NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 243

CARCINOGENESIS STUDIES OF TRICHLOROETHYLENE

(WITHOUT EPICHLOROHYDRIN)

(CAS NO. 79-01-6)

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.

Special note: This Technical Report was peer reviewed in public session and approved by the NTP Board of Scientific Counselors' Technical Reports Review Subcommittee on June 16 and September 22, 1982 [see pages 11-12]. Thereafter, the NTP adopted the policy that the experimental data and laboratory records from all NTP Toxicology and Carcinogenesis Studies not yet printed and distributed would be audited. [A summary of the data audit is presented in Appendix L.] Consequently, printing and distribution of this Technical Report have been delayed, and the format differs from that of Technical Reports peer reviewed more recently. The categories of evidence of carcinogenicity adopted by the NTP in June 1983 were not used to evaluate these data. This final Technical Report supersedes all previous drafts of this report that have been distributed.

NTP TECHNICAL REPORT

ON THE

CARCINOGENESIS STUDIES OF

TRICHLOROETHYLENE

(WITHOUT EPICHLOROHYDRIN)

(CAS NO. 79-01-6)

IN F344/N RATS AND B6C3F$_1$ MICE

(GAVAGE STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 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 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 Studies should be directed to the National Toxicology Program, located at Research Triangle Park, NC 27709 (919-541-3991) or at Room 835B, Westwood Towers, 5401 Westbard Ave., Bethesda, MD 20205 (301-496-1152).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP.

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650).

Single copies of this carcinogenesis studies technical report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

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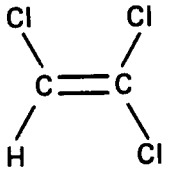


TRICHLOROETHYLENE

CAS NO. 79-01-6
C_2HCl_3 Mol. Wt. 131.40

ABSTRACT

Carcinogenesis studies of epichlorohydrin-free trichloroethylene (TCE) were conducted by administering the test chemical in corn oil by gavage to groups of 50 male and 50 female F344/N rats and B6C3F$_1$ mice. Dosage levels were 500 and 1,000 mg/kg for rats and 1,000 mg/kg for mice. Trichloroethylene was administered five times per week for 103 weeks, and surviving animals were killed between weeks 103 and 107. Groups of 50 rats and 50 mice of each sex received corn oil by gavage on the same schedule and served as vehicle controls. Groups of 50 male and 50 female rats were used as untreated controls.

The dosage levels selected for the 2-year study were based on the results of the 13-week studies. Groups of 10 male and 10 female rats received TCE by gavage at doses of 125 to 2,000 mg/kg (males) and 62.5 to 1,000 mg/kg (females) for 13 weeks. Groups of 10 male and 10 female mice received gavage doses of 375 to 6,000 mg/kg of TCE for 13 weeks. Survival, body weight gains, and previous experience with TCE were used to select doses for the 2-year study. All rats survived the 13-week study, but males receiving 2,000 mg/kg exhibited a 24% difference in final body weight. At the 1,000 mg/kg dose, final body weights for males (-3%) and for females (-2%) were similar to those of controls. The doses selected for the 2-year study in rats were 500 and 1,000 mg/kg for both sexes. The initial doses used in the earlier bioassay in Osborne-Mendel rats were 549 and 1,097 mg/kg for both sexes. A total of 8/10 male mice and 10/10 female mice receiving doses of TCE as high as 1,500 mg/kg survived the 13-week experimental period. The single dosage level selected for the 2-year study in mice was 1,000 mg/kg for both sexes. This dose was less than the high dose used in the earlier bioassay in B6C3F$_1$ mice (2,339 mg/kg for males and 1,739 for females) and was similar to the previous low doses (1,169 mg/kg for males and 869 for females).

In the 2-year study, the survival of both low and high dose male rats and dosed male mice was less ($P \leq 0.005$) than that of the vehicle controls. Mean body weights of dosed rats of each sex were lower than those of the vehicle controls, and after week 65, the decrements in body weight gains were dose related. The mean body weight of dosed male mice was lower than that of the vehicle controls throughout the study, while those of dosed and vehicle control female mice were comparable.

Cytomegaly (toxic nephrosis) of the kidney was observed in 96/98 male and in 97/97 female rats given TCE, with none being found in male or female vehicle control rats. This lesion was more severe in males, particularly in the high dose group. Cytomegaly was observed in 45/50 male mice and in 48/49 female mice administered TCE, and in none of the vehicle controls. Renal tubular cell adenocarcinomas were found in three high dose male rats; these neoplasms were observed in those male rats killed at the end of the study (0/33, 0/20, and 3/16, 19%). The incidence in the high dose male rats at the end of the study was greater ($P<0.05$) than that in the controls. Renal tubular cell adenocarcinomas are considered uncommon occurrences in F344/N rats, with 3/748 (0.4%) being observed in historical vehicle gavage controls. Additional renal tumors in dosed male rats included one transitional cell carcinoma of the renal pelvis and two tubular cell adenomas in low dose animals and one carcinoma of the renal pelvis in a high dose animal. No renal neoplasms were found in vehicle control rats; one untreated control male rat had a transitional cell papilloma of the renal pelvis. In female rats, one tubular cell adenocarcinoma was found in the high dose group.

An increased incidence ($P<0.05$, life table) of peritoneal mesotheliomas was detected in low dose male rats (control, 1/50; low dose, 5/50; high dose, 1/49). Mesotheliomas have been diagnosed in 16/752 (2.1%) historical vehicle control male F344/N rats, and the increased incidence in the present study may have been related to the administration of TCE.

The results in male F344/N rats were considered equivocal for detecting a carcinogenic response because both groups receiving TCE showed significantly reduced survival compared to vehicle controls (35/50, 70%; 20/50, 40%; 16/50, 32%) and because 20% of the animals in the high dose group were killed accidently by gavage error.

Negative trends were observed for chromophobe adenomas of the pituitary gland and for endometrial stromal polyps in female rats. These decreases were not considered to be related to the administration of TCE.

The administration of TCE to mice caused increased incidences of hepatocellular carcinoma in males (control, 8/48; dosed, 31/50; $P<0.001$) and in females (control, 2/48; dosed, 13/49; $P<0.005$). Hepatocellular carcinomas metastasized to the lungs in five dosed male mice and one control male mouse, and none was observed in females. The incidence of hepatocellular adenomas was increased in male mice (control, 7/48; dosed 14/50) and in female mice (control, 4/48; dosed, 16/49; $P<0.05$).

Under the conditions of these studies, epichlorohydrin-free trichloroethylene caused renal tubular-cell neoplasms in male F344/N rats, produced toxic nephrosis in both sexes, and shortened the survival time of males. This experiment in male F344/N rats was considered to be inadequate to evaluate the presence or absence of a carcinogenic response to trichloroethylene. For female F344/N rats receiving trichloroethylene, containing no epichlorohydrin, there was no evidence of carcinogenicity. Trichloroethylene (without epichlorohydrin) was carcinogenic for $B6C3F_1$ mice, causing increased incidences of hepatocellular carcinomas in males and females and of hepatocellular adenomas in females.

CONTRIBUTORS

The carcinogenesis studies of trichloroethylene were conducted at Papanicolaou Cancer Research Institute under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The chronic study was begun in June 1978 and completed in June 1980.

Principal Contributors at Papanicolaou Cancer Research Institute
1155 N.W. 14th Street
Miami, Florida 33136
(Conducted studies and evaluated tissues)

Dr. F. Ahmad
Chemist

Dr. N. Altman
Principal Investigator

Dr. H. Seibold
Pathologist

Ms. N. Thuma
Operations Supervisor

Mr. K. Stephenson
Animal Care Supervisor

Ms. M. Stevens
Chemical Technician

Ms. L. Gorman
Bioassay Coordinator

Principal Contributors at Tracor Jitco
1776 East Jefferson Street
Rockville, Maryland 20852
and
Research Triangle Park
North Carolina 27709
(Prepared preliminary summary report)

E. Cremmins, M.A.
Technical Editor

A. Jacobs, Ph.D.
Bioscience Writer

J. Keller, Ph.D.
Director, Bioassay Program

M. Levy, M.A.
Technical Editor

S. Olin, Ph.D.
Program Associate Director

H. Seifried, Ph.D.
Laboratory Operations Coordinator

M. Stedham, D.V.M.
Pathologist

W. Theriault, Ph.D.
Manager, Technical Reports

J. Tomaszewski, Ph.D.
Chemist

J. Warner, M.S.
Statistician

L. Wijnberg, Ph.D.
Statistician

Principal Contributors at the National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park
Box 12233
North Carolina 27709
(Evaluated experiment, interpreted
results, and reported findings)

John H. Mennear, Ph.D. (Chemical Manager)

Gary Boorman, D.V.M., Ph.D.
R. Chhabra, Ph.D.
M. Dieter, Ph.D.
J. Fielding Douglas, Ph.D.
Charles K. Grieshaber, Ph.D.
Larry Hart, Ph.D.

Joseph Haseman, Ph.D
James Huff, Ph.D.
C.W. Jameson, Ph.D.
Ernest E. McConnell, D.V.M.
John A. Moore, D.V.M.
Raymond Tennant, Ph.D.

NTP Pathology Working Group

The pathology report and selected slides were evaluated on 1 June 1981 by the NTP Pathology Working Group.

Dr. G. Boorman (NTP)
Dr. L. Lomax (NTP)

Dr. E. McConnell (NTP)
Dr. J. Popp (Chemical Institute of Industrial Toxicology)

REVIEWERS

National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee

Margaret Hitchcock, Ph.D. (Chairperson)
Pharmacology/Toxicology
John B. Pierce Foundation Laboratory
New Haven, Connecticut

Curtis Harper, Ph.D. (Principal Reviewer)
Associate Professor of Pharmacology
University of North Carolina
Chapel Hill, North Carolina

Alice Whittemore, Ph.D.*
Biostatistics
Stanford University School of Medicine
Palo Alto, California

Ad Hoc Subcommittee Panel of Experts

Norman Breslow, Ph.D.**
Biostatistics
University of Washington
Seattle, Washington

Robert M. Elashoff, Ph.D. (Principal Reviewer)
Biostatistics
University of California
at Los Angeles
Jonsson Comprehensive Cancer Center
Los Angeles, California

Joseph Highland, Ph.D.**
Toxicology
Environmental Defense Fund
Washington, D.C.

J. Michael Holland, Ph.D., D.V.M.
Pathology
Department of Biology
Oak Ridge National Laboratory
Oak Ridge, Tennessee

Frank Mirer, Ph.D.
Toxicology
International Union, United
Auto Workers
Detroit, Michigan

Robert A. Scala, Ph.D.
Toxicology
Exxon Corporation
East Millstone, New Jersey

Bernard Schwetz, Ph.D., D.V.M.
Toxicology Research Laboratory
Dow Chemical U.S.A.
Midland, Michigan

James Swenberg, Ph.D., D.V.M.
(Principal Reviewer)
Chief of Pathology
Chemical Industry Institute of Toxicology
Research Triangle Park, North Carolina

Stan D. Vesselinovitch, D.V.Sc.*
Departments of Radiology and Pathology
University of Chicago
Chicago, Illinois

Mary Vore, Ph.D.
Pharmacology
University of Kentucky
College of Medicine
Lexington, Kentucky

*Unable to attend June 16, 1982 meeting
**Unable to attend September 22, 1982 meeting

SUMMARY OF PEER REVIEW COMMENTS ON THE CARCINOGENESIS STUDIES OF TRICHLOROETHYLENE (WITHOUT EPICHLOROHYDRIN)

On 16 June and on 22 September 1982 this technical report underwent peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The public review meetings began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences. Research Triangle Park, North Carolina. The following precis represents the critiques made by the principal reviewers, as well as comments from and discussion by the Peer Review Panel, NTP staff, and attendees.

Peer Review Meeting of 16 June 1982

Dr. Swenberg, a principal reviewer for the report on the carcinogenesis studies of trichloroethylene (TCE) without epichlorohydrin, said the conclusion should be restricted to the renal adenocarcinomas in male rats since there was no evidence for progression of the renal adenomas. The adenomas occurred only in low dose animals and were not present at terminal sacrifice, whereas the adenocarcinomas occurred only in the high dose group and were present only at terminal sacrifice. He opined that the high dose was toxic for male and female rats and male mice, and said this indicates the MTD was exceeded, especially since the rats did not die from renal tumors. He objected to the combining of benign and malignant tumors in the text and in certain tables. Dr. Swenberg requested more explanation for the accidental deaths in high dose male rats and on poor tissue accountability. He concluded that the report should be rewritten and at present, he considered the report unacceptable.

As a second principal reviewer, Dr. Harper said the increased incidence of renal tubular adenomas and carcinomas in male rats may have been confounded because the MTD was exceeded. He noted that since only 3/748 (0.4%) historical controls have had renal tubular adenomas, carcinomas, or adenocarcinomas, and carcinoma of the renal pelvis has never been reported in F344/N rats, the findings in the studies should not be minimized by overstating the effects of exceeding the MTD. He commented that caution should be used in statements speculating on the nongenetic mechanism of carcinogenicity; a misunderstanding of the mechanism could lead to an underestimation of the risk associated with human exposure.

As a third principal reviewer, Dr. Elashoff said that based on the 13-week study, the doses chosen for the chronic study were reasonable but the results from the earlier NCI carcinogenesis studies should have suggested the high dose would have been toxic. He agreed with the conclusions for mice; in male mice, the time to death with hepatocellular adenomas was shorter in the high dose than for vehicle controls; yet, the incidence rate was not increased. With regard to male rats, the high dose induced lethal nontumorigenic toxicity with the evidence based upon the small P-value comparing survivorship curves between each dose group and vehicle controls. One result of this lethality in male rats would be to reduce the number of animals at risk for developing tumors leading to unadjusted incidence analysis of low power. Life table or incidental tumor analyses leads to the conclusions that TCE is carcinogenic, and this becomes also a biological conclusion if the predominant nontumorigenic toxicity, cytomegaly, is not associated with the carcinogenic process. On the other hand, if there is an ambiguous relationship between toxicity and carcinogenicity, no clear statement can be made regarding carcinogenicity, and the validity of the studies for male rats becomes questionable.

Dr. Highland stressed that the high mortality from exceeding the MTD as well as from gavage error in high dose male rats could have led to an underestimation of the carcinogenic effect. Dr. Breslow questioned whether the randomization process might have been faulty. He suggested that the abstract should call attention to the fact that five of the hepatocellular carcinomas in dosed male mice versus only one in controls were metastatic as support for the carcinogenic effect. Drs. Schwetz and Elashoff said the report should indicate whether or not the results from the earlier NCI study were considered in dose setting. Dr. Mirer stated that the findings in mice (a high percentage of males with hepatocellular carcinomas at sacrifice) should be emphasized. He cautioned against drawing a conclusion that the renal tumors in male rats were secondary to the toxic nephrosis, and further that these toxic effects should be explored for significance to human industrial exposure. Several panel members called for more balance and perhaps less speculation in the discussion of genetic and nongenetic effects and mechanisms.

Dr. J. Mennear, NTP, responded that the 13-week studies and previous experience were used to select the doses for the 2-year study and the tendency to overestimate the MTD appeared to be a common difficulty with halogenated hydrocarbons, and further discussion would be included. Regarding serology data, Dr. Mennear said serologies were done and would be included in the report. (See pages 29 and 42.)

In discussion from the floor, Mr. L. Schlossberg, Detrex Chemical Industries, read a letter and reports from three scientists who contended that poor survival and renal tumors in male rats, when the MTD was exceeded, may be due to a combination of nongenetic factors such as kidney damage and immune system depression. Others focused on the potential confounding effects of toxicity in male rats, emphasizing that the renal nephrosis was in the same organ as the tumors.

Dr. Scala suggested there were two issues: acceptability of the assay and acceptability of the report. He opined that the assay was marginally acceptable but the report needed to be rewritten to reflect the many comments and the question of balance. Dr. Swenberg proposed the panel defer acceptance until it had a chance to review a revised report, and said the results should be reported whether or not they are adequate or acceptable. He was concerned that there were untreated controls which were not discussed. Dr. J. Huff, NTP, said existence of these controls had been discovered only recently, but should have been brought to the attention of the panel at the outset, and would be described in the revised report.

Dr. Highland moved that the studies on TCE be considered acceptable for reporting. Dr. Harper seconded the motion and this was approved by nine affirmative votes with one abstention (Dr. Schwetz). Dr. Swenberg moved that the technical report be deferred for rewriting. Dr. Harper seconded, and the motion was approved by nine affirmative votes with one abstention (Dr. Schwetz).

Subsequent discussion dealt with what should be covered in a rewrite of the report. Dr. Highland said the untreated controls should be included and discussed; there should be a more balanced discussion of how MTD could have led to either over- or underestimating effects; and there should be a statement about the missing tissues. Dr. Swenberg said the potential complicating factors must be clearly stated, while Dr. Holland asked that nonneoplastic chronic effects not be addressed as confounding factors and that instead, the readers be allowed to draw their own conclusions. Dr. Elashoff said the untreated control data should be included, but a formal statistical analysis of the data should not be done, since the concurrent vehicle controls were the relevant controls for comparison. Dr. Moore concluded that NTP would rewrite the report to be more balanced and agreeable to the viewpoints expressed by the panel members.

Peer Review Meeting of 22 September 1982

Dr. Swenberg, a principal reviewer for the report on the carcinogenesis studies of trichloroethylene (TCE) without epichlorohydrin, agreed with the conclusions as sent to the panel members. Dr. Swenberg questioned whether or not some further comment on the inadequacy of the rat study needed to be added to stress the use of toxic doses and the poor tissue accountability for the pathology.

As a second principal reviewer, Dr. Elashoff agreed with the modified conclusions and mentioned certain issues relating to statistical methodology. As a third principal reviewer, Dr. Harper agreed with the conclusions, yet he questioned whether the decreased survival of male rats could be attributed to exceeding the MTD. He was also concerned about the excessive number of apparent gavage errors.

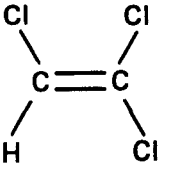
In discussion from the floor, Dr. Z. Bell, PPG Industries, maintained that the current draft report was not adequate for assessing biological significance. He submitted copies of a critique which he asked be made part of the meeting record, and requested that the draft report be returned for further revision and review at the next meeting. Mr. L. Schlossberg, Detrex Chemical Industries, read from reviews commissioned by him which he interpreted as indicating the bioassay was inadequate in rats for establishing the carcinogenicity of TCE. Further, in his opinion, the available epidemiologic and animal evidence indicate TCE is not a carcinogen. Mr. Schlossberg requested that the review of the report be deferred until the data from other ongoing carcinogenesis studies of TCE in different strains of rats are ready for review.

Dr. Swenberg stated that the presentations made by the speakers from the floor related to the male rat findings and were in agreement with the NTP conclusions that the male rat study was considered inadequate. Both Drs. Swenberg and Holland emphasized that the purpose of the peer review panel members was to evaluate the technical report, not the total evidence on the toxicology of the chemical, and to make recommendations as to the acceptability of the report as a reflection of the experimental data. Dr. Mirer requested the mouse findings should be placed first in the summary, since the results

are clear and unequivocal. (In these technical reports, by convention, rats are listed first.) He stated the opinion that the large number of early deaths in the rat study actually increased the difficulty of detecting carcinogenic effects. He questioned how one interprets an excess of tumors in the presence of organ damage; that is, are the tumors secondary to the organ damage or do they result from a separate process? In support of the latter idea, he noted that although kidney damage was observed in female rats and mice of both sexes there was no concomitant increased incidence of renal tumors.

Dr. Swenberg moved that the technical report on the carcinogenesis studies of trichloroethylene be accepted with the minor revisions discussed. Dr. Harper seconded the motion and the technical report on trichloroethylene without epichlorohydrin was approved by nine affirmative votes, with one opposed (Dr. Mirer).

I. INTRODUCTION



TRICHLOROETHYLENE

CAS NO. 79-01-6
C_2HCl_3 Mol. Wt. 131.40

Trichloroethylene (TCE) is an industrial solvent used for vapor degreasing and cold cleaning of fabricated metal parts. TCE has also been used as a carrier solvent for the active ingredients of insecticides and fungicides, as a solvent for waxes, fats, resins, and oils, as an anesthetic for medical and dental use, and as an extractant for spice oleoresins and for caffeine from coffee. Trichloroethylene may be found in printing inks, varnishes, adhesives, paints, lacquers, spot removers, rug cleaners, disinfectants, and cosmetic cleansing fluids. TCE may also be used as a chain terminator in polyvinyl chloride production and as an intermediate in the production of pentachloroethane (Kirk-Othmer, 1963 and 1979; IARC, 1979; Defalque, 1961; Wetterhahn, 1972; U.S. CFR, 1976; Valle-Riestra, 1974; Waters et al., 1977). Trichloroethylene is no longer used with food, drugs, or cosmetics (IARC, 1979; Food Chemical News, 1978). Before 1976, tolerances for TCE in decaffeinated ground coffee were set at 25 ppm (U.S. CFR, 1976).

An estimated 3.5 million workers are exposed to TCE (Page, 1979). The threshhold limit value for TCE is 100 ppm (Federal Register, 1975). In 1979 production of TCE was 319,432,000 pounds (USITC, 1980).

Trichloroethylene has been found in various foodstuffs in England at the following concentrations: packet tea, 60 ppm; pig's liver, 22 ppm; butter, 10 ppm; and fresh bread, 7 ppm (McConnell et al., 1975). Trichloroethylene has also been found in commercial deionized charcoal-filtered water (Dowty et al., 1975) and in drinking water in various cities (Kavlock et al., 1979).

The oral LD_{50} is reported to be 5,200 mg/kg in rats (National Clearinghouse for Poison Control Centers, 1967). The intraperitoneal LD_{50} for mice is 3,200 mg/kg (Klaassen and Plaa, 1966). Trichloroethylene is a central nervous system depressant (Clayton and Clayton, 1981).

The results of mutagenicity testing of TCE are difficult to interpret because few authors provide analytical data regarding the purity of their test materials. The sensitivities of most of these tests are such that the presence of trace levels of potent genotoxic contaminants, such as epichlorohydrin, could affect the results generated. Differences in purity could explain the diversity of results reported from various laboratories. For example, "pure" TCE has been reported to be weakly mutagenic, equivocally mutagenic, or nonmutagenic for *S. typhimurium* TA100 (Baden et al., 1979; Bartsch et al., 1979; Simmon et al., 1977; Waskell, 1978). TCE did not cause mutations in *Salmonella typhimurium* TA98, TA100, TA1535, or TA1537, with or without metabolic activation; using Chinese hamster ovary (CHO) cells, TCE did not induce chromosome aberrations and the results for sister chromatid exchanges were considered equivocal (NTP unpublished results).

The results and conclusions of other workers employing a variety of test methods are similarly inconsistent. Cerna and Kypenova (1977) reported that TCE was mutagenic (without metabolic activation) in *in vitro* tests with *S. typhimurium* TA1535 and 1538 and in host-mediated assays with TA1950, 1951, and 1952. Greim et al. (1975) reported that microsomally activated TCE was slightly mutagenic for *Escherichia coli* K 12, but Loprieno et al. (1979) found no mutagenic activity in a series of short-term tests. Slacik-Erben (1980) studied TCE (99.5% pure) in a dominant lethal test in male Han/BGA NMRI mice and found no mutagenic activity.

Evidence for a carcinogenic effect of TCE was presented by the National Cancer Institute (NCI, 1976) after the completion of a 78-week bioassay of industrial grade (>99% pure) TCE in $B6C3F_1$ mice and Osborne-Mendel rats; without additional TCE administration, rats were observed for another 32 weeks and mice for 12 more weeks. In mice, time-weighted-average gavage doses of 1,169 and 2,339 mg/kg in males and 869 and 1,739 mg/kg in females were associated with significant increases in the incidence of hepatocellular carcinoma. In Osborne-Mendel rats, time-weighted-average gavage doses of 549 and 1,097 mg/kg (both sexes) did not increase the incidence of primary tumors. However, as in several earlier bioassays of chlorinated ethanes and ethylenes (hexachloroethane, NCI, 1978a; 1,1,2,2-tetrachloroethane, NCI, 1978b; 1,1,2-trichloroethane, NCI, 1978c; tetrachloroethylene, NCI, 1977; and pentachloroethane, NTP, 1982), the survival of the rats was compromised by the dosage regimen. The results of most of these earlier carcinogenicity studies have been summarized (Weisburger, 1977) and reviewed (IARC, 1979). The International Agency for Research on Cancer considered the TCE bioassay in Osborne-Mendel rats to be inadequate for evaluation and the bioassay in $B6C3F_1$ mice to provide limited evidence of carcinogenicity; that is, carcinogenic in one species (IARC, 1979). IARC evaluated TCE as being "carcinogenic to mice after its oral administration, producing liver and lung neoplasms" (IARC, 1982).

The interpretation of the earlier TCE study (NCI, 1976) was complicated by the presence of certain contaminants, particularly epichlorohydrin (0.09%) in the test material. Epichlorohydrin had been previously shown to induce local sarcomas in mice following subcutaneous injection (Van Duuren et al., 1974) and has subsequently been reported to cause nasal carcinomas in rats after inhalation exposure (Laskin et al., 1980). Further, epichlorohydrin is a potent mutagen for *S. typhimurium* TA100 (Simmon, 1977). Therefore, although the carcinogenicity of industrial-grade TCE in $B6C3F_1$ mice was firmly established, unequivocal statements regarding its carcinogenicity in rats and the carcinogenicity of pure TCE in mice could not be made.

Results of long-term inhalation studies with purified TCE (less than 0.000025% of each of 5 chlorinated hydrocarbon impurities by gc/ms; stabilized with 0.0015% triethanolamine) have been reported (Henschler et al., 1980). In these studies, male and female Wistar rats, NMRI mice, and Syrian hamsters were exposed to air containing up to 500 ppm of TCE for 18 months (6 hours per day, 5 days per week). This regimen failed to produce compound-related increases in primary tumors in these species. The investigators did report an increase in the incidence of malignant lymphomas in female mice, but the relationship of this lesion to TCE exposure was considered questionable because of the high incidence of lymphomas in control mice.

The evidence for the carcinogenicity of TCE, like that of the chlorinated ethanes and ethylenes tested earlier (hexachloroethane, tetrachloroethane, trichloroethane, tetrachloroethylene, and pentachloroethane) comes mainly from data obtained in experiments conducted in mice. For the most part, the carcinogenic classification of these materials is based upon dose-related increases in the incidences of hepatocellular carcinoma in $B6C3F_1$ mice. Because this is a relatively common tumor in males of this strain of mouse (seen in approximately 18% of control males and 3% of control females), the significance of the lesion is frequently questioned. Also, the reason for the apparent insensitivity of Osborne-Mendel rats to members of this chemical class remains unknown. It may be related to the reduced survival times of dosed animals. Therefore, the failure of the doses to increase tumor incidences in rats could have been due to the animals not surviving long enough to develop the lesions. However, in most of the earlier studies the survival times of both rats and mice were shortened by compound administration. In light of this observation, it is possible that Osborne-Mendel rats are not susceptible to the carcinogenicity of these chemicals. Inter- or intra-species differences in susceptibility to TCE could be mediated through inherited pharmacokinetic factors. Stott et al. (1982) reported that $B6C3F_1$ mice can metabolize more TCE (on a mg/kg basis) than can Osborne-Mendel rats. A similar quantitative difference in TCE metabolism between $B6C3F_1$ mice and Sprague-Dawley rats has recently been reported (Parchman and Magee, 1982). If a carcinogenic effect of TCE requires biotransformation of the parent molecule to a reactive metabolite, the $B6C3F_1$ mouse might be expected to be more sensitive than the Osborne-Mendel rat. Trichloroethylene epoxide has been suggested as an electrophilic metabolite of TCE (Van Duuren,

1975), but Miller and Guengerich (1982) have reported the results of *in vitro* experiments which suggest that the epoxide may not be an intermediate of TCE metabolism.

The possibility of a strain difference in susceptibility to TCE prompted the National Cancer Institute to initiate a series of chronic carcinogenicity studies of a variety of chlorohydrocarbons, including TCE, in several strains of rats. Most of these studies are still in progress; the NTP is preparing draft reports from completed carcinogenesis studies on four strains of rats (Marshall, ACI, Osborne-Mendel, and August) using the oral route, and Dr. C. Maltoni (Institute of Oncology, Bologna, Italy) is currently (August 1983) examining the histopathology portion of TCE inhalation experiments using Sprague-Dawley rats and Swiss and $B6C3F_1$ mice. The comparative testing of epichlorohydrin-free trichloroethylene administered by gavage to $B6C3F_1$ mice and F344/N rats has been completed. This report describes the results of that study.

II. MATERIALS AND METHODS

CHEMICAL ANALYSES

DOSE PREPARATION

THIRTEEN-WEEK STUDY

TWO-YEAR STUDIES

Study Design

Source and Specifications of Test Animals

Animal Maintenance

Clinical Examinations and Pathology

Data Recording and Statistical Methods

CHEMICAL ANALYSES

High purity "Hi-Tri" trichloroethylene was obtained in two lots. Lot No. TB 05-206AA was obtained from Dow Chemical Co. (Richmond, VA) and was used for the 13-week study and for the first 19 months of the 2-year study. Lot No. TB 08-039AA was obtained from Missouri Solvents (Kansas City, MO) and was used for the final 5 months of the 2-year study.

Purity and identity analyses were conducted at Midwest Research Institute. The results of elemental analyses for both lots were consistent with the theoretical values. Twelve impurities with areas totalling less than 0.04% of the area of the major peak were detected in Lot No. TB 05-206AA by gas-liquid chromatography in one system (Appendix G). Eight impurities having areas less than 0.02% that of the major peak were detected in a second system. One impurity with an area of 0.02% that of the major peak was detected in Lot No. TB 08-039AA. The area of all other impurities in this lot totaled less than 0.01% that of the major peak. These impurities were not identified. The infrared and nuclear magnetic resonance spectra of both lots were consistent with the literature spectra. "Hi-Tri" trichloroethylene contains 8 ppm of an amine stabilizer (diisopropylamine) and, if present, no more than 0.001% epichlorohydrin stabilizers as determined by gas chromatography/mass spectrometry.

Throughout the course of this study, the trichloroethylene was stored at 4°C. Papanicolaou periodically analyzed the chemical versus a standard, maintained at −20°C, by gas-liquid chromatography using a 10% OV-101 glass column at 70°C. The chemical showed no decrease in purity over the course of the study, even though a white flocculent material was noticed in the July 1979 reanalysis. A 5-gallon can of this material was returned to Midwest Research Institute for attempted purification. The flocculent material was present at a level of 25-30 ppm (Appendix H). Results of infrared and mass spectroscopy indicated that the precipitate was a mixture of long chain alkene or alkanes and inorganic carbonate. Midwest Research Institute shipped the filtered trichloroethylene back to Papanicolaou in October 1979.

The new lot (TB 08-039AA) was received at Papanicolaou in December 1979 and was used immediately. Both lots were considered to be greater than 99.9% pure.

DOSE PREPARATION

Doses were administered at a constant volume. Mice received 0.5 ml per dose and rats received 1.0 ml per dose. A stock solution of trichloroethylene in corn oil was prepared and appropriately diluted (Table 1). Trichloroethylene in corn oil (1% w/v) was found to be stable for 7 days at room temperature (Appendix I). Later, stock solutions of trichloroethylene in corn oil were found to be stable at 4°C for 4 weeks (Appendix J). Stock solutions were prepared once per week for the first 16 weeks of the study and once per month for the remainder of the study. Stock solutions were analyzed by gas chromatography and found to be within 10% of the target concentrations (Appendix K).

THIRTEEN-WEEK STUDIES

Neither single-dose nor 14-day studies were conducted. Dosage levels for the 13-week study were based on earlier experiences with TCE in rats and mice (NCI, 1976).

Five-week-old male and female F344/N rats and 3-week-old B6C3F$_1$ mice were obtained from Frederick Cancer Research Center. Rats were observed for 2 weeks and mice for 4 weeks. Animals were assigned to cages according to a table of random numbers. Cages were then assigned to dosed and control groups according to another table of random numbers.

Rats and mice were housed five per cage in polycarbonate cages (Table 1). Cages and bedding were changed twice per week. Purina® Lab Chow and water (via an automatic watering system) were available *ad libitum*.

Groups of 10 male rats were administered 0, 125, 250, 500, 1,000, or 2,000 mg/kg trichloroethylene in corn oil by gavage, 5 days per week for 13 weeks. Groups of 10 female rats were administered 0, 62.5, 125, 250, 500, or 1,000 mg/kg, and groups of 10 mice of each sex received 0, 375, 750, 1,500, 3,000, or 6,000 mg/kg on the same schedule. Doses of trichloroethylene were calculated on the basis of mean body weights from the previous weighing period.

Animals were checked for mortality and signs of morbidity twice daily. Each animal was given a clinical examination weekly.

At the end of the 13-week study, survivors were killed with carbon dioxide. Necropsies were performed on animals, unless precluded in whole or in part by autolysis or cannibalization. Thus the number of animals from which organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group. Liver weights from animals of all dosed mouse groups were measured. The following were examined for the control and high dose rats and for the control and the two highest dosed groups of mice: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity, brain, pituitary, and spinal cord. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

TWO-YEAR STUDIES

Study Design

Groups of 50 rats of each sex were administered 500 or 1,000 mg/kg trichloroethylene in corn oil for up to 103 weeks. Groups of 50 mice of each sex were administered 1,000 mg/kg for up to 103 weeks. Doses of trichloroethylene administered were calculated on the basis of mean body weights from the previous weighing period. Groups of 50 rats and mice of each sex received corn oil only and served as vehicle controls (Table 1). In addition, groups of 50 rats of each sex were used as untreated controls. Tumor incidence data from these groups were not used for routine statistical analyses, but the incidences are shown in Appendix A.

Source and Specifications of Test Animals

Five and one-half-week-old male and female F344/N rats and B6C3F$_1$ mice were obtained from Harlan Industries (Indianapolis, IN), observed for 2.5 weeks, and assigned to individual cages according to a table of random numbers. The cages were then assigned to control and dosed groups according to another table of random numbers. Animals that died during the first 1.5 weeks of the study as a result of gavage error were replaced.

Animal Maintenance

Rats were housed five per cage in polycarbonate cages. Mice were housed 10 per cage for the first 8 months and then transferred to smaller cages housing five animals each. Cages and bedding were changed twice per week. Tap water, via an automatic watering system, and diet were available *ad libitum* (Table 1).

The temperature in the animal rooms was 22°-24°C and the humidity was 40%-60%. Ten to fifteen changes of room air per hour were provided. Fluorescent lighting provided illumination 12 hours per day.

Clinical Examinations and Pathology

All animals were observed twice daily for signs of morbidity or mortality. Clinical signs were recorded monthly. Body weights, by cage, were recorded weekly for the first 12 weeks and then every fourth week thereafter. The mean body weight of each group was calculated by dividing the total weight of animals in the group by the number of animals in the group. Moribund animals and animals that survived to the end of the bioassay were killed with carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph nodes, skin, mammary gland, salivary gland, thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, pituitary, and spinal cord.

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

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

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

	13-Week Studies
Experimental Design	
Size of Test Groups	10 males and 10 females of each species
Doses	Male rats: 0, 125, 250, 500, 1,000, or 2,000 mg/kg body weight in corn oil by gavage
	Female rats: 0, 62.5, 125, 250, 500, or 1,000 mg/kg body weight in corn oil by gavage
	Mice: 0, 375, 750, 1,500, 3,000, or 6,000 mg/kg body weight in corn oil by gavage
Duration of Dosing	Five days per week for 13 weeks
Type and Frequency of Observation	Observed twice daily for morbidity and mortality
Necropsy and Histologic Examination	All animals necropsied. All control and high dose rats and the control and the two highest dosed groups of mice were examined histologically
Animals and Animal Maintenance	
Species	F344/N rats; $B6C3F_1$ mice
Animal Source	Frederick Cancer Research Center (Frederick, MD)
Time Held before Start of Test	Rats: 2 weeks Mice: 4 weeks
Age When Placed on Study	Rats: 7 weeks Mice: 7 weeks
Age When Killed	Rats: 20 weeks Mice: 20 weeks
Method of Animal Distribution	Assigned to cages according to a table of random numbers and then to groups according to another table of random numbers
Feed	Purina® Rodent Chow 5001 *ad libitum* (Distributed by O.K. Feed Store, Miami, FL)
Bedding	Sani Chip® hardwood, Pinewood Products Co. (Distributed by O.K. Feed Store, Miami, FL)
Water	Tap water via Edstrom Automatic Watering System (Waterford, WI)
Cages	Polycarbonate, Lab Products (Rochelle Park, NJ); cages changed and sanitized twice weekly; racks sanitized every 2 weeks
Animals per Cage	5
Cage Filters	Cerex spun nylon, Florida Filters (Miami, FL); filters changed every 2 weeks
Animal Room Environment	22°-24°C; 40%-60% relative humidity; 12 hours fluorescent light per day; room air changed 18-20 times per hour
Other Chemicals on Test in Same Room	None
Chemical/Vehicle Mixture	
Preparation	Trichloroethylene was dissolved in Mazola® corn oil so as to allow the proper dose to be contained in 1 ml (rats) or 0.5 ml (mice)
Maximum Storage Time	One week
Storage Conditions	2°-5°C

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

2-Year Studies	
Experimental Design	
Size of Test Groups	50 males and 50 females of each species
Doses	Rats: 0, 500, or 1,000 mg/kg body weight in corn oil by gavage; 1.0 ml per dose Mice: 0 or 1,000 mg/kg body weight in corn oil by gavage; 0.5 ml per dose
Duration of Dosing	Five days per week for 103 weeks
Type and Frequency of Observation	Observed twice daily for morbidity and mortality
Necropsy and Histologic Examination	All animals necropsied and examined histologically
Animals and Animal Maintenance	
Species	F344/N rats; $B6C3F_1$ mice
Animal Source	Harlan Industries (Indianapolis, IN)
Time Held before Start of Test	2.5 weeks
Age When Placed on Study	Rats: 8 weeks Mice: 8 weeks
Age When Killed	Rats: 111-115 weeks Mice: 112-115 weeks
Method of Animal Distribution	Assigned to cages according to a table of random numbers and then to groups according to another table of random numbers
Feed	Purina® Rodent Chow 5001 *ad libitum* (Distributed by O.K. Feed Store, Miami, FL)
Bedding	Sani Chip® hardwood, Pinewood Products Co. (Distributed by O.K. Feed Store, Miami, FL)
Water	Tap water via Edstrom Automatic Watering System (Waterford, WI)
Cages	Polycarbonate, Lab Products (Rochelle Park, NJ); cages changed and sanitized twice weekly; racks sanitized every 2 weeks
Animals per Cage	5 rats per cage; 10 mice per cage for the first 8 months and then 5 per cage
Cage Filters	Cerex spun nylon, Florida Filters (Miami, FL); filters changed every 2 weeks
Animal Room Environment	22°-24°C; 40%-60% relative humidity; 12 hours fluorescent light per day; room air changed 10-15 per hour
Other Chemicals on Test in Same Room	None
Chemical/Vehicle Mixture	
Preparation	Trichloroethylene was dissolved in Mazola® corn oil so as to allow the proper dose to be contained in 1 ml (rats) or 0.5 ml (mice)
Maximum Storage Time	One week for the first 16 weeks and one month thereafter
Storage Conditions	Refrigerated at 2°-5°C in glass bottles sealed with Teflon® septa and aluminum caps

III. RESULTS

RATS

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

THIRTEEN-WEEK STUDIES

All animals survived to the end of the study and only male rats dosed with 2,000 mg/kg/day of TCE exhibited >10% decrements in body weight (Table 2). The body final weight gains for both males and females dosed with 1,000 mg/kg/day or less were considered to be normal.

Histopathological examination of the tissues from animals receiving the highest doses of TCE revealed pulmonary vasculitis, usually involving small veins, in 6/10 males and 6/10 females. This change was also seen in 1/10 male and 1/10 female control animals. Most of these animals also had mild interstitial pneumonitis. Minimal or mild cytomegaly and karyomegaly of the renal tubular epithelial cells in the inner cortex was seen in 8/9 males receiving 2,000 mg/kg/day and the same effect, graded as equivocal or minimal, was seen in 5/10 females that had received the 1,000 mg/kg/day dose. These renal effects were so minimal that they were diagnosed only during a reevaluation of the tissues. The reevaluation was prompted by the production of definite renal toxicity in the 2-year study.

The results of this 13-week study in F344/N rats are essentially similar to those of an earlier 8-week study conducted in Osborne-Mendel rats (NCI, 1976). In that earlier study, only doses in excess of 5,000 mg/kg/day were lethal to rats. Doses of 1,000 mg/kg/day had no effect on body weight gains in males, but depressed weight gains in females by approximately 15%.

In view of the survival of all rats, the minimal effects on weight gain, and the relatively minor nature of the histological changes, dosage levels for the 2-year study were set at 500 and 1,000 mg/kg/day for both sexes.

TABLE 2. SURVIVAL AND MEAN BODY WEIGHTS OF F344/N RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE FOR 13 WEEKS

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weight Relative to Controls *(b)* (Percent)
		Initial	Final	Change	
MALES					
0	10/10	87	312	+225	—
125	10/10	88	292	+204	- 6
250	10/10	92	301	+209	- 4
500	10/10	95	313	+218	0
1,000	10/10	101	303	+202	- 3
2,000	10/10	83	238	+155	-24
FEMALES					
0	10/10	81	181	+100	—
62.5	10/10	72	168	+ 96	- 7
125	10/10	74	179	+105	- 1
250	10/10	75	177	+102	- 2
500	10/10	73	176	+103	- 3
1,000	10/10	76	177	+101	- 2

(a) Number surviving/number per group

(b) Weight Relative to Controls ▫

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

TWO-YEAR STUDIES

Body Weights and Clinical Signs

The growth curves for rats administered 500 or 1,000 mg/kg doses of TCE for 103 weeks are shown in Figure 1, and body weights are summarized in Table 3. The 1,000 mg/kg dose reduced weight gain in male rats, with an 11% decrement relative to controls being observed after 20 weeks. This effect was maintained throughout the experimental period, with high dose males exhibiting a 13% decrement after 99 weeks on study. Although mean body weight for the male rats administered the 500 mg/kg dose appears to be lower than that of the controls (Figure 1), the initial weights were lower than those of the controls (141 g versus 161 g) and therefore the differences in body weight in the 500 mg/kg male rats was not considered compound related. Both dosage levels of TCE reduced body weight gains in female rats, and after these animals were on study for approximately 60 weeks, the decreases in weight gain were dose related.

Gross observations of the appearance and behavior of the rats did not reveal any compound-related clinical signs.

Antibody Titers

Viral antibody titers are shown in Appendix F. At the end of 6 months, positive titers were identified for pneumonia (PVM) and Sendai viruses. Titer values for these viruses diminished over the course of the study and were negative at the 24-month test. Rat corona virus had a significant titer at 24 months.

Survival

Two female rats (one high dose and one vehicle control) were replaced, due to gavage error, during the initial 1.5 weeks of the study. Estimates of the probabilities of survival of male and female rats administered trichloroethylene and those of the vehicle controls are shown by the Kaplan and Meier curves in Figure 2. (The following animals died as a result of gavage error: 1 male vehicle control, 3 low dose males, 10 high dose males, 2 female vehicle controls, 5 low dose females, and 5 high dose females. These animals were censored from the Kaplan and Meier curves at the date of death.) The survival of the dosed male rats was significantly reduced when compared with that of the vehicle controls (low dose, P=0.005; high dose, P=0.001). No significant differences were observed between the dosed males or between any groups of females.

Among male rats, 35/50 (70%) of the controls, 20/50 (40%) of the low dose group, and 16/50 (32%) of the high dose group lived to the end of the study. Among female rats, 37/50 (74%) of the controls, 33/50 (66%) of the low dose group, and 26/50 (52%) of the high dose group lived to the end of the study. The survival data indicated above include one high dose male, two control males, and three control females that died during the termination period of the study (weeks 103-107). For the statistical evaluations of tumor incidences, these animals are considered to have been killed at termination.

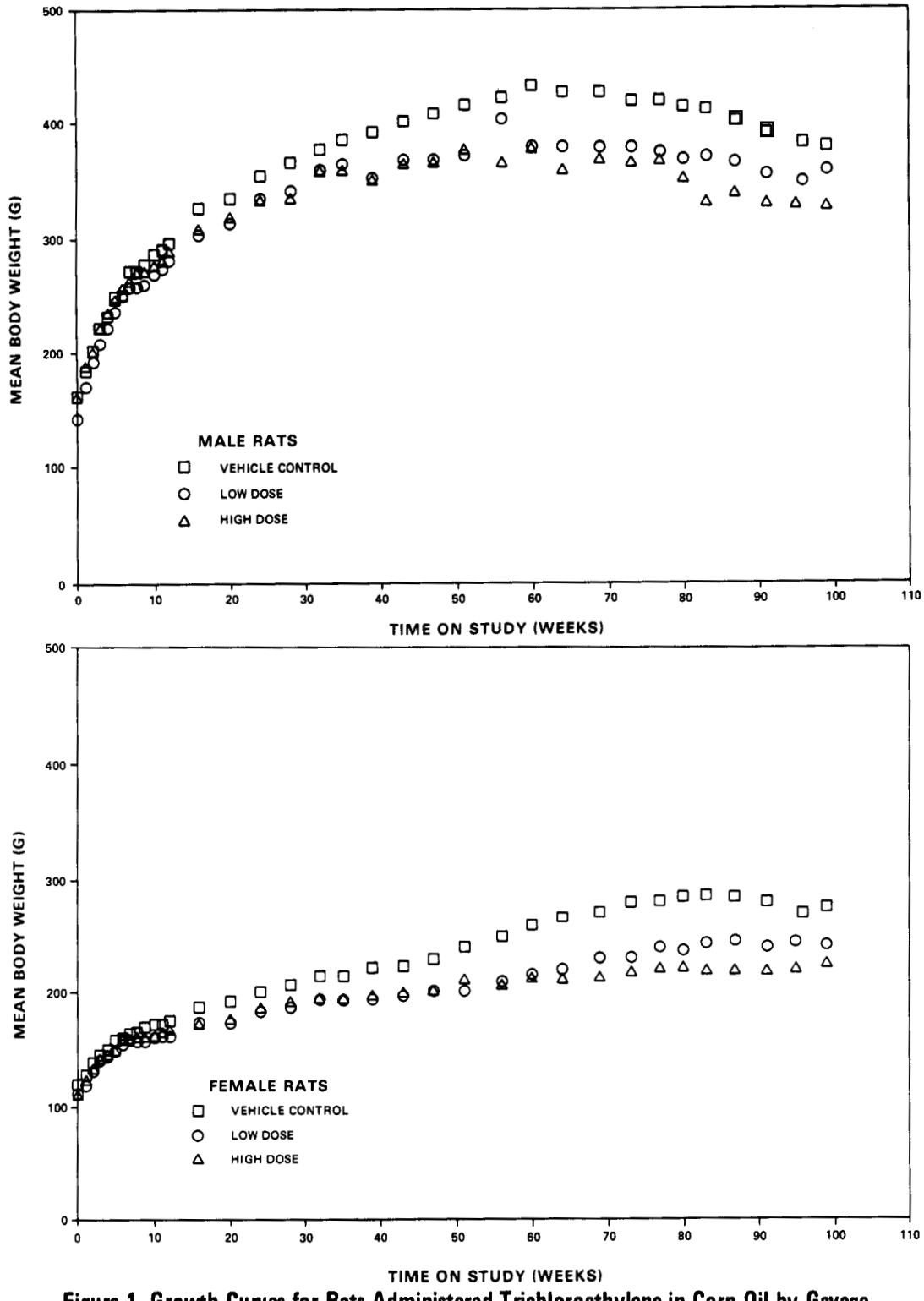


Figure 1. Growth Curves for Rats Administered Trichloroethylene in Corn Oil by Gavage

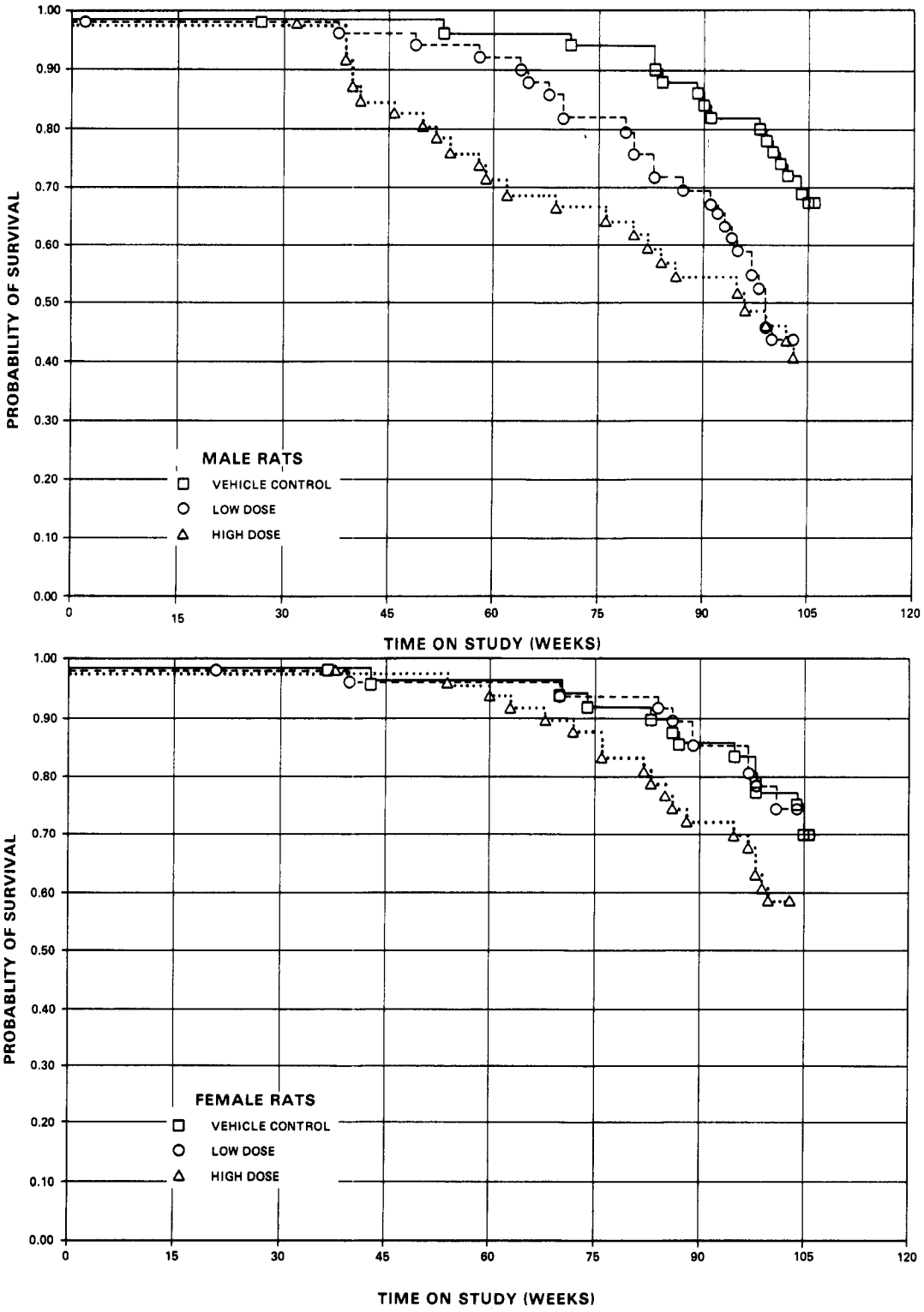


Figure 2. Survival Curves for Rats Administered Trichloroethylene in Corn Oil by Gavage

TABLE 3. MEAN BODY WEIGHTS (RELATIVE TO CONTROLS) OF RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE FOR TWO YEARS

		Mean Body Weight (grams)			Body Weight Relative to Controls *(a)* (Percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males						
	0	161	141	160	-12	- 1
	1	184	169	187	- 8	+ 2
	20	335	314	318	- 6	- 5
	39	392	353	350	-10	-11
	60	433	379	377	-12	-13
	80	414	367	352	-11	-15
	99	378	358	327	- 0	-13
Females						
	0	120	112	111	- 7	- 8
	1	128	119	123	- 7	- 4
	20	191	173	176	- 9	- 8
	39	221	193	197	-13	-11
	60	259	215	212	-17	-18
	80	285	236	221	-17	-22
	99	276	242	225	-12	-18

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

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms 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 and female rat studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2. Tables 4 and 5 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. Because of the reduced survival in dosed male rats, the statistical procedures that adjust for intercurrent mortality (life table and incidental tumor tests) were regarded as more meaningful than the "unadjusted" analysis in the evaluation of tumor incidence data in these groups. Many of the lymph nodes, thymuses, tracheae, pituitaries, thyroids, parathyroids, and ovaries were not examined microscopically. These omissions appear to be the result of faulty histological technique.

Kidney: Renal tubular adenocarcinoma occurred with a significant positive trend in male rats that survived to the end of the study (P=0.009), and the pairwise comparison between the control and high dose groups was significant (terminal incidences: control, 0/33; low dose, 0/20; high dose, 3/16; P=0.028). These tumors were not found in animals that died before the termination of the study. Additional tumors found in the kidneys of male rats included a transitional cell papilloma of the renal pelvis in an untreated control, a transitional-cell carcinoma of the renal pelvis and two tubular cell adenomas in low dose animals and one carcinoma (NOS) of the renal pelvis in a high dose animal. Among female rats, one high dose animal had a renal tubular adenocarcinoma.

Small renal tubular cell adenomas consisted of solid collections of renal tubular epithelial cells filling several contiguous tubules. The tumor cells were enlarged and had abundant cytoplasm, large nuclei, and prominent nucleoli. In larger tumors, there was an increasing degree

of cellular atypia. There was no sharp demarcation between the larger adenomas and the tubular cell adenocarcinomas. The adenocarcinomas contained solid sheets of cells and focal areas of necrosis, and the cells were often quite atypical, with large irregular nuclei and prominent nucleoli. Local invasion was a common feature of these tumors.

Toxic nephrosis, designated "cytomegaly," was present in 98% of the dosed male rats and in 100% of the dosed females, but was not found in any of the vehicle control rats of either sex. The lesion was first noticed in dosed rats that died early in the test and was shown microscopically as frank enlargement of the nucleus and cytoplasm of scattered individual tubular cells that had brush borders and that were located near the cortico-medullary junction.

Progression of the lesion became evident in kidneys taken from rats that died early or were killed during the test. As exposure time increased, affected tubular cells continued to enlarge and additional tubules and tubular cells were affected. Occasionally, some tubules were enlarged or dilated to the extent that they were difficult to identify as tubules. In animals that survived longer, there was a decrease in the numbers of the enlarged cells, the corresponding tubules were dilated, and portions of the basement membrane had a stripped appearance. Special stains (Periodic Acid Schiff) were not useful in attempts to determine if the apparently stripped basement membrane was in fact naked or covered by a thin cytoplasmic membrane extending from the one or more remaining cytomegalic tubular cells. In the most advanced stage, the lesion extended to the subcapsular cortex, where enlarged tubular cells were readily found. Development of cytomegaly did not completely overshadow development of the spontaneous rat nephropathy which also was present but was recognized in a lower percentage of dosed animals than controls.

The cytomegaly was graded in each instance by subjective microscopic evaluation; the designations used as measures of the degree of severity were: slight (1), moderate (2), well marked (3), and severe (4). In this context, slight (1) indicates a subtle change that is often detected only at high microscopic magnifications, involves a limited part of the organ, and probably would not affect the function of the organ. Severe (4) indicates an obvious lesion that is readily visible at low microscopic magnifications, involves a substantial part of the organ, would significantly affect the function of the organ, and might be life threatening. Moderate (2) and well marked (3) are intermediate grades between the two extremes.

The average numerical grade of the lesion in each group of rats was: 0.0 for male and female controls; 2.8 for low dose males; 1.9 for low dose females; 3.1 for high dose males; and 2.7 for high dose females. Cytomegaly was more severe in males than in females, and the high dose males were most severely affected.

Peritoneum: Malignant mesotheliomas were observed in increased incidence in the low dose males compared with the controls ($P=0.042$, life table test; control, 1/50, 2%; low dose, 5/50, 10%; high dose, 0/49, 0%). This tumor was not observed among female rats.

Hematopoietic System: Leukemia occurred in reduced ($P<0.05$) incidence in the low dose female group compared with the controls. Both leukemia and leukemia or lymphoma (combined) occurred in reduced but not statistically significant proportions in the high dose male and high dose female groups. The following incidences of leukemia were observed: males, control, 5/50 (10%); low dose, 5/50 (10%); high dose, 1/49 (2%); females, control, 14/50 (28%); low dose, 4/50 (8%); high dose, 9/50 (18%). A malignant lymphoma was found in one control male rat.

Pituitary: Chromophobe adenomas were observed in decreased incidence in both male and female dosed rats (males: control, 7/42, 17%; low dose, 2/35, 6%; high dose, 1/26; 4%; females: control, 13/37, 35%; low dose, 6/34, 18%; high dose, 6/41, 15%). The pairwise comparison between the high dose and control groups was statistically significant ($P=0.040$, incidental tumor test) for female rats.

Uterus: Endometrial stromal polyps were observed among female rats in a statistically significant negative trend ($P=0.035$, incidental tumor test; control, 15/48, 31%; low dose, 8/48, 17%; high dose, 6/46, 13%).

Testis: Interstitial cell tumors occurred in male rats with a decreased incidence in the high dose group relative to controls (control, 47/49, 96%; low dose, 47/49, 96%; high dose, 32/46, 70%). However, this effect was not statistically significant when survival differences were taken into account (incidental tumor tests).

TABLE 4. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)*

	Untreated Control	Vehicle Control	Low Dose	High Dose
Subcutaneous Tissue: Fibroma				
Tumor Rates				
Overall *(b)*	3/50 (6%)	4/50 (8%)	1/50 (2%)	0/49 (0%)
Adjusted *(c)*		10.2%	5.0%	0.0%
Terminal *(d)*		2/35 (6%)	1/20 (5%)	0/16 (0%)
Statistical Tests *(e)*				
Life Table		P=0.108N	P=0.356N	P=0.208N
Incidental Tumor Test		P=0.064N	P=0.216N	P=0.141N
Cochran-Armitage Trend Test		P=0.027N		
Fisher Exact Test			P=0.181N	P=0.061N
Skin or Subcutaneous Tissue: Fibroma				
Tumor Rates				
Overall *(b)*	3/50 (6%)	4/50 (8%)	1/50 (2%)	1/49 (2%)
Adjusted *(c)*		10.2%	5.0%	6.3%
Terminal *(d)*		2/35 (6%)	1/20 (5%)	1/16 (6%)
Statistical Tests *(e)*				
Life Table		P=0.318N	P=0.356N	P=0.475N
Incidental Tumor Test		P=0.238N	P=0.216N	P=0.373N
Cochran-Armitage Trend Test		P=0.104N		
Fisher Exact Test			P=0.181N	P=0.187N
Lung: Alveolar/Bronchiolar Carcinoma				
Tumor Rates				
Overall *(b)*	1/49 (2%)	3/50 (6%)	2/50 (4%)	2/49 (4%)
Adjusted *(c)*		7.6%	9.5%	10.9%
Terminal *(d)*		2/35 (6%)	1/20 (5%)	1/16 (6%)
Statistical Tests *(e)*				
Life Table		P=0.461	P=0.656	P=0.568
Incidental Tumor Test		P=0.583N	P=0.494N	P=0.639N
Cochran-Armitage Trend Test		P=0.415N		
Fisher Exact Test			P=0.500N	P=0.510N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Tumor Rates				
Overall *(b)*	1/49 (2%)	4/50 (8%)	2/50 (4%)	2/49 (4%)
Adjusted *(c)*		10.4%	9.5%	10.9%
Terminal *(d)*		3/35 (9%)	1/20 (5%)	1/16 (6%)
Statistical Tests *(e)*				
Life Table		P=0.584N	P=0.570N	P=0.669
Incidental Tumor Test		P=0.439N	P=0.368N	P=0.516N
Cochran-Armitage Trend Test		P=0.259N		
Fisher Exact Test			P=0.339N	P=0.349
Hematopoietic System: Leukemia				
Tumor Rates				
Overall *(b)*	11/50 (22%)	5/50 (10%)	5/50 (10%)	1/49 (2%)
Adjusted *(c)*		13.6%	17.9%	5.9%
Terminal *(d)*		4/35 (11%)	2/20 (10%)	0/16 (0%)
Statistical Tests *(e)*				
Life Table		P=0.394N	P=0.336	P=0.368N
Incidental Tumor Test		P=0.255N	P=0.548	P=0.309N
Cochran-Armitage Trend Test		P=0.094N		
Fisher Exact Test			P=0.630	P=0.107N

TABLE 4. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Untreated Control	Vehicle Control	Low Dose	High Dose
Hematopoietic System: Leukemia or Lymphoma				
Tumor Rates				
Overall *(b)*	12/50 (24%)	6/50 (12%)	5/50 (10%)	1/49 (2%)
Adjusted *(c)*		15.4%	17.9%	5.9%
Terminal *(d)*		4/35 (11%)	2/20 (10%)	0/16 (0%)
Statistical Tests *(e)*				
Life Table		P=0.287N	P=0.455	P=0.270N
Incidental Tumor Test		P=0.121N	P=0.512N	P=0.126N
Cochran-Armitage Trend Test		P=0.051N		
Fisher Exact Test			P=0.500N	P=0.059N
Kidney: Tubular-Cell Adenocarcinoma				
Tumor Rates				
Overall *(b)*	0/49 (0%)	0/48 (0%)	0/49 (0%)	3/49 (6%)
Adjusted *(c)*		0.0%	0.0%	18.8%
Terminal *(d)*		0/33 (0%)	0/20 (0%)	3/16 (19%)
Statistical Tests *(e)*				
Life Table		P=0.009	*(f)*	P=0.028
Incidental Tumor Test		P=0.009	*(f)*	P=0.028
Cochran-Armitage Trend Test		P=0.038		
Fisher Exact Test			*(f)*	P=0.125
Kidney: Tubular-Cell Adenoma or Adenocarcinoma				
Tumor Rates				
Overall *(b)*	0/49 (0%)	0/48 (0%)	2/49 (4%)	3/49 (6%)
Adjusted *(c)*		0.0%	5.6%	18.8%
Terminal *(d)*		0/33 (0%)	0/20 (0%)	3/16 (19%)
Statistical Tests *(e)*				
Life Table		P=0.019	P=0.194	P=0.028
Incidental Tumor Test		P=0.030	P=0.327	P=0.028
Cochran-Armitage Trend Test		P=0.084		
Fisher Exact Test			P=0.253	P=0.125
Pituitary: Chromophobe Adenoma				
Tumor Rates				
Overall *(b)*	4/39 (10%) *(g)*	7/42 (17%) *(h)*	2/35 (6%) *(i)*	1/26 (4%)
Adjusted *(c)*		21.2%	8.2%	7.7%
Terminal *(d)*		7/33 (21%)	1/18 (6%)	1/13 (8%)
Statistical Tests *(e)*				
Life Table		P=0.147N	P=0.285N	P=0.258N
Incidental Tumor Test		P=0.125N	P=0.250N	P=0.258N
Cochran-Armitage Trend Test		P=0.150N		
Fisher Exact Test			P=0.128N	P=0.111N
Adrenal: All Pheochromocytomas				
Tumor Rates				
Overall *(b)*	8/45 (18%)	4/45 (9%)	3/42 (7%)	1/44 (2%)
Adjusted *(c)*		13.3%	15.8%	3.2%
Terminal *(d)*		4/30 (13%)	3/19 (16%)	0/16 (0%)
Statistical Tests *(e)*				
Life Table		P=0.348N	P=0.571	P=0.393N
Incidental Tumor Test		P=0.270N	P=0.571	P=0.254N
Cochran-Armitage Trend Test		P=0.140N		
Fisher Exact Test			P=0.539N	P=0.187N

TABLE 4. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Untreated Control	Vehicle Control	Low Dose	High Dose
Thyroid: C-Cell Carcinoma				
Tumor Rates				
Overall *(b)*	0/44 (0%)	2/44 (5%)	3/43 (7%)	0/39 (0%)
Adjusted *(c)*		6.5%	15.9%	0.0%
Terminal *(d)*		2/31 (6%)	2/15 (13%)	0/14 (0%)
Statistical Tests *(e)*				
Life Table		P=0.470N	P=0.231	P=0.425N
Incidental Tumor Test		P=0.429N	P=0.281	P=0.425N
Cochran-Armitage Trend Test		P=0.232N		
Fisher Exact Test			P=0.489	P=0.278N
Thyroid: C-Cell Adenoma or Carcinoma				
Tumor Rates				
Overall *(b)*	5/44 (11%)	4/44 (9%)	3/43 (7%)	0/39 (0%)
Adjusted *(c)*		12.9%	15.9%	0.0%
Terminal *(d)*		4/31 (13%)	2/15 (13%)	0/14 (0%)
Statistical Tests *(e)*				
Life Table		P=0.224N	P=0.464	P=0.202N
Incidental Tumor Test		P=0.197N	P=0.519	P=0.202N
Cochran-Armitage Trend Test		P=0.061N		
Fisher Exact Test			P=0.513N	P=0.074N
Preputial Gland: Adenoma				
Tumor Rates				
Overall *(b)*	4/50 (8%)	4/50 (8%)	0/50 (0%)	1/49 (2%)
Adjusted *(c)*		11.4%	0.0%	6.2%
Terminal *(d)*		4/35 (11%)	0/20 (0%)	1/16 (6%)
Statistical Tests *(e)*				
Life Table		P=0.253N	P=0.154N	P=0.473N
Incidental Tumor Test		P=0.253N	P=0.154N	P=0.473N
Cochran-Armitage Trend Test		P=0.084N		
Fisher Exact Test			P=0.059N	P=0.187N
Preputial Gland: Adenoma or Adenocarcinoma				
Tumor Rates				
Overall *(b)*	4/50 (8%)	5/50 (10%)	1/50 (2%)	3/49 (6%)
Adjusted *(c)*		13.5%	5.0%	13.4%
Terminal *(d)*		4/35 (11%)	1/20 (5%)	1/16 (6%)
Statistical Tests *(e)*				
Life Table		P=0.553	P=0.254	P=0.536
Incidental Tumor Test		P=0.457N	P=0.211N	P=0.541N
Cochran-Armitage Trend Test		P=0.272N		
Fisher Exact Test			P=0.102N	P=0.369N
Testis: Interstitial-Cell Tumor				
Tumor Rates				
Overall *(b)*	44/47 (94%)	47/49 (96%)	47/49 (96%)	32/46 (70%)
Adjusted *(c)*		100.0%	100.0%	96.8%
Terminal *(d)*		35/35 (100%)	20/20 (100%)	14/15 (93%)
Statistical Tests *(e)*				
Life Table		P=0.004	P<0.001	P=0.008
Incidental Tumor Test		P=0.252N	P=0.190	P=0.594N
Cochran-Armitage Trend Test	P<0.001N			
Fisher Exact Test			P=0.691	P=0.001N

TABLE 4. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Untreated Control	Vehicle Control	Low Dose	High Dose
Peritoneum: Malignant Mesothelioma				
Tumor Rates				
Overall *(b)*	1/50 (2%)	1/50 (2%)	5/50 (10%)	0/49 (0%)
Adjusted *(c)*		2.9%	16.1%	0.0%
Terminal *(d)*		1/35 (3%)	0/20 (0%)	0/16 (0%)
Statistical Tests *(e)*				
Life Table		P=0.518	P=0.042	P=0.656N
Incidental Tumor Test		P=0.348N	P=0.274	P=0.656N
Cochran-Armitage Trend Test		P=0.407N		
Fisher Exact Test			P=0.102	P=0.505N
Peritoneum: All Mesotheliomas				
Tumor Rates				
Overall *(b)*	1/50 (2%)	1/50 (2%)	5/50 (10%)	1/49 (2%)
Adjusted *(c)*		2.9%	15.6%	6.3%
Terminal *(d)*		1/35 (3%)	0/20 (0%)	1/16 (6%)
Statistical Tests *(e)*				
Life Table		P=0.286	P=0.042	P=0.578
Incidental Tumor Test		P=0.583	P=0.274	P=0.578
Cochran-Armitage Trend Test		P=0.585		
Fisher Exact Test			P=0.102	P=0.747

(a) Dosed groups received doses of 500 or 1,000 mg/kg of trichloroethylene 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 each dosed group incidence is the P value corresponding to the pairwise comparison 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 test compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).
(f) Not significant; no tumors were observed in dosed or control groups.
(g) Two chromophobe carcinomas, one adenoma, NOS, and one carcinoma, NOS, were also observed.
(h) One chromophobe carcinoma was also observed.
(i) One adenoma, NOS, was also observed.

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

	Untreated Control	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Tumor Rates				
Overall *(b)*	0/49 (0%)	1/50 (2%)	1/49 (2%)	3/50 (6%)
Adjusted *(c)*		2.7%	3.0%	7.5%
Terminal *(d)*		1/37 (3%)	1/33 (3%)	0/26 (0%)
Statistical Tests *(e)*				
Life Table		P=0.151	P=0.736	P=0.246
Incidental Tumor Test		P=0.326	P=0.736	P=0.541
Cochran-Armitage Trend Test		P=0.202		
Fisher Exact Test			P=0.747	P=0.309
Hematopoietic System: Leukemia				
Tumor Rates				
Overall *(b)*	10/49 (20%) *(f)*	14/50 (28%)	4/50 (8%)	9/50 (18%)
Adjusted *(c)*		33.8%	10.7%	29.1%
Terminal *(d)*		10/37 (27%)	2/33 (6%)	6/26 (23%)
Statistical Tests *(e)*				
Life Table		P=0.316N	P=0.019N	P=0.446N
Incidental Tumor Test		P=0.110N	P=0.004N	P=0.182N
Cochran-Armitage Trend Test		P=0.121N		
Fisher Exact Test			P=0.009N	P=0.171N
Pituitary: Chromophobe Adenoma				
Tumor Rates				
Overall *(b)*	18/43 (42%)	13/37 (35%)	6/34 (18%)	6/41 (15%)
Adjusted *(c)*		37.5%	24.0%	22.0%
Terminal *(d)*		9/29 (31%)	5/23 (22%)	3/22 (14%)
Statistical Tests *(e)*				
Life Table		P=0.131N	P=0.135N	P=0.191N
Incidental Tumor Test		P=0.036N	P=0.075N	P=0.040N
Cochran-Armitage Trend Test		P=0.022N		
Fisher Exact Test			P=0.081N	P=0.032N
Pituitary: All Adenomas or Carcinomas				
Tumor Rates				
Overall *(b)*	19/43 (44%)	13/37 (35%)	8/34 (24%)	6/41 (15%)
Adjusted *(c)*		37.5%	30.3%	22.0%
Terminal *(d)*		9/29 (31%)	6/23 (26%)	3/22 (14%)
Statistical Tests *(e)*				
Life Table		P=0.151N	P=0.297N	P=0.191N
Incidental Tumor Test		P=0.038N	P=0.188N	P=0.040N
Cochran-Armitage Trend Test		P=0.024N		
Fisher Exact Test			P=0.209N	P=0.032N
Adrenal: Cortical Adenoma				
Tumor Rates				
Overall *(b)*	2/45 (4%)	1/46 (2%)	2/48 (4%)	3/47 (6%)
Adjusted *(c)*		3.0%	6.1%	12.0%
Terminal *(d)*		1/33 (3%)	2/33 (6%)	3/25 (12%)
Statistical Tests *(e)*				
Life Table		P=0.142	P=0.500	P=0.210
Incidental Tumor Test		P=0.142	P=0.500	P=0.210
Cochran-Armitage Trend Test	P=0.227			
Fisher Exact Test		P=0.516	P=0.317	

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

	Untreated Control	Vehicle Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma				
Tumor Rates				
Overall *(b)*	2/36 (6%) *(g)*	4/41 (10%)	1/45 (2%)	1/44 (2%)
Adjusted *(c)*		10.9%	3.3%	4.2%
Terminal *(d)*		3/34 (9%)	1/30 (3%)	1/24 (4%)
Statistical Tests *(e)*				
Life Table		P=0.168N	P=0.214N	P=0.290N
Incidental Tumor Test		P=0.127N	P=0.168N	P=0.210N
Cochran-Armitage Trend Test		P=0.086N		
Fisher Exact Test			P=0.152N	P=0.159N
Mammary Gland: Fibroadenoma				
Tumor Rates				
Overall *(b)*	10/49 (20%)	9/50 (18%)	12/50 (24%)	4/50 (8%)
Adjusted *(c)*		22.9%	32.6%	14.5%
Terminal *(d)*		7/37 (19%)	9/33 (27%)	3/26 (12%)
Statistical Tests *(e)*				
Life Table		P=0.307N	P=0.240	P=0.285N
Incidental Tumor Test		P=0.169N	P=0.353	P=0.177N
Cochran-Armitage Trend Test		P=0.114N		
Fisher Exact Test			P=0.312	P=0.117N
Uterus: Endometrial Stromal Polyp				
Tumor Rates				
Overall *(b)*	10/45 (22%)	15/48(31%)	8/48 (17%)	6/46 (13%)
Adjusted *(c)*		40.1%	23.1%	21.0%
Terminal *(d)*		13/35(37%)	7/33 (21%)	4/25 (16%)
Statistical Tests *(e)*				
Life Table		P=0.074N	P=0.098N	P=0.120N
Incidental Tumor Test		P=0.035N	P=0.069N	P=0.056N
Cochran-Armitage Trend Test		P=0.019N		
Fisher Exact Test			P=0.075N	P=0.030N
Uterus: Endometrial Stromal Polyp or Sarcoma				
Tumor Rates				
Overall *(b)*	10/45 (22%)	15/48 (31%)	8/48 (17%)	7/46(15%)
Adjusted *(c)*		40.1%	23.1%	23.5%
Terminal *(d)*		13/35 (37%)	7/33 (21%)	4/25(16%)
Statistical Tests *(e)*				
Life Table		P=0.127N	P=0.098N	P=0.193N
Incidental Tumor Test		P=0.060N	P=0.069N	P=0.086N
Cochran-Armitage Trend Test		P=0.037N		
Fisher Exact Test			P=0.075N	P=0.055N

(a) Dosed groups received doses of 500 or 1,000 mg/kg of trichloroethylene 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 each dosed group incidence is the P value corresponding to the pairwise comparison 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 test compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).
(f) One malignant lymphoma, histiocytic type, was also observed.
(g) One C-cell carcinoma was also observed.

THIRTEEN-WEEK STUDIES

The survival, body weight gains, and relative liver weights for mice receiving TCE for 13 weeks are summarized in Table 6. Deaths occurred in all males and 9/10 females receiving 6,000 mg/kg, 7/10 males and 1/10 females receiving 3,000 mg/kg, and 2/10 males and 1/10 females receiving 1,500 mg/kg. Mean body weights of male mice receiving 750, 1,500, or 3,000 mg/kg doses were depressed 11%, 19%, and 17%, respectively, relative to controls. Mean body weights of control and dosed groups of female mice were similar.

Liver weights (both absolute and as a percent of body weight) increased with dose. Liver weights were increased by more than 10% relative to controls for males receiving 750 mg/kg or more and for females receiving 1,500 mg/kg or more.

The most prominent hepatic lesion detected in the mice was centrilobular necrosis, observed in 6/10 males and 1/10 females administered 6,000 mg/kg. Although centrilobular necrosis was not seen in either males or females administered 3,000 mg/kg, 2/10 males had multifocal areas of calcification scattered throughout their livers. These areas of calcification are considered to be evidence of earlier hepatocellular necrosis. Multifocal calcification was also seen in the liver of a single female mouse that survived the 6,000 mg/kg dosage regimen. One female mouse administered 3,000 mg/kg also had an hepatocellular adenoma, an extremely rare lesion in female mice of this age (20 weeks).

As in the rat study, reevaluation of the kidney tissues revealed the presence of mild to moderate cytomegaly and karyomegaly of the renal tubular epithelial cells of the inner cortex. These lesions appear to be a response to repeated doses of TCE, since they were found in only 1 of the 13 males and 10 females that died after receiving doses of 3,000 or 6,000 mg/kg for up to 6 weeks. All four of the male mice that died after receiving the 3,000 mg/kg dose for 7-13 weeks had the lesions, as did all animals that survived the 6,000 mg/kg (1/10 females) and the 3,000 mg/kg doses (3/10 males and 9/10 females). Tissues from mice receiving lower doses of TCE were not examined.

The single dose chosen for the 2-year study in B6C3F$_1$ mice (1,000 mg/kg) was selected on the basis of results of the present 13-week study and the earlier 2-year study (NCI, 1976). While the relatively low incidence of major histopathological lesions among animals administered 3,000 mg/kg and the lack of clinical signs among animals administered 1,500 mg/kg suggested that 1,500 mg/kg might be an acceptable dose level for the 2-year study, the two deaths in males and one death in females at this level indicated toxicity. (The single death in females at 750 mg/kg occurred during week 2 and may not have been due to a toxic effect of trichloroethylene.) Mean liver weights and liver weight/body weight ratios also were increased at 1,500 mg/kg in both males and females, compared to controls. Doses in the range of 1,500 mg/kg were associated with significantly shorter survival times among female mice in the earlier 2-year study. Consequently, the 1,000 mg/kg dose was selected in an attempt to achieve improved survival in the new study.

TABLE 6. SURVIVAL, MEAN BODY WEIGHTS, AND MEAN LIVER WEIGHTS OF MICE ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE FOR 13 WEEKS

Dose (ppm)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weights Relative to Controls *(b)* (Percent)	Mean Liver Weights (Grams)	Relative Liver Weight (Percent of Body Weight)
		Initial	Final	Change			
MALES							
0	10/10	21	36	+15	—	2.10	5.8
375	10/10	20	35	+15	- 3	1.74	5.0
750	10/10	21	32	+11	-11	2.14	6.8
1,500	8/10 *(c)*	19	29	+10	-19	2.27	7.6
3,000	3/10 *(d)*	20	30	+10	-17	2.78	8.5
6,000	0/10 *(e)*	22	—	—	—	—	—
FEMALES							
0	10/10	18	26	+ 8	—	1.40	5.5
375	10/10	17	26	+ 9	0	1.31	5.0
750	9/10 *(f)*	17	26	+ 9	0	1.55	5.8
1,500	9/10 *(g)*	17	26	+ 9	0	1.80	6.5
3,000	9/10 *(g)*	15	26	+11	0	2.06	7.8
6,000	1/10 *(h)*	15	27	+12	+ 4	2.67	9.5

(a) Number surviving/number per group

(b) Weight Relative to Controls =

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

(c) Week of death: 2, 7

(d) Week of death: 1, 6, 6, 7, 9, 10, 13

(e) All mice died during the first week

(f) One mouse died during the second week

(g) One mouse died during the fifth week

(h) Eight mice died during the first week; one mouse died during the third week

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of dosed male mice were lower than those of controls throughout the study (Table 7 and Figure 3). Mean body weights of dosed and control female mice were comparable. No compound-related clinical signs were reported.

TABLE 7. MEAN BODY WEIGHTS (RELATIVE TO CONTROLS) OF MICE ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE FOR TWO YEARS

		Mean Body Weight (grams)		Body Weight Relative to Controls *(a)* (Percent)
	Week No.	Control	Dosed	Dosed
Males				
	0	27	27	0
	1	28	29	+ 4
	20	36	34	- 6
	39	46	39	-15
	60	46	41	-11
	80	46	40	-13
	99	41	37	-10
Females				
	0	21	22	+ 5
	1	22	23	+ 5
	20	28	28	0
	39	35	32	- 9
	60	39	36	- 8
	80	38	39	+ 3
	99	35	33	- 6

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

Antibody Titers

Viral antibody titers are shown in Appendix F. Sendai virus titers were positive at the 6-, 12-, and 18-month tests. At the 24-month test, all titers were negative.

Survival

Ten males (4 vehicle control and 6 dosed) and 11 females (6 vehicle control and 5 dosed) were replaced, due to gavage error, during the initial 1.5 weeks of the study. Estimates of the probabilities of survival of male and female mice administered trichloroethylene at the concentrations used in this bioassay and the estimates for the control groups are shown by the Kaplan and Meier curves in Figure 4. Two male vehicle controls, three dosed males, one female vehicle control, and three dosed females died as a result of gavage error. These animals were censored from the Kaplan and Meier curves at the date of death. The survival of the male dosed group was significantly reduced ($P=0.004$) when compared with that of the controls. No significant difference was observed between the female control and dosed groups.

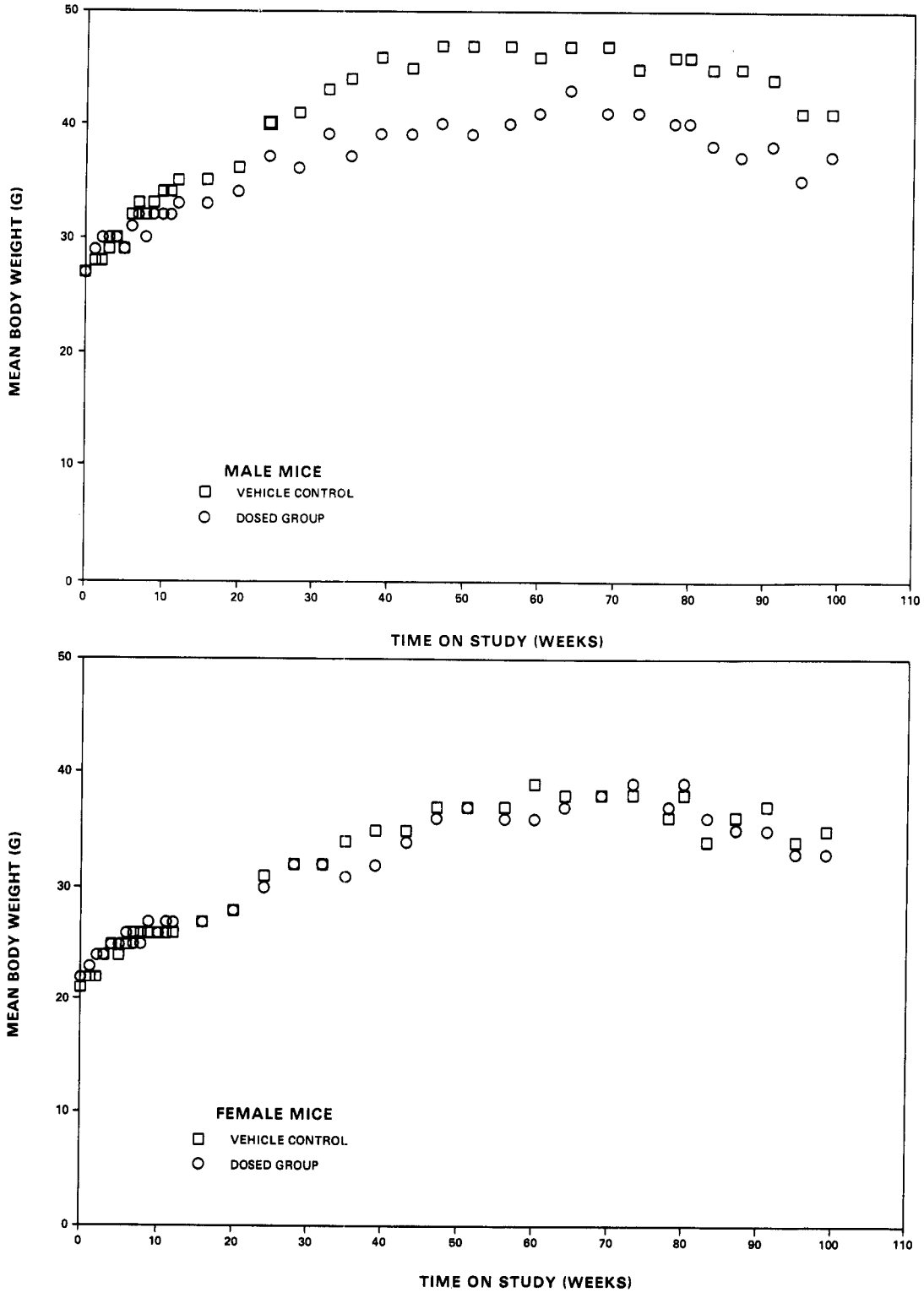


Figure 3. Growth Curves for Mice Administered Trichloroethylene in Corn Oil by Gavage

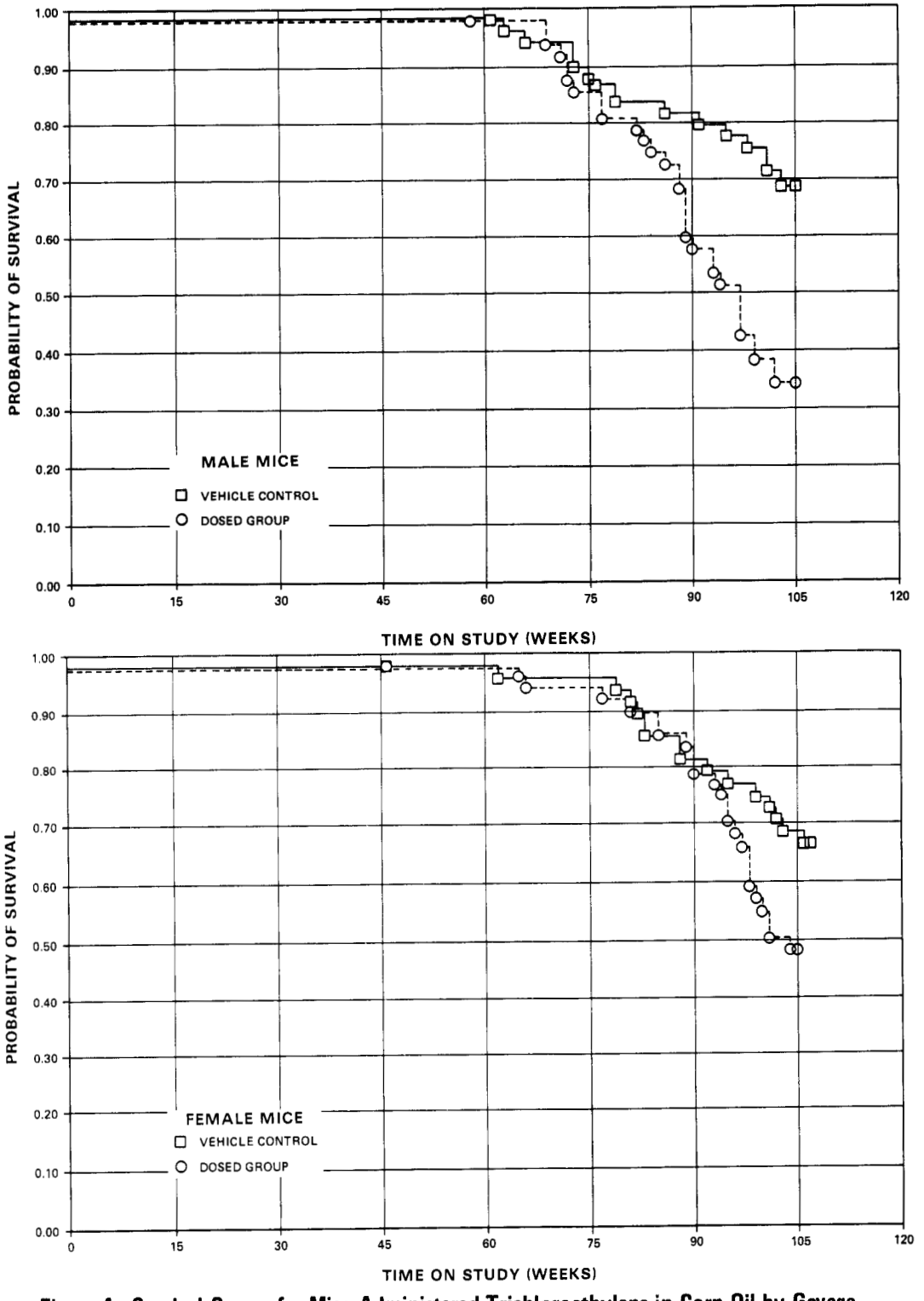


Figure 4. Survival Curves for Mice Administered Trichloroethylene in Corn Oil by Gavage

In male mice, 33/50 (66%) of the controls and 16/50 (32%) of the dosed group lived to the end of the study. In female mice, 32/50 (64%) of the controls and 23/50 (46%) of the dosed group lived to the end of the study. The survival data include four control males, one control female, and one dosed female that died during the termination period of the study (weeks 104-107). For the statistical evaluation of tumor incidences, these animals are considered to have been killed at termination.

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 Appendix D, Tables D1 and D2. Tables 8 and 9 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in either group. Many of the lymph nodes, thymuses, tracheae, pituitaries, thyroids, parathyroids, and ovaries were not examined microscopically. These omissions appear to be the result of faulty histological technique.

Liver: The incidence of hepatocellular carcinoma was significantly increased in dosed male and female mice (males: control, 8/48; dosed, 31/50; $P<0.001$; females: control, 2/48; dosed, 13/49; $P\leq0.002$). In five dosed males and one control male, these tumors metastasized to the lung. The incidence of hepatocellular adenomas was increased in dosed mice (males: control, 7/48; dosed, 14/50; females: control, 4/48; dosed, 16/49; $P<0.05$).

Microscopically, the hepatocellular adenomas were circumscribed areas of distinctive hepatic parenchymal cells with a perimeter of normal appearing parenchyma in which there were areas that appeared to be undergoing compression from expansion of the tumor. Mitotic figures were sparse or absent, but the tumors lacked typical lobular organization.

The hepatocellular carcinomas had markedly abnormal cytology and architecture. Abnormalities in cytology included increased cell size, decreased cell size, cytoplasmic eosinophilia, cytoplasmic basophilia, cytoplasmic vacuolization, cytoplasmic hyaline bodies and variations in nuclear appearance. In many instances, several or all of the abnormalities were present in different areas of the tumor. There also were variations in architecture. Some of the hepatocellular carcinomas had areas of trabecular organization. The general microscopic appearance was that of a diffusely infiltrating hepatocellular tumor that was replacing the normal architectural pattern of the liver. Often the boundary between recognizable tumor and nonneoplastic liver was vague. In some areas, subtle infiltration of tumor cells among persistent remnants of portal areas created a confusion of microscopic details that were difficult to interpret. Mitosis was variable in amount and location.

Lung: Alveolar/bronchiolar adenomas occurred at an increased incidence in dosed female mice (life table, $P=0.040$; control, 0/48; dosed, 4/48). However, the incidence of alveolar/bronchiolar adenoma or carcinoma (combined) was not significantly elevated in dosed female mice.

Hematopoietic System: Lymphoma (all malignant) and lymphoma or leukemia occurred at increased incidences in dosed female mice ($P<0.05$, life table test; lymphoma, control, 7/48, 15%; dosed, 13/49, 27%; lymphoma or leukemia, control, 7/48, 15%; dosed 14/49, 29%). In male mice, these tumors did not occur in statistically significant proportions.

Stomach: Squamous-cell papillomas were found in two dosed female mice, and a squamous cell carcinoma was found in a third dosed female mouse. A squamous cell carcinoma was also found in a male vehicle control.

Kidney: A compound related toxic nephrosis, designated as "cytomegaly," was present in 90% of the dosed male and 98% of the dosed female mice but not in the controls. The pathologic development was basically similar to the comparable cytomegaly found in dosed rats, but it was relatively less severe and did not develop to a stage in which there was extensive loss of cytomegalic epithelial cells and tubular dilation. The cytomegaly in mice was generally graded as slight (1) or moderate (2); in only one instance was a grade of well marked (3) assigned (average numerical grade, 0.0 for control males and females, 1.5 for dosed males, and 1.8 for dosed females). One control male had a renal tubular cell adenoma, and one dosed male had a renal tubular cell adenocarcinoma.

Harderian Gland: Harderian gland adenomas were detected in 4 dosed male and 3 dosed female mice. None were observed in male or female vehicle control mice. Only Harderian glands considered abnormal at necropsy were examined microscopically.

TABLE 8. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)*

	Vehicle Control	Dosed
Lung: Alveolar/Bronchiolar Adenoma		
Tumor Rates		
Overall *(b)*	4/49 (8%)	5/50 (10%)
Adjusted *(c)*	10.5%	27.1%
Terminal *(d)*	2/33 (6%)	4/16 (25%)
Statistical Tests *(e)*		
Life Table		P=0.197
Incidental Tumor Test		P=0.375
Fisher Exact Test		P=0.513
Lung: Alveolar/Bronchiolar Carcinoma		
Tumor Rates		
Overall *(b)*	3/49 (6%)	1/50 (2%)
Adjusted *(c)*	9.1%	4.0%
Terminal *(d)*	3/33 (9%)	0/16 (0%)
Statistical Tests *(e)*		
Life Table		P=0.553N
Incidental Tumor Test		P=0.407N
Fisher Exact Test		P=0.301N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma		
Tumor Rates		
Overall *(b)*	7/49 (14%)	6/50 (12%)
Adjusted *(c)*	19.2%	30.0%
Terminal *(d)*	5/33 (15%)	4/16 (25%)
Statistical Tests *(e)*		
Life Table		P=0.310
Incidental Tumor Test		P=0.575
Fisher Exact Test		P=0.484N
Hematopoietic System: Malignant Lymphoma, Undifferentiated Type		
Tumor Rates		
Overall *(b)*	3/50 (6%)	5/50 (10%)
Adjusted *(c)*	6.7%	17.4%
Terminal *(d)*	0/33 (0%)	1/16 (6%)
Statistical Tests *(e)*		
Life Table		P=0.258
Incidental Tumor Test		P=0.590
Fisher Exact Test		P=0.357
Hematopoietic System: Malignant Lymphoma, Mixed Type		
Tumor Rates		
Overall *(b)*	3/50 (6%)	3/50 (6%)
Adjusted *(c)*	8.8%	14.6%
Terminal *(d)*	2/33 (6%)	1/16 (6%)
Statistical Tests *(e)*		
Life Table		P=0.348
Incidental Tumor Test		P=0.663N
Fisher Exact Test		P=0.661

TABLE 8. ANALYSIS OF PRIMARY TUMORS IN MALE MICE (a) (Continued)

	Vehicle Control	Dosed
Hematopoietic System: Lymphoma, All Malignant		
Tumor Rates		
Overall(b)	11/50 (22%)	13/50 (26%)
Adjusted (c)	25.2%	45.7%
Terminal (d)	3/33 (9%)	3/16 (19%)
Statistical Tests (e)		
Life Table		P=0.116
Incidental Tumor Test		P=0.398N
Fisher Exact Test		P=0.408
Liver: Adenoma		
Tumor Rates		
Overall(b)	7/48 (15%)	14/50 (28%)
Adjusted (c)	20.6%	53.1%
Terminal (d)	6/33 (18%)	6/16 (37%)
Statistical Tests (e)		
Life Table		P=0.002
Incidental Tumor Test		P=0.048
Fisher Exact Test		P=0.084
Liver: Carcinoma		
Tumor Rates		
Overall(b)	8/48 (17%)	31/50 (62%)
Adjusted (c)	22.1%	92.9%
Terminal (d)	6/33 (18%)	14/16 (88%)
Statistical Tests (e)		
Life Table		P<0.001
Incidental Tumor Test		P<0.001
Fisher Exact Test		P<0.001
Liver: Adenoma or Carcinoma		
Tumor Rates		
Overall(b)	14/48 (29%)	39/50 (78%)
Adjusted (c)	38.4%	100%
Terminal (d)	11/33 (33%)	16/16 (100%)
Statistical Tests (e)		
Life Table		P<0.001
Incidental Tumor Test		P<0.001
Fisher Exact Test		P<0.001
Harderian Gland: All Adenomas		
Tumor Rates		
Overall(b)	0/50 (0%)	4/50 (8%)
Adjusted (c)	0.0%	12.0%
Terminal (d)	0/33 (0%)	0/16 (0%)
Statistical Tests (e)		
Life Table		P=0.044
Incidental Tumor Test		P=0.216
Fisher Exact Test		P=0.059

TABLE 8. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)* (Continued)

(a) The dosed group received doses of 1,000 mg/kg of trichloroethylene 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 dosed group incidence is the P value corresponding to the pairwise comparison between the dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Fisher exact test compares directly the overall incidence rates. A negative trend or lower incidence is indicated by N.

TABLE 9. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)*

	Vehicle Control	Dosed
Lung: Alveolar/Bronchiolar Adenoma		
Tumor Rates		
Overall *(b)*	0/48 (0%)	4/48 (8%)
Adjusted *(c)*	0.0%	14.3%
Terminal *(d)*	0/32 (0%)	2/22 (9%)
Statistical Tests *(e)*		
Life Table		P=0.040
Incidental Tumor Test		P=0.064
Fisher Exact Test		P=0.059
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma		
Tumor Rates		
Overall *(b)*	1/48 (2%)	4/48 (8%)
Adjusted *(c)*	2.5%	14.3%
Terminal *(d)*	0/32 (0%)	2/22 (9%)
Statistical Tests *(e)*		
Life Table		P=0.132
Incidental Tumor Test		P=0.184
Fisher Exact Test		P=0.181
Hematopoietic System: Malignant Lymphoma, Undifferentiated Type		
Tumor Rates		
Overall *(b)*	1/48 (2%)	3/49 (6%)
Adjusted *(c)*	2.2%	10.1%
Terminal *(d)*	0/32 (0%)	0/23 (0%)
Statistical Tests *(e)*		
Life Table		P=0.252
Incidental Tumor Test		P=0.476
Fisher Exact Test		P=0.316
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type		
Tumor Rates		
Overall *(b)*	0/48 (0%)	3/49 (6%)
Adjusted *(c)*	0.0%	9.6%
Terminal *(d)*	0/32 (0%)	0/23 (0%)
Statistical Tests *(e)*		
Life Table		P=0.096
Incidental Tumor Test		P=0.324
Fisher Exact Test		P=0.125
Hematopoietic System: Malignant Lymphoma, Histiocytic Type		
Tumor Rates		
Overall *(b)*	1/48 (2%)	3/49 (6%)
Adjusted *(c)*	2.8%	10.9%
Terminal *(d)*	0/32 (0%)	2/23 (9%)
Statistical Tests *(e)*		
Life Table		P=0.228
Incidental Tumor Test		P=0.323
Fisher Exact Test		P=0.316

TABLE 9. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE (a) (Continued)

	Vehicle Control	Dosed
Hematopoietic System: Malignant Lymphoma, Mixed Type		
Tumor Rates		
Overall(b)	3/48 (6%)	2/49 (4%)
Adjusted (c)	9.1%	7.5%
Terminal (d)	2/32 (6%)	1/23 (4%)
Statistical Tests (e)		
Life Table		P=0.636N
Incidental Tumor Test		P=0.424N
Fisher Exact Test		P=0.490N
Hematopoietic System: Lymphoma, All Malignant		
Tumor Rates		
Overall(b)	7/48 (15%)	13/49 (27%)
Adjusted (c)	18.8%	38.0%
Terminal (d)	3/32 (9%)	3/23 (13%)
Statistical Tests (e)		
Life Table		P=0.047
Incidental Tumor Test		P=0.331
Fisher Exact Test		P=0.114
Hematopoietic System: Lymphoma or Leukemia		
Tumor Rates		
Overall(b)	7/48 (15%)	14/49 (29%)
Adjusted (c)	18.8%	39.3%
Terminal (d)	3/32 (9%)	3/23 (13%)
Statistical Tests (e)		
Life Table		P=0.032
Incidental Tumor Test		P=0.287
Fisher Exact Test		P=0.076
Liver: Adenoma		
Tumor Rates		
Overall(b)	4/48 (8%)	16/49 (33%)
Adjusted (c)	12.5%	55.6%
Terminal (d)	4/32 (13%)	11/23 (48%)
Statistical Tests (e)		
Life Table		P<0.001
Incidental Tumor Test		P=0.001
Fisher Exact Test		P=0.003
Liver: Carcinoma		
Tumor Rates		
Overall(b)	2/48 (4%)	13/49 (27%)
Adjusted (c)	6.2%	43.9%
Terminal (d)	2/32 (6%)	8/23 (35%)
Statistical Tests (e)		
Life Table		P<0.001
Incidental Tumor Test		P=0.002
Fisher Exact Test		P=0.002

TABLE 9. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE (a) (Continued)

	Vehicle Control	Dosed
Liver: Adenoma or Carcinoma		
Tumor Rates		
Overall(b)	6/48 (13%)	22/49 (45%)
Adjusted (c)	18.7%	69.7%
Terminal (d)	6/32 (19%)	4/23 (61%)
Statistical Tests (e)		
Life Table		P<0.001
Incidental Tumor Test		P<0.001
Fisher Exact Test		P<0.001
Stomach: Squamous Cell Papilloma or Carcinoma		
Tumor Rates		
Overall(b)	0/47 (0%)	3/47 (6%)
Adjusted (c)	0.0%	8.1%
Terminal (d)	0/32 (0%)	0/22 (0%)
Statistical Tests (e)		
Life Table		P=0.112
Incidental Tumor Test		P=0.261
Fisher Exact Test		P=0.121
Pituitary: Chromophobe Adenoma		
Tumor Rates		
Overall(b)	3/27 (11%)	0/28 (0%)
Adjusted (c)	13.1%	0.0%
Terminal (d)	2/19 (11%)	0/14 (0%)
Statistical Tests (e)		
Life Table		P=0.183N
Incidental Tumor Test		P=0.081N
Fisher Exact Test		P=0.111N
Harderian Gland: Adenoma		
Tumor Rates		
Overall(b)	0/48 (0%)	3/49 (6%)
Adjusted (c)	0.0%	8.3%
Terminal (d)	0/32 (0%)	0/23 (0%)
Statistical Tests (e)		
Life Table		P=0.114
Incidental Tumor Test		P=0.171
Fisher Exact Test		P=0.125

(a) The dosed groups received doses of 1,000 mg/kg of trichloroethylene 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 is the P value associated with the trend test. Beneath the dosed group incidence is the P value corresponding to the pairwise comparison between the dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Fisher exact test compares directly the overall incidence rates. A negative trend or lower incidence is indicated by N.

IV. DISCUSSION AND CONCLUSIONS

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Carcinogenesis studies of epichlorohydrin-free trichloroethylene were conducted by administering the test chemical in corn oil by gavage to groups of 50 male and 50 female F344/N rats and $B6C3F_1$ mice. Trichloroethylene was administered five times per week for 103 weeks, and surviving animals were killed between weeks 103 and 107. Groups of 50 rats and 50 mice of each sex received corn oil by gavage on the same schedule and served as vehicle controls. Groups of 50 male and 50 female rats were used as untreated controls.

Groups of 10 male and 10 female rats received TCE by gavage at doses of 125 to 2,000 mg/kg (males) and 62.5 to 1,000 mg/kg (females) for 13 weeks. Groups of 10 male and 10 female mice received gavage doses of 375 to 6,000 mg/kg of TCE for 13 weeks. Survival, body weight gains, and previous experience with TCE were used to select doses for the 2-year studies. All rats survived the 13-week studies; males receiving 2,000 mg/kg exhibited a 24% difference in final body weight compared to controls. The doses selected for the 2-year study in rats were 500 and 1,000 mg/kg for both sexes. These dose levels were lower than the initial doses used in the earlier bioassay in Osborne-Mendel rats (650 and 1,300 mg/kg for both sexes). Two dose levels were used in the rat portion of the study because TCE had not been tested in a bioassay with F344/N rats, and in the earlier bioassay in Osborne-Mendel rats the chemical was not shown to be carcinogenic.

All male mice receiving 750 mg/kg, 8/10 males given 1,500 mg/kg, and 9/10 female mice administered 750 or 1,500 mg/kg survived the 13-week experimental period. The single dosage level selected for the 2-year study in mice was 1,000 mg/kg for both sexes. This dose was less than the high doses used in the earlier bioassay in $B6C3F_1$ mice (2,339 mg/kg for males and 1,739 for females). A single dose level was used in the mouse study because TCE containing epichlorohydrin had been shown to be carcinogenic in $B6C3F_1$ mice in the earlier bioassay (NCI, 1976). The mice in the present study served as "positive" controls.

The earlier bioassay of TCE (NCI, 1976) established the kidneys of both Osborne-Mendel rats and $B6C3F_1$ mice as target organs for non-neoplastic lesions (toxic nephrosis) induced by long-term administration of TCE. The results of the present study confirmed the effect in $B6C3F_1$ mice, and the data indicate that the kidney is a target organ in F344/N rats as well.

Toxic nephropathy was present in 98% of the dosed male rats, in 100% of the dosed female rats, in 90% of the dosed male mice, and in 98% of the dosed female mice; and was not present in any of the vehicle control rats or mice of either sex. First noticed in rats that died early, the lesions were diagnosed as frank enlargement of the nucleus and cytoplasm of scattered individual tubular cells with brush borders and located near the cortico-medullary junction. Progression of the lesion was evident. As exposure time increased, affected tubular cells continued to enlarge and additional tubules and tubular cells were affected. Occasionally, some tubules were enlarged or dilated to the extent that they were difficult to identify as tubules. Eventually, there was loss of some enlarged cells. Corresponding tubules became dilated and portions of the basement membrane had a stripped appearance. In the most advanced stage, the lesion had progressed to the subcapsular cortex, with enlarged tubular cells. Development of toxic nephropathy did not completely overshadow development of the "spontaneous" rat nephropathy which was recognized in a smaller number of dosed animals than of controls. The toxic nephropathy was graded as slight (1), moderate (2), well marked (3), and severe (4). The numerical value calculated for each group of rats was 0.0 for male and female controls, 2.8 for low dose males, 1.9 for low dose females, 3.1 for high dose males, and 2.7 for high dose females. In mice, the pathologic development was basically similar to the comparable cytomegaly found in dosed rats, but it was relatively less severe and did not develop to a stage in which there was extensive loss of cytomegalic epithelial cells and tubular dilation. The cytomegaly in mice was generally graded as slight (1) or moderate (2); in only one instance was a grade of well marked (3) assigned (average numerical grade, 0.0 for control males and females, 1.5 for dosed males, and 1.8 for dosed females).

In addition to the nonneoplastic renal lesions, the present study has established the kidney of the male F344/N rat as a target organ for neoplastic changes induced by long term administration of TCE. In male rats, the high dose of TCE was associated with a significant ($P<0.05$) increase in the incidence of renal tubular cell adenocarcinoma in rats killed at the end of the experiment (control, 0/33; low dose, 0/20; high dose, 3/16). In addition, two low dose male rats had tubular cell adenoma. Other types of neoplasms found in the kidneys of male rats

included a transitional cell carcinoma of the kidney pelvis in a low dose animal and a carcinoma (NOS) of the renal pelvis in a high dose animal. One high dose female also had a renal adenocarcinoma. No renal neoplasms were found in vehicle control animals, but one untreated control male had a transitional cell papilloma of the renal pelvis.

The primary criterion used to differentiate small tubular cell adenocarcinomas from tubular cell adenomas in this study was evidence of basement membrane invasion. Marked cellular atypia, aggressive growth, and increased mitotic activity characterized the adenocarcinoma. Because of their morphologic similarities, there is little doubt that tubular cell adenomas have the potential to progress to renal adenocarcinomas. For this reason, there is validity in combining renal tubular cell adenomas and adenocarcinomas for determining the carcinogenicity of TCE. The number of renal tubular cell neoplasms in male rats is control, 0/48; low dose, 2/49; and high dose, 3/49.

Renal tumors are rare among F344/N male rats, with 3/748 (0.4%) corn oil control rats in the Bioassay Program having had adenocarcinoma, adenoma, or carcinoma of the renal pelvis (Appendix E, Table E1). All three of these tumors were adenocarcinomas, and all three occurred in animals killed at the end of their respective studies. The incidence of renal tumors among the dosed male rats in this study exceeds both historical and concurrent control rates.

The renal tumors observed in dosed male rats were probably produced by TCE administration; these tumors may have been secondary to the nephrotoxicity. However, TCE produced the same nephrotoxicity in female rats and in both sexes of mice without inducing these tumors; thus, nephrotoxicity did not lead to carcinogenicity in three of four experiments.

Both dose levels of TCE used in this study were toxic for male F344/N rats; the mechanism or causes of the early deaths among rats in this study have not been established. This decreased survival might have reduced the sensitivity of the bioassay to detect a higher incidence of adenocarcinomas or other neoplasms. Ten (20%) high dose male rats were killed accidentally by gavage error (these deaths were not considered to have been due to chemical toxicity and even with these excluded, the decrease in survival of high dose males was significant, P=0.001). There appears to be a dose-response relationship in the incidence of animals accidentally killed by gavage error (males: 1 vehicle control, 3 low dose, 10 high dose; females: 2 vehicle controls, 5 low dose, 5 high dose).

The incidence of mesotheliomas of the peritoneum among low dose male rats was increased (control, 1/50; low dose, 5/50; high dose, 1/49; $P<0.05$). The first mesothelioma to be diagnosed was in a low dose animal during week 64 (the others were at weeks 70, 97, 99, and 100), and 29/50 of the high dose males survived longer than 64 weeks. The mesothelioma found among high dose males was detected at 103 weeks, whereas the one in controls was observed at week 106. The incidence of this tumor in the low dose males exceeds the historical incidence (16/752, 2.1%, Appendix E, Table E2). This increase in mesotheliomas may have been related to the administration of TCE.

The results of the present study with epichlorohydrin-free TCE in mice are similar to those with epichlorohydrin-containing TCE (NCI, 1976). In both studies, TCE administration produced significant increases in the incidence of male and female $B6C3F_1$ mice with hepatocellular carcinoma. In the present study, a higher percentage of dosed male mice dying before the end of the study (16/34, 47%) had hepatocellular carcinoma compared with control males dying early (2/15, 13%). The earliest hepatocellular carcinoma found among dosed males was at week 57, and the earliest diagnosis among control males was at week 75. The incidence of dosed male mice having this tumor detected at the end of the study was 14/16 (88%) versus 6/33 (18%) in the control groups. The incidence of dosed male mice with hepatocellular carcinoma exceeded the rates in either concurrent or historical control groups (31/50, 62%, versus 8/48, 17%, or 120/656, 18%; Appendix E, Table E7). Pulmonary metastasis of the hepatocellular carcinomas was found in 5/31 (16%) dosed males and 1/8 (13%) control males.

The incidence of dosed female mice with hepatocellular carcinoma (13/49, 27%) was seven to nine times greater than that in either concurrent (2/48, 4%) or historical (22/751, 2.9%) control groups. Five of the 13 (31%) dosed females with this tumor died before the end of the study, while both of the control females with hepatocellular carcinoma survived to the scheduled termination. No metastases were found among female mice. Likewise, hepatocellular adenomas were increased in both sexes (males:

control, 3/48; dosed, 8/50; females: control, 2/48; dosed, 8/49).

Harderian gland adenomas were detected in 4/50 (8%) dosed male and 3/49 (6%) dosed female mice, all of which died prior to the end of the study. No Harderian gland tumors were found in control mice. Among males, the incidence was significant by life table analysis ($P<0.05$), but not by the incidental tumor test. The incidental tumor test is the most appropriate method of analysis because this type of tumor is not life threatening. The incidental tumor test also adjusts for the survival differences between dosed and control groups. Historically, Harderian gland tumors occur in 2.4% of male and 0.8% of female B6C3F$_1$ mice (Appendix E, Table E10). Harderian glands were examined microscopically only when found to be grossly abnormal at necropsy; those animals not having visible lesions were not examined similarly.

The increased incidence of dosed female mice with malignant lymphoma ($P<0.05$) and lymphoma or leukemia ($P<0.05$) are not considered to be related to the administration of TCE. The incidence in the concurrent control group was somewhat lower than that in the historical controls, and the incidences in dosed females were within the ranges of historical incidences (Appendix E, Table E9).

Although the incidence of alveolar/bronchiolar adenomas was significantly increased in dosed female mice ($P<0.05$, life table analysis), the significance was lost when adenomas were combined with carcinomas. While this increase in adenomas cannot be ignored, to distinguish between some alveolar/bronchiolar adenomas and carcinomas is sometimes difficult or arbitrary. Therefore, the most meaningful measure of these tumors is considered to be their combined incidence. Because of this, the increased incidence of alveolar/bronchiolar adenomas in dosed female mice is not considered to be due to TCE administration. Using the data available from the previous study (NCI, 1976), IARC considered the increased incidences of lung tumors as being caused by TCE (IARC, 1979; 1982).

Three tumors of the nonglandular stomach were found among dosed female mice, but their incidence was not significantly increased when compared with that of the controls. One animal (dead at week 65) had a squamous cell carcinoma, and two others (dead at week 89 and week 99) had squamous cell papillomas. Squamous cell papillomas have been detected previously in 3/656 (0.5%) gavage control females, while squamous cell carcinomas have never been reported in gavage control females in the Bioassay Program. One vehicle control male in the present study (dead at week 63) had a squamous cell carcinoma. While these stomach lesions in dosed female mice may have been due to the 2-year gavage administration of TCE, their appearance is not considered to be an indication of carcinogenicity per se. The earlier bioassay of TCE (NCI, 1976) did not reveal evidence of chemically-related stomach neoplasms.

In both the rat and mouse portions of this study, many of the lymph nodes, thymuses, tracheae, pituitaries, thyroids, parathyroids, and ovaries were not examined microscopically. These omissions appear to be the result of faulty histological techniques. Because none of these tissues are likely target organs for TCE, these losses are of lesser significance with respect to this study. The results in male F344/N rats were considered equivocal for detecting a carcinogenic response because both groups receiving TCE showed significantly reduced survival compared to vehicle controls (35/50, 70%; 20/50, 40%; 16/50, 32%) and because 20% of the animals in the high dose group were killed accidently by gavage error.

As of August 1983, Dr. C. Maltoni (Institute of Oncology, Bologna, Italy) was examining the histopathological portion of several long term carcinogenesis studies of TCE administered by inhalation at 0, 10, 100, 300, and 600 ppm and for different periods of time up to two years to male and female Sprague-Dawley rats and to male and female Swiss and B6C3F$_1$ mice, and by gavage (0, 50, and 250 mg/kg body weight in olive oil) to male and female Sprague-Dawley rats. Animals were kept until natural death. The studies included 3,500 to 4,000 animals, most of which were treated by inhalation.

Conclusions: Under the conditions of these studies, epichlorohydrin-free trichloroethylene caused renal tubular-cell neoplasms in male F344/N rats, produced toxic nephrosis in both sexes, and shortened the survival time of males. This experiment in male F344/N rats was considered to be inadequate to evaluate the presence or absence of a carcinogenic response to trichloroethylene. For female F344/N rats receiving trichloroethylene, containing no epichlorohydrin, there was no evidence of carcinogenicity. Trichloroethylene (without epichlorohydrin) was carcinogenic for B6C3F$_1$ mice, causing increased incidences of hepatocellular carcinomas in males and females and of hepatocellular adenomas in females.

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	50	50	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50	49
INTEGUMENTARY SYSTEM				
*ABDOMINAL CAVITY	(50)	(50)	(50)	(49)
FIBROUS HISTIOCYTOMA		1 (2%)		
*SKIN	(50)	(50)	(50)	(49)
FIBROMA				1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)	(49)
FIBROMA	3 (6%)	4 (8%)	1 (2%)	
RESPIRATORY SYSTEM				
#LUNG	(49)	(50)	(50)	(49)
CARCINOMA, NOS, METASTATIC				1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)	1 (2%)		
ALVEOLAR/BRONCHIOLAR CARCINOMA		3 (6%)	2 (4%)	2 (4%)
SARCOMA, NOS, UNC PRIM OR META	1 (2%)			
HEMATOPOIETIC SYSTEM				
*MULTIPLE ORGANS	(50)	(50)	(50)	(49)
MALIGNANT LYMPHOMA, NOS		1 (2%)		
LEUKEMIA,NOS	10 (20%)	5 (10%)	5 (10%)	1 (2%)
MONOCYTIC LEUKEMIA	1 (2%)			
#SPLEEN	(45)	(45)	(49)	(44)
SARCOMA, NOS	1 (2%)			
MALIG.LYMPHOMA, UNDIFFER-TYPE	1 (2%)			
CIRCULATORY SYSTEM				
NONE				

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM				
#SALIVARY GLAND	(45)	(45)	(43)	(36)
SQUAMOUS CELL CARCINOMA			1 (2%)	
#LIVER	(49)	(49)	(49)	(49)
NEOPLASTIC NODULE	1 (2%)			1 (2%)
#JEJUNUM	(45)	(48)	(47)	(44)
FIBROSARCOMA				1 (2%)
#LARGE INTESTINE	(41)	(42)	(45)	(39)
FIBROSARCOMA		1 (2%)		
URINARY SYSTEM				
#KIDNEY	(49)	(48)	(49)	(49)
TUBULAR-CELL ADENOMA			2 (4%)	
TUBULAR-CELL ADENOCARCINOMA				3 (6%)
#PERIRENAL TISSUE	(49)	(48)	(49)	(49)
PARAGANGLIOMA, NOS		1 (2%)		
#KIDNEY/PELVIS	(49)	(48)	(49)	(49)
CARCINOMA,NOS				1 (2%)
TRANSITIONAL-CELL PAPILLOMA	1 (2%)			
TRANSITIONAL-CELL CARCINOMA			1 (2%)	
ENDOCRINE SYSTEM				
#PITUITARY	(39)	(42)	(35)	(26)
CARCINOMA,NOS	1 (3%)			
ADENOMA, NOS	1 (3%)		1 (3%)	
CHROMOPHOBE ADENOMA	4 (10%)	7 (17%)	2 (6%)	1 (4%)
CHROMOPHOBE CARCINOMA	2 (5%)	1 (2%)		
#ADRENAL	(45)	(45)	(42)	(44)
CORTICAL ADENOMA	2 (4%)	1 (2%)		
PHEOCHROMOCYTOMA	8 (18%)	3 (7%)	2 (5%)	1 (2%)
PHEOCHROMOCYTOMA, MALIGNANT		1 (2%)	1 (2%)	
#THYROID	(44)	(44)	(43)	(39)
CARCINOMA,NOS		1 (2%)		

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOLLICULAR-CELL ADENOMA	2 (5%)			
C-CELL ADENOMA	5 (11%)	2 (5%)		
C-CELL CARCINOMA		2 (5%)	3 (7%)	
#PARATHYROID	(25)	(22)	(26)	(24)
ADENOMA, NOS				1 (4%)
#PANCREATIC ISLETS	(46)	(47)	(44)	(40)
ISLET-CELL ADENOMA	1 (2%)	2 (4%)	1 (2%)	1 (3%)
REPRODUCTIVE SYSTEM				
*MAMMARY GLAND	(50)	(50)	(50)	(49)
FIBROADENOMA		1 (2%)	1 (2%)	2 (4%)
*PREPUTIAL GLAND	(50)	(50)	(50)	(49)
ADENOMA, NOS	4 (8%)	4 (8%)		1 (2%)
ADENOCARCINOMA, NOS		1 (2%)	1 (2%)	2 (4%)
#TESTIS	(47)	(49)	(49)	(46)
INTERSTITIAL-CELL TUMOR	43 (91%)	46 (94%)	47 (96%)	32 (70%)
#RIGHT TESTIS	(47)	(49)	(49)	(46)
INTERSTITIAL-CELL TUMOR	1 (2%)	1 (2%)		
NERVOUS SYSTEM				
#BRAIN/MENINGES	(49)	(50)	(49)	(48)
GRANULAR-CELL TUMOR, NOS	1 (2%)			
#BRAIN	(49)	(50)	(49)	(48)
GLIOMA, NOS			1 (2%)	1 (2%)
SPECIAL SENSE ORGANS				
NONE				
MUSCULOSKELETAL SYSTEM				
NONE				

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES				
*THORAX	(50)	(50)	(50)	(49)
FIBROMA		1 (2%)		
*PERITONEUM	(50)	(50)	(50)	(49)
MESOTHELIOMA, NOS				1 (2%)
MESOTHELIOMA, MALIGNANT	1 (2%)	1 (2%)	5 (10%)	
ALL OTHER SYSTEMS				
*MULTIPLE ORGANS	(50)	(50)	(50)	(49)
SARCOMA, NOS, UNC PRIM OR META			1 (2%)	
LEG				
SYNOVIAL SARCOMA			1	
ANIMAL DISPOSITION SUMMARY				
ANIMALS INITIALLY IN STUDY	50	50	50	50
NATURAL DEATH@	12	8	20	22
MORIBUND SACRIFICE	7	8	7	3
SCHEDULED SACRIFICE				
TERMINAL SACRIFICE	31	33	20	15
DOSING ACCIDENT				
ACCIDENTALLY KILLED, NDA				
ACCIDENTALLY KILLED, NOS		1	3	10
ANIMAL MISSING				
ANIMAL MISSEXED				
OTHER CASES				

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY				
TOTAL ANIMALS WITH PRIMARY TUMORS*	48	48	48	34
TOTAL PRIMARY TUMORS	96	92	79	53
TOTAL ANIMALS WITH BENIGN TUMORS	47	47	47	32
TOTAL BENIGN TUMORS	76	74	57	40
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	14	18	11
TOTAL MALIGNANT TUMORS	17	17	21	11
TOTAL ANIMALS WITH SECONDARY TUMORS#				1
TOTAL SECONDARY TUMORS				1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	1		2
TOTAL UNCERTAIN TUMORS	2	1		2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC	1		1	
TOTAL UNCERTAIN TUMORS	1		1	

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

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	49	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	50	50
INTEGUMENTARY SYSTEM				
*SKIN	(49)	(50)	(50)	(50)
KERATOACANTHOMA		1 (2%)		
*SUBCUT TISSUE	(49)	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA			1 (2%)	
FIBROMA		1 (2%)		
FIBROSARCOMA	1 (2%)			
RESPIRATORY SYSTEM				
#LUNG	(49)	(50)	(49)	(50)
ADENOCARCINOMA, NOS, METASTATIC				1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA		1 (2%)	1 (2%)	2 (4%)
ALVEOLAR/BRONCHIOLAR CARCINOMA				1 (2%)
HEMATOPOIETIC SYSTEM				
*MULTIPLE ORGANS	(49)	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)			
LEUKEMIA,NOS	10 (20%)	14 (28%)	4 (8%)	9 (18%)
CIRCULATORY SYSTEM				
#HEART	(49)	(50)	(49)	(50)
ADENOCARCINOMA, NOS, METASTATIC				1 (2%)
DIGESTIVE SYSTEM				
*INTESTINAL TRACT	(49)	(50)	(50)	(50)
ADENOCA IN ADENOMATOUS POLYP			1 (2%)	

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#LIVER	(49)	(50)	(48)	(48)
NEOPLASTIC NODULE	1 (2%)		1 (2%)	1 (2%)
#STOMACH	(46)	(50)	(48)	(43)
SQUAMOUS CELL PAPILLOMA				1 (2%)
#ILEUM	(44)	(47)	(45)	(45)
FIBROSARCOMA	1 (2%)			
URINARY SYSTEM				
#KIDNEY	(48)	(50)	(49)	(48)
TUBULAR-CELL ADENOCARCINOMA				1 (2%)
ENDOCRINE SYSTEM				
#PITUITARY	(43)	(37)	(34)	(41)
CARCINOMA,NOS			1 (3%)	
CHROMOPHOBE ADENOMA	18 (42%)	13 (35%)	6 (18%)	6 (15%)
CHROMOPHOBE CARCINOMA	1 (2%)			
ACIDOPHIL CARCINOMA			1 (3%)	
#ADRENAL	(45)	(46)	(48)	(47)
CORTICAL ADENOMA	2 (4%)	1 (2%)	2 (4%)	3 (6%)
PHEOCHROMOCYTOMA	1 (2%)	1 (2%)		2 (4%)
#THYROID	(36)	(41)	(45)	(44)
FOLLICULAR-CELL ADENOMA			1 (2%)	1 (2%)
C-CELL ADENOMA	2 (6%)	4 (10%)	1 (2%)	1 (2%)
C-CELL CARCINOMA	1 (3%)			
REPRODUCTIVE SYSTEM				
*MAMMARY GLAND	(49)	(50)	(50)	(50)
ADENOMA, NOS			1 (2%)	1 (2%)
ADENOCARCINOMA, NOS				1 (2%)
SARCOMA, NOS		1 (2%)		
FIBROADENOMA	10 (20%)	9 (18%)	12 (24%)	4 (8%)
*CLITORAL GLAND	(49)	(50)	(50)	(50)
ADENOMA, NOS		1 (2%)		

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ADENOCARCINOMA, NOS	1 (2%)			
#UTERUS	(45)	(48)	(48)	(46)
ADENOMA, NOS			1 (2%)	
ADENOCARCINOMA, NOS			1 (2%)	
SARCOMA, NOS		1 (2%)		
ENDOMETRIAL STROMAL POLYP	10 (22%)	15 (31%)	8 (17%)	6 (13%)
ENDOMETRIAL STROMAL SARCOMA		1 (2%)		1 (2%)
#UTERUS/ENDOMETRIUM	(45)	(48)	(48)	(46)
ADENOMA, NOS	1 (2%)			
ADENOCARCINOMA, NOS	1 (2%)		1 (2%)	
ADENOCA IN ADENOMATOUS POLYP			1 (2%)	
#OVARY	(44)	(46)	(47)	(44)
THECOMA		1 (2%)		
GRANULOSA-CELL TUMOR			1 (2%)	
NERVOUS SYSTEM				
#BRAIN/MENINGES	(48)	(50)	(50)	(49)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)	
#BRAIN	(48)	(50)	(50)	(49)
CHROMOPHOBE CARCINOMA, INVASIVE	1 (2%)			
ASTROCYTOMA				1 (2%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS				
NONE				
MUSCULOSKELETAL SYSTEM				
NONE				
BODY CAVITIES				
*ABDOMINAL CAVITY	(49)	(50)	(50)	(50)
SARCOMA, NOS			1 (2%)	
ALL OTHER SYSTEMS				
NONE				

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY				
ANIMALS INITIALLY IN STUDY	50	50	50	50
NATURAL DEATHa	18	7	7	14
MORIBUND SACRIFICE	7	7	5	5
SCHEDULED SACRIFICE				
TERMINAL SACRIFICE	25	34	33	26
DOSING ACCIDENT				
ACCIDENTALLY KILLED, NDA				
ACCIDENTALLY KILLED, NOS		2	5	5
ANIMAL MISSING				
ANIMAL MISSEXED				
OTHER CASES				
TUMOR SUMMARY				
TOTAL ANIMALS WITH PRIMARY TUMORS*	40	38	31	30
TOTAL PRIMARY TUMORS	62	65	47	42
TOTAL ANIMALS WITH BENIGN TUMORS	31	33	24	22
TOTAL BENIGN TUMORS	44	48	33	27
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	16	12	14
TOTAL MALIGNANT TUMORS	17	17	12	14
TOTAL ANIMALS WITH SECONDARY TUMORS#	1		1	1
TOTAL SECONDARY TUMORS	1		1	2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1		2	1
TOTAL UNCERTAIN TUMORS	1		2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC				
TOTAL UNCERTAIN TUMORS				

a INCLUDES AUTOLYZED ANIMALS

* 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 TRICHLOROETHYLENE

UNTREATED CONTROL

ANIMAL NUMBER	64202	64552	65255	65546	65590	66033	66346	66465	66552	67233	67330	67494	67551	68862	70271	70807	71177	71919	72071	72707	73446	74363	74431
WEEKS ON STUDY	106	106	106	106	106	106	071	106	106	106	090	079	106	106	071	080	100	106	106	089	106	103	102
INTEGUMENTARY SYSTEM																							
SUBCUTANEOUS TISSUE	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	X	+	+	+	+	+	+
FIBROMA																	X					X	
RESPIRATORY SYSTEM																							
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																							
SARCOMA, NOS, UNC PRIM OR META																							
TRACHEA	+	+	+	+	+	+	-	+	-	-	+	+	+	-	+	+	-	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																							
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+
SARCOMA, NOS																							
MALIG.LYMPHOMA, UNDIFFER-TYPE																							
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
PANCREAS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-
LARGE INTESTINE	+	-	+	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	-
URINARY SYSTEM																							
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
KIDNEY/PELVIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL PAPILLOMA											X												
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-
ENDOCRINE SYSTEM																							
PITUITARY	+	+	+	-	+	-	+	+	+	+	+	+	-	+	+	+	-	-	+	+	+	+	+
CARCINOMA,NOS																							
ADENOMA, NOS		X													X							X	
CHROMOPHOBE ADENOMA						X																	
CHROMOPHOBE CARCINOMA																							
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	=
CORTICAL ADENOMA														X								X	
PHEOCHROMOCYTOMA			X			X		X															
THYROID	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA	X	X																					X
C-CELL ADENOMA											X									X	X		
PARATHYROID	-	-	+	+	-	+	+	+	-	+	-	-	+	+	+	-	+	+	+	+	-	-	-
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+
ISLET-CELL ADENOMA																							
REPRODUCTIVE SYSTEM																							
MAMMARY GLAND	+	+	N	N	+	+	+	+	N	+	+	N	N	N	+	+	N	N	+	+	+	+	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
INTERSTITIAL-CELL TUMOR	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																X							
NERVOUS SYSTEM																							
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULAR-CELL TUMOR, NOS																							
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
MESOTHELIOMA, MALIGNANT																						X	
ALL OTHER SYSTEMS																							
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS					X	X							X			X		X	X		X		X
MONOCYTIC 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 A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) UNTREATED CONTROL

ANIMAL NUMBER	745	749	755	757	759	761	766	769	770	772	780	784	785	789	792	800	803	805	806	811	812	819	822	825	838	TOTAL
WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	101	101	106	102	096	105	081	106	106	106	106	106	106	065	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	N	50M
FIBROMA		X																				X				3
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA																				X						1
SARCOMA, NOS, UNC PRIM OR META																									X	1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	+	45
SARCOMA, NOS		X																								1
MALIG.LYMPHOMA, UNDIFFER-TYPE										X																1
LYMPH NODES	-	+	+	-	+	-	-	+	+	-	+	A	+	-	-	+	-	+	+	+	+	+	-	+	-	28
THYMUS	-	+	-	-	+	-	-	-	+	+	-	A	-	+	+	-	-	-	+	-	+	+	+	+	-	22
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	+	+	45
LIVER	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	X	+	+	+	+	+	+	49
NEOPLASTIC NODULE																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	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	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	46
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	48
STOMACH	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	48
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	45
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	~	+	+	-	-	41
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	49
KIDNEY/PELVIS	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRANSITIONAL-CELL PAPILLOMA																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	=	+	=	44
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	=	+	=	+	+	+	+	+	+	+	=	+	+	=	+	+	+	+	+	+	=	39
CARCINOMA,NOS																					X					1
ADENOMA, NOS										X																1
CHROMOPHOBE ADENOMA																	X									4
CHROMOPHOBE CARCINOMA													X													2
ADRENAL	+	=	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	=	45
CORTICAL ADENOMA																										2
PHEOCHROMOCYTOMA			X			X														X		X			3
THYROID	+	+	+	+	=	+	+	+	+	+	+	+	+	+	+	+	=	+	+	+	+	+	+	+	=	44
FOLLICULAR-CELL ADENOMA																										2
C-CELL ADENOMA						X																				5
PARATHYROID	-	-	+	+	-	-	+	+	+	-	-	A	+	-	-	-	-	+	-	+	+	+	-	+	-	25
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	46
ISLET-CELL ADENOMA	X																									1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	N	+	N	+	+	N	+	+	N	N	+	+	N	+	+	N	+	+	N	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	47
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X		X	X	X	X	X	X	X		44
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	-	+	+	+	+	+	+	+	+	-	46
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	50M
ADENOMA, NOS								X			X							X							4
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	49
GRANULAR-CELL TUMOR, NOS																		X								1
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, MALIGNANT																										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						10
MONOCYTIC 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 A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF TRICHLOROETHYLENE

VEHICLE CONTROL

ANIMAL NUMBER	64 14	64 16	64 17	64 18	65 14	66 19	67 16	68 10	68 11	68 15	68 19	69 13	69 15	69 18	70 14	70 18	71 11	71 15	71 16	71 18	72 11	72 12	72 13	72 14	73 15
WEEKS ON STUDY	100 6	100 6	090 1	100 6	100 2	100 6	100 6	100 2	100 6	100 5	100 6	100 6	100 6	100 6	100 6	100 0	083 3	098 8	100 6	100 6	100 6	100 6	100 6	100 6	100 6
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE FIBROMA	+	+	+	+	+	+	+	+	+	+ X	N	+	+	+	+	+	+	N	+	+	+	+	+ X	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA ALVEOLAR/BRONCHIOLAR CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	-	+	+	+	-	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+
LYMPH NODES	+	-	+	-	+	+	-	-	+	+	-	-	-	-	-	+	+	-	+	+	-	-	-	-	-
THYMUS	+	-	-	+	-	+	-	-	+	-	+	+	-	-	+	-	+	-	+	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE FIBROSARCOMA	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
URINARY SYSTEM																									
KIDNEY PARAGANGLIOMA, NOS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	-	+	+	+	+	-	-	+	+	-	+	+	+	+	-	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY CHROMOPHOBE ADENOMA CHROMOPHOBE CARCINOMA	+	+	-	+	-	+	+	+	+	+ X	+	+	+	+ X	+	-	+	+	+	-	+	+ X	+	+	+
ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT	+	-	+	+	+	+	+ X	+	+ X	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID CARCINOMA,NOS C-CELL ADENOMA C-CELL CARCINOMA	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+
PARATHYROID	+	+	-	+	+	+	-	-	-	+	-	+	+	-	+	+	+	-	-	-	+	-	-	+	
PANCREATIC ISLETS ISLET-CELL ADENOMA	+ X	-	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND FIBROADENOMA	N	+	+	+	+	+	+	N	N	+	N	+	N	N	+	+	N X	N	+	N	N	N	+	+	N
TESTIS INTERSTITIAL-CELL TUMOR	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	-	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND ADENOMA, NOS ADENOCARCINOMA, NOS	N	N	N X	N	N	N X	N	N	N	N X	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
PLEURA FIBROMA	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
PERITONEUM FIBROUS HISTIOCYTOMA MESOTHELIOMA, MALIGNANT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	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	N X	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 A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	740	746	748	750	751	754	760	764	765	771	774	777	786	788	791	793	801	806	811	817	821	826	827	830	836	840	TOTAL
WEEKS ON STUDY	084	106	106	106	106	099	104	053	089	027	106	106	106	106	071	106	090	106	106	106	106	106	111	106	083	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																											
SUBCUTANEOUS TISSUE	+	+	N	+	N	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA						X			X																		4
RESPIRATORY SYSTEM																											
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																				X							1
ALVEOLAR/BRONCHIOLAR CARCINOMA					X			X																			3
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	44
HEMATOPOIETIC SYSTEM																											
BONE MARROW	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
LYMPH NODES	+	-	-	+	-	-	-	-	-	+	-	-	-	-	+	+	+	+	-	-	-	+	-	-	-	-	18
THYMUS	-	-	-	+	+	-	-	-	-	+	+	-	-	-	-	+	-	-	+	-	+	+	+	-	+		19
CIRCULATORY SYSTEM																											
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																											
SALIVARY GLAND	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	45
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	N	N	50M
PANCREAS	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
STOMACH	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+		47
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	-		42
FIBROSARCOMA									X																		1
URINARY SYSTEM																											
KIDNEY	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PARAGANGLIOMA, NOS												X															1
URINARY BLADDER	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	-		40
ENDOCRINE SYSTEM																											
PITUITARY	+	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	42
CHROMOPHOBE ADENOMA				X									X	X							X						7
CHROMOPHOBE CARCINOMA																						X					1
ADRENAL	+	-	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	45
CORTICAL ADENOMA																											1
PHEOCHROMOCYTOMA																X											3
PHEOCHROMOCYTOMA, MALIGNANT					X																						1
THYROID	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	X	+	+	+	+	+	+	+	+	+	44
CARCINOMA,NOS																	X										1
C-CELL ADENOMA																		X		X							2
C-CELL CARCINOMA																X							X				2
PARATHYROID	-	-	-	-	-	+	-	-	+	-	+	+	-	+	-	+	-	-	+	-	-	-	+	-	+		22
PANCREATIC ISLETS	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ISLET-CELL ADENOMA																											2
REPRODUCTIVE SYSTEM																											
MAMMARY GLAND	+	N	N	N	N	+	N	N	N	N	N	+	+	+	N	+	+	+	+	N	+	+	+	N	+		50M
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	X	X	X	X	47
PROSTATE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	47
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																	X		X								4
ADENOCARCINOMA, NOS																											1
NERVOUS SYSTEM																											
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BODY CAVITIES																											
PLEURA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
FIBROMA											X																1
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	N	50M
FIBROUS HISTIOCYTOMA																									X		1
MESOTHELIOMA, MALIGNANT																											1
ALL OTHER SYSTEMS																											
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIGNANT LYMPHOMA, NOS															X												1
LEUKEMIA,NOS			X		X											X											5

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 A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF TRICHLOROETHYLENE

LOW DOSE

ANIMAL NUMBER	641	643	650	658	661	662	666	668	670	677	678	679	684	691	692	694	697	699	700	703	705	712	714	728	729
WEEKS ON STUDY	103	098	068	094	058	080	103	103	097	103	083	103	095	103	103	080	103	083	103	103	099	099	103	100	103
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE FIBROMA	+	+	N	N	N	+	N	+	+	+	+	+	+	+	N	N	N	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	X	+
TRACHEA	+	+	+	-	+	+	+	+	+	+	-	-	+	-	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	-	+	+	-	+	+	-	+	-	+	+	-	-	-	+	+	-	-	-	+	-	+	-	-
THYMUS	-	-	+	-	+	+	+	-	+	-	-	-	-	-	-	+	+	-	-	-	-	+	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND SQUAMOUS CELL CARCINOMA	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+ X	-	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	-	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+
URINARY SYSTEM																									
KIDNEY TUBULAR-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+ X	+	+	+	+	+	+	+	+	+
KIDNEY/PELVIS TRANSITIONAL-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS CHROMOPHOBE ADENOMA	+	+	+	+	-	+	+	+ X	+	+	+	+	+	+	-	+	+	+	+ X	+	-	-	+	+	+
ADRENAL PHEOCHROMOCYTOMA PHEOCHROMOCYTOMA, MALIGNANT	+	+	+	+	+	+	+	+	+	+ X	-	+ X	-	+	+	-	+	+	-	+	+	+	+ X	+	+
THYROID C-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+ X	+	+	+	-	-	+	+	+	+	+
PARATHYROID	+	+	-	+	-	+	+	-	+	+	+	-	+	-	+	+	-	+	-	-	-	+	+	+	-
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	-	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND FIBROADENOMA	+	N	N	+	N	+	N	N	+	+	+	+	N	N	+ X	N	N	+	N	+	+	+	+	+	+
TESTIS INTERSTITIAL-CELL TUMOR	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	-	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X	+ X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND ADENOCARCINOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N v	N	N	N	N	N	N	N	N	N	N
NERVOUS SYSTEM																									
BRAIN GLIOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
PERITONEUM MESOTHELIOMA, MALIGNANT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N X	N	
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS SARCOMA, NOS, UNC PRIM OR META LEUKEMIA,NOS	N X	N	N	N	N	N X	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N X	N	N
LEG NOS SYNOVIAL SARCOMA				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) LOW DOSE

ANIMAL NUMBER / WEEKS ON STUDY	730 070	731 038	732 002	739 088	746 091	758 113	776 103	778 103	779 103	790 058	795 103	797 087	802 097	814 070	816 064	820 103	821 079	823 092	824 103	828 049	829 065	831 103	833 093	835 099	839 091	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	N	+	N	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	50*
FIBROMA								X																		1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR CARCINOMA																										2
TRACHEA	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	43
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	-	+	+	+	+	-	+	-	+	+	-	+	+	-	+	-	+	+	+	-	-	+	+	+	+	29
THYMUS	-	+	-	-	-	-	-	-	+	+	-	+	-	-	-	-	-	-	-	-	-	-	-	+	-	13
CIRCULATORY SYSTEM																										
HEART	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	43
SQUAMOUS CELL CARCINOMA																										1
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	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	44
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TUBULAR-CELL ADENOMA																		X								2
KIDNEY/PELVIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRANSITIONAL-CELL CARCINOMA																	X									1
URINARY BLADDER	-	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	-	42
ENDOCRINE SYSTEM																										
PITUITARY	+	-	-	+	-	+	-	+	+	-	+	+	-	+	-	+	+	-	+	-	+	+	+	-	-	35
ADENOMA, NOS																										1
CHROMOPHOBE ADENOMA												X														2
ADRENAL	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	+	+	42
PHEOCHROMOCYTOMA																										2
PHEOCHROMOCYTOMA, MALIGNANT																										1
THYROID	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	43
C-CELL CARCINOMA				X			X																			3
PARATHYROID	-	-	-	-	+	+	-	-	-	+	-	+	+	+	+	-	+	+	-	-	-	+	-	+	-	26
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	44
ISLET-CELL ADENOMA																								X		1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	+	+	+	+	N	+	N	N	N	+	N	N	+	N	+	+	N	N	+	+	+	+	50*
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	X	X	X	47
PROSTATE	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	45
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	50*
ADENOCARCINOMA, NOS																										1
NERVOUS SYSTEM																										
BRAIN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GLIOMA, NOS	X																									1
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	50*
MESOTHELIOMA, MALIGNANT													X	X	X											5
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N	50*
SARCOMA, NOS, UNC PRIM OR META																										1
LEUKEMIA,NOS																									X	5
LEG NOS																										
SYNOVIAL SARCOMA																										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 TRICHLOROETHYLENE

HIGH DOSE

ANIMAL NUMBER	649	651	653	657	667	671	682	683	687	688	690	696	701	706	709	710	713	725	726	733	737	738	741	747	752
WEEKS ON STUDY	084	040	102	041	103	103	052	103	039	036	095	076	082	103	059	096	086	099	103	050	040	039	031	042	037
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	N	+	+	+	N	A	N	+	N	+	+	N	+	N	+	+	N	N	N	+	N	+
FIBROMA					X																				
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, METASTATIC 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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
BILE DUCT	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
PANCREAS	+	+	+	-	+	+	-	+	A	-	+	+	-	+	+	+	+	+	+	-	-	-	+	+	+
ESOPHAGUS	+	+	+	-	+	+	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	-	+	+	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA	X																								
LARGE INTESTINE	+	-	+	-	+	+	-	+	A	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA						X																			
KIDNEY/PELVIS	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS																									
URINARY BLADDER	+	+	+	+	+	+	=	+	A	+	+	+	=	+	=	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	=	+	+	+	+	+	=	A	=	+	=	+	+	=	+	+	+	+	=	=	=	+	=	=
CHROMOPHOBE ADENOMA																									
ADRENAL	+	+	+	+	+	+	=	+	A	+	+	+	+	+	+	+	=	+	+	+	+	=	+	+	+
PHEOCHROMOCYTOMA															X										
THYROID	+	+	=	=	+	=	+	+	A	+	+	=	+	+	+	+	+	=	+	+	+	+	+	+	=
PARATHYROID	+	+	=	=	=	=	=	=	A	=	=	=	+	=	+	+	=	=	+	+	+	+	=	=	=
ADENOMA, NOS																									
PANCREATIC ISLETS	+	+	+	=	+	+	=	+	A	=	+	+	=	+	+	+	+	+	+	=	=	=	+	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	+	N	+	+	N	N	A	N	+	N	+	+	N	+	+	N	N	N	N	N	+	N	N
FIBROADENOMA																									
TESTIS	+	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X		X		X	X		X			X	X	X	X	X	X	X	X	X				X	X	
PROSTATE	+	+	+	+	+	+	-	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	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
ADENOMA, NOS																X		X					X		
ADENOCARCINOMA, NOS																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GLIOMA, NOS																							X		
BODY CAVITIES																									
PERITONEUM	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
MESOTHELIOMA, NOS																									
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
LEUKEMIA, NOS			X																						

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

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

ANIMAL NUMBER	75356	75685	76239	76311	76917	76808	77308	77505	78113	78203	78303	78807	79411	79613	79806	79905	80407	80902	81003	81315	81523	83354	83737	TOTAL TISSUES TUMORS
WEEKS ON STUDY	046	085	039	033	035	078	088	058	103	032	033	080	031	031	062	058	052	029	033	029	039	069	054	033	033
INTEGUMENTARY SYSTEM																									
SKIN	+	N	N	+	N	+	+	N	+	N	+	+	+	N	+	N	+	+	+	+	+	+	+	+	49*
FIBROMA																									1
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA, NOS, METASTATIC													X												1
ALVEOLAR/BRONCHIOLAR CARCINOMA																		X							2
TRACHEA	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	-	-	+	+	38
HEMATOPOIETIC SYSTEM																									
BONE MARROW	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	-	+	+	+	+	39
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	44
LYMPH NODES	+	+	+	+	-	-	-	-	-	-	-	+	+	+	-	-	-	+	-	-	+	+	+	-	24
THYMUS	+	-	-	+	+	+	+	-	-	-	-	-	+	+	-	-	-	+	+	+	-	-	-	+	22
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	-	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	36
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	49*
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	40
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	45
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	46
SMALL INTESTINE	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	44
FIBROSARCOMA																									1
LARGE INTESTINE	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	39
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TUBULAR-CELL ADENOCARCINOMA																							X	X	3
KIDNEY/PELVIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA,NOS														X											1
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	+	+	+	-	+	41
ENDOCRINE SYSTEM																									
PITUITARY	-	+	-	+	+	+	+	-	+	-	-	-	+	+	-	-	-	-	+	-	-	+	-	+	26
CHROMOPHOBE ADENOMA				X																					1
ADRENAL	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	44
PHEOCHROMOCYTOMA																									1
THYROID	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	-	+	+	39
PARATHYROID	-	-	+	+	-	-	+	+	+	+	-	-	+	+	+	+	-	-	+	-	+	-	+	+	24
ADENOMA, NOS							X																		1
PANCREATIC ISLETS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	40
ISLET-CELL ADENOMA									X																1
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	+	N	N	N	N	+	N	+	+	+	N	N	N	N	N	+	+	+	+	N	+	+	49*
FIBROADENOMA												X													X	2
TESTIS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	46
INTERSTITIAL-CELL TUMOR		X		X	X	X	X		X	X	X	X	X			X	X		X		X	X		X	32
PROSTATE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	45
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	49*
ADENOMA, NOS																									1
ADENOCARCINOMA, NOS																									2
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	48
GLIOMA, NOS																									1
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	49*
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	49*
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 A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF TRICHLOROETHYLENE

UNTREATED CONTROL

ANIMAL NUMBER	001	004	005	006	007	010	012	020	022	032	034	036	852	854	857	863	866	872	875	876	878	883	884	889	894
WEEKS ON STUDY	092	092	106	084	107	106	084	106	107	106	104	106	106	106	105	107	106	107	107	097	106	074	106	098	107
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE FIBROSARCOMA	N	N	+	+	+	+	+ X	+	+	+	+	N	+	+	+	N	+	+	+	+	N	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	-	+	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	-	-	-	+	+	-	+	-	-	+	-	-	-	-	-	+	-	+	+	+	-	+	+	+	+
THYMUS	-	-	+	-	+	-	-	+	-	+	+	-	-	-	+	+	+	+	+	+	-	-	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GILLBLADDER & 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	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+ X	+	+	+
FIBROSARCOMA																									
LARGE INTESTINE	+	-	+	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	-	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CHROMOPHOBE ADENOMA						X		X	X	X		X		X		X	X	X					X		X
CHROMOPHOBE CARCINOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA												X					X								
PHEOCHROMOCYTOMA									X																
THYROID	+	+	+	+	+	-	+	+	-	+	+	+	+	-	-	+	+	-	+	+	+ X	-	+	-	+
C-CELL ADENOMA	X																								
C-CELL CARCINOMA																									
PARATHYROID	-	-	+	+	-	-	+	+	-	+	-	-	+	-	-	+	+	-	+	+	+	-	+	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	N	+	+	+	+
FIBROADENOMA				X				X	X			X							X						
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS																									
UTERUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
ADENOCARCINOMA, NOS					X		X				X										X	X	X		
ENDOMETRIAL STROMAL POLYP																									
OVARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CHROMOPHOBE CARCINOMA, INVASIVE																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		X						X		X	X			X	X	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 A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) UNTREATED CONTROL

ANIMAL NUMBER	89 51	89 81	89 91	90 00	90 31	91 10	91 11	91 14	91 18	92 40	93 13	93 81	94 11	94 51	94 81	95 00	95 81	96 31	96 81	97 11	98 21	98 41	99 61	99 71	99 81	TOTAL TISSUES TUMORS
WEEKS ON STUDY	09 1	10 0	10 6	10 7	10 6	10 4	10 6	10 7	08 9	09 0	07 7	08 8	10 2	10 8	07 6	09 7	07 3	10 7	09 8	10 6	10 6	09 5	10 6	06 6	10 3	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	N	+	+	N	+	+	+	N	A	+	+	+	+	+	+	+	+	+	+	+	+	+	N	49*
FIBROSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRACHEA	+	+	+	+	+	+	+	+	+	-	A	+	+	-	+	-	+	+	-	+	+	+	-	+		40
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	-	+	+	+	+	+	+	47
SPLEEN	+	-	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	-	-	-	-	-	-	+	+	+	A	+	-	-	+	-	+	+	-	-	+	-	+	-	+	23
THYMUS	+	-	-	+	+	-	-	+	-	-	A	+	+	-	+	-	-	-	-	+	+	-	+	+	-	23
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	46
LIVER	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASTIC NODULE			X																							1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
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	N	N	N	49*
PANCREAS	+	-	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	46
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	-	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	46
SMALL INTESTINE	+	-	+	+	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	44
FIBROSARCOMA																										1
LARGE INTESTINE	+	-	+	-	+	+	-	+	+	+	A	+	+	+	+	+	+	+	+	+	-	-	+	+	+	39
URINARY SYSTEM																										
KIDNEY	+	-	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	A	-	+	+	+	+	-	+	+	+	+	-	+	+	+	41
ENDOCRINE SYSTEM																										
PITUITARY	-	-	+	+	+	-	+	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	-	-	43
CHROMOPHOBE ADENOMA							X	X				X	X			X					X		X			18
CHROMOPHOBE CARCINOMA																				X						1
ADRENAL	+	-	+	+	+	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	-	45
CORTICAL ADENOMA																										2
PHEOCHROMOCYTOMA																										1
THYROID	-	+	+	+	+	+	+	+	+	-	A	+	+	+	+	-	+	+	-	+	+	+	-	-	+	36
C-CELL ADENOMA							X																			2
C-CELL CARCINOMA																										1
PARATHYROID	-	+	-	+	+	+	+	-	-	-	A	-	+	+	+	-	+	+	-	-	-	-	-	-	-	22
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	N	+	+	+	+	A	+	+	+	N	+	+	+	N	+	+	+	N	+	N	49*
FIBROADENOMA			X		X				X				X				X									10
PREPUTIAL/CLITORAL GLAND	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	49*
ADENOCARCINOMA, NOS										X																1
UTERUS	+	-	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	45
ADENOMA, NOS																		X								1
ADENOCARCINOMA, NOS																			X							1
ENDOMETRIAL STROMAL POLYP			X					X	X	X																10
OVARY	+	-	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	-	+	-	+	44
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CHROMOPHOBE CARCINOMA, INVASIVE																				X						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	49*
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	X																									1
LEUKEMIA,NOS		X													X									X		10

* 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 TRICHLOROETHYLENE

VEHICLE CONTROL

ANIMAL NUMBER	0033	0039	0151	0214	0247	0270	0308	0388	0400	0411	8433	8444	8455	8477	8499	8539	8599	8600	8667	8700	8731	8771	9011	9022	9099
WEEKS ON STUDY	106	106	106	107	106	106	106	106	086	106	106	106	106	095	106	106	106	037	106	083	106	106	043	106	106
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N	N	+	+	
KERATOACANTHOMA											X														
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N	N	+	+	
FIBROMA																						X			
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
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	+	+	-	-	+	+	+	+	-	+	+	+	-	+	-	+	+	-	-	+	+	+	-	+	
CHROMOPHOBE ADENOMA												X								X		X		X	
ADRENAL	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA																								X	
THYROID	-	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	+	+	+	
C-CELL ADENOMA									X		X														
PARATHYROID	-	+	+	-	+	-	+	+	-	-	+	+	-	-	-	+	+	-	-	+	-	+	+	+	
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	N	+	
SARCOMA, NOS																									
FIBROADENOMA	X				X			X														X		X	
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
SARCOMA, NOS																									
ENDOMETRIAL STROMAL POLYP		X					X	X	X				X		X	X	X								
ENDOMETRIAL STROMAL SARCOMA																									
OVARY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
THECOMA																									
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	
LEUKEMIA,NOS	X		X						X		X		X							X					X

+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
: 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	9115	9116	9117	9119	9123	9126	9127	9128	9129	9130	9132	9133	9134	9136	9143	9147	9149	9151	9152	9154	9162	9175	9176	9181	9194	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1 0 6	1 0 6	0 7 4	0 9 8	0 8 7	0 7 0	1 0 6	1 0 6	0 3 7	1 0 5	1 0 6	1 0 4	1 0 6	1 0 5	1 0 9	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 6	1 0 9	1 0 6	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	50*
KERATOACANTHOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	50*
FIBROMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	-	+	+	+	+	+	-	+	+	-	-	+	-	+	-	-	+	-	-	+	-	-	+	+	26
THYMUS	+	-	-	-	+	-	+	+	+	+	+	-	+	-	-	-	+	+	-	-	+	+	-	-	-	25
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	+	+	+	+	+	+	+	+	41
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	37
CHROMOPHOBE ADENOMA				X	X		X			X	X			X				X				X		X		13
ADRENAL	+	+	+	+	+	+	+	+		+	+	-	+	+	+	+	+	-	+	+	-	+	+	+	+	46
CORTICAL ADENOMA								X																		1
PHEOCHROMOCYTOMA																										1
THYROID	+	+	-	-	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	41
C-CELL ADENOMA																X				X						4
PARATHYROID	+	-	-	-	-	-	+	+	+	+	+	-	-	-	-	+	+	+	+	+	+	+	-	+	+	29
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	+	+	+	N	N	+	+	+	N	+	+	+	+	N	+	+	+	+	+	+	+	+	50*
SARCOMA, NOS																			X							1
FIBROADENOMA				X	X					X												X				9
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	50*
ADENOMA, NOS							X																			1
UTERUS	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
SARCOMA, NOS			X																							1
ENDOMETRIAL STROMAL POLYP										X							X	X	X		X	X		X		15
ENDOMETRIAL STROMAL SARCOMA																	X									1
OVARY	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	46
THECOMA												X														1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
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	50*
LEUKEMIA,NOS		X					X				X				X	X	X							X		14

* 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 TRICHLOROETHYLENE

LOW DOSE

ANIMAL NUMBER	0 1 4	0 2 5	0 2 6	0 2 9	0 3 1	0 3 7	8 4 1	8 4 2	8 5 0	8 5 1	8 5 6	8 6 1	8 6 2	8 6 5	8 6 9	8 7 1	8 7 9	8 8 0	8 8 1	8 8 2	8 8 6	8 9 0	8 9 1	8 9 2	8 9 6
WEEKS ON STUDY	1 0 4	0 9 7	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 1	0 2 1	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 0	1 0 4	1 0 4	0 8 9	1 0 4
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+
SQUAMOUS CELL CARCINOMA																									
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
NEOPLASTIC NODULE																									X
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
SMALL INTESTINE	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	-	+	+	-	+	+	+	+	+	+	+	-	+	-	+	-	-	-
CARCINOMA,NOS																X									
CHROMOPHOBE ADENOMA						X			X	X															
ACIDOPHIL CARCINOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
CORTICAL ADENOMA					X								X												
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
C-CELL ADENOMA																									
PARATHYROID	-	+	+	-	-	+	-	+	-	-	+	-	+	-	-	-	-	-	+	+	-	+	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	+	N	+	+
ADENOMA, NOS								X																	
FIBROADENOMA	X			X	X	X						X					X								
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ADENOMA, NOS														X					X						
ADENOCARCINOMA, NOS																									
ADENOCA IN ADENOMATOUS POLYP																									
ENDOMETRIAL STROMAL POLYP							X	X					X			X	X						X		
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
GRANULOSA-CELL TUMOR																		X							
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																									
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
SARCOMA, 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		X							X															X	
INTESTINAL TRACT																									
ADENOCA IN ADENOMATOUS POLYP												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 A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) LOW DOSE

ANIMAL NUMBER	906	908	920	925	937	939	940	942	946	953	957	960	964	966	967	969	977	978	979	985	989	992	993	995	999	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	104	101	104	104	037	104	070	104	104	053	084	083	104	098	104	040	104	097	104	104	089	086	083	104	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	N	N	+	+	+	+	+	+	+	A	+	+	N	+	+	+	+	+	+	+	50*
SQUAMOUS CELL CARCINOMA							X																			1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
TRACHEA	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	-	+	-	-	-	+	-	+	+	+	-	+	+	-	+	-	-	+	+	-	+	+	+	+	-	25
THYMUS	+	-	-	+	+	+	-	-	+	+	-	+	+	-	-	+	+	+	-	+	+	-	+	-	-	26
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	-	+	+	+	+	+	+	-	+	-	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	42
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	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
STOMACH	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	45
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ENDOCRINE SYSTEM																										
PITUITARY	+	-	+	+	+	-	-	+	+	-	+	+	-	+	+	+	-	-	+	-	+	+	+	+	+	34
CARCINOMA,NOS																										1
CHROMOPHOBE ADENOMA				X	X									X												6
ACIDOPHIL CARCINOMA			X																							1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CORTICAL ADENOMA																										2
THYROID	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	45
FOLLICULAR-CELL ADENOMA									X																	1
C-CELL ADENOMA							X																			1
PARATHYROID	+	-	-	+	+	+	-	-	-	-	-	-	+	+	+	+	+	-	-	-	+	+	-	-	-	20
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	N	N	N	+	N	N	+	+	N	N	50*
ADENOMA, NOS																										1
FIBROADENOMA		X								X		X		X	X							X				12
UTERUS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS																										1
ADENOCARCINOMA, NOS		X																								2
ADENOCA IN ADENOMATOUS POLYP															X											1
ENDOMETRIAL STROMAL POLYP					X																	X				8
OVARY	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
GRANULOSA-CELL TUMOR																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA, METASTAT							X																			1
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	50*
SARCOMA, 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	50*
LEUKEMIA,NOS				X																						4
INTESTINAL TRACT																										
ADENOCA IN ADENOMATOUS POLYP																										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 TRICHLOROETHYLENE

HIGH DOSE

ANIMAL NUMBER	001	002	008	011	013	016	017	018	023	028	033	035	039	042	046	048	055	058	064	068	074	085	088	087	088	093
WEEKS ON STUDY	095	103	060	031	031	031	031	082	076	031	031	031	097	063	031	031	031	072	031	031	054	031	086	088	088	103
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																								X		
ALVEOLAR/BRONCHIOLAR ADENOMA																		X				X				
ALVEOLAR/BRONCHIOLAR CARCINOMA								X																		
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
SPLEEN	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
LYMPH NODES	-	-	-	+	-	+	-	+	+	-	-	-	+	+	-	-	+	+	+	+	+	+	+	+	+	+
THYMUS	-	+	-	+	-	-	-	-	-	+	-	-	+	+	-	-	+	-	-	+	+	-	-	+	+	+
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																								X		
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE		X																								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
STOMACH	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
SQUAMOUS CELL PAPILLOMA																	X									
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
LARGE INTESTINE	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	-	-		
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
TUBULAR-CELL ADENOCARCINOMA																										
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	-	+	
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	
CHROMOPHOBE ADENOMA	X	X									X		X													
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CORTICAL ADENOMA				X											X											
PHEOCHROMOCYTOMA				X																						
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	
FOLLICULAR-CELL ADENOMA							X			X																
C-CELL ADENOMA																										
PARATHYROID	+	+	+	+	-	+	-	-	+	-	-	-	+	+	+	+	-	-	+	+	+	+	+	+	-	
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	N	N	+	N	+	+	+	+	N	N	N	+	N	+	+	+	+	+	+	
ADENOMA, NOS																								X		
ADENOCARCINOMA, NOS																										
FIBROADENOMA					X																					
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	
ENDOMETRIAL STROMAL POLYP							X						X		X											
ENDOMETRIAL STROMAL SARCOMA	X																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
ASTROCYTOMA																										
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS			X				X		X		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 A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED) HIGH DOSE

ANIMAL NUMBER	897	904	905	907	912	913	921	922	935	944	955	959	961	965	970	972	973	974	980	983	986	987	988	990	991	TOTAL
WEEKS ON STUDY	046	099	103	103	103	052	098	083	103	103	081	103	103	103	100	103	103	085	038	098	103	103	076	041	068	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC																										1
ALVEOLAR/BRONCHIOLAR ADENOMA																										2
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	-	45
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	-	+	46
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	-	+	+	+	A	+	+		44
LYMPH NODES	-	+	-	-	+	-	-	+	+	-	+	-	+	-	+	+	-	+	-	-	-	+	A	-	+	26
THYMUS	+	-	+	-	+	+	+	-	-	-	+	-	-	+	-	+	+	-	-	-	-	+	A	+	+	22
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC																										1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	46
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	48
NEOPLASTIC NODULE																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	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	50*
PANCREAS	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	A	+	+	44
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	-	+	+	+	A	+	+	43
SQUAMOUS CELL PAPILLOMA																										1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	A	+	+	45
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	-	+	-	A	+	+		40
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+	48
TUBULAR-CELL ADENOCARCINOMA							X																			1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	A	+	+	44
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	-	-	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	A	+	+	41
CHROMOPHOBE ADENOMA															X							X				6
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	A	+	+	47
CORTICAL ADENOMA																	X	X								3
PHEOCHROMOCYTOMA																	X									2
THYROID	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	-	44
FOLLICULAR-CELL ADENOMA																										1
C-CELL ADENOMA																										1
PARATHYROID	-	+	-	-	+	-	+	+	+	+	+	-	-	-	-	-	+	+	-	-	-	+	A	-	-	26
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	+	N	+	N	+	+	+	+	+	+	N	N	+	+	+	+	N	+	+	N	N	N	+	50*
ADENOMA, NOS					X																					1
ADENOCARCINOMA, NOS																										1
FIBROADENOMA								X		X			X													4
UTERUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	X	+	X	+	X	-	+	+	+	A	+	46
ENDOMETRIAL STROMAL POLYP																										6
ENDOMETRIAL STROMAL SARCOMA																										1
OVARY	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	+	+	A	+	+	44
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	49
ASTROCYTOMA		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	50*
LEUKEMIA,NOS				X					X							X				X						9

* 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 TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	DOSED GROUP
ANIMALS INITIALLY IN STUDY	50	50
ANIMALS NECROPSIED	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50
INTEGUMENTARY SYSTEM		
NONE		
RESPIRATORY SYSTEM		
#LUNG	(49)	(50)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)	5 (10%)
ALVEOLAR/BRONCHIOLAR ADENOMA	4 (8%)	5 (10%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	3 (6%)	1 (2%)
HEMATOPOIETIC SYSTEM		
#BRAIN/MENINGES	(48)	(49)
MALIGNANT RETICULOSIS	1 (2%)	
*CRANIAL NERVE	(50)	(50)
MALIGNANT RETICULOSIS	1 (2%)	
*MULTIPLE ORGANS	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)	3 (6%)
MALIG.LYMPHOMA, UNDIFFER-TYPE	3 (6%)	5 (10%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2 (4%)	2 (4%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	2 (4%)	
MALIGNANT LYMPHOMA, MIXED TYPE	2 (4%)	3 (6%)
PLASMA-CELL TUMOR	1 (2%)	
#SPLEEN	(48)	(42)
MALIGNANT LYMPHOMA, MIXED TYPE	1 (2%)	
CIRCULATORY SYSTEM		
#LIVER	(48)	(50)
HEMANGIOSARCOMA	1 (2%)	

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
DIGESTIVE SYSTEM		
#LIVER	(48)	(50)
HEPATOCELLULAR ADENOMA	7 (15%)	14 (28%)
HEPATOCELLULAR CARCINOMA	8 (17%)	31 (62%)
#STOMACH	(48)	(47)
SQUAMOUS CELL CARCINOMA	1 (2%)	
URINARY SYSTEM		
#KIDNEY	(49)	(50)
TUBULAR-CELL ADENOMA	1 (2%)	
TUBULAR-CELL ADENOCARCINOMA		1 (2%)
ENDOCRINE SYSTEM		
#ADRENAL	(32)	(36)
CORTICAL ADENOMA	1 (3%)	
PHEOCHROMOCYTOMA	1 (3%)	
REPRODUCTIVE SYSTEM		
NONE		
NERVOUS SYSTEM		
#BRAIN/MENINGES	(48)	(49)
SARCOMA, NOS	1 (2%)	
#BRAIN	(48)	(49)
NEOPLASM, NOS, MALIGNANT		1 (2%)
SPECIAL SENSE ORGANS		
*HARDERIAN GLAND	(50)	(50)
ADENOMA, NOS		2 (4%)
PAPILLARY ADENOMA		1 (2%)
ACINAR-CELL ADENOMA		1 (2%)
MUSCULOSKELETAL SYSTEM		
NONE		

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
BODY CAVITIES		
NONE		
ALL OTHER SYSTEMS		
*MULTIPLE ORGANS	(50)	(50)
CARCINOMA,NOS		1 (2%)
ANIMAL DISPOSITION SUMMARY		
ANIMALS INITIALLY IN STUDY	50	50
NATURAL DEATH@	14	28
MORIBUND SACRIFICE	5	3
SCHEDULED SACRIFICE		
ACCIDENTALLY KILLED	2	3
TERMINAL SACRIFICE	29	16
ANIMAL MISSING		
@ INCLUDES AUTOLYZED ANIMALS		
TUMOR SUMMARY		
TOTAL ANIMALS WITH PRIMARY TUMORS*	33	45
TOTAL PRIMARY TUMORS	42	71
TOTAL ANIMALS WITH BENIGN TUMORS	13	22
TOTAL BENIGN TUMORS	14	23
TOTAL ANIMALS WITH MALIGNANT TUMORS	25	39
TOTAL MALIGNANT TUMORS	27	48
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	5
TOTAL SECONDARY TUMORS	1	5
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 TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	DOSED GROUP
ANIMALS INITIALLY IN STUDY	50	50
ANIMALS MISSING	2	1
ANIMALS NECROPSIED	48	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	49
INTEGUMENTARY SYSTEM		
NONE		
RESPIRATORY SYSTEM		
#LUNG	(48)	(48)
ALVEOLAR/BRONCHIOLAR ADENOMA		4 (8%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	
HEMATOPOIETIC SYSTEM		
#BRAIN/MENINGES	(48)	(48)
MALIGNANT RETICULOSIS	1 (2%)	
*CRANIAL NERVE	(48)	(49)
MALIGNANT RETICULOSIS	1 (2%)	
*MULTIPLE ORGANS	(48)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)	2 (4%)
MALIG.LYMPHOMA, UNDIFFER-TYPE	1 (2%)	3 (6%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		3 (6%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)	2 (4%)
MALIGNANT LYMPHOMA, MIXED TYPE	3 (6%)	2 (4%)
MYELOMONOCYTIC LEUKEMIA		1 (2%)
#SPLEEN	(47)	(48)
MALIGNANT LYMPHOMA, NOS	1 (2%)	
#LIVER	(48)	(49)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)
CIRCULATORY SYSTEM		
*ADIPOSE TISSUE	(48)	(49)
HEMANGIOMA	1 (2%)	
DIGESTIVE SYSTEM		
#LIVER	(48)	(49)
HEPATOCELLULAR ADENOMA	4 (8%)	16 (33%)
HEPATOCELLULAR CARCINOMA	2 (4%)	13 (27%)
#STOMACH	(47)	(47)
SQUAMOUS CELL PAPILLOMA		2 (4%)
SQUAMOUS CELL CARCINOMA		1 (2%)
URINARY SYSTEM		
NONE		

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
ENDOCRINE SYSTEM		
#PITUITARY	(27)	(28)
CHROMOPHOBE ADENOMA	3 (11%)	
#ADRENAL	(36)	(37)
CORTICAL ADENOMA	1 (3%)	
PHEOCHROMOCYTOMA	2 (6%)	
#ADRENAL/CAPSULE	(36)	(37)
SARCOMA, NOS		1 (3%)
#THYROID	(33)	(31)
FOLLICULAR-CELL ADENOMA		1 (3%)
REPRODUCTIVE SYSTEM		
*MAMMARY GLAND	(48)	(49)
FIBROSARCOMA	1 (2%)	
#UTERUS	(47)	(49)
SARCOMA, NOS		1 (2%)
LEIOMYOMA		1 (2%)
ENDOMETRIAL STROMAL POLYP		2 (4%)
NEURILEMOMA, MALIGNANT	1 (2%)	
#OVARY	(27)	(31)
ADENOCARCINOMA, NOS	1 (4%)	
PAPILLARY ADENOMA		1 (3%)
NERVOUS SYSTEM		
#BRAIN/MENINGES	(48)	(48)
MENINGIOMA		1 (2%)
SPECIAL SENSE ORGANS		
*HARDERIAN GLAND	(48)	(49)
ADENOMA, NOS		3 (6%)
MUSCULOSKELETAL SYSTEM		
NONE		
BODY CAVITIES		
NONE		
ALL OTHER SYSTEMS		
*MULTIPLE ORGANS	(48)	(49)
SQUAMOUS CELL CARCINOMA, METASTA		1 (2%)
SITE UNKNOWN		
NEOPLASM, NOS	1	
ANIMAL DISPOSITION SUMMARY		
ANIMALS INITIALLY IN STUDY	50	50
**NATURAL DEATH@	12	16
**MORIBUND SACRIFICE	4	8
SCHEDULED SACRIFICE	2	
ACCIDENTALLY KILLED	1	3
TERMINAL SACRIFICE	29	22
ANIMAL MISSING	2	1

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED
** INCLUDES ANIMALS THAT DIED BEFORE OR AFTER THE BEGINNING OF THE TERMINATION PERIOD

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
TUMOR SUMMARY		
TOTAL ANIMALS WITH PRIMARY TUMORS*	21	38
TOTAL PRIMARY TUMORS	27	61
TOTAL ANIMALS WITH BENIGN TUMORS	9	23
TOTAL BENIGN TUMORS	11	50
TOTAL ANIMALS WITH MALIGNANT TUMORS	13	30
TOTAL MALIGNANT TUMORS	15	31
TOTAL ANIMALS WITH SECONDARY TUMORS#		1
TOTAL SECONDARY TUMORS		1
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 B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF TRICHLOROETHYLENE

VEHICLE CONTROL

ANIMAL NUMBER	341	343	344	345	346	348	349	350	351	353	354	357	358	359	360	364	368	369	370	371	374	378	379	380	381
WEEKS ON STUDY	107	107	107	075	107	063	107	098	071	107	076	066	071	071	073	107	107	107	106	107	101	101	101	103	107
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																X									
ALVEOLAR/BRONCHIOLAR ADENOMA													X												
ALVEOLAR/BRONCHIOLAR CARCINOMA	X						X																		
TRACHEA	+	-	-	-	-	+	-	-	-	+	+	+	-	-	+	+	-	+	+	+	+	-	+	-	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, MIXED TYPE																									
LYMPH NODES	+	-	-	-	-	+	-	+	+	+	+	+	+	-	+	+	-	-	+	+	-	+	+	+	
THYMUS	+	-	+	-	-	-	-	-	-	-	-	-	+	+	-	-	+	+	-	-	+	-	+	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	-	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA							X	X		X				X						X				X	
HEPATOCELLULAR CARCINOMA				X						X			X			X									X
HEMANGIOSARCOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	+	N	+	N	+	N	N	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	N
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA						X																			
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+
LARGE INTESTINE	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	-	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA																									
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	-	-	-	-	-	-	-	+	+	-	-	-	+	+	-	+	-	+	-	-	+	-
ADRENAL	-	-	+	+	+	+	-	+	-	-	+	+	-	-	+	-	+	+	+	+	-	+	+	+	-
CORTICAL ADENOMA					X																				
PHEOCHROMOCYTOMA																									
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
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
NERVES	N	N	N	N	N	+	N	+	+	N	+	N	N	N	+	N	N	N	N	N	N	N	N	N	N
MALIGNANT RETICULOSIS																									
BRAIN	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS			X																						
MALIGNANT RETICULOSIS																									
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
MALIGNANT LYMPHOMA, NOS																									
MALIG.LYMPHOMA, UNDIFFER-TYPE											X				X										
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE								X																	
MALIG.LYMPHOMA, HISTIOCYTIC TYPE												X													
MALIGNANT LYMPHOMA, MIXED TYPE																									
PLASMA-CELL TUMOR																								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 B3. MALE MICE: TUMOR PATHOLOGY (CONTINUED) VEHICLE CONTROL

ANIMAL NUMBER	38 06	38 07	39 02	39 03	39 04	39 09	40 01	40 03	40 05	41 01	41 03	41 04	41 05	41 08	42 03	42 05	42 09	43 01	43 06	43 08	43 09	54 06	57 05	60 01	61 03	TOTAL TISSUES TUMORS
WEEKS ON STUDY	06 6	10 7	09 5	10 7	10 7	06 1	09 1	10 7	08 6	10 7	10 7	10 7	10 7	10 5	10 7	10 7	10 7	10 7	07 9	10 6	10 1	10 1	10 1	10 7	07 3	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	49
HEPATOCELLULAR CARCINOMA, METASTA																										1
ALVEOLAR/BRONCHIOLAR ADENOMA							X	X																	X	4
ALVEOLAR/BRONCHIOLAR CARCINOMA														X												3
TRACHEA	+	-	+	-	-	-	-	-	-	-	-	+	-	-	+	+	+	-	+	+	A	-	+	-	+	23
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	49
PLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	48
MALIGNANT LYMPHOMA, MIXED TYPE												X														1
LYMPH NODES	+	+	+	+	+	+	+	+	+	-	-	-	-	-	+	+	-	+	-	-	A	+	+	-	+	31
THYMUS	-	-	-	-	-	-	-	+	+	-	-	+	+	-	+	-	-	+	-	-	A	-	+	+	-	16
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	-	-	+	+	+	+	+	+	+	+	+	-	-	+	-	-	-	+	A	+	+	-	+	37
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	-	48
HEPATOCELLULAR ADENOMA																								X		7
HEPATOCELLULAR CARCINOMA		X		X					X																	8
HEMANGIOSARCOMA			X																							1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	-	48
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	N	N	+	N	+	+	+	+	+	+	+	N	+	+	N	N	+	+	+	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	48
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	48
SQUAMOUS CELL CARCINOMA																										1
SMALL INTESTINE	+	-	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-	A	+	+	+	+	43
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	+	-	-	+	-	+	-	+	+	+	-	A	+	+	+	+	36
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	49
TUBULAR-CELL ADENOMA							X																			1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	-	+	47
ENDOCRINE SYSTEM																										
PITUITARY	-	-	-	+	-	-	-	-	+	-	+	-	-	+	+	-	-	-	+	-	A	+	+	-	-	18
ADRENAL	+	+	+	+	-	+	+	+	+	+	-	+	+	+	-	+	-	+	+	+	A	+	-	-	-	32
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA														X												1
THYROID	+	-	+	-	+	-	+	-	-	-	-	+	+	+	+	+	+	-	-	+	A	+	+	+	-	31
PARATHYROID	+	-	+	-	-	-	-	-	-	-	-	-	-	+	-	+	+	-	-	+	A	-	+	-	-	18
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	50*
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	49
PROSTATE	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	44
NERVOUS SYSTEM																										
NERVES	+	N	N	N	N	+	+	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	50*
MALIGNANT RETICULOSIS						X																				1
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	48
SARCOMA, NOS																										1
MALIGNANT RETICULOSIS						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	50*
MALIGNANT LYMPHOMA, NOS	X																									1
MALIG.LYMPHOMA, UNDIFFER-TYPE																									X	3
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE									X																	2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																				X						2
MALIGNANT LYMPHOMA, MIXED TYPE														X												2
PLASMA-CELL TUMOR																		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 TRICHLOROETHYLENE

DOSED GROUP

ANIMAL NUMBER	342	347	352	355	356	361	362	363	365	366	373	375	376	377	382	383	384	388	389	390	391	395	398	400	402
WEEKS ON STUDY	105	077	105	084	101	089	077	071	089	069	105	091	041	058	094	105	099	097	093	082	088	105	083	093	102
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA												X							X						
ALVEOLAR/BRONCHIOLAR ADENOMA				X	X												X								
ALVEOLAR/BRONCHIOLAR CARCINOMA															X										
TRACHEA	-	-	+	-	+	-	+	+	+	+	-	+	+	+	-	-	-	+	-	+	+	-	+	-	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	A	A	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+
LYMPH NODES	-	+	+	+	+	+	A	A	+	-	-	-	+	-	+	-	+	+	+	+	+	+	-	-	-
THYMUS	-	-	+	-	-	+	A	A	-	-	+	-	+	-	-	+	-	+	-	-	-	+	+	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	-
LIVER	+	+	+	+	+	+	/	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA			X			X												X	X			X			X
HEPATOCELLULAR CARCINOMA	X		X	X	X				X	X	X	X		X	X	X				X		X	X	X	X
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	N	N	+	+	N	N	+	N	+	+	+	N	+	+	+	+	N	N	N	+	+	N	+
PANCREAS	+	+	+	+	+	+	+	A	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA																							X		
URINARY BLADDER	+	+	+	+	+	+	+	A	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	-	-	-	+	A	A	+	-	-	-	+	-	+	+	+	-	-	+	-	+	+	+	-
ADRENAL	+	+	+	+	+	+	+	A	+	+	-	+	+	-	+	-	-	+	+	+	+	-	+	-	+
THYROID	-	-	-	-	+	-	A	A	-	+	+	+	+	+	+	-	-	-	-	+	+	-	+	+	+
PARATHYROID	-	-	-	-	+	-	A	A	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	-	+	+	-	+	+	A	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASM, NOS, MALIGNANT																		X							
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS		X								X															
PAPILLARY ADENOMA																									
ACINAR-CELL ADENOMA				X																					
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																									
MALIGNANT LYMPHOMA, NOS			Y																				X		
ALL OTHER SYSTEMS (CONT)																									
MALIG.LYMPHOMA, UNDIFFER-TYPE		X			X	X														X					
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									X
MALIGNANT LYMPHOMA, MIXED TYPE																									

+: 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) DOSED GROUP

ANIMAL NUMBER / WEEKS ON STUDY	040 088	040 105	040 869	040 972	041 089	041 105	041 957	042 072	042 097	042 105	042 605	042 705	043 060	043 205	043 289	043 334	043 486	043 505	043 717	044 009	054 197	054 305	054 838	054 949	055 105	055 902	055 912	TOTAL TISSUES	TOTAL TUMORS
RESPIRATORY SYSTEM																													
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
HEPATOCELLULAR CARCINOMA, METASTA					X						X															X		5	
ALVEOLAR/BRONCHIOLAR ADENOMA						X																	X					5	
ALVEOLAR/BRONCHIOLAR CARCINOMA																												1	
TRACHEA	+	-	+	-	-	-	-	+	-	+	-	+	+	+	-	+	+	-	-	+	+	+	-	-	+			27	
HEMATOPOIETIC SYSTEM																													
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			49	
SPLEEN	+	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+			42	
LYMPH NODES	+	-	-	-	-	+	+	-	+	-	+	+	-	-	+	+	+	+	+	+	+	-	+	+	+			30	
THYMUS	-	+	-	-	-	+	-	-	-	-	+	-	-	-	-	-	+	-	+	-	+	+	-	-	-			15	
CIRCULATORY SYSTEM																													
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+			49	
DIGESTIVE SYSTEM																													
SALIVARY GLAND	+	-	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	-			40	
LIVER																													
HEPATOCELLULAR ADENOMA	X		X	X										X		X	X					X		X			14	
HEPATOCELLULAR CARCINOMA	X	X			X	X	X	X		X	X	X					X				X	X	X	X	X			31	
BILE DUCT	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			50	
GALLBLADDER & COMMON BILE DUCT	+	N	N	+	+	+	N	N	+	+	N	+	+	+	N	N	+	N	+	N	+	+	+	+	+			50*	
PANCREAS	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+			46	
ESOPHAGUS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	-	+	+			44	
STOMACH	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+			47	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+			47	
LARGE INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	-			45	
URINARY SYSTEM																													
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			50	
TUBULAR-CELL ADENOCARCINOMA																												1	
URINARY BLADDER	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			47	
ENDOCRINE SYSTEM																													
PITUITARY	+	+	-	+	-	-	-	-	-	-	-	-	-	+	+	+	-	+	+	+	-	-	-	-	+			22	
ADRENAL	-	+	+	+	+	-	+	+	+	+	+	-	+	-	-	+	+	-	+	+	+	-	+	+	+			36	
THYROID	-	-	-	+	+	+	+	+	+	-	-	+	-	+	+	+	+	-	+	+	+	+	-	+	+			29	
PARATHYROID	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	+	-	-	-				7	
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			50*	
TESTIS	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			49	
PROSTATE	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			44	
NERVOUS SYSTEM																													
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+			49	
NEOPLASM, NOS, MALIGNANT																												1	
SPECIAL SENSE ORGANS																													
HARDERIAN 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			50*	
ADENOMA, NOS																					X							2	
PAPILLARY ADENOMA																												1	
ACINAR-CELL ADENOMA																												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			50*	
CARCINOMA,NOS																												1	
MALIGNANT LYMPHOMA, NOS	X														X													3	
ALL OTHER SYSTEMS (CONT)																													
MALIG.LYMPHOMA, UNDIFFER-TYPE																					X							5	
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																											X	2	
MALIGNANT LYMPHOMA, MIXED TYPE									X										X			X						3	

* 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 TRICHLOROETHYLENE

VEHICLE CONTROL

ANIMAL NUMBER	44113	44436	44457	44469	44488	44499	45002	45113	45364	45407	45707	45802	45907	46004	46407	46808	46909	47010	47107	47407	47809	48004	48606
WEEKS ON STUDY	1 0 7	0 8 8	1 0 7	1 0 7	0 7 9	0 4 6	0 9 9	0 8 2	1 0 7	0 6 4	1 0 7	1 0 7	1 0 7	0 9 2	0 8 7	0 4 1	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	0 8 3	1 0 7
RESPIRATORY SYSTEM																							
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA																							
TRACHEA	+	-	+	-	+	+	+	-	-	M	-	-	-	+	+	M	-	-	+	+	-	-	+
HEMATOPOIETIC SYSTEM																							
BONE MARROW	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
SPLEEN	+		+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS			X																				
LYMPH NODES	+	-	-	-	+	-	-	-	-	M	+	+	-	-	+	M	+	-	-	+	-	+	+
THYMUS	+	-	-	+	+	-	-	+	-	M	+	+	-	-	+	M	-	+	+	+	-	+	-
CIRCULATORY SYSTEM																							
HEART	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																							
SALIVARY GLAND	+	+	+	+	-	+	+	+	-	M	+	+	-	+	+	M	-	+	+	+	+	+	-
LIVER	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA											X							X					
HEPATOCELLULAR CARCINOMA																							
BILE DUCT	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	N	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	-	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	-	+	+	-	+	+
STOMACH	+	-	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	-	+	+
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	M	+	+	-	+	+	M	-	+	+	+	+	+	+
URINARY SYSTEM																							
KIDNEY	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	-	+	+	+	M	+	+	+	+	+	M	+	+	+	+	-	+	+
ENDOCRINE SYSTEM																							
PITUITARY	+	-	+	-	-	-	-	+	+	M	-	+	-	+	+	M	-	+	-	+	+	+	+
CHROMOPHOBE ADENOMA												X								X			
ADRENAL	-	+	+	+	+	+	+	+	+	M	+	+	-	+	+	M	+	-	+	+	+	+	-
CORTICAL ADENOMA																	X						
PHEOCHROMOCYTOMA																							
THYROID	+	-	+	-	+	+	+	+	-	M	+	-	-	+	+	M	+	-	+	+	-	-	+	+	-
PARATHYROID	-	-	-	-	-	+	+	-	-	M	-	-	-	-	-	M	+	-	-	-	-	-	-	-	-
REPRODUCTIVE SYSTEM																							
MAMMARY GLAND	+	N	+	N	+	+	+	N	+	M	+	+	+	+	+	M	+	N	+	+	+	+	+
FIBROSARCOMA	X																						
UTERUS	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+
NEURILEMOMA, MALIGNANT																					X		
OVARY	+	-	+	-	-	+	-	-	+	M	+	+	+	+	+	M	-	+	+	-	-	-	+	+	-
ADENOCARCINOMA, NOS						X																	
NERVOUS SYSTEM																							
NERVE	N	+	N	N	N	+	N	+	N	M	N	N	N	+	+	M	N	N	N	N	N	N	+	N
MALIGNANT RETICULOSIS																							
BRAIN	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+
MALIGNANT RETICULOSIS																							
ALL OTHER SYSTEMS																							
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	M	N	N	N	N	N	M	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS					X																				
MALIG.LYMPHOMA, UNDIFFER-TYPE							X																		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																					X				
MALIGNANT LYMPHOMA, MIXED TYPE																									
SITE UNKNOWN										M						M							
NEOPLASM, NOS																							
ADIPOSE TISSUE										M						M							
HEMANGIOMA																	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	487	492	493	494	499	501	503	505	506	511	512	513	514	515	518	528	529	531	536	544	553	554	555	556	558	TOTAL
WEEKS ON STUDY	107	107	105	107	088	107	107	083	081	062	107	107	106	107	107	103	107	101	095	102	107	105	107	107	106	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ALVEOLAR/BRONCHIOLAR CARCINOMA					X																					1
TRACHEA	+	+	-	-	+	+	+	+	+	+	+	+	+	-	-	-	-	+	+	+	+	-	-	+	+	28
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	47
MALIGNANT LYMPHOMA, NOS																										1
LYMPH NODES	+	-	-	+	-	-	-	A	+	-	+	+	-	-	-	+	-	+	+	+	+	+	-	-	+	22
THYMUS	+	-	+	+	-	+	+	A	-	-	-	+	-	+	+	+	-	+	-	-	+	+	-	+	-	25
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	47
DIGESTIVE SYSTEM																										
SALIVARY GLAND	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	39
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEPATOCELLULAR ADENOMA		X																				X				4
HEPATOCELLULAR CARCINOMA			-	-																				X	X	2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	+	N	+	N	+	+	+	+	+	+	+	N	+	+	N	N	+	N	N	48*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	45
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SMALL INTESTINE	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	-	+	+	+	-	+	+	+	+	41
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY BLADDER	+	+	+	+	+	+	+	A	-	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	41
ENDOCRINE SYSTEM																										
PITUITARY	-	+	-	-	+	+	+	+	-	-	+	+	-	+	-	+	+	+	-	-	-	+	+	-	-	27
CHROMOPHOBE ADENOMA																		X								3
ADRENAL	+	-	-	+	+	-	+	A	+	+	-	-	-	+	+	+	-	+	+	+	+	+	+	+	+	36
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA									X									X								2
THYROID	+	+	-	-	+	+	+	A	+	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+	+	33
PARATHYROID	+	-	-	-	+	-	-	A	-	-	+	+	+	-	+	-	-	-	-	+	+	-	-	-	-	11
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	+	+	+	+	N	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	48*
FIBROSARCOMA																										1
UTERUS	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
NEURILEMOMA, MALIGNANT																										1
OVARY	+	-	+	-	+	-	+	A	-	+	-	+	+	-	-	-	+	-	+	-	+	+	+	+	+	27
ADENOCARCINOMA, NOS																										1
NERVOUS SYSTEM																										
NERVES	N	N	N	N	+	N	N	N	+	+	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	48*
MALIGNANT RETICULOSIS										X																1
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
MALIGNANT RETICULOSIS										X																
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
MALIGNANT LYMPHOMA, NOS																		X								1
MALIG.LYMPHOMA, UNDIFFER-TYPE																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
MALIGNANT LYMPHOMA, MIXED TYPE																X									X	3
SITE UNKNOWN																										
NEOPLASM, NOS									X																	1
ADIPOSE TISSUE																										
HEMANGIOMA																										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 TRICHLOROETHYLENE

DOSED GROUP

ANIMAL NUMBER	44201	44707	45206	47906	41611	46201	46303	46606	46707	47201	47301	47506	47604	47707	48201	48301	48406	48501	48808	48901	49001	49101	49505	49601	49707
WEEKS ON STUDY	09 8	09 7	10 4	07 7	01 1	00 4	00 5	00 4	09 8	00 4	01 5	06 5	08 4	08 2	01 5	01 1	08 1	08 5	04 1	09 3	00 5	01 5	08 2	08 2	01 5
RESPIRATORY SYSTEM																									
UNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA	X		X								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
HEPATOCELLULAR CARCINOMA							X			X	X				X					X		X			X
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	+	+	N	+	+	N	+	N	N	N	+	+	+	+	+	N	+	N	+	+	+	N	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																									
SQUAMOUS CELL CARCINOMA												X													
SMALL INTESTINE	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	-	-	-	+	+	+	+	+	-	-	+	-	+	-	+	+	-	-	+	+	+	-	+	-	-
ADRENAL	+	-	-	-	+	-	+	+	+	-	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+
SARCOMA, NOS													X												
THYROID	+	-	+	-	+	-	+	-	+	-	+	+	+	+	+	+	+	-	+	-	+	-	+	+	+
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	-	-	-	-	-	-	-	-	-	-	+	-	+	+	+	-	+	-	+	-	-	-	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	N	+	N	N	N	+	+	+	+	N	+	+	+	+	N	N	N	+	+	N
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
LEIOMYOMA																									
ENDOMETRIAL STROMAL POLYP										X															
OVARY	+	+	-	+	-	+	+	+	+	+	+	-	+	+	-	-	+	-	-	+	+	-	+	-	+
PAPILLARY ADENOMA						X																			
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MENINGIOMA																	X								
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS		X																							
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, METASTAT												X													
MALIGNANT LYMPHOMA, NOS																X									
MALIG.LYMPHOMA, UNDIFFER-TYPE					X																				
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE									X																
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			X															X							
MALIGNANT LYMPHOMA, MIXED TYPE	X						X																		
MYELOMONOCYTIC 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 B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED) DOSED GROUP

ANIMAL NUMBER	500	502	504	507	508	509	510	516	517	519	520	521	524	526	527	530	532	534	537	540	542	545	547	550	552	TOTAL
WEEKS ON STUDY	105	104	096	076	090	094	105	066	105	105	105	090	091	089	099	105	105	098	105	104	100	104	046	095	085	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ALVEOLAR/BRONCHIOLAR ADENOMA																									X	4
TRACHEA	-	+	+	M	+	-	-	+	-	+	-	+	+	+	+	-	+	-	-	-	-	-	-	+		27
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	48
LYMPH NODES	+	-	+	M	+	+	+	+	+	+	-	+	-	+	-	-	-	+	+	+	-	+	+	+	+	36
THYMUS	-	+	-	M	-	-	-	-	+	+	+	-	-	-	-	-	+	-	+	+	-	+	-	+	+	17
CIRCULATORY SYSTEM																										
HEART	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	-	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	35
LIVER	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA									X									X	X	X	X			X	X	16
HEPATOCELLULAR CARCINOMA		X											X		X		X							X	X	11
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																X										1
BILE DUCT	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	+	+	M	+	+	+	N	+	+	N	N	+	+	N	+	+	+	N	+	N	+	+	+	+	49*
PANCREAS	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	-	-	+	M	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	43
STOMACH	+	-	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	47
SQUAMOUS CELL PAPILLOMA													X	X												2
SQUAMOUS CELL CARCINOMA																										1
SMALL INTESTINE	+	-	+	M	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	-	+	+	M	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	44
URINARY SYSTEM																										
KIDNEY	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	M	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	-	-	+	+	+	43
ENDOCRINE SYSTEM																										
PITUITARY	+	+	-	M	-	+	-	+	-	-	-	+	+	+	+	+	+	-	-	+	-	+	+	+	+	28
ADRENAL	+	+	+	M	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	37
SARCOMA, NOS																										1
THYROID	-	+	+	M	-	+	+	+	-	+	-	+	+	+	+	+	-	+	-	-	-	-	+	-	+	31
FOLLICULAR-CELL ADENOMA							X																			1
PARATHYROID	-	+	-	M	-	-	-	-	-	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	+	13
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	M	+	+	N	+	N	+	+	N	N	+	+	N	+	+	+	+	N	+	+	+	+	49*
UTERUS	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SARCOMA, NOS															X											1
LEIOMYOMA																				X						1
ENDOMETRIAL STROMAL POLYP																								X		2
OVARY	+	-	+	M	+	+	-	-	+	-	+	+	+	-	-	+	-	-	+	-	+	+	+	+	+	31
PAPILLARY ADENOMA																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
MENINGIOMA																										1
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
ADENOMA, NOS					X							X														3
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
SQUAMOUS CELL CARCINOMA, METASTAT																										1
MALIGNANT LYMPHOMA, NOS												X														2
MALIG.LYMPHOMA, UNDIFFER-TYPE					X																X					3
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE			X															X								3
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										2
MALIGNANT LYMPHOMA, MIXED TYPE								X																		2
MYELOMONOCYTIC LEUKEMIA																										1

* ANIMALS NECROPSIED

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

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

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	50	50	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50	49
INTEGUMENTARY SYSTEM				
NONE				
RESPIRATORY SYSTEM				
*NASAL CAVITY	(50)	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			2 (4%)	
INFLAMMATION, ACUTE				1 (2%)
#TRACHEA	(45)	(44)	(43)	(38)
LACERATED WOUND		2 (5%)	3 (7%)	1 (3%)
PENETRATING WOUND			1 (2%)	
FOREIGN MATERIAL, NOS				3 (8%)
#LUNG/BRONCHIOLE	(49)	(50)	(50)	(49)
HYPERPLASIA, EPITHELIAL			1 (2%)	
#LUNG	(49)	(50)	(50)	(49)
EMPHYSEMA, ALVEOLAR				2 (4%)
COLLAPSE	3 (6%)	3 (6%)	2 (4%)	1 (2%)
CONGESTION, NOS	4 (8%)	3 (6%)	9 (18%)	24 (49%)
CONGESTION, PASSIVE	1 (2%)			1 (2%)
EDEMA, NOS	3 (6%)	1 (2%)	3 (6%)	6 (12%)
HEMORRHAGE	4 (8%)	6 (12%)	12 (24%)	12 (24%)
INFLAMMATION, NOS			1 (2%)	
BRONCHOPNEUMONIA, FOCAL				1 (2%)
INFLAMMATION, FOCAL	2 (4%)		1 (2%)	1 (2%)
INFLAMMATION, DIFFUSE		1 (2%)		
INFLAMMATION, INTERSTITIAL	3 (6%)	1 (2%)		1 (2%)
PNEUMONIA, ASPIRATION		2 (4%)		
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	8 (16%)	20 (40%)	3 (6%)	5 (10%)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)		1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CALCIFICATION, FOCAL				1 (2%)
FOREIGN MATERIAL, NOS		1 (2%)	4 (8%)	3 (6%)
HEMOGLOBIN PIGMENT	1 (2%)			
HEMOSIDEROSIS			1 (2%)	
ALVEOLAR MACROPHAGES	2 (4%)	2 (4%)		1 (2%)
HYPERPLASIA, ADENOMATOUS		1 (2%)	1 (2%)	
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)			
HEMATOPOIETIC SYSTEM				
#SPLEEN	(45)	(45)	(49)	(44)
CONGESTION, NOS	2 (4%)	2 (4%)	1 (2%)	4 (9%)
CONGESTION, CHRONIC PASSIVE	1 (2%)			
FIBROSIS	1 (2%)			
FIBROSIS, FOCAL	1 (2%)			1 (2%)
NECROSIS, FOCAL		1 (2%)		
INFARCT, NOS	1 (2%)			
HEMOSIDEROSIS	1 (2%)	2 (4%)		3 (7%)
HYPERPLASIA, NODULAR				1 (2%)
HYPERPLASIA, NOS	1 (2%)			
HYPERPLASIA, RETICULUM CELL	1 (2%)			
HYPERPLASIA, LYMPHOID		1 (2%)		
HEMATOPOIESIS	4 (9%)	2 (4%)	6 (12%)	3 (7%)
ERYTHROPOIESIS	1 (2%)			
#LYMPH NODE	(28)	(18)	(29)	(24)
HEMORRHAGE				1 (4%)
HYPERPLASIA, NOS	1 (4%)			
#MANDIBULAR L. NODE	(28)	(18)	(29)	(24)
HEMORRHAGE			2 (7%)	1 (4%)
#MESENTERIC L. NODE	(28)	(18)	(29)	(24)
LYMPHEDEMA				1 (4%)
HEMORRHAGE	2 (7%)	2 (11%)	1 (3%)	1 (4%)
#LUNG	(49)	(50)	(50)	(49)
LEUKEMOID REACTION	1 (2%)			
#LIVER	(49)	(49)	(49)	(49)
LEUKEMOID REACTION		1 (2%)		
#THYMUS	(22)	(19)	(13)	(22)
HEMORRHAGE			1 (8%)	2 (9%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INVOLUTION, NOS			1 (8%)	
CIRCULATORY SYSTEM				
*ABDOMINAL CAVITY	(50)	(50)	(50)	(49)
PERIARTERITIS	1 (2%)			
#SPLEEN	(45)	(45)	(49)	(44)
THROMBUS, ORGANIZED	1 (2%)			
#LUNG	(49)	(50)	(50)	(49)
PERIVASCULITIS	2 (4%)	1 (2%)		
#HEART	(49)	(50)	(49)	(48)
THROMBOSIS, NOS			1 (2%)	
THROMBUS, MURAL	1 (2%)		1 (2%)	
INFLAMMATION, FOCAL			2 (4%)	3 (6%)
INFLAMMATION, ACUTE FOCAL		1 (2%)		
INFLAMMATION, CHRONIC FOCAL				1 (2%)
FIBROSIS	23 (47%)	15 (30%)	6 (12%)	6 (13%)
FIBROSIS, FOCAL	14 (29%)	20 (40%)	14 (29%)	10 (21%)
FIBROSIS, CONDENSATION	1 (2%)			
PERIARTERITIS	1 (2%)			
NECROSIS, FOCAL				2 (4%)
NECROSIS, DIFFUSE	1 (2%)			
CALCIFICATION, METASTATIC	1 (2%)			
#MYOCARDIUM	(49)	(50)	(49)	(48)
INFLAMMATION, FOCAL				1 (2%)
FIBROSIS			2 (4%)	
*PANCREATIC ARTERY	(50)	(50)	(50)	(49)
ARTERIOSCLEROSIS, NOS	1 (2%)			
#LIVER	(49)	(49)	(49)	(49)
THROMBOSIS, NOS				1 (2%)
THROMBUS, ORGANIZED				2 (4%)
*MESENTERY	(50)	(50)	(50)	(49)
PERIARTERITIS	1 (2%)			
*GENITAL SYSTEM	(50)	(50)	(50)	(49)
PERIARTERITIS	1 (2%)			

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM				
#SALIVARY GLAND	(45)	(45)	(43)	(36)
HEMORRHAGE			1 (2%)	
INFLAMMATION, NOS			1 (2%)	1 (3%)
INFLAMMATION, FOCAL			1 (2%)	
INFLAMMATION ACUTE AND CHRONIC				1 (3%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)		
ATROPHY, NOS	1 (2%)			1 (3%)
ATROPHY, FOCAL				1 (3%)
#LIVER	(49)	(49)	(49)	(49)
CONGESTION, NOS	1 (2%)	2 (4%)	2 (4%)	7 (14%)
CONGESTION, PASSIVE		2 (4%)		
CONGESTION, ACUTE PASSIVE		1 (2%)	1 (2%)	1 (2%)
CONGESTION, CHRONIC PASSIVE	1 (2%)			
INFLAMMATION, NOS	1 (2%)		1 (2%)	
INFLAMMATION, FOCAL	1 (2%)	5 (10%)		1 (2%)
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)		
ABSCESS, CHRONIC				1 (2%)
CHOLANGIOFIBROSIS	1 (2%)			
PARASITISM			1 (2%)	
NECROSIS, FOCAL	5 (10%)	1 (2%)	1 (2%)	1 (2%)
NECROSIS, CENTRAL	1 (2%)	2 (4%)	2 (4%)	1 (2%)
METAMORPHOSIS FATTY	3 (6%)	5 (10%)		1 (2%)
PIGMENTATION, NOS	1 (2%)			
KARYOPYKNOSIS				1 (2%)
CYTOPLASMIC VACUOLIZATION	1 (2%)	3 (6%)	1 (2%)	
BASOPHILIC CYTO CHANGE	14 (29%)	3 (6%)	3 (6%)	
CLEAR-CELL CHANGE	1 (2%)	2 (4%)	3 (6%)	4 (8%)
ATROPHY, FOCAL				1 (2%)
HYPERPLASIA, SECONDARY				1 (2%)
#INTRAHEPATIC BILE DU	(49)	(49)	(49)	(49)
HYPERPLASIA, FOCAL			1 (2%)	
#PANCREAS	(46)	(47)	(44)	(40)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)		
FIBROSIS, FOCAL	1 (2%)			
NECROSIS, HEMORRHAGIC	1 (2%)			
ATROPHY, NOS	1 (2%)	2 (4%)	1 (2%)	
ATROPHY, FOCAL	2 (4%)	5 (11%)	5 (11%)	2 (5%)
#ESOPHAGUS	(48)	(47)	(50)	(45)
LACERATED WOUND				1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
PENETRATING WOUND				2 (4%)
IMPACTION, NOS	1 (2%)			
#STOMACH	(48)	(47)	(48)	(46)
CYST, NOS			1 (2%)	
INFLAMMATION, CHRONIC FOCAL				1 (2%)
CALCIFICATION, METASTATIC	1 (2%)			
#GASTRIC MUCOSA	(48)	(47)	(48)	(46)
ULCER, NOS	1 (2%)			
FIBROSIS	1 (2%)			
#PYLORUS	(48)	(47)	(48)	(46)
ATROPHY, NOS	1 (2%)			
#DUODENUM	(45)	(48)	(47)	(44)
ECTOPIA		1 (2%)		
#ILEUM	(45)	(48)	(47)	(44)
PARASITISM	1 (2%)			
#COLON	(41)	(42)	(45)	(39)
ULCER, ACUTE	1 (2%)			
PARASITISM	5 (12%)	9 (21%)	9 (20%)	4 (10%)
#COLONIC MUCOSA	(41)	(42)	(45)	(39)
FIBROSIS	1 (2%)			
*RECTUM	(50)	(50)	(50)	(49)
INFLAMMATION, ACUTE	1 (2%)			
PARASITISM		2 (4%)		2 (4%)
URINARY SYSTEM				
#KIDNEY	(49)	(48)	(49)	(49)
CONGENITAL HYPOPLASIA		1 (2%)		
CYST, NOS	1 (2%)	1 (2%)		
CONGESTION, NOS		1 (2%)	1 (2%)	
HEMORRHAGE				1 (2%)
GLOMERULONEPHRITIS, MEMBRANOUS	1 (2%)			
INFLAMMATION, ACUTE FOCAL		1 (2%)		
GLOMERULONEPHRITIS, SUBACUTE	1 (2%)			
NEPHROPATHY	43 (88%)	41 (85%)	29 (59%)	18 (37%)
DEGENERATION, GRANULAR		1 (2%)		

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
METAMORPHOSIS FATTY		1 (2%)		
CALCIFICATION, FOCAL		2 (4%)		
CALCIFICATION, METASTATIC	1 (2%)			
PIGMENTATION, NOS	2 (4%)	1 (2%)	5 (10%)	
HEMOSIDEROSIS	2 (4%)			
CYTOMEGALY			48 (98%)	48 (98%)
HYPERPLASIA, TUBULAR CELL				1 (2%)
#RIGHT KIDNEY	(49)	(48)	(49)	(49)
NEPHROPATHY			1 (2%)	
#LEFT KIDNEY	(49)	(48)	(49)	(49)
HYPOPLASIA, NOS			1 (2%)	
#KIDNEY/CORTEX	(49)	(48)	(49)	(49)
HEMORRHAGE				1 (2%)
ENDOCRINE SYSTEM				
#PITUITARY	(39)	(42)	(35)	(26)
CYST, NOS	1 (3%)	1 (2%)		
HYPERPLASIA, FOCAL	1 (3%)			
HYPERPLASIA, CHROMOPHOBE-CELL	1 (3%)	1 (2%)	1 (3%)	
#ADRENAL	(45)	(45)	(42)	(44)
AGENESIS			1 (2%)	
HEMORRHAGE	1 (2%)			
CALCIFICATION, FOCAL				1 (2%)
ANGIECTASIS	5 (11%)	4 (9%)	1 (2%)	2 (5%)
#ADRENAL CORTEX	(45)	(45)	(42)	(44)
HEMORRHAGE		1 (2%)		1 (2%)
NECROSIS, FOCAL	2 (4%)	1 (2%)		
METAMORPHOSIS FATTY	1 (2%)		1 (2%)	1 (2%)
HYPERPLASIA, FOCAL		1 (2%)	1 (2%)	1 (2%)
#ADRENAL MEDULLA	(45)	(45)	(42)	(44)
HYPERPLASIA, FOCAL	1 (2%)	2 (4%)		
#THYROID	(44)	(44)	(43)	(39)
CYST, NOS			1 (2%)	
HYPERPLASIA, C-CELL	9 (20%)	8 (18%)	1 (2%)	
#PARATHYROID	(25)	(22)	(26)	(24)
HYPERPLASIA, FOCAL			1 (4%)	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM				
*MAMMARY GLAND	(50)	(50)	(50)	(49)
CYST, NOS		1 (2%)		
LACTATION	4 (8%)	1 (2%)	1 (2%)	
*PREPUTIAL GLAND	(50)	(50)	(50)	(49)
INFLAMMATION, CALC GRANULOMATOUS			1 (2%)	
#PROSTATE	(46)	(47)	(45)	(45)
EDEMA, NOS			1 (2%)	
INFLAMMATION, NOS	5 (11%)	3 (6%)	2 (4%)	1 (2%)
INFLAMMATION, FOCAL	18 (39%)	21 (45%)	7 (16%)	5 (11%)
INFLAMMATION, DIFFUSE	1 (2%)			
INFLAMMATION ACUTE AND CHRONIC	1 (2%)			
INFLAMMATION, CHRONIC FOCAL	1 (2%)			
CORPORA AMYLACEA	31 (67%)	20 (43%)	25 (56%)	17 (38%)
HYPERPLASIA, FOCAL	2 (4%)	2 (4%)	4 (9%)	4 (9%)
*SEMINAL VESICLE	(50)	(50)	(50)	(49)
COLLAPSE		1 (2%)		1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)			
HYPOPLASIA, NOS				1 (2%)
ATROPHY, NOS			2 (4%)	
#TESTIS	(47)	(49)	(49)	(46)
CRYPTORCHISM				1 (2%)
CALCIFICATION, FOCAL				1 (2%)
ATROPHY, NOS				1 (2%)
ATROPHY, FOCAL		1 (2%)	1 (2%)	
ASPERMATOGENESIS	3 (6%)	1 (2%)	2 (4%)	2 (4%)
HYPOSPERMATOGENESIS			1 (2%)	1 (2%)
HYPERPLASIA, INTERSTITIAL CELL	2 (4%)			3 (7%)
#LEFT TESTIS	(47)	(49)	(49)	(46)
ATROPHY, NOS		1 (2%)		
HYPERPLASIA, INTERSTITIAL CELL	1 (2%)			
NERVOUS SYSTEM				
#BRAIN	(49)	(50)	(49)	(48)
NECROSIS, FOCAL		1 (2%)		

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS				
*EYE	(50)	(50)	(50)	(49)
LACERATED WOUND		1 (2%)		
*TARSAL GLAND	(50)	(50)	(50)	(49)
CYST, NOS			1 (2%)	
*HARDERIAN GLAND	(50)	(50)	(50)	(49)
INFLAMMATION, FOCAL			2 (4%)	
INFLAMMATION ACUTE AND CHRONIC	1 (2%)			
INFLAMMATION, CHRONIC FOCAL	2 (4%)	3 (6%)	5 (10%)	13 (27%)
*EUSTACHIAN TUBE	(50)	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)		
MUSCULOSKELETAL SYSTEM				
*MUSCLE HIP/THIGH	(50)	(50)	(50)	(49)
NECROSIS, NOS	1 (2%)		1 (2%)	
NECROSIS, FOCAL		1 (2%)		
BODY CAVITIES				
*ABDOMINAL CAVITY	(50)	(50)	(50)	(49)
NECROSIS, FAT				1 (2%)
INFARCT, NOS		1 (2%)		
*PERITONEUM	(50)	(50)	(50)	(49)
INFLAMMATION, CHRONIC				1 (2%)
INFARCT, NOS				1 (2%)
*PERITONEAL CAVITY	(50)	(50)	(50)	(49)
HEMORRHAGE, CHRONIC			1 (2%)	
HEMOPERITONEUM			1 (2%)	
FOREIGN MATERIAL, NOS				1 (2%)
*PLEURAL CAVITY	(50)	(50)	(50)	(49)
FOREIGN MATERIAL, NOS				1 (2%)
*MESENTERY	(50)	(50)	(50)	(49)
INFARCT, NOS		4 (8%)	6 (12%)	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFARCT, HEALED	1 (2%)	1 (2%)		
ALL OTHER SYSTEMS				
*MULTIPLE ORGANS	(50)	(50)	(50)	(49)
JAUNDICE, NOS	1 (2%)	1 (2%)		
ADIPOSE TISSUE				
HEMORRHAGE			1	
INFLAMMATION, FOCAL			1	
INFARCT, NOS	1	3	3	5
OMENTUM				
INFARCT, NOS				1
SPECIAL MORPHOLOGY SUMMARY				
AUTO/NECROPSY/HISTO PERF	1			
AUTOLYSIS/NO NECROPSY				1

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

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	49	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	50	50
INTEGUMENTARY SYSTEM				
*SUBCUT TISSUE	(49)	(50)	(50)	(50)
ABSCESS, NOS			1 (2%)	
GRANULOMA, FOREIGN BODY		1 (2%)		
RESPIRATORY SYSTEM				
*NASAL CAVITY	(49)	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC			1 (2%)	
#TRACHEA	(40)	(46)	(46)	(45)
LACERATED WOUND			2 (4%)	
FOREIGN MATERIAL, NOS			1 (2%)	1 (2%)
#LUNG/BRONCHUS	(49)	(50)	(49)	(50)
INFLAMMATION, NOS		1 (2%)		
#LUNG	(49)	(50)	(49)	(50)
FOREIGN BODY, NOS		1 (2%)		
EMPHYSEMA, ALVEOLAR	1 (2%)		1 (2%)	
COLLAPSE	2 (4%)	1 (2%)	1 (2%)	
CONGESTION, NOS	8 (16%)	5 (10%)	6 (12%)	13 (26%)
EDEMA, NOS	7 (14%)	2 (4%)	3 (6%)	5 (10%)
HEMORRHAGE	2 (4%)	6 (12%)	13 (27%)	12 (24%)
BRONCHOPNEUMONIA, NOS	1 (2%)			
INFLAMMATION, NOS				1 (2%)
INFLAMMATION, FOCAL	5 (10%)	3 (6%)	1 (2%)	2 (4%)
INFLAMMATION, INTERSTITIAL			1 (2%)	
INFLAMMATION, ACUTE FOCAL			1 (2%)	
INFLAMMATION, CHRONIC FOCAL	10 (20%)	23 (46%)	11 (22%)	7 (14%)
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)	
FOREIGN MATERIAL, NOS		1 (2%)		4 (8%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ALVEOLAR MACROPHAGES	2 (4%)		1 (2%)	
HYPERPLASIA, ADENOMATOUS		1 (2%)		
HEMATOPOIETIC SYSTEM				
#BONE MARROW	(47)	(46)	(48)	(46)
HEMORRHAGE		1 (2%)		
HYPERPLASIA, ERYTHROID	1 (2%)			
HYPERPLASIA, GRANULOCYTIC			1 (2%)	
HYPOPLASIA, HEMATOPOIETIC				1 (2%)
#SPLEEN	(47)	(50)	(49)	(44)
CONGESTION, NOS	2 (4%)		1 (2%)	
INFLAMMATION ACUTE AND CHRONIC			1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)			1 (2%)
FIBROSIS, DIFFUSE				
INFARCT, NOS	1 (2%)			
HEMOSIDEROSIS	6 (13%)	4 (8%)	3 (6%)	5 (11%)
LYMPHOID DEPLETION				1 (2%)
HYPERPLASIA, FOCAL	1 (2%)			
HEMATOPOIESIS	3 (6%)	1 (2%)	3 (6%)	5 (11%)
ERYTHROPOIESIS	1 (2%)			
#LYMPH NODE	(23)	(26)	(25)	(26)
INFLAMMATION, FOCAL				1 (4%)
#MANDIBULAR L. NODE	(23)	(26)	(25)	(26)
PLASMACYTOSIS		1 (4%)		
#MESENTERIC L. NODE	(23)	(26)	(25)	(26)
EDEMA, NOS		1 (4%)		
HEMORRHAGE	1 (4%)			
PLASMACYTOSIS	1 (4%)			
#LIVER	(49)	(50)	(48)	(48)
ERYTHROPOIESIS			1 (2%)	
#ADRENAL	(45)	(46)	(48)	(47)
HEMATOPOIESIS	1 (2%)			
#THYMUS	(23)	(25)	(26)	(22)
HEMORRHAGE			1 (4%)	
INVOLUTION, NOS		1 (4%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM				
#LUNG	(49)	(50)	(49)	(50)
PERIVASCULITIS	2 (4%)			
#HEART	(49)	(50)	(49)	(50)
INFLAMMATION, FOCAL	2 (4%)			1 (2%)
INFLAMMATION, MULTIFOCAL	1 (2%)			
INFLAMMATION, CHRONIC FOCAL	1 (2%)			1 (2%)
FIBROSIS	14 (29%)	3 (6%)	1 (2%)	1 (2%)
FIBROSIS, FOCAL	5 (10%)	3 (6%)	8 (16%)	4 (8%)
SCAR		1 (2%)		
NECROSIS, FOCAL			1 (2%)	
#MYOCARDIUM	(49)	(50)	(49)	(50)
FIBROSIS	1 (2%)			
CALCIFICATION, FOCAL		1 (2%)		
*AORTA	(49)	(50)	(50)	(50)
PERIARTERITIS		1 (2%)		
#ADRENAL	(45)	(46)	(48)	(47)
THROMBOSIS, NOS	1 (2%)			
DIGESTIVE SYSTEM				
#SALIVARY GLAND	(46)	(48)	(42)	(46)
INFLAMMATION, NOS		1 (2%)		
#LIVER	(49)	(50)	(48)	(48)
CYST, NOS				1 (2%)
CONGESTION, NOS	1 (2%)			
CONGESTION, PASSIVE	1 (2%)	1 (2%)		
HEMORRHAGE	1 (2%)			
INFLAMMATION, FOCAL	8 (16%)	12 (24%)	8 (17%)	7 (15%)
INFLAMMATION, MULTIFOCAL	1 (2%)		1 (2%)	
INFLAMMATION, CHRONIC FOCAL			1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)			
CHOLANGIOFIBROSIS		1 (2%)		
NECROSIS, FOCAL	1 (2%)	3 (6%)	4 (8%)	
NECROSIS, CENTRAL	2 (4%)			
METAMORPHOSIS FATTY	5 (10%)	6 (12%)	3 (6%)	2 (4%)
PIGMENTATION, NOS	1 (2%)	2 (4%)	2 (4%)	1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CYTOPLASMIC CHANGE, NOS				1 (2%)
CYTOPLASMIC VACUOLIZATION			9 (19%)	2 (4%)
BASOPHILIC CYTO CHANGE	27 (55%)	27 (54%)	3 (6%)	2 (4%)
EOSINOPHILIC CYTO CHANGE		1 (2%)	1 (2%)	1 (2%)
CLEAR-CELL CHANGE	1 (2%)		6 (13%)	7 (15%)
DEPLETION, GLYCOGEN		1 (2%)		
HYPERPLASIA, NODULAR	1 (2%)			
#INTRAHEPATIC BILE DU	(49)	(50)	(48)	(48)
HYPERPLASIA, NOS	1 (2%)			
#PANCREAS	(46)	(48)	(47)	(44)
DILATATION/DUCTS		1 (2%)		
INFLAMMATION, FOCAL				1 (2%)
ATROPHY, NOS		1 (2%)		
ATROPHY, FOCAL	1 (2%)	2 (4%)	1 (2%)	
#ESOPHAGUS	(49)	(48)	(47)	(50)
LACERATED WOUND				1 (2%)
PENETRATING WOUND			1 (2%)	1 (2%)
PERFORATING WOUND		1 (2%)		
IMPACTION, NOS		2 (4%)		
#STOMACH	(46)	(50)	(48)	(43)
ULCER, NOS	1 (2%)	1 (2%)		
INFLAMMATION, ACUTE FOCAL		1 (2%)		
#GASTRIC MUCOSA	(46)	(50)	(48)	(43)
ULCER, ACUTE		1 (2%)		
#DUODENUM	(44)	(47)	(45)	(45)
ADHESION, NOS	1 (2%)			
#COLON	(39)	(47)	(45)	(40)
PARASITISM	6 (15%)	4 (9%)	6 (13%)	2 (5%)
*RECTUM	(49)	(50)	(50)	(50)
PARASITISM	2 (4%)		1 (2%)	1 (2%)
URINARY SYSTEM				
*URINARY TRACT	(49)	(50)	(50)	(50)
DILATATION, NOS	1 (2%)			
#KIDNEY	(48)	(50)	(49)	(48)
CONGENITAL HYDRONEPHROSIS				1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYDRONEPHROSIS	2 (4%)			
CYST, NOS			1 (2%)	
HEMATOMA, NOS			1 (2%)	
INFLAMMATION, INTERSTITIAL		1 (2%)		
GLOMERULONEPHRITIS, MEMBRANOUS	1 (2%)			
PYELONEPHRITIS, ACUTE				1 (2%)
FIBROSIS, DIFFUSE		1 (2%)		
NEPHROPATHY	24 (50%)	9 (18%)	4 (8%)	2 (4%)
NEPHROSIS, NOS	1 (2%)	2 (4%)		
INFARCT, NOS		2 (4%)		
CALCIFICATION, FOCAL	8 (17%)	9 (18%)	9 (18%)	2 (4%)
PIGMENTATION, NOS		1 (2%)	1 (2%)	
HEMOSIDEROSIS	1 (2%)			
CYTOMEGALY			49 (100%)	48 (100%)
#KIDNEY/CORTEX	(48)	(50)	(49)	(48)
NECROSIS, HEMORRHAGIC			1 (2%)	
#URINARY BLADDER	(41)	(41)	(46)	(44)
EDEMA, NOS	1 (2%)	1 (2%)		
ENDOCRINE SYSTEM				
#PITUITARY	(43)	(37)	(34)	(41)
CYST, NOS	1 (2%)	4 (11%)		3 (7%)
MULTIPLE CYSTS		1 (3%)		
HEMORRHAGE	2 (5%)	1 (3%)		1 (2%)
HEMORRHAGIC CYST			1 (3%)	
HEMOSIDEROSIS		1 (3%)		
HYPERPLASIA, CHROMOPHOBE-CELL			1 (3%)	
ANGIECTASIS	1 (2%)			
#ADRENAL	(45)	(46)	(48)	(47)
NECROSIS, CORTICAL		1 (2%)		1 (2%)
METAMORPHOSIS FATTY			1 (2%)	
HYPERPLASIA, FOCAL				1 (2%)
ANGIECTASIS	7 (16%)	7 (15%)	11 (23%)	8 (17%)
#ADRENAL CORTEX	(45)	(46)	(48)	(47)
HEMORRHAGE	1 (2%)	2 (4%)	1 (2%)	
METAMORPHOSIS FATTY	3 (7%)	2 (4%)		1 (2%)
HYPERTROPHY, FOCAL				1 (2%)
HYPERPLASIA, FOCAL	2 (4%)		1 (2%)	5 (11%)
#ADRENAL MEDULLA	(45)	(46)	(48)	(47)
HYPERPLASIA, FOCAL		2 (4%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#THYROID	(36)	(41)	(45)	(44)
HYPERPLASIA, C-CELL	15 (42%)	8 (20%)	7 (16%)	3 (7%)
REPRODUCTIVE SYSTEM				
*MAMMARY GLAND	(49)	(50)	(50)	(50)
RETENTION OF CONTENT			1 (2%)	
GALACTOCELE	2 (4%)	1 (2%)	2 (4%)	2 (4%)
INFLAMMATION, NOS	1 (2%)			
CYSTIC DISEASE	1 (2%)			
LACTATION	3 (6%)		1 (2%)	1 (2%)
#UTERUS	(45)	(48)	(48)	(46)
PROLAPSE				1 (2%)
HYDROMETRA		2 (4%)	1 (2%)	3 (7%)
CYST, NOS			1 (2%)	
MULTIPLE CYSTS			1 (2%)	
CONGESTION, NOS	1 (2%)			
HEMORRHAGE	1 (2%)			
HEMATOMETRA	1 (2%)			
INFLAMMATION, CHRONIC		1 (2%)		
#UTERUS/ENDOMETRIUM	(45)	(48)	(48)	(46)
CYST, NOS			1 (2%)	1 (2%)
MULTIPLE CYSTS				2 (4%)
FIBROSIS	2 (4%)			
HYPERPLASIA, CYSTIC		1 (2%)	1 (2%)	
#OVARY	(44)	(46)	(47)	(44)
CYST, NOS	1 (2%)	5 (11%)	2 (4%)	2 (5%)
FOLLICULAR CYST, NOS			1 (2%)	
FIBROSIS, DIFFUSE		1 (2%)		
NERVOUS SYSTEM				
#BRAIN/MENINGES	(48)	(50)	(50)	(49)
FIBROSIS, FOCAL			1 (2%)	
#BRAIN	(48)	(50)	(50)	(49)
GLIOSIS				1 (2%)
NECROSIS, HEMORRHAGIC	1 (2%)			
CALCIFICATION, FOCAL		1 (2%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS				
*EYE	(49)	(50)	(50)	(50)
CATARACT		1 (2%)		
*EYE/CORNEA	(49)	(50)	(50)	(50)
ULCER, ACUTE	1 (2%)			
CALCIFICATION, FOCAL				1 (2%)
*HARDERIAN GLAND	(49)	(50)	(50)	(50)
INFLAMMATION, FOCAL		1 (2%)		
INFLAMMATION ACUTE AND CHRONIC	1 (2%)			
INFLAMMATION, CHRONIC FOCAL	5 (10%)		7 (14%)	19 (38%)
MUSCULOSKELETAL SYSTEM				
*COSTOCHONDRAL SYNCHO	(49)	(50)	(50)	(50)
NECROSIS, FOCAL				1 (2%)
*MUSCLE OF HEAD	(49)	(50)	(50)	(50)
INFLAMMATION, CHRONIC				1 (2%)
*MUSCLE HIP/THIGH	(49)	(50)	(50)	(50)
NECROSIS, NOS	2 (4%)			
NECROSIS, FOCAL		1 (2%)		
BODY CAVITIES				
*PERITONEUM	(49)	(50)	(50)	(50)
INFARCT, NOS			1 (2%)	
*MESENTERY	(49)	(50)	(50)	(50)
NECROSIS, FAT				1 (2%)
INFARCT, NOS			2 (4%)	3 (6%)
INFARCT, ACUTE		1 (2%)		
ALL OTHER SYSTEMS				
*MULTIPLE ORGANS	(49)	(50)	(50)	(50)
CALCIFICATION, METASTATIC		1 (2%)		
JAUNDICE, NOS	2 (4%)			

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ADIPOSE TISSUE				
INFARCT, NOS	2	3	1	1
INFARCT, FOCAL				1
INFARCT, ACUTE			1	
INFARCT, HEALED		1		
OMENTUM				
INFARCT, NOS			1	
SPECIAL MORPHOLOGY SUMMARY				
AUTO/NECROPSY/HISTO PERF				1
AUTOLYSIS/NO NECROPSY	1			

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

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	DOSED GROUP
ANIMALS INITIALLY IN STUDY	50	50
ANIMALS NECROPSIED	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50
INTEGUMENTARY SYSTEM		
*SKIN	(50)	(50)
EPIDERMAL INCLUSION CYST		1 (2%)
ULCER, NOS		1 (2%)
ACARIASIS	1 (2%)	8 (16%)
*SUBCUT TISSUE	(50)	(50)
ABSCESS, CHRONIC	1 (2%)	
RESPIRATORY SYSTEM		
*NASAL CAVITY	(50)	(50)
INFLAMMATION, SUPPURATIVE		3 (6%)
*LARYNX	(50)	(50)
ULCER, ACUTE		1 (2%)
#TRACHEA	(23)	(27)
PENETRATING WOUND		1 (4%)
HEMORRHAGE		1 (4%)
#LUNG/BRONCHIOLE	(49)	(50)
HYPERPLASIA, FOCAL		1 (2%)
#LUNG	(49)	(50)
CONGESTION, NOS	3 (6%)	12 (24%)
EDEMA, NOS		2 (4%)
HEMORRHAGE	6 (12%)	7 (14%)
BRONCHOPNEUMONIA, FOCAL	9 (18%)	6 (12%)
PNEUMONIA, ASPIRATION	1 (2%)	1 (2%)
BRONCHOPNEUMONIA, CHRONIC	3 (6%)	
INFLAMMATION, CHRONIC FOCAL	4 (8%)	3 (6%)
FOREIGN MATERIAL, NOS		1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
PIGMENTATION, NOS	1 (2%)	
ALVEOLAR MACROPHAGES	2 (4%)	
HYPERPLASIA, ADENOMATOUS		1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)	
HEMATOPOIETIC SYSTEM		
#BONE MARROW	(49)	(49)
HYPERPLASIA, GRANULOCYTIC	3 (6%)	2 (4%)
#SPLEEN	(48)	(42)
ATROPHY, NOS		1 (2%)
HYPERPLASIA, NOS	1 (2%)	
HYPERPLASIA, FOCAL	1 (2%)	
HYPERPLASIA, LYMPHOID	3 (6%)	1 (2%)
HEMATOPOIESIS		3 (7%)
ERYTHROPOIESIS		1 (2%)
#LYMPH NODE	(31)	(30)
ABSCESS, NOS	1 (3%)	
PLASMACYTOSIS	1 (3%)	
#PANCREATIC L.NODE	(31)	(30)
HEMORRHAGE		1 (3%)
#MESENTERIC L. NODE	(31)	(30)
HEMORRHAGE	9 (29%)	7 (23%)
INFLAMMATION, ACUTE		1 (3%)
HYPERPLASIA, LYMPHOID	1 (3%)	
#LIVER	(48)	(50)
HEMATOPOIESIS	1 (2%)	1 (2%)
#PEYER'S PATCH	(43)	(47)
HYPERPLASIA, LYMPHOID		1 (2%)
#THYMUS	(16)	(15)
INVOLUTION, NOS		1 (7%)
CIRCULATORY SYSTEM		
*LARYNGEAL MUSCLE	(50)	(50)
PERIARTERITIS	1 (2%)	

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
#HEART	(49)	(49)
FIBROSIS, FOCAL		1 (2%)
PERIARTERITIS	1 (2%)	
NECROSIS, HEMORRHAGIC	1 (2%)	
INFARCT, ACUTE	1 (2%)	
CALCIFICATION, FOCAL		2 (4%)
MELANIN	2 (4%)	
#LIVER	(48)	(50)
THROMBOSIS, NOS		1 (2%)
THROMBUS, ORGANIZED		1 (2%)
#PANCREAS	(47)	(46)
PERIARTERITIS		1 (2%)
DIGESTIVE SYSTEM		
#SALIVARY GLAND	(37)	(40)
INFLAMMATION, CHRONIC FOCAL	1 (3%)	1 (3%)
#LIVER	(48)	(50)
INFLAMMATION, FOCAL	2 (4%)	1 (2%)
NECROSIS, NOS		1 (2%)
NECROSIS, FOCAL	1 (2%)	4 (8%)
INFARCT, NOS	1 (2%)	1 (2%)
INFARCT, FOCAL		1 (2%)
METAMORPHOSIS FATTY	2 (4%)	
PIGMENTATION, NOS		1 (2%)
CYTOPLASMIC VACUOLIZATION	1 (2%)	
CYTOLOGIC ALTERATION, NOS	1 (2%)	1 (2%)
HYPERPLASIA, FOCAL	1 (2%)	1 (2%)
*GALLBLADDER	(50)	(50)
NECROSIS, NOS		1 (2%)
#PANCREAS	(47)	(46)
CYST, NOS	1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	2 (4%)
ATROPHY, NOS	1 (2%)	
#ESOPHAGUS	(48)	(44)
LACERATED WOUND		1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
HEMORRHAGE		1 (2%)
INFLAMMATION, NOS	1 (2%)	1 (2%)
INFLAMMATION, FOCAL		1 (2%)
#STOMACH	(48)	(47)
INFLAMMATION, NOS		2 (4%)
INFLAMMATION, FOCAL		2 (4%)
INFLAMMATION, PSEUDOMEMBRANOUS	1 (2%)	
ULCER, ACUTE	1 (2%)	2 (4%)
HYPERKERATOSIS		2 (4%)
#GASTRIC MUCOSA	(48)	(47)
INFLAMMATION, NOS	1 (2%)	1 (2%)
INFLAMMATION, FOCAL	6 (13%)	
URINARY SYSTEM		
#KIDNEY	(49)	(50)
CYST, NOS		1 (2%)
GLOMERULONEPHRITIS, NOS		2 (4%)
GLOMERULONEPHRITIS, FOCAL		2 (4%)
INFLAMMATION, FOCAL		1 (2%)
PYELONEPHRITIS, FOCAL	1 (2%)	
PYELONEPHRITIS, ACUTE		1 (2%)
GLOMERULONEPHRITIS, CHRONIC		1 (2%)
INFLAMMATION, CHRONIC FOCAL		1 (2%)
PYELONEPHRITIS, HEALED	1 (2%)	
NEPHROSIS, NOS	1 (2%)	
METAMORPHOSIS FATTY	2 (4%)	
CALCIFICATION, FOCAL	19 (39%)	3 (6%)
CYTOPLASMIC VACUOLIZATION	1 (2%)	
CYTOMEGALY		45 (90%)
METAPLASIA, OSSEOUS	1 (2%)	
#KIDNEY/CORTEX	(49)	(50)
CYTOMEGALY		1 (2%)
#PERIRENAL TISSUE	(49)	(50)
INFARCT, FOCAL	1 (2%)	
#URINARY BLADDER	(47)	(47)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	
ENDOCRINE SYSTEM		
#ADRENAL	(32)	(36)
INFLAMMATION, ACUTE	1 (3%)	

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
#ADRENAL CORTEX	(32)	(36)
HEMORRHAGE		1 (3%)
HYPERPLASIA, FOCAL	1 (3%)	
#THYROID	(31)	(29)
CYSTIC FOLLICLES		1 (3%)
REPRODUCTIVE SYSTEM		
#PROSTATE	(44)	(44)
INFLAMMATION, ACUTE	1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE		1 (2%)
HYPERPLASIA, NOS	1 (2%)	
*SEMINAL VESICLE	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)	
#TESTIS	(49)	(49)
HEMORRHAGE		1 (2%)
CALCIFICATION, FOCAL		1 (2%)
*EPIDIDYMIS	(50)	(50)
SPERMATOCELE		1 (2%)
INFLAMMATION, SUPPURATIVE		1 (2%)
GRANULOMA, SPERMATIC	1 (2%)	
NERVOUS SYSTEM		
#BRAIN	(48)	(49)
NECROSIS, ISCHEMIC		1 (2%)
CALCIFICATION, FOCAL	6 (13%)	5 (10%)
SPECIAL SENSE ORGANS		
*NASOLACRIMAL DUCT	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)
*HARDERIAN GLAND	(50)	(50)
HYPERPLASIA, FOCAL		1 (2%)
*MIDDLE EAR	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)	
METAPLASIA, SQUAMOUS		1 (2%)
MUSCULOSKELETAL SYSTEM		
*VERTEBRAL COLUMN	(50)	(50)
ABSCESS, CHRONIC	1 (2%)	
*THORACIC VERTEBRA	(50)	(50)
FRACTURE, NOS		1 (2%)
BODY CAVITIES		
*THORAX	(50)	(50)
HEMOPNEUMOTHORAX		1 (2%)
*THORACIC CAVITY	(50)	(50)
HEMOTHORAX		1 (2%)
*MEDIASTINUM	(50)	(50)
ABSCESS, CHRONIC	1 (2%)	
*ABDOMINAL CAVITY	(50)	(50)
HEMOPERITONEUM		1 (2%)
*PERITONEUM	(50)	(50)
INFLAMMATION, NOS		1 (2%)
INFLAMMATION, CHRONIC		1 (2%)
*PERICARDIUM	(50)	(50)
INFLAMMATION, NOS	1 (2%)	
*MESENTERY	(50)	(50)
INFLAMMATION, ACUTE		1 (2%)
ALL OTHER SYSTEMS		
NECK		
ABSCESS, NOS		1
ADIPOSE TISSUE		
INFARCT, NOS	1	

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
PLEURAL CAVITY		
HEMOTHORAX		1
SPECIAL MORPHOLOGY SUMMARY		
AUTO/NECROPSY/HISTO PERF		2
AUTO/NECROPSY/NO HISTO	1	

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

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE ADMINISTERED TRICHLOROETHYLENE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	DOSED GROUP
ANIMALS INITIALLY IN STUDY	50	50
ANIMALS MISSING	2	1
ANIMALS NECROPSIED	48	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	49
INTEGUMENTARY SYSTEM		
*SKIN	(48)	(49)
ACARIASIS	10 (21%)	
RESPIRATORY SYSTEM		
*NASAL CAVITY	(48)	(49)
INFLAMMATION, SUPPURATIVE	1 (2%)	3 (6%)
INFLAMMATION, CHRONIC		1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)
#LUNG	(48)	(48)
CONGESTION, NOS	4 (8%)	7 (15%)
HEMORRHAGE	2 (4%)	6 (13%)
BRONCHOPNEUMONIA, FOCAL	14 (29%)	5 (10%)
INFLAMMATION, ACUTE FOCAL	1 (2%)	
BRONCHOPNEUMONIA, CHRONIC	3 (6%)	2 (4%)
INFLAMMATION, CHRONIC FOCAL		1 (2%)
HEMOSIDEROSIS		4 (8%)
ALVEOLAR MACROPHAGES	1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM		
*MULTIPLE ORGANS	(48)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)	
#BONE MARROW	(48)	(49)
HYPERPLASIA, GRANULOCYTIC	2 (4%)	5 (10%)
#SPLEEN	(47)	(48)
INFLAMMATION WITH FIBROSIS		1 (2%)
HEMOSIDEROSIS		1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
HYPERPLASIA, RETICULUM CELL	1 (2%)	
HYPERPLASIA, LYMPHOID	4 (9%)	2 (4%)
HEMATOPOIESIS	3 (6%)	1 (2%)
ERYTHROPOIESIS		2 (4%)
#MESENTERIC L. NODE	(22)	(36)
HEMORRHAGE	3 (14%)	7 (19%)
HYPERPLASIA, RETICULUM CELL	1 (5%)	
*VERTEBRAL COLUMN	(48)	(49)
MYELOFIBROSIS	28 (58%)	10 (20%)
#LIVER	(48)	(49)
HEMATOPOIESIS	2 (4%)	
#THYMUS	(25)	(17)
INVOLUTION, NOS		1 (6%)
CIRCULATORY SYSTEM		
#BRAIN/MENINGES	(48)	(48)
PERIARTERITIS		1 (2%)
*MULTIPLE ORGANS	(48)	(49)
PERIARTERITIS	1 (2%)	
#LUNG	(48)	(48)
PERIVASCULITIS	2 (4%)	1 (2%)
#HEART	(47)	(48)
CALCIFICATION, FOCAL		2 (4%)
#LIVER	(48)	(49)
THROMBOSIS, NOS		1 (2%)
DIGESTIVE SYSTEM		
#SALIVARY GLAND	(39)	(35)
INFLAMMATION, ACUTE		1 (3%)
INFLAMMATION, CHRONIC FOCAL	10 (26%)	4 (11%)
#LIVER	(48)	(49)
INFLAMMATION, NOS		1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
INFLAMMATION, FOCAL	9 (19%)	14 (29%)
NECROSIS, FOCAL	1 (2%)	1 (2%)
NECROSIS, CENTRAL	1 (2%)	
INFARCT, NOS		1 (2%)
CYTOPLASMIC VACUOLIZATION	1 (2%)	1 (2%)
CLEAR-CELL CHANGE		1 (2%)
#PANCREAS	(47)	(49)
DILATATION/DUCTS	3 (6%)	
HEMORRHAGE		1 (2%)
ABSCESS, NOS		1 (2%)
INFLAMMATION, CHRONIC FOCAL		2 (4%)
INFLAMMATION WITH FIBROSIS		1 (2%)
ATROPHY, NOS	2 (4%)	
ATROPHY, FATTY		1 (2%)
#ESOPHAGUS	(45)	(43)
DILATATION, NOS		1 (2%)
#STOMACH	(47)	(47)
INFLAMMATION, NOS		1 (2%)
INFLAMMATION, FOCAL	1 (2%)	
INFLAMMATION, ACUTE		1 (2%)
#GASTRIC MUCOSA	(47)	(47)
INFLAMMATION, NOS	3 (6%)	8 (17%)
ULCER, NOS		1 (2%)
INFLAMMATION, FOCAL	2 (4%)	
INFLAMMATION, CHRONIC		1 (2%)
#PEYER'S PATCH	(45)	(44)
HYPERPLASIA, NOS		1 (2%)
#DUODENUM	(45)	(44)
ULCER, NOS		1 (2%)
ULCER, ACUTE		1 (2%)
*RECTUM	(48)	(49)
INFLAMMATION, NOS	1 (2%)	
INFLAMMATION, ACUTE		1 (2%)
URINARY SYSTEM		
#KIDNEY	(48)	(49)
CAST, NOS		1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
CONGESTION, NOS		1 (2%)
GLOMERULONEPHRITIS, NOS	1 (2%)	1 (2%)
PYELONEPHRITIS, FOCAL		1 (2%)
INFLAMMATION, ACUTE FOCAL	1 (2%)	
GLOMERULONEPHRITIS, SUBACUTE	1 (2%)	
GLOMERULONEPHRITIS, CHRONIC		1 (2%)
INFLAMMATION, CHRONIC FOCAL		1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	
DEGENERATION, NOS	1 (2%)	
CALCIFICATION, FOCAL		1 (2%)
PIGMENTATION, NOS	1 (2%)	
CYTOMEGALY		48 (98%)
#URINARY BLADDER	(41)	(43)
EDEMA, NOS		3 (7%)
INFLAMMATION, CHRONIC	2 (5%)	
ENDOCRINE SYSTEM		
#PITUITARY	(27)	(28)
HEMORRHAGE	1 (4%)	
HYPERPLASIA, CHROMOPHOBE-CELL		1 (4%)
#ADRENAL	(36)	(37)
CYST, NOS	1 (3%)	
CONGESTION, NOS		1 (3%)
HEMORRHAGE		1 (3%)
AMYLOID, NOS		1 (3%)
#ADRENAL CORTEX	(36)	(37)
HYPERPLASIA, FOCAL		1 (3%)
#THYROID	(33)	(31)
CYSTIC FOLLICLES		3 (10%)
REPRODUCTIVE SYSTEM		
*MAMMARY GLAND	(48)	(49)
GALACTOCELE		1 (2%)
#UTERUS	(47)	(49)
HYDROMETRA	2 (4%)	
HEMORRHAGE	1 (2%)	

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
PYOMETRA	1 (2%)	2 (4%)
INFLAMMATION, CHRONIC	1 (2%)	
#CERVIX UTERI	(47)	(49)
INFLAMMATION, CHRONIC		1 (2%)
HYPERPLASIA, FOCAL		1 (2%)
#UTERUS/ENDOMETRIUM	(47)	(49)
EDEMA, NOS	1 (2%)	
INFLAMMATION, ACUTE	1 (2%)	
HYPERPLASIA, NOS	2 (4%)	
HYPERPLASIA, CYSTIC	31 (66%)	28 (57%)
#OVARY	(27)	(31)
CYST, NOS	9 (33%)	3 (10%)
FOLLICULAR CYST, NOS		1 (3%)
LUTEINIZED FOLLIC CYST	1 (4%)	
CORPUS HEMORRHAGICUM CYST		2 (6%)
PAROVARIAN CYST		1 (3%)
HEMORRHAGIC CYST		1 (3%)
NERVOUS SYSTEM		
#BRAIN/MENINGES	(48)	(48)
INFLAMMATION WITH FIBROSIS		1 (2%)
#BRAIN	(48)	(48)
INFLAMMATION, FOCAL		1 (2%)
INFLAMMATION, ACUTE FOCAL		1 (2%)
CALCIFICATION, FOCAL	13 (27%)	5 (10%)
*SPINAL CORD	(48)	(49)
CYST, NOS		1 (2%)
*SCIATIC NERVE	(48)	(49)
DEGENERATION, MYELIN		1 (2%)
SPECIAL SENSE ORGANS		
*EYE/CORNEA	(48)	(49)
ULCER, PERFORATED	1 (2%)	
*EYE APPENDAGE	(48)	(49)
INFLAMMATION, ACUTE		1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	DOSED GROUP
*HARDERIAN GLAND	(48)	(49)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	2 (4%)
*MIDDLE EAR	(48)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)
MUSCULOSKELETAL SYSTEM		
*BONE	(48)	(49)
FIBROUS OSTEODYSTROPHY		1 (2%)
*SKULL	(48)	(49)
INFLAMMATION WITH FIBROSIS		1 (2%)
BODY CAVITIES		
*MEDIASTINUM	(48)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)
*ABDOMINAL VISCERA	(48)	(49)
NECROSIS, FAT	1 (2%)	
*PLEURA	(48)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)
*MESENTERY	(48)	(49)
NECROSIS, NOS	1 (2%)	
ALL OTHER SYSTEMS		
*MULTIPLE ORGANS	(48)	(49)
PIGMENTATION, NOS	1 (2%)	
NECK		
PENETRATING WOUND	1	
ADIPOSE TISSUE		
INFLAMMATION ACUTE AND CHRONIC	1	
OMENTUM		
INFARCT, NOS		1

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

APPENDIX E

HISTORICAL INCIDENCES OF TUMORS IN F344/N RATS AND B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE FOR TWO YEARS

TABLE E1. HISTORICAL INCIDENCE OF RENAL TUBULAR-CELL ADENOMAS, CARCINOMAS, OR ADENOCARCINOMAS IN MALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Total	Diagnosis
Frederick	0/52	—
Gulf South	1/244	Adenocarcinoma (1/50)
Hazleton	0/50	—
Litton	1/130	Adenocarcinoma (1/50)
Mason	0/25	—
Papanicolaou	0/48 *(b)*	—
Southern	1/199	Adenocarcinoma (1/50)
Total	3/748 (0.40%)	

(a) Data as of June 15, 1981 for studies of at least 104 weeks.
(b) This study.

TABLE E2. HISTORICAL INCIDENCE OF MESOTHELIOMAS IN MALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Total	Site	Designation
Frederick	1/52	Tunica vaginalis	NOS
Gulf South	4/245	Hepatic capsule	NOS
		Testis *(b)*	NOS
		Peritoneum *(b)*	NOS
		Multiple organs	NOS
Hazleton	0/50	—	—
Litton	1/130	Testis	Malignant
Mason	2/25	Body cavities, NOS *(b)*	NOS
		Body cavities, NOS *(b)*	Malignant
Papanicolaou	1/50 *(c)*	Peritoneum	Malignant
Southern	7/200	Multiple organs *(b)*	Malignant
		Heart *(b)*	Malignant
		Peritoneum *(b)*	Malignant
		Pleura *(b)*	Malignant
		Mesentery *(b)*	Malignant
		Tunica vaginalis (2) *(b)*	NOS
Total	16/752 (2.1%)		
Range:	High, 3/50; Low, 0/50		

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) Indicates multiple tumors within a group. Range: High, 3/50; Low, 0/50
(c) This study.

TABLE E3. HISTORICAL INCIDENCE OF PITUITARY TUMORS IN MALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Carcinoma NOS	Adenoma NOS	Chromophobe Adenoma	Chromophobe Carcinoma
Frederick	4/52 (7.7%)	12/52 (23.1%)	0/52 (0.0%)	0/52 (0.0%)
Gulf South	0/224 (0.0%)	42/224 (18.8%)	21/224 (9.4%)	0/224 (0.0%)
Hazleton	0/43 (0.0%)	0/43 (0.0%)	4/43 (9.3%)	0/43 (0.0%)
Litton	0/121 (0.0%)	2/121 (1.7%)	9/121 (7.4%)	1/121 (0.8%)
Mason	0/22 (0.0%)	0/22 (0.0%)	2/22 (9.1%)	0/22 (0.0%)
Papanicolaou	0/42 (0.0%)*(b)*	0/42 (0.0%)*(b)*	7/42 (16.7%)*(b)*	1/42 (2.4%)*(b)*
Southern	1/194 (0.5%)	36/194 (18.6%)	0/194 (0.0%)	0/194 (0.0%)
Total	5/698 (0.7%)	92/698 (13.2%)	43/698 (6.2%)	2/698 (0.3%)
Overall Historical Range				
High	4/52	14/44	20/48	1/42
Low	0/50	0/43	0/52	0/52

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

TABLE E4. HISTORICAL INCIDENCE OF PITUITARY TUMORS IN FEMALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Carcinoma NOS	Adenoma NOS	Chromophobe Adenoma	Chromophobe Carcinoma
Frederick	7/49 (14.3%)	18/49 (36.7%)	0/49 (0.0%)	0/49 (0.0%)
Gulf South	5/228 (2.2%)	74/228 (32.5%)	23/228 (10.1%)	0/228 (0.0%)
Hazleton	0/50 (0.0%)	0/50 (0.0%)	14/50 (28.0%)	0/50 (0.0%)
Litton	0/126 (0.0%)	1/126 (0.8%)	49/126 (38.9%)	3/126 (2.3%)
Mason	0/23 (0.0%)	0/23 (0.0%)	7/23 (30.4%)	0/23 (0.0%)
Papanicolaou	0/37 (0.0%)*(b)*	0/37 (0.0%)*(b)*	13/37 (35.1%)*(b)*	0/37 (0.0%)*(b)*
Southern	3/194 (1.5%)	56/194 (28.9%)	0/194 (0.0%)	0/194 (0.0%)
Total	15/707 (2.1%)	149/707 (21.1%)	106/707 (15.0%)	3/707 (0.42%)
Overall Historical Range				
High	7/49	25/49	25/50	2/50
Low	0/50	0/50	0/49	0/49

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

TABLE E5. HISTORICAL INCIDENCE OF UTERINE TUMORS IN FEMALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Endometrial Stromal Polyp	Endometrial Stromal Sarcoma
Frederick	17/51 (33.3%)	2/51 (3.9%)
Gulf South	35/224 (15.6%)	3/224 (1.3%)
Hazleton	16/48 (33.3%)	1/48 (2.1%)
Litton	21/127 (16.5%)	1/127 (0.8%)
Mason	4/24 (16.7%)	0/24 (0.0%)
Papanicolaou	15/48 (31.3%)*(b)*	1/48 (2.1%)*(b)*
Southern	45/200 (22.5%)	7/200 (3.5%)
Total	153/722 (21.2%)	15/722 (2.1%)
Overall Historical Range		
High	17/51	3/50
Low	3/45	0/45

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

TABLE E6. HISTORICAL INCIDENCE OF HEMATOPOIETIC TUMORS IN FEMALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Leukemia	Lymphoma	Lymphoma or Leukemia
Frederick	13/52 (25.0%)	0/52 (0.0%)	13/52 (25.0%)
Gulf South	23/245 (9.4%)	6/245 (2.4%)	29/245 (11.8%)
Hazleton	2/50 (4.0%)	1/50 (2.0%)	3/50 (6.0%)
Litton	28/130 (21.5%)	2/130 (1.5%)	30/130 (23.1%)
Mason	0/24 (0.0%)	0/24 (0.0%)	0/24 (0.0%)
Papanicolaou	14/50 (28.0%)*(b)*	0/50 (0.0%)*(b)*	14/50 (28.0%)*(b)*
Southern	21/200 (10.5%)	2/200 (1.0%)	23/200 (11.5%)
Total	101/751 (13.4%)	11/751 (1.5%)	112/751 (14.9%)
Overall Historical Range			
High	21/50	3/49	22/50
Low	1/49	0/52	2/50

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

TABLE E7. HISTORICAL INCIDENCE OF LIVER TUMORS IN MALE B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Adenoma	Carcinoma	Adenoma or Carcinoma
Frederick	0/50 (0.0%)	4/50 (8.0%)	4/50 (8.0%)
Gulf South	27/190 (14.2%)	32/190 (16.8%)	59/190 (31.1%)
Litton	6/119 (5.0%)	18/119 (15.1%)	24/119 (20.2%)
Mason	8/50 (16.0%)	5/50 (10.0%)	13/50 (26.0%)
Papanicolaou	3/48 (6.3%)*(b)*	8/48 (16.7%)*(b)*	11/48 (22.9%)*(b)*
Southern	18/199 (9.0%)	53/199 (26.6%)	67/199 (33.7%)
Total	62/656 (9.5%)	120/656 (18.3%)	178/656 (27.1%)
Overall Historical Range			
High	10/48	18/50	22/50
Low	0/50	4/50	4/50

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

TABLE E8. HISTORICAL INCIDENCE OF LIVER TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Adenoma	Carcinoma	Adenoma or Carcinoma
Frederick	0/50 (0.0%)	2/50 (4.0%)	2/50 (4.0%)
Gulf South	13/285 (4.6%)	8/285 (2.8%)	21/285 (7.4%)
Litton	2/118 (1.7%)	3/118 (2.5%)	5/118 (4.2%)
Mason	5/50 (10.0%)	2/50 (4.0%)	7/50 (14.0%)
Papanicolaou	2/48 (4.2%)*(b)*	2/48 (4.2%)*(b)*	4/48 (8.3%)*(b)*
Southern	6/200 (3.0%)	5/200 (2.5%)	11/200 (5.5%)
Total	28/751 (3.7%)	22/751 (2.9%)	50/751 (6.7%)
Overall Historical Range			
High	5/50	4/48	7/50
Low	0/50	0/50	1/50

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

TABLE E9. HISTORICAL INCIDENCE OF HEMATOPOIETIC TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Leukemia	Lymphoma	Lymphoma or Leukemia
Frederick	2/50 (4.0%)	4/50 (8.0%)	6/50 (12.0%)
Gulf South	16/292 (5.5%)	44/292 (15.1%)	60/292 (20.5%)
Litton	5/119 (4.2%)	30/119 (25.2%)	34/119 (28.6%)
Mason	0/50 (0.0%)	15/50 (30.0%)	15/50 (30.0%)
Papanicolaou	0/48 (0.0%)*(b)*	7/48 (14.6%)*(b)*	7/48 (14.6%)*(b)*
Southern	1/200 (0.5%)	26/200 (13.0%)	27/200 (13.5%)
Total	24/759 (3.2%)	126/759 (16.6%)	149/759 (19.6%)
Overall Historical Range			
High	9/49	16/50	20/49
Low	0/50	2/48	5/50

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

TABLE E10. INCIDENCE OF HARDERIAN GLAND TUMORS IN B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Laboratory	Males	Females
Frederick	0/50 (0.0%)	0/50 (0.0%)
Gulf South	0/191 (0.0%)	0/292 (0.0%)
Litton	2/120 (1.7%)	3/119 (2.5%)
Mason	3/50 (6.0%)	0/50 (0.0%)
Papanicolaou	0/50 (0.0%)*(b)*	0/48 (0.0%)*(b)*
Southern	11/200 (5.5%)	3/200 (1.5%)
Total	16/661 (2.4%)	6/759 (0.8%)
Overall Historical Range		
High	4/50	2/50
Low	0/50	0/50

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.
(b) This study.

APPENDIX F

SENTINEL ANIMAL SEROLOGY DATA FOR THE TRICHLOROETHYLENE STUDIES

APPENDIX F

A. METHODS

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

Fifteen B6C3F$_1$ mice of both sexes and 15 F344/N rats of both sexes are selected at the time of randomization and allocation of the animals to the various study groups. Five animals of each designated sentinel group are killed at 6, 12, and 18 months on study. Data from animals surviving 24 months are collected from 5/50 randomly selected control animals of each sex and species. The blood from each animal is collected and clotted and the serum is separated. The serum is cooled on ice and shipped to Microbiological Associates' Comprehensive Animal Diagnostic Service for determination of the viral titers. The following tests are performed:

	Hemagglutination Inhibition	Complement Fixation	Elisa*
Mice	PVM (Pneumonia virus of mice) Reo 3 (Reovirus 3) GDVII (Theilor's encephalomyelitis virus) Poly (Polyoma virus) Sendai (Sendai virus) MVM (Minute virus of mice) Ectro (Ectromelia virus)	M. Ad. (Mouse adenovirus) LCM (Lymphocytic choriomeningitis virus)	MHV (Mouse hepatitis virus)
Rats	PVM (Pneumonia virus of mice) Sendai (Sendai virus) KRV (Kilham rat virus) H-1 (Toolan's H-1 virus)	RCV (Rat corona virus)	

* Elisa = Enzyme-linked immunosorbent assay

B. RESULTS

See Tables F1 and F2.

TABLE F1. MURINE VIRUS ANTIBODY DETERMINATIONS FOR RATS IN THE 2-YEAR STUDY OF TRICHLOROETHYLENE

Sample No.	Sex	Hemagglutination Inhibition			Complement Fixation	
		PVM	KRV	H-1	RCV	Sendai
SIX MONTHS						
834	F	80	—	—	—	—
835	F	80	—	—	—	1280
836	F	160	—	—	—	80
837	F	320	—	—	—	640
838	M	320	—	—	—	80
839	M	160	—	—	—	160
840	M	320	—	—	—	40
841	M	320	—	—	—	80
842	M	320	—	40	—	160
843	F	160	20	80	—	160
TWELVE MONTHS						
158	M	20	—	—	—	20
159	M	40	—	—	—	20
160	M	80	—	—	—	20
161	M	20	—	—	—	40
162	M	10	—	—	—	20
163	F	—	—	—	—	80
164	F	80	—	—	—	10
165	F	—	—	—	—	10
166	F	80	—	—	—	10
167	F	80	—	—	—	20
EIGHTEEN MONTHS						
289	M	80	—	—	—	20
290	M	80	—	—	—	—
291	M	80	—	—	—	10
292	M	80	—	—	—	20
293	M	80	—	—	—	10
294	F	—	—	—	—	10
295	F	80	—	—	—	40
296	F	80	—	—	—	20
297	F	80	—	—	—	40
TWENTY-FOUR MONTHS						
164	M	—	—	—	40	—
165	M	—	—	—	20	—
166	M	—	—	—	80	—
167	M	—	—	—	80	—
168	M	—	—	—	40	—
169	F	—	—	—	40	—
170	F	—	—	—	80	—
171	F	—	—	—	80	—
172	F	—	—	—	80	—
173	F	—	—	—	80	—
Significant Titer		20	20	20	10	10

TABLE F2. MURINE VIRUS ANTIBODY DETERMINATIONS FOR MICE IN THE 2-YEAR STUDY OF TRICHLOROETHYLENE

Sample Number	Sex	Hemagglutination Inhibition						Complement Fixation			
		PVM	Reo 3	GDVII	Poly	MVM	Ectro	Sendai	M. Ad	MHV	LCM
SIX MONTHS											
824	F	—	—	—	—	—	—	80	—	—	—
825	F	—	—	—	—	—	—	40	*(a)*	80	—
826	F	—	—	—	—	—	—	160	—	20	—
827	F	—	—	—	—	—	—	40	—	20	—
828	F	—	—	—	—	—	—	80	—	10	—
829	M	—	—	—	—	—	—	80	—	20	—
830	M	—	—	—	—	—	—	20	—	20	—
831	M	—	—	—	—	—	—	80	—	20	—
832	M	—	—	—	—	—	—	80	*(a)*	20	*(a)*
833	M	—	—	—	—	—	—	80	—	20	—
TWELVE MONTHS											
168	M	—	—	—	—	—	—	20	—	—	—
169	M	—	—	—	—	—	—	10	—	—	—
170	M	—	—	—	—	—	—	20	—	—	—
171	M	—	—	—	—	—	—	20	—	—	—
172	M	—	—	—	—	—	—	40	—	—	—
173	F	10	—	—	—	—	—	—	—	—	—
174	F	20	—	—	—	—	—	20	—	—	—
175	F	20	—	—	—	—	—	10	—	—	—
176	F	20	—	—	—	—	—	10	—	—	—
177	F	20	—	—	—	—	—	40	—	—	—
EIGHTEEN MONTHS											
298	M	10	—	—	—	—	—	—	—	—	—
299	M	—	—	—	—	—	—	10	—	—	—
300	M	—	—	—	—	—	—	10	—	—	—
301	M	—	—	—	—	—	—	—	—	—	—
302	M	—	—	—	—	—	—	10	—	—	—
303	F	—	—	*(b)*	—	—	—	40	—	—	—
304	F	10	—	*(b)*	—	—	—	80	—	—	*(c)*
305	F	40	—	—	—	—	—	—	—	—	—
306	F	20	—	—	—	—	—	10	—	—	—
307	F	80	—	—	—	—	—	40	—	—	—
TWENTY-FOUR MONTHS											
174	M	—	—	—	—	—	—	—	—	—	—
175	M	—	—	—	—	—	—	—	—	—	—
176	M	—	—	—	—	—	—	—	—	—	—
177	M	—	—	—	—	—	—	—	—	—	—
178	M	—	—	—	—	—	—	—	—	—	—
179	F	—	—	—	—	—	—	—	—	—	—
180	F	—	—	—	—	—	—	—	—	—	—
181	F	—	—	—	—	—	—	—	—	—	—
182	F	—	—	—	—	—	—	—	—	—	—
183	F	—	—	—	—	—	—	—	—	—	—
Significant Titer		20	20	20	20	20	20	10	10	10	10

(a) Anticomplimentary serum
(b) Serum agglutinates RBCs
(c) Serum reacts with control antigen

APPENDIX G

ANALYSIS OF TRICHLOROETHYLENE
(LOT NUMBERS TB 05-206AA AND TB 08-039AA)
MIDWEST RESEARCH INSTITUTE

APPENDIX G

A. ELEMENTAL ANALYSIS

Element	C	H	Cl
Theory	18.28	0.77	80.95
Lot No. TB05-206AA			
Determined	18.31	0.78	80.69
	18.45	0.80	80.85
Lot No. TB08-039AA			
Determined	18.29	0.80	80.78
	18.15	0.81	80.95

B. WATER ANALYSIS

(Karl Fischer)

Lot No. TB05-206AA — 0.0097 ± 0.0020(δ)%

Lot No. TB08-039AA — < 0.003%

C. BOILING POINT

Lot No. TB05-206AA

Determined	Literature Value
b.p.: 86.0° ± 0.8 (δ)°C at 737 mm (visual, micro boiling point); 84.5°-87°C (DuPont 900 DTA)	b.p. 86.7°C at 760 mm (Gallant, 1966)

D. INDEX OF REFRACTION

Lot No. TB05-206AA

Determined	Literature Value
n_D^{20} 1.4766 ± 0.0002 (δ)	n_D^{20} 1.4766 (Backman et al., 1950)

E. DENSITY

Lot no. TB05-206AA

Determined	Literature Value
d_{23}^{22} 1.46315 ± 0.00002 (δ)	d^{23} 1.458 read from graph (Gallant, 1966)

F. GAS CHROMATOGRAPHY

1. Lot No. TB05-206AA
   Instrument: Tracor MT 220
   Detector: Flame ionization
   Inlet temperature: 200°C
   Detector temperature: 255°C

APPENDIX G

a. System 1

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°-200°C at 10°C/min

Results: Major peak and 12 impurities. The total area of the impurities was less than 0.04% of the major peak.

Peak	Retention Time (min)	Retention Time (Relative to Trichloroethylene)	Area (Percent of Trichloroethylene)
1	0.3	0.10	trace, < 0.001
2	1.2	0.40	trace, < 0.001
3	1.4	0.47	0.002
4	2.0	0.67	0.001
5	2.1	0.70	trace, < 0.001
6	2.4	0.80	0.001
7	3.0	1.00	100
8	7.4	2.47	0.001
9	7.9	2.63	0.02
10	9.8	3.27	trace, < 0.001
11	10.3	3.43	0.003
12	11.8	3.93	trace, < 0.001
13	12.4	4.13	0.003

b. System 2

Column: 20% SP 2100/0.1% Carbowax 1500 on 80/100 Supelcoport, 1.8m x 4 mm I.D., glass

Oven temperature program: 50°C, 5 min; 50°-170°C at 10°C/min

Results: Major peak and eight impurities. All impurities have areas less than 0.01% of the area of the major peak. The total area of the impurities was less than 0.02 of the major peak.

Peak	Retention Time (min)	Retention Time (Relative to Trichloroethylene)	Area (Percent of Trichloroethylene)
1	2.6	0.50	0.0005
2	3.8	0.73	0.0004
3	5.2	1.00	100
4	7.4	1.42	0.002
5	7.7	1.48	0.002
6	8.8	1.69	0.004
7	9.4	1.81	0.0005
8	10.2	1.96	0.0005
9	13.9	2.67	0.002

2. Lot No. TB08-039AA

Instrument: Varian 3700

Detector: Flame ionization

Inlet temperature: 200°C

Carrier Gas: Nitrogen

Carrier Flow Rate: 70 cc/min

a. System 1

Detector Temperature: 250°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 for 5 min; then 50°C to 200°C/min at 10°C/min

Samples Injected: Neat liquid (3.5 μl) and solutions of 1.0 and 0.5% (v/v) trichloroethylene in o-dichlorobenzene to quantitate the major peak and check for detector overload.

Results: Major peak and one impurity after the major peak with an area 0.02% of the major peak.

Peak	Retention Time (min)	Retention Time (Relative to Major Peak)	Area (Percent of Major Peak)
1	3.9	1.00	1.00
2	11.2	2.87	0.02

b. System 2

Detector Temperature: 240°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, for 5 min, then 50°C to 170°C at 10°C/min

Samples Injected: Neat liquid (3 μl) and solutions of 1.0% and 0.5% trichloroethylene in o-dichlorobenzene to quantitate the major peak and check for detector overload.

Results: Major peak and one impurity after the major peak with an area 0.02% of the of the major peak.

Peak	Retention Time (min)	Retention Time (Relative to Major Peak)	Area (Percent of Major Peak)
1	6.3	1.00	100
2	8.3	1.32	0.01

G. SPECTRAL DATA

1. Infrared

a. Lot No. TB05-206AA

Instrument: Beckman IR-12
Cell: 0.015 mm liquid cell, sodium chloride windows
Results: See Figure 5

Spectrum consistent with literature spectrum (Sadtler Standard Spectra)

b. Lot No. TB08-039AA

Instrument: Beckman IR-12
Cell: Thin film between silver chloride plates
Results: See Figure 6

Spectrum consistent with literature spectrum (Sadtler Standard Spectra)

2. Ultraviolet/Visible

a. Lot No. TB05-206AA

Instrument: Cary 118.

No absorbance between 800 and 350 nm (visible range). No maximum between 208 and 350 nm (ultraviolet range), but a gradual increase in absorbance toward the solvent cutoff at 208 nm.

No maximum observed in the in the near ultraviolet range. (Lacher et al., 1950)

Concentration: 1 mg/ml

Solvent: Methanol

b. Lot No. TB08-039AA

Instrument: Cary 118.

No absorbance between 800 and 350 nm (visible region) at a concentration of 1% (v/v). No absorbance maximum between 350 and 215 nm (ultraviolet region) but a gradual increase in absorbance toward 215 nm at a concentration of 0.0004% (v/v).

3. Nuclear Magnetic Resonance

a. Lot Nos. TB05-206AA and TB08-039AA

Instrument: Varian HA-100
Solvent: Neat, tetramethylsilane added.
Assignments: (see Figures 7 and 8)

Consistent with literature spectrum (Sadtler Standard Spectra)

b. Lot No. TB05-206AA:

(a) s, δ 6.34 ppm

Integration Ratio:
(a) 1.00

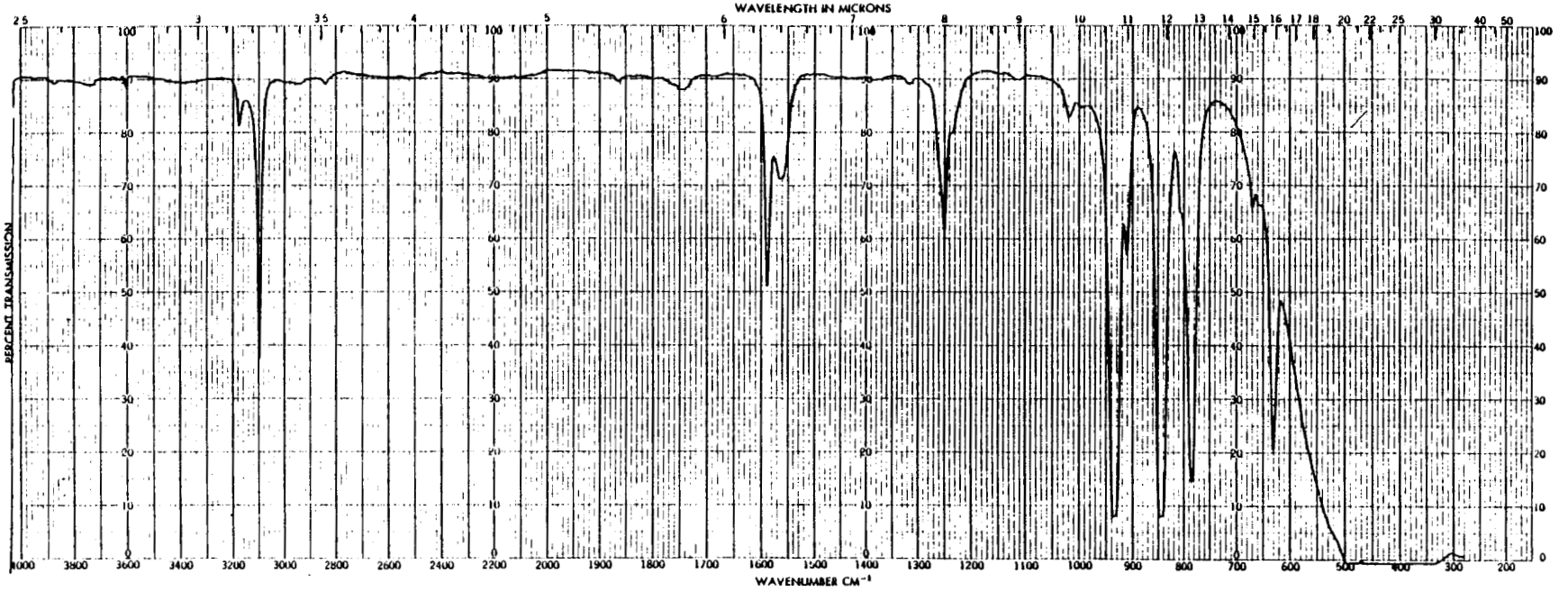

Figure 5. Infrared Absorption Spectrum of Trichloroethylene (Lot No. TB05-206AA)

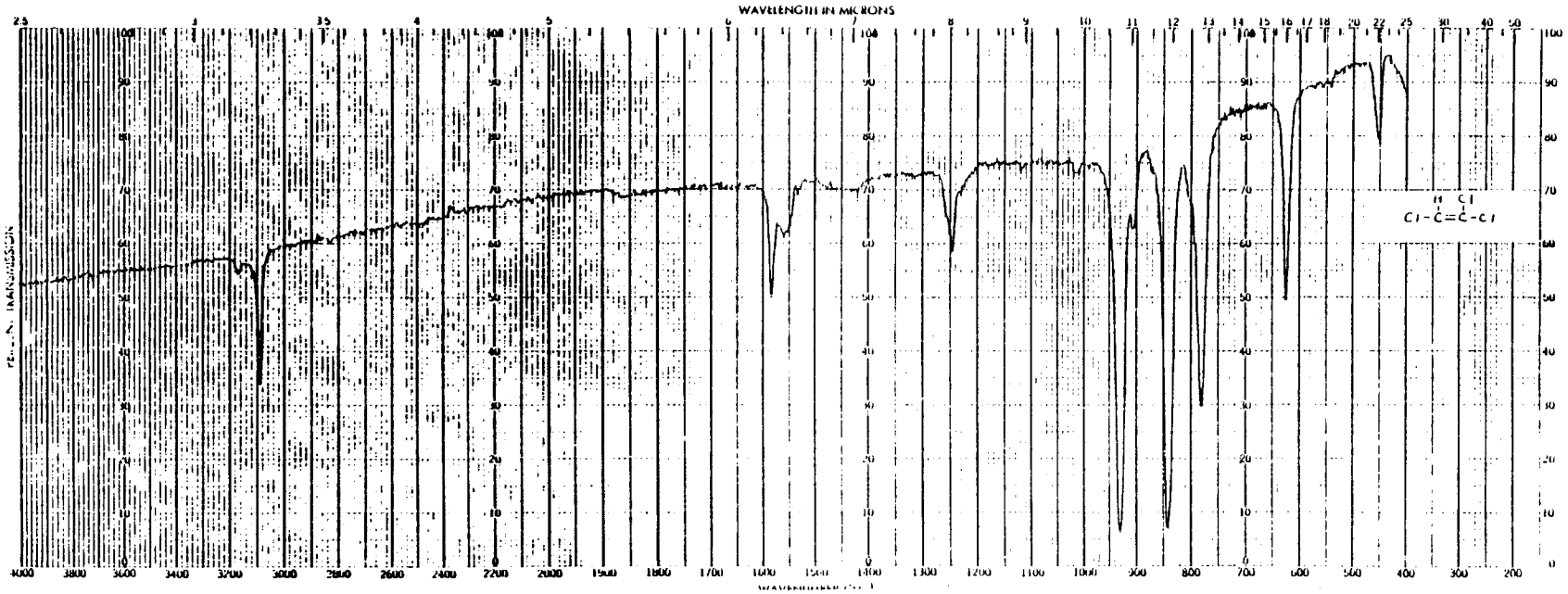

Figure 6. Infrared Absorption Spectrum of Trichloroethylene (Lot No. TB08-039AA)

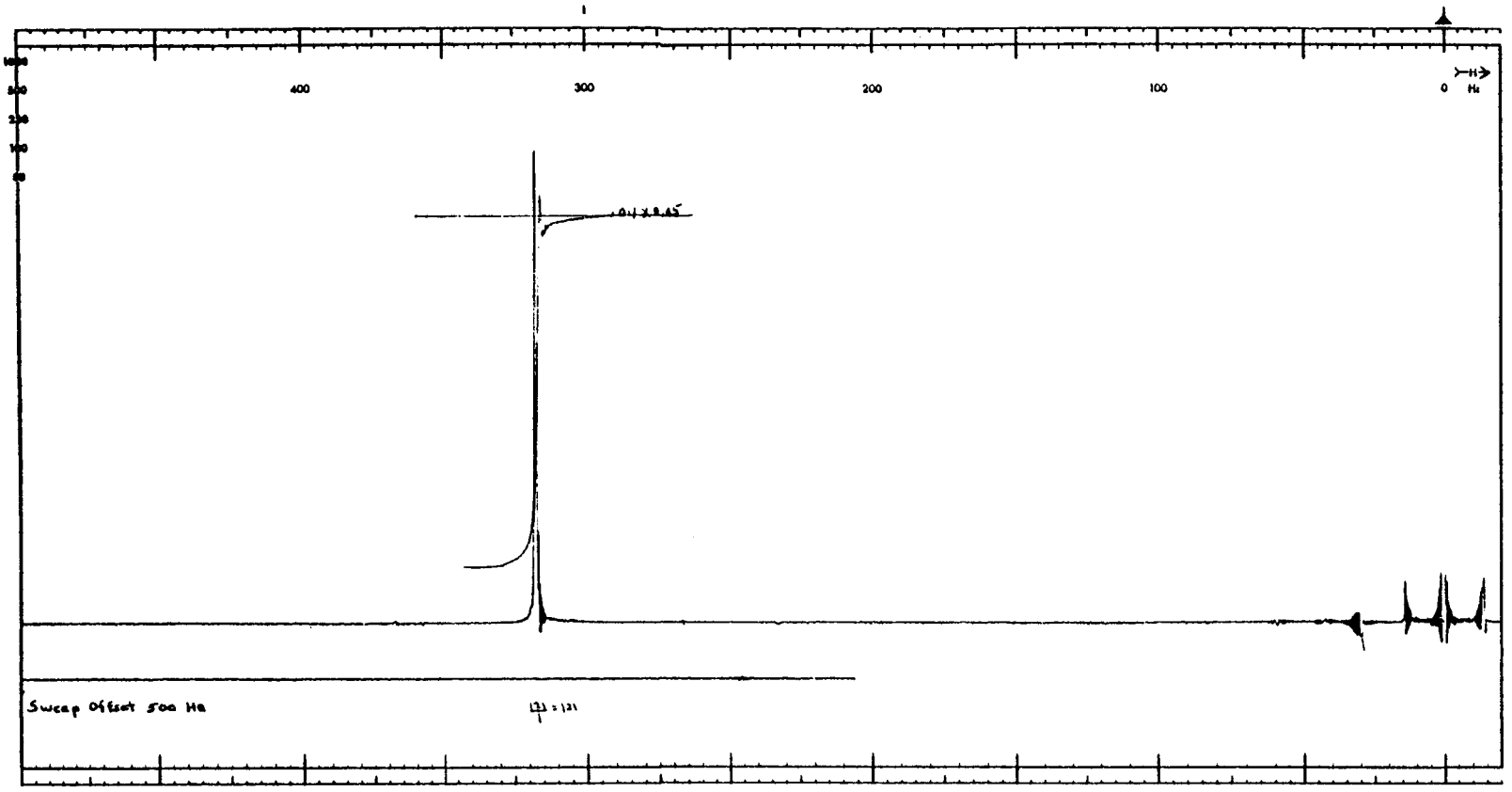

Figure 7. Nuclear Magnetic Resonance Spectrum of Trichloroethylene (Lot No. TB05-206AA)

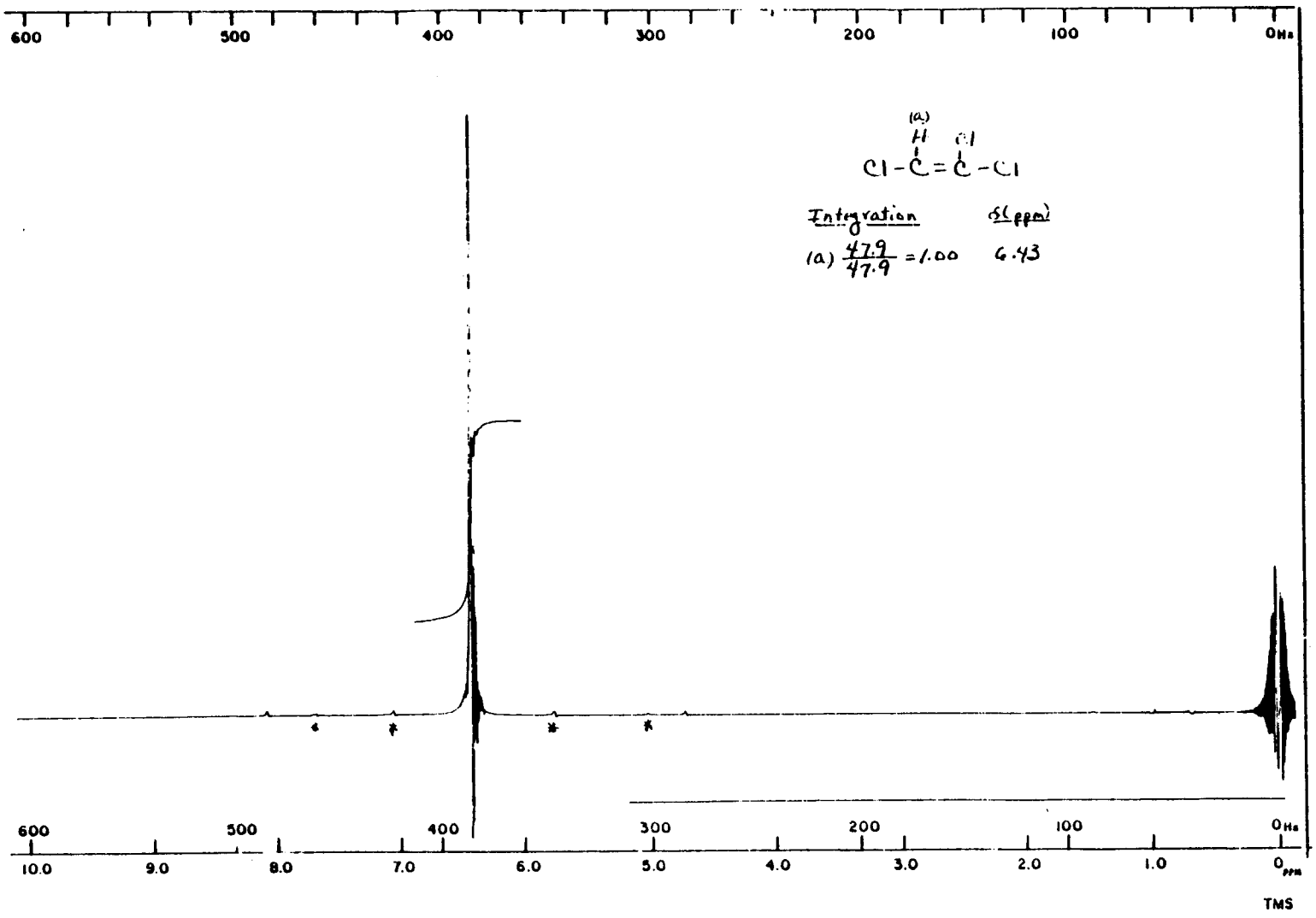

Figure 8. Nuclear Magnetic Resonance Spectrum of Trichloroethylene (Lot No. TB08-039AA)

c. Lot No. TB08-039AA:

(a) s, δ 6.43 ppm

H. QUANTITATION OF THE AMOUNT OF EPICHLOROHYDRIN PRESENT IN LOT NO. TB05-206AA

Analysis by Gas Chromatography

1. System

Instrument: Varian 3700

Detector: Flame ionization

Inlet Temperature: 200°C

Detector Temperature: 250°C

Carrier Gas: Nitrogen; 70 cc/min

Column: 80/100 Carbopack C/0.1% SP 1000; 1.8 m x 4 mm I.D.; glass

Oven Temperature Program: 50°C, isothermal

2. Results

Trichloroethylene, when injected as a neat liquid on the above system, had a retention time of 16.0 min and contained a peak at a retention time of 7.2 min with a shoulder at 7.6 min. The shoulder was enhanced by addition of authentic epichlorohydrin to the sample (0.001%, v/v, relative to trichloroethylene).

3. Conclusions

Calculation of the amount of epichlorohydrin present in the unspiked sample by the standard addition method shows that if epichlorohydrin is present in trichloroethylene, it is present at a level less than or equal to 0.001% (v/v).

I. IDENTIFICATION OF THE IMPURITY IN LOT NO. TB05-206AA (H-2)

Analysis by Gas Chromatography/Mass Spectrometry

1. System

Instrument: Varian 311-A Mass Spectrometer interfaced via a single-stage glass jet separator to a Varian 2700 Gas Chromatograph. Data handled by an Incos 2300 Data System.

Column: 80/100 Carbopack C/0.1% SP-1000; 1.8 m x 2 mm I.D., glass.

Column Oven Temperature: Ambient

Heated Zone Temperatures:

Inlet: 170°C

Transfer line: 300°C; Helium separator: 275°C

Carrier: Helium, 30 cc/min.

Scan Range: 5 - 350 amu

Scan Times (sec): up:2.50; top:0.00
down:0.00; bottom:0.50

Accelerator Voltage: 3000

Electron Multiplier Voltage: -2000

Resolution: 801

Sample Injected: 5 μl of neat trichloroethylene

2. Results

The impurity corresponding to the peak reported in H-2 (with a retention time of 7.2 minutes) eluted in 9.65 min on this system. The spectrum obtained from this peak and a literature spectrum of n-pentane are given below.

Spectrum of Impurity		Literature Spectrum of N-Pentane (Eight peak index of mass spectra)	
m/e	Relative Abundance (% of m/e 43)	m/e	Relative Abundance Index, 1970) (% of m/e 43)
43	100	43	100
41	62	42	59
42	61	41	41
39	26	27	34
27	25	29	25
29	17	39	14
57	11	57	13
72	7	72	9

3. Conclusions

The impurity with the retention time of 7.2 min., reported in the trichloroethylene special report (H-2), was identified on the basis of its mass spectrum as n-pentane.

APPENDIX H

IDENTIFICATION OF FOREIGN MATERIAL FOUND IN TRICHLOROETHYLENE (LOT NO. TB05-206AA)

APPENDIX H

PURPOSE

To identify foreign material found in a sample of trichloroethylene.

ANALYSIS

A. UNDISSOLVED SOLIDS

The original sample of this lot of trichloroethylene was received in a 55-gallon drum and then transferred to 5-gallon drums. The contents of two of these drums were filtered through ashless filter paper. The material was air dried and then weighed. Ten gallons (85 kg) of trichloroethylene were found to contain 260 mg of undissolved solid material. This represents undissolved solids at a level of 3 ppm. The empty drums were then cut open and visually inspected. None of the solids had remained in the drums. The drums were found to be uncoated on the inside, and patches of light corrosion were found, probably due to the action of HCl.

B. DISSOLVED SOLIDS

The amount of dissolved solids was determined by evaporating 100-ml aliquots of filtered trichloroethylene to dryness and then weighing the residue. The trichloroethylene was found to contain dissolved solids at a level of 25.6 ± 1.7 (δ) ppm.

C. MELTING-POINT DETERMINATION

A Buchi Model 510 melting point apparatus was used to determine the melting characteristics of the foreign material. No melting was observed. At 110°C, the sample began to darken and continued to darken until complete decomposition was evident at 290°C.

D. ELEMENTAL ANALYSIS

1. C, H, N, and Cl (a)

Element	Percent Found in Foreign Material
C	41.29
H	4.21
N	< 0.05
Cl	0.95

(a) Analysis performed by Galbraith Laboratories, Inc., 2323 Sycamore Drive, Knoxville, Tennessee 37921.

APPENDIX H

E. SPARK-SOURCE MASS SPECTROMETRY *(a)*

Concentrations are in ppm wt. in Foreign Material

Uranium	<1.2	Terbium	<0.24	Ruthenium	<0.49	Vanadium	0.96
Thorium	<2.4	Gadolinium	<1.0	Molybdenum	0.61	Titanium	58
Bismuth	2.5	Europium	<0.47	Niobium	<0.24	Scandium	<0.47
Lead	31	Samarium	<1.2	Zirconium	0.71	Calcium	>1%
Thallium	<3.0	Neodymium	<1.8	Yttrium	6.2	Potassium	>0.5%
Mercury	NR	Praseodymium	0.90	Strontium	39	Chlorine	≃1,800
Gold	<0.30	Cerium	2.0	Rubidium	0.95	Sulfur	≃1,600
Platinum	<0.87	Lanthanum	1.6	Bromine	17	Phosphorus	≃4,000
Iridium	<0.46	Barium	3.4	Selenium	<0.47	Silicon	>0.5%
Osmium	<0.70	Cesium		Arsenic	<1.2	Aluminum	600
Rhenium	Internal	Iodine	2.9	Germanium	<0.14	Magnesium	>1%
	Standard	Tellurium		Gallium	0.37	Sodium	>1%
Tungsten	<1.2	Antimony	<0.52	Zinc	380	Fluorine	300
Tantalum	<0.45	Tin	3.1	Copper	990	Oxygen	NR
Hafnium	<2.8	Indium	Internal	Nickel	1.4	Nitrogen	NR
Lutetium	<0.43		Standard	Cobalt	1.3	Carbon	NR
Ytterbium	<0.99	Cadmium	0.18	Iron	≃3,100	Boron	10
Thulium	<0.72	Silver	0.78	Manganese	360	Beryllium	<0.24
Erbium	<1.8	Palladium	<0.58	Chromium	38	Lithium	8.6
Holmium	<0.26	Rhodium	<0.15				
Dysprosium	<0.27						

NOTE: All elements for which values are not entered <0.1 ppm wt. NR - Not reported.

(a) Analysis performed by Camp Dresser and McKee, Inc., 11455 W. 48th Avenue, Wheat Ridge, Colorado, 80033.

F. FREE ACID TITRATION

Titration of aliquots of trichloroethylene with 0.01N sodium hydroxide indicated the presence of 6.14 ± 0.25 (δ) ppm free acid (as HCl).

G. INFRARED SPECTROSCOPY

Instrument: Beckman IR-12

Cell: Thin film on silver chloride plates

Sample Preparation: Toluene suspension of precipitated material

Results: The absorbance at 2530, 1795, 1440, and 700 cm^{-1} are characteristic of calcium carbonate. The other absorbances at 2930, 2860, 976, and 912 cm^{-1} are compatible with an unsaturated hydrocarbon. (See Figure 9.)

H. DIRECT INLET MASS SPECTROMETRY

The 70 eV mass spectrum given below was obtained from the foreign material. The spectrum indicates that the material was a mixture. Alkane and alkene fragmentation series were clearly evident. However, it was felt that the spectrum obtained may not be representative of the compound because of the nonvolatile and thermally unstable nature of the material (see Section C). Spectra obtained from low density polyethylene, silicon rubber, and Teflon® did not correspond to the spectrum of the foreign material.

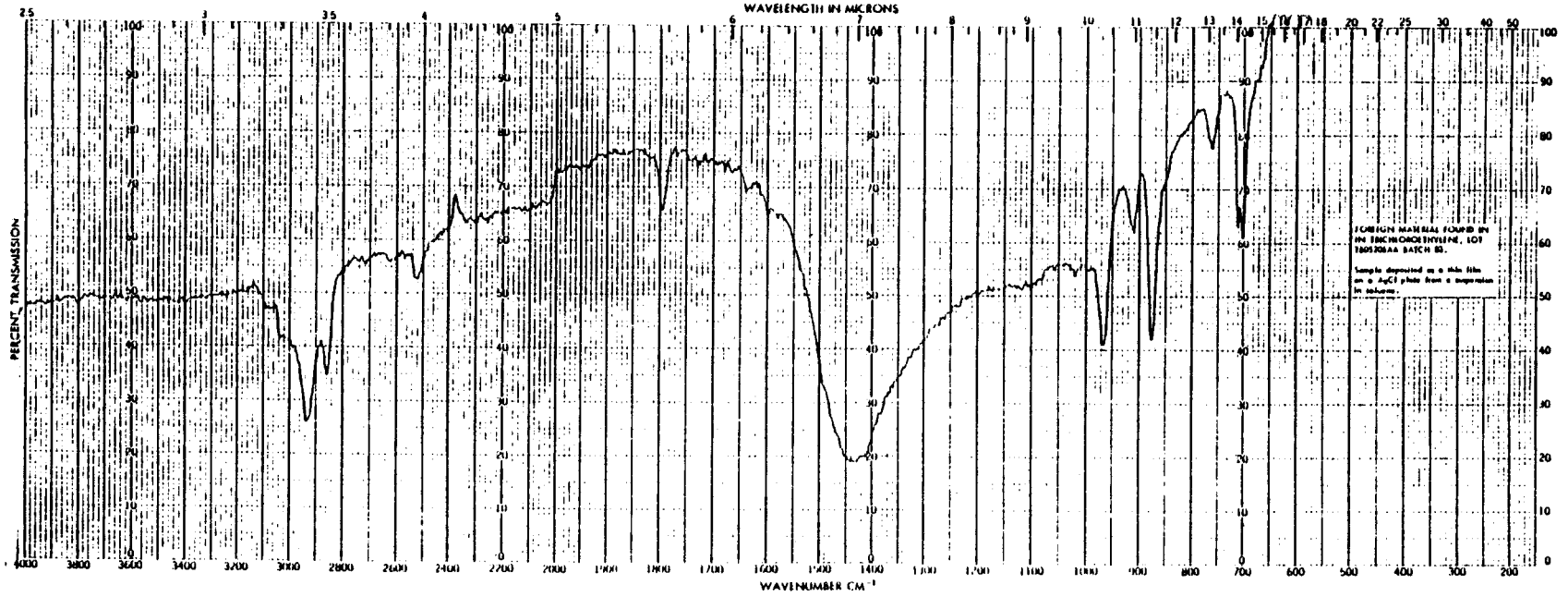

Figure 9. Infrared Absorption Spectrum of Precipitate Found in Trichloroethylene (Lot No. TB05-206AA)

Spectrum Obtained from Foreign Material

M/E	Relative Abundance (% of M/E 69)	M/E	Relative Abundance (% of M/E 69)
69	100	237	20
55	94	185	19
98	92	137	18
83	75	121	18
57	60	99	18
97	60	59	17
81	56	54	17
129	55	87	17
73	52	125	17
95	51	108	16
43	50	151	15
41	49	80	15
67	48	93	15
44	41	42	14
71	38	79	14
60	36	124	14
85	36	39	14
84	35	239	13
311	35	94	13
96	35	107	13
135	34	138	13
70	32	152	12
111	32	171	12
109	30	53	12
56	30	126	11
112	26	101	11
313	26	29	11
236	24	143	11
123	22	72	11
339	21	61	10
110	21	89	10
116	21	91	10
		113	10
		149	10
		157	10
		165	10
		115	10

SUMMARY OF ANALYTICAL DATA

The precipitated material was present in the trichloroethylene at a level of 3 ppm. Non-volatile and non-filterable residue was present at a level of 25.6 ± 1.7 (δ) ppm.

Elemental analysis indicated the precipitate contained 41.29% carbon, 4.21% hydrogen, 0.95% chlorine, and no detectable nitrogen. Spark-source mass spectrometry indicated the presence of calcium, magnesium, and sodium at levels greater than 1% and of potassium at levels greater than 0.5%.

The dried precipitate was a fibrous type material which decomposed on heating. Decomposition began at 110°C and was completed at 290°C.

The infrared spectroscopy (Figure 9) indicated that the material was a mixture of calcium carbonate and probably an unsaturated hydrocarbon. Mass spectroscopy also indicated that the material was a mixture probably containing alkane and alkene materials.

APPENDIX I

ANALYSIS OF TRICHLOROETHYLENE IN CORN OIL FOR STABILITY OF TRICHLOROETHYLENE AT ROOM TEMPERATURE

MIDWEST RESEARCH INSTITUTE

APPENDIX I

A. SAMPLE PREPARATION

A 1% (w/v) sample solution of trichloroethylene 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 trichloroethylene (exactly measured for each sample) was added via a 100 μl syringe. The samples were shaken and stored at room temperature from 1 to 7 days.

B. EXTRACTION AND ANALYSIS

Each sample was 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, using the following system:

Instrument: Tracor MT 220

Column: Chromosorb 102, 60/80 mesh, 1.8 x 2 mm I.D., glass

Detection: Flame ionization

Oven Temperature: 160°C, isothermal

Detector Temperature: 260°C

Inlet Temperature: 200°C

Retention Time of Compound: 4.15 min

C. RESULTS

End of Day	Average Percent in Chemical/Vehicle Mixture *(a)*
1	1.00 ± 0.05
2	0.96 ± 0.05
3	0.99 ± 0.05
4	0.98 ± 0.05
5	1.00 ± 0.05
6	0.98 ± 0.05
7	0.99 ± 0.05

(a) Corrected for an average spiked recovery yield of 61.7% ± 0.9%.
Theoretical percent in chemical/vehicle mixture, 1.00.

D. CONCLUSION

Trichloroethylene mixed with corn oil is stable for 7 days at room temperature.

APPENDIX J

ANALYSIS OF TRICHLOROETHYLENE IN CORN OIL FOR STABILITY OF TRICHLOROETHYLENE AT 4 °C

PAPANICOLAOU CANCER RESEARCH INSTITUTE

APPENDIX J

A. STABILITY OF CHEMICAL

The stability of a stock solution at 4° C was determined. The method of analysis was that described in Appendix G.

B. RESULTS

No. Weeks after Mixing	μg of TCE per μl of Sample Injected for Target Concentrations of: 59.5	235.5
1	60.4	240
2	59.2	236.9
3	56.9	236.9
4	58.4	236.9
5	56.9	235.3
6	57.3	235.3
7	55.4	227.6
8	55.8	239.9

APPENDIX K

ANALYSIS OF TRICHLOROETHYLENE IN CORN OIL FOR CONCENTRATION OF TRICHLOROETHYLENE

PAPANICOLAOU CANCER RESEARCH INSTITUTE

APPENDIX K

Analysis of dosage mixtures was performed using gas chromatography. The specifications are as follows:

Gas Chromatograph:	Varian 3700 with CDS III Integrator
Detector:	FID
Detector Temp.:	200° C
Injector Temp.:	130° C
Oven Temp.:	70° C (isothermal)
Attenuator:	512 x 10^{-10}
Column:	10% OV-101 on 100/120 Supelcoport
Column Material:	10 ft. x 1/8 in. stainless steel until 4/28/80; After 4/28/80, 15 ft. x 1/4 in. glass column

The method of analysis was changed on March 16, 1979 to use an internal standard. Previously, the concentration of TCE in dosage mixtures was calculated from the percent recovery after the TCE-corn oil mixture was extracted into methanol. This recovery usually ran about 65% and was abandoned for a more reliable method, the internal standard method, which was performed as follows: an aliquot (2 ml) of a TCE-corn oil mixture was diluted to 25 ml with internal standard solution containing 0.5 mg/ml octane in chloroform. A 3-μl aliquot of this mixture was injected into the gas chromatograph. If the sample was too concentrated (i.e., if the peak went off-scale), the solution was re-diluted as stated above (2 ml to 25 ml internal standard solution).

Results of analyses are presented in Table K1.

TABLE K1. ANALYSIS OF TRICHLOROETHYLENE/CORN OIL MIXTURES

Date mixed	Concentration of Trichloroethylene in Corn Oil *(a)*	
	Target Conc. (mg/ml)	Actual Conc. (mg/ml)
5/18/78	55	50.8
	55	52
	113	105.4
	50	49.2
	50	48.1
5/26/78	51.8	47.7
	141.5	127.1
	54	52.3
6/01/78	166.5	175.3
6/08/78	57.4	54.6
	193.8	189.2
6/15/78	202	213.8
	60	60
6/21/78	30.2	27.7
6/22/78	60.8	60.8
	220.6	226.1
6/29/78	59.4	62.3
	235.7	238.4
7/06/78	248	253
	58.5	58.8
7/13/78	257.5	261.5
	62.4	60
7/20/78	265	270.7
	63	61.5
8/03/78	271.2	264.5
	64.2	61.9
8/10/78	276.5	285.3
	64.5	63.1
8/17/78	281	286.1
	64.5	63.1
8/24/78	65.5	63.1
	289	293.8
8/31/78	288.8	299.9
	65.5	64.6
9/20/78	308.5	309.9
	66	66.9
10/19/78	318	316.8
	318	334.5
11/16/78	333.5	322.1
12/08/78	164.3	164.4
12/14/78	72.5	66.6
	170.0	175.4

TABLE K1. ANALYSIS OF TRICHLOROETHYLENE/CORN OIL MIXTURES (Continued)

Date mixed	Concentration of Trichloroethylene in Corn Oil *(a)*	
	Target Conc. (mg/ml)	Actual Conc. (mg/ml)
12/28/78	200.0	210.6
1/11/79	78.5	77.2
	356.6	354.8
	225.4	214.7
2/07/79	357.5	364.1
	74.9	69.0
	242.2	251.2
	182.8	175.4
3/07/79	156	168.4
	728.4	
4/04/79	(758.4) *(b)*	765.1
	156.9	165.8
	68.0	69.8
	544.2	570.6
	519.8	545.9
5/01/79	729.8	736.9
	161.9	175.8
	561.6	601.4
	524.5	562.0
5/30/79	751.6	756.1
	573.0	602.1
	535.2	547.1
	156.5	164.5
6/27/79	161.2	166.6
	730.2	731.0
	561.2	584.5
	548.2	567.8
7/25/79	755.0	778.1
	164.4	164.6
8/21/79	85.4	84.7
	716.2	680.5
	732.8	662.0
9/19/79	164.8	161.5
10/15/79	325.3	319.1
10/17/79	164.8	157.1
	730.0	664.0
12/10/79	546.0	506.8
12/14/79	533.3	512.6
	663.6	625.7
1/09/80	577.2	566.7
2/06/80	70.6	70.6
	74.4	76.8
3/05/80	75.8	74.3
	330.4	358.9
4/02/80	69.7	72.2
4/30/80	327.3	330.2

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

(b) Analysis by Midwest Research Institute.

APPENDIX L

AUDIT SUMMARY

APPENDIX L
AUDIT SUMMARY

The pathology specimens, experimental data, study documents, and draft (August 1983) of NTP Technical Report No. 243 for the 2-year studies of trichloroethylene in rats and mice were audited at the NTP Archives. The audits included review of:

1. records concerning animal receipt, quarantine, randomization, and disposition prior to the start of dosing;

2. in-life records including protocol, correspondence, animal identification, animal husbandry, environmental conditions, dosing, external masses, mortality, and serology;

3. body weight and clinical observation data for a random 10% sample of animals in each study group;

4. test chemical records;

5. postmortem records for individual animals concerning date of death, disposition code, condition code, tissue accountability, correlation of masses or clinical signs recorded at or near the last in-life observation with gross observations and microscopic diagnoses, consistency of data entry on necropsy record forms, and correlation between gross observations and microscopic diagnoses;

6. inventory for wet tissue bags from all animals, and residual wet tissues from a random 10% sample of animals in each study group, plus other relevant cases, to evaluate the integrity of individual animal identity and the thoroughness of necropsy and trimming procedure performance;

7. blocks and slides of tissues from all animals in the high-dose and vehicle-control groups to examine for proper inventory, labeling, matching of tissue sections, and preservation;

8. microscopic diagnoses for a random 10% sample of animals, plus 100% of the changes in diagnoses made to preliminary pathology tables, to verify their incorporation into the final pathology tables; and

9. the extent of correlation between the data, factual information, and procedures for the two-year studies as presented in the draft Technical Report and the study records available at the NTP Archives.

These studies were conducted before Good Laboratory Practice standards for documentation were adopted. Not surprisingly, the archival records were found to be incomplete and sometimes inconsistent with respect to specific details; however, they did contain sufficient documentation to generally support the data, results, and statements of fact presented in the Technical Report. For example, study protocols, animal breeding records, and animal room environment records were incomplete or absent, but the partial study records, site-visit reports, and laboratory reports for the studies indicate that the procedures specified in the contract for the work were followed. Also, although raw data to support the results reported from analysis of dosage mixtures were not present, complete records for the independent analysis of samples sent to a referee laboratory were; the combined records demonstrate that dosage mixtures were prepared and analyzed properly.

Following audit of the pathology specimens, a thorough review of preserved livers for all mice was performed, additional diagnoses were made, and results were incorporated into the Technical Report. All of the findings from audit of the draft Technical Report were evaluated by NTP staff and appropriate changes were incorporated into the final report.

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

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