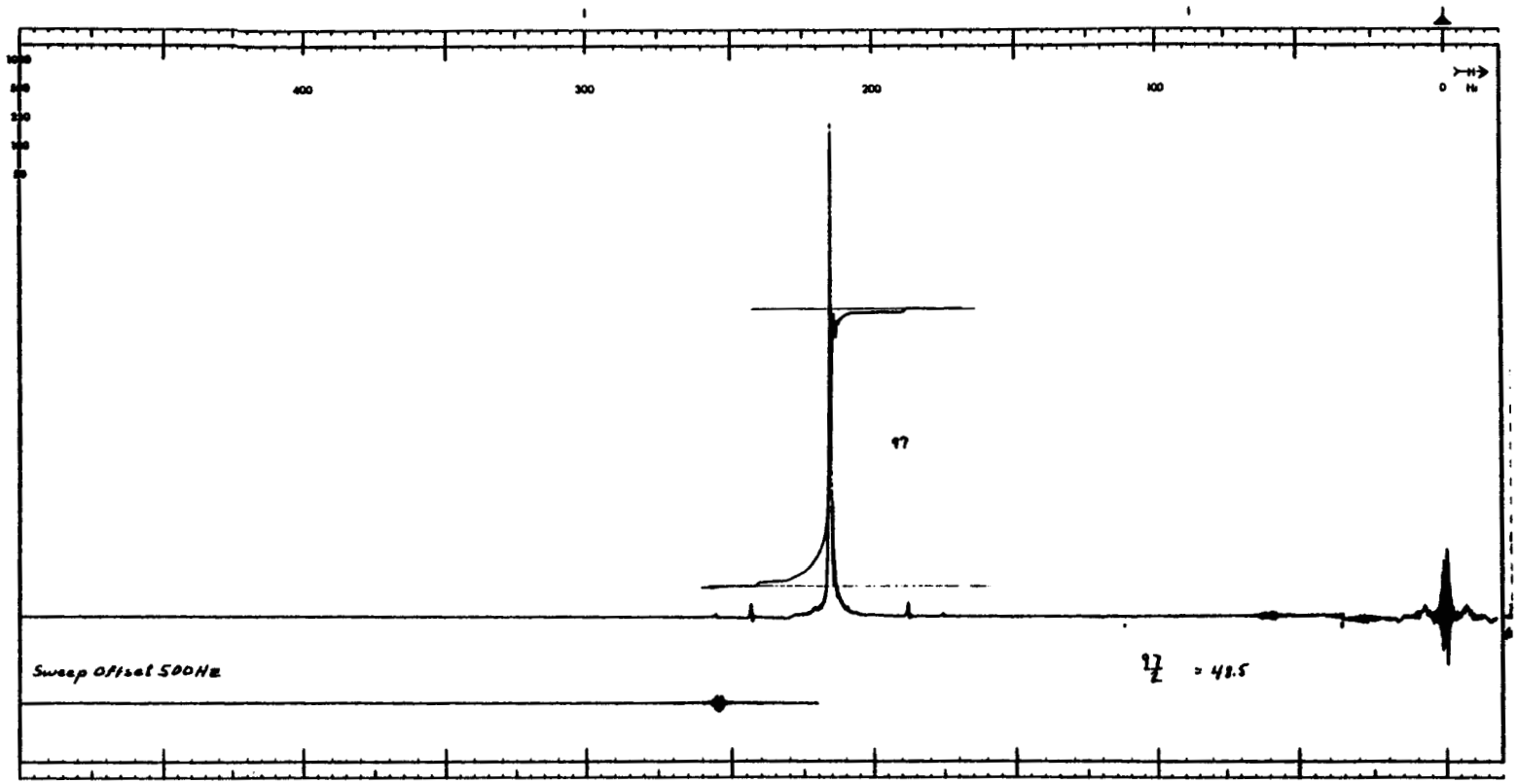

Figure 6. Nuclear Magnetic Resonance Spectrum of 1,1,1,2-Tetrachloroethane (Lot No. 102957)

APPENDIX F

ANALYSIS OF 1,1,1,2-TETRACHLOROETHANE (LOT NO. KB081977)) MIDWEST RESEARCH INSTITUTE

APPENDIX F

A. ELEMENTAL ANALYSIS

Element	C	H	Cl
Theory	14.31	1.20	84.49
Determined	14.30	1.20	84.57
	14.42	1.21	84.32

B. WATER ANALYSIS (Karl Fischer)

0.042 ± 0.001 (δ)%

C. TITRATION FOR ACIDIC COMPONENTS

Titration with sodium hydroxide

37.7 ± 1.20 (δ) ppm (assumed to be HCl)

D. VAPOR-PHASE CHROMATOGRAPHY

1. Impurity Detection

Instrument: Tracor MT-220
Detector: Flame ionization
Carrier gas: Nitrogen
Carrier flow rate: 70 cc/min.

a. System 1

Inlet temperature: 195°C
Detector temperature: 210°C
Column: 10% Carbowax 20M-TPA on 80/100 Chromosorb W(AW), 1.8 m x 4 mm I.D., glass
Oven temperature program: 50°C, 5 min.; 50° to 200°C at 10°C/min.
Sample injected: 5 μl neat liquid, diluted to 0.5% and 0.25% in hexanes to quantitate major peak and check for overloading

Results: Major peak and two impurities. The areas of the two impurities totaled 0.07% of the area of the major peak.

Peak	Retention Time (min.)	Retention Time (Relative to 1,1,1,2-Tetrachloroethane)	Area (Percent of 1,1,1,2-Tetrachloroethane)
1	0.61	0.05	0.02
2	4.80	0.41	0.05
3	11.71	1.00	100

b. System 2

Inlet temperature: 200°C
Detector temperature: 225°C
Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm I.D., glass
Oven temperature program: 50°C, 5 min.; 50° to 170°C, 10°C/min.
Sample injected: 5 μl neat liquid, diluted to 1.0% and 0.5% to quantitate major peak and check for overloading.
Results: Major peak and two impurities. Areas of the two impurities total 0.08% of the area of the major peak.

Peak	Retention Time (min.)	Retention Time (Relative to 1,1,1,2-Tetrachloroethane)	Area (Percent of 1,1,1,2-Tetrachloroethane)
1	9.87	0.94	0.05
2	10.47	1.00	100
3	12.50	1.19	0.03

2. Identification and Quantitation of Impurities

Instrument: Tracor MT-220
Detector: Flame ionization
Carrier gas: Nitrogen
Carrier flow rate: 70 cc/min.
Column: 20% SP-2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm I.D., glass

a. System 1 (Tetrachloroethylene)

Inlet temperature: 130°C
Detector temperature: 200°C
Oven temperature program: 70°C isothermal
Standards (4 μl) of 0.04% tetrachloroethylene in pentane were injected. Tetrachloroethylene had a retention time of 7.1 minutes. Neat 1,1,1,2-tetrachloroethane had a peak with a retention time of 7.1 minutes, when injected under the same conditions, which was enhanced by the addition of tetrachloroethylene. Tetrachloroethylene in the sample was quantitated against a 0.04% standard in pentane.

Conclusions: The sample contained 0.062% ± 0.001 (δ)% tetrachloroethylene.

b. System 2 (Pentachloroethane)

Inlet temperature: 140°C
Detector temperature: 215°C
Oven Temperature program: 100°C isothermal
Standards (4 μl) of 0.02% pentachloroethane in pentane were injected. Pentachloroethane had a retention time of 6.6 minutes. Neat 1,1,1,2-tetrachloroethane had a peak with a retention time of 6.6 minutes which, when injected under the same conditions, was enhanced by the addition of pentachloroethane. Pentachloroethane in the sample was quantitated against a 0.02% standard in pentane.

Conclusions: The sample contained 0.052% ± 0.001 (δ) % pentachloroethane.

c. System 3 (1,1,2,2-Tetrachloroethane)

Inlet temperature: 140°C
Detector temperature: 215°C
Oven temperature program: 80°C isothermal
Standards (6 μl) were injected containing 0.01% 1,1,2,2-tetrachloroethane in pentane. 1,1,2,2-Tetrachloroethane had a retention time of 8.0 minutes. Neat 1,1,1,2-tetrachloroethane had a peak with a retention time of 8.0 minutes, when injected under the same conditions, which was enhanced by the addition of 1,1,2,2-tetrachloroethane. 1,1,2,2-Tetrachloroethane in the sample was quantitated against the 0.01% standard in pentane.

Conclusions: The sample contained less than 0.01% 1,1,2,2-tetrachloroethane.

E. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY

Instrument: Varian MAT CH4B mass spectrometer interfaced via a Watson-Biemann helium separator to a Tracor MT 2000 MF vapor-phase chromatograph. Data processed by a Varian 620/i computer.

Vapor-phase chromatograph column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm I.D., glass
Inlet temperature: 170°C
Oven temperature program: 100°C, 2 min.; 100° to 170°C at 10°C/min.
Carrier gas: Helium
Carrier gas flow rate: 30 cc/min.
Sample injected: 1 μl neat liquid
Results: Major peak and 5 impurities as shown in Table F1.

Note: While the mass spectrum of pentachloroethane was significantly different from the literature spectrum, it was consistent with mass spectra obtained previously for pentachloroethane on the same mass spectrometer. Some variation in relative intensities was observed, but the larger peaks in this spectrum were prominent in all spectra recorded at Midwest Research Institute.

TABLE F1. VAPOR-PHASE CHROMATOGRAPHY DATA

Peak	Retention Time (min.)	Retention Time (Relative to 1,1,1,2-Tetrachloroethane)	Corresponding Peak by FID Section D-1-b *(a)*
1	4.3	0.6	not reported (<0.01)
2	6.2	0.8	not reported (<0.01)
3	6.7	0.9	1
4	7.3	1.0	2
5 shoulder	8.1	1.1	not reported (<0.01)
6	9.8	1.3	3

Specific ion searches were also done for masses 83 and 97 characteristic of 1,1,2-trichloroethane; masses 49 and 62 characteristic of 1,2-dichloroethane; and masses 43 and 58 characteristic of acetone. Masses 83 and 97 were observed together only under the major peak and peak no. 6 at longer retention time than the major peak. Masses 49 and 62 were observed together only under the major peak. Masses 43 and 58 were not observed together (Table F2).

Conclusions: The sample contained trichloroethylene; a hydrocarbon similar in structure to 2,6-dimethylundecane; tetrachloroethylene; 1,1,2,2-tetrachloroethane; pentachloroethane; and 1,1,1,2-tetrachloroethane, the major component. It did not contain 1,1,2-trichloroethane, acetone, or 1,2-dichloroethane at levels greater than 0.01%.

TABLE F2. MASS SPECTROMETRY DATA

				Literature	
Peak	Mass	Percent of Base Peak	Identity	Mass	Percent of Base Peak
1	134	31	Trichloroethylene *(a)*	134	30
	132	87		132	94
	130	100		130	98
	99	7		99	11
	97	52		97	64
	95	84		95	100
	62	7		62	10
	60	33		60	31
2	98	1	2,6-Dimethyl-	98	8
	85	1	undecane or	85	6
	71	16	similar hydro-	71	36
	70	5	carbon *(a)*	70	8
	57	100		57	100
	56	42		56	14
	44	9		44	7
	43	18		43	20

(a) Eight peak index.

TABLE F2. MASS SPECTROMETRY DATA *(Continued)*

Peak	Mass	Percent of Base Peak	Identity	Literature Mass	Literature Percent of Base Peak
3	168	42	Tetrachloroethylene *(a)*	168	48
	166	100		166	100
	164	73		164	78
	133	15		133	20
	131	51		131	62
	129	52		129	64
	96	11		96	14
	94	15		94	21
4	135	28	1,1,1,2-Tetra-	135	32
	133	97	chloroethane *(a)*	133	96
	131	98		131	100
	121	29		121	26
	119	95		119	78
	117	100		117	82
	97	21		97	20
	95	31		95	28
5	168	2 (6) *(b)*	1,1,2,2-Tetra-	168	8
	131	98 (>100)	chloroethane *(a)*	131	8
	95	31 (>100)		95	11
	87	3 (9)		87	10
	85	17 (60)		85	63
	83	29 (100)		83	100
	61	33 (>100)		61	8
	60	15 (53)		60	8
6	169	25	Pentachloro-	169	48
	167	56	ethane *(a)*	167	100
	166	2		166	60
	165	49		165	78
	164	1		164	46
	132	30		119	97
	130	34		117	99
	119	77		82	61
	117	80			
	83	100			
	82	14			

(a) Eight peak index.

(b) The numbers in parentheses are calculated based on the largest peaks in the literature spectrum of the identified compound being the base peak.

F. SPECTRAL DATA

1. Infrared

Instrument: Perkin-Elmer 137
Cell: Thin film between AgCl plates
Results: See Figure 7

Consistent with literature spectrum, which was recorded from 400 to 1,200 cm^{-1} (Bernstein, 1950)

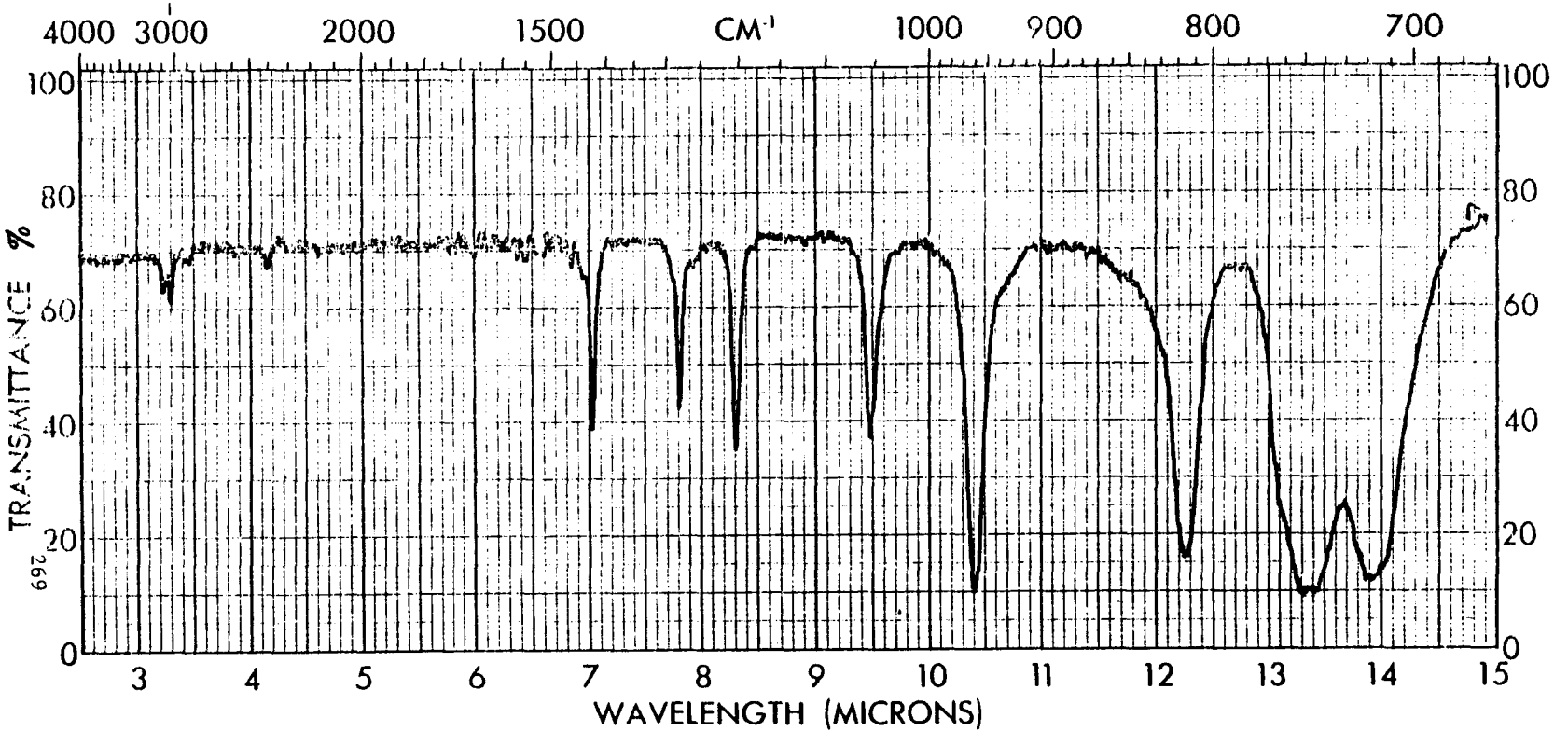

Figure 7. Infrared Absorption Spectrum of 1,1,1,2-Tetrachloroethane (Lot No. KB081977)

2. Ultraviolet/Visible

Instrument: Cary 118. No absorbance between 350 and 800 nm (visible region). No maximum between 212 and 350 nm (ultraviolet region), but a gradual increase in absorbance toward the solvent cut-off at 212 nm. Concentration: 1%, 0.1%, and 0.01% Solvent: Methanol	No literature reference found.

3. Nuclear Magnetic Resonance

Instrument: Varian EM-360 60 MHz Solvent: Neat, tetramethyl silane added Assignments: See Figure 8 (a) s, δ 4.29 ppm Integration Ratios: (a) 2.00	Literature Values: ν = 258.2 cps at 60 MHz = 4.31 ppm (McClellan and Nicksic, 1965)

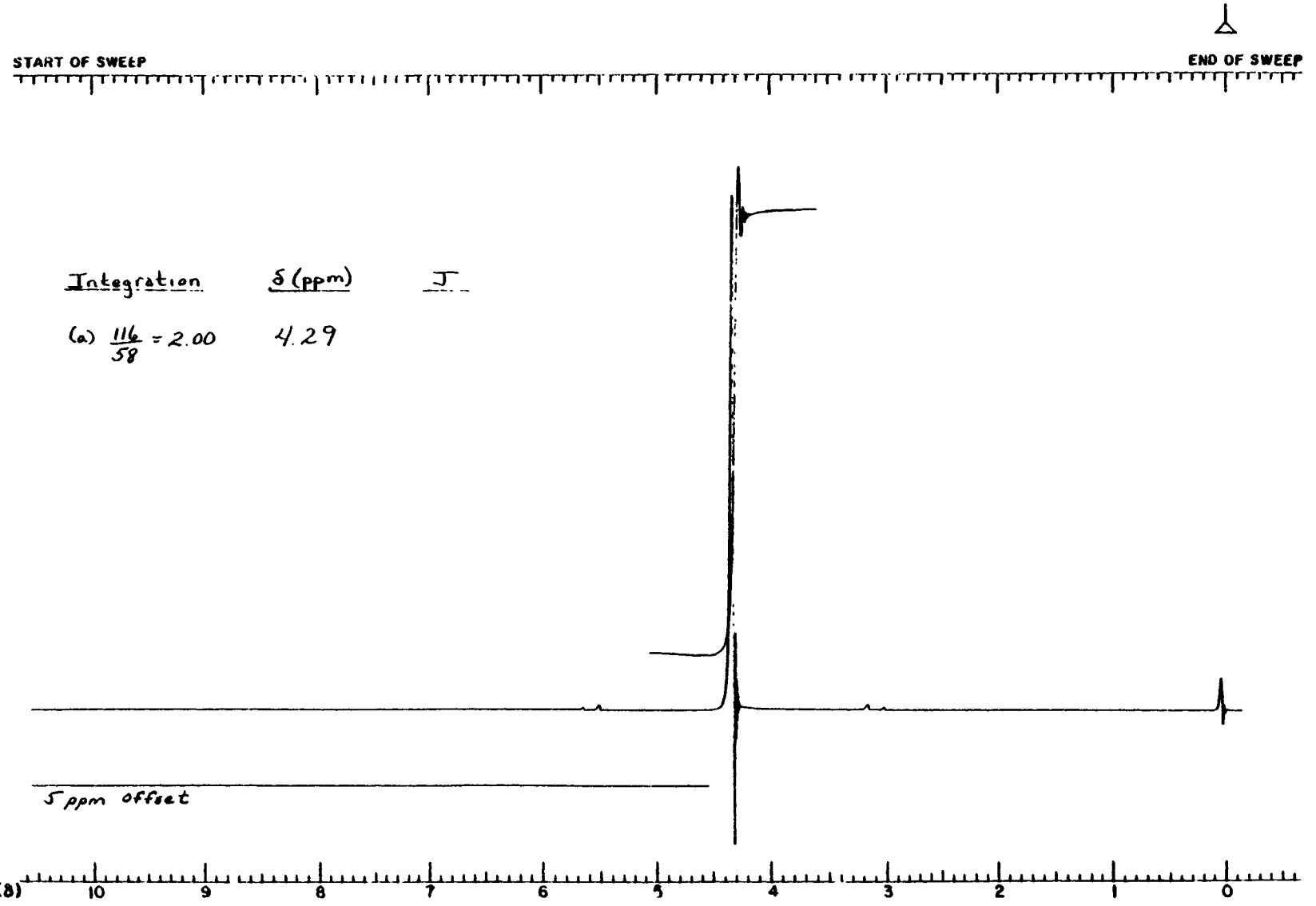

Figure 8. Nuclear Magnetic Resonance Spectrum of 1,1,1,2-Tetrachloroethane (Lot No. KB081977)

APPENDIX G

STABILITY ANALYSIS OF 1,1,1,2-TETRACHLOROETHANE IN CORN OIL

MIDWEST RESEARCH INSTITUTE

APPENDIX G

A. SAMPLE PREPARATION

A 1% (w/v) sample solution of 1,1,1,2-tetrachloroethane in corn oil was prepared for each day of the study as follows: 10 ml of corn oil was transferred into a 50-ml Hypo-vial, the vial was sealed, and then approximately 95 mg of 1,1,1,2-tetrachloroethane was added via a 100-μl syringe. The samples were shaken and stored at room temperature from 1 to 7 days, respectively.

B. EXTRACTION AND ANALYSIS

The samples were extracted with 20 ml of methanol, which was injected into the sample vial via a 10-ml syringe. Samples for analysis were withdrawn directly from the top methanol layer in the vial and analyzed by vapor-phase chromatography, according to the following systems.

Days 1 through 3:

Instrument: Bendix 2500
Column: Chromosorb 102, 100/120 mesh, glass, 1.8 m x 4 mm I.D.
Detection: Flame ionization
Oven temperature: 250°C, isothermal
Detector temperature: 295°C
Inlet temperature: 250°C

Days 4 through 7:

Instrument: Tracor MT-220
Column: 10% Carbowax 20 M on 80/100 Chromosorb W AW, glass, 1.8 m x 4 mm I.D.
Detection: Flame ionization
Oven temperature: 90°C, isothermal
Inlet temperature: 200°C
Detector temperature: 265°C

C. RESULTS

End of Day	Average Percent Compound *(a)*
1	1.02 ± 0.05
2	0.99 ± 0.05
3	1.06 ± 0.05
4	0.99 ± 0.05
5	1.02 ± 0.05
6	0.94 ± 0.05
7	0.99 ± 0.05

(a) Corrected for a spiked recovery value of 65.8%.

D. CONCLUSION

1,1,1,2-Tetrachloroethane mixed in corn oil is stable for 7 days at room temperature.

APPENDIX H

ANALYSIS OF 1,1,1,2-TETRACHLOROETHANE IN CORN OIL FOR CONCENTRATIONS OF 1,1,1,2-TETRACHLOROETHANE

GULF SOUTH RESEARCH INSTITUTE

APPENDIX H

Samples of selected dose preparations administered during the chronic study were analyzed for concentrations of 1,1,1,2-tetrachloroethane in corn oil.

Duplicate 1.0-ml samples of corn oil containing tetrachloroethane were diluted with benzene to a final volume of 10 ml. The resulting concentration was 5 mg/ml. Four μl aliquots for gas chromatography injections were used.

Reference standards were prepared by diluting pure tetrachloroethane (1.5532 g/ml) by a factor of 1:500 with benzene. This dilution yielded a concentration of 3.1064 mg/ml, injected in 5 μl aliquots.

Instrument: MT 220
Column: 20% SP 2100
Detector temperature: 250°C
Column temperature: 100°C
Inlet temperature: 230°C
Carrier gas: N_2
Flow: 30 ml/min.
Detector: Flame ionization
Retention time for 1,1,1,2-tetrachloroethane: 3.94 minutes
Results: See Table H1

TABLE H1. CONCENTRATION OF 1,1,1,2-TETRACHLOROETHANE IN CORN OIL

Date Mixed	Week Used	Concentration of 1,1,1,2-Tetrachloroethane for Target Concentration of 50 mg/ml *(a)*
1/03/78	1/04/78	48.4
2/23/78	2/24/78	46.4
4/13/78	4/14/78	48.0
6/15/78	6/16/78	47.0
7/07/78	7/08/78	54.0
11/23/78	11/24/78	48.9
2/08/79	2/09/79	52.0
5/03/79	5/04/79	51.8
8/17/79	8/18/79	53.0
10/25/79	10/26/79	50.0
Mean (mg/ml)		49.9
Standard deviation		2.6
Coefficent of variation (%)		5.6
Range (mg/ml)		46.4-54.0
Number of samples		10

(a) The data presented are the average of the results of duplicate analyses.

APPENDIX I

CUMULATIVE MEAN BODY WEIGHT CHANGE OF ANIMALS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE IN THE CHRONIC STUDY

TABLE I1. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF RATS ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE IN THE CHRONIC STUDY

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males	0	138 *(b)*	137 *(b)*	136 *(b)*		
	2	39	38	50	- 3	+28
	23	229	232	236	+ 1	+ 3
	43	276	273	277	- 1	0
	63	287	290	304	+ 1	+ 6
	83	318	326	311	+ 3	- 2
	103	294	301	287	+ 2	- 2
Females	0	108 *(b)*	110 *(b)*	105 *(b)*		
	2	17	25	28	+47	+65
	23	92	93	97	+ 1	+ 5
	43	117	113	110	- 3	- 6
	63	142	139	141	- 2	- 1
	83	172	154	163	-10	- 5
	103	170	166	175	- 2	+ 3

(a) Weight change of the dosed group relative to that of the controls = $\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$

(b) Initial weight.

TABLE I2. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF MICE ADMINISTERED 1,1,1,2-TETRACHLOROETHANE BY GAVAGE IN THE CHRONIC STUDY

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males	0	25 *(b)*	25 *(b)*	26 *(b)*		
	2	1	2	0	+100	-100
	23	17	15	11	- 12	- 35
	43	23	19	12	- 17	- 48
	63	22	20	13	- 9	- 41
	83	20	19	—	- 5	—
	103	18	19	—	+ 6	—
Females	0	20 *(b)*	20 *(b)*	19 *(b)*		
	2	- 1	+ 1	+ 1	*(c)*	*(c)*
	23	9	9	9	0	0
	43	17	18	13	+ 6	- 24
	63	22	22	16	0	- 27
	83	25	22	—	- 12	—
	103	19	19	—	0	—

(a) Weight change of the dosed group relative to that of the controls = $\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$

(b) Initial weight.

(c) Controls lost weight.

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