NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 384

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF 1,2,3,-TRICHLOROPROPANE

(CAS NO. 96-18-4)

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

FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Technical Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals. The prechronic and chronic studies were conducted in compliance with Food and Drug Administration (FDA) Good Laboratory Practice Regulations, and all aspects of the chronic studies were subjected to retrospective quality assurance audits before being presented for public review.

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology and carcinogenesis studies are chosen primarily on the basis of human exposure, level of production, and chemical structure. Selection *per se* is not an indicator of a chemical's carcinogenic potential.

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NTP TECHNICAL REPORT

ON THE

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CONTENTS

ABSTRACT

$ClH_2CCHClCH_2Cl$

1,2,3-TRICHLOROPROPANE

CAS No. 96-18-4

Chemical Formula: $C_3H_5Cl_3$ Molecular Weight: 147.44

Synonyms: Allyl trichloride, glycerol trichlorohydrin, glyceryl trichlorohydrin, trichlorohydrin

1,2,3-Trichloropropane is a colorless liquid used as a paint and varnish remover, solvent, and degreasing agent, and as a crosslinking agent in the synthesis of polysulfides and hexafluoropropylene. 1,2,3-Trichloropropane may be found as an impurity in certain nematocides and soil fumigants and as a contaminant of drinking and ground water. Studies on the toxic and carcinogenic effects of 1,2,3-trichloropropane were initiated because of the close structural relationship of this chemical to other short-chain halogenated compounds that were demonstrated to be carcinogenic in experimental animals, and because of the potential for human exposure. Toxicology and carcinogenicity studies were conducted by administering 1,2,3-trichloropropane (greater than 99% pure) in corn oil by gavage to groups of F344/N rats and B6C3F_1 mice for 17 weeks and 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium* strains, mouse lymphoma cells, and Chinese hamster ovary cells.

17-Week Studies: Groups of 20 male and 20 female rats received 1,2,3-trichloropropane in corn oil by gavage at doses of 8, 16, 32, 63, 125, or 250 mg/kg body weight 5 days per week for up to 17 weeks; 30 male and 30 female rats received corn oil alone and served as controls. Animals were evaluated at 8 or 17 weeks. All rats in the 250 mg/kg groups died by week 5. One male and four female rats in the 125 mg/kg groups died during the study.The mean body weight gains and final mean body weights of males receiving 63 mg/kg and of males and females receiving 125 mg/kg were lower than those of the controls. Hematocrit values, hemoglobin concentrations, and erythrocyte counts decreased with dose in males and females. Serum alanine aminotransferase, aspartate aminotransferase, and sorbitol dehydrogenase activities were significantly increased in some female rats receiving 125 mg/kg. Serum pseudocholinesterase activity decreased with dose in females. Increases in kidney and liver weights were related to chemical administration. The principal toxic lesions associated with the administration of 1,2,3-trichloropropane to rats were hepatocellular necrosis, karyomegaly, and biliary hyperplasia of the liver; renal tubule necrosis, regeneration, and karyomegaly of the kidney; and necrosis and inflammation of the nasal olfactory and respiratory epithelium.

Groups of 20 male and 20 female mice received 1,2,3-trichloropropane in corn oil by gavage at doses of 8, 16, 32, 63, 125, or 250 mg/kg 5 days per week for up to 17 weeks; 30 male and 30 female mice received corn oil alone and served as controls. Sixteen male and seven female mice in the 250 mg/kg groups died by week 4. The final mean body weights and mean body weight gains of dosed mice were similar to those of the controls, except those of 250 mg/kg males, which were lower than those of controls. The principal toxic lesions

associated with the administration of 1,2,3-trichloropropane were hepatocellular necrosis and karyomegaly of the liver; necrosis, regeneration, and hyperplasia of the bronchiolar epithelium in the lung; and acanthosis (hyperplasia) and hyperkeratosis of the forestomach epithelium.

2-Year Studies: Groups of 60 male and 60 female rats received 0, 3, 10, or 30 mg 1,2,3-trichloropropane/kg body weight in corn oil by gavage 5 days per week for up to 104 weeks. Selection of 30 mg/kg as the high dose in these studies was based on the following chemical-related effects in the 17-week studies: deaths and liver and kidney lesions at 125 and 250 mg/kg and reduced final mean body weights and mean body weight gains at 63 mg/kg or greater.

Groups of 60 male and 60 female mice received 0, 6, 20, or 60 mg 1,2,3-trichloropropane/kg body weight in corn oil by gavage 5 days per week for up to 104 weeks. Selection of 60 mg/kg as the high dose was based on chemical-related deaths and lesions of the liver, lung, and forestomach at 125 and 250 mg/kg in the 17-week studies.

15-Month Interim Evaluations: Up to 10 rats and 10 mice from each dose group were evaluated at 15 months. Absolute and relative liver and kidney weights of dosed rats were significantly greater than those of the controls. Chemical-related nonneoplastic lesions and neoplasms of the forestomach, oral mucosa, pancreas (males), kidney, mammary gland (females), preputial gland, and clitoral gland were observed in dosed rats. Chemical-related nonneoplastic lesions and neoplasms of the forestomach and liver (females) were observed in dosed mice.

Survival and Body Weight in the 2-Year Studies: Survival of male and female rats receiving 10 or 30 mg/kg 1,2,3-trichloropropane was significantly lower than that of controls. Two-year survival rates of male rats were: control, 34/50; 3 mg/kg, 32/50; 10 mg/kg, 14/49; 30 mg/kg, 0/52; and of females were: 31/50, 30/49, 8/52, 0/52. At 30 mg/kg, survival was markedly reduced due to chemical-related neoplasms, and survivors were killed in weeks 67 (females) or 77 (males). Final mean body weights of 30 mg/kg rats were 13% lower for males and 12% lower for females than those of controls; mean body weights of 3 and 10 mg/kg rats were similar to controls.

Survival rates of mice receiving 6, 20, or 60 mg/kg 1,2,3-trichloropropane were also significantly lower than those of controls. Two-year survival rates of male mice were: 42/52, 18/51, 0/54, 0/56; and of female mice were: 41/50, 13/50, 0/51, 0/55. Because of reduced survival at 20 and 60 mg/kg due to chemical-related neoplasms, survivors were killed in weeks 73 (60 mg/kg females), 79 (60 mg/kg males), or 89 (20 mg/kg males and females). Final mean body weights were 16% lower for 60 mg/kg males, 18% lower for 60 mg/kg females, and 13% lower for 20 mg/kg males than those of controls. Final mean body weights of 6 mg/kg males and females and 20 mg/kg females were similar to controls.

Neoplasms and Nonneoplastic Lesions in the 2-Year Studies: Administration of 1,2,3-trichloropropane to rats induced benign and malignant neoplasms of the oral mucosa (pharynx and tongue), forestomach, and preputial and clitoral glands in males and females; benign neoplasms of the exocrine pancreas and kidney in males, and malignant neoplasms of the mammary gland in females. The incidences of squamous cell papillomas and carcinomas of the oral mucosa were significantly increased in 10 and 30 mg/kg rats, while the incidences of squamous cell papillomas or carcinomas (combined) of the forestomach were significantly increased in all dosed groups. The incidence of pancreatic acinar adenoma was significantly increased in dosed males, but not in dosed females. Similarly, the incidence of adenoma of the kidney was significantly increased in 10 and 30 mg/kg male rats only. The incidences of adenoma or carcinoma (combined) of the preputial gland in 30 mg/kg males and of the clitoral gland in 10 and 30 mg/kg females (homologous organs) were significantly increased. The incidence of adenocarcinoma of the mammary gland was significantly increased in the 10 and 30 mg/kg females. The incidences of Zymbal's gland carcinomas were increased in 30 mg/kg males and females. Adenocarcinomas of the intestine occurred in small numbers of dosed rats and may have been chemical related.

In mice, the incidence of squamous cell carcinoma of the oral mucosa was significantly increased only in 60 mg/kg females. In contrast, the incidences of squamous cell papilloma and carcinoma of the forestomach were significantly increased in all groups of dosed mice. The incidences of hepatocellular adenoma or carcinoma (combined) were significantly increased in all dosed groups of males

and 60 mg/kg females. The incidences of harderian gland adenoma were significantly increased in 20 mg/kg males and in 60 mg/kg males and females. The incidences of uterine adenoma, adenocarcinoma, and stromal polyp were significantly increased in 60 mg/kg females.

Genetic Toxicology: 1,2,3-Trichloropropane was mutagenic *in vitro* in the presence of S9 metabolic activation. At two laboratories, positive responses were obtained for mutagenicity in *Salmonella typhimurium* strains TA97, TA98, TA100, and TA1535 in the presence of S9; no mutagenic activity was observed in TA1537, with or without S9. 1,2,3-Trichloropropane induced trifluorothymidine resistance in L5178Y mouse lymphoma cells with, but not without, S9. In cultured Chinese hamster ovary cells, sister chromatid exchanges and chromosomal aberrations were induced by 1,2,3-trichloropropane; however, significant increases in the endpoints of both cytogenetic effects occurred only in the presence of S9.

Conclusions: Under the conditions of these 2-year gavage studies, there was *clear evidence of carcinogenic activity** of 1,2,3-trichloropropane in male F344/N rats based on increased incidences of squamous cell papillomas and carcinomas of the oral mucosa and forestomach, adenomas of the pancreas and kidney, adenomas or carcinomas of the preputial gland, and carcinomas of the Zymbal's gland. Adenomatous polyps and adenocarcinomas of the intestine may have been related to chemical administration. There was *clear evidence of carcinogenic activity* of 1,2,3-trichloropropane in female F344/N rats based on increased incidences of squamous cell papillomas and carcinomas of the oral mucosa and forestomach, adenomas or carcinomas of the clitoral gland, adenocarcinomas of the mammary gland, and carcinomas of the Zymbal's gland. Adenocarcinomas of the intestine may have been related to chemical administration.

There was *clear evidence of carcinogenic activity* of 1,2,3-trichloropropane in male B6C3F_1 mice based on increased incidences of squamous cell papillomas and carcinomas of the forestomach, hepatocellular adenomas or carcinomas of the liver, and harderian gland adenomas. Squamous cell papillomas of the oral mucosa may have been related to chemical administration. There was *clear evidence of carcinogenic activity* of 1,2,3-trichloropropane in female B6C3F_1 mice based on increased incidences of squamous cell carcinomas of the oral mucosa, squamous cell papillomas and carcinomas of the forestomach, hepatocellular adenomas or carcinomas of the liver, harderian gland adenomas, and uterine adenomas, adenocarcinomas, and stromal polyps.

Nonneoplastic lesions associated with exposure to 1,2,3-trichloropropane included increased severity of nephropathy in male rats and increased incidences of basal cell and squamous hyperplasia of the forestomach, acinar hyperplasia of the pancreas, renal tubule hyperplasia, and preputial or clitoral gland hyperplasia in male and female rats. Increased incidences of squamous hyperplasia of the forestomach and eosinophilic foci in the liver in male and female mice were chemical related.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 10. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 12.

Summary of the 2-Year Carcinogenicity and Genetic Toxicology Studies of 1,2,3-Trichloropropane

Variable	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Doses	0, 3, 10, or 30 mg/kg in corn oil by gavage	0, 3, 10, or 30 mg/kg in corn oil by gavage	0, 6, 20, or 60 mg/kg in corn oil by gavage	0, 6, 20, or 60 mg/kg in corn oil by gavage
Body weights	30 mg/kg group lower than controls	30 mg/kg group lower than controls	20 and 60 mg/kg groups lower than controls	60 mg/kg group lower than controls
2-Year survival rates	34/50, 32/50, 14/49, 0/52	31/50, 30/49, 8/52, 0/52	42/52, 18/51, 0/54, 0/56	41/50, 13/50, 0/51, 0/55
Nonneoplastic effects	Forestomach: basal cell hyperplasia (0/50, 5/50, 8/49, 7/52); squamous hyperplasia (3/50, 28/50, 13/49, 6/52) Pancreas: acinar hyperplasia (28/50, 46/50, 46/49, 48/52) Kidney: renal tubule hyperplasia (0/50, 1/50, 21/49, 29/52); nephropathy severity grades (2.0, 2.0, 2.6, 2.4) Preputial gland: focal hyperplasia (0/49, 0/47, 1/49, 1/50)	Forestomach: basal cell hyperplasia (0/50, 8/49, 4/51, 6/52); squamous hyperplasia (1/50, 25/49, 11/51, 15/52) Pancreas: acinar hyperplasia (5/50, 14/49, 24/52, 9/52) Kidney: renal tubule hyperplasia (0/50, 2/47, 3/52, 10/51) Clitoral gland: focal hyperplasia (0/46, 2/46, 3/50, 3/51)	Forestomach: squamous hyperplasia (8/52, 29/51, 27/54, 34/56) Liver: eosinophilic focus (2/52, 3/51, 8/54, 32/56)	Forestomach: squamous hyperplasia (10/50, 15/49, 14/51, 31/55) Liver: eosinophilic focus (0/50, 6/50, 9/51, 34/55)
Neoplastic effects	Oral cavity: squamous cell papilloma (0/50, 4/50, 9/49, 19/52); squamous cell carcinoma (1/50, 0/50, 11/49, 25/52) Forestomach: squamous cell papilloma (0/50, 29/50, 33/49, 38/52); squamous cell carcinoma (0/50, 9/50, 27/49, 13/52) Pancreas: acinar adenoma (5/50, 21/50, 36/49, 29/52)	Oral cavity: squamous cell papilloma (1/50, 5/49, 10/52, 18/52); squamous cell carcinoma (0/50, 1/49, 21/52, 21/52) Forestomach: squamous cell papilloma (0/50, 13/49, 32/51, 16/52); squamous cell carcinoma (0/50, 3/49, 9/51, 4/52) Clitoral gland: adenoma (5/46, 10/46, 13/50, 10/51); carcinoma (0/46, 0/46, 4/50, 6/51)	Forestomach: squamous cell papilloma (3/52, 28/51, 22/54, 33/56); squamous cell carcinoma (0/52, 40/51, 50/54, 51/56) Liver: hepatocellular adenoma (11/52, 18/51, 21/54, 29/56); hepatocellular adenoma or carcinoma (13/52, 24/51, 24/54, 31/56) Harderian gland: adenoma (1/52, 2/51, 10/54, 11/56)	Oral cavity: squamous cell carcinoma (0/50, 0/50, 1/51, 5/55) Forestomach: squamous cell papilloma (0/50, 23/50, 18/51, 29/55); squamous cell carcinoma (0/50, 46/50, 49/51, 49/55) Liver: hepatocellular adenoma (6/50, 9/50, 8/51, 31/55); hepatocellular adenoma or carcinoma (7/50, 11/50, 8/51, 31/55)

Summary of the 2-Year Carcinogenicity and Genetic Toxicology Studies of 1,2,3-Trichloropropane (continued)

Variable	Male F344/N Rats	Female F344/N Rats	Male $B6C3F_1$ Mice	Female $B6C3F_1$ Mice
Neoplastic effects (continued)	Kidney: renal tubule adenoma (0/50, 2/50, 20/49, 21/52) Preputial gland: adenoma (5/49, 3/47, 5/49, 11/50); carcinoma (0/49, 3/47, 3/49, 5/50) Zymbal's gland: carcinoma (0/50, 0/50, 0/49, 3/52)	Mammary gland: adenocarcinoma (1/50, 6/49, 12/52, 21/52) Zymbal's gland: carcinoma (0/50, 1/49, 0/52, 3/52)		Harderian gland: adenoma (2/50, 6/50, 7/51, 10/55) Uterus: adenoma (0/50, 1/50, 0/51, 3/55); adenocarcinoma (0/50, 4/50, 3/51, 6/55); stromal polyp (0/50, 2/50, 1/51, 6/55)
Uncertain findings	Intestine: adenocarcinoma (0/50, 0/50, 2/49, 1/52); adenomatous polyp (0/50, 0/50, 0/49, 2/52)	Intestine: adenocarcinoma (0/50, 0/49, 1/52, 2/52)	Oral cavity: squamous cell papilloma (0/52, 0/51, 0/54, 2/56)	None
Level of evidence of carcinogenic activity	Clear evidence	Clear evidence	Clear evidence	Clear evidence

Genetic toxicology

Salmonella typhimurium gene mutations:	Positive with S9 in strains TA97, TA98, TA100, and TA1535 Negative with or without S9 in strain TA1537
L5178Y mouse lymphoma gene mutations:	Positive with S9 Negative without S9
Sister chromatid exchanges Chinese hamster ovary cells *in vitro*:	Positive with S9 Negative without S9
Chromosomal aberrations Chinese hamster ovary cells *in vitro*:	Positive with S9 Equivocal without S9

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

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

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

- **Clear evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.
- **Some evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.
- **Equivocal evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemical related.
- **No evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing no chemical-related increases in malignant or benign neoplasms.
- **Inadequate study** of carcinogenic activity is demonstrated by studies that, because of major qualitative or quantitative limitations, cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

When a conclusion statement for a particular experiment is selected, consideration must be given to key factors that would extend the actual boundary of an individual category of evidence. Such consideration should allow for incorporation of scientific experience and current understanding of long-term carcinogenesis studies in laboratory animals, especially for those evaluations that may be on the borderline between two adjacent levels. These considerations should include:

- adequacy of the experimental design and conduct;
- occurrence of common versus uncommon neoplasia;
- progression (or lack thereof) from benign to malignant neoplasia as well as from preneoplastic to neoplastic lesions;
- some benign neoplasms have the capacity to regress but others (of the same morphologic type) progress. At present, it is impossible to identify the difference. Therefore, where progression is known to be a possibility, the most prudent course is to assume that benign neoplasms of those types have the potential to become malignant;
- combining benign and malignant tumor incidence known or thought to represent stages of progression in the same organ or tissue;
- latency in tumor induction;
- multiplicity in site-specific neoplasia;
- metastases;
- supporting information from proliferative lesions (hyperplasia) in the same site of neoplasia or in other experiments (same lesion in another sex or species);
- presence or absence of dose relationships;
- statistical significance of the observed tumor increase;
- concurrent control tumor incidence as well as the historical control rate and variability for a specific neoplasm;
- survival-adjusted analyses and false positive or false negative concerns;
- structure-activity correlations; and
- in some cases, genetic toxicology.

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the NTP draft Technical Report on 1,2,3-trichloropropane on July 9, 1991, are listed below. Subcommittee members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, subcommittee members have five major responsibilities in reviewing NTP studies:

- ! to ascertain that all relevant literature data have been adequately cited and interpreted,
- ! to determine if the design and conditions of the NTP studies were appropriate,
- ! to ensure that the Technical Report presents the experimental results and conclusions fully and clearly,
- ! to judge the significance of the experimental results by scientific criteria, and
- ! to assess the evaluation of the evidence of carcinogenic activity and other observed toxic responses.

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SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On July 9, 1991, the draft Technical Report on the toxicology and carcinogenesis studies of 1,2,3-trichloropropane received public review by the National Toxicology Program Board of Scientific Counselors Technical Reports Review Subcommittee. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. R.D. Irwin, NIEHS, introduced the toxicology and carcinogenesis studies of 1,2,3-trichloropropane by discussing the uses, human exposure, and rationale for the study, describing the experimental design, reporting on survival and body weight effects, and commenting on chemical-related neoplasms and nonneoplastic lesions in rats and mice. The proposed conclusions were *clear evidence of carcinogenic activity* in male and female rats and mice.

Dr. Goodman, a principal reviewer, agreed with the proposed conclusions. He asked whether any of the clinical findings in male rats could have been due to the severe chemical-induced nephropathy. Dr. Irwin said that although the neoplasm response was quite strong, one could not unequivocally rule out a contribution by the nephropathy. Dr. Goodman commented on the four widely used *in vitro* tests for genetic toxicity, and noted that the three assays for mutagenesis in mouse lymphoma cells and chromosome aberrations and sister chromatid exchanges in Chinese hamster ovary cells added nothing to the ability of tests for mutagenesis in *Salmonella typhimurium* to predict carcinogenicity of chemicals in long-term rodent studies. Therefore, he thought presentation of data from these assays should be very limited in this and other reports. Dr. S.L. Eustis, NIEHS, responded that the staff would reconsider their approach to the genetic toxicology presentation and discussion in the reports.

Dr. McKnight, the second principal reviewer, agreed with the proposed conclusions in principle. However, she suggested that Zymbal's gland neoplasms should be included as support for clear evidence in male and female rats, noting that these neoplasms occur with statistically significant trends in both sexes and the incidences in the high-dose groups exceed the ranges observed in historical control groups for both sexes. Dr. McKnight said that an explanation should be given for why gavage was used in these studies, as occupational exposure occurs mainly by inhalation, and there is also potential for human exposure via drinking water contamination and dermal exposure. Dr. Irwin commented that due to the presence of 1,2,3-trichloropropane in ground and surface water, the numbers of people exposed orally may exceed those exposed by any other route.

Dr. Zeise, the third principal reviewer, also agreed in principle with the proposed conclusions. She supported Dr. McKnight's call to include Zymbal's gland neoplasms in rats under clear evidence, and proposed that oral cavity squamous cell papillomas be added to the evidence for male mice. Dr. J.K. Haseman, NIEHS, noted that the inclusion of oral cavity neoplasms as part of the evidence for carcinogenicity in the other three experimental groups added weight to the proposed association with chemical treatment for these uncommon neoplasms in male mice. Dr. Zeise argued that squamous cell papillomas or carcinomas of the skin and liver neoplasms in male rats as well as squamous cell carcinomas of the large intestine in female mice should be included in the conclusions as findings that "may have been related to chemical treatment." Dr. Eustis said that discussion of these neoplasms could be added to the results.

Mr. Beliczky stated that, in view of the widespread human exposure in polymer manufacture and when the chemical is used as a solvent for degreasing and paint stripping, there needed to be more emphasis and information in the report on dermal exposure and absorption. Dr. Davis pursued the issue of how the route of administration is selected; i.e., was this the route of primary human exposure or was the gavage route chosen to maximize the ability to detect a carcinogenic response? Dr. Eustis said NTP takes into consideration the route of human exposure but cost is also considered — two feed studies can be conducted for about the same cost as one inhalation study. Dr. R.A. Griesemer, NIEHS, added that the agency or party nominating a chemical for study may specify a particular route of exposure. In this case, because of considerable

ground water contamination, there was an interest in oral exposures from the start.

Dr. Goodman moved that the Technical Report on 1,2,3-trichloropropane be accepted with the revisions discussed and the conclusions as written for male and female rats and mice, *clear evidence of carcinogenic activity*. Mr. Beliczky seconded the motion.

Dr. McKnight offered an amendment that Zymbal's gland neoplasms be added to the list of neoplasms on which the level of evidence is based in male and female rats. Dr. Davis seconded the amendment and it was accepted by seven yes to three no votes (Drs. Bailey, Carlson, and Garman). The original motion by Dr. Goodman was then accepted unanimously with ten votes.

INTRODUCTION

$ClH_2CCHClCH_2Cl$

1,2,3-TRICHLOROPROPANE

CAS No. 96-18-4

Chemical Formula: $C_3H_5Cl_3$ Molecular Weight: 147.44

Synonyms: Allyl trichloride, glycerol trichlorohydrin, glyceryl trichlorohydrin, trichlorohydrin

PHYSICAL AND CHEMICAL PROPERTIES

1,2,3-Trichloropropane is a colorless liquid with a strong acidic odor. It has a boiling point of 156° C (760 mm Hg), a vapor pressure of 3 mm Hg at 25° C, a specific gravity of 1.370 g/mL, and a flash point of 71.1° C (*Hawley's*, 1987). 1,2,3-Trichloropropane is only slightly soluble in water but freely soluble in alcohol and ether.

PRODUCTION, USE, AND HUMAN EXPOSURE

1,2,3-Trichloropropane is manufactured by chlorination of propylene at low temperatures (*Hawley's*, 1987). Two manufacturing facilities had a combined annual production greater than 10,000 pounds in 1985 (USEPA, 1987). 1,2,3-Trichloropropane is commonly used as a paint and varnish remover, solvent, and degreasing agent, but the extent of these uses is uncertain. 1,2,3-Trichloropropane is used as a crosslinking agent in the synthesis of polysulfides and hexafluoropropylene, and it may be found as an impurity in certain nematocides and soil fumigants (Aharonson, 1987).

Occupational exposure to 1,2,3-trichloropropane occurs primarily by inhalation of vapors during its manufacture and formulation into polymers and during its use as a solvent and degreasing agent. From a survey conducted from 1981 to 1983, NIOSH estimated that 492 workers may have been exposed to 1,2,3-trichloropropane in the United States (NIOSH, 1990). In 1980, the American Conference of Governmental Industrial Hygienists recommended a threshold limit value of 50 ppm in air to prevent hepatotoxicity and a short-term exposure limit of 75 ppm to prevent eye and mucosal irritation (ACGIH, 1980). The Occupational Safety and Health Administration's permissible exposure limit of 10 ppm per 8-hour work shift became effective December 30, 1992.

1,2,3-Trichloropropane has been detected in drinking and ground water in various parts of the United States. In 1976, 1,2,3-trichloropropane was found in the drinking water from the Carrollton Water Plant in New Orleans at levels less than 0.2 µg/L (Keith *et al.*, 1976). The chemical was also found in drinking water in Ames, Iowa, although concentration levels were not reported (USEPA, 1976). In 1983, drinking water from wells on the island of

Oahu, Hawaii, contained concentrations ranging from 200 to 2,800 ng/L (Oki and Giambelluca, 1987), and in California, 1,2,3-trichloropropane was detected in ground water at concentrations ranging from 0.1 to 5 ppb (Cohen, 1986). Surface water from the Delaware River Basin contained trichloropropane (an unspecified isomer) at concentrations of less than 1 µg/L in three percent of the samples (Dewalle and Chian, 1978). Unspecified concentrations of 1,2,3-trichloropropane were found in sea water from Narragansett Bay in Rhode Island (Wakeham *et al.*, 1983).

METABOLISM AND DISTRIBUTION

Pharmacokinetic studies in male F344/N rats after intravenous administration of 1,2,3-trichloropropane showed that the chemical is rapidly distributed and eliminated (Volp *et al.*, 1984; Mahmood *et al.*, 1991). The pharmacokinetics of 1,2,3-trichloropropane and 1,2-dibromo-3-chloropropane are similar, but the biological half-lives of the two chemicals vary tenfold. At comparable doses, 1,2,3-trichloropropane has a 23-hour half-life, while 1,2-dibromo-3-chloropropane has a half-life of only 2.5 hours (Gingell *et al.*, 1987; Mahmood *et al.*, 1991). The major urinary metabolite of 1,2,3-trichloropropane in F344/N rats was identified as *N*-acetyl-*S*-(3-chloro-2-hydroxypropyl)cysteine. This metabolite was also present in urine from male B6C3F_1 mice, but several unidentified metabolites were present in greater amounts. Approximately 20% of the radioactivity from 2-[^{14}C]-1,2,3-trichloropropane was eliminated as $^{14}CO_2$ in both rats and mice. The major biliary metabolite in male rats was identified as 2-(*S*-glutathionyl)malonic acid (Mahmood *et al.*, 1991). In a nuclear magnetic resonance spectroscopy study using ^{13}C-labeled 1,2,3-trichloropropane in male rats, 2,3-dichloropropionic acid was also identified as a urinary metabolite (Weber *et al.*, 1991). Formation of these metabolites indicates that oxidation and glutathione conjugation play a major role in the metabolism of 1,2,3-trichloropropane.

Mahmood *et al.* (1991) examined the disposition and metabolism of 2-[^{14}C]-1,2,3-trichloropropane after single oral doses of 30 mg/kg by corn oil gavage to male and female F344/N rats and 30 or 60 mg/kg to male B6C3F_1 mice. Six hours after dosing, the highest concentration of radioactivity in the tissue of male rats was found in the forestomach, glandular stomach, intestine, adipose tissue, kidney, and liver.

At 60 hours after dosing, the liver, kidney, and forestomach contained the greatest amount of residual radioactivity in male and female rats and in male mice. The presence of nonextractable radioactivity in the liver, kidney, and forestomach of rats and male mice 60 hours after dosing is an indication that the residual material was covalently bound. The tissue distribution and relative concentration of 1,2,3-trichloropropane-derived radioactivity was similar in male and female rats 24 hours after dosing. In contrast, 60 hours after dosing the concentration of radioactivity was higher in the tissues of female rats than in male rats, although significantly higher in only the forestomach and spleen.

Male mice eliminated 1,2,3-trichloropropane-derived radioactivity more rapidly than did male rats, even at higher doses. In male mice receiving 30 mg/kg of 2-[^{14}C]-1,2,3-trichloropropane, 6 of the 14 tissues evaluated had significantly lower radioactivity than did the same tissues in rats, and no tissues from male mice contained significantly higher amounts of radioactivity than tissues from male rats. Even after administration of 60 mg/kg of 2-[^{14}C]-1,2,3-trichloropropane, tissues of male mice did not accumulate higher levels of radioactivity than male rats receiving 30 mg/kg, with the exception of the forestomach, which contained significantly more radioactivity 60 hours after dosing than was found in male rats.

TOXICITY

Acute and subchronic toxicity of 1,2,3-trichloropropane has been studied by inhalation, gavage, dermal exposure, and ingestion of drinking water.

Inhalation Studies

In one study, 15 mice were exposed to 5,000 ppm 1,2,3-trichloropropane for 20 minutes. Eight mice died within 2 days, and four of the remaining mice died 7 to 10 days later from liver damage. In a similar study, 7 of 10 mice exposed to 2,500 ppm 1,2,3-trichloropropane daily for 10 minutes died during the 10-day study (McOmie and Barnes, 1949).

Johannsen *et al.* (1988) used acute and subchronic rat studies to determine the adequacy of the occupational inhalation exposure limit of 10 ppm 1,2,3-trichloropropane. In 4-week pilot studies, groups of five male and 5 female rats were exposed 6 hours a day for 5 days a week to 0, 100, 300, 600, or 900 ppm 1,2,3-trichloropropane. After a single

exposure, nine of ten rats in the 900 ppm group died, three in the 600 ppm group died, and one in the 300 ppm group died. At the end of the study, liver weights were increased in rats exposed to concentrations of 100 ppm and higher. Spleen weights of 300 ppm females and ovary weights of 300 and 600 ppm females were lower than those of the controls. In a 13-week inhalation study with 15 rats of each sex exposed to 5, 15, or 50 ppm 1,2,3-trichloropropane, no exposure-related deaths occurred. Liver weights were increased in all exposure groups, and hepatocellular hypertrophy was present in all exposed male groups. Lung hyperplasia occurred in rats exposed to 5 or 15 ppm and splenic hematopoiesis occurred only in female rats. In a second 13-week study, rats exposed to 0, 0.5, and 1.5 ppm 1,2,3-trichloropropane had no chemical-related gross or microscopic lesions.

Groups of five male and five female rats and guinea pigs were exposed to 800, 2,100, or 5,000 ppm 1,2,3-trichloropropane for 30 minutes. Minimal depression of the central nervous system occurred at 800 ppm but narcosis and convulsions were present at the higher concentrations (USEPA, 1989). Two rats and six guinea pigs in the 5,000 ppm group died, and one male rat in the 2,100 ppm group died. Fourteen days after the exposure, the only histopathologic lesion observed was adrenal corticomedullary necrosis.

In a clinical chemistry study, Drew *et al.* (1978) reported a marked increase in the activity of serum enzymes in male CD rats following a single 4-hour exposure to 500 ppm of 1,2,3-trichloropropane vapor.

Gavage Studies

Smyth *et al.* (1962) evaluated the acute toxicity of the trichloropropanes. The LD_{50} for 1,2,3-trichloropropane was determined to be 450 mg/kg based on a single gavage dose to five nonfasted Carworth-Wistar male rats followed by a 14-day observation period.

Dermal Studies

1,2,3-Trichloropropane, which is absorbed through the skin, was found to be an "intense skin irritant" in rabbits, due in part to its lipid-solvent properties (McOmie and Barnes, 1949). In a 15-day period, seven rabbits received 10 applications of 2 mL of 1,2,3-trichloropropane per 100 cm^2 skin, resulting in pain, subdermal hemorrhage, and the death of one rabbit. The remaining six rabbits survived and healed within 6 weeks. The LD_{50} in rabbits for a single dermal exposure was determined to be 2,500 mg/kg, which was considered to be high for dermal exposure (Smyth *et al.*, 1962).

Drinking Water Studies

Groups of 10 male and 10 female Sprague-Dawley rats received 1,2,3-trichloropropane in drinking water *ad libitum* at concentrations of 1, 10, 100, or 1,000 mg/L for 13 weeks (Villeneuve *et al.*, 1985). The growth rates were decreased in high-dose males and females. Chemical-related differences in clinical chemistry parameters included elevated serum cholesterol levels in females and increased hepatic aminopyrine demethylase and aniline hydroxylase activities in males. Mild histologic changes occurred in the liver, thyroid gland, and kidney at 1,000 mg/L. Three animals died during the study, but the deaths were not considered to be chemical related. The no-effect level of 1,2,3-trichloropropane in drinking water was determined to be 100 mg/L.

CARCINOGENICITY

No carcinogenicity studies of 1,2,3-trichloropropane in experimental animals or epidemiology studies of potential carcinogenicity in humans were found in the literature.

GENETIC TOXICITY

1,2,3-Trichloropropane contains two chlorinated methyl groups which are structural alerts to potential DNA reactivity (Ashby and Tennant, 1988). Although there has not been extensive testing for genotoxic activity, particularly *in vivo*, the data indicate that 1,2,3-trichloropropane is active *in vitro* with S9 activation. 1,2,3-Trichloropropane induced gene mutations in *Salmonella typhimurium* strains TA97, TA98, TA100, and TA1535 in the presence of S9 (Stolzenberg and Hine, 1980; Haworth *et al.*, 1983; Ratpan and Plaumann, 1988) and induced sister chromatid exchanges in V79 cells (hamster) with S9 (von der Hude *et al.*, 1987). 1,2,3-Trichloropropane did not induce unscheduled DNA synthesis in hepatocytes of male F344/N rats tested *in vitro* (Mirsalis *et al.*, 1983; Williams *et al.*, 1989) or *in vivo* (Mirsalis *et al.*, 1983). Negative results were also obtained in an *in vivo* test for induction of dominant lethal mutations in male Sprague-Dawley rats treated daily with 80 mg/kg 1,2,3-trichloropropane for 5 days (Saito-Suzuki *et al.*, 1982).

STUDY RATIONALE

Similar short-chain halogenated compounds have been studied in rats and mice, and the majority were carcinogenic. Moreover, 1,2,3-trichloropropane might be used in industry as a replacement for these compounds that are known to be carcinogenic. The oral gavage route was selected for the NTP 17-week and 2-year studies to maximize systemic exposure.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF 1,2,3-TRICHLOROPROPANE

1,2,3-Trichloropropane was obtained from the Shell Chemical Company (Houston, TX) in one lot (JG32449), which was used throughout the 17-week and 2-year studies. The purity, elemental, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO), and confirmed by the study laboratories, Hazleton Laboratories America (Vienna, VA) for the 17-week studies and EG&G Mason Research Institute (Worcester, MA) for the 2-year studies. The methods and results of these studies are detailed in Appendix H.

The chemical, a clear, colorless, nonviscous liquid, was identified as 1,2,3-trichloropropane by physical properties and infrared, ultraviolet/visible, and nuclear magnetic resonance spectroscopy. The purity of 1,2,3-trichloropropane was greater than 99%, as determined by elemental analyses, Karl Fischer water analysis, titration of acid groups, and two gas chromatography systems.

Stability studies using gas chromatography indicated that 1,2,3-trichloropropane was stable as a bulk chemical for at least 2 weeks at temperatures up to 60° C. Throughout the studies, the bulk chemical was stored in the dark at 5° C at the study laboratories. The identity and stability of the bulk chemical was monitored by infrared spectroscopy and gas chromatography periodically during all phases of the studies by the study laboratories. Identity was confirmed and no change in purity was detected.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

Dose formulations were prepared by mixing 1,2,3-trichloropropane and corn oil (Table H1). Studies were conducted by the analytical chemistry laboratory to determine the stability of 1,2,3-trichloropropane in corn oil. Gas chromatographic methods were used to confirm that the dose formulations were stable when stored for 3 weeks in the dark at room temperature. Samples of the solutions were also stable when exposed for 3 hours to ambient air and light in order to mimic dosing conditions. The dose formulations were stored in sealed amber serum vials in the dark at room temperature for up to 7 days during the 17-week studies and at 4° C for up to 3 weeks during the 2-year studies.

The study laboratories and the analytical chemistry laboratory conducted periodic analyses of the 1,2,3-trichloropropane dose formulations with gas chromatography as described in Appendix H. Analysis of dose formulations during the 17-week studies indicated that 91% (52 of 57 samples) were within 10% of the target concentrations (Tables H2 and H3). During the 2-year studies, the dose formulations were analyzed after mixing at approximately 8-week intervals (Table H4) and 92% (44 of 48 samples) were within 10% of the target concentrations. Monthly analyses of the corn oil vehicle by the study laboratory showed peroxide levels below the acceptable level of 10 mEq/kg throughout the 2-year studies. Referee analyses of dose formulations performed by the analytical chemistry laboratory were in good agreement with the results of the study laboratories (Table H5).

17-WEEK STUDIES

The 17-week studies were conducted to determine the cumulative toxic effects of repeated gavage doses of 1,2,3-trichloropropane and to determine appropriate doses to be used in the 2-year studies. Data on the acute toxic effects of repeated exposure to 1,2,3-trichloropropane were available in the literature and were considered adequate for determining the dose levels for the 17-week studies.

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Facility (Frederick, MD) and were observed for 15 days before the studies began. At the end of the studies, serologic analyses were performed on up to 5 male and 5 female sentinel rats and mice using the protocols of the NTP Sentinel Animal Program

(Appendix J). The average age was 57 days for rats and 50 days for mice when the studies began. Groups of 30 male and 30 female rats and mice were assigned to the control group; 20 males and 20 females (19 male rats in the 125 mg/kg group) of each species received 1,2,3-trichloropropane in corn oil by gavage at doses of 8, 16, 32, 63, 125, or 250 mg/kg body weight, 5 days per week for 8 or 17 weeks. Animals were housed five per cage, and water and feed were available *ad libitum*. Animals were observed twice daily and clinical observations were recorded weekly. Animals were weighed at the start of the study and weekly thereafter. The right testis and epididymis were weighed at the 8-week interim evaluation. At the end of the 17-week studies, the brain, right epididymis, heart, right kidney, liver, lung, right testis, and thymus were weighed. Twenty-four-hour urine samples were collected from animals held in metabolism cages prior to the 8-week and terminal evaluations. Blood samples for hematology were collected from the retro-orbital sinus prior to urine collection, and blood for clinical chemistry was collected from the abdominal aorta at necropsy. Further experimental details are presented in Table 1.

Necropsies were performed on all animals. Complete histopathologic examinations were performed on all animals killed moribund or found dead during the studies, all controls, rats receiving 125 mg/kg, and mice receiving 125 (males) and 250 mg/kg. Selected tissues from other dose groups were also examined are listed in Table 1.

2-YEAR STUDIES

Study Design

Groups of 60 male and 60 female rats and mice were administered 1,2,3-trichloropropane in corn oil by gavage 5 days per week at doses of 0, 3, 10, or 30 mg/kg for rats and 0, 6, 20, or 60 mg/kg for mice. Ten male and 10 female rats and mice from each dose group were designated for 15-month interim evaluations. Due to high mortality, surviving 30 mg/kg rats were evaluated at 77 (males) or 67 (females) weeks, surviving 20 mg/kg mice were evaluated at 89 weeks, and surviving 60 mg/kg mice were evaluated at 79 (males) or 73 (females) weeks.

Source and Specification of Animals

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Facility (Frederick, MD) for use in the 2-year studies. Rats were quarantined 10 days (males) or 14 days (females), and mice were quarantined 13 days (males) or 14 days (females). Five rats and five mice of each sex were randomly selected and killed for serologic viral screen, parasite examination, and gross observation for disease. Animals were approximately 6 weeks old when the studies began. The health of the animals was monitored during the course of the studies according to the protocols of the NTP Sentinel Animal Program (Appendix J).

Animal Maintenance

Rats were housed five per cage and mice were housed individually throughout the studies. Feed and water were available *ad libitum*. Cages were rotated vertically on their racks every 2 weeks. Information on feed composition and contaminants is provided in Appendix I. Further details of animal maintenance are given in Table 1.

Clinical Examinations and Pathology

All animals were observed twice daily and clinical findings were recorded at the time of weighing or as necessary. Animals were weighed at study initiation, weekly for 13 weeks, and monthly thereafter. Organ weights were recorded for the brain, liver, and right kidney of all animals at the 15-month interim evaluations. Blood was collected for hematology and clinical chemistry from all animals prior to necropsy at the 15-month interim evaluations. Further experimental details are presented in Table 1.

Necropsies were performed on all animals and all organs and tissues were examined for gross lesions. All major tissues were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 4 to 6 µm, and stained with hematoxylin and eosin for microscopic examination. Complete histopathologic examinations were performed on all rats and mice. The organs examined are listed in Table 1.

Upon completion of the microscopic evaluation by the laboratory pathologist, pathology data were entered into the Toxicology Data Management System (TDMS). The slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit for accuracy of labeling and animal identification, and for thoroughness of tissue trimming. The slides,

individual animal data records, and pathology tables were evaluated by an independent pathology quality assessment laboratory. The individual animal records and pathology tables were compared for accuracy, slide and tissue counts were verified, and histotechnique was evaluated. All tissues with a diagnosis of neoplasia, all tissues from a randomly selected 10% of the control and high-dose rats and mice, the kidney, pancreas, forestomach, preputial and clitoral gland of rats, and the forestomach, liver, lung, and uterus of mice were reevaluated microscopically by a quality assessment pathologist.

The quality assessment report and slides were submitted to the NTP Pathology Working Group (PWG). The PWG consisted of the quality assessment pathologist and other pathologists experienced in rodent toxicologic pathology. This group examined the tissues without knowledge of dose groups or previously rendered diagnoses. When the consensus opinion of the PWG differed from that of the laboratory pathologist, the diagnosis was changed to reflect a consensus of contractor pathologists and the PWG. Details of these review procedures have been described by Maronpot and Boorman (1982) and Boorman *et al.* (1985). For subsequent analysis of pathology data, the diagnosed lesions for each tissue type were evaluated separately or combined according to the guidelines of McConnell *et al.* (1986).

Statistical Methods

Survival Analyses

The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals were censored from the survival analyses at the time they were found dead of other than natural causes or were found to be missing; animals dying from natural causes were not censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) life table test to identify dose-related trends. All reported P values for the survival analyses are two sided.

Calculation of Incidence

Appendix Tables A1, B1, C1, and D1 present the incidences of neoplasms in male rats, female rats, male mice, and female mice. Tables A5, B5, C5, and D5 summarize the incidences of nonneoplastic lesions in male and female rats and mice. The incidence of neoplasms or nonneoplastic lesions is given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators include only those animals for which the site was examined histologically. However, when microscopic examination was required to detect lesions (e.g., skin or mammary gland neoplasms) prior to histologic sampling, or when lesions had multiple potential sites of occurrence (e.g., mononuclear cell leukemia), the denominators consist of the number of animals on which a necropsy was performed.

Analysis of Neoplasm Incidence

In these studies, large numbers of dosed rats and mice died or were killed moribund early in the studies. These deaths were considered to be due primarily to oral cavity, forestomach, and malignant mammary gland neoplasms. Consequently, for these particular lesions, primary emphasis in the analysis of neoplasm incidence was given to the life table test (Cox, 1972; Tarone, 1975), a survival-adjusted procedure appropriate for rapidly lethal neoplasms. For incidental neoplasms, the statistical method used was a logistic regression analysis, which assumed that the diagnosed neoplasms were discovered as the result of death from an unrelated cause and thus did not affect the risk of death. In this approach, neoplasm prevalence was modeled as a logistic function of chemical exposure and time. Both linear and quadratic terms in time were incorporated initially, and the quadratic term was eliminated if it did not significantly enhance the fit of the model. The dosed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and Haseman (1986). When neoplasms are incidental, this comparison of the time-specific neoplasm prevalences also provides a comparison of the time-specific neoplasm incidences (McKnight and Crowley, 1984). Markedly reduced survival in dosed animals (due largely to increased incidences of lethal neoplasms) reduced the power of logistic regression to detect carcinogenic effects in some instances. When this occurred, primary emphasis was given to the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart *et al.*, 1979), procedures that are based on the overall proportion of neoplasm-bearing animals.

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

Historical Control Data

Although the concurrent control group is always the first and most appropriate control group used for evaluation, there are certain instances in which historical control data can be helpful in the overall assessment of neoplasm incidence. Consequently, control neoplasm incidences from the NTP historical control database (Haseman *et al.*, 1984, 1985) are included in the NTP reports for neoplasms appearing to show compound-related effects.

Analysis of Continuous Variables

Two approaches were employed to assess the significance of pairwise comparisons between dosed and control groups in the analysis of continuous variables. Organ and body weight data, which have approximately normal distributions, were analyzed using the multiple comparison procedures of Dunnett (1955) and Williams (1971, 1972). Clinical chemistry, hematology, and urinalysis data which typically have skewed distributions, were analyzed using multiple comparison methods of Dunn (1964) and Shirley (1977). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of dose-response trends and to determine whether a trend-sensitive test (Williams' or Shirley's test) was more appropriate for pairwise comparisons than a test that does not assume a monotonic dose-response trend (Dunnett's or Dunn's test). Average nephropathy severity values were analyzed for significance using the Mann-Whitney U test (Hollander and Wolfe, 1973).

QUALITY ASSURANCE METHODS

The 17-week and 2-year studies were conducted in compliance with FDA Good Laboratory Practice Regulations (21 CFR Part 58). In addition, as study records were submitted to the NTP Archives, they were audited retrospectively by an independent quality assurance contractor. Separate audits covering completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and preliminary review draft of the NTP Technical Report were conducted. Audit procedures and findings are presented in the reports, which are on file at the NIEHS. The audit findings were reviewed and assessed by NTP staff so that all had been resolved or were otherwise addressed during the preparation of this Technical Report.

GENETIC TOXICITY

The genetic toxicity of 1,2,3-trichloropropane was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium*, sister chromatid exchanges and chromosomal aberrations in Chinese hamster ovary cells, and mutations in mouse lymphoma cells. The protocols for these studies and the results are given in Appendix E.

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of 1,2,3-Trichloropropane

17-Week Studies	2-Year Studies
Study Laboratory Hazleton Laboratories America (Vienna, VA)	EG&G Mason Research Institute (Worcester, MA)
Strain and Species Rats: F344/N Mice: $B6C3F_1$	Rats: F344/N Mice: $B6C3F_1$
Animal Source Frederick Cancer Research Facility (Frederick, MD)	Frederick Cancer Research Facility (Frederick, MD)
Date of Birth Rats: 3 January 1982 (median date) Mice: 2 February 1982 (median date)	Rats: week of 21 April 1985 Mice: week of 12 June 1985
Time Held Before Study 15 days	Rats: 10 days (males), 14 days (females) Mice: 13 days (males), 14 days (females)
Average Age When Study Began Rats: 57 days (median age) Mice: 50 days (median age)	6 weeks
Doses 0, 8, 16, 32, 63, 125, or 250 mg/kg 1,2,3-trichloropropane in 5 mL/kg (rats) or 10 mL/kg (mice) corn oil by gavage	Rats: 0, 3, 10, or 30 mg/kg 1,2,3-trichloropropane in 5 mL/kg corn oil by gavage Mice: 0, 6, 20, or 60 mg/kg 1,2,3-trichloropropane in 10 mL/kg corn oil by gavage
Size of Study Groups 30 males and 30 females in the control groups; 20 males and 20 females in the dosed groups	60 males and 60 females
Date of First Dose Rats: 25 February 1982 Mice: 24 March 1982	Rats: 3 June 1985 (males); 5 June 1985 (females) Mice: 25 June 1985 (males); 28 June 1985 (females)
Duration of Dosing Rats: 125-127 days Mice: 125 days	15-Month interim evaluation: Rats: 65 weeks (males); 67 weeks (females) Mice: 66 weeks 2-Year study: Rats: 0, 3, and 10 mg/kg, 103 weeks (males), 104 weeks (females); 30 mg/kg, 77 weeks (males), 67 weeks (females) Mice: 0 and 6 mg/kg, 103 weeks (males), 104 weeks (females); 20 mg/kg, 89 weeks; 60 mg/kg, 79 weeks (males), 73 weeks (females)

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of 1,2,3-Trichloropropane (continued)

17-Week Studies	2-Year Studies
Date of Last Dose Rats: 30 June 1982 Mice: 27 July 1982	15-Month interim evaluation: Rats: 25-27 August 1986 (males); 9-11 September 1986 (females) Mice: 23-25 September 1986 (males); 30 September- 2 October 1986 (females) 2-Year study: Rats: 0, 3, and 10 mg/kg, 22 May 1987 (males), 2 June 1987 (females); 30 mg/kg, 17 November 1986 (males), 11 September 1986 (females) Mice: 0 and 6 mg/kg, 15 June 1987 (males), 24 June 1987 (females); 20 mg/kg, 7 March 1987; 60 mg/kg, 29 December 1986 (males), 19 November 1986 (females)
Method of Animal Distribution Animals of each sex were randomly assigned to dose groups by weight class.	Animals of obvious weight extremes were culled, then animals of each sex were randomly assigned to distribution cages from which they were randomly assigned to dose groups.
Animals per Cage 5	Rats: 5 Mice: 1
Method of Animal Identification Rats: Ear tags Mice: Ear punch	Toe clip
Diet NIH-07 Rat and Mouse Ration, open formula, powdered (Zeigler Bros., Inc., Gardners, PA), available *ad libitum*, changed weekly	NIH-07 Rat and Mouse Ration, open formula, mash (Zeigler Bros., Inc., Gardners, PA), available *ad libitum*, changed weekly
Feeders Stainless steel (Hazleton Systems, Inc., Aberdeen, MD), changed once weekly	Rats: Stainless steel, gang style (Hoeltge, Inc., Cincinnati, OH), changed weekly Mice: Stainless steel (Lab Products, Inc., Rochelle Park, NJ), changed once weekly
Water Tap water (Aberdeen, MD) via automatic watering system (Hazleton Systems, Inc., Aberdeen, MD), available *ad libitum*	Tap water (City of Worcester Water Supply, MA) via automatic watering system with outside valve (Edstrom Industries Inc., Waterford, WI), available *ad libitum*, changed once every 2 weeks
Cages Solid-bottom polycarbonate (Hazleton Systems, Inc., Aberdeen, MD)	Solid-bottom polycarbonate (Lab Products, Inc., Rochelle Park, NJ)
Bedding Heat-treated hardwood chips (P.J. Murphy Forest Products, Mt. Pruitt, PA), changed twice weekly	BetaChips (Northeastern Products Corp., Warrensburg, NY), changed twice weekly

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of 1,2,3-Trichloropropane (continued)

	17-Week Studies	2-Year Studies
Cage Filters	Reemay spun-bonded polyester filters (National Paper Company, Baltimore, MD), changed once every 2 weeks	Nonwoven fiber filters (Snow Filtration, Cincinnati, OH), changed once every 2 weeks
Animal Room Environment	Temperature: 21°-26° C Relative humidity: 32%-86% (rats), 20%-82% (mice) Fluorescent light: 12 hours/day Room air changes: 10-12 changes/hour	Average Temperature: 22°-23° C (rats), 22° C (mice) Average relative humidity: 48% (rats), 47% (mice) Fluorescent light: 12 hours/day Room air changes: more than 10 changes/hour
Necropsy Dates	8-Week interim evaluation: Rats: 27-29 April 1982 Mice: 26-27 May 1982 17-Week study: Rats: 29 June to 1 July 1982 Mice: 27-29 July 1982	15-Month interim evaluation: Rats: 26-28 August 1986 (males); 10-12 September 1986 (females) Mice: 24-26 September 1986 (males); 1-3 October 1986 (females) 2-Year study: Rats: 0, 3, and 10 mg/kg, 1-9 June 1987 (males), 10-16 June 1987 (females); 30 mg/kg, 18 November 1986 (males), 10-12 September 1986 (females) Mice: 0 and 6 mg/kg, 23-24 June 1987 (males), 30 June -1 July 1987 (females); 20 mg/kg, 9 March 1987; 60 mg/kg, 30 December 1986 (males), 20 November 1986 (females)
Average Age When Killed	Rats: 182 days Mice: 160 days	Rats: 73 weeks (30 mg/kg females), 83 weeks (30 mg/kg males), 110-113 weeks (0, 3, and 10 mg/kg groups) Mice: 80 weeks (60 mg/kg females), 86 weeks (60 mg/kg males), 95 weeks (20 mg/kg dose groups), 111 weeks (0 and 6 mg/kg males), 112 weeks (0 and 6 mg/kg females)
Type and Frequency of Observation	Observed twice/day; weighed initially and once/week; clinical observations recorded once/week	Observed twice/day; weighed initially, once/week for 13 weeks, once/month thereafter; clinical observations recorded at weighing
Necropsy Examinations	Necropsy performed on all animals. At 8-week interim evaluations, the right epididymis and testis were weighed. At study termination, the following organs of all animals were weighed: brain, right epididymis, heart, right kidney, liver, lungs, right testis, and thymus.	Necropsy performed on all animals. At 15 months, the brain, right kidney, and liver were weighed.

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of 1,2,3-Trichloropropane (continued)

17-Week Studies	2-Year Studies
Clinical Pathology At 8 and 17 weeks, blood and urine samples were collected from all animals. ***Hematology:*** hematocrit, hemoglobin, erythrocytes, leukocytes, monocytes, and eosinophils ***Clinical chemistry:*** urea nitrogen, creatinine, sodium, potassium, chloride, phosphorus, total protein, albumin, globulin, albumin/globulin ratio, total bilirubin, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, sorbitol dehydrogenase, and pseudocholinesterase ***Urinalysis:*** Specific gravity	At 15 months, blood was collected from all animals. ***Hematology:*** hematocrit, hemoglobin, erythrocytes, mean erythrocyte volume, mean erythrocyte hemoglobin, mean erythrocyte hemoglobin concentration, and leukocyte count and differential ***Clinical chemistry:*** alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, creatine kinase, lactate dehydrogenase, sorbitol dehydrogenase, and 5'-nucleotidase
Histopathologic Examinations Complete histopathologic examination was performed on all animals found dead or killed moribund, on 0 and 125 mg/kg rats, and on 0, 125 (males), and 250 mg/kg mice. In addition to gross lesions, tissues examined included adrenal gland, bile duct (rats), bone and marrow, brain, clitoral gland (rats), epididymis, esophagus, gallbladder (mice), heart, kidney, large intestine (cecum, colon, and rectum), liver, lung, lymph nodes (mandibular and mesenteric), mammary gland, nose, ovary (rats), pancreas, parathyroid gland, pituitary gland, preputial gland (rats) prostate gland, salivary gland, skin, small intestine (duodenum, jejunum, and ileum), spleen, stomach (forestomach and glandular stomach), testes, thymus (mice), thyroid gland, trachea, urinary bladder, and uterus (rats). Organs examined from 63 mg/kg rats at 8 weeks included bone and marrow, heart, kidney, liver, nose, spleen, stomach, and uterus. At the end of the studies, organs examined from 32 and 63 mg/kg rats included: adrenal gland (females only), bone and marrow (except 32 mg/kg males), kidney, liver (except 32 mg/kg females), nose (63 mg/kg only), spleen, and thymus (except 32 mg/kg females). At the end of the studies, organs examined from other mouse groups (except 8 mg/kg) included spleen (except 16 mg/kg males), lung (except 16 mg/kg mice and 32 mg/kg males), forestomach (except 16 and 32 mg/kg groups), and liver (125 mg/kg females only).	Complete histopathologic examinations were performed on all animals. In addition to gross lesions, tissues examined included adrenal gland, bone and bone marrow, brain, clitoral gland (rats), epididymis, esophagus, gallbladder (mice), heart, kidney, large intestine (cecum, colon, rectum), liver, lung, lymph nodes (mandibular and mesenteric), mammary gland, nose, ovary, pancreas (islets), parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, seminal vesicles, skin, small intestine (duodenum, jejunum, ileum), spleen, stomach (forestomach, glandular), testes, thymus, thyroid gland, trachea, urinary bladder, and uterus. Mice: Tissues routinely examined microscopically included adrenal gland, bone and bone marrow, brain, epididymis, esophagus, gallbladder, gross lesions, heart, kidney, large intestine (cecum, colon, rectum), liver, lung, lymph nodes (mandibular and mesenteric), mammary gland (females), nose, ovary, pancreas (islets), parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, seminal vesicles, skin, small intestine (duodenum, jejunum, ileum), spleen, stomach (forestomach, glandular), testes, thymus, thyroid gland, trachea, urinary bladder, uterus, and gross lesions.

RESULTS

RATS

17-Week Studies

All female rats receiving 250 mg/kg 1,2,3-trichloropropane died by week 2 and all males receiving the same dose died by week 5 (Table 2). At 125 mg/kg, one male died by the end of week 5 and four females died during the studies. No other chemical-related deaths occurred. One control female was killed after escaping during week 6. At 125 mg/kg, mean body weight gains were significantly lower than those of the controls; final mean body weights were 21% lower than the controls for males and 24% lower for females (Table 2). Mean body weight gain of males receiving 63 mg/kg was also lower than that of the controls, and the final mean body weight was 11% lower than controls. Final mean body weights and mean body weight gains of the other dosed groups were similar to those of controls.

TABLE 2
Survival and Mean Body Weights of Rats in the 17-Week Gavage Studies of 1,2,3-Trichloropropane

Dose (mg/kg)	8-Week Interim Evaluation[a]	Survival[b]	Mean Body Weight (g)[c]			Final Weight Relative to Controls (%)
			Initial	Final	Change	
Male						
0	10	20/20	176 ± 3	389 ± 5	213 ± 5	
8	10	10/10	172 ± 8	393 ± 8	222 ± 10	101
16	10	10/10	178 ± 8	372 ± 12	194 ± 7	96
32	10	10/10	175 ± 7	386 ± 5	211 ± 7	99
63	10	10/10	171 ± 7	345 ± 6**	174 ± 8**	89
125[d]	9	9/10	180 ± 9	306 ± 7**	122 ± 7**	79
250[e]	0	0/10	175 ± 7	-[f]	-	-
Female						
0[g]	10	19/20	128 ± 1	216 ± 2	88 ± 2	
8	10	10/10	130 ± 2	216 ± 4	87 ± 3	100
16	10	10/10	134 ± 3	225 ± 6	91 ± 6	104
32	10	10/10	128 ± 1	216 ± 3	88 ± 2	100
63	10	10/10	128 ± 2	208 ± 3	80 ± 2	96
125[h]	9	7/10	129 ± 2	165 ± 7**	36 ± 6**	76
250[i]	0	0/10	126 ± 3	-	-	-

** Significantly different ($P \leq 0.01$) from the control group by Williams' or Dunnett's test
[a] Number of animals killed for the 8-week interim evaluation
[b] Number of animals surviving/number initially in group minus animals killed for the 8-week interim evaluation
[c] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the studies.
[d] Week of death: 5
[e] Week of death: 12 in week 1, 6 in week 2, 1 in week 3, 1 in week 5
[f] No data calculated due to 100% mortality in this group
[g] One was killed after escaping from cage in week 6.
[h] Week of death: 5, 8, 9, 13
[i] Week of death: 16 in week 1, 4 in week 2

Emaciation, debilitation, or lethargy occurred in rats receiving 250 mg/kg and dying of severe hepatic or renal toxicity. No other clinical findings were associated with the administration of 1,2,3-trichloropropane.

Absolute liver weights of all dosed males and relative liver weights of males that received 32 mg/kg or more, and both absolute and relative liver weights of females that received 16 mg/kg or more were significantly greater than those of the controls (Table F1). Absolute and relative kidney weights of males that received 32 mg/kg or more and of females that received 63 or 125 mg/kg were significantly greater than those of the controls. This dose-related trend of increased liver and kidney weights in rats receiving 1,2,3-trichloropropane was consistent with the clinical pathology and histopathology findings. Differences in absolute or relative brain and heart weights were considered to be related to decreases in body weight rather than to organ toxicity.

A decreased erythrocyte mass, as evidenced by lower mean hematocrit, hemoglobin, and erythrocyte counts, was observed at the 8-week interim evaluations in rats receiving 16 mg/kg or more (Table G1). Erythrocyte morphology in these groups did not reveal an increase in polychromasia, suggesting that the anemia was nonregenerative and possibly associated with a depression in erythropoiesis.

Most of the biologically significant differences in clinical chemistry parameters were related to the liver. At the 8-week interim evaluations, female rats were more severely affected than males (Table G1). Total bilirubin values were higher in 63 and 125 mg/kg male and female groups, indicating either increased free bilirubin production or decreased hepatocellular uptake, conjugation, or excretion of bilirubin. Females in the 125 mg/kg group also exhibited prominent increases in alanine aminotransferase, aspartate aminotransferase, and sorbitol dehydrogenase activities.

Of these enzymes, alanine aminotransferase and sorbitol dehydrogenase are quite liver specific in rats, and even though aspartate aminotransferase has a wide tissue distribution, it is probable that the increase in serum aspartate aminotransferase is from the liver. Increases in these enzymes indicate ongoing hepatocellular damage with subsequent enzyme leakage. A significant decrease in pseudocholinesterase values occurred in all dosed female groups. In the absence of specific inhibitors, the observed decreases suggest depressed synthesis due to hepatocellular damage. Significant decreases in urea nitrogen and creatinine were also observed in females receiving 63 or 125 mg/kg.

In general, the trends in hematologic and clinical chemistry parameters observed at the 8-week interim evaluations were also evident at the end of the 17-week studies (Table G2). In addition to the increases in liver enzymes, the urea nitrogen values were significantly decreased in males receiving 125 mg/kg and in females receiving 32 mg/kg or more. Pseudocholinesterase values were significantly decreased in males receiving 63 or 125 mg/kg and in females receiving 8 mg/kg or more.

In rats administered 1,2,3-trichloropropane, the principal toxic lesions occurred in the liver, kidney, and nasal turbinates (Table 3). Rats receiving 250 mg/kg that died within the first several weeks of the studies had severe hepatic toxicity characterized by multifocal, centrilobular hepatocellular necrosis. The hepatocellular necrosis was more extensive in female rats, especially those dying within the first few days of dosing. Karyomegaly (nuclear enlargement) of hepatocytes was also noted. At the 8-week interim evaluations, similar hepatic lesions were observed primarily in females receiving 125 mg/kg. Hepatocellular necrosis in the 125 mg/kg groups was generally less extensive than that in the 250 mg/kg animals that died during the studies; lesion location was randomly distributed rather than centrilobular. Multifocal hemorrhage and bile duct hyperplasia were also seen in females receiving 125 mg/kg.

In rats dying during the studies, severe nephrotoxicity was observed primarily in females and to a lesser extent in males. The condition was characterized by diffuse acute tubule necrosis in the outer stripe of the outer medulla in rats that died during the first few days of dosing. Rats surviving the first few days of dosing exhibited regenerative hyperplasia of the tubule epithelium, karyomegaly of individual epithelial cells, and multifocal necrosis. At the 8-week interim evaluations, nephrotoxicity was observed in the 125 mg/kg groups and was primarily characterized by a regenerative hyperplasia with karyomegaly. At the end of the studies, kidney lesions similar to those observed at the interim

TABLE 3
Incidences of Selected Lesions in Rats at the 8-Week Interim Evaluations and in the 17-Week Gavage Studies of 1,2,3-Trichloropropane

Dose	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg	250 mg/kg
Male							
8-Week Interim Evaluation[a]							
Liver[b]	10	10	10	10	10	9	20
Necrosis[c]	0	0	0	0	0	0	20**
Degeneration	0	0	0	0	0	0	2
Karyomegaly	0	0	0	0	0	0	9**
Hemorrhage	0	0	0	0	0	0	1
Kidney	10	10	10	10	10	9	20
Necrosis	0	0	0	0	0	1	14**
Regenerative hyperplasia	0	0	0	0	10**	9**	9**
Karyomegaly	0	0	0	0	0	3	9**
Nasal turbinates	10	10	10	10	10	9	20
Epithelial attenuation	0	0	0	0	2	0	13**
Epithelial necrosis	0	0	0	0	0	2	14**
Acute inflammation	0	0	0	0	0	0	12**
Chronic inflammation	0	0	0	0	0	1	4
17-Week Study[d]							
Liver	20	10	10	10	10	10	
Necrosis	0	0	0	1	1	1	
Degeneration	0	0	0	0	0	0	
Karyomegaly	0	0	0	0	0	1	
Hemorrhage	0	0	0	0	0	1	
Kidney	20	10	10	10	10	10	
Necrosis	0	0	0	0	0	1	
Regenerative hyperplasia	0	0	0	0	0	10**	
Karyomegaly	0	0	0	0	0	10**	
Nasal turbinates	20	10	10	10	10	9	
Epithelial attenuation	0	0	0	0	0	4**	
Epithelial necrosis	0	0	0	0	0	3*	
Acute inflammation	0	0	0	0	1	0	
Chronic inflammation	0	0	0	0	0	5**	

(continued)

TABLE 3
Incidences of Selected Lesions in Rats at the 8-Week Interim Evaluations and in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

Dose	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg	250 mg/kg
Female							
8-Week Interim Evaluation							
Liver	10	10	10	10	10	9	20
Necrosis	0	0	0	0	0	7**	20**
Hemorrhage	0	0	0	0	0	5*	7**
Karyomegaly	0	0	0	0	0	1	1
Bile duct	10	10	10	10	10	9	20
Hyperplasia	0	0	0	0	0	6**	0
Kidney	10	10	10	10	10	9	20
Necrosis	0	0	0	0	0	0	20**
Regenerative hyperplasia	0	0	0	0	10**	9**	4**
Karyomegaly	0	0	0	0	1	9**	4
Nasal turbinates	10	10	10	10	10	9	20
Epithelial attenuation	0	0	0	0	1	6**	13**
Epithelial necrosis	0	0	0	0	0	5*	19**
Acute inflammation	0	0	0	0	1	0	12**
Chronic inflammation	0	0	0	0	1	2	4
17-Week Study							
Liver	20	10	10	10	10	11	
Necrosis	0	0	0	0	0	11**	
Karyomegaly	0	0	0	0	0	11**	
Hemorrhage	0	0	0		0	1	
Bile duct	20	10	10	10	10	11	
Hyperplasia	0	0	0	0	0	9**	
Kidney	20	10	10	10	10	11	
Necrosis	0	0	0	0	0	0	
Regenerative hyperplasia	0	0	0	0	0	10**	
Karyomegaly	0	0	0	0	0	11**	
Nasal turbinates	20	10	10	10	10	11	
Epithelial attenuation	0	0	0	0	0	5**	
Epithelial necrosis	0	0	0	0	0	2	
Acute inflammation	0	0	0	0	0	2	
Chronic inflammation	2	0	0	0	0	1	

* Significantly different (P 0.05) from the control group by the Fisher exact test
** P 0.01
[a] Includes rats killed at the 8-week interim evaluations and all 250 mg/kg rats.
[b] Number of rats with organ examined microscopically
[c] Number of animals with lesion
[d] Includes rats killed at the end of the 17-week studies and those dying or killed moribund during the studies.

evaluations occurred along with proteinaceous casts and an increase in the severity of chronic inflammation (chronic nephropathy).

Lesions were observed in the nasal passages of rats that died early. Extensive necrosis of the olfactory and respiratory epithelium and acute inflammation were most severe in the dorsal posterior region of the nasal turbinates, particularly in animals dying during the first few days of the studies. Other lesions included multifocal necrosis and epithelium attenuation, subepithelial fibrosis, and inflammation. At 8 weeks, the nasal lesions were seen primarily in females receiving 125 mg/kg. At the end of the studies, nasal lesions were also seen in males receiving 125 mg/kg and were similar to those found in females.

Lesions seen less frequently in rats dying during the studies included thymic lymphoid depletion and hypocellularity of stemal bone marrow (primarily in males). At 8 weeks, sternal marrow hypocellularity was observed in both sexes, and uterine hypoplasia was observed in some females. Splenic atrophy occurred in dosed males and hypocellularity of the sternal bone marrow occurred in dosed female rats. In addition, uterine hypoplasia, adrenal cortical cell vacuolation, and myocardial chronic inflammation occurred in some dosed females. One nasopharyngeal squamous cell carcinoma was observed in a 125 mg/kg female that died during the study.

Dose Selection Rationale: All rats receiving 250 mg/kg and one male and three females receiving 125 mg/kg died with severe toxicity-related lesions of the liver and kidney. In addition, groups receiving 63 mg/kg or more had lower mean body weight gains and increased liver and kidney weights, indicating that a dose of 63 mg/kg would be too high for the 2-year studies. Based on these results, 30 mg/kg was selected as the high dose for the 2-year studies in rats. Doses of 3 and 10 mg/kg were chosen to provide adequate dose-response data.

2-Year Studies

15-Month Interim Evaluations

At the 15-month interim evaluations, neoplasms of the forestomach, oral mucosa (tongue and pharynx), pancreas (males), kidney, mammary gland (females), preputial gland, and clitoral gland occurred primarily in rats receiving 10 or 30 mg/kg (Tables A1 and B1). Nearly all 30 mg/kg rats had squamous cell papillomas of the forestomach, and two females and one male had squamous cell carcinomas of the forestomach. About half of the 10 mg/kg rats (4/10 males and 5/8 females) also had forestomach neoplasms. Squamous cell papillomas or carcinomas arising from the lingual or pharyngeal mucosa also occurred in several 30 mg/kg rats and renal tubule adenomas were seen in 5/8 of the 30 mg/kg males. A few rats in one or more of the dosed groups had neoplasms of the preputial gland, clitoral gland, mammary gland (females), pancreas (males), and other organs. Nonneoplastic lesions attributed to chemical administration were also observed in the forestomach and kidney of dosed rats (Tables A5 and B5). Focal hyperplasia of the stratified squamous epithelium of the forestomach was observed in some dosed rats. The incidence of nephropathy in females and the severity of nephropathy in males were increased in rats receiving 10 and 30 mg/kg. Focal hyperplasia of the renal tubule epithelium was also seen in several dosed male and female rats.

Hematologic evaluations of dosed rats showed a chemical-related decrease in hematocrit and hemoglobin concentrations especially in the 30 mg/kg groups (Table G3). The total leukocyte counts were also significantly higher in the 30 mg/kg groups primarily due to increased numbers of segmented neutrophils. The decreased hematocrit may have been caused by depressed erythropoiesis or by blood loss from neoplasms in the forestomach or oral mucosa, while the increase in leukocytes was likely due to inflammation associated with the chemical-induced neoplasms. Significant increases in serum 5'-nucleotidase and alanine aminotransferase occurred in 30 mg/kg males, but not in females. Marginal differences in other clinical chemistry parameters in dosed groups were not considered chemical related.

Survival

Estimates of 2-year survival probabilities for male and female rats are shown in Table 4 and in the Kaplan-Meier curves in Figure 1. Survival of male and female rats receiving 10 or 30 mg/kg was significantly lower than that of the controls. Most female rats receiving 30 mg/kg were killed moribund or died between weeks 3 and 65 from chemical-related neoplasms; the few surviving females were killed at the 15-month interim evaluation. Most 30 mg/kg male rats were killed moribund between week 45 and week 77, when all surviving males were killed. The male and female 30 mg/kg groups were terminated because additional relevant information would not be gained by allowing them to live longer.

Body Weights and Clinical Findings

Mean body weights of male and female rats receiving 3 or 10 mg/kg were similar to those of the controls throughout the studies (Figure 2 and Tables 5 and 6). Mean body weights of male rats receiving 30 mg/kg were consistently lower than the controls after about week 15. After week 53, mean body weights of 30 mg/kg males remained at least 5% lower than the controls until week 77 when all surviving males were killed. Beginning at about week 58, mean body weights of the surviving 30 mg/kg females were 5% lower than those of controls.

Of the clinical findings, none were considered to be directly related to organ toxicity other than those associated with chemical-induced neoplasms of the oral mucosa, forestomach, or mammary gland. The clinical findings in rats killed moribund or dying before the end of the studies included emaciation, lethargy, diarrhea, dyspnea, and tissue masses. The moribund condition of rats receiving 10 and 30 mg/kg was associated with one or more of these clinical findings. In most of these rats, the clinical findings and moribund condition were attributed to chemical-induced neoplasms of the oral mucosa or forestomach.

TABLE 4
Survival of Rats in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	10	10	10	8
Natural deaths	2	2	4	0
Moribund	13	16	30	43
Accidental deaths[a]	1	0	1	0
Scheduled sacrifice in week 77	0	0	0	9
Missexed[a]	0	0	1	0
Animals surviving to study termination	34	32	14	0
Percent probability of survival at end of study[b]	70	64	30	0
Mean survival days[c]	647	661	596	465
Survival analysis[d]	P<0.001	P=0.884	P<0.001	P<0.001
Female				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	10	10	8	8
Natural deaths	2	2	2	2
Moribund	17	17	42	49
Scheduled sacrifice in week 67	0	0	0	1
Missexed[a]	0	1	0	0
Animals surviving to study termination	31	30	8	0
Percent probability of survival at end of study	62	62	16	0
Mean survival days	649	654	580	366
Survival analysis	P<0.001	P=1.000N	P<0.001	P<0.001

[a] Censored from survival analyses
[b] Kaplan-Meier determinations
[c] Mean of all deaths (uncensored, censored, terminal sacrifice)
[d] The entry under the "Vehicle Control" column is associated with the life table trend test (Tarone, 1975). Subsequent entries are the results of pairwise tests (Cox, 1972). Lower mortality in a dose group is indicated by N.

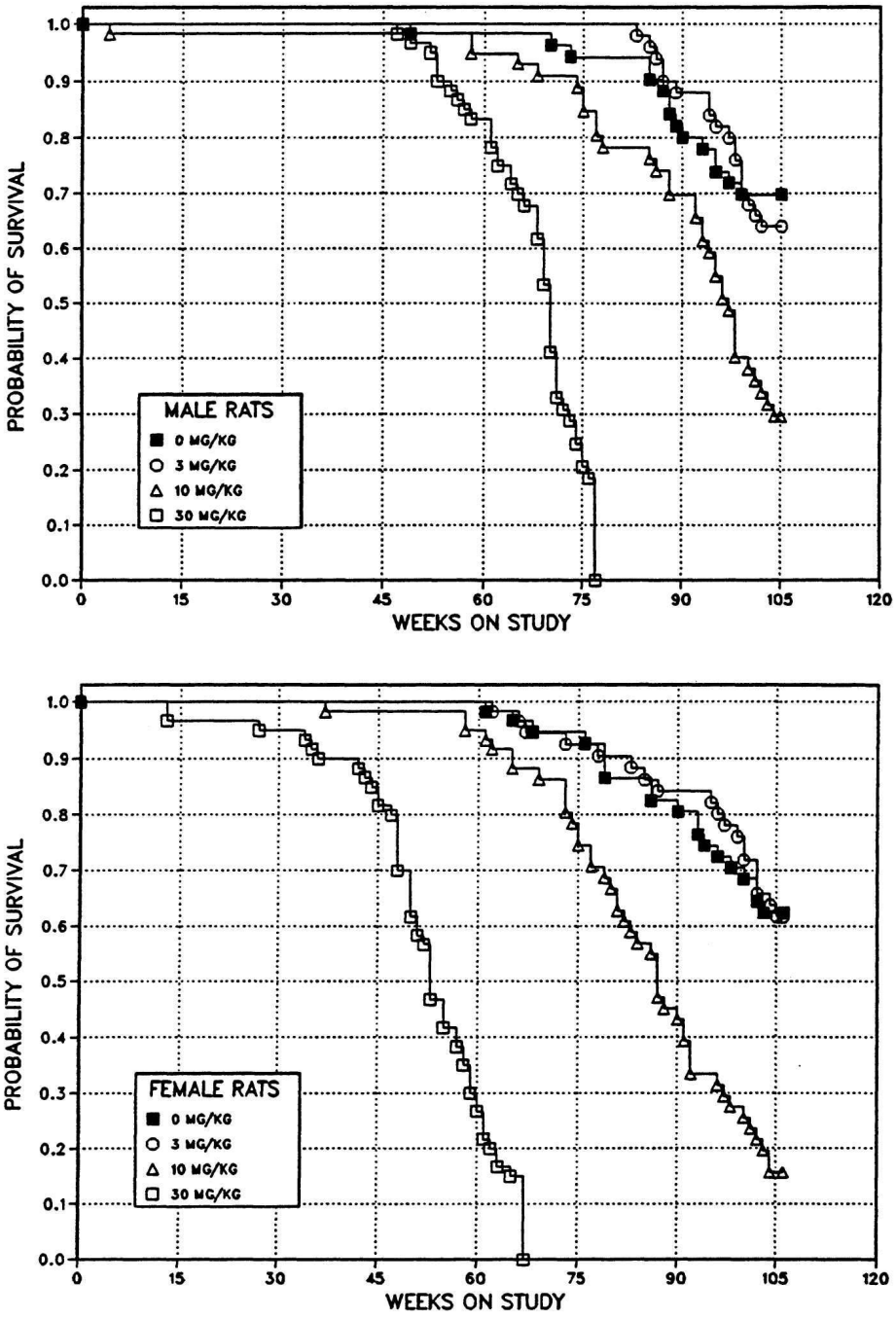


FIGURE 1
Kaplan-Meier Survival Curves for Male and Female Rats Administered 1,2,3-Trichloropropane by Gavage for 2 Years

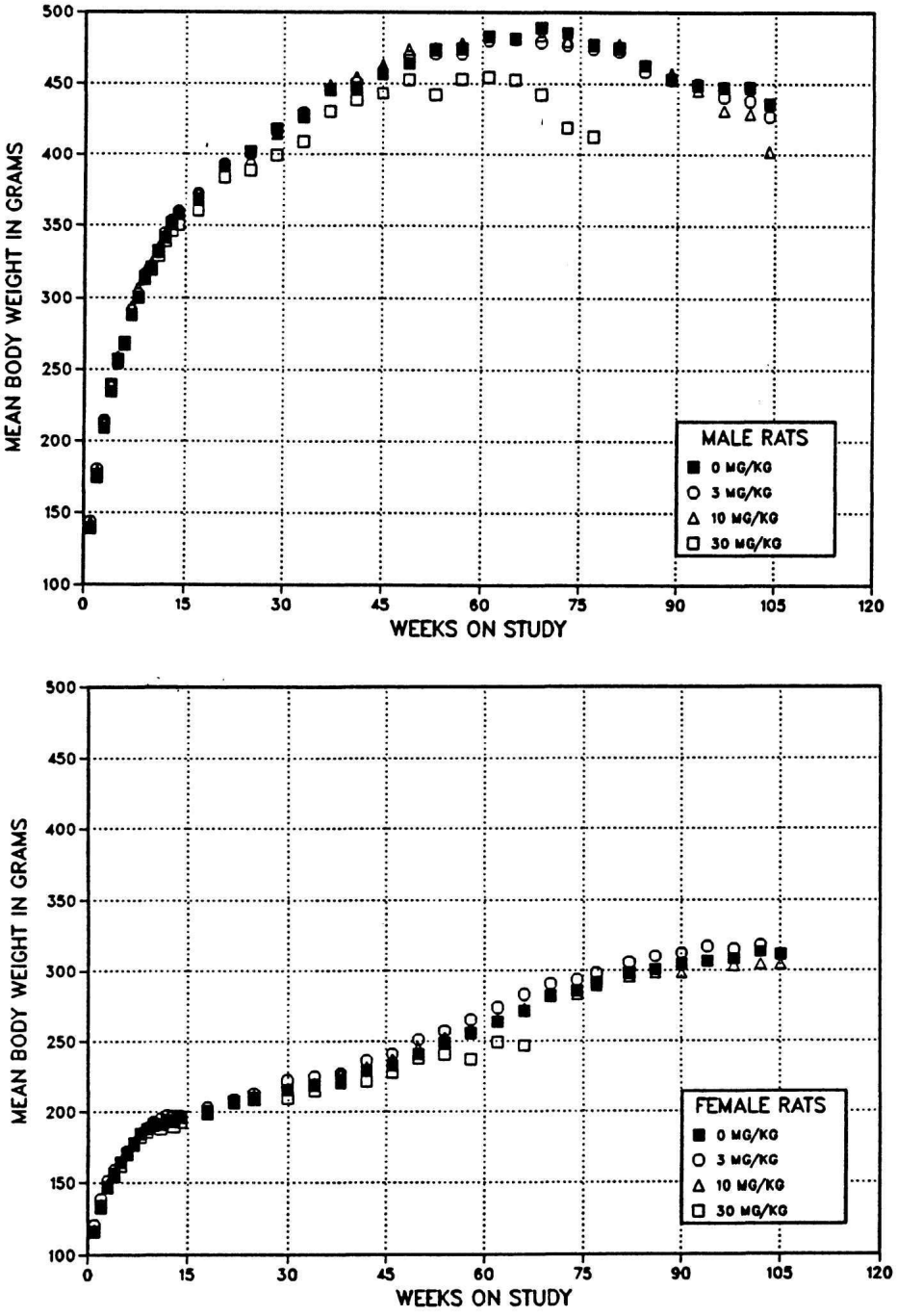


FIGURE 2
Growth Curves for Male and Female Rats Administered 1,2,3-Trichloropropane by Gavage for 2 Years

TABLE 5
Mean Body Weights and Survival of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane

Weeks on Study	Vehicle Control		3 mg/kg			10 mg/kg			30 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	139	60	143	103	60	143	103	60	139	100	60
2	175	60	180	103	60	178	102	60	176	101	60
3	209	60	214	102	60	214	102	59	212	101	60
4	235	60	238	101	60	240	102	59	239	102	60
5	255	60	254	100	60	259	102	58	257	101	60
6	267	60	269	101	60	269	101	58	269	101	60
7	288	60	291	101	60	294	102	58	288	100	60
8	300	60	303	101	60	307	102	58	301	100	60
9	313	60	316	101	60	319	102	58	314	100	60
10	321	60	321	100	60	324	101	58	319	99	60
11	332	60	332	100	60	335	101	58	329	99	60
12	341	60	345	101	60	345	101	58	339	99	60
13	351	60	353	101	60	353	101	58	347	99	60
14	358	60	360	101	60	359	100	58	351	98	60
17	368	60	372	101	60	373	101	58	361	98	60
21	391	60	393	101	60	392	100	58	384	98	60
25	402	60	400	100	60	396	99	58	389	97	60
29	418	60	416	100	60	414	99	58	399	95	60
33	427	60	429	100	60	426	100	57	409	96	60
37	445	60	446	100	60	449	101	57	430	97	60
41	447	60	451	101	60	454	102	57	438	98	60
45	457	60	459	100	60	464	102	57	443	97	60
49	464	60	469	101	60	474	102	57	453	98	59
53	474	59	471	99	60	475	100	57	442	93	57
57	474	59	471	99	60	478	101	57	453	96	52
61	483	59	480	99	60	483	100	55	455	94	50
65[a]	481	59	481	100	60	481	100	54	452	94	43
69	489	49	479	98	50	484	99	43	443	91	30
73	485	48	477	98	50	480	99	43	419	86	15
77	477	47	474	99	50	477	100	40	413	87	9[b]
81	475	47	473	100	50	477	100	37			
85	463	47	458	99	49	463	100	37			
89	453	40	453	100	45	457	101	33			
93	449	39	450	100	44	445	99	31			
97	447	36	441	99	41	431	96	24			
101	447	34	438	98	34	429	96	18			
104	436	34	427	98	32	402	92	15			
Terminal sacrifice		34			32			14			
Mean for weeks											
1-13	271		274	101		75	101		271	100	
14-52	418		420	100		420	100		406	97	
53-104	467		462	99		462	99		440	94	

[a] Interim evaluation occurred during week 65 for all groups.
[b] Surviving members of the 30 mg/kg group were killed at week 77.

TABLE 6
Mean Body Weights and Survival of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane

Weeks on Study	Vehicle Control		3 mg/kg			10 mg/kg			30 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	116	60	120	103	60	118	102	60	116	100	60
2	133	60	139	105	60	135	102	60	134	101	60
3	147	60	151	103	59	149	101	60	147	100	60
4	156	60	159	102	59	157	101	60	154	99	60
5	164	60	164	100	59	165	101	60	161	98	60
6	171	60	172	101	59	171	100	60	169	99	60
7	178	60	178	100	59	179	101	60	176	99	60
8	184	60	185	101	59	185	101	60	182	99	60
9	188	60	189	101	59	188	100	60	186	99	60
10	191	60	193	101	59	192	101	60	190	99	60
11	191	60	195	102	59	191	100	60	188	98	60
12	193	60	197	102	59	195	101	60	194	101	60
13	193	60	197	102	59	197	102	60	189	98	58
14	196	60	197	101	59	198	101	60	192	98	58
18	201	60	203	101	59	200	100	60	199	99	58
22	206	60	209	101	59	209	101	60	207	100	58
25	210	60	213	101	59	212	101	60	208	99	58
30	216	60	222	103	59	216	100	60	210	97	57
34	219	60	225	103	59	220	100	60	215	98	57
38	222	60	227	102	59	227	102	59	221	100	54
42	229	60	237	103	59	232	101	59	222	97	54
46	233	60	241	103	59	237	102	59	228	98	49
50	241	60	251	104	59	245	102	59	238	99	42
54	249	60	258	104	59	253	102	59	241	97	28
58	256	60	265	104	59	258	101	59	237	93	22
62	264	59	274	104	59	265	100	56	249	95	13
66[a]	271	58	283	104	58	273	101	53	247	91	9[b]
70	282	47	291	103	46	283	100	44			
74	286	47	294	103	45	283	99	41			
77	291	46	298	102	45	289	99	36			
82	298	43	306	103	44	296	99	32			
86	301	43	310	103	42	299	99	29			
90	305	41	313	103	41	299	98	23			
94	307	38	318	104	41	307	100	17			
98	309	36	316	102	38	304	98	15			
102	314	33	318	101	34	305	97	12			
Terminal sacrifice		31			31			8			
Mean for weeks											
1-13	170		172	101		171	101		168	99	
14-52	217		223	103		220	101		214	99	
53-102	287		296	103		286	100		244	85	

[a] Interim evaluation occurred during week 67.
[b] Surviving members of the 30 mg/kg group were killed at week 67.

Sentinel Animals

Serum samples from sentinel animals were negative for virus antibodies throughout the studies, except the 18-month serum sample of one female rat which was positive for pneumonia virus of mice (PVM) (Table J1). Other serum samples at 18 months and at subsequent periods were negative for PVM.

Pathology and Statistical Analyses of Results

Statistically significant or biologically noteworthy neoplasms or nonneoplastic lesions of the oral mucosa, forestomach, pancreas, kidney, preputial gland, clitoral gland, mammary gland, Zymbal's gland, intestine, skin, and liver occurred in rats receiving 1,2,3-trichloropropane. The occurrence, statistical analyses, and historical incidence of these lesions in the 2-year studies are presented in Appendix A for male rats and Appendix B for female rats.

Oral Mucosa (Pharynx and Tongue): The oral mucosa and tissues of the mouth of all rats were examined for gross lesions at necropsy; tissues were selected for microscopic examination when a lesion was observed. In male rats, 72% of the 30 mg/kg group and 32% of the 10 mg/kg group had exophytic papillary or nodular masses arising primarily from the mucosa of the pharyngeal palate or tongue. In female rats, 62% of the 30 mg/kg group and 47% of the 10 mg/kg group had similar lesions. The masses in the oral mucosa were squamous cell papillomas or carcinomas. The incidences of squamous cell papillomas and squamous cell carcinomas were significantly increased in rats receiving 10 and 30 mg/kg (Tables 7, A3, and B3).

The squamous cell papillomas and carcinomas of the oral mucosa constituted a morphologic continuum and were similar to those of the forestomach. The papillomas were exophytic, branching papillary structures consisting of a thickened stratified squamous epithelium overlying a thin connective tissue core. Although most of the squamous cell carcinomas were well differentiated and had a similar exophytic papillary or verrucous structure, they also exhibited invasion of the underlying tissues by cords of squamous epithelium; a few carcinomas metastasized to distant organs.

Forestomach: Exophytic papillary or nodular masses similar to those in the oral mucosa were also observed in the forestomach of many dosed male and female rats at necropsy. The masses were squamous cell papillomas or squamous cell carcinomas arising from the stratified squamous epithelium of the forestomach. Multiple squamous cell papillomas or carcinomas often occurred in the same rat, and in some rats, the neoplasms were so extensive that it was difficult to discern if they represented a single neoplasm or the confluent growth of multiple neoplasms. The incidences of squamous cell papilloma or carcinoma (combined) were significantly increased in all dosed groups (Tables 8, A3, and B3). The incidences of forestomach neoplasms, particularly squamous cell carcinomas, and the incidences of multiple neoplasms were generally higher in males than in females at the same dose levels (Tables A1 and B1). The incidence of squamous cell carcinoma in males and the incidence of forestomach neoplasms in females were slightly higher in rats receiving 10 mg/kg than in rats receiving 30 mg/kg (Table 8). This was perhaps due to the lower survival of the 30 mg/kg groups and the competing risks from squamous cell carcinomas of the tongue in males (Table A3) or mammary gland adenocarcinomas in females (Table B3).

The incidence of focal hyperplasia of the stratified squamous epithelium also increased in rats receiving 1,2,3-trichloropropane (Tables A5 and B5). Hyperplasia consisted of prominent, downward-extending ridges of basal cells (basal cell hyperplasia) or thickened epithelium forming short rugae or papillae (squamous hyperplasia). Hyperplasia, squamous cell papilloma, and squamous cell carcinoma of the forestomach constituted a morphologic continuum; the squamous cell papillomas and carcinomas were similar to those of the oral mucosa.

Pancreas: Male rats exhibited a dose-related increased incidence of pancreatic acinar adenoma (Tables 9 and A3), and the incidence of adenoma in each dosed group was significantly increased. Adenocarcinomas occurred in two 10 mg/kg males, the group with the highest incidence of adenomas, and in one 30 mg/kg male.

TABLE 7
Incidence of Oral Mucosa Neoplasms in Rats in the 2-Year Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
Squamous Cell Papilloma[b]				
15-Month interim evaluation[c]	0/10 (0%)	0/10 (0%)	1/10 (10%)	3/8 (38%)
2-Year study[d]	0/50 (0%)	4/50 (8%)	9/49 (18%)	19/52 (37%)
Logistic regression test[e]	P<0.001	P=0.069	P<0.001	P<0.001
Squamous Cell Carcinoma[f]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
2-Year study	1/50 (2%)	0/50 (0%)	11/49 (22%)	25/52 (48%)
Life table test[e]	P<0.001	P=0.512N	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.512N	P<0.001	P<0.001
Squamous Cell Papilloma or Squamous Cell Carcinoma[b]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	3/8 (38%)
2-Year study	1/50 (2%)	4/50 (8%)	18/49 (37%)	40/52 (77%)
Life table test	P<0.001	P=0.173	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.192	P<0.001	P<0.001
Female				
Squamous Cell Papilloma[b]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	3/8 (38%)
2-Year study	1/50 (2%)	5/49 (10%)	10/52 (19%)	18/52 (35%)
Logistic regression test	P<0.001	P=0.106	P=0.003	P<0.001
Squamous Cell Carcinoma[g]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
2-Year study	0/50 (0%)	1/49 (2%)	21/52 (40%)	21/52 (40%)
Life table test	P<0.001	P=0.493	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.493	P<0.001	P<0.001
Squamous Cell Papilloma or Squamous Cell Carcinoma[h]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	5/8 (63%)
2-Year study	1/50 (2%)	6/49 (12%)	28/52 (54%)	32/52 (62%)
Life table test	P<0.001	P=0.064	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.061	P<0.001	P<0.001

[a] Incidences include neoplasms of the pharynx and tongue.
[b] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 3/820 (0.4% ± 0.8%); range 0%-2%
[c] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluations
[d] Number of neoplasm-bearing animals/number of animals necropsied at the end of the studies
[e] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. For all tests, a lower incidence in a dose group is indicated by N.
[f] Historical incidence: 0/820
[g] Historical incidence: 2/820 (0.2% ± 0.7%); range 0%-2%
[h] Historical incidence: 5/820 (0.6% ± 1.0%); range 0%-2%

TABLE 8
Incidence of Forestomach Neoplasms in Rats in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
Squamous Cell Papilloma[a]				
15-Month interim evaluation[b]	0/10 (0%)	2/10 (20%)	3/10 (30%)	8/8 (100%)
2-Year study[c]	0/50 (0%)	29/50 (58%)	33/49 (67%)	38/52 (73%)
Logistic regression test[d]	P<0.001	P<0.001	P<0.001	P<0.001
Squamous Cell Carcinoma[e]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	1/8 (13%)
2-Year study	0/50 (0%)	9/50 (18%)	27/49 (55%)	13/52 (25%)
Life table test[d]	P<0.001	P=0.003	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.003	P<0.001	P=0.001
Squamous Cell Papilloma or Squamous Cell Carcinoma[f]				
15-Month interim evaluation	0/10 (0%)	2/10 (20%)	4/10 (40%)	8/8 (100%)
2-Year study	0/50 (0%)	33/50 (66%)	42/49 (86%)	43/52 (83%)
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Female				
Squamous Cell Papilloma[g]				
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	5/8 (63%)	7/8 (88%)
2-Year study	0/50 (0%)	13/49 (27%)	32/51 (63%)	17/52 (33%)
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Squamous Cell Carcinoma[e]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
2-Year study	0/50 (0%)	3/49 (6%)	9/51 (18%)	4/52 (8%)
Life table test	P<0.001	P=0.121	P<0.001	P=0.001
Logistic regression test	P<0.001	P=0.124	P<0.001	P=0.046
Squamous Cell Papilloma or Squamous Cell Carcinoma[f]				
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	5/8 (63%)	8/8 (100%)
2-Year study	0/50 (0%)	16/49 (33%)	37/51 (73%)	19/52 (37%)
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 4/820 (0.5% ± 1.2%); range 0%-4%
[b] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluations
[c] Number of neoplasm-bearing animals/number of animals necropsied at the end of the studies
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal.
[e] Historical incidence: 0/820
[f] Historical incidence: 4/820 (0.5% ± 1.2%); range 0%-4%
[g] Historical incidence: 2/820 (0.2% ± 0.7%); range 0%-2%

TABLE 9
Incidence of Selected Pancreatic Acinar Lesions in Rats in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
Hyperplasia				
15-Month interim evaluation[a]	0/10 (0%)	2/10 (20%)	7/10 (70%)	8/8 (100%)
2-Year study[b]				
Acinus, hyperplasia (single or multiple)	28/50 (56%)	46/50 (92%)	46/49 (94%)	48/52 (92%)
Logistic regression test[c]	P<0.001	P<0.001	P<0.001	P<0.001
Adenoma[d]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	2/8 (25%)
2-Year study	5/50 (10%)	21/50 (42%)	36/49 (73%)	29/52 (56%)
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Adenocarcinoma[e]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
2-Year study	0/50 (0%)	0/50 (0%)	2/49 (4%)	1/52 (2%)
Adenoma or Adenocarcinoma[f]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	2/8 (25%)
2-Year study	5/50 (10%)	21/50 (42%)	36/49 (75%)	29/52 (56%)
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Female				
Hyperplasia				
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	0/8 (0%)	2/8 (25%)
2-Year study	5/50 (10%)	14/49 (29%)	24/52 (46%)	9/52 (17%)
Logistic regression test	P<0.001	P=0.013	P<0.001	P=0.009
Adenoma[g]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
2-Year study	0/50 (0%)	0/49 (0%)	2/52 (4%)	0/52 (0%)

[a] Number of lesion-bearing animals/number of animals with pancreas examined microscopically at the 15-month interim evaluations
[b] Number of lesion-bearing animals/number of animals with pancreas examined microscopically at the end of the studies
[c] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The logistic regression test regards these lesions as nonfatal.
[d] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 57/815 (7.0% ± 9.4%); range 0%-32%.
[e] Historical incidence: 0/815
[f] Historical incidence: 57/815 (7.0% ± 9.4%); range 0%-32%
[g] Historical incidence: 8/810 (1.0% ± 1.5%); range 0%-4%

Focal hyperplasia of the pancreatic acini occurred in 56% of the control males and ranged from 92% to 94% in groups of dosed males (Tables 9 and A5). The incidence of hyperplasia in each dosed group was greater than that in controls. The incidence of hyperplasia of the pancreas in all dosed groups of females was also significantly increased. Adenomas were observed in two 10 mg/kg females (Tables 9 and A1). The lower incidence of pancreatic acinar hyperplasia or adenoma in females compared with males in the same dosed groups is consistent with the lower spontaneous rate of proliferative pancreatic lesions in females.

A morphologic continuum was observed from focal acinar hyperplasia to adenoma to adenocarcinoma. These proliferative acinar lesions varied from small nodules about 1 mm in diameter to large, multilobulated nodular masses over 1 cm in diameter. Although the increase in size was generally associated with progressive loss of normal architectural features and greater cellular atypia, no definitive histologic criteria distinguished focal hyperplasia from adenoma or adenoma from early adenocarcinoma. Foci of hyperplasia were circumscribed lesions with a prominent glandular pattern which resulted from enlargement of the acini. Similar proliferative lesions greater than 3 mm in diameter were generally diagnosed as adenoma. Some of the larger adenomas were multinodular and the acinar cells were arranged in prominent branching tubules rather than blunt acini. The few adenocarcinomas had heterogeneous growth patterns and cellular atypia.

Kidney: Focal hyperplasia of the renal tubule epithelium occurred in many male rats receiving 10 and 30 mg/kg (Tables 10 and A5). The incidences of hyperplasia in these groups were significantly increased. The increased incidence of hyperplasia in the 10 and 30 mg/kg males was accompanied by a concomitant, statistically significant increased incidence of renal tubule adenomas (Tables 10 and A3). Hyperplasia and adenoma sometimes occurred in the same rat, and about half the affected males had multiple, usually two, adenomas. In female rats, the incidence of hyperplasia was significantly increased in the 10 and 30 mg/kg groups. An adenocarcinoma in a 30 mg/kg female was the only renal tubule neoplasm observed in female rats.

Focal hyperplasia, as diagnosed in these studies, adenoma, and adenocarcinoma constituted a morphologic continuum. Hyperplasia was distinguished from tubule regeneration, which commonly accompanies the degenerative changes of nephropathy, by stratification of the epithelium (loss of basement membrane dependency) and cellular atypia. Focal hyperplasia, as viewed in one or more cross sections of a tubule, consisted of at least three distinct layers of epithelial cells partially or completely filling the tubule lumen. Adenomas were nodular masses usually larger than the diameter of approximately five tubules and nearly all were detected only during microscopic examination. The adenomas were usually solid, although some had dilated cavities. The cells composing the adenomas were generally uniform and arranged in solid clusters or, less frequently, tubular or papillary formations separated by a delicate stroma. The one adenocarcinoma found in the 30 mg/kg female was a large neoplasm with a heterogeneous growth pattern, cellular pleomorphism, and cellular atypia.

Nephropathy occurred in nearly all control and dosed males, but the severity of renal disease increased in male rats receiving 10 or 30 mg/kg (Table 10). In males, the mean severity of nephropathy was 2.0 for both the controls and 3 mg/kg groups, 2.6 for the 10 mg/kg group, and 2.4 for the 30 mg/kg group. Of the 30 mg/kg males with nephropathy, 20/52 were moderately severe and 3/52 were marked; in contrast, the control males had 10/50 with moderate nephropathy and 1/50 with marked nephropathy. The severity and extent of the renal lesions typically increased with age, and the shortened life span of the 30 mg/kg males compared to 10 mg/kg males may explain why the mean severity of nephropathy in the 30 mg/kg group was lower than in the 10 mg/kg group. The incidence and severity of spontaneous nephropathy is generally lower in female rats than in male rats of similar age; in these studies, there was no apparent increased incidence of spontaneous nephropathy in dosed female rats.

Nephropathy was characterized by a spectrum of degenerative changes involving the glomeruli, tubules, and interstitium. It consisted of thickening (duplication) of the glomerulus and tubule basement membranes, glomerulosclerosis, degeneration and atrophy of the tubule epithelium with dilatation

TABLE 10
Incidence of Selected Renal Tubule Lesions in Rats in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
Hyperplasia				
15-Month interim evaluation[a]	0/10 (0%)	0/10 (0%)	2/10 (20%)	6/8 (75%)
2-Year study[b]	0/50 (0%)	1/50 (2%)	21/49 (43%)	29/52 (56%)
Logistic regression test[c]	P<0.001	P=0.487	P<0.001	P<0.001
Adenoma[d]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	5/8 (63%)
2-Year study	0/50 (0%)	2/50 (4%)	20/49 (41%)	21/52 (40%)
Logistic regression test	P<0.001	P=0.225	P<0.001	P<0.001
Nephropathy				
15-Month interim evaluation	10/10 (100%)	10/10 (100%)	10/10 (100%)	8/8 (100%)
2-Year study	48/50 (96%)	50/50 (100%)	48/49 (98%)	52/52 (100%)
Severity grade				
Minimal (1)	13 (27%)	14 (28%)	6 (13%)	3 (6%)
Mild (2)	24 (50%)	25 (50%)	16 (33%)	26 (50%)
Moderate (3)	10 (21%)	8 (16%)	15 (31%)	20 (38%)
Marked (4)	1 (2%)	3 (60%)	11 (23%)	3 (6%)
Mean severity	2.0	2.0	2.6	2.4
Female				
Hyperplasia				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
2-Year study	0/50 (0%)	2/47 (4%)	3/52 (6%)	10/51 (20%)
Logistic regression test	P<0.001	P=0.226	P=0.023	P=0.006
Adenocarcinoma[e]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
2-Year study	0/50 (0%)	0/47 (0%)	0/52 (0%)	1/51 (2%)
Nephropathy				
15-month interim evaluation	0/10 (0%)	0/10 (0%)	1/8 (13%)	3/8 (38%)
2-Year study	18/50 (36%)	21/47 (45%)	17/52 (33%)	5/51 (10%)

[a] Number of lesion-bearing animals/number of animals with kidney examined microscopically at the 15-month interim evaluations
[b] Number of lesion-bearing animals/number of animals with kidney examined microscopically at the end of the studies
[c] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The logistic regression test regards these lesions as nonfatal.
[d] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 6/820 (0.7% ± 1.0%); range 0%-2%.
[e] Historical incidence: 0/819

and cast formation, regeneration of the epithelium, interstitial fibrosis, and chronic inflammation. The severity of nephropathy was judged by the extent of the disease process. Involvement of less than 25% of the renal tubules was considered minimal (grade 1), 25% to 50% was mild (grade 2), 50% to 75% was moderate (grade 3), and greater than 75% was marked (grade 4).

Preputial Gland and Clitoral Gland: The preputial gland in males and the clitoral gland in females are homologous organs. They are paired, modified sebaceous glands lying in the subcutaneous tissue lateral to the base of the penis or clitoris. In dosed males, preputial gland adenomas or carcinomas (combined) occurred with a significant positive trend, and the incidence in 30 mg/kg males was significantly increased (Tables 11 and A3). In dosed females, a similar significant positive trend for clitoral gland neoplasms occurred, and the incidences in both the 10 and 30 mg/kg groups were significantly increased. Several rats, particularly in the 10 or 30 mg/kg groups, had bilateral neoplasms (Tables A1 and B1). Focal hyperplasia of the preputial or clitoral gland was observed in several dosed males and females (Tables A5 and B5).

Mammary Gland: Adenocarcinomas of the mammary gland occurred with a dose-related increased incidence in female rats (Tables 12 and B3), and the incidences in the 10 and 30 mg/kg groups were significantly increased. Although fibroadenomas occurred more frequently in the 3 and 10 mg/kg females than in the controls, only the incidence in the 10 mg/kg group was significantly increased. Adenomas of the mammary gland occurred in one control, three 10 mg/kg, and one 30 mg/kg female.

The adenomas were discrete, nonencapsulated masses consisting of regularly arranged alveoli or ductules lined by a single layer of well-differentiated epithelium. They were distinguished from fibroadenomas by the lack of a proliferating stroma. Whereas the adenomas were relatively small, the fibroadenomas were often many centimeters in diameter and had a prominent connective tissue component. The adenocarcinomas were less well circumscribed and exhibited a broad range of histologic patterns including papillary, ductular, or alveolar structures and combinations of these patterns. The neoplastic epithelium formed single or multiple layers, and small solid clusters of cells were sometimes present. Cellular pleomorphism and atypia were present to varying degrees.

Unlike the development of neoplasms in many other tissues in rats, no clear morphologic continuum was apparent for the development of mammary gland adenocarcinomas. The reason that definitive preneoplastic lesions were not identified may be related to the wide dispersion and separation of mammary ducts and alveoli in the mammary fat and the method of sampling. Studies have shown that adenocarcinomas often arise from areas of ductule hyperplasia; progression is usually rapid and distinct morphologically benign stages are not often seen. Although adenocarcinomas have been observed arising within fibroadenomas, this generally occurs only in a low percentage of animals, and fibroadenomas are usually considered end-stage benign neoplasms.

Zymbal's Gland: The Zymbal's glands are specialized sebaceous glands about 3 to 5 mm in diameter lying anteroventral to the orifices of the external ears. Zymbal's glands were examined microscopically when they were observed to be grossly abnormal or enlarged at necropsy. Carcinomas of the Zymbal's gland occurred in one 3 mg/kg and three 30 mg/kg females and in three 30 mg/kg males; none occurred in the controls (Tables 13, A3, and B3). One 30 mg/kg female rat examined at the 15-month interim evaluation also had a carcinoma.

Zymbal's gland carcinomas are relatively fast growing and highly invasive, producing weight loss and debilitation. Thus, the life table test is considered the most appropriate analysis. The trend test was highly significant for both males and females, but only the incidence in 30 mg/kg females was significantly greater than that in controls (Tables 13 and B3). Zymbal's gland carcinomas are relatively uncommon in F344/N rats. The incidence of this neoplasm in NTP historical controls is 10/820 in males and 5/820 in females (Tables A4e and B4e). Although the incidences of Zymbal's gland carcinoma in rats receiving 30 mg/kg were low and close to the highest incidence in historical controls, the mean life span of these groups was considerably shortened by the development of neoplasms at other sites and was shorter than that of historical controls. Thus, the Zymbal's gland carcinomas were considered to be related to the administration of 1,2,3-trichloropropane.

TABLE 11
Incidence of Preputial Gland and Clitoral Gland Neoplasms in Rats in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male (Preputial Gland)				
Adenoma[a]				
15-Month interim evaluation[b]	0/10 (0%)	0/10 (0%)	1/10 (10%)	0/8 (0%)
2-Year study[c]	5/49 (10%)	3/47 (6%)	5/49 (10%)	11/50 (22%)
Logistic regression test[d]	P=0.002	P=0.363N	P=0.404	P=0.023
Carcinoma[e]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/8 (13%)
2-Year study	0/49 (0%)	3/47 (6%)	3/49 (6%)	5/50 (10%)
Logistic regression test	P=0.103	P=0.118	P=0.152	P=0.164
Adenoma or Carcinoma[f]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	1/8 (13%)
2-Year study	5/49 (10%)	6/47 (13%)	8/49 (16%)	16/50 (32%)
Logistic regression test	P<0.001	P=0.491	P=0.163	P=0.007
Female (Clitoral Gland)				
Adenoma[g]				
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	1/8 (13%)	2/8 (25%)
2-Year study	5/46 (11%)	10/46 (22%)	13/50 (26%)	10/51 (20%)
Logistic regression test	P<0.001	P=0.098	P=0.001	P=0.030
Carcinoma[h]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
2-Year study	0/46 (0%)	0/46 (0%)	4/50 (8%)	6/51 (12%)
Logistic regression test	P=0.404	-[i]	P=0.176	P=0.246
Adenoma or Carcinoma[j]				
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	1/8 (13%)	2/8 (25%)
2-Year study	5/46 (11%)	10/46 (22%)	17/50 (34%)	15/51 (29%)
Logistic regression test	P<0.001	P=0.098	P<0.001	P=0.013

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 38/820 (4.6% ± 4.2%) range 0%-12%
[b] Number of neoplasm-bearing animals/number of animals with preputial or clitoral gland examined microscopically at the 15-month interim evaluations
[c] Number of neoplasm-bearing animals/number of animals with preputial or clitoral gland examined microscopically at the end of the studies
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The logistic regression test regards these lesions as nonfatal. For all tests, a lower incidence in a dose group is indicated by **N**.
[e] Historical incidence: 22/820 (2.7% ± 4.0%); range 0%-12%
[f] Historical incidence: 60/820 (7.3% ± 5.9%); range 0%-20%
[g] Historical incidence: 62/820 (7.6% ± 5.4%); range 0%-20%
[h] Historical incidence: 12/820 (1.5% ± 1.9%); range 0%-6%
[i] Not applicable; no neoplasms in animal group
[j] Historical incidence: 74/820 (9.0% ± 6.0%); range 2%-22%

TABLE 12
Incidence of Mammary Gland Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Adenoma[a]				
15-Month interim evaluation[b]	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
2-Year study[c]	1/50 (2%)	0/49 (0%)	3/52 (6%)	0/52 (0%)
Logistic regression test[d]	P=0.337	P=0.497N	P=0.256	P=0.625
Fibroadenoma[e]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
2-Year study	15/50 (30%)	23/49 (47%)	20/52 (38%)	1/52 (2%)
Logistic regression test	P=0.249	P=0.078	P=0.016	P=0.306N
Adenocarcinoma[f]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
2-Year study	1/50 (2%)	6/49 (12%)	12/52 (23%)	21/52 (40%)
Life table test[d]	P<0.001	P=0.059	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.057	P=0.003	P=0.014

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 8/820 (1.0% ± 1.8%) range 0%-6%
[b] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluations
[c] Number of neoplasm-bearing animals/number of animals necropsied at the end of the studies
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The life table test regards neoplasms in animals dying prior to terminal kill as being, directly or indirectly, the cause of death. The logistic regression test regards these lesions as nonfatal. For all tests, a lower incidence in a dose group is indicated by **N**.
[e] Historical incidence: 314/820 (38.3% ± 10.8%); range 18%-56%
[f] Historical incidence: 25/820 (3.0% ± 2.6%); range 0%-8%

Intestine: Adenomatous polyps or adenocarcinomas of the intestine occurred in two males and one female receiving 10 mg/kg and three males and two females receiving 30 mg/kg; none occurred in the controls (Tables A2 and B2). The number of rats affected in any particular dose group was low and not significantly greater than the number of affected controls; however, intestinal neoplasms are uncommon in F344/N rats. The incidences of small intestine neoplasms in NTP historical controls are 1/820 (males) and 0/820 (females) (Tables A4g and B4h), and the historical control incidences for large intestine neoplasms are 0/820 (males) and 1/820 (females) (Tables A4h and B4i). In view of the reduced survival and shortened life span of 30 mg/kg rats, the few neoplasms of the intestine observed in this dose group may have been chemical related.

Skin: There was a dose-related increased incidence of squamous cell papillomas and squamous cell papillomas or carcinomas (combined) in male rats (Table A3). However, the incidences of squamous cell papillomas or carcinomas in any male dose group were not significantly greater than those in the controls. Therefore, these neoplasms were not considered to be chemical related.

Liver: Significant positive trends for hepatocellular adenoma or carcinoma (combined) occurred in male rats (Table A3). Since the combined incidence of hepatocellular adenoma or carcinoma was not significantly increased in any dose group, these neoplasms were not considered to be related to 1,2,3-trichloropropane administration.

TABLE 13
Incidence of Zymbal's Gland Carcinomas in Rats in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
Carcinoma[a]				
15-Month interim evaluation[b]	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
2-Year study[c]	0/50 (0%)	0/50 (0%)	0/49 (0%)	3/52 (6%)
Life table test[d]	P=0.005	-[e]	-	P=0.093
Logistic regression test[d]	P=0.058	-	-	P=0.441
Female				
Carcinoma[f]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
2-Year study	0/50 (0%)	1/49 (2%)	0/52 (0%)	3/52 (6%)
Life table test	P<0.001	P=0.506	-	P=0.003
Logistic regression test	P=0.028	P=0.503	-	P=0.103

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 10/820 (1.2% ± 1.6%) range 0%-5%
[b] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluations
[c] Number of neoplasm-bearing animals/number of animals necropsied at the end of the studies
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The life table test regards neoplasms in animals dying prior to terminal kill as being, directly or indirectly, the cause of death. The logistic regression test regards these lesions as nonfatal.
[e] Not applicable; no neoplasms in animal group
[f] Historical incidence: 5/820 (0.6% ± 1.2%); range 0%-4%

MICE

17-Week Studies

In mice receiving 250 mg/kg, 16 males died by the end of week 4 and 7 females died by the end of week 2 (Table 14). In addition, one 250 mg/kg female died after the last day of chemical administration but before necropsy evaluation. No other chemical-related deaths occurred. Final mean body weights and mean body weight gains of dosed mice were similar to those of the controls, except for lower mean body weight gains in surviving males in the 250 mg/kg group. No clinical findings in mice were related to the administration of 1,2,3-trichloropropane.

TABLE 14
Survival and Mean Body Weights of Mice in the 17-Week Gavage Studies of 1,2,3-Trichloropropane

Dose (mg/kg)	8-Week Interim Evaluation[a]	Survival[b]	Mean Body Weight (g)[c] Initial	Final	Change	Final Weight Relative to Controls (%)
Male						
0[d]	10	18/20	21.6 ± 0.5	32.3 ± 0.6	10.9 ± 0.5	
8	10	10/10	20.7 ± 0.5	32.6 ± 0.5	10.9 ± 0.6	101
16[e]	9	10/10	21.4 ± 0.4	31.6 ± 0.6	10.3 ± 0.5	98
32[f]	9	10/10	20.8 ± 0.5	33.2 ± 0.8	11.6 ± 0.7	103
63[e]	9	10/10	21.6 ± 0.4	32.1 ± 0.5	10.9 ± 0.5	99
125[g]	8	8/10	20.7 ± 0.5	33.9 ± 0.8	12.7 ± 0.7	105
250[h]	2	2/10	21.9 ± 0.4	29.7 ± 0.9	6.1 ± 0.2**	92
Female						
0[d]	10	18/20	16.8 ± 0.2	24.2 ± 0.4	7.4 ± 0.3	
8	10	10/10	17.1 ± 0.3	24.4 ± 0.7	7.6 ± 0.4	101
16[i]	9	8/10	16.4 ± 0.3	25.7 ± 0.9	8.8 ± 0.6	106
32	10	10/10	17.4 ± 0.3	25.0 ± 0.4	7.7 ± 0.4	103
63[e]	9	10/10	17.4 ± 0.3	25.7 ± 1.2	8.7 ± 0.9	106
125[f]	9	10/10	17.0 ± 0.2	25.9 ± 0.8	8.8 ± 0.6	107
250[j]	6	7/10	16.4 ± 0.3	25.0 ± 0.7	8.4 ± 0.4	103

** Significantly different ($P \leq 0.01$) from the control group by Williams' or Dunnett's test
[a] Number of animals killed for the 8-week interim evaluation
[b] Number of animals surviving/number initially in group minus animals killed for the 8-week interim evaluations
[c] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the studies.
[d] Week of death: 2, 2
[e] Week of death: 2
[f] Week of death: 1
[g] Week of death: 1, 1, 1, 2
[h] Week of death: 6 week 1, 1 week 2, 9 week 4
[i] Week of death: 1, 3, 11
[j] Week of death: 1, 1, 1, 1, 1, 2, 2

At 17 weeks, absolute and relative liver weights increased with dose and were significantly greater than those of the controls in males receiving 125 mg/kg and females receiving 125 or 250 mg/kg (Table F3). These dose-related increased liver weights in mice were consistent with the histopathologic findings. No differences in hematologic or clinical chemistry parameters were considered related to the administration of 1,2,3-trichloropropane (Tables G4 and G5).

In mice administered 1,2,3-trichloropropane for up to 17 weeks, the principal toxic lesions occurred in the liver, lung, and forestomach. The incidences of selected chemical-related lesions observed at the 8-week interim evaluations and the incidences of lesions in animals dying early or surviving to the end of the 17-week studies are shown in Table 15. In mice receiving 250 mg/kg, the liver and lung lesions were generally more severe in those dying before the end of the studies than in those surviving to the end of the studies. Similar, but less severe, lesions were also seen at the 8-week interim evaluations in males receiving 125 mg/kg and females receiving 250 mg/kg. Lesions of the forestomach were observed primarily in animals surviving until the end of the studies.

The lesions in the liver consisted of focal hepatocellular necrosis, often located in the subserosal parenchyma, and did not occur with a lobular distribution. Hepatocellular degeneration associated with fatty change and karyomegaly were also observed. Necrosis, regeneration, and hyperplasia of the bronchiolar epithelium were observed primarily in the lungs of mice receiving 250 mg/kg that died early. The bronchiolar lesions were characterized by focal or multifocal desquamation of necrotic cells in the airways, flattened epithelium with loss of differentiated cells (regeneration occurred presumably to replace lost cells or to cover the denuded basement membranes), and thickened epithelium with an increase in goblet cells (hyperplasia). Minimal, but morphologically similar, lung changes were noted in the 125 mg/kg males and females at the end of the studies. At the 8-week interim evaluations and at the end of the studies, a number of male and female mice receiving 250 mg/kg had minimal acanthosis (hyperplasia) or hyperkeratosis of the forestomach. Additionally, one female in the 250 mg/kg group died of malignant lymphoma 2 days prior to the end of the studies.

Dose Selection Rationale: In the 17-week studies, 16/20 males and 7/20 females receiving 250 mg/kg died before the end of the studies. Moreover, lesions of the liver and lung in mice receiving 125 or 250 mg/kg were considered potentially life threatening with prolonged administration of the chemical, thus precluding the use of doses of 125 mg/kg or more in the 2-year studies. A high dose of 60 mg/kg was selected for the 2-year studies with lower doses of 6 and 20 mg/kg to provide adequate dose-response data.

TABLE 15
Incidences of Selected Lesions in Mice at the 8-Week Interim Evaluations and in the 17-Week Gavage Studies of 1,2,3-Trichloropropane[a]

Dose	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg	250 mg/kg
Male							
8-Week Interim Evaluation							
Liver[b]	10	10	10	10	9	8	1
Necrosis[c]	0	0	0	0	0	6**	0
Karyomegaly	0	0	0	0	0	1	0
Lung/bronchiole	10	10	10	10	9	8	1
Regeneration	0	0	1	0	0	1	1
Forestomach	10	10	10	10	9	8	1
Hyperkeratosis	0	0	0	0	0	6**	1
17-Week Study							
Liver	10	10	10	10	10	12	19
Necrosis	1	0	0	0	0	1	14**
Karyomegaly	0	0	0	0	0	1	11**
Lung/bronchiole	10	10	10	10	10	12	19
Regeneration	0	0	0	0	0	9**	14**
Hyperplasia	0	0	0	0	0	0	2
Necrosis	0	0	0	0	0	0	3
Forestomach	10	10	10	10	10	12	19
Hyperkeratosis	0	0	0	0	0	7**	4
Acanthosis[d]	0	0	0	0	0	2	1

(continued)

TABLE 15
Incidences of Selected Lesions in Mice at the 8-Week Interim Evaluations and in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

Dose	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg	250 mg/kg
Female							
8-Week Interim Evaluation							
Liver	10	10	10	10	10	8	6
Necrosis	0	0	0	0	0	0	4**
Karyomegaly	0	0	0	0	0	0	2
Lung/bronchiole	10	10	10	10	10	8	6
Regeneration	0	0	0	0	0	0	5**
Forestomach	10	10	10	10	10	8	6
Hyperkeratosis	4	0	0	0	0	0	6*
Acanthosis	0	0	0	0	0	0	1
17-Week Study							
Liver	10	10	10	10	9	12	14
Necrosis	0	0	0	0	0	1	5*
Karyomegaly	0	0	0	0	0	0	1
Lung	10	10	10	10	9	12	14
Regeneration	0	0	0	0	7**	10**	7**
Hyperplasia	0	0	0	0	0	0	2
Necrosis	0	0	0	0	0	0	1
Forestomach	10	10	10	10	9	12	14
Hyperkeratosis	0	0	0	0	7**	9**	8**
Acanthosis	0	0	0	0	5*	8**	7**

* Significantly different ($P \leq 0.05$) from the control group by the Fisher exact test
** $P \leq 0.01$
[a] Male and female mice designated for the interim evaluations that died during the studies are included in the number of animals examined at the end of the studies.
[b] Number of mice with organ examined microscopically
[c] Number of animals with lesions
[d] The term acanthosis was used synonymously with hyperplasia.

2-Year Studies

15-Month Interim Evaluations

At the 15-month interim evaluations, nonneoplastic lesions or neoplasms of the forestomach and liver occurred primarily in 20 and 60 mg/kg mice and were similar to those seen in animals killed moribund or dying before and after the 15-month interim evaluations. Squamous cell papillomas or squamous cell carcinomas of the forestomach occurred in all 60 mg/kg male mice, in 88% of the 6 mg/kg males, in all 20 and 60 mg/kg female mice, and in 60% of the 6 mg/kg female mice (Tables C1 and D1). Most mice receiving 20 and 60 mg/kg had both squamous cell papillomas and carcinomas, whereas mice in the 6 mg/kg groups generally had a single squamous cell papilloma. Focal hyperplasia of the forestomach epithelium also occurred in all dosed female mice, in all 6 and 60 mg/kg males, and in 83% of the 20 mg/kg males (Tables C5 and D5).

Evaluations of hematologic parameters showed a chemical-related decrease in erythrocyte counts, hematocrit, and hemoglobin concentrations in male and female mice receiving 20 or 60 mg/kg (Table G6). The decrease in hematocrit may have been related to depression of hematopoiesis or to blood loss from neoplasms in the forestomach. Total leukocyte counts, principally increased numbers of segmented neutrophils, were substantially higher in 60 mg/kg mice likely due to inflammation associated with the chemical-induced neoplasms. No other differences in clinical chemistry parameters were considered to be related to the administration of 1,2,3-trichloropropane.

Hepatocellular adenomas were observed in all 60 mg/kg females and in two 60 mg/kg males; similar benign liver neoplasms were observed in only one male and one female control (Tables C1 and D1). Eosinophilic foci, a possible precursor of adenoma, were seen in all 60 mg/kg females.

Survival

Estimates of 2-year survival probabilities for male and female mice are shown in Table 16 and in the Kaplan-Meier curves in Figure 3. Survival of all dosed groups of male and female mice was significantly lower than that of the controls. Early deaths of 60 mg/kg mice between weeks 53 and 70 were due to the development of chemical-related neoplasms, primarily in the forestomach. Of the surviving 60 mg/kg mice, the males were killed in week 79 and the females were killed in week 73. Survival of the 20 mg/kg mice dropped sharply after week 65, also due to chemical-induced neoplasms, and continued to decline until the surviving mice in these groups were killed at week 89. The male and female 20 and 60 mg/kg groups were terminated because additional relevant information would not be gained by allowing them to live longer.

Body Weights and Clinical Findings

The mean body weights of 60 mg/kg male mice were consistently lower than those of the controls after week 21 (Figure 4 and Table 17). The final mean body weight of 60 mg/kg males at week 77 was 16% lower than that of the controls. The mean body weight of 20 mg/kg males was within 5% of that of the controls until week 85, but was 13% lower than that of the controls at week 89 when all surviving 20 mg/kg males were killed. The final mean body weight of the 6 mg/kg males at week 103 was 8% lower than the controls.

Weekly mean body weights of the 60 mg/kg female mice were consistently lower than those of the controls after week 29; the final mean body weight of this group at week 69 was 18% lower than that of the controls (Table 18 and Figure 4). Body weights of 6 and 20 mg/kg female mice were within 7% of that of the controls throughout the study.

No clinical findings were considered to be directly related to organ toxicity other than those associated with chemical-induced neoplasms. The clinical findings in mice killed moribund or dying before the end of the studies included emaciation, lethargy, or tissue masses.

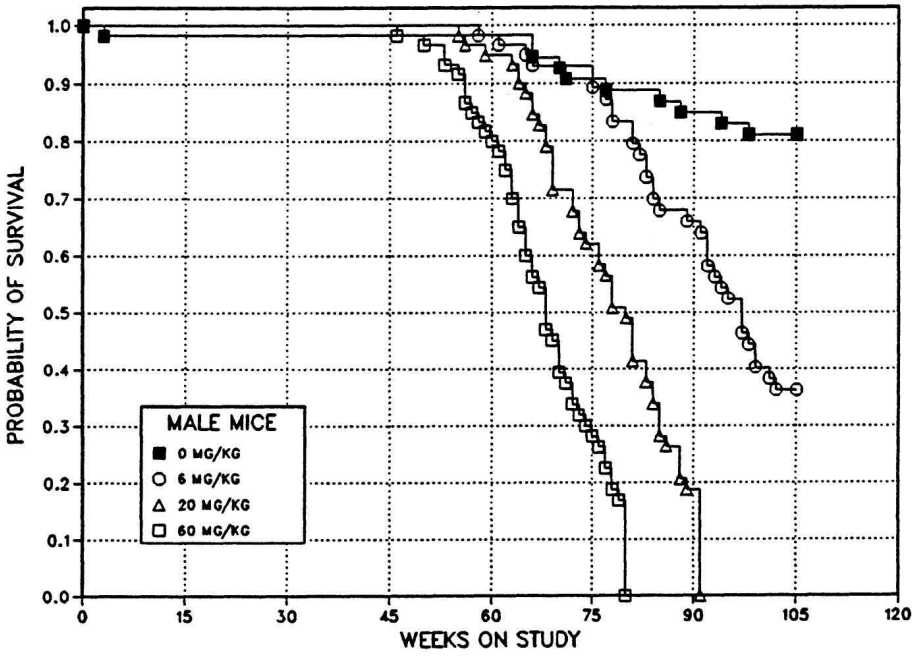
Sentinel Animals

Serum samples from sentinel mice tested for virus and *Mycoplasma* antibodies were negative throughout the studies, except for samples from several males and females at 10 and 11 months, which were positive for Reovirus 3 (Reo 3), and one from a female, which was positive for *Mycoplasma arthritidis* at 11 months (Table J1). Subsequent serum samples were negative for Reo 3 and *Mycoplasma arthritidis*.

TABLE 16
Survival of Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Male				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	8	8	6	4
Natural deaths	7	7	4	3
Moribund	3	26	40	44
Scheduled sacrifice	0	0	10	9
Missexed[a]	0	1	0	0
Animals surviving to study termination	42	18	0	0
Percent probability of survival at end of study[b]	81	36	0	0
Mean survival days[c]	655	617	531	470
Survival analysis[d]	P<0.001	P<0.001	P<0.001	P<0.001
Female				
Animals initially in study	60	60	60	60
15-Month interim evaluation[a]	10	10	9	5
Natural deaths	1	3	4	1
Moribund	8	34	37	48
Accidental deaths[a]	0	0	1	0
Scheduled sacrifice	0	0	9	6
Animals surviving to study termination	41	13	0	0
Percent probability of survival at end of study	82	26	0	0
Mean survival days	661	601	515	453
Survival analysis	P<0.001	P<0.001	P<0.001	P<0.001

[a] Censored from survival analyses
[b] Kaplan-Meier determinations
[c] Mean of all deaths (uncensored, censored, terminal sacrifice)
[d] The entry under the "Vehicle Control" column is associated with the life table trend test (Tarone, 1975). Subsequent entries are the results of pairwise tests (Cox, 1972).



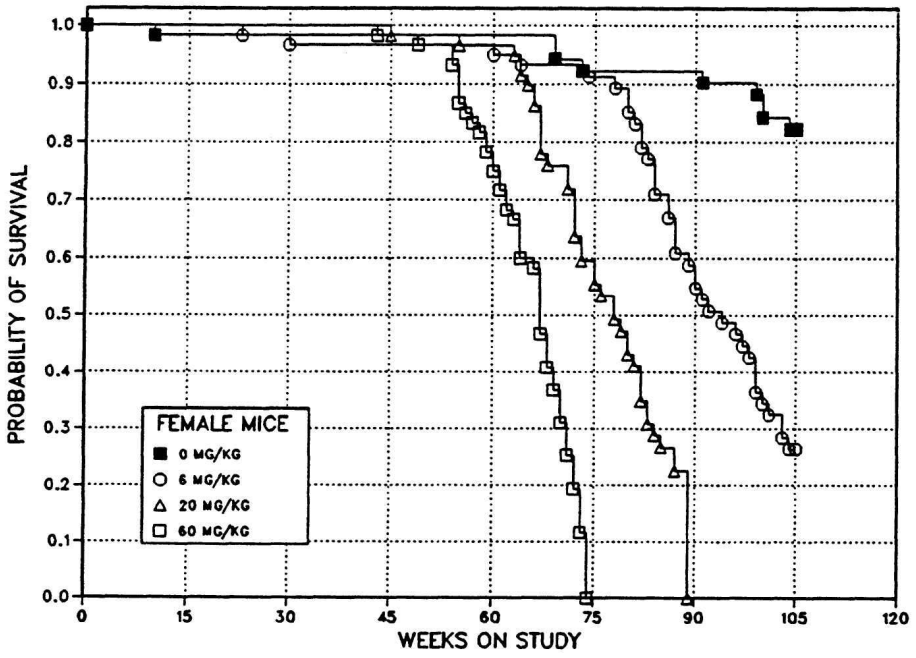


FIGURE 3
Kaplan-Meier Survival Curves for Male and Female Mice Administered 1,2,3-Trichloropropane by Gavage for 2 Years

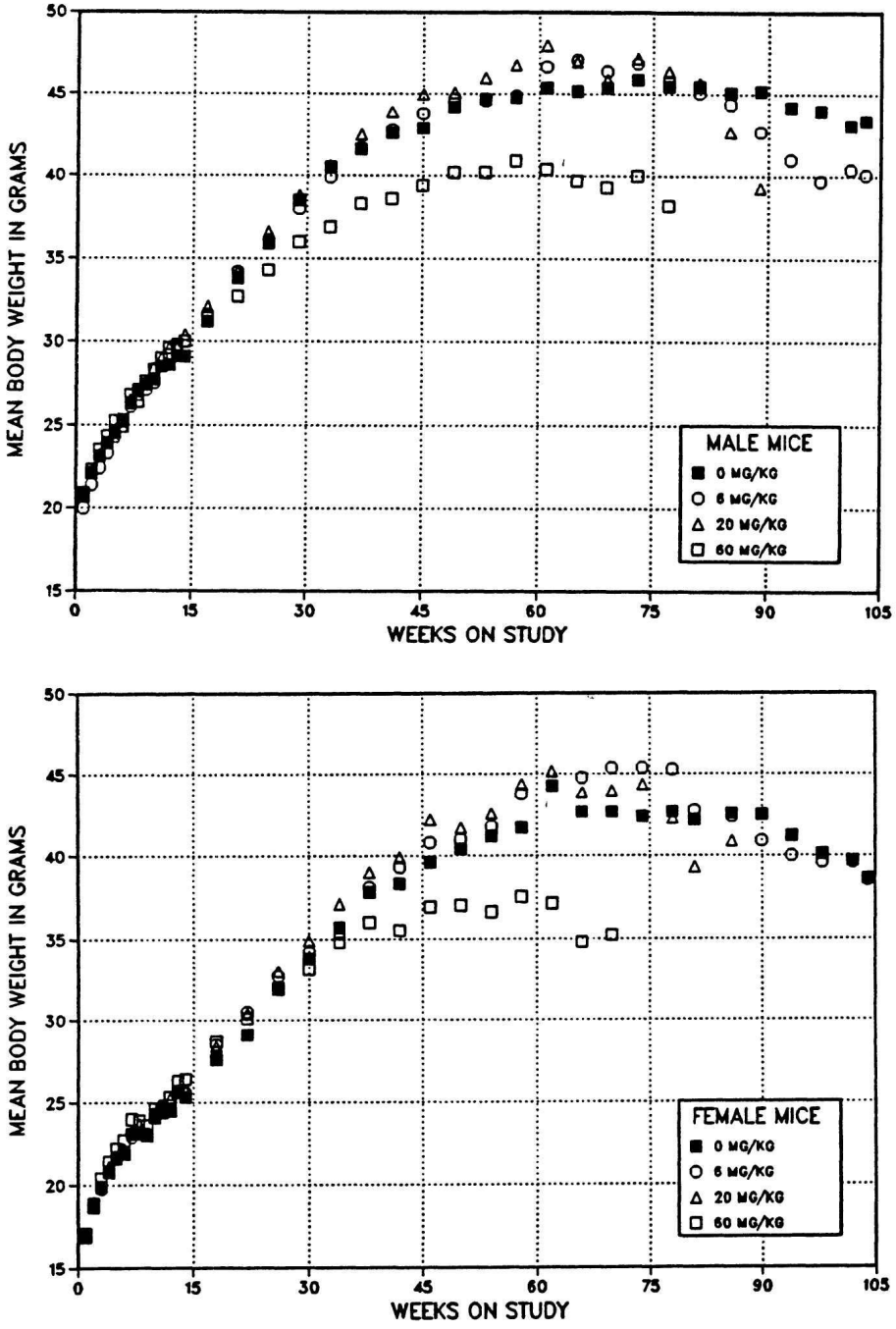


FIGURE 4
Growth Curves for Male and Female Mice Administered 1,2,3-Trichloropropane by Gavage for 2 Years

TABLE 17
Mean Body Weights and Survival of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane

Weeks on Study	Vehicle Control		6 mg/kg			20 mg/kg			60 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	20.9	60	20.0	96	60	20.7	99	60	20.8	100	60
2	22.1	60	21.4	97	60	22.2	101	60	22.3	101	60
3	23.1	60	22.4	97	60	23.2	100	60	23.5	102	60
4	23.9	59	23.3	98	60	23.9	100	60	24.3	102	60
5	24.5	59	24.3	99	60	24.7	101	60	25.2	103	60
6	25.3	59	24.9	98	60	24.9	98	60	25.2	100	60
7	26.3	59	26.1	99	60	26.5	101	60	26.8	102	60
8	27.1	59	26.8	99	60	27.0	100	60	26.4	97	60
9	27.4	59	27.1	99	60	27.6	101	60	27.6	101	60
10	27.7	59	27.5	99	60	28.4	103	60	28.3	102	60
11	28.5	59	28.5	100	60	29.0	102	60	29.0	102	60
12	28.6	59	29.2	102	60	29.6	104	60	29.6	104	60
13	29.1	59	29.5	101	60	29.7	102	60	29.8	102	60
14	29.1	59	30.0	103	60	30.4	105	60	30.0	103	60
17	31.2	59	31.6	101	60	32.1	103	60	31.2	100	60
21	33.8	59	34.2	101	60	34.2	101	60	32.7	97	60
25	35.9	59	36.1	101	60	36.6	102	60	34.3	96	60
29	38.5	59	38.0	99	60	38.8	101	60	36.0	94	60
33	40.5	59	39.9	99	60	40.6	100	60	36.9	91	60
37	41.6	59	41.7	100	60	42.5	102	60	38.3	92	60
41	42.6	59	42.8	101	60	43.9	103	60	38.6	91	60
45	42.9	59	43.8	102	60	45.0	105	60	39.4	92	60
49	44.2	59	44.7	101	60	45.1	102	60	40.2	91	59
53	44.7	59	44.6	100	60	46.0	103	60	40.2	90	58
57	44.8	59	44.9	100	60	46.8	105	58	40.9	91	52
61	45.4	59	46.7	103	59	48.0	106	57	40.4	89	48
65	45.2	59	47.1	104	58	47.0	104	54	39.7	88	39
69[a]	45.4	49	46.4	102	48	45.9	101	42	39.3	87	25
73	45.9	47	46.9	102	48	47.2	103	34	40.0	87	18
77	45.5	46	45.8	101	46	46.4	102	31	38.2	84	14[b]
81	45.5	46	45.1	99	41	45.7	100	22			
85	45.1	46	44.4	98	36	42.7	95	18			
89	45.2	44	42.7	95	35	39.3	87	11[c]			
93	44.2	44	41.0	93	29						
97	44.0	43	39.7	90	26						
101	43.1	42	40.4	94	20						
103	43.4	42	40.1	92	18						
Terminal sacrifice		42			18						
Mean for weeks											
1-13	25.7		25.5	99		26.0	101		26.1	101	
14-52	38.0		38.3	101		38.9	102		35.8	95	
53-103	44.8		44.0	98		45.5	101		39.8	88	

[a] Interim evaluation occurred.
[b] Surviving members of the 60 mg/kg group were killed at week 79.
[c] Surviving members of the 20 mg/kg group were killed at week 89.

TABLE 18
Mean Body Weights and Survival of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane

Weeks on Study	Vehicle Control		6 mg/kg			20 mg/kg			60 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	17.1	60	17.1	100	60	17.0	99	60	16.9	99	60
2	19.4	60	19.3	100	60	19.4	100	60	19.6	101	60
3	20.8	60	20.8	100	60	21.1	101	59	21.4	103	60
4	21.6	60	21.7	101	60	21.7	101	59	22.2	103	60
5	21.9	60	22.0	101	60	22.2	101	59	22.7	104	60
7	23.1	60	22.9	99	60	23.2	100	59	24.0	104	60
8	23.1	60	23.1	100	60	23.4	101	59	23.8	103	60
9	24.1	60	24.3	101	60	24.3	101	59	24.6	102	60
10	24.4	59	24.8	102	60	24.8	102	59	24.5	100	60
11	24.5	59	24.8	101	60	25.2	103	59	25.3	103	60
13	25.4	59	25.6	101	60	25.7	101	59	26.3	104	60
17	27.6	59	28.5	103	60	28.4	103	59	28.7	104	60
21	29.1	59	30.5	105	60	30.4	105	59	30.1	103	60
25	31.9	59	32.7	103	59	33.0	103	59	32.0	100	60
29	33.8	59	34.2	101	59	34.9	103	59	33.1	98	60
33	35.7	59	35.3	99	58	37.1	104	59	34.8	98	60
38	37.8	59	38.1	101	58	39.0	103	59	36.0	95	60
41	38.3	59	39.3	103	58	39.9	104	59	35.5	93	60
45	39.6	59	40.8	103	58	42.2	107	58	36.9	93	59
49	40.4	59	41.0	102	58	41.7	103	58	37.0	92	58
53	41.2	59	41.8	102	58	42.6	103	58	36.6	89	58
57	41.7	59	43.8	105	58	44.4	107	57	37.5	90	50
61	44.3	59	44.3	100	57	45.2	102	57	37.1	84	44
65	42.7	59	44.8	105	56	43.9	103	53	34.8	82	36
69[a]	42.7	47	45.4	106	46	44.0	103	37	35.2	82	19[b]
73	42.4	47	45.4	107	46	44.4	105	29			
77	42.7	46	45.3	106	45	42.3	99	26			
81	42.2	46	42.8	101	42	39.3	93	21			
86	42.6	46	42.4	100	35	40.9	96	13[c]			
89	42.5	46	40.9	96	30						
94	41.2	45	40.0	97	25						
98	40.1	45	39.6	99	21						
102	39.7	42	39.6	100	16						
104	38.6	42	38.5	100	14						
Terminal sacrifice		41			13						
Mean for weeks											
1-13	22.3		22.4	100		22.5	101		22.8	102	
14-52	34.9		35.6	102		36.6	104		33.8	97	
53-104	41.8		42.5	102		43.0	101		36.2	85	

[a] Interim evaluation occurred.
[b] Surviving members of the 60 mg/kg group were killed at week 73.
[c] Surviving members of the 20 mg/kg group were killed at week 89.

Pathology and Statistical Analyses of Results

Statistically significant or biologically noteworthy neoplasms or nonneoplastic lesions of the oral mucosa, forestomach, liver, harderian gland, uterus, and large intestine occurred in mice receiving 1,2,3-trichloropropane. The occurrence, statistical analyses, and historical incidences of these lesions in the NTP 2-year studies are presented in Appendix C for male mice and Appendix D for female mice.

Oral Mucosa (Pharynx and Tongue): In contrast to dosed rats, there were few neoplasms of the oral mucosa in dosed mice. Nevertheless, squamous cell carcinomas arising from the pharyngeal or lingual mucosa were observed in one 20 mg/kg and five 60 mg/kg females, and none were seen in the controls (Tables 19 and D3). The incidence of squamous cell carcinoma in the 60 mg/kg females was significantly increased by the life table analysis. Squamous cell papillomas were seen in one control and one 20 mg/kg female. No squamous cell carcinomas were observed in the oral mucosa of males, but squamous cell papillomas were observed in two 60 mg/kg males (Tables 19 and C1).

Squamous cell papillomas and carcinomas of the oral mucosa are rare spontaneous neoplasms of mice. None were observed in the 700 male and 698 female NTP historical controls (Tables C4a and D4a). Although it is clear that the squamous cell carcinomas in females are due to the administration of 1,2,3-trichloropropane, it is uncertain if the two squamous cell papillomas in 60 mg/kg males were chemical related.

Forestomach: Exophytic papillary or nodular masses similar to those in the forestomach of rats were observed in the forestomach of nearly all dosed male and female mice at necropsy (Tables 20, C3, and D3). The masses were squamous cell papillomas or carcinomas arising from the stratified squamous epithelium of the forestomach. Multiple or single squamous cell papillomas or squamous cell papillomas and carcinomas often occurred in the same mouse, and in some mice the neoplasms were so extensive that it was difficult to determine if they constituted a single neoplasm or the confluent growth of several neoplasms. The incidences of squamous cell papilloma or carcinoma in each dosed male and female mouse group were significantly increased. There was no apparent difference in the incidences of these neoplasms between sexes.

A dose-related increase in the incidence of focal hyperplasia of the stratified squamous epithelium also occurred in male mice receiving 1,2,3-trichloropropane (Table C5). However, the incidence of hyperplasia in female mice was markedly increased only in the 60 mg/kg group (Table D5). Hyperplasia consisted of focally thickened epithelium forming short rugae or papillae (squamous hyperplasia). Hyperplasia, squamous cell papilloma, and squamous cell carcinoma of the forestomach constituted a morphologic continuum, and the squamous cell papillomas and carcinomas were morphologically similar to those seen in rats.

Liver: Hepatocellular adenoma and adenoma or carcinoma (combined) occurred with a significant positive trend in dosed male and female mice (Tables 21, C3, and D3), and the incidences in 20 and 60 mg/kg males and 60 mg/kg females were significantly greater than in controls. The incidence of hepatocellular carcinoma, however, was significantly increased only in 6 mg/kg males. Many mice in the 60 mg/kg groups had multiple adenomas or both adenoma and carcinoma (Tables C2 and D2).

Eosinophilic foci occurred more frequently in 20 and 60 mg/kg male mice, and in all dosed groups of female mice than in controls; eosinophilic foci occurred in over 50% of females in the 60 mg/kg group (Tables C5 and D5). Basophilic foci were seen in small numbers of dosed male mice, but not in the controls. No apparent pattern in the incidences of clear cell or mixed cell foci occurred in dosed mice.

Foci are classified according to the predominant staining characteristics of the hepatocyte cytoplasm. The degree of cytoplasmic basophilia is usually related to the amount of rough endoplasmic reticulum and ribosomes, whereas "clear" cells are usually filled with glycogen. Mixed cell foci consist of mixtures of clear cells and either basophilic or eosinophilic cells. The various types of foci are believed to be precursors of hepatocellular adenoma. Adenomas also consist of hepatocytes with eosinophilic, basophilic, or clear cytoplasm. Adenomas are distinguished from foci on the basis of altered growth pattern (organization of the hepatic plates) and the extent of loss of lobular architecture within the mass. Carcinomas exhibit a greater degree of altered growth pattern with prominent trabeculae, cytologic pleomorphism, and cellular atypia.

TABLE 19
Incidence of Oral Mucosa Neoplasms in Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Male				
Squamous Cell Papilloma[b]				
15-Month interim evaluation[c]	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
2-Year study[d]	0/52 (0%)	0/51 (0%)	0/54 (0%)	2/56 (4%)
Logistic regression test[e]	P=0.075	-[f]	-	P=0.311
Female				
Squamous Cell Papilloma[g]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
2-Year study	1/50 (2%)	0/50 (0%)	1/51 (2%)	0/55 (0%)
Squamous Cell Carcinoma[g]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
2-Year study	0/50 (0%)	0/50 (0%)	1/51 (2%)	5/55 (10%)
Life table test[e]	P<0.001	-	P=0.370	P=0.006
Logistic regression test	P=0.008	-	P=0.552	P=0.128
Squamous Cell Papilloma or Squamous Cell Carcinoma[g]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
2-Year study	1/50 (2%)	0/50 (0%)	2/51 (4%)	5/55 (9%)
Life table test	P<0.001	P=0.728N	P=0.086	P=0.006
Logistic regression test	P=0.024	P=0.728N	P=0.365	P=0.212

[a] Incidences include neoplasms of the pharynx and tongue.
[b] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 0/700
[c] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluations
[d] Number of neoplasm-bearing animals/number of animals necropsied at the end of the studies
[e] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. A lower incidence in a dose group is indicated by N.
[f] Not applicable; no neoplasms in animal group
[g] Historical incidence: 0/698

TABLE 20
Incidence of Forestomach Neoplasms in Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Male				
Squamous Cell Papilloma[a]				
15-Month interim evaluation[b]	0/8 (0%)	7/8 (88%)	3/6 (50%)	2/4 (50%)
2-Year study[c]	3/52 (6%)	28/51 (55%)	22/54 (41%)	33/56 (59%)
Logistic regression test[d]	P<0.001	P<0.001	P<0.001	P<0.001
Squamous Cell Carcinoma[e]				
15-Month interim evaluation	0/8 (0%)	1/8 (13%)	4/6 (67%)	4/4 (100%)
2-Year study	0/52 (0%)	40/51 (78%)	50/54 (93%)	51/56 (91%)
Life table test[d]	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Squamous Cell Papilloma or Squamous Cell Carcinoma[f]				
15-Month interim evaluation	0/8 (0%)	7/8 (88%)	4/6 (67%)	4/4 (100%)
2-Year study	3/52 (6%)	50/51 (98%)	53/54 (98%)	55/56 (98%)
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Female				
Squamous Cell Papilloma[g]				
15-Month interim evaluation	0/10 (0%)	5/10 (50%)	9/9 (100%)	4/5 (80%)
2-Year study	0/50 (0%)	23/50 (46%)	18/51 (35%)	29/55 (53%)
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Squamous Cell Carcinoma[h]				
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	6/9 (67%)	2/5 (40%)
2-Year study	0/50 (0%)	46/50 (92%)	49/51 (96%)	49/55 (89%)
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Squamous Cell Papilloma or Squamous Cell Carcinoma[i]				
15-Month interim evaluation	0/10 (0%)	6/10 (60%)	9/9 (100%)	5/5 (100%)
2-Year study	0/50 (0%)	48/50 (96%)	50/51 (98%)	54/55 (98%)
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 19/700 (2.7% ± 3.7%); range 0%-14%
[b] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluations
[c] Number of neoplasm-bearing animals/number of animals necropsied at the end of the studies
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal.
[e] Historical incidence: 2/700 (0.3% ± 0.7%); range 0%-2%
[f] Historical incidence: 21/700 (3.0% ± 3.9%); range 0%-14%
[g] Historical incidence: 24/698 (3.4% ± 3.1%); range 0%-10%
[h] Historical incidence: 3/698 (0.4% ± 1.2%); range 0%-4%
[i] Historical incidence: 27/698 (3.9% ± 3.5%); range 0%-10%

TABLE 21
Incidence of Liver Neoplasms in Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Male				
Hepatocellular Adenoma[a]				
15-Month interim evaluation[b]	1/8 (13%)	0/8 (0%)	0/6 (0%)	2/4 (50%)
2-Year study[c]	11/52 (21%)	18/51 (35%)	21/54 (39%)	29/56 (52%)
Logistic regression test[d]	P<0.001	P=0.073	P=0.028	P<0.001
Hepatocellular Carcinoma[e]				
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	1/6 (17%)	0/4 (0%)
2-Year study	4/52 (8%)	11/51 (22%)	5/54 (9%)	3/56 (5%)
Logistic regression test	P=0.533	P=0.015	P=0.194	P=0.666
Hepatocellular Adenoma or Carcinoma[f]				
15-Month interim evaluation	1/8 (13%)	0/8 (0%)	1/6 (17%)	2/4 (50%)
2-Year study	13/52 (25%)	24/51 (47%)	24/54 (44%)	31/56 (55%)
Logistic regression test	P<0.001	P=0.008	P=0.007	P<0.001
Female				
Hepatocellular Adenoma[g]				
15-Month interim evaluation	1/10 (10%)	0/10 (0%)	1/9 (11%)	5/5 (100%)
2-Year study	6/50 (12%)	9/50 (18%)	8/51 (16%)	31/55 (56%)
Logistic regression test	P<0.001	P=0.164	P=0.057	P<0.001
Hepatocellular Carcinoma[h]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
2-Year study	1/50 (2%)	3/50 (6%)	0/51 (0%)	2/55 (4%)
Logistic regression test	P=0.259	P=0.242	-[i]	P=0.395
Hepatocellular Adenoma or Carcinoma[j]				
15-Month interim evaluation	1/10 (10%)	0/10 (0%)	1/9 (11%)	5/5 (100%)
2-Year study	7/50 (14%)	11/50 (22%)	8/51 (16%)	31/55 (56%)
Logistic regression test	P<0.001	P=0.093	P=0.067	P<0.001

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 162/699 (23.2% ± 11.7%); range 4%-40%
[b] Number of neoplasm-bearing animals/number of animals with liver examined microscopically at the 15-month interim evaluations
[c] Number of neoplasm-bearing animals/number of animals with liver examined microscopically at the end of the studies
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The logistic regression test regards these lesions as nonfatal.
[e] Historical incidence: 122/699 (17.5% ± 5.8%); range 10%-32%
[f] Historical incidence: 261/699 (37.3% ± 11.6%); range 14%-52%
[g] Historical incidence: 59/697 (8.5% ± 6.6%); range 2%-26%
[h] Historical incidence: 35/697 (5.0% ± 3.7%); range 2%-14%
[i] Not applicable; no neoplasms in animal group
[j] Historical incidence: 88/697 (12.6% ± 8.0%); range 2%-34%

Harderian Gland: The harderian gland is a specialized lacrimal gland located medial and posterior to the globe of the eye. Harderian glands were microscopically examined only when they were observed to be abnormal or enlarged at necropsy. Harderian gland adenomas occurred with a significant positive trend in dosed male mice, and the incidences in the 20 and 60 mg/kg groups were significantly increased by both the Fisher exact and logistic regression tests (Tables 22 and C3). There was a similar positive trend in female mice and the incidence in 60 mg/kg females was significantly increased by the Fisher exact test (Tables 22 and D3). In NTP historical control mice, harderian gland adenomas have occurred in 40/700 males (Table C4c) and in 20/698 females (Table D4c). Although the incidence of adenomas in the concurrent control group of male mice is slightly less than that of historical controls, incidences of neoplasms in the 20 and 60 mg/kg groups exceeded the upper boundary of the historical control range, despite the lower survival and shortened life span of these groups. Similarly, incidences of neoplasms in the female dose groups exceeded the historical control range. Thus, the increased incidences of harderian gland adenomas in mice were considered to be chemical related.

TABLE 22
Incidence of Harderian Gland Neoplasms in Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Male				
Adenoma[a]				
15-Month interim evaluation[b]	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
2-Year study[c]	1/52 (2%)	2/51 (4%)	10/54 (19%)	11/56 (20%)
Logistic regression test[d]	P=0.001	P=0.449	P=0.002	P=0.008
Cochran-Armitage test[d]	P=0.001			
Fisher exact test[d]		P=0.494	P=0.004	P=0.002
Female				
Adenoma[e]				
15-Month interim evaluation	1/10 (10%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
2-Year study	2/50 (4%)	6/50 (12%)	7/51 (14%)	10/55 (18%)
Logistic regression test	P=0.004	P=0.191	P=0.077	P=0.060
Cochran-Armitage test	P=0.040			
Fisher exact test		P=0.245	P=0.161	P=0.037

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 40/700 (5.7% ± 4.4%); range 0%-16%
[b] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluations
[c] Number of neoplasm-bearing animals/number of animals necropsied at the end of the studies
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall rates.
[e] Historical incidence: 20/698 (2.9% ± 2.2%); range 0%-6%

Uterus: Stromal polyps of the uterus were significantly increased in 60 mg/kg female mice (Tables 23 and D3). Uterine stromal polyps are relatively uncommon spontaneous neoplasms and have been observed in 11/698 of the historical controls (Table D4e). Since the incidence in the 60 mg/kg group exceeded the upper boundary of historical controls despite the lower survival and shortened life span of the group, the increased incidence of stromal polyps was considered to be chemical related.

The incidences of epithelial neoplasms (adenomas or adenocarcinomas combined) of the uterine endometrium were also significantly increased in all dosed groups of female mice (Tables 23 and D3). The majority of neoplasms observed were adenocarcinomas, but adenomas were seen in one 6 mg/kg and four 60 mg/kg females. Uterine endometrial neoplasms have been seen infrequently in NTP historical controls; the incidence in female mice is 3/698 (Table D4e). The uterine endometrial adenomas and adenocarcinomas in dosed female mice were considered to be related to the administration of 1,2,3-trichloropropane, since the incidences in each group exceeded the range in historical controls and were significantly greater than the concurrent controls.

Large Intestine: One squamous cell carcinoma occurred in a 60 mg/kg female mouse and another occurred in a 20 mg/kg female mouse (Table D1).

GENETIC TOXICOLOGY

1,2,3-Trichloropropane was tested for mutagenicity in *Salmonella typhimurium* by two laboratories using a preincubation protocol with and without Aroclor 1254-induced male Sprague-Dawley rat or induced Syrian hamster liver S9 (Table E1; Haworth *et al.*, 1983). Mutagenic activity was observed in strains TA97, TA100, and TA1535 in the presence of either species of S9; for strain TA98, one laboratory reported increases in revertant colonies with either species of S9, and a second laboratory reported mutagenic activity only with induced hamster S9. No increase in revertants was observed in TA1537 with or without S9.

In the mouse lymphoma assay, a positive response was obtained with 1,2,3-trichloropropane for induction of trifluorothymidine resistance in L5178Y cells in the presence of Aroclor 1254-induced male Fischer rat liver S9; the lowest effective dose was 0.01 µL (Table E2). Without S9, no induction of trifluorothymidine resistance was noted at doses below those which produced precipitation of 1,2,3-trichloropropane.

In cytogenetic tests with Chinese hamster ovary cells, 1,2,3-trichloropropane induced both sister chromatid exchanges (Table E3) and chromosomal aberrations (Table E4) in the presence of Aroclor 1254-induced male Sprague-Dawley rat liver S9; neither endpoint was significantly elevated in the absence of S9. In the single chromosomal aberrations trial without S9, an elevation in chromosomal aberrations was noted for the 943.7 µg/mL dose but the trend analysis was not significant and the call for this trial was therefore concluded to be questionable. Severe chemical-induced cytotoxicity reduced the number of scorable cells in this trial. In the chromosomal aberrations test with S9, the first trial was invalidated due to a lack of metaphase I cells available for analysis at two of the four doses tested. In trial 2, a strong induction of chromosomal aberrations was noted, along with marked cytotoxicity. The relationship, if any, between cytotoxicity and increased chromosomal aberrations has not been defined (Scott *et al.*, 1991). In the case of 1,2,3-trichloropropane, marked cytotoxicity occurred in all three chromosomal aberration trials, yet a clear induction of chromosomal aberrations was noted in only one trial. In conclusion, 1,2,3-trichloropropane demonstrated mutagenic activity in each of the *in vitro* assays conducted, and this mutagenic activity was dependent upon S9 activation.

TABLE 23
Incidence of Uterine Neoplasms in Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Stromal Polyp[a]				
15-Month interim evaluation[b]	0/10 (0%)	0/10 (0%)	1/9 (11%)	1/5 (20%)
2-Year study[c]	0/50 (0%)	2/50 (4%)	1/51 (2%)	6/54 (11%)
Logistic regression test[d]	P=0.023	P=0.165	P=0.378	P=0.074
Cochran-Armitage test[d]	P=0.002			
Fisher exact test[d]		P=0.248	P=0.248	P=0.006
Endometrium: Adenoma				
15-month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	1/5 (20%)
2-Year study	0/50 (0%)	1/50 (2%)	0/51 (0%)	3/54 (6%)
Logistic regression test	P=0.009	P=0.272	-[e]	P=0.134
Cochran-Armitage test	P=0.011			
Fisher exact test		P=0.500	-	P=0.059
Endometrium: Adenocarcinoma				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	2/5 (40%)
2-Year study	0/50 (0%)	4/50 (8%)	3/51 (6%)	6/54 (11%)
Logistic regression test	P<0.001	P=0.007	P=0.050	P=0.017
Cochran-Armitage test	P=0.006			
Fisher exact test		P=0.059	P=0.122	P=0.003
Endometrium: Adenoma or Adenocarcinoma[f]				
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	3/5 (10%)
2-Year study	0/50 (0%)	5/50 (10%)	3/51 (6%)	9/54 (17%)
Logistic regression test	P<0.001	P=0.002	P=0.050	P=0.030
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.029	P=0.122	P<0.001

[a] Historical incidence for 2-year NTP corn oil gavage studies with control groups (mean ± standard deviation): 11/698 (1.6% ± 2.0%); range 0%-6%
[b] Number of neoplasm-bearing animals/number of animals necropsied at the 15-month interim evaluation
[c] Number of neoplasm-bearing animals/number of animals necropsied at the end of the study
[d] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the vehicle controls and that dosed group. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall rates.
[e] Not applicable; no neoplasms in animal group
[f] Historical incidence: 3/698 (0.4% ± 0.9%); range 0%-2%

DISCUSSION AND CONCLUSIONS

1,2,3-Trichloropropane is a colorless liquid used as a paint and varnish remover, solvent, degreasing agent, and crosslinking agent in the synthesis of polysulfides and hexafluoropropylene. The chemical may be found as an impurity in certain nematocides and soil fumigants and has been found as a contaminant of drinking and ground water. 1,2,3-Trichloropropane was evaluated in toxicity and carcinogenicity studies because of its close structural relationship to other short-chain halogenated compounds which have been shown to be carcinogenic in experimental animals and because of the potential for human exposure.

In the 2-year studies, administration of 1,2,3-trichloropropane in corn oil by gavage to rats and mice produced high incidences of neoplasms at several sites. A carcinogenic response was evident at all dose levels even though the lowest dose administered to rats (3 mg/kg) and mice (6 mg/kg) in these studies was approximately one-tenth the maximum tolerated dose predicted by the results of the 17-week studies. Considering the proportion of rats and mice in the low-dose groups with chemical-induced neoplasms of the forestomach, carcinogenic activity might have been detected at even lower doses. Neoplasms of the forestomach in rats and mice, the oral mucosa in rats, and the mammary gland in female rats were the principal cause of death of most animals dying or killed moribund before the end of the studies. The mortality associated with chemical-induced neoplasms was so great that the 30 mg/kg rats and 20 and 60 mg/kg mice were killed before the end of the 2-year studies.

Squamous cell papillomas or carcinomas arising from the stratified squamous epithelium of the oral mucosa were observed in 72% of male rats and 62% of female rats receiving 30 mg/kg 1,2,3-trichloropropane. The mucosal epithelium of the forestomach of rats is a stratified squamous epithelium similar to that of the oral mucosa, and the neoplasms in the forestomach were morphologically similar to those in the oral mucosa. The percentage of 30 mg/kg male rats with forestomach squamous cell papillomas or carcinomas was nearly twice that of 30 mg/kg females (males, 85%; females, 45%).

The lower survival of the 30 mg/kg groups and the risk of developing neoplasms at other sites may explain the apparent incongruities in the dose-response between males and females and between the 10 and 30 mg/kg groups. For example, the proportion of 30 mg/kg female rats with neoplasms of the oral mucosa was slightly lower than that of males, while the incidence of these neoplasms was higher in 10 mg/kg females. This was likely due to the shorter life span of 30 mg/kg females and the competing risk from the development of mammary gland adenocarcinomas. Similarly, the greater incidence of forestomach carcinomas in 10 mg/kg male rats compared to 30 mg/kg male rats is due to the shorter life span of the 30 mg/kg males and the competing risk from neoplasms of the oral mucosa (42% of 30 mg/kg males had squamous cell carcinomas of the oral mucosa).

Chemical-related increased incidences of preputial and clitoral gland neoplasms were also seen in rats. The preputial and clitoral glands are modified sebaceous glands believed to secrete pheromones or pheromone-like substances which affect some aspects of sexual behavior. Chemicals shown to induce preputial or clitoral gland neoplasms generally are mutagens in the *Salmonella* assay and also induce neoplasms of the Zymbal's gland, skin, mammary gland, or combinations of these organs (Copeland-Haines and Eustis, 1990).

Administration of 1,2,3-trichloropropane to male rats was associated with the development of benign neoplasms in the pancreas and kidney, in contrast to the malignant neoplasms of the oral mucosa and forestomach. The pancreatic and renal adenomas generally appeared later than the forestomach and oral mucosa neoplasms. The shorter life span of the 30 mg/kg groups as well as the apparent lower susceptibility of the pancreas and kidney to 1,2,3trichloropropane-induced neoplasms may have contributed to the lack of progression and development of malignant neoplasms in these organs. Although few pancreatic or renal adenomas occurred in dosed female rats, the incidence of focal hyperplasia was increased in these organs. The proliferative lesions diagnosed as hyperplasia in the pancreas

and kidney were considered preneoplastic because of the morphologic continuum and the frequent occurrence with chemical-induced neoplasms in these organs. The potential rates of progression or regression of these preneoplastic lesions are unknown and may likely vary with the chemical and dosage.

In contrast to rats, there were few neoplasms of the oral mucosa in dosed mice. Nevertheless, because of the rare occurrence of these neoplasms in historical controls, the few that were observed in the 60 mg/kg females were considered chemical related. The forestomach was the principal organ for a carcinogenic response in mice; nearly all dosed mice had squamous cell papillomas, carcinomas, or both. Unlike rats, carcinogenic responses were also observed in the liver, harderian gland, and uterus.

The genetic toxicity studies of 1,2,3-trichloropropane are part of a larger effort by the NTP to develop a database that would permit the evaluation of the contribution of these four *in vitro* short-term genetic toxicity tests to predicting chemical carcinogenicity in experimental animals. These *in vitro* tests were developed to study mechanisms of chemical-induced DNA damage, but their use has been extended to the prediction of carcinogenicity based on the somatic mutation theory and electrophilic theory of chemical carcinogenesis (Miller and Miller, 1977; Straus, 1981; Crawford, 1985). Although mutations can be detected in *S. typhimurium* and mouse lymphoma cells, neither of the specific gene loci tested appear to be related to the cellular changes that occur in the induction of neoplasia in humans or animals. Moreover, none of the chromosomal aberrations or sister chromatid exchanges observed in Chinese hamster ovary cells have been clearly related to heritable changes involved in the induction or progression of neoplasia. Thus, a positive response in any of these tests by a chemical that produces increases in neoplasm incidences in rodents does not necessarily implicate a specific mechanism of carcinogenicity involving DNA damage in the intact animal. Nevertheless, there is a strong correlation between structural alerts to DNA reactivity (electrophilicity), mutagenicity in *S. typhimurium*, and carcinogenicity in two rodent species at single or multiple tissue sites (Ashby and Tennant, 1991), providing support for the electrophilic theory of chemical carcinogenesis in a subset of chemical carcinogens. The reader is referred to the article by Ashby and Tennant (1991) for details regarding the correlation of structural alerts (or absence thereof), mutagenicity, and carcinogenicity results of 301 chemicals in the NTP database.

The S9-dependent genetic toxicity of 1,2,3-trichloropropane is consistent with the strong carcinogenic response in rats and mice in the present studies and with the recently proposed mechanisms of bioactivation and metabolism of this chemical and similar short-chain halogenated hydrocarbons.

Recent evidence indicates that 1,2,3,-trichloropropane can be metabolized by two major pathways in rats and mice (Anders *et al.*, 1988). One proposed pathway involves oxidation by mixed function oxidases in the liver. 1,2-Dichloropropionic acid, 2-chloroethanol, 3-(*S*-glutathionyl)lactic acid, ethylene glycol, oxalic acid (Weber *et al.*, 1991) and 2-glutathionyl malonic acid (Mahmood *et al.*, 1991) have been identified in the urine of F344/N rats administered 1,2,3-trichloropropane. The formation of these metabolites is consistent with a degradation pathway involving mixed function oxidase catalyzed oxygenation of 1,2,3-trichloropropane on a terminal carbon to yield a chlorohydrin, followed by additional reactions that result in formation of the observed metabolites. Weber *et al.* (1991) and Mahmood *et al.* (1991) have proposed specific schemes that account for the observed urinary metabolites, starting with the initial formation of a chlorohydrin. In addition, the 2- and 3-carbon metabolites generated in these pathways can be further metabolized to the major 1,2,3-trichloropropane metabolite, CO_2. Disposition and pharmacokinetic studies have demonstrated that following oral or intravenous administration of radio-labeled 1,2,3-trichloropropane to F344/N rats or $B6C3F_1$ mice, 20% to 25% (rats) or 15% to 20% (mice) of the radiolabel is eliminated as radioactive CO_2 (Volp *et al.*, 1984; Mahmood *et al.*, 1991).

The second major metabolic pathway of 1,2,3-trichloropropane involves glutathione transferase (GST) catalyzed formation of glutathione conjugates in the liver. Once formed, the conjugates can undergo additional biotransformation in the liver or be excreted in bile or plasma. Conjugates reaching the kidney are further processed to mercapturates, while conjugates excreted in the bile may be processed by intestinal microflora and reabsorbed.

The probable initial glutathione conjugate formed from 1,2,3-trichloropropane is *S*-(2,3-dichloropropyl)glutathione; however, the absence of this conjugate in urine or bile indicates that it undergoes additional processing. This may involve additional metabolic transformations or an internal displacement reaction in which the chlorine atom on carbon 2 is displaced by nucleophilic attack of the sulfur atom of glutathione to produce a three-membered cyclic episulfonium ion. This highly reactive bifunctional compound may act as an alkylating or crosslinking agent and react with cellular macromolecules, or react with water to form *S*-(3-chloro-2-hydroxypropyl)glutathione or *S*-(2-chloro-3-hydroxypropyl)glutathione. The former conjugate can be converted to *S*-(3-chloro-2-hydroxypropyl)mercapturic acid, a metabolite identified in the urine of F344/N rats administered 1,2,3-trichloropropane (Weber *et al.*, 1991), whereas the latter can form a hydroxy episulfonium ion capable of alkylating cellular constituents or reacting with water.

Hepatocellular necrosis and other cytotoxic liver lesions which occurred in the 17-week studies summarized in the current report, as well as the hepatocellular lesions reported in the studies of Weber and Sipes (1990), are the type of toxic response expected from the *in situ* formation of a reactive chemical species such as an episulfonium ion.

The formation of glutathione conjugates in the liver and their subsequent processing in the kidney may play a major role in the nephrotoxicity of 1,2,3-trichloropropane. During the 17-week studies, severe nephrotoxicity characterized by acute diffuse renal tubule cell necrosis occurred in rats. Cysteine-*S*-conjugates formed from glutathione-*S*-conjugates may be transported into renal proximal tubule cells and converted to cytotoxic intermediates. By analogy to the reaction described previously for the corresponding glutathione metabolite in the liver, *S*-(2,3-dichloropropyl)cysteine transported into renal proximal tubule cells or formed *in situ*, would undergo internal displacement to form episulfonium ions which react with cellular macromolecules in the renal tubules. Consistent with the role of episulfonium ion formation in nephrotoxicity is the observation that when *S*-(3-chloropropyl)cysteine is taken up by renal proximal tubule cells it cannot form a cyclic episulfonium ion due to the lack of a displaceable group on the number 2 carbon and is, therefore, not a nephrotoxin in F344/N rats.

The study by Mahmood *et al.* (1991) demonstrated the presence of significantly elevated quantities of nonextractable radioactivity in the forestomach, liver, and kidneys 6, 24, and 60 hours after oral administration of 1,2,3-trichloropropane to F344/N rats, and 60 hours after oral administration to B6C3F$_1$ mice. The presence of covalently bound radioactivity in these tissues is consistent with the *in situ* formation of alkylating species such as the episulfonium ion, and in the 2-year studies, exposure to 1,2,3-trichloropropane caused marked increases in neoplasms in these tissues as well as in several other tissues in rats and mice.

The results of both the gavage and inhalation studies of 1,2-dibromo-3-chloropropane (DBCP; NCI, 1978; NTP, 1982) are comparable to the results of the 1,2,3-trichloropropane gavage study. DBCP structure, urinary metabolites, and proposed metabolism are very similar to that of 1,2,3-trichloropropane. Both involve mixed function oxidase catalyzed oxygenation as well as conjugation with glutathione and episulfonium ion formation. Although the degradation scheme proposed for DBCP includes an alternate pathway involving radical-initiated reactions, the radical intermediates would behave like other cytotoxic reactive species such as the episulfonium ion, and the expected toxic response (cytotoxicity, necrosis) would be similar to that resulting from the *in situ* formation of any reactive species capable of reacting with cellular macromolecules.

The gavage studies were conducted by administering DBCP in corn oil at doses of 15 or 29 mg/kg to Osborne-Mendel rats for 78 weeks or at doses of 114 or 219 mg/kg to B6C3F$_1$ mice for 60 weeks (NCI, 1978a). Because of reduced survival associated with the presence of neoplasms of the forestomach, the surviving high-dose rats were necropsied after 64 weeks of chemical exposure, the low-dose rats after 78 weeks, the high-dose mice after 47 weeks, and the low-dose mice after 60 weeks. Nonneoplastic proliferative lesions occurred in the kidneys of all groups of rats and mice and these lesions might have developed into neoplasms if the studies had been of longer duration.

During the inhalation studies, rats and mice were exposed to 0.6 or 3 ppm DBCP vapor 6 hours per day, 5 days per week for 2 years (NTP, 1982). The survival of high-dose rats was reduced as a result of morbidity associated with the presence of neoplasms of the nose and oral mucosa. The incidence of renal tubule neoplasms was also increased in both sexes. The survival of high-dose mice was reduced by morbidity associated with the presence of neoplasms of the nose and lung. In addition, nonneoplastic proliferative lesions were present in the renal tubules of both rats and mice and in the forestomach of female rats and both sexes of mice.

The close parallel between the target organs and the spectrum of lesions associated with exposure to 1,2,3-trichloropropane and DBCP, even when chemical administration was by two different routes, is consistent with and supports the proposal that similar toxic mechanisms are involved. With both compounds, neoplasms occurred at the administration site (forestomach for 1,2,3-trichloropropane by gavage and lung for DBCP by inhalation); however, nonneoplastic toxic lesions occurred in the forestomach of female rats and both sexes of mice in the DBCP inhalation study, and in the lungs of mice in the 17-week studies of 1,2,3-trichloro-propane, consistent with the formation of a reactive metabolite(s) in these tissues. The stronger response in the forestomach in the gavage studies would be expected because of the much higher local concentration of chemical at the administration site.

Several other 2- or 3-carbon halogenated aliphatic compounds similar to 1,2,3-trichloropropane and DBCP have also been evaluated in NTP studies. 1,2-Dichloroethane was administered by gavage in corn oil to Osborne-Mendel rats and $B6C3F_1$ mice; however, the period of chemical administration was 78 weeks rather than 104 weeks (NCI, 1978b). Neoplasms associated with chemical exposure included squamous cell carcinomas of the forestomach and hemangiosarcomas of the circulatory system in male rats, mammary gland adenocarcinomas in female rats, alveolar/bronchiolar adenomas in male and female mice, and mammary gland adenocarcinomas, endometrial stromal polyps and endometrial sarcomas in female mice.

1,2-Dichloroethane is a potent nephrotoxin that undergoes GST-catalyzed conversion to the corresponding glutathione conjugate, *S*-(2-chloroethyl) glutathione, which can be processed in the kidney to *S*-(2-chloroethyl)cysteine, another potent nephrotoxin. In contrast, *S*-ethyl cysteine and *S*-(2-hydroxyethyl)cysteine, which cannot form episulfonium ions, are not nephrotoxic. Moreover, *S*-(2-hydroxyethyl)cysteine, the expected product from the reaction of the corresponding episulfonium ion with water, is a urinary metabolite of rats administered 1,2-dichloroethane. Similar arguments can be made to explain the nephrotoxicity of 1,2-dibromoethane. *S*-[(2-N7-guanyl)ethyl]glutathione, the expected conjugate produced by the reaction of the 7 nitrogen of guanine with the episulfonium ion to form 1,2-dibromoethane, has been isolated from tissues of exposed rats, suggesting that the episulfonium ion is a formidable alkylating agent.

Two other short-chain halogenated hydrocarbons have been evaluated in 2-year studies by the NTP. 1,2-Dichloropropane administered by gavage produced a marginal increase in mammary gland adenocarcinomas in female rats and an increase in hepatocellular adenomas in mice, but produced no indication of kidney toxicity in either rats or mice at the doses administered (NTP, 1986). The structure of 1,2-dichloropropane suggests that it would be subjected to oxidation by mixed function oxidases on the unsubstituted carbon. Hutson *et al*. (1971) found that 40% of the administered [^{14}C]1,2-dichloropropane was expired through the lungs within 96 hours after dosing, of which half (20% of the administered dose) was CO_2. A major urinary metabolite of 1,2-dichloropropane in rats is *N*-acetyl-*S*-(2-hydroxypropyl)cysteine (Jones and Gibson, 1980), suggesting a possible GST-catalyzed formation of *S*-(2-chloropropyl)glutathione. In theory, this compound could undergo internal displacement of the chlorine on carbon 2 with the resulting formation of an episulfonium ion. The presence of the adjacent methyl group would be expected to sufficiently reduce the reactivity of the chlorine on the 2 carbon to prevent this reaction from competing with the oxidative pathway. *N*-acetyl-*S*-(2-hydroxypropyl)cysteine could arise from conjugate formation between 2-hydroxychloropropane, formed in the oxidative pathway, and glutathione.

The other halogenated hydrocarbon studied by the NTP was hexachloroethane, which produced significant nephrotoxicity in prechronic studies and increases in kidney neoplasm incidence in male rats (NTP, 1989). This compound appears to be extensively conjugated and excreted predominantly in the

bile. In dosed rabbits, only 5% of the hexachloroethane appeared in the urine 3 days after administration, and it was present as di- and trichloroethanol, mono-, di-, and trichloroacetic acid, and oxalic acid (Jondorf *et al.*, 1957). Up to 24% of the administered dose was exhaled as the parent compound, tetrachloroethylene, 1,1,2,2-tetra-chloroethane, and CO_2. These results suggest that hexachloroethane is metabolized by an oxidative pathway similar to that of 1,2,3-trichloropropane, as well as by GST-catalyzed glutathione conjugate formation. It is unlikely, however, that the glutathione or cysteine conjugates of hexachloroethane form episulfonium ions. The extensive halogen substitution of the 2 carbon of the ethane resides in close proximity to the sulfur atom of glutathione or cysteine and significantly reduces their nucleophilicity and, thus, effectively reduces the ability to displace chlorine.

The absence of either a toxic or carcinogenic response in the liver of animals exposed to hexachloroethane, combined with the response observed in the kidney, suggests that another mechanism is responsible for the nephrotoxicity and renal carcinogenic response. One possibility involves the formation of toxic products from the action of the renal cysteine β-lyase on the cysteine-*S*-conjugates of hexachloroethane. This enzyme acts on amino acid substrates and catalyzes β-elimination reactions to ammonia, pyruvic acid, and a cysteine conjugate. The conjugate is an alkyl-thiol derivative from the parent compound which may be unstable or be further converted to toxic products. Because the kidney is a major site of cysteine β-lyase activity, this toxic mechanism is relatively specific to the kidney. The nephrotoxicity of numerous polyhalogenated alkenes depends on β-lyase activation of the corresponding polyhalogenated cysteine conjugates derived from the parent alkenes (Anders *et al.*, 1988; Lock, 1988), and similar conjugates would be formed from hexachloroethane. β-lyase activation, therefore, is a probable contributor to the nephrotoxicity of hexachloroethane. Renal β-lyase activation has recently been shown to be an important pathway of toxification of polyhalogenated alkenes in primary cultures of human proximal tubule cells (Chen *et al.*, 1990).

CONCLUSIONS

Under the conditions of these 2-year gavage studies, there was *clear evidence of carcinogenic activity** of 1,2,3-trichloropropane in male F344/N rats based on increased incidences of squamous cell papillomas and carcinomas of the oral mucosa and forestomach, adenomas of the pancreas and kidney, adenomas or carcinomas of the preputial gland, and carcinomas of the Zymbal's gland. Adenomatous polyps and adenocarcinomas of the intestine may have been related to chemical administration. There was *clear evidence of carcinogenic activity* of 1,2,3-trichloropropane in female F344/N rats based on increased incidences of squamous cell papillomas and carcinomas of the oral mucosa and forestomach, adenomas or carcinomas of the clitoral gland, adenocarcinomas of the mammary gland, and carcinomas of the Zymbal's gland. Adenocarcinomas of the intestine may have been related to chemical administration.

There was *clear evidence of carcinogenic activity* of 1,2,3-trichloropropane in male $B6C3F_1$ mice based on increased incidences of squamous cell papillomas and carcinomas of the forestomach, hepatocellular adenomas or carcinomas of the liver, and harderian gland adenomas. Squamous cell papillomas of the oral mucosa may have been related to chemical administration. There was *clear evidence of carcinogenic activity* of 1,2,3-trichloropropane in female $B6C3F_1$ mice based on increased incidences of squamous cell carcinomas of the oral mucosa, squamous cell papillomas and carcinomas of the forestomach, hepatocellular adenomas or carcinomas of the liver, harderian gland adenomas, and uterine adenomas, adenocarcinomas, and stromal polyps.

Nonneoplastic lesions associated with exposure to 1,2,3-trichloropropane included increased severity of nephropathy in male rats and increased incidences of basal cell and squamous hyperplasia of the forestomach, acinar hyperplasia of the pancreas, renal tubule hyperplasia, and preputial or clitoral gland hyperplasia in male and female rats. Increased incidences of squamous hyperplasia of the forestomach and eosinophilic foci in the liver in male and female mice were chemical related.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 10. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 12.

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APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR GAVAGE STUDY OF 1,2,3-TRICHLOROPROPANE

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	8
Early deaths				
Accidental deaths	1		1	
Moribund	13	16	30	43
Natural deaths	2	2	4	
Scheduled sacrifice				9
Survivors				
Terminal sacrifice	34	32	14	
Missexed			1	
Animals examined microscopically	60	60	59	60
15-Month Interim Evaluation				
Alimentary System				
Pancreas	(10)	(10)	(10)	(8)
Adenoma				1 (13%)
Acinus, adenoma			1 (10%)	
Acinus, adenoma, multiple				1 (13%)
Pharynx			(1)	(1)
Palate, papilloma squamous				1 (100%)
Stomach, forestomach	(10)	(10)	(10)	(8)
Papilloma squamous		2 (20%)	3 (30%)	8 (100%)
Squamous cell carcinoma			1 (10%)	1 (13%)
Tongue	(10)		(2)	(3)
Papilloma squamous			1 (50%)	2 (67%)
Papilloma squamous, multiple				1 (33%)
Cardiovascular System				
None				
Endocrine System				
Pituitary gland	(10)	(10)	(10)	(8)
Pars distalis, adenoma		2 (20%)	1 (10%)	
Thyroid gland	(10)	(10)	(10)	(8)
C-cell, adenoma				1 (13%)
General Body System				
None				

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
15-Month Interim Evaluation (continued)				
Genital System				
Epididymis	(10)	(10)	(10)	(8)
Mesothelioma malignant, metastatic, testes			1 (10%)	
Preputial gland	(10)	(10)	(10)	(8)
Adenoma			1 (10%)	
Carcinoma				1 (13%)
Testes	(10)	(10)	(10)	(8)
Bilateral, interstitial cell, adenoma	3 (30%)	1 (10%)	6 (60%)	6 (75%)
Interstitial cell, adenoma	5 (50%)	5 (50%)	4 (40%)	2 (25%)
Tunic, mesothelioma malignant			1 (10%)	
Hematopoietic System				
None				
Integumentary System				
Skin	(10)	(9)	(10)	(8)
Papilloma squamous				3 (38%)
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)	(10)	(10)	(8)
Alveolar/bronchiolar adenoma				1 (13%)
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(8)
Renal tubule, adenoma				4 (50%)
Renal tubule, adenoma, multiple				1 (13%)
Systemic Lesions				
Multiple organs[b]	(10)	(10)	(10)	(8)
Mesothelioma malignant			1 (10%)	

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study				
Alimentary System				
Intestine large, colon	(50)	(50)	(48)	(52)
Adenocarcinoma, multiple			1 (2%)	
Polyp adenomatous				1 (2%)
Intestine large, rectum	(49)	(50)	(47)	(52)
Polyp adenomatous				1 (2%)
Intestine small, duodenum	(49)	(50)	(48)	(52)
Squamous cell carcinoma, metastatic, stomach			1 (2%)	
Intestine small, ileum	(49)	(50)	(47)	(51)
Squamous cell carcinoma, metastatic, stomach			1 (2%)	
Intestine small, jejunum	(49)	(50)	(47)	(52)
Adenocarcinoma			1 (2%)	1 (2%)
Squamous cell carcinoma, metastatic, stomach			1 (2%)	
Liver	(50)	(50)	(49)	(52)
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Hepatocellular carcinoma			1 (2%)	2 (4%)
Hepatocellular adenoma	1 (2%)	1 (2%)	3 (6%)	1 (2%)
Sarcoma, metastatic, skin	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		1 (2%)	2 (4%)	
Mesentery	(4)	(9)	(11)	(3)
Sarcoma, metastatic, skin	1 (25%)			
Pancreas	(50)	(50)	(49)	(52)
Adenoma		1 (2%)	1 (2%)	
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Mixed tumor benign	1 (2%)			
Sarcoma, metastatic, skin	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		1 (2%)	1 (2%)	
Acinus, adenocarcinoma			2 (4%)	1 (2%)
Acinus, adenoma	5 (10%)	6 (12%)	4 (8%)	5 (10%)
Acinus, adenoma, multiple		14 (28%)	31 (63%)	24 (46%)
Pharynx	(1)	(5)	(17)	(15)
Palate, papilloma squamous		2 (40%)	1 (6%)	3 (20%)
Palate, squamous cell carcinoma	1 (100%)		11 (65%)	7 (47%)
Salivary glands	(50)	(50)	(49)	(52)
Adenoma				1 (2%)
Stomach, forestomach	(50)	(50)	(49)	(52)
Papilloma squamous		17 (34%)	24 (49%)	24 (46%)
Papilloma squamous, multiple		12 (24%)	9 (18%)	14 (27%)
Squamous cell carcinoma		9 (18%)	17 (35%)	12 (23%)
Squamous cell carcinoma, multiple			10 (20%)	1 (2%)
Stomach, glandular	(50)	(50)	(49)	(52)
Tongue	(4)	(8)	(11)	(44)
Papilloma squamous		2 (25%)	8 (73%)	16 (36%)
Papilloma squamous, multiple				2 (5%)
Squamous cell carcinoma				19 (43%)
Tooth	(1)		(1)	
Adamantinoma benign	1 (100%)			

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Cardiovascular System				
Heart	(50)	(49)	(49)	(52)
Carcinoma, metastatic, lung			1 (2%)	
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Squamous cell carcinoma, metastatic, stomach			1 (2%)	
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(48)	(51)
Squamous cell carcinoma, metastatic, stomach			1 (2%)	
Bilateral, medulla, osteosarcoma, metastatic, bone	1 (2%)			
Adrenal gland, medulla	(49)	(50)	(48)	(51)
Pheochromocytoma malignant	1 (2%)	1 (2%)	2 (4%)	
Pheochromocytoma complex	1 (2%)			
Pheochromocytoma benign	8 (16%)	7 (14%)	12 (25%)	
Bilateral, pheochromocytoma benign	2 (4%)		1 (2%)	
Islets, pancreatic	(50)	(50)	(49)	(52)
Adenoma	9 (18%)	4 (8%)	3 (6%)	1 (2%)
Carcinoma	1 (2%)			
Pituitary gland	(48)	(48)	(49)	(51)
Pars distalis, adenoma	9 (19%)	12 (25%)	7 (14%)	2 (4%)
Pars distalis, adenoma, multiple		1 (2%)		
Pars distalis, fibrous histiocytoma, metastatic, kidney			1 (2%)	
Thyroid gland	(50)	(49)	(49)	(51)
Sarcoma, metastatic, skin	1 (2%)			
C-cell, adenoma	4 (8%)	14 (29%)	4 (8%)	5 (10%)
C-cell, adenoma, multiple		1 (2%)		
C-cell, carcinoma		1 (2%)	2 (4%)	
Follicular cell, adenoma	1 (2%)	1 (2%)	2 (4%)	2 (4%)
Follicular cell, carcinoma			1 (2%)	
General Body System				
None				
Genital System				
Epididymis	(50)	(49)	(49)	(52)
Sarcoma, metastatic, skin	1 (2%)			
Penis				(1)
Squamous cell carcinoma				1 (100%)
Preputial gland	(49)	(47)	(49)	(50)
Adenoma	5 (10%)	3 (6%)	5 (10%)	8 (16%)
Carcinoma		2 (4%)	3 (6%)	4 (8%)
Bilateral, adenoma				3 (6%)
Bilateral, carcinoma		1 (2%)		1 (2%)
Prostate	(48)	(50)	(49)	(52)
Adenoma			2 (4%)	

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Genital System (continued)				
Seminal vesicle	(49)	(48)	(48)	(52)
Squamous cell carcinoma, metastatic, stomach		1 (2%)	1 (2%)	
Testes	(50)	(50)	(49)	(52)
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Sarcoma, metastatic, skin	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		1 (2%)		
Bilateral, interstitial cell, adenoma	40 (80%)	40 (80%)	36 (73%)	36 (69%)
Interstitial cell, adenoma	7 (14%)	8 (16%)	9 (18%)	8 (15%)
Hematopoietic System				
Blood	(2)	(3)	(3)	
Bone marrow	(50)	(50)	(49)	(52)
Carcinoma, metastatic, thyroid gland		1 (2%)		
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Osteosarcoma, metastatic, bone		1 (2%)		
Lymph node	(50)	(50)	(49)	(52)
Mediastinal, carcinoma, metastatic, thyroid gland		1 (2%)		
Mediastinal, fibrous histiocytoma, metastatic, kidney			1 (2%)	
Renal, fibrous histiocytoma, metastatic, kidney			1 (2%)	
Lymph node, mandibular	(50)	(50)	(48)	(52)
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Sarcoma, metastatic, ear			1 (2%)	
Lymph node, mesenteric	(50)	(49)	(47)	(51)
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Hemangioma				1 (2%)
Squamous cell carcinoma, metastatic, stomach				2 (4%)
Spleen	(50)	(50)	(49)	(52)
Fibroma	2 (4%)			
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Hemangioma				1 (2%)
Sarcoma, metastatic, skin	1 (2%)			
Thymus	(49)	(48)	(41)	(48)
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Epithelial cell, thymoma benign				1 (2%)
Integumentary System				
Mammary gland	(44)	(44)	(34)	(41)
Fibroadenoma	2 (5%)	3 (7%)	1 (3%)	
Fibroadenoma, multiple			1 (3%)	
Skin	(50)	(49)	(48)	(51)
Basal cell carcinoma				1 (2%)
Keratoacanthoma	2 (4%)	2 (4%)	1 (2%)	2 (4%)
Papilloma squamous		2 (4%)		2 (4%)
Squamous cell carcinoma			1 (2%)	1 (2%)
Trichoepithelioma	1 (2%)		1 (2%)	
Subcutaneous tissue, fibroma	1 (2%)	2 (4%)	5 (10%)	1 (2%)
Subcutaneous tissue, fibroma, multiple	1 (2%)		1 (2%)	
Subcutaneous tissue, sarcoma	1 (2%)	1 (2%)	1 (2%)	

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Musculoskeletal System				
Bone	(50)	(50)	(49)	(52)
Osteosarcoma	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Skeletal muscle	(2)	(3)	(5)	(3)
Adenocarcinoma, metastatic, uncertain primary site				1 (33%)
Fibrous histiocytoma, metastatic			1 (20%)	
Squamous cell carcinoma, metastatic, stomach		1 (33%)	2 (40%)	1 (33%)
Nervous System				
Brain	(50)	(49)	(49)	(52)
Astrocytoma malignant	1 (2%)			
Glioma malignant			1 (2%)	
Peripheral nerve			(1)	
Squamous cell carcinoma, metastatic, pharynx			1 (100%)	
Respiratory System				
Lung	(50)	(49)	(49)	(52)
Alveolar/bronchiolar adenoma	2 (4%)	1 (2%)	2 (4%)	1 (2%)
Alveolar/bronchiolar carcinoma			1 (2%)	
Carcinoma			1 (2%)	
Fibrous histiocytoma, metastatic, kidney			1 (2%)	
Osteosarcoma, metastatic, bone	1 (2%)	1 (2%)		
Sarcoma, metastatic, skin	1 (2%)			
Squamous cell carcinoma, metastatic, skin				1 (2%)
Squamous cell carcinoma, metastatic, stomach		1 (2%)	1 (2%)	
Mediastinum, squamous cell carcinoma, metastatic, stomach			1 (2%)	
Nose	(50)	(50)	(49)	(52)
Squamous cell carcinoma		1 (2%)		1 (2%)
Special Senses System				
Ear		(1)	(2)	
Sarcoma		1 (100%)	2 (100%)	
Zymbal's gland				(4)
Carcinoma				3 (75%)
Urinary System				
Kidney	(50)	(50)	(49)	(52)
Adenoma			2 (4%)	2 (4%)
Fibrous histiocytoma, metastatic			1 (2%)	
Sarcoma, metastatic	1 (2%)			
Squamous cell carcinoma, metastatic, stomach			1 (2%)	
Renal tubule, adenoma		2 (4%)	8 (16%)	10 (19%)
Renal tubule, adenoma, multiple			10 (20%)	9 (17%)
Renal tubule, oncocytoma benign			1 (2%)	
Transitional epithelium, carcinoma			1 (2%)	
Urinary bladder	(49)	(50)	(47)	(52)
Melanoma malignant, metastatic, testes	1 (2%)			

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Systemic Lesions				
Multiple organs	(50)	(50)	(49)	(52)
Leukemia mononuclear	16 (32%)	11 (22%)	9 (18%)	6 (12%)
Lymphoma malignant histiocytic		1 (2%)		
Lymphoma malignant lymphocytic			1 (2%)	
Mesothelioma malignant	3 (6%)	4 (8%)	3 (6%)	2 (4%)
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	8	8	10	8
2-Year study	50	50	47	52
Total primary neoplasms				
15-Month interim evaluation	8	10	19	34
2-Year study	130	192	268	252
Total animals with benign neoplasms				
15-Month interim evaluation	8	8	10	8
2-Year study	49	50	46	49
Total benign neoplasms				
15-Month interim evaluation	8	10	17	32
2-Year study	104	158	195	188
Total animals with malignant neoplasms				
15-Month interim evaluation			2	2
2-Year study	22	28	37	45
Total malignant neoplasms				
15-Month interim evaluation			2	2
2-Year study	26	34	73	64
Total animals with secondary neoplasms[d]				
15-Month interim evaluation			1	
2-Year study	5	7	9	5
Total secondary neoplasms				
15-Month interim evaluation			1	
2-Year study	23	20	44	10
Total animals with malignant neoplasms uncertain primary site				
2-Year study				1

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms
[d] Secondary neoplasms: metastatic neoplasms or neoplasms invasive to an adjacent organ

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control

Number of Days on Study	340	485	506	589	591	605	610	614	614	618	628	648	663	663	677	692	731	731	731	731	731	731	731	731	731	731
Carcass ID Number	00015	00065	00044	00114	00142	00035	00085	00025	00082	00224	00105	00074	00073	00094	00084	00104	00034	00053	00054	00071	00072	00081	00083	00091	00092
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																										
Sarcoma, metastatic, skin											X															
Mesentery	+	+									+			+												
Mesothelioma malignant, metastatic, testes		X																								
Sarcoma, metastatic, skin											X															
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes		X																			X					
Mixed tumor benign																										
Sarcoma, metastatic, skin											X															
Acinus, adenoma																			X							X
Pharynx																			+							
Palate, squamous cell carcinoma																			X							
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue				+																	+	+				
Tooth	+																									
Adamantinoma benign	X																									
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, medulla, osteosarcoma, metastatic, bone					X																					

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	731	731	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	737	737	
Carcass ID Number	00093	00113	00111	00112	00121	00222	00223	00232	00333	00341	00443	00451	00552	00561	00662	00663	00664	01212	01223	01231	01011	01202	01213	01141	01152	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma															X											1
Sarcoma, metastatic, skin																										1
Mesentery																										4
Mesothelioma malignant, metastatic, testes																										1
Sarcoma, metastatic, skin																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesothelioma malignant, metastatic, testes																										2
Mixed tumor benign															X											1
Sarcoma, metastatic, skin																										1
Acinus, adenoma		X					X													X						5
Pharynx																										1
Palate, squamous cell carcinoma																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue															+											4
Tooth																										1
Adamantinoma benign																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, medulla, osteosarcoma, metastatic, bone																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	340	485	506	589	591	605	610	614	614	618	628	648	663	663	677	692	731	731	731	731	731	731	731	731	731
Carcass ID Number	00015	00065	00444	01144	01442	00035	00885	02525	00882	02424	01055	00744	00773	00994	00884	01044	00344	00553	00554	00711	00722	00881	00883	00891	00892
Endocrine System (continued)																									
Adrenal gland, medulla	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma complex																									
Pheochromocytoma benign													X									X			
Bilateral, pheochromocytoma benign															X										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma									X			X						X	X						
Carcinoma																									
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma												X	X			X	X		X						
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin											X														
C-cell, adenoma								X										X							
Follicular cell, adenoma																									
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes		X																			X				
Sarcoma, metastatic, skin											X														
Preputial gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma			X																X						
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes																					X				
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin											X														
Bilateral, interstitial cell, adenoma						X			X	X	X	X	X	X	X			X	X	X	X	X	X	X	X
Interstitial cell, adenoma			X	X	X		X	X									X								
Hematopoietic System																									
Blood						+																			
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	731	731	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	737	737	
Carcass ID Number	00093	00113	00112	00121	00202	00223	00232	00333	00341	00433	00451	00523	00621	00622	00663	00644	01211	01222	01331	01101	01202	01303	01411	01512	01612	**Total Tissues/ Tumors**
Endocrine System (continued)																										
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																				X						1
Pheochromocytoma complex																								X		1
Pheochromocytoma benign				X						X					X			X					X	X		8
Bilateral, pheochromocytoma benign																X										2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma						X					X		X					X		X						9
Carcinoma																			X							1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	48
Pars distalis, adenoma					X												X					X		X		9
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skin																										1
C-cell, adenoma								X																X		4
Follicular cell, adenoma									X																	1
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesothelioma malignant, metastatic, testes														X												3
Sarcoma, metastatic, skin																										1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma		X				X											X									5
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	48
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	49
Mesothelioma malignant, metastatic, testes																										1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, skin																										1
Bilateral, interstitial cell, adenoma	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	40
Interstitial cell, adenoma														X												7
Hematopoietic System																										
Blood														+												2
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	340	485	506	589	591	605	610	614	614	618	628	648	663	663	667	692	731	731	731	731	731	731	731	731	731
Carcass ID Number	00015	00065	00044	00144	00422	00035	00085	00025	00082	00024	00105	00074	00073	00094	00084	00104	00034	00053	00054	00071	00072	00081	00083	00091	00092
Hematopoietic System (continued)																									
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
Mesothelioma malignant, metastatic, testes																									
Sarcoma, metastatic, skin											X														
Thymus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	+	+	+	M	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																									X
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																		X	X						
Trichoepithelioma																									
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, fibroma, multiple								X																	
Subcutaneous tissue, sarcoma											X														
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma					X																				
Skeletal muscle		+																							
Mesothelioma malignant, metastatic, testes		X																							
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant														X											
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma														X											X
Mesothelioma malignant, metastatic, testes																					X				
Osteosarcoma, metastatic, bone					X																				
Sarcoma, metastatic, skin											X														
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	731	731	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	736	737	737	737	737	737	737	
Carcass ID Number	00093	00113	00011	00012	00021	00022	00023	00032	00033	00041	00043	00051	00052	00061	00062	00063	00064	00121	00122	00231	00101	00112	00023	00113	00112	00113	**Total Tissues/ Tumors**
Hematopoietic System (continued)																											
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma											X					X											2
Mesothelioma malignant, metastatic, testes														X													1
Sarcoma, metastatic, skin																											1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Integumentary System																											
Mammary gland	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Fibroadenoma																			X								2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Keratoacanthoma																											2
Trichoepithelioma																								X			1
Subcutaneous tissue, fibroma												X															1
Subcutaneous tissue, fibroma, multiple																											1
Subcutaneous tissue, sarcoma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																											1
Skeletal muscle														+													2
Mesothelioma malignant, metastatic, testes														X													2
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																											2
Mesothelioma malignant, metastatic, testes																											1
Osteosarcoma, metastatic, bone																											1
Sarcoma, metastatic, skin																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	340	485	506	589	591	605	610	614	614	618	628	648	663	663	677	692	731	731	731	731	731	731	731	731	731	731
Carcass ID Number	00015	00065	00444	01144	01422	00355	00855	00255	00082	00824	01015	00744	00773	00994	00844	01044	00344	00534	00544	00711	00072	00881	00883	00991	00992	
Special Senses System																										
Eye														+												
Lacrimal gland																										+
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic											X															
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Melanoma malignant, metastatic, testes																					X					
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X				X				X								X	X			
Mesothelioma malignant		X																			X					

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	7 3 1	7 3 1	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7			
Carcass ID Number	0 0 9 3	0 1 1 3	0 0 1 1	0 1 1 2	0 2 1	0 2 2	0 2 3	0 3 2	0 3 3	0 4 1	0 4 3	0 5 1	0 5 2	0 6 1	0 6 2	0 6 3	0 6 4	0 1 2 1	0 1 2 2	0 3 1 1	0 1 1	0 1 2	0 1 3	0 1 1	0 1 1	0 1 2		**Total Tissues/ Tumors**	
Special Senses System																													
Eye					+																						2		
Lacrimal gland																											1		
Urinary System																													
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50		
Sarcoma, metastatic																											1		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+		49		
Melanoma malignant, metastatic, testes																											1		
Systemic Lesions																													
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50		
Leukemia mononuclear			X		X					X	X	X	X	X			X			X			X	X		16		
Mesothelioma malignant														X													3		

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg

Number of Days on Study	577	591	600	603	603	621	654	656	663	678	685	685	689	692	692	694	703	710	730	730	730	730	730	730	730
Carcass ID Number	02155	01655	01444	01184	01185	02225	02445	01553	01833	01335	01334	01544	01664	02244	02344	01552	01193	01433	01331	01323	01333	01441	01422	01511	01611
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Squamous cell carcinoma, metastatic, stomach													X												
Mesentery		+		+	+					+		+				+		+							
Mesothelioma malignant, metastatic, testes																		X							
Fat, mesothelioma malignant, metastatic, testes												X													
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X								
Squamous cell carcinoma, metastatic, stomach													X												
Acinus, adenoma											X	X									X			X	
Acinus, adenoma, multiple																X									X
Pharynx			+									+						+				+			
Palate, papilloma squamous																		X				X			
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous							X	X				X			X					X	X		X		X
Papilloma squamous, multiple						X								X			X		X						
Squamous cell carcinoma			X			X							X												X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue				+								+				+				+				+	
Papilloma squamous																X								X	
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	
Carcass ID Number	01662	01663	01671	01772	01773	01792	02001	02002	02011	02012	02013	02014	02021	02022	02023	02181	02182	02191	02231	02232	02233	02241	02242	02243	02244	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma		X																								1
Squamous cell carcinoma, metastatic, stomach																										1
Mesentery			+											+												9
Mesothelioma malignant, metastatic, testes																										1
Fat, mesothelioma malignant, metastatic, testes																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																										1
Squamous cell carcinoma, metastatic, stomach																										1
Acinus, adenoma	X		X																							6
Acinus, adenoma, multiple		X		X		X	X		X	X		X		X	X		X	X		X						14
Pharynx							+																			5
Palate, papilloma squamous																										2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous	X			X	X	X			X					X	X							X	X			17
Papilloma squamous, multiple		X					X			X	X					X	X	X							X	12
Squamous cell carcinoma							X		X	X		X	X													9
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tongue				+								+									+					8
Papilloma squamous																										2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	577	591	600	603	603	621	654	656	663	678	685	685	689	692	692	694	703	710	730	730	730	730	730	730	730
Carcass ID Number	02155	01655	01444	01184	01885	02255	02445	01553	01833	01335	01334	01544	01664	02244	02344	01552	01193	01443	01331	01323	01333	01441	01422	01511	01661
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant											X														
Pheochromocytoma benign			X													X					X				
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma				X																					X
Parathyroid gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X	X	X	X				X								X			X		X	X	
Pars distalis, adenoma, multiple														X											
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
C-cell, adenoma						X	X	X									X			X				X	
C-cell, adenoma, multiple																									
C-cell, carcinoma														X											
Follicular cell, adenoma																									
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes						X						X						X							
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X					X			
Carcinoma							X									X									
Bilateral, carcinoma											X														
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes												X													
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Squamous cell carcinoma, metastatic, stomach													X												
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach													X												
Bilateral, interstitial cell, adenoma		X		X			X	X	X	X		X	X	X	X	X	X	X	X	X	X			X	X
Interstitial cell, adenoma	X				X						X											X	X		

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	
Carcass ID Number	01662	01663	01671	01772	01773	01792	02001	02002	02011	02112	02113	02114	02121	02222	02223	02181	02182	02191	02231	02232	02233	02241	02242	02243	02244	**Total Tissues/ Tumors**
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Pheochromocytoma benign	X							X							X	X										7
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma						X														X						4
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Pars distalis, adenoma		X										X		X												12
Pars distalis, adenoma, multiple																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell, adenoma	X	X			X								X	X				X	X	X						14
C-cell, adenoma, multiple																								X		1
C-cell, carcinoma																										1
Follicular cell, adenoma	X																									1
General Body System																										
None																										
Genital System																										
Epididymis		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesothelioma malignant, metastatic, testes																				X						4
Preputial gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	47
Adenoma				X																						3
Carcinoma																										2
Bilateral, carcinoma																										1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesothelioma malignant, metastatic, testes																										1
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	48
Squamous cell carcinoma, metastatic, stomach																										1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach																										1
Bilateral, interstitial cell, adenoma	X	X		X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X		X	X	40
Interstitial cell, adenoma			X									X											X			8

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	577	591	600	603	603	621	654	656	663	678	685	685	689	692	692	694	703	710	730	730	730	730	730	730	730
Carcass ID Number	02155	01655	01444	01184	01885	02225	02445	01553	01183	01335	01334	01544	01664	02244	02344	01552	01993	01143	01331	01323	01333	01341	01442	01551	01661
Hematopoietic System																									
Blood		+								+															
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, thyroid gland														X											
Osteosarcoma, metastatic, bone															X										
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, carcinoma, metastatic, thyroid gland														X											
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	M	+	+	+	M	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+
Fibroadenoma											X										X				
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma													X										X		
Mesothelioma malignant, metastatic, testes						X																			
Papilloma squamous													X												
Scrotum, mesothelioma malignant, metastatic, testes												X													
Subcutaneous tissue, fibroma														X											
Subcutaneous tissue, sarcoma									X																
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma															X										
Skeletal muscle										+			+					+							
Mesothelioma malignant, metastatic, testes																		X							
Squamous cell carcinoma, metastatic, stomach													X												
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	
Carcass ID Number	01662	01663	01671	01772	01773	01792	02001	02002	02011	02112	02113	02114	02201	02222	02223	02281	02182	02192	02291	02332	02333	02341	02442	02443	02444		**Total Tissues/ Tumors**
Hematopoietic System																											
Blood	+																										3
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Carcinoma, metastatic, thyroid gland																											1
Osteosarcoma, metastatic, bone																											1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Mediastinal, carcinoma, metastatic, thyroid gland																											1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Integumentary System																											
Mammary gland	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+		44
Fibroadenoma																						X					3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+		49
Keratoacanthoma																											2
Mesothelioma malignant, metastatic, testes																											1
Papilloma squamous														X													2
Scrotum, mesothelioma malignant, metastatic, testes																											1
Subcutaneous tissue, fibroma													X														2
Subcutaneous tissue, sarcoma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Osteosarcoma																											1
Skeletal muscle																											3
Mesothelioma malignant, metastatic, testes																											1
Squamous cell carcinoma, metastatic, stomach																											1
Nervous System																											
Brain	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	577	591	600	603	603	621	654	656	663	678	685	685	689	692	692	694	703	710	730	730	730	730	730	730	730	730
Carcass ID Number	02155	01655	01444	01184	01185	02225	02445	01535	01183	01335	01344	01544	01644	02244	02344	02152	01933	01143	01331	01323	01333	01411	01422	01511	01611	
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	
Alveolar/bronchiolar adenoma																										
Osteosarcoma, metastatic, bone															X											
Squamous cell carcinoma, metastatic, stomach													X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma						X																				
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Special Senses System																										
Ear																						+				
Sarcoma																						X				
Harderian gland									+																	
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Renal tubule, adenoma																						X				
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear		X								X								X					X			
Lymphoma malignant histiocytic								X																		
Mesothelioma malignant						X						X						X								

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	731	
Carcass ID Number	01662	01663	01671	01772	01773	01792	02001	02002	02201	02211	02213	02214	02221	02222	02223	02181	02182	02191	02331	02332	02333	02441	02442	02443	02444	**Total Tissues/ Tumors**
Respiratory System																												
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49		
Alveolar/bronchiolar adenoma					X																					1		
Osteosarcoma, metastatic, bone																										1		
Squamous cell carcinoma, metastatic, stomach																										1		
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50		
Squamous cell carcinoma																										1		
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50		
Special Senses System																												
Ear																										1		
Sarcoma																										1		
Harderian gland																										1		
Urinary System																												
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50		
Renal tubule, adenoma																								X		2		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50		
Systemic Lesions																												
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50		
Leukemia mononuclear	X											X	X	X		X					X		X		11		
Lymphoma malignant histiocytic																										1		
Mesothelioma malignant																				X						4		

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg

Number of Days on Study	025	225	404	404	449	472	514	520	524	536	538	540	590	596	612	614	638	641	649	649	655	660	663	668
Carcass ID Number	02915	03155	03305	03325	03324	03535	03233	02664	03444	02744	02271	02293	03352	02844	03331	03511	02254	02553	02633	03044	02552	02622	02733	03443
Alimentary System																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, multiple														X										
Intestine large, rectum	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach													X											
Intestine small, ileum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach													X											
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma													X											
Squamous cell carcinoma, metastatic, stomach													X											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, kidney																	X							
Hepatocellular carcinoma																								
Hepatocellular adenoma																								
Squamous cell carcinoma, metastatic, stomach													X											
Mesentery	+			+									+								+	+		
Mesothelioma malignant, metastatic, testes													X											
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								X
Fibrous histiocytoma, metastatic, kidney																	X							
Mesothelioma malignant, metastatic, testes													X											
Squamous cell carcinoma, metastatic, stomach													X											
Acinus, adenocarcinoma																								
Acinus, adenoma														X			X				X			
Acinus, adenoma, multiple						X			X		X				X	X				X		X	X	
Pharynx				+					+		+									+	+		+	
Palate, papilloma squamous																								
Palate, squamous cell carcinoma				X							X												X	
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	669	678	684	685	685	686	698	701	709	720	728	729	729	729	729	729	729	729	729	729	729	729	730	730	
Carcass ID Number	03644	03342	02661	03303	03331	03222	02521	03114	03321	03313	03636	02722	02822	02833	02922	03011	03022	03111	03212	03414	03421	03616	03621	02811	02921	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma, multiple																										1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Squamous cell carcinoma, metastatic, stomach																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Squamous cell carcinoma, metastatic, stomach																										1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenocarcinoma																										1
Squamous cell carcinoma, metastatic, stomach																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrous histiocytoma, metastatic, kidney																										1
Hepatocellular carcinoma	X																									1
Hepatocellular adenoma									X									X						X		3
Squamous cell carcinoma, metastatic, stomach																		X								2
Mesentery						+				+					+				+	+		+				11
Mesothelioma malignant, metastatic, testes																				X		X				3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																										1
Fibrous histiocytoma, metastatic, kidney																										1
Mesothelioma malignant, metastatic, testes																				X		X				3
Squamous cell carcinoma, metastatic, stomach																										1
Acinus, adenocarcinoma										X					X											2
Acinus, adenoma			X																							4
Acinus, adenoma, multiple	X	X		X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	31
Pharynx		+		+				+	+	+				+				+	+	+	+	+				17
Palate, papilloma squamous		X																								1
Palate, squamous cell carcinoma				X				X	X	X				X						X	X	X				11
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	025	225	404	404	449	472	514	520	524	536	538	540	590	596	612	614	638	641	649	649	655	660	663	668
Carcass ID Number	02915	03155	03035	03255	03244	03533	03233	02644	03444	02744	02711	02933	03552	02844	03331	03511	02544	02533	02663	03044	02552	02622	02733	03443
Alimentary System (continued)																								
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous			X				X			X		X				X	X	X	X	X	X			
Papilloma squamous, multiple						X									X							X		
Squamous cell carcinoma													X	X	X				X	X			X	
Squamous cell carcinoma, multiple																X						X		X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue												+									+		+	
Papilloma squamous												X									X		X	
Tooth																			+					
Cardiovascular System																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, lung																		X						
Fibrous histiocytoma, metastatic, kidney																	X							
Squamous cell carcinoma, metastatic, stomach														X										
Endocrine System																								
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach													X											
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pheochromocytoma malignant																								
Pheochromocytoma benign														X	X					X				X
Bilateral, pheochromocytoma benign																								
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																						X		
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																						X		X
Pars distalis, fibrous histiocytoma, metastatic, kidney																	X							
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																								
C-cell, carcinoma																								
Follicular cell, adenoma																								
Follicular cell, carcinoma																								

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	669	678	684	685	685	686	698	701	709	720	728	729	729	729	729	729	729	729	729	729	729	730	730	
Carcass ID Number	03644	03362	02661	03603	03311	03222	02551	03114	03212	03113	03663	02722	02822	02833	02932	03011	03302	03111	03412	03341	03421	03611	03622	02811	02921	**Total Tissues/ Tumors**
Alimentary System (continued)																										
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papilloma squamous	X	X		X	X		X	X		X	X	X		X		X			X	X					X	24
Papilloma squamous, multiple			X			X									X		X				X			X		9
Squamous cell carcinoma	X							X	X		X		X	X					X	X		X	X	X		17
Squamous cell carcinoma, multiple					X	X				X		X				X		X			X					10
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue	+				+		+				+		+	+	+					+						11
Papilloma squamous	X						X						X	X	X											8
Tooth																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, lung																										1
Fibrous histiocytoma, metastatic, kidney																										1
Squamous cell carcinoma, metastatic, stomach																										1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Squamous cell carcinoma, metastatic, stomach																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pheochromocytoma malignant														X			X									2
Pheochromocytoma benign		X		X			X			X			X	X	X									X		12
Bilateral, pheochromocytoma benign																X										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma															X				X							3
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma		X								X			X		X								X			7
Pars distalis, fibrous histiocytoma, metastatic, kidney																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell, adenoma					X		X						X										X			4
C-cell, carcinoma						X														X						2
Follicular cell, adenoma		X		X																						2
Follicular cell, carcinoma												X														1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	025	225	404	404	449	472	514	520	524	536	538	540	590	596	612	614	638	641	649	649	655	660	663	668
Carcass ID Number	02915	03155	03305	03325	03324	03553	03233	02664	03444	02744	02771	02293	03552	02844	03331	03511	02254	02553	02663	03304	02525	02622	02736	03443
General Body System																								
None																								
Genital System																								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes													X											
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																X				X				
Carcinoma			X				X																	
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes													X											
Squamous cell carcinoma, metastatic, stomach														X										
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, kidney																	X							
Bilateral, interstitial cell, adenoma						X	X	X	X		X	X				X	X	X	X	X	X	X	X	X
Interstitial cell, adenoma			X		X								X	X	X									
Hematopoietic System																								
Blood									+											+				
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, kidney																	X							
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, fibrous histiocytoma, metastatic, kidney																	X							
Renal, fibrous histiocytoma, metastatic, kidney																	X							
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, kidney																	X							
Sarcoma, metastatic, ear																								

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	669	678	684	685	685	686	698	701	709	720	728	729	729	729	729	729	729	729	729	729	729	729	730	730	
Carcass ID Number	03644	03352	02661	03303	03331	03322	02551	03114	03321	03113	03663	02772	02822	02883	02992	03001	03302	03111	03112	03441	03442	03361	03662	02811	02991	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesothelioma malignant, metastatic, testes																				X		X				2
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma									X								X					X				5
Carcinoma													X													3
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma						X											X									2
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Mesothelioma malignant, metastatic, testes																						X				2
Squamous cell carcinoma, metastatic, stomach																										1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrous histiocytoma, metastatic, kidney																										1
Bilateral, interstitial cell, adenoma	X	X	X		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X	X		36
Interstitial cell, adenoma				X					X												X				X	9
Hematopoietic System																										
Blood																	+									3
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrous histiocytoma, metastatic, kidney																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mediastinal, fibrous histiocytoma, metastatic, kidney																										1
Renal, fibrous histiocytoma, metastatic, kidney																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Fibrous histiocytoma, metastatic, kidney																										1
Sarcoma, metastatic, ear															X											1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	025	225	404	404	449	472	514	520	524	536	538	540	590	596	612	614	638	641	649	649	655	660	663	668
Carcass ID Number	02915	03155	03305	03325	03524	03553	03623	02664	03444	02274	02711	02093	03552	02844	03331	03511	02254	02533	02663	03044	02525	02622	02733	03443
Hematopoietic System (continued)																								
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, kidney																	X							
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, kidney																	X							
Thymus	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	M	+	+	+	+	+	M
Fibrous histiocytoma, metastatic, kidney																	X							
Integumentary System																								
Mammary gland	+	+	+	+	+	M	+	+	M	M	+	+	M	M	+	+	M	+	+	M	+	+	M	M
Fibroadenoma																								
Fibroadenoma, multiple																								
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Keratoacanthoma																								
Mesothelioma malignant, metastatic, testes													X											
Squamous cell carcinoma														X										
Trichoepithelioma																								
Subcutaneous tissue, fibroma									X															
Subcutaneous tissue, fibroma, multiple																								
Subcutaneous tissue, sarcoma																								X
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma										X														
Skeletal muscle		+											+	+			+					+		
Fibrous histiocytoma, metastatic																	X							
Squamous cell carcinoma, metastatic, stomach													X	X										
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Glioma malignant																		X						
Peripheral nerve																								
Squamous cell carcinoma, metastatic, pharynx																								
Spinal cord					+												+							

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	669	678	684	685	685	686	698	701	709	720	728	729	729	729	729	729	729	729	729	729	729	729	730	730	
Carcass ID Number	03642	03362	02661	03033	03311	03222	02521	03114	03021	03313	03363	02722	02822	02883	02932	03001	03022	03112	03312	03414	03422	03612	03662	02811	02921	**Total Tissues/ Tumors**
Hematopoietic System (continued)																										
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Fibrous histiocytoma, metastatic, kidney																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrous histiocytoma, metastatic, kidney																										1
Thymus	M	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	41
Fibrous histiocytoma, metastatic, kidney																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	M	+	+	+	M	M	+	M	+	+	+	M	+	+	+	+	M	+	+	34
Fibroadenoma																X										1
Fibroadenoma, multiple																				X						1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Keratoacanthoma																		X								1
Mesothelioma malignant, metastatic, testes																										1
Squamous cell carcinoma																										1
Trichoepithelioma										X																1
Subcutaneous tissue, fibroma												X		X			X				X					5
Subcutaneous tissue, fibroma, multiple							X																			1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Osteosarcoma																										1
Skeletal muscle																										5
Fibrous histiocytoma, metastatic																										1
Squamous cell carcinoma, metastatic, stomach																										2
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Glioma malignant																										1
Peripheral nerve				+																						1
Squamous cell carcinoma, metastatic, pharynx				X																						1
Spinal cord																										2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	025	225	404	404	449	472	514	520	524	536	538	540	590	596	612	614	638	641	649	649	655	660	663	668
Carcass ID Number	02915	03155	03035	03325	03424	03553	03233	02644	03444	02744	02711	02933	03552	02844	03331	03511	02254	02553	02663	03044	02552	02622	02733	03443
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																								
Alveolar/bronchiolar carcinoma																								
Carcinoma																		X						
Fibrous histiocytoma, metastatic, kidney																	X							
Squamous cell carcinoma, metastatic, stomach														X										
Mediastinum, squamous cell carcinoma, metastatic, stomach														X										
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																								
Ear																								
Sarcoma																								
Eye							+		+													+		
Harderian gland																								
Urinary System																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								
Fibrous histiocytoma, metastatic																	X							
Mesothelioma malignant, metastatic, testes																								
Squamous cell carcinoma, metastatic, stomach													X											
Renal tubule, adenoma																						X		
Renal tubule, adenoma, multiple																								X
Renal tubule, oncocytoma benign																								
Transitional epithelium, carcinoma																								
Urinary bladder	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																								
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear													X							X				X
Lymphoma malignant lymphocytic																						X		
Mesothelioma malignant													X											

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	669	678	684	685	685	686	698	701	709	720	728	729	729	729	729	729	729	729	729	729	729	729	730	730	
Carcass ID Number	03644	03362	02661	03303	03311	03322	02521	03114	03321	03113	03633	02722	02822	02883	02992	03012	03022	03111	03312	03441	03422	03361	03622	02811	02991	**Total Tissues/ Tumors**
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma			X																			X				2
Alveolar/bronchiolar carcinoma													X													1
Carcinoma																										1
Fibrous histiocytoma, metastatic, kidney																										1
Squamous cell carcinoma, metastatic, stomach																										1
Mediastinum, squamous cell carcinoma, metastatic, stomach																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	48
Special Senses System																										
Ear	+														+											2
Sarcoma	X														X											2
Eye	+							+			+											+				7
Harderian gland				+																						1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma		X							X																	2
Fibrous histiocytoma, metastatic																										1
Mesothelioma malignant, metastatic, testes																						X				1
Squamous cell carcinoma, metastatic, stomach																										1
Renal tubule, adenoma			X	X			X	X			X			X					X							8
Renal tubule, adenoma, multiple	X				X	X									X	X	X	X			X	X				10
Renal tubule, oncocytoma benign				X																						1
Transitional epithelium, carcinoma																			X							1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	47
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leukemia mononuclear			X							X			X				X			X		X				9
Lymphoma malignant lymphocytic																										1
Mesothelioma malignant																				X		X				3

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg

Number of Days on Study	327	337	361	368	369	369	382	388	395	401	423	424	425	432	432	444	448	452	459	470	470	473	478	479	480	481
Carcass ID Number	04355	04555	04055	03885	03844	04455	03755	04115	03744	04885	04255	04884	03955	03944	04554	04444	03732	03822	04655	03811	04233	04644	04022	04755	03722	04001
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp adenomatous																										
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+
Polyp adenomatous																	X									
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																		X								
Hepatocellular adenoma																										
Mesentery																										
Mesothelioma malignant, metastatic, testes																										
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenocarcinoma																										
Acinus, adenoma																					X			X		
Acinus, adenoma, multiple											X			X								X	X			X
Pharynx											+	+		+			+							+		+
Palate, papilloma squamous												X														
Palate, squamous cell carcinoma											X			X			X							X		X
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous				X			X					X	X	X	X	X							X	X		
Papilloma squamous, multiple					X													X	X			X	X		X	
Squamous cell carcinoma											X								X							
Squamous cell carcinoma, multiple																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+
Papilloma squamous		X									X	X	X	X		X					X		X		X	X
Papilloma squamous, multiple																										
Squamous cell carcinoma	X			X	X	X		X		X					X			X	X	X		X		X		
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	484	484	485	487	487	487	493	493	494	495	501	511	512	512	519	520	527	534	534	534	534	534	534	534	534	534	
Carcass ID Number	04431	04432	04482	03922	04422	04663	04421	04433	04453	04474	04473	04452	04472	04481	04462	04413	04422	03711	03911	03393	04111	04122	04441	04511	04611	04471	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	51
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Polyp adenomatous																				X							1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Polyp adenomatous																											1
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenocarcinoma				X																							1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hepatocellular carcinoma																							X				2
Hepatocellular adenoma																X											1
Mesentery										+												+			+		3
Mesothelioma malignant, metastatic, testes										X																	1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Acinus, adenocarcinoma																						X					1
Acinus, adenoma																							X	X	X		5
Acinus, adenoma, multiple	X	X	X		X	X	X		X	X	X	X	X	X	X		X	X	X		X	X				X	24
Pharynx		+		+			+			+		+		+	+					+				+			15
Palate, papilloma squamous							X													X							3
Palate, squamous cell carcinoma		X										X															7
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenoma	X																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Papilloma squamous	X		X		X		X	X	X		X	X	X	X	X	X	X	X								X	24
Papilloma squamous, multiple		X								X										X	X	X	X	X	X		14
Squamous cell carcinoma	X			X	X	X			X		X			X	X				X					X			12
Squamous cell carcinoma, multiple												X															1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Tongue	+	+	+	+	+	+	+	+	+	+	+		+		+	+	+			+			+	+	+	+	44
Papilloma squamous	X	X						X	X	X	X																16
Papilloma squamous, multiple																				X			X				2
Squamous cell carcinoma				X		X							X		X	X	X								X		19
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	327	337	361	368	369	369	382	388	395	401	423	424	425	432	432	444	448	452	459	470	470	473	478	479	480	481
Carcass ID Number	04355	04555	04055	03885	03844	04445	03755	04115	03744	04855	04255	04484	03955	03944	04544	04473	03732	03822	04655	03811	04233	04644	04022	04755	03721	04001
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																								X		
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+
Pituitary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																										
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																						X			X	
Follicular cell, adenoma													X												X	
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma malignant, metastatic, testes																										
Penis																										+
Squamous cell carcinoma																										X
Preputial gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																			X			X		X		
Carcinoma							X							X												
Bilateral, adenoma																				X						
Bilateral, carcinoma																X										
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma			X					X						X	X		X	X	X	X	X	X	X	X		X
Interstitial cell, adenoma						X					X	X	X			X									X	
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																										
Squamous cell carcinoma, metastatic, stomach																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	484	484	485	487	487	487	493	493	494	495	501	511	512	512	519	520	527	534	534	534	534	534	534	534	534	
Carcass ID Number	04431	04432	04482	03992	04422	04463	04421	04433	04455	04474	04473	04552	04572	04581	04662	04613	04422	03711	03991	03933	04111	04121	04414	04551	04661	04671	**Total Tissues/ Tumors**
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenoma																											1
Parathyroid gland	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pars distalis, adenoma		X																		X							2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	51
C-cell, adenoma																X				X			X				5
Follicular cell, adenoma																											2
General Body System																											
None																											
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Mesothelioma malignant, metastatic, testes								X		X																	2
Penis																											1
Squamous cell carcinoma																											1
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma						X								X	X						X					X	8
Carcinoma			X		X																						4
Bilateral, adenoma											X												X				3
Bilateral, carcinoma																											1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Bilateral, interstitial cell, adenoma	X		X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	36
Interstitial cell, adenoma						X														X							8
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node, mesenteric	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hemangioma							X																				1
Squamous cell carcinoma, metastatic, stomach					X						X																2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	327	337	361	368	369	369	382	388	395	401	423	424	425	432	432	444	448	452	459	470	470	473	478	479	480	481
Carcass ID Number	04355	04555	04055	03885	03844	04445	03775	04115	03774	04485	04425	04484	03995	03944	04544	04474	03732	03882	04655	03811	04233	04464	04402	04475	03721	04001
Hematopoietic System (continued)																										
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																										
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Epithelial cell, thymoma benign																										
Integumentary System																										
Mammary gland	+	M	M	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Basal cell carcinoma																								X		
Keratoacanthoma																							X			
Papilloma squamous																										
Squamous cell carcinoma																										
Scrotum, mesothelioma malignant, metastatic, testes																										
Subcutaneous tissue, fibroma																										
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																									X	
Skeletal muscle																										
Adenocarcinoma, metastatic, uncertain primary site																										
Mesothelioma malignant, metastatic, testes																										
Squamous cell carcinoma, metastatic, stomach																										
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																										
Squamous cell carcinoma, metastatic, skin														X												
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																										
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	484	484	485	487	487	487	493	493	494	495	501	511	512	512	519	520	527	534	534	534	534	534	534	534	534	534	534	
Carcass ID Number	04431	04432	04482	03992	04422	04463	04421	04433	04453	04474	04473	04452	04472	04481	04462	04413	04422	03771	03991	03933	04411	04122	04414	04451	04561	04671		**Total Tissues/ Tumors**
Hematopoietic System (continued)																												
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hemangioma			X																									1
Thymus	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	48
Epithelial cell, thymoma benign												X																1
Integumentary System																												
Mammary gland	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	M	+	+	+	41
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Basal cell carcinoma																												1
Keratoacanthoma							X																					2
Papilloma squamous																						X				X		2
Squamous cell carcinoma	X																											1
Scrotum, mesothelioma malignant, metastatic, testes								X																				1
Subcutaneous tissue, fibroma																X												1
Musculoskeletal System																												
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Osteosarcoma																												1
Skeletal muscle					+					+	+																	3
Adenocarcinoma, metastatic, uncertain primary site					X																							1
Mesothelioma malignant, metastatic, testes										X																		1
Squamous cell carcinoma, metastatic, stomach											X																	1
Nervous System																												
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Respiratory System																												
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Alveolar/bronchiolar adenoma									X																			1
Squamous cell carcinoma, metastatic, skin																												1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Squamous cell carcinoma																					X							1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	327	337	361	368	369	369	382	388	395	401	423	424	425	432	432	444	448	452	459	470	470	473	478	479	480	481
Carcass ID Number	04355	04555	04055	03885	03844	04445	03775	04115	03744	04485	04425	04484	03995	03944	04545	04443	03732	03822	04465	03811	04233	04644	04022	04475	03722	04041
Special Senses System																										
Eye			+													+	+	+								+
Harderian gland																	+									
Zymbal's gland			+						+				+	+												
Carcinoma									X				X	X												
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Renal tubule, adenoma																		X			X					X
Renal tubule, adenoma, multiple											X									X				X	X	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																			X				X			
Mesothelioma malignant																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	4 8 4	4 8 4	4 8 5	4 8 7	4 8 7	4 8 7	4 9 3	4 9 3	4 9 4	4 9 5	5 0 1	5 1 1	5 1 2	5 1 2	5 1 9	5 2 0	5 2 7	5 3 4	5 3 4	5 3 4	5 3 4	5 3 4	5 3 4	5 3 4	5 3 4	5 3 4	
Carcass ID Number	0 4 3 1	0 4 3 2	0 4 8 2	0 3 9 2	0 4 2 2	0 4 6 3	0 4 2 1	0 4 4 3	0 4 5 3	0 4 7 4	0 4 7 3	0 4 5 2	0 4 7 2	0 4 8 1	0 4 6 2	0 4 1 3	0 4 4 2	0 3 7 1	0 3 9 1	0 3 9 3	0 4 1 1	0 4 1 2	0 4 4 1	0 4 5 1	0 4 6 1	0 4 7 1	**Total Tissues/ Tumors**
Special Senses System																											
Eye							+	+			+																8
Harderian gland																							+				2
Zymbal's gland																											4
Carcinoma																											3
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenoma																X				X							2
Renal tubule, adenoma				X				X		X		X						X					X	X			10
Renal tubule, adenoma, multiple		X			X	X													X		X						9
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 2
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 2
Leukemia mononuclear							X								X		X						X				6
Mesothelioma malignant								X		X																	2

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	10/60 (17%)	7/60 (12%)	13/58 (22%)	0/59 (0%)
Adjusted rate[b]	27.6%	19.7%	54.1%	0.0%
15-Month interim evaluation[c]	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate[d]	8/34 (24%)	5/32 (16%)	5/14 (36%)	0/0 (0%)
First incidence (days)	663	600	596	-[f]
Life table test[e]	P=0.009	P=0.322N	P=0.013	-
Logistic regression test[e]	P=0.419	P=0.256N	P=0.076	P=0.842N
Cochran-Armitage test[e]	P=0.004N			
Fisher exact test[e]		P=0.301N	P=0.289	P<0.001N
Adrenal Medulla: Benign, Complex, or Malignant Pheochromocytoma				
Overall rate	11/60 (18%)	8/60 (13%)	14/58 (24%)	0/59 (0%)
Adjusted rate	30.4%	21.7%	59.2%	0.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	9/34 (26%)	5/32 (16%)	6/14 (43%)	0/0 (0%)
First incidence (days)	663	600	596	-
Life table test	P=0.007	P=0.327N	P=0.009	-
Logistic regression test	P=0.397	P=0.261N	P=0.065	P=0.853N
Cochran-Armitage test	P=0.002N			
Fisher exact test		P=0.309N	P=0.293	P<0.001N
Kidney (Renal Tubule): Adenoma				
Overall rate	0/60 (0%)	2/60 (3%)	20/59 (34%)	26/60 (43%)
Adjusted rate	0.0%	6.3%	76.3%	85.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	5/8 (63%)
Terminal rate	0/34 (0%)	2/32 (6%)	8/14 (57%)	0/0 (0%)
First incidence (days)	-	729 (T)	660	423
Life table test	P<0.001	P=0.225	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.225	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.248	P<0.001	P<0.001
Large and Small Intestine: Adenomatous Polyp or Adenocarcinoma				
Overall rate	0/60 (0%)	0/60 (0%)	2/59 (3%)	3/60 (5%)
Adjusted rate	0.0%	0.0%	5.4%	16.9%
15-Month interim evaluation	1/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	0/34 (0%)	0/32 (0%)	0/14 (0%)	0/0 (0%)
First incidence (days)	-	-	590	448
Life table test	P<0.001	-	P=0.193	P=0.020
Logistic regression test	P=0.094	-	P=0.247	P=0.239
Cochran-Armitage test	P=0.037			
Fisher exact test		-	P=0.244	P=0.122
Liver: Hepatocellular Adenoma				
Overall rate	1/60 (2%)	1/60 (2%)	3/59 (5%)	1/60 (2%)
Adjusted rate	2.9%	3.1%	19.3%	9.1%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	1/34 (3%)	1/32 (3%)	2/14 (14%)	0/0 (0%)
First incidence (days)	729 (T)	729 (T)	709	520
Life table test	P=0.002	P=0.748	P=0.076	P=0.214
Logistic regression test	P=0.054	P=0.748	P=0.120	P=0.601
Cochran-Armitage test	P=0.618N			
Fisher exact test		P=0.752N	P=0.303	P=0.752N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	1/60 (2%)	1/60 (2%)	4/59 (7%)	3/60 (5%)
Adjusted rate	2.9%	3.1%	22.6%	21.2%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	1/34 (3%)	1/32 (3%)	2/14 (14%)	0/0 (0%)
First incidence (days)	729 (T)	729 (T)	669	452
Life table test	P<0.001	P=0.748	P=0.034	P=0.009
Logistic regression test	P=0.011	P=0.748	P=0.073	P=0.216
Cochran-Armitage test	P=0.223			
Fisher exact test		P=0.752N	P=0.177	P=0.309
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	2/60 (3%)	1/59 (2%)	4/59 (7%)	2/60 (3%)
Adjusted rate	5.5%	3.2%	20.6%	7.9%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/8 (13%)
Terminal rate	1/34 (3%)	1/31 (3%)	2/14 (14%)	0/0 (0%)
First incidence (days)	663	729 (T)	641	452 (I)
Life table test	P=0.001	P=0.510N	P=0.118	P=0.120
Logistic regression test	P=0.132	P=0.491N	P=0.209	P=0.610
Cochran-Armitage test	P=0.547			
Fisher exact test		P=0.506N	P=0.332	P=0.691N
Mammary Gland: Fibroadenoma				
Overall rate	2/60 (3%)	3/60 (5%)	2/59 (3%)	0/60 (0%)
Adjusted rate	5.9%	8.6%	14.3%	0.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	2/34 (6%)	2/32 (6%)	2/14 (14%)	0/0 (0%)
First incidence (days)	729 (T)	685	729 (T)	-
Life table test	P=0.595	P=0.490	P=0.352	-
Logistic regression test	P=0.701	P=0.520	P=0.352	-
Cochran-Armitage test	P=0.117N			
Fisher exact test		P=0.500	P=0.684	P=0.248N
Oral Cavity (Pharynx and Tongue): Squamous Cell Papilloma				
Overall rate	0/60 (0%)	4/60 (7%)	10/59 (17%)	22/60 (37%)
Adjusted rate	0.0%	11.7%	39.3%	61.5%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	3/8 (38%)
Terminal rate	0/34 (0%)	2/32 (6%)	3/14 (21%)	0/0 (0%)
First incidence (days)	-	694	452 (I)	337
Life table test	P<0.001	P=0.062	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.069	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.059	P<0.001	P<0.001
Oral Cavity (Pharynx and Tongue): Squamous Cell Carcinoma				
Overall rate	1/60 (2%)	0/60 (0%)	11/59 (19%)	25/60 (42%)
Adjusted rate	2.9%	0.0%	47.6%	65.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	1/34 (3%)	0/32 (0%)	4/14 (29%)	0/0 (0%)
First incidence (days)	729 (T)	-	404	327
Life table test	P<0.001	P=0.512N	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.512N	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.500N	P=0.002	P<0.001

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Oral Cavity (Pharynx and Tongue): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	1/60 (2%)	4/60 (7%)	19/59 (32%)	43/60 (72%)
Adjusted rate	2.9%	11.7%	66.4%	85.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	3/8 (38%)
Terminal rate	1/34 (3%)	2/32 (6%)	6/14 (43%)	0/0 (0%)
First incidence (days)	729 (T)	694	404	327
Life table test	P<0.001	P=0.173	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.192	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.182	P<0.001	P<0.001
Pancreas: Adenoma				
Overall rate	5/60 (8%)	21/60 (35%)	37/59 (63%)	31/60 (52%)
Adjusted rate	14.7%	58.0%	100.0%	96.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	2/8 (25%)
Terminal rate	5/34 (15%)	17/32 (53%)	14/14 (100%)	0/0 (0%)
First incidence (days)	729 (T)	685	450 (I)	423
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Pancreas: Adenoma or Carcinoma				
Overall rate	5/60 (8%)	21/60 (35%)	37/59 (63%)	31/60 (52%)
Adjusted rate	14.7%	58.0%	100.0%	96.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	2/8 (25%)
Terminal rate	5/34 (15%)	17/32 (53%)	14/14 (100%)	0/0
First incidence (days)	729 (T)	685	450 (I)	423
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Pancreatic Islets: Adenoma				
Overall rate	9/60 (15%)	4/60 (7%)	3/59 (5%)	1/60 (2%)
Adjusted rate	24.4%	11.3%	17.3%	3.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	7/34 (21%)	3/32 (9%)	2/14 (14%)	0/0 (0%)
First incidence (days)	614	603	660	479
Life table test	P=0.436	P=0.132N	P=0.387N	P=0.395
Logistic regression test	P=0.392N	P=0.100N	P=0.175N	P=0.712N
Cochran-Armitage test	P=0.015N			
Fisher exact test		P=0.120N	P=0.067N	P=0.008N
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	10/60 (17%)	4/60 (7%)	3/59 (5%)	1/60 (2%)
Adjusted rate	27.2%	11.3%	17.3%	3.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	8/34 (24%)	3/32 (9%)	2/14 (14%)	0/0 (0%)
First incidence (days)	614	603	660	479
Life table test	P=0.504	P=0.087N	P=0.320N	P=0.395
Logistic regression test	P=0.343N	P=0.061N	P=0.126N	P=0.724N
Cochran-Armitage test	P=0.010N			
Fisher exact test		P=0.077N	P=0.040N	P=0.004N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Pharynx: Squamous Cell Papilloma				
Overall rate	0/60 (0%)	2/60 (3%)	1/59 (2%)	4/60 (7%)
Adjusted rate	0.0%	6.1%	4.2%	19.2%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/8 (13%)
Terminal rate	0/34 (0%)	1/32 (3%)	0/14 (0%)	0/0 (0%)
First incidence (days)	-	710	678	424
Life table test	P<0.001	P=0.230	P=0.425	P=0.009
Logistic regression test	P=0.046	P=0.247	P=0.458	P=0.196
Cochran-Armitage test	P=0.048			
Fisher exact test		P=0.248	P=0.496	P=0.059
Pharynx: Squamous Cell Carcinoma				
Overall rate	1/60 (2%)	0/60 (0%)	11/59 (19%)	7/60 (12%)
Adjusted rate	2.9%	0.0%	47.6%	21.8%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	1/34 (3%)	0/32 (0%)	4/14 (29%)	0/0 (0%)
First incidence (days)	729 (T)	-	404	423
Life table test	P<0.001	P=0.512N	P<0.001	P=0.001
Logistic regression test	P=0.003	P=0.512N	P<0.001	P=0.114
Cochran-Armitage test	P=0.015			
Fisher exact test		P=0.500N	P=0.002	P=0.031
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	9/58 (16%)	15/58 (26%)	8/59 (14%)	2/59 (3%)
Adjusted rate	25.1%	34.3%	35.8%	14.5%
15-Month interim evaluation	0/10 (0%)	2/10 (20%)	1/10 (10%)	0/8 (0%)
Terminal rate	6/32 (19%)	6/31 (19%)	3/14 (21%)	0/0 (0%)
First incidence (days)	648	450 (I)	450 (I)	484
Life table test	P=0.111	P=0.150	P=0.214	P=0.049
Logistic regression test	P=0.153N	P=0.139	P=0.519	P=0.615
Cochran-Armitage test	P=0.003N			
Fisher exact test		P=0.126	P=0.485N	P=0.025N
Preputial Gland: Adenoma				
Overall rate	5/59 (8%)	3/57 (5%)	6/59 (10%)	11/58 (19%)
Adjusted rate	13.6%	9.6%	25.6%	55.5%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	0/8 (0%)
Terminal rate	4/34 (12%)	2/29 (7%)	2/14 (14%)	0/0 (0%)
First incidence (days)	506	703	450 (I)	459
Life table test	P<0.001	P=0.421N	P=0.154	P<0.001
Logistic regression test	P=0.002	P=0.363N	P=0.404	P=0.023
Cochran-Armitage test	P=0.014			
Fisher exact test		P=0.378N	P=0.500	P=0.083
Preputial Gland: Carcinoma				
Overall rate	0/59 (0%)	3/57 (5%)	3/59 (5%)	6/58 (10%)
Adjusted rate	0.0%	7.4%	10.9%	15.9%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/8 (13%)
Terminal rate	0/34 (0%)	0/29 (0%)	1/14 (7%)	0/0 (0%)
First incidence (days)	-	654	404	382
Life table test	P<0.001	P=0.143	P=0.070	P=0.005
Logistic regression test	P=0.103	P=0.118	P=0.152	P=0.164
Cochran-Armitage test	P=0.021			
Fisher exact test		P=0.115	P=0.122	P=0.013

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Preputial Gland: Adenoma or Carcinoma				
Overall rate	5/59 (8%)	6/57 (11%)	9/59 (15%)	17/58 (29%)
Adjusted rate	13.6%	16.4%	34.6%	62.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	1/8 (13%)
Terminal rate	4/34 (12%)	2/29 (7%)	3/14 (21%)	0/0 (0%)
First incidence (days)	506	654	404	382
Life table test	P<0.001	P=0.463	P=0.028	P<0.001
Logistic regression test	P<0.001	P=0.491	P=0.163	P=0.007
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.476	P=0.197	P=0.004
Skin: Squamous Cell Papilloma				
Overall rate	0/60 (0%)	2/60 (3%)	0/59 (0%)	5/60 (8%)
Adjusted rate	0.0%	5.7%	0.0%	27.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	3/8 (38%)
Terminal rate	0/34 (0%)	1/32 (3%)	0/14 (0%)	0/0 (0%)
First incidence (days)	-	689	-	450 (I)
Life table test	P<0.001	P=0.242	-	P=0.001
Logistic regression test	P=0.023	P=0.248	-	P=0.111
Cochran-Armitage test	P=0.010			
Fisher exact test		P=0.248	-	P=0.029
Skin: Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	2/60 (3%)	1/59 (2%)	6/60 (10%)
Adjusted rate	0.0%	5.7%	2.8%	30.5%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	3/8 (38%)
Terminal rate	0/34 (0%)	1/32 (3%)	0/14 (0%)	0/0 (0%)
First incidence (days)	-	689	596	450 (I)
Life table test	P<0.001	P=0.242	P=0.455	P<0.001
Logistic regression test	P=0.014	P=0.248	P=0.512	P=0.073
Cochran-Armitage test	P=0.005			
Fisher exact test		P=0.248	P=0.496	P=0.014
Skin: Trichoepithelioma, Keratoacanthoma, Squamous Cell Papilloma, Squamous Cell Carcinoma, or Basal Cell Carcinoma				
Overall rate	3/60 (5%)	3/60 (5%)	3/59 (5%)	9/60 (15%)
Adjusted rate	8.8%	8.7%	15.4%	38.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	3/8 (38%)
Terminal rate	3/34 (9%)	2/32 (6%)	1/14 (7%)	0/0 (0%)
First incidence (days)	729 (T)	689	596	450 (I)
Life table test	P<0.001	P=0.645	P=0.305	P<0.001
Logistic regression test	P=0.002	P=0.647N	P=0.494	P=0.034
Cochran-Armitage test	P=0.014			
Fisher exact test		P=0.660N	P=0.652	P=0.063
Skin (Subcutaneous Tissue): Fibroma				
Overall rate	2/60 (3%)	2/60 (3%)	6/59 (10%)	1/60 (2%)
Adjusted rate	5.2%	5.7%	34.0%	9.1%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	1/34 (3%)	1/32 (3%)	4/14 (29%)	0/0 (0%)
First incidence (days)	614	692	524	520
Life table test	P=0.001	P=0.690	P=0.016	P=0.214
Logistic regression test	P=0.189	P=0.682N	P=0.068	P=0.814
Cochran-Armitage test	P=0.373N			
Fisher exact test		P=0.691N	P=0.131	P=0.500N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Skin (Subcutaneous Tissue): Fibroma or Sarcoma				
Overall rate	3/60 (5%)	3/60 (5%)	7/59 (12%)	1/60 (2%)
Adjusted rate	7.6%	8.0%	36.5%	9.1%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	1/34 (3%)	1/32 (3%)	4/14 (29%)	0/0 (0%)
First incidence (days)	614	663	524	520
Life table test	P=0.002	P=0.646N	P=0.024	P=0.214
Logistic regression test	P=0.353	P=0.652N	P=0.086	P=0.694N
Cochran-Armitage test	P=0.229N			
Fisher exact test		P=0.660N	P=0.154	P=0.309N
Stomach (Forestomach): Squamous Cell Papilloma				
Overall rate	0/60 (0%)	31/60 (52%)	36/59 (61%)	46/60 (77%)
Adjusted rate	0.0%	74.8%	89.0%	97.7%
15-Month interim evaluation	0/10 (0%)	2/10 (20%)	3/10 (30%)	8/8 (100%)
Terminal rate	0/34 (0%)	22/32 (69%)	10/14 (71%)	0/0 (0%)
First incidence (days)	-	450 (I)	404	368
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Stomach (Forestomach): Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	9/60 (15%)	28/59 (47%)	14/60 (23%)
Adjusted rate	0.0%	24.3%	89.4%	57.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	1/8 (13%)
Terminal rate	0/34 (0%)	6/32 (19%)	11/14 (79%)	0/0 (0%)
First incidence (days)	-	600	450 (I)	423
Life table test	P<0.001	P=0.003	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.003	P<0.001	P=0.001
Cochran-Armitage test	P=0.012			
Fisher exact test		P=0.001	P<0.001	P<0.001
Stomach (Forestomach): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	35/60 (58%)	46/59 (78%)	51/60 (85%)
Adjusted rate	0.0%	80.8%	100.0%	100.0%
15-Month interim evaluation	0/10 (0%)	2/10 (20%)	4/10 (40%)	8/8 (100%)
Terminal rate	0/34 (0%)	24/32 (75%)	14/14 (100%)	0/0 (0%)
First incidence (days)	-	450 (I)	404	368
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Testes: Adenoma				
Overall rate	55/60 (92%)	54/60 (90%)	55/59 (93%)	52/60 (87%)
Adjusted rate	100.0%	100.0%	100.0%	100.0%
15-Month interim evaluation	8/10 (80%)	6/10 (60%)	10/10 (100%)	8/8 (100%)
Terminal rate	34/34 (100%)	32/32 (100%)	14/14 (100%)	0/0 (0%)
First incidence (days)	450 (I)	450 (I)	404	361
Life table test	P<0.001	P=0.566N	P<0.001	P<0.001
Logistic regression test	P=0.016	P=0.339N	P=0.151	P=0.057
Cochran-Armitage test	P=0.223N			
Fisher exact test		P=0.500N	P=0.511	P=0.279N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Thyroid Gland (C-cell): Adenoma				
Overall rate	4/60 (7%)	15/59 (25%)	4/59 (7%)	6/59 (10%)
Adjusted rate	10.9%	41.6%	22.5%	38.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/8 (13%)
Terminal rate	3/34 (9%)	11/31 (35%)	2/14 (14%)	0/0 (0%)
First incidence (days)	614	621	685	452 (I)
Life table test	P<0.001	P=0.005	P=0.253	P<0.001
Logistic regression test	P=0.040	P=0.006	P=0.443	P=0.113
Cochran-Armitage test	P=0.273N			
Fisher exact test		P=0.005	P=0.632	P=0.361
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rate	4/60 (7%)	16/59 (27%)	6/59 (10%)	6/59 (10%)
Adjusted rate	10.9%	43.1%	32.5%	38.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	1/8 (13%)
Terminal rate	3/34 (9%)	11/31 (35%)	3/14 (21%)	0/0 (0%)
First incidence (days)	614	621	685	452 (I)
Life table test	P<0.001	P=0.003	P=0.062	P<0.001
Logistic regression test	P=0.024	P=0.003	P=0.171	P=0.113
Cochran-Armitage test	P=0.234N			
Fisher exact test		P=0.003	P=0.361	P=0.361
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rate	1/60 (2%)	1/59 (2%)	3/59 (5%)	2/59 (3%)
Adjusted rate	2.9%	3.2%	15.1%	5.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	1/34 (3%)	1/31 (3%)	1/14 (7%)	0/0 (0%)
First incidence (days)	729 (T)	729 (T)	678	425
Life table test	P=0.002	P=0.741	P=0.116	P=0.160
Logistic regression test	P=0.116	P=0.741	P=0.185	P=0.553
Cochran-Armitage test	P=0.395			
Fisher exact test		P=0.748	P=0.303	P=0.494
Tongue: Squamous Cell Papilloma				
Overall rate	0/60 (0%)	2/60 (3%)	9/59 (15%)	21/60 (35%)
Adjusted rate	0.0%	5.9%	36.7%	59.3%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	3/8 (38%)
Terminal rate	0/34 (0%)	1/32 (3%)	3/14 (21%)	0/0 (0%)
First incidence (days)	-	694	452 (I)	337
Life table test	P<0.001	P=0.236	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.248	P=0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.248	P=0.001	P<0.001
Tongue: Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	0/60 (0%)	0/59 (0%)	19/60 (32%)
Adjusted rate	0.0%	0.0%	0.0%	57.5%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	0/34 (0%)	0/32 (0%)	0/14 (0%)	0/0 (0%)
First incidence (days)	-	-	-	327
Life table test	P<0.001	-	-	P<0.001
Logistic regression test	P<0.001	-	-	P=0.004
Cochran-Armitage test	P<0.001			
Fisher exact test		-	-	P<0.001

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Tongue: Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	2/60 (3%)	9/59 (15%)	40/60 (67%)
Adjusted rate	0.0%	5.9%	36.7%	83.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	3/8 (38%)
Terminal rate	0/34 (0%)	1/32 (3%)	3/14 (21%)	0/0 (0%)
First incidence (days)	-	694	452 (I)	327
Life table test	P<0.001	P=0.236	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.248	P=0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.248	P=0.001	P<0.001
Zymbal's Gland: Carcinoma				
Overall rate	0/60 (0%)	0/60 (0%)	0/59 (0%)	3/60 (5%)
Adjusted rate	0.0%	0.0%	0.0%	6.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	0/34 (0%)	0/32 (0%)	0/14 (0%)	0/0 (0%)
First incidence (days)	-	-	-	395
Life table test	P=0.005	-	-	P=0.093
Logistic regression test	P=0.058	-	-	P=0.441
Cochran-Armitage test	P=0.009			
Fisher exact test		-	-	P=0.122
All Organs: Mononuclear Cell Leukemia				
Overall rate	16/60 (27%)	11/60 (18%)	9/59 (15%)	6/60 (10%)
Adjusted rate	42.6%	30.5%	42.0%	34.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/10 (0%)	0/8 (0%)
Terminal rate	13/34 (38%)	8/32 (25%)	4/14 (29%)	0/0 (0%)
First incidence (days)	605	591	590	459
Life table test	P<0.001	P=0.216N	P=0.459	P<0.001
Logistic regression test	P=0.152	P=0.141N	P=0.311N	P=0.219
Cochran-Armitage test	P=0.022N			
Fisher exact test		P=0.191N	P=0.096N	P=0.016N
All Organs: Malignant Mesothelioma				
Overall rate	3/60 (5%)	4/60 (7%)	4/59 (7%)	2/60 (3%)
Adjusted rate	7.8%	10.4%	18.1%	10.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/10 (10%)	0/8 (0%)
Terminal rate	2/34 (6%)	1/32 (3%)	2/14 (14%)	0/0 (0%)
First incidence (days)	485	621	450 (I)	493
Life table test	P=0.034	P=0.505	P=0.228	P=0.217
Logistic regression test	P=0.606N	P=0.509	P=0.469	P=0.732N
Cochran-Armitage test	P=0.332N			
Fisher exact test		P=0.500	P=0.491	P=0.500N
All Organs: Benign Neoplasms				
Overall rate	57/60 (95%)	58/60 (97%)	56/59 (95%)	57/60 (95%)
Adjusted rate	100.0%	100.0%	100.0%	100.0%
15-Month interim evaluation	8/10 (80%)	8/10 (80%)	10/10 (100%)	8/8 (100%)
Terminal rate	34/34 (100%)	32/32 (100%)	14/14 (100%)	0/0 (0%)
First incidence (days)	340	450 (I)	404	337
Life table test	P<0.001	P=0.445	P<0.001	P<0.001
Logistic regression test	P=0.026	P=0.656	P=0.268	P=0.072
Cochran-Armitage test	P=0.524N			
Fisher exact test		P=0.500	P=0.652N	P=0.660N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
All Organs: Malignant Neoplasms				
Overall rate	22/60 (37%)	28/60 (47%)	40/59 (68%)	47/60 (78%)
Adjusted rate	54.1%	60.5%	97.3%	93.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	2/10 (20%)	2/8 (25%)
Terminal rate	16/34 (47%)	14/32 (44%)	13/14 (93%)	0/0 (0%)
First incidence (days)	485	591	404	327
Life table test	P<0.001	P=0.199	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.222	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.177	P<0.001	P<0.001
All Organs: Benign and Malignant Neoplasms				
Overall rate	58/60 (97%)	58/60 (97%)	57/59 (97%)	60/60 (100%)
Adjusted rate	100.0%	100.0%	100.0%	100.0%
15-Month interim evaluation	8/10 (80%)	8/10 (80%)	10/10 (100%)	8/8 (100%)
Terminal rate	34/34 (100%)	32/32 (100%)	14/14 (100%)	0/0 (0%)
First incidence (days)	340	450 (I)	404	327
Life table test	P<0.001	P=0.512	P<0.001	P<0.001
Logistic regression test	P=0.005	P=0.566N	P=0.264	P=0.036
Cochran-Armitage test	P=0.157			
Fisher exact test		P=0.691N	P=0.684N	P=0.248

(T)Terminal sacrifice
(I)15-Month interim evaluation
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, epididymis, heart, kidney, larynx, liver, lung, nose, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] 15-Month interim evaluation began on day 450
[d] Observed incidence at terminal kill
[e] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by **N**.
[f] Not applicable; no neoplasms in animal group

TABLE A4a
Historical Incidence of Oral Cavity Neoplasms in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Squamous Cell Papilloma	Squamous Cell Carcinoma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	0/50	0/50
Tribromomethane	0/50	0/50	0/50
Hexachloroethane	0/50	0/50	0/50
Phenylbutazone	0/50	0/50	0/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	0/60	0/60	0/60
Overall Historical Incidence			
Total	3/820 (0.4%)[b]	0/820 (0.0%)	3/820 (0.4%)
Standard deviation	0.8%		0.8%
Range	0%-2%		0%-2%

[a] Data as of 3 April 1991
[b] Numerator includes two pharyngeal tumors and one lingual tumor

TABLE A4b
Historical Incidence of Forestomach Neoplasms in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Squamous Cell Papilloma	Squamous Cell Carcinoma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	0/50	0/50
Tribromomethane	0/50	0/50	0/50
Hexachloroethane	0/50	0/50	0/50
Phenylbutazone	0/50	0/50	0/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	0/60	0/60	0/60
Overall Historical Incidence			
Total	4/820 (0.5%)	0/820	4/820 (0.5%)
Standard deviation	1.2%		1.2%
Range	0%-4%		0%-4%

[a] Data as of 3 April 1991

TABLE A4c
Historical Incidence of Pancreatic Neoplasms in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	1/50	0/50	1/50
Tribromomethane	1/50	0/50	1/50
Hexachloroethane	0/50	0/50	0/50
Phenylbutazone	3/50	0/50	3/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	0/59	0/59	0/59
Overall Historical Incidence			
Total	57/815 (7.0%)	0/815	57/815 (7.0%)
Standard deviation	9.4%		9.4%
Range	0%-32%		0%-32%

[a] Data as of 3 April 1991

TABLE A4d
Historical Incidence of Renal Tubule Neoplasms in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	1/50	1/50
Tribromomethane	1/50	0/50	1/50
Hexachloroethane	1/50	0/50	1/50
Phenylbutazone	0/50	0/50	0/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	1/60	0/60	1/60
Overall Historical Incidence			
Total	6/820 (0.7%)	2/820 (0.2%)	8/820 (1.0%)
Standard deviation	1.0%	0.7%	1.3%
Range	0%-2%	0%-2%	0%-4%

[a] Data as of 3 April 1991

TABLE A4e
Historical Incidence of Zymbal's Gland Neoplasms in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	1/50	1/50
Tribromomethane	0/50	1/50	1/50
Hexachloroethane	0/50	1/50	1/50
Phenylbutazone	0/50	2/50	2/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	0/60	3/60	3/60
Overall Historical Incidence			
Total	2/820 (0.2%)	10/820 (1.2%)	12/820 (1.5%)
Standard deviation	1.0%	1.6%	2.0%
Range	0%-4%	0%-5%	0%-6%

[a] Data as of 3 April 1991

TABLE A4f
Historical Incidence of Preputial Gland Neoplasms in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	1/50	2/50	3/50
Tribromomethane	4/50	6/50	10/50
Hexachloroethane	1/50	0/50	1/50
Phenylbutazone	2/50	0/50	2/50
Probenecid	6/50	0/50	6/50
Titanocene•2Cl	4/60	1/60	5/60
Overall Historical Incidence			
Total	38/820 (4.6%)	22/820 (2.7%)	60/820 (7.3%)
Standard deviation	4.2%	4.0%	5.9%
Range	0%-12%	0%-12%	0%-20%

[a] Data as of 3 April 1991

TABLE A4g
Historical Incidence of Carcinoma of the Small Intestine in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls
Historical Incidence at EG&G Mason Research Institute	
2,4-Diaminophenol•2HCl	0/50
Tribromomethane	0/50
Hexachloroethane	0/50
Phenylbutazone	0/50
Probenecid	0/50
Titanocene•2Cl	0/60
Overall Historical Incidence	
Total	1/820 (0.1%)[b]
Standard deviation	0.5%
Range	0%-2%

[a] Data as of 3 April 1991. Current NTP historical neoplasm pooling convention recodes adenocarcinoma to carcinoma.
[b] Numerator specifies one jejunal carcinoma.

TABLE A4h
Historical Incidence of Carcinoma of the Large Intestine in Male F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls
Historical Incidence at EG&G Mason Research Institute	
2,4-Diaminophenol•2HCl	0/50
Tribromomethane	0/50
Hexachloroethane	0/50
Phenylbutazone	0/50
Probenecid	0/50
Titanocene•2Cl	0/60
Overall Historical Incidence	
Total	0/820

[a] Data as of 3 April 1991. Current NTP historical neoplasm pooling convention recodes adenocarcinoma to carcinoma.

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	10	8
Early deaths				
Accidental deaths	1		1	
Moribund	13	16	30	43
Natural deaths	2	2	4	
Scheduled sacrifice				9
Survivors				
Terminal sacrifice	34	32	14	
Missexed			1	
Animals examined microscopically	60	60	59	60
15-Month Interim Evaluation				
Alimentary System				
Esophagus	(10)	(10)	(10)	(8)
Hyperkeratosis				2 (25%)
Liver	(10)	(10)	(10)	(8)
Basophilic focus	4 (40%)	1 (10%)	6 (60%)	4 (50%)
Clear cell focus			2 (20%)	2 (25%)
Eosinophilic focus		2 (20%)		1 (13%)
Fatty change, focal	8 (80%)	5 (50%)	2 (20%)	
Hepatodiaphragmatic nodule			2 (20%)	
Bile duct, hyperplasia	1 (10%)	2 (20%)	5 (50%)	8 (100%)
Pancreas	(10)	(10)	(10)	(8)
Acinus, hyperplasia		2 (20%)	7 (70%)	8 (100%)
Stomach, forestomach	(10)	(10)	(10)	(8)
Hyperplasia, basal cell		2 (20%)	4 (40%)	2 (25%)
Tongue	(10)		(2)	(3)
Inflammation, chronic active			1 (50%)	1 (33%)
Cardiovascular System				
Heart	(10)	(10)	(10)	(8)
Cardiomyopathy	6 (60%)	8 (80%)	9 (90%)	5 (63%)
Endocrine System				
Adrenal gland, medulla	(10)	(10)	(10)	(8)
Hyperplasia	1 (10%)			
Pituitary gland	(10)	(10)	(10)	(8)
Pars distalis, angiectasis		1 (10%)		
Pars distalis, hyperplasia			1 (10%)	
Thyroid gland	(10)	(10)	(10)	(8)
C-cell, hyperplasia	1 (10%)	1 (10%)		1 (13%)
Follicular cell, hyperplasia				1 (13%)
General Body System				
None				

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
15-Month Interim Evaluation (continued)				
Genital System				
Testes	(10)	(10)	(10)	(8)
Interstitial cell, hyperplasia	10 (100%)	10 (100%)	7 (70%)	6 (75%)
Hematopoietic System				
None				
Integumentary System				
Skin	(10)	(9)	(10)	(8)
Acanthosis		1 (11%)		
Hemorrhage		1 (11%)		
Hyperkeratosis				1 (13%)
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)	(10)	(10)	(8)
Alveolar epithelium, hyperplasia				1 (13%)
Nose	(10)	(10)	(10)	(8)
Fungus	2 (20%)	1 (10%)		
Hyperkeratosis	1 (10%)			
Inflammation, acute		1 (10%)		
Respiratory epithelium, metaplasia, squamous	1 (10%)			
Special Senses System				
Eye		(2)		
Lens, cataract		1 (50%)		
Urinary System				
Kidney	(10)	(10)	(10)	(8)
Nephropathy	10 (100%)	10 (100%)	10 (100%)	8 (100%)
Renal tubule, hyperplasia			2 (20%)	6 (75%)
Urinary bladder	(10)	(10)	(10)	(8)
Calculus gross observation		1 (10%)	1 (10%)	
Calculus micro observation only	1 (10%)	1 (10%)	1 (10%)	

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study				
Alimentary System				
Esophagus	(50)	(49)	(49)	(51)
Hyperkeratosis	2 (4%)	3 (6%)	8 (16%)	33 (65%)
Inflammation, acute	1 (2%)			
Necrosis			1 (2%)	1 (2%)
Intestine large, colon	(50)	(50)	(48)	(52)
Edema	1 (2%)			
Intestine small, duodenum	(49)	(50)	(48)	(52)
Inflammation, acute			1 (2%)	
Intestine small, ileum	(49)	(50)	(47)	(51)
Ulcer		1 (2%)		
Intestine small, jejunum	(49)	(50)	(47)	(52)
Diverticulum				1 (2%)
Inflammation, chronic active			1 (2%)	
Metaplasia, osseous			1 (2%)	
Liver	(50)	(50)	(49)	(52)
Basophilic focus	8 (16%)	7 (14%)	12 (24%)	6 (12%)
Clear cell focus	2 (4%)	5 (10%)	2 (4%)	3 (6%)
Congestion	1 (2%)			
Cyst				1 (2%)
Eosinophilic focus				2 (4%)
Fatty change, focal	3 (6%)	4 (8%)	1 (2%)	1 (2%)
Fibrosis	1 (2%)			1 (2%)
Hepatodiaphragmatic nodule		3 (6%)	4 (8%)	2 (4%)
Hyperplasia		1 (2%)		2 (4%)
Infarct				2 (4%)
Mixed cell focus	7 (14%)	8 (16%)	6 (12%)	7 (13%)
Pigmentation	1 (2%)			
Bile duct, hyperplasia			1 (2%)	12 (23%)
Mesentery	(4)	(9)	(11)	(3)
Fat, fibrosis			1 (9%)	
Fat, hemorrhage			1 (9%)	
Fat, inflammation, chronic active	1 (25%)		1 (9%)	1 (33%)
Fat, mineralization	1 (25%)	2 (22%)	4 (36%)	
Fat, necrosis		4 (44%)	3 (27%)	
Fat, pigmentation		1 (11%)		1 (33%)
Pancreas	(50)	(50)	(49)	(52)
Hyperplasia				1 (2%)
Acinus, atrophy	10 (20%)	13 (26%)	8 (16%)	2 (4%)
Acinus, hyperplasia	28 (56%)	44 (88%)	46 (94%)	48 (92%)
Acinus, hyperplasia, multiple		2 (4%)		
Artery, inflammation, chronic active	6 (12%)	2 (4%)	1 (2%)	
Pharynx	(1)	(5)	(17)	(15)
Hyperplasia, basal cell				1 (7%)
Hyperplasia, squamous				1 (7%)
Palate, hyperplasia, basal cell		1 (20%)		2 (13%)
Palate, hyperplasia, squamous			1 (6%)	1 (7%)
Palate, ulcer			1 (6%)	
Salivary glands	(50)	(50)	(49)	(52)
Duct, metaplasia, squamous		1 (2%)	2 (4%)	6 (12%)
Stomach	(50)	(50)	(49)	(52)
Hyperplasia, squamous				1 (2%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Stomach, forestomach	(50)	(50)	(49)	(52)
Cyst epithelial inclusion		1 (2%)		
Hyperplasia, basal cell		5 (10%)	8 (16%)	7 (13%)
Hyperplasia, squamous	3 (6%)	28 (56%)	13 (27%)	6 (12%)
Inflammation, chronic active	1 (2%)	1 (2%)	2 (4%)	
Ulcer	1 (2%)	2 (4%)	7 (14%)	2 (4%)
Stomach, glandular	(50)	(50)	(49)	(52)
Fibrosis	1 (2%)			
Hyperplasia				2 (4%)
Mineralization			1 (2%)	
Tongue	(4)	(8)	(11)	(44)
Acanthosis			2 (18%)	
Hyperkeratosis	3 (75%)	2 (25%)	1 (9%)	5 (11%)
Hyperplasia, basal cell	1 (25%)			2 (5%)
Hyperplasia, squamous		1 (13%)		
Inflammation, acute			1 (9%)	16 (36%)
Cardiovascular System				
Heart	(50)	(49)	(49)	(52)
Cardiomyopathy	33 (66%)	35 (71%)	28 (57%)	22 (42%)
Fibrosis			1 (2%)	
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(48)	(51)
Degeneration, fatty		1 (2%)		
Hyperplasia			1 (2%)	1 (2%)
Adrenal gland, medulla	(49)	(50)	(48)	(51)
Hyperplasia	9 (18%)	8 (16%)	9 (19%)	3 (6%)
Islets, pancreatic	(50)	(50)	(49)	(52)
Hyperplasia	5 (10%)	2 (4%)	1 (2%)	2 (4%)
Parathyroid gland	(47)	(46)	(47)	(46)
Hyperplasia	1 (2%)		1 (2%)	1 (2%)
Pituitary gland	(48)	(48)	(49)	(51)
Pars distalis, angiectasis	7 (15%)	9 (19%)	3 (6%)	1 (2%)
Pars distalis, cyst	3 (6%)	1 (2%)	2 (4%)	
Pars distalis, hyperplasia	7 (15%)	11 (23%)	13 (27%)	10 (20%)
Pars distalis, hyperplasia, multifocal	1 (2%)			
Pars intermedia, hyperplasia			1 (2%)	
Thyroid gland	(50)	(49)	(49)	(51)
C-cell, hyperplasia	4 (8%)	2 (4%)	8 (16%)	3 (6%)
Follicle, cyst		1 (2%)	1 (2%)	
Follicular cell, hyperplasia		1 (2%)	1 (2%)	3 (6%)
General Body System				
None				

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Genital System				
Preputial gland	(49)	(47)	(49)	(50)
Abscess	2 (4%)			2 (4%)
Hyperplasia			1 (2%)	1 (2%)
Inflammation, chronic active	1 (2%)		1 (2%)	
Prostate	(48)	(50)	(49)	(52)
Hyperplasia	7 (15%)	4 (8%)	10 (20%)	2 (4%)
Inflammation, acute			1 (2%)	
Inflammation, chronic active	1 (2%)		1 (2%)	
Testes	(50)	(50)	(49)	(52)
Interstitial cell, hyperplasia	6 (12%)	4 (8%)	6 (12%)	18 (35%)
Seminiferous tubule, atrophy	5 (10%)	5 (10%)	3 (6%)	
Hematopoietic System				
Bone marrow	(50)	(50)	(49)	(52)
Myelofibrosis		1 (2%)		
Lymph node	(50)	(50)	(49)	(52)
Mediastinal, angiectasis	1 (2%)		2 (4%)	1 (2%)
Mediastinal, infiltration cellular, polymorphonuclear				1 (2%)
Mediastinal, pigmentation	1 (2%)	2 (4%)	2 (4%)	3 (6%)
Lymph node, mandibular	(50)	(50)	(48)	(52)
Angiectasis	1 (2%)			
Degeneration	1 (2%)	1 (2%)	1 (2%)	
Infiltration cellular, plasma cell	1 (2%)			1 (2%)
Inflammation, granulomatous			1 (2%)	
Lymph node, mesenteric	(50)	(49)	(47)	(51)
Angiectasis		1 (2%)		
Degeneration		1 (2%)		
Hemorrhage			1 (2%)	
Infiltration cellular, histiocyte	1 (2%)		1 (2%)	
Spleen	(50)	(50)	(49)	(52)
Fibrosis	1 (2%)	5 (10%)	1 (2%)	2 (4%)
Hematopoietic cell proliferation	15 (30%)	24 (48%)	31 (63%)	31 (60%)
Hemorrhage	1 (2%)			
Infiltration cellular, histiocyte	1 (2%)			
Mineralization			1 (2%)	
Pigmentation		2 (4%)		
Thymus	(49)	(48)	(41)	(48)
Cyst				1 (2%)
Depletion lymphoid			1 (2%)	1 (2%)
Epithelial cell, hyperplasia	4 (8%)	2 (4%)		2 (4%)
Integumentary System				
Mammary gland	(44)	(44)	(34)	(41)
Galactocele	1 (2%)	3 (7%)	2 (6%)	
Hyperplasia		1 (2%)		

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Integumentary System (continued)				
Skin	(50)	(49)	(48)	(51)
Fibrosis	2 (4%)			
Hyperkeratosis		1 (2%)	2 (4%)	2 (4%)
Inflammation, chronic active	4 (8%)			1 (2%)
Necrosis	2 (4%)			
Musculoskeletal System				
Bone	(50)	(50)	(49)	(52)
Fibrous osteodystrophy			1 (2%)	
Skeletal muscle	(2)	(3)	(5)	(3)
Inflammation, acute			1 (20%)	
Nervous System				
None				
Respiratory System				
Lung	(50)	(49)	(49)	(52)
Edema			1 (2%)	
Fibrosis	1 (2%)			
Hemorrhage		1 (2%)		
Infiltration cellular, histiocyte	1 (2%)	3 (6%)		
Inflammation, acute			4 (8%)	1 (2%)
Alveolar epithelium, hyperplasia				3 (6%)
Mediastinum, inflammation, acute	1 (2%)			
Nose	(50)	(50)	(49)	(52)
Fungus	6 (12%)	5 (10%)	6 (12%)	1 (2%)
Inflammation, acute	7 (14%)	6 (12%)	10 (20%)	6 (12%)
Nasolacrimal duct, inflammation, acute			1 (2%)	
Respiratory epithelium, hyperplasia	1 (2%)	3 (6%)		1 (2%)
Respiratory epithelium, metaplasia, squamous	1 (2%)	1 (2%)		
Special Senses System				
Eye	(2)		(7)	(8)
Synechia	1 (50%)		1 (14%)	1 (13%)
Lens, cataract	1 (50%)		4 (57%)	4 (50%)
Retina, atrophy			1 (14%)	
Harderian gland		(1)	(1)	(2)
Hemorrhage		1 (100%)		
Hyperplasia			1 (100%)	
Zymbal's gland				(4)
Necrosis				1 (25%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Urinary System				
Kidney	(50)	(50)	(49)	(52)
Cyst		1 (2%)	3 (6%)	
Hydronephrosis			1 (2%)	
Hyperplasia				1 (2%)
Necrosis		1 (2%)	1 (2%)	
Nephropathy	48 (96%)	50 (100%)	48 (98%)	52 (100%)
Bilateral, hydronephrosis			1 (2%)	
Cortex, mineralization			3 (6%)	
Renal tubule, hyperplasia		1 (2%)	21 (43%)	29 (56%)
Renal tubule, hyperplasia, eosinophil				2 (4%)
Urinary bladder	(49)	(50)	(47)	(52)
Calculus gross observation				4 (8%)
Calculus micro observation only				4 (8%)

[a] Number of animals examined microscopically at site and number of animals with lesion

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR GAVAGE STUDY OF 1,2,3-TRICHLOROPROPANE

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	8	8
Early deaths				
Moribund	17	17	42	49
Natural deaths	2	2	2	2
Scheduled sacrifice				1
Survivors				
Terminal sacrifice	31	30	8	
Missexed		1		
Animals examined microscopically	60	59	60	60
15-Month Interim Evaluation				
Alimentary System				
Intestine small, jejunum	(10)	(10)	(8)	(8)
Adenocarcinoma				1 (13%)
Pharynx				(4)
Palate, papilloma squamous				1 (25%)
Palate, squamous cell carcinoma				1 (25%)
Stomach, forestomach	(10)	(10)	(8)	(8)
Papilloma squamous			4 (50%)	6 (75%)
Papilloma squamous, multiple		1 (10%)	1 (13%)	1 (13%)
Squamous cell carcinoma				1 (13%)
Squamous cell carcinoma, multiple				1 (13%)
Tongue	(10)		(1)	(4)
Papilloma squamous				2 (50%)
Squamous cell carcinoma				1 (25%)
Cardiovascular System				
None				
Endocrine System				
Pituitary gland	(10)	(10)	(8)	(8)
Pars distalis, adenoma	1 (10%)	1 (10%)		2 (25%)
Thyroid gland	(10)	(10)	(8)	(8)
C-cell, adenoma		1 (10%)		
General Body System				
None				
Genital System				
Clitoral gland	(10)	(10)	(8)	(8)
Adenoma		1 (10%)	1 (13%)	2 (25%)
Uterus	(10)	(10)	(8)	(8)
Polyp stromal		1 (10%)		1 (13%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
15-Month Interim Evaluation (continued)				
Hematopoietic System				
None				
Integumentary System				
Mammary gland	(10)	(9)	(8)	(7)
Adenocarcinoma				1 (14%)
Adenoma				1 (14%)
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
Zymbal's gland				(1)
Carcinoma				1 (100%)
Urinary System				
None				
2-Year Study				
Alimentary System				
Intestine large, colon	(49)	(47)	(52)	(51)
Adenocarcinoma				1 (2%)
Intestine small, jejunum	(49)	(47)	(52)	(52)
Adenocarcinoma			1 (2%)	1 (2%)
Liver	(50)	(49)	(52)	(52)
Hepatocellular adenoma			1 (2%)	
Sarcoma, metastatic, pharynx				1 (2%)
Mesentery	(2)	(5)	(4)	(1)
Nephroblastoma, metastatic, kidney				1 (100%)
Pancreas	(50)	(49)	(52)	(52)
Acinus, adenoma			2 (4%)	
Pharynx	(1)	(3)	(18)	(19)
Squamous cell carcinoma				1 (5%)
Palate, papilloma squamous	1 (100%)	2 (67%)	5 (28%)	2 (11%)
Palate, squamous cell carcinoma		1 (33%)	10 (56%)	14 (74%)
Salivary glands	(50)	(49)	(52)	(52)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Stomach	(50)	(49)	(52)	(52)
Papilloma squamous				1 (2%)
Squamous cell carcinoma			1 (2%)	
Squamous cell carcinoma, multiple				1 (2%)
Stomach, forestomach	(50)	(49)	(51)	(52)
Papilloma squamous		10 (20%)	26 (51%)	12 (23%)
Papilloma squamous, multiple		3 (6%)	6 (12%)	4 (8%)
Squamous cell carcinoma		3 (6%)	5 (10%)	3 (6%)
Squamous cell carcinoma, multiple			3 (6%)	
Stomach, glandular	(50)	(49)	(52)	(51)
Tongue		(4)	(20)	(31)
Papilloma squamous		3 (75%)	5 (25%)	16 (52%)
Squamous cell carcinoma			13 (65%)	7 (23%)
Cardiovascular System				
Heart	(50)	(49)	(52)	(50)
Adenocarcinoma, metastatic, mammary gland		1 (2%)		
Endocrine System				
Adrenal gland, cortex	(49)	(48)	(52)	(50)
Adenoma	1 (2%)			
Adrenal gland, medulla	(49)	(47)	(52)	(50)
Adenocarcinoma, metastatic, mammary gland		1 (2%)		
Pheochromocytoma malignant	2 (4%)			
Pheochromocytoma benign	5 (10%)	2 (4%)	1 (2%)	
Islets, pancreatic	(50)	(48)	(52)	(52)
Adenoma	2 (4%)	2 (4%)		1 (2%)
Carcinoma	1 (2%)	1 (2%)		
Pituitary gland	(50)	(48)	(51)	(51)
Pars distalis, adenoma	28 (56%)	29 (60%)	12 (24%)	3 (6%)
Thyroid gland	(50)	(47)	(52)	(52)
Bilateral, C-cell, adenoma		1 (2%)		
C-cell, adenoma	4 (8%)	3 (6%)	4 (8%)	
C-cell, carcinoma		1 (2%)		
Follicular cell, adenoma			3 (6%)	2 (4%)
Follicular cell, carcinoma		1 (2%)		
General Body System				
None				
Genital System				
Clitoral gland	(46)	(46)	(50)	(51)
Adenoma	4 (9%)	10 (22%)	10 (20%)	10 (20%)
Carcinoma			3 (6%)	5 (10%)
Bilateral, adenoma	1 (2%)		3 (6%)	
Bilateral, carcinoma			1 (2%)	1 (2%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Genital System (continued)				
Ovary	(50)	(48)	(52)	(52)
Nephroblastoma, metastatic, kidney				1 (2%)
Thecoma benign			1 (2%)	
Bilateral, hemangioma				1 (2%)
Uterus	(50)	(48)	(52)	(52)
Hemangioma		1 (2%)		
Polyp stromal	7 (14%)	3 (6%)	6 (12%)	
Sarcoma		1 (2%)	1 (2%)	
Sarcoma stromal	3 (6%)			
Bilateral, polyp stromal	2 (4%)	1 (2%)	1 (2%)	
Endometrium, adenoma		1 (2%)	2 (4%)	
Hematopoietic System				
Blood	(5)	(4)	(3)	
Bone marrow	(50)	(48)	(52)	(52)
Lymph node	(50)	(49)	(52)	(52)
Mediastinal, sarcoma, metastatic, pharynx				1 (2%)
Lymph node, mandibular	(48)	(49)	(52)	(50)
Adenocarcinoma, metastatic, mammary gland		1 (2%)		
Sarcoma, metastatic, pharynx				1 (2%)
Squamous cell carcinoma, metastatic, pharynx			1 (2%)	1 (2%)
Lymph node, mesenteric	(50)	(48)	(51)	(49)
Spleen	(50)	(47)	(52)	(51)
Sarcoma, metastatic, pharynx				1 (2%)
Thymus	(46)	(46)	(51)	(50)
Epithelial cell, thymoma benign		1 (2%)		
Integumentary System				
Mammary gland	(47)	(46)	(45)	(43)
Adenocarcinoma	1 (2%)	6 (13%)	11 (24%)	19 (44%)
Adenocarcinoma, multiple			1 (2%)	2 (5%)
Adenoma	1 (2%)		2 (4%)	
Adenoma, multiple			1 (2%)	
Fibroadenoma	13 (28%)	15 (33%)	12 (27%)	1 (2%)
Fibroadenoma, multiple	2 (4%)	8 (17%)	8 (18%)	
Skin	(50)	(49)	(51)	(51)
Papilloma squamous			1 (2%)	
Squamous cell carcinoma	1 (2%)		1 (2%)	
Subcutaneous tissue, fibroma		1 (2%)		
Subcutaneous tissue, hemangiosarcoma			1 (2%)	
Subcutaneous tissue, sarcoma	1 (2%)		1 (2%)	
Musculoskeletal System				
Skeletal muscle		(1)		

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Nervous System				
Brain	(50)	(49)	(52)	(52)
Astrocytoma malignant			1 (2%)	
Peripheral nerve				(2)
Squamous cell carcinoma, metastatic, pharynx				2 (100%)
Respiratory System				
Lung	(50)	(48)	(51)	(52)
Adenocarcinoma, metastatic, mammary gland		1 (2%)	1 (2%)	2 (4%)
Alveolar/bronchiolar adenoma	2 (4%)	1 (2%)	1 (2%)	
Alveolar/bronchiolar carcinoma			1 (2%)	
Hemangiosarcoma, metastatic, skin			1 (2%)	
Sarcoma, metastatic, pharynx				1 (2%)
Squamous cell carcinoma		1 (2%)		
Special Senses System				
Ear	(1)		(1)	(2)
Sarcoma			1 (100%)	
Eye	(4)	(5)	(9)	(19)
Histiocytic sarcoma				1 (5%)
Harderian gland	(1)		(1)	(9)
Adenoma				1 (11%)
Zymbal's gland		(1)		(3)
Carcinoma		1 (100%)		3 (100%)
Urinary System				
Kidney	(50)	(47)	(52)	(51)
Adenocarcinoma, metastatic, mammary gland		1 (2%)		
Histiocytic sarcoma, metastatic				1 (2%)
Nephroblastoma				1 (2%)
Renal tubule, adenocarcinoma				1 (2%)
Urinary bladder	(49)	(46)	(52)	(52)
Systemic Lesions				
Multiple organs[b]	(50)	(49)	(52)	(52)
Histiocytic sarcoma				1 (2%)
Leukemia mononuclear	13 (26%)	17 (35%)	14 (27%)	

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	1	4	5	8
2-Year study	48	46	51	48
Total primary neoplasms				
15-Month interim evaluation	1	5	6	23
2-Year study	95	130	183	115
Total animals with benign neoplasms				
15-Month interim evaluation	1	4	5	8
2-Year study	41	44	46	32
Total benign neoplasms				
15-Month interim evaluation	1	5	6	16
2-Year study	73	97	113	54
Total animals with malignant neoplasms				
15-Month interim evaluation				5
2-Year study	20	25	46	43
Total malignant neoplasms				
15-Month interim evaluation				7
2-Year study	22	33	70	61
Total animals with secondary neoplasms[d]				
2-Year study		1	3	7
Total secondary neoplasms				
2-Year study		5	3	13

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms
[d] Secondary neoplasms: metastatic neoplasms or neoplasms invasive to an adjacent organ

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control

Number of Days on Study	424	450	474	526	547	550	550	597	601	626	645	647	652	670	683	699	708	714	717	738	738	738	738	738	738
Carcass ID Number	06315	06155	06554	05955	05564	06551	06553	06574	05555	06223	05633	05594	06005	06604	06643	06422	05543	05573	06334	05442	05544	05545	05525	05533	05561
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery																		+							+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pharynx																									
Palate, papilloma squamous																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Adenoma																								X	
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Pheochromocytoma malignant																									X
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									X
Carcinoma																			X						
Parathyroid gland	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma			X	X		X					X		X		X	X		X	X	X	X		X	X	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma				X																					

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	738	738	738	738	738	738	738	738	738	738	738	738	738	740	741	741	741	741	741	741	742	742	742	742	742	742	
Carcass ID Number	05662	05571	05572	05581	05582	05583	05584	05591	05592	05593	06631	06632	06652	05541	05543	05551	06603	06633	06641	06601	06602	06611	06612	06621	06622		**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Mesentery																											2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Pharynx						+																					1
Palate, papilloma squamous						X																					1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Adenoma																											1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Pheochromocytoma malignant								X																			2
Pheochromocytoma benign						X					X		X							X			X				5
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Adenoma				X																							2
Carcinoma																											1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+		47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Pars distalis, adenoma	X	X		X	X	X	X					X		X	X	X	X	X	X	X				X			28
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
C-cell, adenoma							X				X		X														4

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	4 2 4	4 5 0	4 7 4	5 2 6	5 4 7	5 5 0	5 5 0	5 9 7	6 0 1	6 2 6	6 4 5	6 4 7	6 5 2	6 7 0	6 8 3	6 9 9	7 0 8	7 1 4	7 1 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8
Carcass ID Number	0 6 3 5	0 6 1 5	0 6 5 4	0 5 9 5	0 5 6 4	0 6 5 1	0 6 5 3	0 5 7 4	0 5 5 5	0 6 2 3	0 5 6 3	0 5 9 4	0 6 0 5	0 6 0 4	0 6 4 3	0 6 4 2	0 5 5 4	0 5 7 3	0 6 3 4	0 5 4 2	0 5 4 4	0 5 4 5	0 5 5 2	0 5 5 3	0 5 6 1
General Body System																									
None																									
Genital System																									
Clitoral gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																			X						
Bilateral, adenoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal					X										X								X		
Sarcoma stromal	X												X	X											
Bilateral, polyp stromal																									
Hematopoietic System																									
Blood										+							+								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma		X																							
Adenoma																		X							
Fibroadenoma			X			X						X					X					X			
Fibroadenoma, multiple									X																
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																				X					
Subcutaneous tissue, sarcoma																			X						
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 4 0	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 5 6 2	0 5 7 1	0 5 7 2	0 5 8 1	0 5 8 2	0 5 8 3	0 5 8 4	0 5 9 1	0 5 9 2	0 5 9 3	0 6 3 1	0 6 3 2	0 6 5 2	0 5 4 1	0 5 4 3	0 5 5 1	0 6 0 3	0 6 3 3	0 6 4 1	0 6 0 1	0 6 0 2	0 6 1 1	0 6 1 2	0 6 2 1	0 6 2 2	**Total Tissues/ Tumors**
General Body System																										
None																										
Genital System																										
Clitoral gland	+	M	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4 6
Adenoma	X										X			X												4
Bilateral, adenoma																									X	1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	49
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Polyp stromal			X		X							X			X											7
Sarcoma stromal																										3
Bilateral, polyp stromal										X								X								2
Hematopoietic System																										
Blood		+						+										+								5
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4 8
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Thymus	+	M	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	4 6
Integumentary System																										
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	47
Adenocarcinoma																										1
Adenoma																										1
Fibroadenoma			X	X	X							X					X		X	X	X					13
Fibroadenoma, multiple																X										2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Squamous cell carcinoma																										1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	4 2 4	4 5 0	4 7 4	5 2 6	5 4 7	5 5 0	5 5 0	5 9 7	6 0 1	6 2 6	6 4 5	6 4 7	6 5 2	6 7 0	6 8 3	6 9 9	7 0 8	7 1 4	7 1 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 6 3 5	0 6 1 5	0 6 5 4	0 5 9 5	0 5 6 4	0 6 5 1	0 6 5 3	0 5 7 4	0 5 5 5	0 6 2 3	0 5 6 3	0 5 9 4	0 6 0 5	0 6 0 4	0 6 4 3	0 6 4 2	0 5 5 4	0 5 7 3	0 6 3 4	0 5 4 2	0 5 4 4	0 5 4 5	0 5 5 2	0 5 5 3	0 5 6 1	
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Alveolar/bronchiolar adenoma											X															
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Special Senses System																										
Ear																+										
Eye		+		+							+						+									
Harderian gland		+																								
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Urinary bladder	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear								X	X	X					X		X							X		

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 4 0	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 1	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	7 4 2	
Carcass ID Number	0 5 6 2	0 5 7 1	0 5 7 2	0 5 8 1	0 5 8 2	0 5 8 3	0 5 8 4	0 5 9 1	0 5 9 2	0 5 9 3	0 6 3 1	0 6 3 2	0 6 5 2	0 5 4 1	0 5 4 3	0 5 5 1	0 6 0 3	0 6 3 3	0 6 4 1	0 6 6 1	0 6 0 2	0 6 1 1	0 6 1 2	0 6 2 1	0 6 2 2	**Total Tissues/ Tumors**
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma						X																				2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Special Senses System																										
Ear																										1
Eye																										4
Harderian gland																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Leukemia mononuclear		X						X	X		X							X	X	X						13

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg

Number of Days on Study	434	460	469	510	545	580	589	604	664	670	677	690	695	696	708	713	713	725	729	736	736	736	736	736
Carcass ID Number	07225	06885	07555	07663	06664	06744	07744	07544	07004	07332	07444	07222	06955	07433	07033	06633	07622	07211	06883	06722	06733	06922	06933	06944
Alimentary System																								
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery							+	+						+										
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pharynx									+										+					
Palate, papilloma squamous									X										X					
Palate, squamous cell carcinoma																								
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous				X											X		X				X		X	
Papilloma squamous, multiple																								
Squamous cell carcinoma																X								
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue											+												+	
Papilloma squamous											X												X	
Tooth							+	+																
Cardiovascular System																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland			X																					
Endocrine System																								
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland			X																					
Pheochromocytoma benign																		X						

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	736	736	736	737	737	737	737	737	737	737	737	737	737	737	737	737	737	737	737	738	738	738	738	738	738	
Carcass ID Number	07011	07014	07015	06661	06662	06671	06681	06682	06691	07002	07011	07012	07013	07033	07034	07041	07042	07053	07061	07031	07051	07052	07071	07072	07073	**Total Tissues/ Tumors**
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mesentery		+																			+					5
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pharynx												+														3
Palate, papilloma squamous																										2
Palate, squamous cell carcinoma												X														1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papilloma squamous	X		X						X		X											X				10
Papilloma squamous, multiple					X			X					X													3
Squamous cell carcinoma																		X			X					3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tongue								+											+							4
Papilloma squamous																			X							3
Tooth																										2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, mammary gland																										1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	47
Adenocarcinoma, metastatic, mammary gland																										1
Pheochromocytoma benign		X																								2

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	434	460	469	510	545	580	589	604	664	670	677	690	695	696	708	713	713	725	729	736	736	736	736	736	
Carcass ID Number	07225	06855	07555	07663	06664	06744	07744	07544	07044	07332	07444	07022	06995	07433	07033	06633	07623	07221	06833	06722	06733	06922	06933	06944	
Endocrine System (continued)																									
Islets, pancreatic	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma																									
Carcinoma														X											
Parathyroid gland	+	+	+	+	+	+	+	M	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	
Pituitary gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Pars distalis, adenoma			X				X	X						X	X	X		X	X	X				X	
Thyroid gland	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	
Bilateral, C-cell, adenoma																									
C-cell, adenoma							X										X	X							
C-cell, carcinoma																									
Follicular cell, carcinoma																									
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	
Adenoma									X		X							X				X			
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Oviduct	+	+	+	+	+	+	+	+		+	+			+		+	+			+	+		+		
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Hemangioma																									
Polyp stromal									X																
Sarcoma																									
Bilateral, polyp stromal																									
Endometrium, adenoma																			X						
Hematopoietic System																									
Blood											+	+		+				+							
Bone marrow	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenocarcinoma, metastatic, mammary gland			X																						
Lymph node, mesenteric	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Spleen	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Thymus	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Epithelial cell, thymoma benign												X													

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	736	736	736	737	737	737	737	737	737	737	737	737	737	737	737	737	737	737	737	738	738	738	738	738	738	
Carcass ID Number	07011	07014	07015	06661	06662	06671	06681	06682	06691	07022	07711	07712	07713	07733	07734	07741	07742	07753	07761	07731	07751	07752	07771	07772	07773	**Total Tissues/ Tumors**
Endocrine System (continued)																										
Isletsp ancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																				X		X				2
Carcinoma																										1
Parathyroidg land	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	M	+	+	+	+	+	+	+	43
Pituitarg land	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma				X		X	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X	X	29
Thyroidg land	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Bilateral, C-cell, adenoma																	X									1
C-cell, adenoma																										3
C-cell, carcinoma																					X					1
Follicular cell, carcinoma																		X								1
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	46
Adenoma						X			X			X				X					X			X		10
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Oviduct				+	+	+	+	+						+	+	+	+	+	+	+	+	+	+	+		32
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Hemangioma													X													1
Polyp stromal					X																X					3
Sarcoma															X											1
Bilateral, polyp stromal											X															1
Endometrium, adenoma																										1
Hematopoietic System																										
Blood																										4
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, mammary gland																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	46
Epithelial cell, thymoma benign																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	434	460	469	510	545	580	589	604	664	670	677	690	695	696	708	713	713	725	729	736	736	736	736	736	736
Carcass ID Number	07225	06885	07555	07633	06664	06674	07744	07544	07704	07732	07444	07222	06955	07433	07033	06633	06622	07211	06833	06672	06733	06922	06933	06944	06694
Integumentary System																									
Mammary gland	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma			X														X						X		
Fibroadenoma								X		X		X			X		X					X			
Fibroadenoma, multiple														X				X			X		X		
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibroma				X																					
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle														+											
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland			X																						
Alveolar/bronchiolar adenoma																									
Squamous cell carcinoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye			+	+																					
Zymbal's gland																+									
Carcinoma																X									
Urinary System																									
Kidney	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland			X																						
Urinary bladder	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X	X									X	X		X		X		X		X	X	X			

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 3 mg/kg (continued)

Number of Days on Study	7 3 6	7 3 6	7 3 6	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 7	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	7 3 8	
Carcass ID Number	0 7 0 1	0 7 1 4	0 7 1 5	0 6 6 1	0 6 6 2	0 6 6 7 1	0 6 8 1	0 6 8 2	0 6 9 1	0 7 0 2	0 7 1 1	0 7 1 2	0 7 1 3	0 7 3 3	0 7 3 4	0 7 4 1	0 7 4 2	0 7 5 3	0 7 6 1	0 7 3 1	0 7 5 1	0 7 5 2	0 7 7 1	0 7 7 2	0 7 7 3	**Total Tissues/ Tumors**
Integumentary System																											
Mammary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4	6
Adenocarcinoma				X											X	X										6	
Fibroadenoma							X		X	X					X					X	X	X		X	X	15	
Fibroadenoma, multiple						X						X					X						X			8	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4	9
Subcutaneous tissue, fibroma																										1	
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Skeletal muscle																										1	
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Respiratory System																											
Lung	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48	
Adenocarcinoma, metastatic, mammary gland																										1	
Alveolar/bronchiolar adenoma																						X				1	
Squamous cell carcinoma														X												1	
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Special Senses System																											
Eye										+										+			+			5	
Zymbal's gland																										1	
Carcinoma																										1	
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47	
Adenocarcinoma, metastatic, mammary gland																										1	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	4	6
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4	9
Leukemia mononuclear		X		X						X					X		X	X							X	17	

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg

Number of Days on Study	255	405	405	424	434	450	451	479	505	510	510	513	520	521	538	538	550	557	561	563	572	581	584	598	604	605
Carcass ID Number	08144	08555	08665	08825	08045	07995	08885	08355	08755	07944	08744	08033	07933	08944	07922	08133	08933	08344	08552	07911	08833	08122	08244	08844	08333	08223
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																										
Mesentery		+											+												+	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma																										
Pharynx			+												+	+	+		+			+			+	
Palate, papilloma squamous			X												X		X									
Palate, squamous cell carcinoma																X						X			X	
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																										
Stomach, forestomach	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous							X	X	X	X	X	X				X			X	X	X	X	X			X
Papilloma squamous, multiple																									X	
Squamous cell carcinoma																										
Squamous cell carcinoma, multiple																										
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue						+		+				+	+	+	+	+		+	+	+				+	+	
Papilloma squamous								X																	X	
Squamous cell carcinoma												X	X		X	X		X	X	X				X		
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	6 0 8	6 0 8	6 1 2	6 2 8	6 3 4	6 3 7	6 4 1	6 4 2	6 4 3	6 6 9	6 7 6	6 8 3	6 9 9	7 0 1	7 0 9	7 2 1	7 2 5	7 2 5	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 6	7 3 8	7 3 8	
Carcass ID Number	0 8 1 1	0 8 8 2	0 8 6 3	0 7 8 5	0 8 7 3	0 7 8 2	0 8 3 1	0 8 0 2	0 8 5 1	0 8 9 2	0 8 9 1	0 8 0 1	0 8 4 3	0 8 7 2	0 8 4 2	0 8 4 1	0 8 3 2	0 8 6 2	0 7 8 1	0 7 8 3	0 7 8 4	0 8 2 1	0 8 2 2	0 8 6 1	0 8 7 1	0 8 8 1	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenocarcinoma													X														1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hepatocellular adenoma																				X							1
Mesentery	+																										4
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Acinus, adenoma														X										X			2
Pharynx		+		+			+				+		+	+				+			+		+		+	18
Palate, papilloma squamous																					X		X				5
Palate, squamous cell carcinoma		X		X			X				X		X					X						X			10
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Squamous cell carcinoma											X																1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Papilloma squamous			X		X					X			X	X	X			X	X	X		X	X		X	X	26
Papilloma squamous, multiple						X						X					X				X			X			6
Squamous cell carcinoma							X						X			X			X						X		5
Squamous cell carcinoma, multiple				X					X											X							3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Tongue						+				+						+			+	+			+	+		+	20
Papilloma squamous										X									X	X							5
Squamous cell carcinoma						X										X							X	X		X	13
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Pheochromocytoma benign																						X					1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	255	405	405	424	434	450	451	479	505	510	510	513	520	521	538	538	550	557	561	563	572	581	584	598	604	605
Carcass ID Number	08144	08555	08665	08825	08045	07995	08855	08335	08775	07945	08744	08033	07933	08944	07922	08133	08933	08344	08522	07911	08833	08122	08244	08844	08343	08223
Endocrine System (continued)																										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	M	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pars distalis, adenoma													X		X		X				X					
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma												X														
Follicular cell, adenoma															X											
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+
Adenoma																X										X
Carcinoma					X	X			X																	
Bilateral, adenoma										X																
Bilateral, carcinoma							X																			
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thecoma benign																										
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal						X											X		X						X	
Sarcoma												X														
Bilateral, polyp stromal																										
Endometrium, adenoma																										
Hematopoietic System																										
Blood																		+								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, pharynx																										
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	608	608	612	628	634	637	641	642	643	669	676	683	699	701	709	721	725	725	736	736	736	736	736	736	738	738	
Carcass ID Number	08111	08812	08863	07885	08773	07882	08831	08802	08851	08892	08891	08801	08843	08872	08422	08411	08323	08622	07881	08833	07884	08221	08222	08261	08771	08881	**Total Tissues/ Tumors**
Endocrine System (continued)																											
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Parathyroid gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pars distalis, adenoma	X						X	X						X			X	X				X				X	12
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
C-cell, adenoma			X	X		X																					4
Follicular cell, adenoma											X								X								3
General Body System																											
None																											
Genital System																											
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma										X			X						X		X	X	X	X		X	10
Carcinoma																											3
Bilateral, adenoma					X												X										3
Bilateral, carcinoma																											1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Thecoma benign										X																	1
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Polyp stromal					X																	X					6
Sarcoma																											1
Bilateral, polyp stromal																									X		1
Endometrium, adenoma																			X			X					2
Hematopoietic System																											
Blood								+													+						3
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Squamous cell carcinoma, metastatic, pharynx																		X									1
Lymph node, mesenteric	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	2 5 5	4 0 5	4 0 5	4 2 4	4 3 4	4 5 0	4 5 1	4 7 9	5 0 5	5 1 0	5 1 0	5 1 3	5 2 0	5 2 1	5 3 8	5 3 8	5 5 0	5 5 7	5 6 1	5 6 3	5 7 2	5 8 1	5 8 4	5 9 8	6 0 4	6 0 5
Carcass ID Number	0 8 1 4	0 8 5 5	0 8 6 5	0 8 2 5	0 8 0 5	0 7 9 5	0 8 8 5	0 8 3 5	0 8 7 5	0 7 9 4	0 8 7 4	0 8 0 3	0 7 9 3	0 8 9 4	0 7 9 2	0 8 1 3	0 8 9 3	0 8 3 4	0 8 5 2	0 7 9 1	0 8 8 3	0 8 1 2	0 8 2 4	0 8 8 4	0 8 3 3	0 8 2 3
Integumentary System																										
Mammary gland	+	M	+	+	M	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma				X				X		X				X		X					X					
Adenocarcinoma, multiple																	X									
Adenoma														X												
Adenoma, multiple																							X			
Fibroadenoma										X	X							X	X					X		X
Fibroadenoma, multiple																									X	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																										
Squamous cell carcinoma																										
Subcutaneous tissue, hemangiosarcoma																										
Subcutaneous tissue, sarcoma																										
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant	X																									
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland								X																		
Alveolar/bronchiolar adenoma										X																
Alveolar/bronchiolar carcinoma																			X							
Hemangiosarcoma, metastatic, skin																										
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+
Special Senses System																										
Ear											+															
Sarcoma											X															
Eye						+	+	+				+	+													
Harderian gland																							+			

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	608	608	612	628	634	637	641	642	643	669	676	683	699	701	709	721	725	725	736	736	736	736	736	736	738	738	
Carcass ID Number	08111	08812	08863	07885	08773	07882	08831	08002	08851	08892	08891	08801	08843	08872	08842	08411	08322	08622	07881	07833	07884	08821	08822	08861	08771	08881	**Total Tissues/ Tumors**
Integumentary System																											
Mammary gland	+	M	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Adenocarcinoma	X		X																				X	X		X	11
Adenocarcinoma, multiple																											1
Adenoma																		X									2
Adenoma, multiple																											1
Fibroadenoma	X									X				X							X			X	X		12
Fibroadenoma, multiple												X			X	X		X	X	X						X	8
Skin	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Papilloma squamous																						X					1
Squamous cell carcinoma						X																					1
Subcutaneous tissue, hemangiosarcoma															X												1
Subcutaneous tissue, sarcoma									X																		1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Astrocytoma malignant																											1
Respiratory System																											
Lung	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenocarcinoma, metastatic, mammary gland																											1
Alveolar/bronchiolar adenoma																											1
Alveolar/bronchiolar carcinoma																											1
Hemangiosarcoma, metastatic, skin															X												1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Special Senses System																											
Ear																											1
Sarcoma																											1
Eye					+		+		+				+														9
Harderian gland																											1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	255	405	405	424	434	450	451	479	505	510	510	513	520	521	538	538	550	557	561	563	572	581	584	598	604	605
Carcass ID Number	08144	08555	08665	08825	08805	07995	08885	08355	08775	07944	08744	08033	07933	08944	07922	08133	08933	08344	08522	07911	08833	08122	08244	08844	08333	08223
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear			X									X			X			X								

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 10 mg/kg (continued)

Number of Days on Study	0608	0608	0612	0628	0634	0637	0641	0642	0643	0669	0676	0683	0699	0701	0709	0721	0725	0725	0736	0736	0736	0736	0736	0736	0738	0738	
Carcass ID Number	0081 1	0088 1 2	0086 3	0078 5	0087 3	0078 2	0083 1	0080 2	0085 1	0089 2	0089 1	0080 1	0084 3	0087 2	0084 2	0084 1	0083 2	0086 2	0078 1	0078 3	0078 4	0082 1	0082 2	0086 1	0087 1	0088 1	**Total Tissues/ Tumors**
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Leukemia mononuclear				X	X			X			X		X				X				X	X		X		X	14

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg

Number of Days on Study	085	085	184	233	239	251	294	297	307	310	311	325	330	331	331	336	336	336	345	345	345	345	345	352	354	361
Carcass ID Number	09044	09055	09665	09555	10115	10144	09644	09355	09445	09155	09933	09544	10505	09144	09755	09225	09535	09744	09113	09433	09443	09843	09855	09633	09033	09224
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																										
Intestine large, rectum	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, pharynx												X														
Mesentery			+																							
Nephroblastoma, metastatic, kidney			X																							
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pharynx												+	+					+						+	+	
Squamous cell carcinoma																										
Palate, papilloma squamous																		X								
Palate, squamous cell carcinoma													X											X	X	
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																										
Squamous cell carcinoma, multiple																										
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous												X											X			
Papilloma squamous, multiple																										
Squamous cell carcinoma												X														
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Tongue				+			+	+	+	+				+			+	+	+						+	
Papilloma squamous				X						X							X								X	
Squamous cell carcinoma							X	X	X										X							
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	367	367	371	371	371	371	381	385	385	397	399	400	402	407	408	412	416	416	422	423	424	434	441	441	451	464	
Carcass ID Number	09213	10133	09902	09934	09942	09952	09983	09901	09955	09941	09962	10121	09961	09973	09922	09982	09972	09994	10111	09933	10044	09912	09932	09971	09992	09951	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenocarcinoma																			X								1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenocarcinoma														X													1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Sarcoma, metastatic, pharynx																											1
Mesentery																							M				1
Nephroblastoma, metastatic, kidney																											1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Pharynx								+	+	+	+	+		+	+	+	+			+	+		+		+	+	19
Squamous cell carcinoma																							X				1
Palate, papilloma squamous																									X		2
Palate, squamous cell carcinoma								X		X	X	X		X	X	X	X			X	X					X	14
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Papilloma squamous																										X	1
Squamous cell carcinoma, multiple												X															1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Papilloma squamous							X		X					X	X	X			X	X	X	X			X		12
Papilloma squamous, multiple				X				X			X												X				4
Squamous cell carcinoma	X																									X	3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tongue	+	+	+	+		+	+	+	+	+	+	+		+		+	+	+	+		+	+	+	+		+	31
Papilloma squamous		X				X	X	X	X			X				X	X				X	X	X	X			16
Squamous cell carcinoma										X								X	X								7
Cardiovascular System																											
Heart		+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	085	085	184	233	239	251	294	297	307	310	311	325	330	331	331	336	336	336	345	345	345	345	345	352	354	361
Carcass ID Number	09044	09055	09665	09555	10115	10144	09644	09935	09445	09915	09933	09554	10055	09914	09755	09925	09553	09744	09913	09433	09944	09844	09855	09663	09903	09924
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	M
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma															X						X					
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma										X																
General Body System																										
Tissue NOS												+														
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma										X		X							X		X		X		X	
Carcinoma														X	X						X					
Bilateral, carcinoma																X										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nephroblastoma, metastatic, kidney			X																							
Bilateral, hemangioma																										
Oviduct	+	+								+	+	+		+		+		+	+						+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, sarcoma, metastatic, pharynx												X														
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, pharynx												X														
Squamous cell carcinoma, metastatic, pharynx																										
Lymph node, mesenteric	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, pharynx												X														
Thymus	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	367	367	371	371	371	371	381	385	385	397	399	400	402	407	408	412	416	416	422	423	424	434	441	441	451	464	
Carcass ID Number	09233	10133	09902	09934	09942	09952	09983	09901	09955	09941	09962	10122	09961	09973	09922	09982	09972	09994	10011	09933	10042	09912	09932	09971	09992	09951	**Total Tissues/ Tumors**
Endocrine System																											
Adrenal gland		+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex		+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla		+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenoma											X																1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pars distalis, adenoma																									X		3
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Follicular cell, adenoma																			X								2
General Body System																											
Tissue NOS																											1
Genital System																											
Clitoral gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma							X				X					X									X		10
Carcinoma		X												X													5
Bilateral, carcinoma																											1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Nephroblastoma, metastatic, kidney																											1
Bilateral, hemangioma					X																						1
Oviduct	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	36
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Mediastinal, sarcoma, metastatic, pharynx																											1
Lymph node, mandibular	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, metastatic, pharynx																											1
Squamous cell carcinoma, metastatic, pharynx																	X										1
Lymph node, mesenteric	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Sarcoma, metastatic, pharynx																											1
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	085	085	184	233	239	251	294	297	307	310	311	325	330	331	331	336	336	336	345	345	345	345	345	352	354	361
Carcass ID Number	09004	09005	09965	09555	10115	10144	09644	09935	09445	09915	09933	09954	10055	09914	09755	09925	09553	09744	09913	09443	09443	09844	09855	09663	09033	09024
Integumentary System																										
Mammary gland	M	+	+	+	+	+	+	M	M	+	+	+	+	M	M	+	+	M	+	+	+	M	+	+	+	M
Adenocarcinoma					X	X					X		X			X	X			X			X		X	
Adenocarcinoma, multiple																										
Fibroadenoma																										
Skin	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve																										
Squamous cell carcinoma, metastatic, pharynx																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland																										
Sarcoma, metastatic, pharynx												X														
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Ear																										
Eye												+			+				+	+	+	+	+	+	+	+
Histiocytic sarcoma												X														
Harderian gland																		+								
Adenoma																										
Zymbal's gland																		+								
Carcinoma																		X								
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic												X														
Nephroblastoma			X																							
Renal tubule, adenocarcinoma																										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma												X														

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 30 mg/kg (continued)

Number of Days on Study	3 6 7	3 6 7	3 7 1	3 7 1	3 7 1	3 7 1	3 8 1	3 8 5	3 8 5	3 9 7	3 9 9	4 0 0	4 0 2	4 0 7	4 0 8	4 1 2	4 1 6	4 1 6	4 2 2	4 2 3	4 2 4	4 3 4	4 4 1	4 4 1	4 5 1	4 6 4	
Carcass ID Number	0 9 2 3	1 0 1 3	0 9 0 2	0 9 3 4	0 9 4 2	0 9 5 2	0 9 8 3	0 9 0 1	0 9 9 5	0 9 4 1	0 9 6 2	1 0 1 2	0 9 6 1	0 9 7 3	0 9 2 2	0 9 8 2	0 9 7 2	0 9 9 4	1 0 1 1	0 9 3 3	1 0 0 4	0 9 1 2	0 9 3 2	0 9 7 1	0 9 9 2	0 9 9 5	**Total Tissues/ Tumors**
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	43
Adenocarcinoma	X			X	X	X		X	X		X	X	X									X					19
Adenocarcinoma, multiple																							X		X		2
Fibroadenoma			X																								1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Peripheral nerve												+			+												2
Squamous cell carcinoma, metastatic, pharynx												X			X												2
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adenocarcinoma, metastatic, mammary gland					X																				X		2
Sarcoma, metastatic, pharynx																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Special Senses System																											
Ear																		+								+	2
Eye						+	+					+		+	+					+			+		+	+	19
Histiocytic sarcoma																											1
Harderian gland					+							+		+	+	+	+			+					+		9
Adenoma																	X										1
Zymbal's gland																							+			+	3
Carcinoma																							X			X	3
Urinary System																											
Kidney	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma, metastatic																											1
Nephroblastoma																											1
Renal tubule, adenocarcinoma															X												1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Histiocytic sarcoma																											1

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Adrenal Medulla: Benign Pheochromocytoma				
Overall rate[a]	5/59 (8%)	2/57 (4%)	1/60 (2%)	0/58 (0%)
Adjusted rate[b]	16.7%	6.5%	12.5%	0.0%
15-Month interim evaluation[c]	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate[d]	5/30 (17%)	1/29 (3%)	1/8 (13%)	0/0 (0%)
First incidence (days)	736 (T)	725	736 (T)	-[f]
Life table test[e]	P=0.757N	P=0.226N	P=0.601N	-
Logistic regression test[e]	P=0.702N	P=0.210N	P=0.601N	-
Cochran-Armitage test[e]	P=0.032N			
Fisher exact test[e]		P=0.234N	P=0.100N	P=0.030N
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rate	7/59 (12%)	2/57 (4%)	1/60 (2%)	0/58 (0%)
Adjusted rate	23.3%	6.5%	12.5%	0.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	7/30 (23%)	1/29 (3%)	1/8 (13%)	0/0 (0%)
First incidence (days)	736 (T)	725	736 (T)	-
Life table test	P=0.540N	P=0.085N	P=0.430N	-
Logistic regression test	P=0.476N	P=0.075N	P=0.430N	-
Cochran-Armitage test	P=0.012N			
Fisher exact test		P=0.090N	P=0.029N	P=0.007N
Clitoral Gland: Adenoma				
Overall rate	5/56 (9%)	11/56 (20%)	14/58 (24%)	12/59 (20%)
Adjusted rate	17.0%	31.5%	83.1%	49.4%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	1/8 (13%)	2/8 (25%)
Terminal rate	4/28 (14%)	7/29 (24%)	6/8 (75%)	0/0 (0%)
First incidence (days)	717	465 (I)	463 (I)	310
Life table test	P<0.001	P=0.105	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.098	P=0.001	P=0.030
Cochran-Armitage test	P=0.187			
Fisher exact test		P=0.088	P=0.026	P=0.071
Clitoral Gland: Carcinoma				
Overall rate	0/56 (0%)	0/56 (0%)	4/58 (7%)	6/59 (10%)
Adjusted rate	0.0%	0.0%	7.5%	15.5%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	0/28 (0%)	0/29 (0%)	0/8 (0%)	0/0 (0%)
First incidence (days)	-	-	434	331
Life table test	P<0.001	-	P=0.059	P=0.004
Logistic regression test	P=0.404	-	P=0.176	P=0.246
Cochran-Armitage test	P=0.003			
Fisher exact test		-	P=0.064	P=0.016
Clitoral Gland: Adenoma or Carcinoma				
Overall rate	5/56 (9%)	11/56 (20%)	18/58 (31%)	17/59 (29%)
Adjusted rate	17.0%	31.5%	84.4%	56.2%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	1/8 (13%)	2/8 (25%)
Terminal rate	4/28 (14%)	7/29 (24%)	6/8 (75%)	0/0 (0%)
First incidence (days)	717	465 (I)	434	310
Life table test	P<0.001	P=0.105	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.098	P<0.001	P=0.013
Cochran-Armitage test	P=0.020			
Fisher exact test		P=0.088	P=0.003	P=0.006

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Large and Small Intestine: Adenomatous Polyp or Adenocarcinoma				
Overall rate	0/60 (0%)	0/59 (0%)	1/60 (2%)	3/60 (5%)
Adjusted rate	0.0%	0.0%	7.1%	20.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	0/31 (0%)	0/30 (0%)	0/8 (0%)	0/0 (0%)
First incidence (days)	-	-	699	407
Life table test	P<0.001	-	P=0.318	P=0.021
Logistic regression test	P=0.029	-	P=0.383	P=0.181
Cochran-Armitage test	P=0.022			
Fisher exact test		-	P=0.500	P=0.122
Mammary Gland: Adenoma				
Overall rate	1/60 (2%)	0/59 (0%)	3/60 (5%)	1/60 (2%)
Adjusted rate	3.0%	0.0%	15.2%	16.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	0/31 (0%)	0/30 (0%)	0/8 (0%)	0/0 (0%)
First incidence (days)	714	-	521	465 (I)
Life table test	P=0.022	P=0.506N	P=0.109	P=0.455
Logistic regression test	P=0.337	P=0.497N	P=0.256	P=0.625
Cochran-Armitage test	P=0.560			
Fisher exact test		P=0.504N	P=0.309	P=0.752N
Mammary Gland: Carcinoma				
Overall rate	1/60 (2%)	6/59 (10%)	12/60 (20%)	22/60 (37%)
Adjusted rate	1.7%	17.7%	51.7%	63.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	0/31 (0%)	4/30 (13%)	3/8 (38%)	0/0 (0%)
First incidence (days)	450	469	424	239
Life table test	P<0.001	P=0.059	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.057	P=0.003	P=0.014
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.054	P=0.001	P<0.001
Mammary Gland: Adenoma or Carcinoma				
Overall rate	2/60 (3%)	6/59 (10%)	14/60 (23%)	23/60 (38%)
Adjusted rate	4.7%	17.7%	58.0%	70.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
Terminal rate	0/31 (0%)	4/30 (13%)	3/8 (38%)	0/0 (0%)
First incidence (days)	450	469	424	239
Life table test	P<0.001	P=0.135	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.132	P=0.002	P=0.009
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.131	P=0.001	P<0.001
Mammary Gland: Fibroadenoma				
Overall rate	15/60 (25%)	23/59 (39%)	20/60 (33%)	1/60 (2%)
Adjusted rate	40.1%	61.6%	88.2%	3.1%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	10/31 (32%)	16/30 (53%)	6/8 (75%)	0/0 (0%)
First incidence (days)	474	604	510	371
Life table test	P<0.001	P=0.081	P<0.001	P=0.375
Logistic regression test	P=0.249	P=0.078	P=0.016	P=0.306N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.075	P=0.211	P<0.001N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Mammary Gland: Fibroadenoma or Adenoma				
Overall rate	16/60 (27%)	23/59 (39%)	22/60 (37%)	2/60 (3%)
Adjusted rate	41.9%	61.6%	88.9%	19.3%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	10/31 (32%)	16/30 (53%)	6/8 (75%)	0/0 (0%)
First incidence (days)	474	604	510	371
Life table test	P<0.001	P=0.118	P<0.001	P=0.152
Logistic regression test	P=0.168	P=0.114	P=0.012	P=0.524N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.108	P=0.163	P<0.001N
Mammary Gland: Fibroadenoma, Adenoma, or Adenocarcinoma				
Overall rate	17/60 (28%)	26/59 (44%)	29/60 (48%)	24/60 (40%)
Adjusted rate	42.9%	67.8%	95.3%	71.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
Terminal rate	10/31 (32%)	18/30 (60%)	7/8 (88%)	0/0 (0%)
First incidence (days)	450	469	424	239
Life table test	P<0.001	P=0.065	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.057	P=0.002	P=0.078
Cochran-Armitage test	P=0.315			
Fisher exact test		P=0.055	P=0.019	P=0.124
Oral Cavity (Pharynx and Tongue): Squamous Cell Papilloma				
Overall rate	1/60 (2%)	5/59 (8%)	10/60 (17%)	21/60 (35%)
Adjusted rate	3.2%	14.1%	58.7%	75.5%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	3/8 (38%)
Terminal rate	1/31 (3%)	2/30 (7%)	4/8 (50%)	0/0 (0%)
First incidence (days)	736 (T)	664	405	233
Life table test	P<0.001	P=0.112	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.106	P=0.003	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.100	P=0.004	P<0.001
Oral Cavity (Pharynx and Tongue): Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	1/59 (2%)	21/60 (35%)	23/60 (38%)
Adjusted rate	0.0%	3.3%	72.5%	73.9%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
Terminal rate	0/31 (0%)	1/30 (3%)	3/8 (38%)	0/0 (0%)
First incidence (days)	-	736 (T)	513	294
Life table test	P<0.001	P=0.493	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.493	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.496	P<0.001	P<0.001
Oral Cavity (Pharynx and Tongue): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	1/60 (2%)	6/59 (10%)	28/60 (47%)	37/60 (62%)
Adjusted rate	3.2%	17.2%	90.3%	91.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	5/8 (63%)
Terminal rate	1/31 (3%)	3/30 (10%)	6/8 (75%)	0/0 (0%)
First incidence (days)	736 (T)	664	405	233
Life table test	P<0.001	P=0.064	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.061	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.054	P<0.001	P<0.001

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Pancreatic Islets: Adenoma or Carcinoma				
Overall rate	3/60 (5%)	3/58 (5%)	0/60 (0%)	1/60 (2%)
Adjusted rate	9.4%	9.3%	0.0%	4.2%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	2/31 (6%)	2/30 (7%)	0/8 (0%)	0/0 (0%)
First incidence (days)	717	696	-	399
Life table test	P=0.305	P=0.653	P=0.408N	P=0.318
Logistic regression test	P=0.649	P=0.652N	P=0.331N	P=0.667
Cochran-Armitage test	P=0.191N			
Fisher exact test		P=0.644	P=0.122N	P=0.309N
Pharynx: Squamous Papilloma				
Overall rate	1/60 (2%)	2/59 (3%)	5/60 (8%)	3/60 (5%)
Adjusted rate	3.2%	5.6%	30.2%	26.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	1/31 (3%)	0/30 (0%)	2/8 (25%)	0/0 (0%)
First incidence (days)	736 (T)	664	405	336
Life table test	P<0.001	P=0.508	P=0.012	P=0.030
Logistic regression test	P=0.145	P=0.505	P=0.092	P=0.242
Cochran-Armitage test	P=0.323			
Fisher exact test		P=0.494	P=0.103	P=0.309
Pharynx: Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	1/59 (2%)	10/60 (17%)	16/60 (27%)
Adjusted rate	0.0%	3.3%	45.6%	61.5%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	0/31 (0%)	1/30 (3%)	1/8 (13%)	0/0 (0%)
First incidence (days)	-	736 (T)	538	330
Life table test	P<0.001	P=0.493	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.493	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.496	P<0.001	P<0.001
Pituitary Gland (Pars Distalis): Adenoma				
Overall rate	29/60 (48%)	30/58 (52%)	12/59 (20%)	5/59 (8%)
Adjusted rate	70.0%	76.4%	57.1%	36.3%
15-Month interim evaluation	1/10 (10%)	1/10 (10%)	0/8 (0%)	2/8 (25%)
Terminal rate	19/31 (61%)	21/30 (70%)	2/8 (25%)	0/0 (0%)
First incidence (days)	463 (I)	465 (I)	520	331
Life table test	P=0.004	P=0.459	P=0.486	P=0.027
Logistic regression test	P=0.300N	P=0.498	P=0.028N	P=0.622N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.427	P=0.001N	P<0.001N
Stomach (Forestomach): Squamous Cell Papilloma				
Overall rate	0/60 (0%)	14/59 (24%)	37/60 (62%)	24/60 (40%)
Adjusted rate	0.0%	39.6%	100.0%	95.3%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	5/8 (63%)	7/8 (88%)
Terminal rate	0/31 (0%)	10/30 (33%)	8/8 (100%)	0/0 (0%)
First incidence (days)	-	463 (I)	451	325
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Stomach (Forestomach): Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	3/59 (5%)	9/60 (15%)	6/60 (10%)
Adjusted rate	0.0%	9.4%	57.6%	48.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
Terminal rate	0/31 (0%)	2/30 (7%)	3/8 (38%)	0/0 (0%)
First incidence (days)	-	713	628	325
Life table test	P<0.001	P=0.121	P<0.001	P=0.001
Logistic regression test	P<0.001	P=0.124	P<0.001	P=0.046
Cochran-Armitage test	P=0.058			
Fisher exact test		P=0.119	P=0.001	P=0.014
Stomach (Forestomach): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	17/59 (29%)	42/60 (70%)	27/60 (45%)
Adjusted rate	0.0%	47.3%	100.0%	100.0%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	5/8 (63%)	8/8 (100%)
Terminal rate	0/31 (0%)	12/30 (40%)	8/8 (100%)	0/0 (0%)
First incidence (days)	-	463 (I)	451	325
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Thyroid Gland (C-cell): Adenoma				
Overall rate	4/60 (7%)	5/57 (9%)	4/60 (7%)	0/60 (0%)
Adjusted rate	11.6%	12.9%	14.8%	0.0%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	0/8 (0%)	0/8 (0%)
Terminal rate	3/31 (10%)	1/30 (3%)	0/8 (0%)	0/0 (0%)
First incidence (days)	526	465 (I)	513	-
Life table test	P=0.542	P=0.492	P=0.243	-
Logistic regression test	P=0.171N	P=0.472	P=0.569	P=0.676N
Cochran-Armitage test	P=0.032N			
Fisher exact test		P=0.467	P=0.641N	P=0.059N
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rate	4/60 (7%)	6/57 (11%)	4/60 (7%)	0/60 (0%)
Adjusted rate	11.6%	15.9%	14.8%	0.0%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	0/8 (0%)	0/8 (0%)
Terminal rate	3/31 (10%)	2/30 (7%)	0/8 (0%)	0/0 (0%)
First incidence (days)	526	465 (I)	513	-
Life table test	P=0.529	P=0.365	P=0.243	-
Logistic regression test	P=0.183N	P=0.345	P=0.569	P=0.676N
Cochran-Armitage test	P=0.024N			
Fisher exact test		P=0.339	P=0.641N	P=0.059N
Thyroid Gland (Follicular Cell): Adenoma				
Overall rate	0/60 (0%)	0/57 (0%)	3/60 (5%)	2/60 (3%)
Adjusted rate	0.0%	0.0%	20.1%	8.1%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	0/31 (0%)	0/30 (0%)	1/8 (13%)	0/0 (0%)
First incidence (days)	-	-	538	310
Life table test	P<0.001	-	P=0.026	P=0.099
Logistic regression test	P=0.151	-	P=0.078	P=0.609
Cochran-Armitage test	P=0.160			
Fisher exact test		-	P=0.122	P=0.248

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rate	0/60 (0%)	1/57 (2%)	3/60 (5%)	2/60 (3%)
Adjusted rate	0.0%	3.3%	20.1%	8.1%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	0/31 (0%)	1/30 (3%)	1/8 (13%)	0/0 (0%)
First incidence (days)	-	736 (T)	538	310
Life table test	P<0.001	P=0.493	P=0.026	P=0.099
Logistic regression test	P=0.137	P=0.493	P=0.078	P=0.609
Cochran-Armitage test	P=0.264			
Fisher exact test		P=0.487	P=0.122	P=0.248
Tongue: Squamous Cell Papilloma				
Overall rate	0/60 (0%)	3/59 (5%)	5/60 (8%)	18/60 (30%)
Adjusted rate	0.0%	9.1%	33.4%	65.2%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	2/8 (25%)
Terminal rate	0/31 (0%)	2/30 (7%)	2/8 (25%)	0/0 (0%)
First incidence (days)	-	677	479	233
Life table test	P<0.001	P=0.124	P=0.002	P<0.001
Logistic regression test	P<0.001	P=0.123	P=0.017	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.119	P=0.029	P<0.001
Tongue: Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	0/59 (0%)	13/60 (22%)	8/60 (13%)
Adjusted rate	0.0%	0.0%	57.0%	34.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	0/31 (0%)	0/30 (0%)	3/8 (38%)	0/0 (0%)
First incidence (days)	-	-	513	294
Life table test	P<0.001	-	P<0.001	P<0.001
Logistic regression test	P=0.011	-	P<0.001	P=0.100
Cochran-Armitage test	P=0.005			
Fisher exact test		-	P<0.001	P=0.003
Tongue: Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	3/59 (5%)	18/60 (30%)	26/60 (43%)
Adjusted rate	0.0%	9.1%	77.1%	78.3%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	3/8 (38%)
Terminal rate	0/31 (0%)	2/30 (7%)	5/8 (63%)	0/0 (0%)
First incidence (days)	-	677	479	233
Life table test	P<0.001	P=0.124	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.123	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.119	P<0.001	P<0.001
Uterus: Stromal Polyp				
Overall rate	9/60 (15%)	5/59 (8%)	7/60 (12%)	1/60 (2%)
Adjusted rate	26.4%	13.7%	36.0%	11.1%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	0/8 (0%)	1/8 (13%)
Terminal rate	7/31 (23%)	3/30 (10%)	2/8 (25%)	0/0 (0%)
First incidence (days)	547	463 (I)	450	463 (I)
Life table test	P=0.126	P=0.207N	P=0.143	P=0.455
Logistic regression test	P=0.435N	P=0.192N	P=0.581	P=0.751
Cochran-Armitage test	P=0.016N			
Fisher exact test		P=0.207N	P=0.395N	P=0.008N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Uterus: Stromal Sarcoma				
Overall rate	3/60 (5%)	0/59 (0%)	0/60 (0%)	0/60 (0%)
Adjusted rate	6.8%	0.0%	0.0%	0.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	0/31 (0%)	0/30 (0%)	0/8 (0%)	0/0 (0%)
First incidence (days)	424	-	-	-
Life table test	P=0.407N	P=0.116N	P=0.233N	P=0.786N
Logistic regression test	P=0.073N	P=0.127N	P=0.087N	P=0.143N
Cochran-Armitage test	P=0.134N			
Fisher exact test		P=0.125N	P=0.122N	P=0.122N
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rate	12/60 (20%)	5/59 (8%)	7/60 (12%)	1/60 (2%)
Adjusted rate	31.4%	13.7%	36.0%	11.1%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	0/8 (0%)	1/8 (13%)
Terminal rate	7/31 (23%)	3/30 (10%)	2/8 (25%)	0/0 (0%)
First incidence (days)	424	463 (I)	450	463 (I)
Life table test	P=0.289	P=0.065N	P=0.355	P=0.584
Logistic regression test	P=0.134N	P=0.059N	P=0.293N	P=0.344N
Cochran-Armitage test	P=0.005N			
Fisher exact test		P=0.061N	P=0.159N	P=0.001N
Zymbal's Gland: Carcinoma				
Overall rate	0/60 (0%)	1/59 (2%)	0/60 (0%)	4/60 (7%)
Adjusted rate	0.0%	2.9%	0.0%	36.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	1/8 (13%)
Terminal rate	0/31 (0%)	0/30 (0%)	0/8 (0%)	0/0 (0%)
First incidence (days)	-	713	-	336
Life table test	P<0.001	P=0.506	-	P=0.003
Logistic regression test	P=0.028	P=0.503	-	P=0.103
Cochran-Armitage test	P=0.011			
Fisher exact test		P=0.496	-	P=0.059
All Organs: Mononuclear Cell Leukemia				
Overall rate	13/60 (22%)	17/59 (29%)	14/60 (23%)	0/60 (0%)
Adjusted rate	34.9%	44.1%	69.3%	0.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	0/8 (0%)
Terminal rate	8/31 (26%)	10/30 (33%)	4/8 (50%)	0/0 (0%)
First incidence (days)	597	434	405	-
Life table test	P=0.025	P=0.265	P=0.005	-
Logistic regression test	P=0.323N	P=0.262	P=0.164	P=0.372N
Cochran-Armitage test	P<0.001N			
Fisher exact test		P=0.246	P=0.500	P<0.001N
All Organs: Benign Neoplasms				
Overall rate	42/60 (70%)	48/59 (81%)	51/60 (85%)	40/60 (67%)
Adjusted rate	93.2%	100.0%	100.0%	100.0%
15-Month interim evaluation	1/10 (10%)	4/10 (40%)	5/8 (63%)	8/8 (100%)
Terminal rate	28/31 (90%)	30/30 (100%)	8/8 (100%)	0/0 (0%)
First incidence (days)	463 (I)	463 (I)	405	233
Life table test	P<0.001	P=0.164	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.073	P<0.001	P<0.001
Cochran-Armitage test	P=0.129N			
Fisher exact test		P=0.109	P=0.040	P=0.422N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
All Organs: Malignant Neoplasms				
Overall rate	20/60 (33%)	25/59 (42%)	46/60 (77%)	48/60 (80%)
Adjusted rate	47.2%	62.9%	100.0%	94.9%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/8 (0%)	5/8 (63%)
Terminal rate	10/31 (32%)	16/30 (53%)	8/8 (100%)	0/0 (0%)
First incidence (days)	424	434	255	184
Life table test	P<0.001	P=0.236	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.216	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.204	P<0.001	P<0.001
All Organs: Benign and Malignant Neoplasms				
Overall rate	49/60 (82%)	50/59 (85%)	56/60 (93%)	56/60 (93%)
Adjusted rate	98.0%	100.0%	100.0%	100.0%
15-Month interim evaluation	1/10 (10%)	4/10 (40%)	5/8 (63%)	8/8 (100%)
Terminal rate	30/31 (97%)	30/30 (100%)	8/8 (100%)	0/0 (0%)
First incidence (days)	424	434	255	184
Life table test	P<0.001	P=0.455	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.436	P=0.001	P<0.001
Cochran-Armitage test	P=0.036			
Fisher exact test		P=0.420	P=0.048	P=0.048

(T)Terminal sacrifice
(I)15-Month interim evaluation
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, salivary gland, spleen, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] 15-Month interim evaluation began on day 463
[d] Observed incidence at terminal kill
[e] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by **N**.
[f] Not applicable; no neoplasms in animal group

TABLE B4a
Historical Incidence of Oral Cavity Neoplasms in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Squamous Cell Papilloma	Squamous Cell Carcinoma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	0/50	0/50
Tribromomethane	0/50	0/50	0/50
Hexachloroethane	0/50	0/50	0/50
Phenylbutazone	0/50	0/50	0/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	0/60	0/60	0/60
Overall Historical Incidence			
Total	3/820 (0.4%)	2/820 (0.2%)	5/820 (0.6%)
Standard deviation	0.8%	0.7%	1.0%
Range	0%-2%	0%-2%	0%-2%

[a] Data as of 3 April 1991

TABLE B4b
Historical Incidence of Forestomach Neoplasms in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Squamous Cell Papilloma	Squamous Cell Carcinoma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	0/50	0/50
Tribromomethane	1/50	0/50	1/50
Hexachloroethane	0/50	0/50	0/50
Phenylbutazone	1/50	0/50	1/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	0/60	0/60	0/60
Overall Historical Incidence			
Total	2/820 (0.2%)	0/820	2/820 (0.2%)
Standard deviation	0.7%		0.7%
Range	0%-2%		0%-2%

[a] Data as of 3 April 1991

TABLE B4c
Historical Incidence of Pancreatic Neoplasms in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/49	0/49	0/49
Tribromomethane	1/48	0/48	1/48
Hexachloroethane	0/48	0/48	0/48
Phenylbutazone	1/50	0/50	1/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	1/60	0/60	1/60
Overall Historical Incidence			
Total	8/810 (1.0%)	0/810	8/810 (1.0%)
Standard deviation	1.5%		1.5%
Range	0%-4%		0%-4%

[a] Data as of 3 April 1991

TABLE B4d
Historical Incidence of Renal Tubule Neoplasms in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	0/50	0/50
Tribromomethane	0/50	0/50	0/50
Hexachloroethane	0/50	0/50	0/50
Phenylbutazone	0/50	0/50	0/50
Probenecid	0/50	0/50	0/50
Titanocene•2Cl	0/60	0/60	0/60
Overall Historical Incidence			
Total	1/819 (0%)	0/819 (0%)	1/819 (0%)
Standard deviation	0.5%		0.5%
Range	0%-2%		0%-2%

[a] Data as of 3 April 1991

TABLE B4e
Historical Incidence of Zymbal's Gland Neoplasms in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	0/50	0/50	0/50
Tribromomethane	0/50	0/50	0/50
Hexachloroethane	0/50	2/50	2/50
Phenylbutazone	0/50	0/50	0/50
Probenecid	0/50	0/50	
Titanocene•2Cl	0/60	0/60	0/60
Overall Historical Incidence			
Total	0/820 (0.0%)	5/820 (0.6%)	5/820 (0.6%)
Standard deviation		1.2%	1.2%
Range		0%-4%	0%-4%

[a] Data as of 3 April 1991

TABLE B4f
Historical Incidence of Clitoral Gland Neoplasms in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	2/50	1/50	3/50
Tribromomethane	0/50	1/50	1/50
Hexachloroethane	3/50	1/50	4/50
Phenylbutazone	5/50	0/50	5/50
Probenecid	3/50	0/50	
Titanocene•2Cl	12/60	1/60	13/60
Overall Historical Incidence			
Total	62/820 (7.6%)	12/820 (1.5%)	74/820 (9.0%)
Standard deviation	5.4%	1.9%	6.0%
Range	0%-20%	0%-6%	2%-22%

[a] Data as of 3 April 1991

TABLE B4g
Historical Incidence of Mammary Gland Neoplasms in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls			
	Fibroadenoma	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute				
2,4-Diaminophenol•2HCl	17/50	0/50	3/50	3/50
Tribromomethane	22/50	0/50	1/50	1/50
Hexachloroethane	28/50	0/50	0/50	0/50
Phenylbutazone	22/50	0/50	1/50	1/50
Probenecid	24/50	0/50	3/50	3/50
Titanocene•2Cl	26/60	1/60	3/60	4/60
Overall Historical Incidence				
Total	314/820 (38.3%)	8/820 (1.0%)	25/820 (3.0%)	335/820 (40.9%)
Standard deviation	10.8%	1.8%	2.6%	9.9%
Range	18%-56%	0%-6%	0%-8%	22%-58%

[a] Data as of 3 April 1991

TABLE B4h
Historical Incidence of Carcinoma of the Small Intestine in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls
Historical Incidence at EG&G Mason Research Institute	
2,4-Diaminophenol•2HCl	0/50
Tribromomethane	0/50
Hexachloroethane	0/50
Phenylbutazone	0/50
Probenecid	0/50
Titanocene•2Cl	0/60
Overall Historical Incidence	
Total	0/820

[a] Data as of 3 April 1991. Current NTP historical neoplasm pooling convention recodes adenocarcinoma to carcinoma.

TABLE B4i
Historical Incidence of Carcinoma of the Large Intestine in Female F344/N Rats Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls
Historical Incidence at EG&G Mason Research Institute	
2,4-Diaminophenol•2HCl	1/50
Tribromomethane	0/50
Hexachloroethane	0/50
Phenylbutazone	0/50
Probenecid	0/50
Titanocene•2Cl	0/60
Overall Historical Incidence	
Total	1/820 (0.1%)
Standard deviation	0.5%
Range	0%-2%

[a] Data as of 3 April 1991. Current NTP historical neoplasm pooling convention recodes adenocarcinoma to carcinoma.

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	8	8
Early deaths				
Moribund	17	17	42	49
Natural deaths	2	2	2	2
Scheduled sacrifice				1
Survivors				
Terminal sacrifice	31	30	8	
Missexed		1		
Animals examined microscopically	60	59	60	60
15-Month Interim Evaluation				
Alimentary System				
Esophagus	(10)	(10)	(8)	(8)
Hyperkeratosis				2 (25%)
Liver	(10)	(10)	(8)	(8)
Basophilic focus	3 (30%)	2 (20%)	3 (38%)	5 (63%)
Clear cell focus			1 (13%)	
Eosinophilic focus		2 (20%)		1 (13%)
Hepatodiaphragmatic nodule	1 (10%)		1 (13%)	1 (13%)
Bile duct, hyperplasia			1 (13%)	3 (38%)
Pancreas	(10)	(10)	(8)	(8)
Acinus, hyperplasia		1 (10%)		2 (25%)
Stomach, forestomach	(10)	(10)	(8)	(8)
Hyperplasia, basal cell		2 (20%)	1 (13%)	3 (38%)
Hyperplasia, squamous		1 (10%)	4 (50%)	1 (13%)
Stomach, glandular	(10)	(10)	(8)	(8)
Hyperplasia				1 (13%)
Tongue	(10)		(1)	(4)
Hyperkeratosis				2 (50%)
Cardiovascular System				
Heart	(10)	(10)	(8)	(8)
Cardiomyopathy			1 (13%)	2 (25%)
Endocrine System				
Pituitary gland	(10)	(10)	(8)	(8)
Pars distalis, angiectasis		1 (10%)		1 (13%)
Pars distalis, cyst	2 (20%)	1 (10%)	1 (13%)	
Pars distalis, hyperplasia	3 (30%)	3 (30%)	2 (25%)	1 (13%)
Thyroid gland	(10)	(10)	(8)	(8)
Follicular cell, hyperplasia				1 (13%)
General Body System				
None				

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
15-Month Interim Evaluation (continued)				
Genital System				
Ovary	(10)	(10)	(8)	(8)
Cyst		1 (10%)	1 (13%)	
Uterus	(10)	(10)	(8)	(8)
Decidual reaction		1 (10%)		
Hematopoietic System				
Spleen	(10)	(10)	(8)	(8)
Fibrosis	1 (10%)			
Hematopoietic cell proliferation				1 (13%)
Integumentary System				
Skin	(10)	(10)	(8)	(8)
Inflammation, acute				1 (13%)
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
Eye			(2)	
Lens, cataract			1 (50%)	
Retina, atrophy			1 (50%)	
Urinary System				
Kidney	(10)	(10)	(8)	(8)
Nephropathy			1 (13%)	3 (38%)
Renal tubule, hyperplasia				2 (25%)
2-Year Study				
Alimentary System				
Esophagus	(48)	(49)	(52)	(52)
Hyperkeratosis	1 (2%)		15 (29%)	29 (56%)
Intestine large, cecum	(49)	(47)	(52)	(52)
Atrophy				2 (4%)
Epithelium, hyperplasia				1 (2%)
Intestine large, colon	(49)	(47)	(52)	(51)
Diverticulum			1 (2%)	

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Liver	(50)	(49)	(52)	(52)
Basophilic focus	20 (40%)	27 (55%)	17 (33%)	5 (10%)
Bile stasis			1 (2%)	
Clear cell focus		1 (2%)	1 (2%)	1 (2%)
Eosinophilic focus	1 (2%)		2 (4%)	2 (4%)
Fatty change, diffuse	1 (2%)			
Fatty change, focal	3 (6%)	2 (4%)	2 (4%)	
Fibrosis			1 (2%)	
Hepatodiaphragmatic nodule	1 (2%)	3 (6%)	10 (19%)	5 (10%)
Hepatodiaphragmatic nodule, multiple	1 (2%)			
Hyperplasia	2 (4%)	3 (6%)	1 (2%)	1 (2%)
Inflammation, granulomatous	6 (12%)	5 (10%)		
Mineralization				1 (2%)
Mitotic alteration			1 (2%)	
Mixed cell focus	4 (8%)	6 (12%)	3 (6%)	
Necrosis		1 (2%)		4 (8%)
Bile duct, hyperplasia				2 (4%)
Mesentery	(2)	(5)	(4)	(1)
Fat, inflammation, chronic active	1 (50%)			
Fat, necrosis	1 (50%)	4 (80%)	3 (75%)	
Pancreas	(50)	(49)	(52)	(52)
Acinus, atrophy	10 (20%)	9 (18%)	9 (17%)	3 (6%)
Acinus, hyperplasia	5 (10%)	14 (29%)	24 (46%)	9 (17%)
Pharynx	(1)	(3)	(18)	(19)
Hyperplasia, squamous			1 (6%)	
Palate, abscess			1 (6%)	1 (5%)
Palate, hyperplasia, basal cell	1 (100%)		1 (6%)	1 (5%)
Palate, hyperplasia, squamous			1 (6%)	
Salivary glands	(50)	(49)	(52)	(52)
Inflammation, chronic active				1 (2%)
Duct, metaplasia, squamous		5 (10%)	3 (6%)	
Stomach, forestomach	(50)	(49)	(51)	(52)
Hyperplasia, basal cell		8 (16%)	4 (8%)	6 (12%)
Hyperplasia, squamous	1 (2%)	25 (51%)	11 (22%)	15 (29%)
Inflammation, chronic active	1 (2%)	1 (2%)		1 (2%)
Mineralization		2 (4%)		
Ulcer	1 (2%)	1 (2%)	2 (4%)	1 (2%)
Stomach, glandular	(50)	(49)	(52)	(51)
Hyperplasia				1 (2%)
Mineralization		2 (4%)		1 (2%)
Tongue		(4)	(20)	(31)
Acanthosis				3 (10%)
Hyperkeratosis			1 (5%)	1 (3%)
Hyperplasia, squamous		1 (25%)		
Inflammation, acute		1 (25%)	6 (30%)	
Cardiovascular System				
Heart	(50)	(49)	(52)	(50)
Cardiomyopathy	18 (36%)	22 (45%)	16 (31%)	7 (14%)
Artery, inflammation, chronic active		1 (2%)		

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Endocrine System				
Adrenal gland, cortex	(49)	(48)	(52)	(50)
Degeneration, fatty		2 (4%)	1 (2%)	
Hyperplasia		2 (4%)	1 (2%)	
Adrenal gland, medulla	(49)	(47)	(52)	(50)
Hyperplasia	7 (14%)	5 (11%)	3 (6%)	
Islets, pancreatic	(50)	(48)	(52)	(52)
Hyperplasia			1 (2%)	
Metaplasia		1 (2%)	2 (4%)	1 (2%)
Pituitary gland	(50)	(48)	(51)	(51)
Pars distalis, angiectasis	19 (38%)	20 (42%)	11 (22%)	3 (6%)
Pars distalis, cyst	10 (20%)	6 (13%)	10 (20%)	1 (2%)
Pars distalis, hyperplasia	21 (42%)	19 (40%)	23 (45%)	6 (12%)
Pars intermedia, cyst			3 (6%)	
Pars intermedia, hyperplasia	1 (2%)			
Thyroid gland	(50)	(47)	(52)	(52)
C-cell, hyperplasia	7 (14%)	7 (15%)	8 (15%)	
Follicle, cyst			1 (2%)	
Follicle, hemorrhage	1 (2%)			
Follicular cell, hyperplasia		3 (6%)	1 (2%)	1 (2%)
General Body System				
None				
Genital System				
Clitoral gland	(46)	(46)	(50)	(51)
Hyperplasia		2 (4%)	3 (6%)	3 (6%)
Necrosis			3 (6%)	
Ovary	(50)	(48)	(52)	(52)
Cyst	4 (8%)	2 (4%)	7 (13%)	3 (6%)
Interstitial cell, hyperplasia				1 (2%)
Uterus	(50)	(48)	(52)	(52)
Cyst	2 (4%)			
Decidual reaction			1 (2%)	
Inflammation, chronic active	1 (2%)			
Endometrium, hyperplasia	1 (2%)	1 (2%)		1 (2%)
Hematopoietic System				
Bone marrow	(50)	(48)	(52)	(52)
Myelofibrosis	1 (2%)			
Lymph node	(50)	(49)	(52)	(52)
Mediastinal, pigmentation	3 (6%)	3 (6%)	5 (10%)	
Pancreatic, pigmentation	2 (4%)			
Lymph node, mandibular	(48)	(49)	(52)	(50)
Degeneration			4 (8%)	
Lymph node, mesenteric	(50)	(48)	(51)	(49)
Angiectasis	4 (8%)	2 (4%)		

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Hematopoietic System (continued)				
Spleen	(50)	(47)	(52)	(51)
Angiectasis	1 (2%)			
Depletion lymphoid				3 (6%)
Fibrosis	2 (4%)		1 (2%)	
Hematopoietic cell proliferation	25 (50%)	27 (57%)	40 (77%)	31 (61%)
Infiltration cellular, histiocyte	1 (2%)		1 (2%)	
Thymus	(46)	(46)	(51)	(50)
Depletion lymphoid				2 (4%)
Epithelial cell, hyperplasia	1 (2%)		4 (8%)	
Integumentary System				
Mammary gland	(47)	(46)	(45)	(43)
Galactocele	11 (23%)	15 (33%)	11 (24%)	1 (2%)
Skin	(50)	(49)	(51)	(51)
Acanthosis	1 (2%)	1 (2%)		
Hyperkeratosis	1 (2%)			
Inflammation, chronic active	1 (2%)	1 (2%)		
Necrosis				1 (2%)
Musculoskeletal System				
Bone	(50)	(49)	(52)	(51)
Hyperostosis		1 (2%)		
Nervous System				
Brain	(50)	(49)	(52)	(52)
Hemorrhage	1 (2%)			
Hydrocephalus		1 (2%)		
Hyperplasia, reticulum cell			1 (2%)	
Inflammation, acute			1 (2%)	
Respiratory System				
Lung	(50)	(48)	(51)	(52)
Edema	1 (2%)			
Embolus tumor				1 (2%)
Fibrosis	1 (2%)	1 (2%)		
Infiltration cellular, histiocyte	5 (10%)	2 (4%)	5 (10%)	
Inflammation, acute	1 (2%)		2 (4%)	
Alveolar epithelium, hyperplasia	2 (4%)	2 (4%)	2 (4%)	1 (2%)
Nose	(50)	(49)	(52)	(52)
Fungus				1 (2%)
Inflammation, acute	2 (4%)	1 (2%)	2 (4%)	6 (12%)

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
2-Year Study (continued)				
Special Senses System				
Eye	(4)	(5)	(9)	(19)
Hemorrhage	1 (25%)			2 (11%)
Inflammation, acute			2 (22%)	2 (11%)
Synechia	1 (25%)	1 (20%)	2 (22%)	
Lens, cataract		1 (20%)	2 (22%)	5 (26%)
Retina, atrophy		2 (40%)	3 (33%)	
Urinary System				
Kidney	(50)	(47)	(52)	(51)
Cyst	1 (2%)			
Infarct		1 (2%)		
Nephropathy	18 (36%)	21 (45%)	17 (33%)	5 (10%)
Cortex, mineralization	1 (2%)	1 (2%)		5 (10%)
Papilla, mineralization	1 (2%)	1 (2%)		
Renal tubule, hyperplasia		2 (4%)	3 (6%)	10 (20%)
Renal tubule, regeneration				3 (6%)

[a] Number of animals examined microscopically at site and number of animals with lesion

APPENDIX C
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR GAVAGE STUDY OF 1,2,3-TRICHLOROPROPANE

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	8	8	6	4
Early deaths				
Moribund	3	26	40	44
Natural deaths	7	7	4	3
Scheduled sacrifice			10	9
Survivors				
Terminal sacrifice	42	18		
Missexed		1		
Animals examined microscopically	60	59	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(8)	(8)	(6)	(4)
Hepatocellular carcinoma			1 (17%)	
Hepatocellular adenoma	1 (13%)			
Hepatocellular adenoma, multiple				2 (50%)
Squamous cell carcinoma, metastatic, stomach				2 (50%)
Stomach, forestomach	(8)	(8)	(6)	(4)
Papilloma squamous		4 (50%)	1 (17%)	2 (50%)
Papilloma squamous, multiple		3 (38%)	2 (33%)	
Squamous cell carcinoma		1 (13%)	2 (33%)	4 (100%)
Squamous cell carcinoma, multiple			2 (33%)	
Cardiovascular System				
None				
Endocrine System				
Thyroid gland	(7)	(8)	(6)	(4)
Follicular cell, adenoma			1 (17%)	
General Body System				
None				
Genital System				
None				
Hematopoietic System				
Spleen	(8)	(8)	(6)	(4)
Squamous cell carcinoma, metastatic, stomach			1 (17%)	
Integumentary System				
None				

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
15-Month Interim Evaluation (continued)				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(8)	(8)	(6)	(4)
Alveolar/bronchiolar adenoma		1 (13%)		1 (25%)
Alveolar/bronchiolar adenoma, multiple				2 (50%)
Squamous cell carcinoma, metastatic, stomach				1 (25%)
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Gallbladder	(47)	(46)	(51)	(55)
Sarcoma, metastatic, stomach				1 (2%)
Squamous cell carcinoma, metastatic, stomach			2 (4%)	1 (2%)
Intestine large, cecum	(51)	(49)	(53)	(55)
Intestine small, duodenum	(49)	(48)	(54)	(53)
Intestine small, ileum	(50)	(51)	(54)	(55)
Squamous cell carcinoma, metastatic, stomach				1 (2%)
Lymphoid tissue, histiocytic sarcoma		1 (2%)	1 (2%)	
Intestine small, jejunum	(49)	(48)	(54)	(55)
Adenoma	1 (2%)			1 (2%)
Squamous cell carcinoma, metastatic, stomach				2 (4%)
Liver	(52)	(51)	(54)	(56)
Hemangioma		1 (2%)		
Hemangiosarcoma	3 (6%)			
Hepatocellular carcinoma	4 (8%)	8 (16%)	5 (9%)	3 (5%)
Hepatocellular carcinoma, multiple		3 (6%)		
Hepatocellular adenoma	9 (17%)	11 (22%)	13 (24%)	6 (11%)
Hepatocellular adenoma, multiple	2 (4%)	7 (14%)	8 (15%)	23 (41%)
Histiocytic sarcoma	1 (2%)	1 (2%)	1 (2%)	
Sarcoma, metastatic, stomach				1 (2%)
Squamous cell carcinoma, metastatic, stomach		13 (25%)	31 (57%)	27 (48%)
Mesentery	(4)	(15)	(17)	(16)
Hemangiosarcoma, metastatic, liver	1 (25%)			
Histiocytic sarcoma			1 (6%)	
Histiocytic sarcoma, metastatic, liver	1 (25%)			
Sarcoma, metastatic, skeletal muscle			1 (6%)	
Squamous cell carcinoma, metastatic, stomach		13 (87%)	14 (82%)	15 (94%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Pancreas	(52)	(50)	(53)	(55)
Histiocytic sarcoma		1 (2%)	1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Sarcoma, metastatic, stomach				1 (2%)
Squamous cell carcinoma, metastatic, stomach		12 (24%)	16 (30%)	11 (20%)
Salivary glands	(52)	(51)	(54)	(56)
Stomach	(52)	(51)	(54)	(56)
Histiocytic sarcoma			1 (2%)	
Stomach, forestomach	(52)	(51)	(54)	(56)
Papilloma squamous	3 (6%)	13 (25%)	14 (26%)	22 (39%)
Papilloma squamous, multiple		15 (29%)	8 (15%)	11 (20%)
Sarcoma				1 (2%)
Squamous cell carcinoma		26 (51%)	17 (31%)	32 (57%)
Squamous cell carcinoma, multiple		14 (27%)	33 (61%)	19 (34%)
Tongue	(2)	(1)	(1)	(3)
Papilloma squamous				2 (67%)
Cardiovascular System				
Heart	(52)	(51)	(54)	(56)
Histiocytic sarcoma			1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		1 (2%)		
Endocrine System				
Adrenal gland, cortex	(52)	(51)	(51)	(54)
Histiocytic sarcoma		1 (2%)		
Squamous cell carcinoma, metastatic, stomach		2 (4%)		
Thyroid gland	(50)	(51)	(54)	(56)
Histiocytic sarcoma			1 (2%)	
Follicular cell, adenoma	1 (2%)	1 (2%)		
Follicular cell, carcinoma			1 (2%)	
General Body System				
Tissue NOS		(1)		
Squamous cell carcinoma, metastatic, stomach		1 (100%)		
Genital System				
Epididymis	(52)	(51)	(54)	(56)
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		6 (12%)	5 (9%)	2 (4%)
Prostate	(51)	(50)	(54)	(53)
Squamous cell carcinoma, metastatic, stomach			2 (4%)	2 (4%)
Seminal vesicle	(52)	(51)	(54)	(56)
Squamous cell carcinoma, metastatic, stomach		6 (12%)	9 (17%)	1 (2%)
Testes	(52)	(51)	(53)	(56)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Hematopoietic System				
Bone marrow	(52)	(51)	(54)	(56)
Hemangiosarcoma	1 (2%)			
Histiocytic sarcoma		1 (2%)	1 (2%)	
Lymph node	(52)	(51)	(54)	(56)
Axillary, histiocytic sarcoma			1 (2%)	
Bronchial, squamous cell carcinoma, metastatic, stomach				1 (2%)
Iliac, squamous cell carcinoma, metastatic, stomach		1 (2%)		
Mediastinal, histiocytic sarcoma		1 (2%)	1 (2%)	
Mediastinal, sarcoma, metastatic, stomach				1 (2%)
Mediastinal, squamous cell carcinoma, metastatic, stomach		8 (16%)	4 (7%)	3 (5%)
Pancreatic, squamous cell carcinoma, metastatic, stomach		1 (2%)		
Lymph node, mandibular	(50)	(49)	(51)	(50)
Histiocytic sarcoma		1 (2%)	1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Lymph node, mesenteric	(48)	(48)	(52)	(54)
Histiocytic sarcoma		1 (2%)	1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		6 (13%)	12 (23%)	5 (9%)
Mediastinal, squamous cell carcinoma, metastatic, stomach				1 (2%)
Spleen	(52)	(51)	(54)	(56)
Hemangioma	1 (2%)	1 (2%)		
Hemangiosarcoma	2 (4%)			
Histiocytic sarcoma		1 (2%)	1 (2%)	
Sarcoma, metastatic, skeletal muscle			1 (2%)	
Squamous cell carcinoma, metastatic, stomach		3 (6%)	8 (15%)	5 (9%)
Thymus	(47)	(40)	(47)	(46)
Histiocytic sarcoma			1 (2%)	
Squamous cell carcinoma, metastatic, stomach		3 (8%)		1 (2%)
Integumentary System				
Skin	(52)	(50)	(54)	(55)
Prepuce, papilloma squamous	1 (2%)			
Subcutaneous tissue, hemangioma			1 (2%)	
Subcutaneous tissue, hemangiosarcoma	1 (2%)			
Subcutaneous tissue, sarcoma		1 (2%)		
Musculoskeletal System				
Bone	(52)	(51)	(54)	(56)
Osteosarcoma		1 (2%)		
Skeletal muscle	(1)	(13)	(14)	(9)
Histiocytic sarcoma			1 (7%)	
Sarcoma			1 (7%)	
Sarcoma, metastatic, stomach				1 (11%)
Squamous cell carcinoma, metastatic, stomach		12 (92%)	11 (79%)	7 (78%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Nervous System				
Brain	(52)	(50)	(54)	(56)
Squamous cell carcinoma, metastatic, stomach				1 (2%)
Respiratory System				
Lung	(52)	(51)	(54)	(56)
Alveolar/bronchiolar adenoma	6 (12%)	9 (18%)	3 (6%)	5 (9%)
Alveolar/bronchiolar adenoma, multiple	1 (2%)	2 (4%)		1 (2%)
Alveolar/bronchiolar carcinoma	1 (2%)		2 (4%)	
Hemangiosarcoma, metastatic, liver	1 (2%)			
Hepatocellular carcinoma, metastatic, liver		3 (6%)	1 (2%)	1 (2%)
Histiocytic sarcoma		1 (2%)	1 (2%)	
Histiocytic sarcoma, metastatic, liver	1 (2%)			
Sarcoma, metastatic, stomach				1 (2%)
Squamous cell carcinoma, metastatic, stomach		6 (12%)	12 (22%)	6 (11%)
Nose	(52)	(51)	(54)	(56)
Histiocytic sarcoma			1 (2%)	
Special Senses System				
Harderian gland	(1)	(3)	(11)	(13)
Adenoma	1 (100%)	2 (67%)	10 (91%)	11 (85%)
Urinary System				
Kidney	(52)	(51)	(54)	(56)
Histiocytic sarcoma			1 (2%)	
Squamous cell carcinoma, metastatic, stomach		2 (4%)		
Urinary bladder	(52)	(50)	(53)	(56)
Systemic Lesions				
Multiple organs[b]	(52)	(51)	(54)	(56)
Histiocytic sarcoma	1 (2%)	1 (2%)	1 (2%)	
Lymphoma malignant histiocytic		1 (2%)		
Lymphoma malignant lymphocytic	1 (2%)			1 (2%)
Lymphoma malignant undifferentiated cell	4 (8%)	3 (6%)		

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	1	7	5	4
2-Year study	29	50	54	56
Total primary neoplasms				
15-Month interim evaluation	1	9	9	11
2-Year study	44	120	117	138
Total animals with benign neoplasms				
15-Month interim evaluation	1	7	4	3
2-Year study	19	42	42	47
Total benign neoplasms				
15-Month interim evaluation	1	8	4	7
2-Year study	26	62	57	82
Total animals with malignant neoplasms				
15-Month interim evaluation		1	4	4
2-Year study	15	43	52	54
Total malignant neoplasms				
15-Month interim evaluation		1	5	4
2-Year study	18	58	60	56
Total animals with secondary neoplasms[d]				
15-Month interim evaluation			1	2
2-Year study	2	23	37	35
Total secondary neoplasms				
15-Month interim evaluation			1	3
2-Year study	9	99	129	99

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms
[d] Secondary neoplasms: metastatic neoplasms or neoplasms invasive to an adjacent organ

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control

Number of Days on Study	016	458	458	486	495	533	592	615	655	682	729	729	729	729	729	729	729	729	729	729	729	730	730	730	730
Carcass ID Number	0011	0121	0361	0551	0501	0311	0441	0111	0101	0191	0021	0031	0041	0061	0071	0081	0131	0151	0161	0251	0371	0601	0141	0181	0201	0211
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	+	+	A	+	A	M	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	A	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma						X		X																		
Hepatocellular carcinoma							X																		X	
Hepatocellular adenoma				X			X		X	X									X						X	
Hepatocellular adenoma, multiple																										
Histiocytic sarcoma					X																					
Mesentery					+	+				+																
Hemangiosarcoma, metastatic, liver						X																				
Histiocytic sarcoma, metastatic, liver					X																					
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver					X																					
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous				X																X						
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue															+											
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver					X																					

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	
Carcass ID Number	02211	02311	02411	02811	02911	03011	03411	03511	03811	03911	04011	04111	04211	04311	04511	04611	04711	04811	05111	05211	05311	05411	05511	05611	05811	05911	**Total Tissues/ Tumors**
Alimentary System																												
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																			X								1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hemangiosarcoma																						X					3
Hepatocellular carcinoma							X				X																4
Hepatocellular adenoma		X										X											X				9
Hepatocellular adenoma, multiple					X									X													2
Histiocytic sarcoma																											1
Mesentery											+																4
Hemangiosarcoma, metastatic, liver																											1
Histiocytic sarcoma, metastatic, liver																											1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Histiocytic sarcoma, metastatic, liver																											1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Papilloma squamous																X											3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Tongue																			+								2
Cardiovascular System																												
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Histiocytic sarcoma, metastatic, liver																											1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	0 1 6	4 5 8	4 5 8	4 8 6	4 9 5	5 3 3	5 9 2	6 1 5	6 5 5	6 8 2	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 0 1 1	0 1 2 1	0 3 6 1	0 5 5 1	0 5 0 1	0 3 1 1	0 4 4 1	0 1 1 1	0 1 0 1	0 1 9 1	0 0 2 1	0 0 3 1	0 0 4 1	0 0 6 1	0 0 7 1	0 0 8 1	0 1 3 1	0 1 5 1	0 1 6 1	0 2 5 1	0 3 7 1	0 6 0 1	0 1 4 1	0 1 8 1	0 2 0 1	0 2 1 1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	M	+	M	+	+	M	+	+	M	M	+	M	+	M	+	+	M	+	M	+	+	+	+	+	+	M
Pituitary gland	+	+	+	I	+	+	+	+	+	+	+	M	+	M	+	+	+	+	M	M	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																										
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver					X																					
Preputial gland			+	+			+	+	+		+	+	+	+			+	+	+	+		+		+		
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma								X																		
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, liver					X																					
Lymph node, mesenteric	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Histiocytic sarcoma, metastatic, liver					X																					
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma													X													
Hemangiosarcoma								X					X													
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prepuce, papilloma squamous													X													
Subcutaneous tissue, hemangiosarcoma								X																		

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	
Carcass ID Number	02211	02311	02411	02811	02911	03011	03411	03511	03811	03911	04011	04411	04211	04311	04511	04611	04711	04811	05111	05211	05311	05411	05511	05611	05811	05911				**Total Tissues/ Tumors**
Endocrine System																														
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+				51
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Parathyroid gland	M	+	+	+	+	+	+	+	M	M	M	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+				36
Pituitary gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				46
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				50
Follicular cell, adenoma																							X							1
General Body System																														
None																														
Genital System																														
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Histiocytic sarcoma, metastatic, liver																														1
Preputial gland	+					+	+	+		+	+		+		+	+	+		+	+	+	+	+	+		+				32
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Hematopoietic System																														
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Hemangiosarcoma																														1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+				50
Histiocytic sarcoma, metastatic, liver																														1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+				48
Histiocytic sarcoma, metastatic, liver																														1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Hemangioma																														1
Hemangiosarcoma																														2
Thymus	M	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+				47
Integumentary System																														
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M				
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Prepuce, papilloma squamous																														1
Subcutaneous tissue, hemangiosarcoma																														1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	0 1 6	4 5 8	4 5 8	4 8 6	4 9 5	5 3 3	5 9 2	6 1 5	6 5 5	6 8 2	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0
Carcass ID Number	0 0 1 1	0 1 2 1	0 3 6 1	0 0 5 1	0 5 0 1	0 3 1 1	0 4 4 1	0 1 1 1	0 1 1 1	0 1 0 1	0 1 9 1	0 0 2 1	0 0 3 1	0 0 4 1	0 0 6 1	0 0 7 1	0 0 8 1	0 1 3 1	0 1 5 1	0 1 6 1	0 2 5 1	0 3 7 1	0 6 0 1	0 1 4 1	0 1 8 1	0 2 0 1	0 2 1 1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle										+																
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal cord																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma		X									X		X													
Alveolar/bronchiolar adenoma, multiple																										
Alveolar/bronchiolar carcinoma																										
Hemangiosarcoma, metastatic, liver						X																				
Histiocytic sarcoma, metastatic, liver					X																					
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Eye																										
Harderian gland																										
Adenoma																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma					X																					
Lymphoma malignant lymphocytic										X																
Lymphoma malignant undifferentiated cell type																								X		

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	730	
Carcass ID Number	02211	02311	02411	02811	02911	03011	03411	03511	03811	03911	04011	04411	04211	04311	04511	04611	04711	04811	05111	05211	05311	05411	05511	05611	05811	05911				**Total Tissues/ Tumors**
Musculoskeletal System																														
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Skeletal muscle																														1
Nervous System																														
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Spinal cord																										+				1
Respiratory System																														
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Alveolar/bronchiolar adenoma					X						X														X					6
Alveolar/bronchiolar adenoma, multiple																			X											1
Alveolar/bronchiolar carcinoma															X															1
Hemangiosarcoma, metastatic, liver																														1
Histiocytic sarcoma, metastatic, liver																														1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Special Senses System																														
Eye																+							+							2
Harderian gland																							+							1
Adenoma																							X							1
Urinary System																														
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Systemic Lesions																														
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				52
Histiocytic sarcoma																														1
Lymphoma malignant lymphocytic																														1
Lymphoma malignant undifferentiated cell type				X					X																	X				4

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg

Number of Days on Study	400	424	451	458	520	520	535	541	541	561	561	571	577	581	583	585	590	620	636	639	639	641	645	652	660
Carcass ID Number	09111	09611	12001	10331	11011	11151	06991	06661	08111	08331	08881	10811	09001	09991	08551	08991	11411	11131	09551	09921	10111	07711	07331	07811	09711
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	+	+	+	M	A	+	+	+	+	+	+	M	+	+	+	+	+	+	A	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	A	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoid tissue, histiocytic sarcoma																		X							
Intestine small, jejunum	+	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma									X																
Hepatocellular carcinoma													X												X
Hepatocellular carcinoma, multiple														X											
Hepatocellular adenoma						X				X	X		X					X							
Hepatocellular adenoma, multiple														X							X				
Histiocytic sarcoma																		X							
Squamous cell carcinoma, metastatic, stomach						X			X		X					X	X			X				X	X
Mesentery		+				+		+			+					+	+			+		+		+	+
Squamous cell carcinoma, metastatic, stomach		X				X		X			X					X	X			X		X		X	X
Pancreas	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																		X							
Squamous cell carcinoma, metastatic, stomach								X			X					X			X	X		X		X	
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous				X	X		X						X		X	X									
Papilloma squamous, multiple																		X					X		X
Squamous cell carcinoma		X	X		X		X	X	X	X	X	X			X	X			X	X	X	X		X	
Squamous cell carcinoma, multiple						X							X	X			X								X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																									
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																									X

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	677	678	678	680	688	690	707	710	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	07911	07411	10511	08001	08671	10411	06811	06111	06211	06311	06511	07211	07511	07611	08411	08611	08711	09411	10211	10611	10911	11111	11211	11611	11711	11811	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymphoid tissue, histiocytic sarcoma																											1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hemangioma																											1
Hepatocellular carcinoma	X		X	X				X										X								X	8
Hepatocellular carcinoma, multiple																						X			X		3
Hepatocellular adenoma					X							X		X		X						X			X		11
Hepatocellular adenoma, multiple		X									X							X		X				X			7
Histiocytic sarcoma																											1
Squamous cell carcinoma, metastatic, stomach		X			X	X						X														X	13
Mesentery				+	+		+						+				+										15
Squamous cell carcinoma, metastatic, stomach				X	X		X																				13
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																											1
Squamous cell carcinoma, metastatic, stomach		X		X	X	X	X																				12
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Papilloma squamous	X	X									X				X				X				X	X			13
Papilloma squamous, multiple						X	X	X	X				X			X	X	X		X	X	X			X		15
Squamous cell carcinoma		X		X	X	X	X	X					X		X	X	X										26
Squamous cell carcinoma, multiple			X							X		X		X				X	X			X	X			X	14
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Tongue																									+		1
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Squamous cell carcinoma, metastatic, stomach																											1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	400	424	451	458	520	520	535	541	541	561	561	571	577	581	583	585	590	620	636	639	639	641	645	652	660
Carcass ID Number	09111	09611	20101	03101	10101	15101	06901	06601	08101	08301	08801	08101	09001	09901	08501	08901	11401	11301	09501	09201	10101	07701	07301	07801	09701
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																		X							
Squamous cell carcinoma, metastatic, stomach																						X			
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	+	+	M	+	+	M	+	M	+	M	M	+	+	+	M	+	+	+	+	M	M
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	A	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																									
General Body System																									
Tissue NOS		+																							
Squamous cell carcinoma, metastatic, stomach		X																							
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																X			X	X		X			
Preputial gland		+		+	+	+	+	+	+		+	+			+		+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach		X						X							X				X						
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																		X							
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Iliac, squamous cell carcinoma, metastatic, stomach																									
Mediastinal, histiocytic sarcoma																		X							
Mediastinal, squamous cell carcinoma, metastatic, stomach								X								X			X	X		X		X	X
Pancreatic, squamous cell carcinoma, metastatic, stomach																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	677	678	678	680	688	690	707	710	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	07911	07411	10511	08001	08671	10411	06811	06111	06211	06311	06511	07211	07511	07611	07841	08611	08711	09411	10211	10611	10911	11111	11211	11611	11711	11811		**Total Tissues/ Tumors**
Endocrine System																												
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Histiocytic sarcoma																												1
Squamous cell carcinoma, metastatic, stomach		X																										2
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Parathyroid gland	+	M	+	M	+	+	+	+	+	M	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+		37
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Follicular cell, adenoma										X																		1
General Body System																												
Tissue NOS																												1
Squamous cell carcinoma, metastatic, stomach																												1
Genital System																												
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Squamous cell carcinoma, metastatic, stomach				X			X																					6
Preputial gland		+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+		41
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Squamous cell carcinoma, metastatic, stomach		X					X																					6
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Hematopoietic System																												
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Histiocytic sarcoma																												1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Iliac, squamous cell carcinoma, metastatic, stomach				X																								1
Mediastinal, histiocytic sarcoma																												1
Mediastinal, squamous cell carcinoma, metastatic, stomach							X																					8
Pancreatic, squamous cell carcinoma, metastatic, stomach												X																1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	400	424	451	458	520	520	535	541	541	561	561	571	577	581	583	585	590	620	636	639	639	641	645	652	660
Carcass ID Number	09111	09611	12011	10331	11011	11151	06991	06661	08111	08331	08881	08101	09011	09911	08551	08911	11411	11311	09551	09921	10111	07711	07731	07811	09711
Hematopoietic System (continued)																									
Lymph node, mandibular	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Histiocytic sarcoma																		X							
Lymph node, mesenteric	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+
Histiocytic sarcoma																		X							
Squamous cell carcinoma, metastatic, stomach								X			X									X					
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Histiocytic sarcoma																		X							
Squamous cell carcinoma, metastatic, stomach											X								X						
Thymus	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	M	M	+	+	+	M
Squamous cell carcinoma, metastatic, stomach																			X			X		X	
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, sarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma							X																		
Skeletal muscle		+				+		+			+				+	+	+			+		+		+	+
Squamous cell carcinoma, metastatic, stomach		X				X		X			X				X	X	X					X		X	X
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma		X							X		X						X								
Alveolar/bronchiolar adenoma, multiple																			X						
Hepatocellular carcinoma, metastatic, liver													X												X
Histiocytic sarcoma																		X							
Squamous cell carcinoma, metastatic, stomach															X		X		X						X
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	677	678	678	680	688	690	707	710	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	07911	07411	10511	08011	00671	10411	06811	06611	06211	06311	06511	07211	07511	07611	08411	08611	08711	09411	10211	10611	10911	11111	11211	11611	11711	11811		**Total Tissues/ Tumors**
Hematopoietic System (continued)																												
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Histiocytic sarcoma																												1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Histiocytic sarcoma																												1
Squamous cell carcinoma, metastatic, stomach		X		X		X																						6
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Hemangioma	X																											1
Histiocytic sarcoma																												1
Squamous cell carcinoma, metastatic, stomach												X																3
Thymus	A	M	+	+	+	M	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+		40
Squamous cell carcinoma, metastatic, stomach																												3
Integumentary System																												
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M		
Skin	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Subcutaneous tissue, sarcoma																						X						1
Musculoskeletal System																												
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Osteosarcoma																												1
Skeletal muscle			+				+																					13
Squamous cell carcinoma, metastatic, stomach			X				X																					12
Nervous System																												
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Respiratory System																												
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Alveolar/bronchiolar adenoma	X														X			X				X				X		9
Alveolar/bronchiolar adenoma, multiple		X																										2
Hepatocellular carcinoma, metastatic, liver																									X			3
Histiocytic sarcoma																												1
Squamous cell carcinoma, metastatic, stomach				X			X																					6
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	400	424	451	458	520	520	535	541	541	561	561	571	577	581	583	585	590	620	636	639	639	641	645	652	660
Carcass ID Number	09111	09611	20101	03101	10101	11511	06991	06611	08111	08331	08881	08101	09091	09991	08551	08991	11411	11311	09551	09921	10111	07711	07331	07811	09711
Special Senses System																										
Ear																		+								
Eye																					+					
Harderian gland															+						+		+			
Adenoma																					X		X			
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Squamous cell carcinoma, metastatic, stomach											X														X	
Urinary bladder	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma																		X								
Lymphoma malignant histiocytic																										
Lymphoma malignant undifferentiated cell type																									X	

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	677	678	688	680	688	690	707	710	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	07911	07411	10511	08011	08611	10741	06811	06611	06211	06311	06511	07211	07511	07611	07711	08411	08811	08611	08711	09411	10211	10611	10911	11111	11211	11611	11711	11811	**Total Tissues/ Tumors**
Special Senses System																													
Ear																													1
Eye																													1
Harderian gland																													3
Adenoma																													2
Urinary System																													
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Squamous cell carcinoma, metastatic, stomach																													2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																													
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Histiocytic sarcoma																													1
Lymphoma malignant histiocytic													X																1
Lymphoma malignant undifferentiated cell type						X																			X				3

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg

Number of Days on Study	385	388	410	436	445	445	452	458	458	469	472	473	477	477	477	478	498	498	505	505	514	526	527	535	540	540	542	560
Carcass ID Number	12211	14511	17511	12411	12611	14911	17811	14211	17111	14711	15811	17911	12111	12311	16811	15411	13911	14011	16611	17311	15011	12911	14611	13411	12711	16711	16511	16011
Alimentary System																												
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																						X						
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoid tissue, histiocytic sarcoma																										X		
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma													X															
Hepatocellular adenoma			X	X								X	X						X	X	X							
Hepatocellular adenoma, multiple																X								X				
Histiocytic sarcoma																										X		
Squamous cell carcinoma, metastatic, stomach	X	X	X		X					X					X	X	X		X	X	X	X	X		X		X	X
Mesentery			+		+						+				+		+	+				+				+	+	+
Histiocytic sarcoma																										X		
Sarcoma, metastatic, skeletal muscle																												
Squamous cell carcinoma, metastatic, stomach			X		X						X				X		X	X				X					X	X
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Squamous cell carcinoma, metastatic, stomach			X							X					X	X	X	X				X					X	X
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous					X		X					X		X				X					X		X			X
Papilloma squamous, multiple						X		X	X																			
Squamous cell carcinoma	X	X	X		X	X							X					X						X	X			
Squamous cell carcinoma, multiple				X						X	X	X		X	X	X		X	X	X	X	X	X				X	X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																						+						

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	561	561	561	563	576	577	582	582	590	591	592	597	610	611	616	623	623	623	623	623	623	623	623	623	623	623	
Carcass ID Number	13001	13071	16091	13331	17461	14111	12881	14441	15311	13811	14311	18001	16111	15211	15511	13111	13211	13515	13611	15611	15911	16211	16311	17011	17211	17411	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	51
Squamous cell carcinoma, metastatic, stomach					X																						2
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Lymphoid tissue, histiocytic sarcoma																											1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Hepatocellular carcinoma										X					X						X			X			5
Hepatocellular adenoma					X	X			X						X	X							X				13
Hepatocellular adenoma, multiple							X						X	X				X		X					X		8
Histiocytic sarcoma																											1
Squamous cell carcinoma, metastatic, stomach	X		X	X	X		X			X	X	X		X	X	X	X	X		X						X	31
Mesentery	+				+				+		+		+	+			+										17
Histiocytic sarcoma																											1
Sarcoma, metastatic, skeletal muscle									X																		1
Squamous cell carcinoma, metastatic, stomach	X				X						X			X			X										14
Pancreas	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Histiocytic sarcoma																											1
Squamous cell carcinoma, metastatic, stomach					X		X	X			X			X			X								X		16
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Histiocytic sarcoma																											1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Papilloma squamous							X							X		X	X		X							X	14
Papilloma squamous, multiple						X															X	X	X	X			8
Squamous cell carcinoma		X		X					X	X	X	X						X	X								17
Squamous cell carcinoma, multiple	X		X		X	X	X	X					X	X	X	X	X			X	X	X	X	X	X	X	33
Stomach, glandular	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Tongue																											1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	385	388	410	436	445	445	452	458	458	469	472	473	477	477	477	478	498	498	505	505	514	526	527	535	540	540	542	560
Carcass ID Number	12211	14511	17511	12411	12611	14911	17811	14211	17111	14711	15811	17911	12111	12311	16811	15411	13911	14011	16611	17311	15011	12911	14611	13411	12711	16711	16511	16011
Cardiovascular System																												
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Endocrine System																												
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	M
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	M	+	+	+	+
Pituitary gland	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Follicular cell, carcinoma							X																					
General Body System																												
None																												
Genital System																												
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																						X						X
Preputial gland	+	M	+						+			+	M	+	+	+	+	+	+	+	+	+	+	+	+			+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																												X
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach			X													X	X	X								X	X	
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Hematopoietic System																												
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Axillary, histiocytic sarcoma																										X		
Mediastinal, histiocytic sarcoma																										X		
Mediastinal, squamous cell carcinoma, metastatic, stomach			X							X																		

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	561	561	561	563	576	577	582	582	590	591	592	597	610	611	616	623	623	623	623	623	623	623	623	623	623	623	623	
Carcass ID Number	13001	13071	16091	13331	17611	14111	12821	14441	15311	13811	14311	18011	16111	15211	15511	13111	13321	13511	13611	15611	15911	16211	16311	17011	17211	17411		**Total Tissues/ Tumors**
Cardiovascular System																												
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Histiocytic sarcoma																												1
Endocrine System																												
Adrenal gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Adrenal gland, cortex	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Adrenal gland, medulla	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+		49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+		53
Parathyroid gland	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	M	M	+	+	+	+	+	+	+	M	+		44
Pituitary gland	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+		50
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Histiocytic sarcoma																												1
Follicular cell, carcinoma																												1
General Body System																												
None																												
Genital System																												
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Squamous cell carcinoma, metastatic, stomach					X							X					X											5
Preputial gland	+	+	+	+	+	+	+	+	+	+			+	+		+	+	+	+	+			+	+	+	+		39
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Squamous cell carcinoma, metastatic, stomach					X																							2
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Squamous cell carcinoma, metastatic, stomach											X	X					X											9
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		53
Hematopoietic System																												
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Histiocytic sarcoma																												1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Axillary, histiocytic sarcoma																												1
Mediastinal, histiocytic sarcoma																												1
Mediastinal, squamous cell carcinoma, metastatic, stomach					X												X											4

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	385	388	410	436	445	445	452	458	458	469	472	473	477	477	477	478	498	498	505	505	514	526	527	535	540	540	542	560
Carcass ID Number	12211	14511	17511	12411	12611	14911	17811	14211	17111	14711	15811	17911	12111	12311	16811	15411	13911	14011	16611	17311	15011	12911	14611	13411	12711	16711	16511	16011
Hematopoietic System (continued)																												
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Lymph node, mesenteric	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Squamous cell carcinoma, metastatic, stomach										X					X					X	X	X					X
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										X		
Sarcoma, metastatic, skeletal muscle																												
Squamous cell carcinoma, metastatic, stomach													X				X						X					X
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	M
Histiocytic sarcoma																										X		
Integumentary System																												
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangioma																												
Musculoskeletal System																												
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle			+								+				+		+	+				+				+	+	
Histiocytic sarcoma																										X		
Sarcoma																												
Squamous cell carcinoma, metastatic, stomach			X								X						X	X				X					X	
Nervous System																												
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																												
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma		X																		X								
Alveolar/bronchiolar carcinoma																												
Hepatocellular carcinoma, metastatic, liver																												
Histiocytic sarcoma																										X		
Squamous cell carcinoma, metastatic, stomach					X					X						X	X					X			X			X

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	561	561	561	563	576	577	582	582	590	591	592	597	610	611	616	623	623	623	623	623	623	623	623	623	623	623	
Carcass ID Number	13001	13071	13691	13331	17461	14111	12811	14441	15331	13811	14431	18001	16111	15211	15511	13111	13321	13351	13611	15611	15591	16211	16311	17011	17211	17411	**Total Tissues/ Tumors**
Hematopoietic System (continued)																											
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	51
Histiocytic sarcoma																											1
Lymph node, mesenteric	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Histiocytic sarcoma																											1
Squamous cell carcinoma, metastatic, stomach	X				X					X	X	X					X										12
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Histiocytic sarcoma																											1
Sarcoma, metastatic, skeletal muscle									X																		1
Squamous cell carcinoma, metastatic, stomach											X	X			X					X							8
Thymus	+	+	+	M	+	+	+	M	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	47
Histiocytic sarcoma																											1
Integumentary System																											
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Subcutaneous tissue, hemangioma																									X		1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Skeletal muscle					+			+	+		+						+	+									14
Histiocytic sarcoma																											1
Sarcoma									X																		1
Squamous cell carcinoma, metastatic, stomach					X			X			X						X	X									11
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Alveolar/bronchiolar adenoma											X																3
Alveolar/bronchiolar carcinoma									X									X									2
Hepatocellular carcinoma, metastatic, liver															X												1
Histiocytic sarcoma																											1
Squamous cell carcinoma, metastatic, stomach										X	X				X		X	X									12

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	385	388	410	436	445	445	452	458	458	469	472	473	477	477	477	478	498	498	505	505	514	526	527	535	540	540	542	560	
Carcass ID Number	12211	14511	17511	12411	12261	14991	17811	14211	17111	14711	15811	17911	12111	12311	16811	15411	13911	14011	16611	17311	15011	12991	14611	13411	12711	16711	16511	16011	
Respiratory System (continued)																													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma																										X			
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Special Senses System																													
Ear				+																									
Eye										+										+									
Harderian gland														+						+				+	+				
Adenoma																				X				X	X				
Urinary System																													
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma																										X			
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																													
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma																										X			

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	561	561	561	563	576	577	582	582	590	591	592	597	610	611	616	623	623	623	623	623	623	623	623	623	623	623	623	
Carcass ID Number	13001	13071	16091	13331	17611	14111	12881	14411	15311	13811	14311	18011	16111	15211	15511	13112	13235	13611	15611	15591	16221	16311	17011	17721	17741	**Total Tissues/ Tumors**
Respiratory System (continued)																												
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Histiocytic sarcoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Special Senses System																												
Ear																										1
Eye																										2
Harderian gland			+					+		+	+		+			+					+					11
Adenoma			X					X		X	X		X			X					X					10
Urinary System																												
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Histiocytic sarcoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Systemic Lesions																												
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Histiocytic sarcoma																										1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg

Number of Days on Study	322	350	366	368	379	388	389	392	393	406	413	417	423	428	429	435	437	437	442	444	445	452	452	455	458	461	465	470	471
Carcass ID Number	22201	21881	23331	19001	23991	20211	22411	22711	23611	20911	18111	23511	23001	21411	20711	18511	19811	20311	21111	18711	21611	21211	21511	22611	20611	20811	22001	20011	19211
Alimentary System																													
Esophagus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, stomach															X														
Squamous cell carcinoma, metastatic, stomach																													
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																													
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																													
Squamous cell carcinoma, metastatic, stomach																												X	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma							X																			X			
Hepatocellular adenoma	X	X											X										X						
Hepatocellular adenoma, multiple																					X							X	
Sarcoma, metastatic, stomach															X														
Squamous cell carcinoma, metastatic, stomach			X		X				X			X	X	X		X		X	X	X	X	X		X				X	X
Mesentery			+							+		+	+			+			+			+		+			+	+	
Squamous cell carcinoma, metastatic, stomach			X									X	X			X			X			X		X			X	X	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, stomach															X														
Squamous cell carcinoma, metastatic, stomach						X							X			X			X									X	X
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous	X		X				X			X				X						X	X	X		X	X	X	X	X	
Papilloma squamous, multiple																	X	X											
Sarcoma															X														
Squamous cell carcinoma		X	X	X	X	X			X	X	X	X	X	X		X	X	X	X	X	X	X	X	X		X	X		
Squamous cell carcinoma, multiple								X																	X			X	X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																												+	
Papilloma squamous																												X	

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	471	473	478	488	490	490	497	499	504	507	514	520	532	534	539	541	542	553	554	554	554	554	554	554	554	554	554	
Carcass ID Number	22251	22311	18311	23411	19111	23711	21011	21911	19611	20111	24011	18811	18911	22911	21311	21171	18611	19711	18211	18411	19411	19911	20411	20511	22811	23211	23811	**Total Tissues/ Tumors**
Alimentary System																												
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Sarcoma, metastatic, stomach																												1
Squamous cell carcinoma, metastatic, stomach															X													1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	53
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Squamous cell carcinoma, metastatic, stomach															X													1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	55
Adenoma																										X		1
Squamous cell carcinoma, metastatic, stomach															X													2
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	56
Hepatocellular carcinoma																							X					3
Hepatocellular adenoma					X																			X				6
Hepatocellular adenoma, multiple	X	X		X		X			X		X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	23
Sarcoma, metastatic, stomach																												1
Squamous cell carcinoma, metastatic, stomach				X		X	X	X		X				X	X		X	X				X		X	X			27
Mesentery					+	+		+				+			+									+				16
Squamous cell carcinoma, metastatic, stomach					X	X		X				X			X									X				15
Pancreas	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Sarcoma, metastatic, stomach																												1
Squamous cell carcinoma, metastatic, stomach				X		X									X			X						X				11
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	56
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	56
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	56
Papilloma squamous		X					X			X		X		X	X	X	X					X						22
Papilloma squamous, multiple			X					X			X		X						X	X	X		X				X	11
Sarcoma																												1
Squamous cell carcinoma	X		X			X			X					X		X		X		X				X		X	32
Squamous cell carcinoma, multiple		X		X	X		X	X		X	X	X	X		X		X					X	X	X		X		19
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	56
Tongue								+											+									3
Papilloma squamous																			X									2

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	322	350	366	368	379	388	389	392	393	406	413	417	423	428	429	435	437	437	442	444	445	452	452	455	458	461	465	470	471
Carcass ID Number	22021	21881	23331	19001	23091	20221	22441	22771	23631	20991	18111	23531	23001	21041	20771	18511	19881	20311	21111	18771	21161	21221	21151	22261	20661	20881	20201	20091	19211
Cardiovascular System																													
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																													
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	M	+	+	+	+	+	M	+	+	M	M	+	+	+	+	M	+	+	+	+	+	M	+	+	+	M	+
Pituitary gland	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																													
None																													
Genital System																													
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																													
Preputial gland			+		+	+	+	+	+	+	+		+	+	+	+		+					+			+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																													
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																													
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																													
Blood																													
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bronchial, squamous cell carcinoma, metastatic, stomach																													
Mediastinal, sarcoma, metastatic, stomach															X														
Mediastinal, squamous cell carcinoma, metastatic, stomach																			X										

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	471	473	478	488	490	490	497	499	504	507	514	520	532	534	539	541	542	553	554	554	554	554	554	554	554	554	554	554	
Carcass ID Number	22251	22311	18331	23411	19111	23711	21011	21991	19611	20111	24011	18811	18911	22911	21311	21711	18611	19711	18211	18411	19411	19911	20411	20511	22811	23211	23811		**Total Tissues/ Tumors**
Cardiovascular System																													
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Endocrine System																													
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+		54
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+		54
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+		54
Islets, pancreatic	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		55
Parathyroid gland	+	+	M	M	M	M	+	+	+	+	+	M	M	+	+	M	M	+	+	+	M	M	+	+	+	+	+		39
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		54
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
General Body System																													
None																													
Genital System																													
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Squamous cell carcinoma, metastatic, stomach																		X						X					2
Preputial gland	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				42
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+		53
Squamous cell carcinoma, metastatic, stomach																								X		X			2
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Squamous cell carcinoma, metastatic, stomach																								X					1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Hematopoietic System																													
Blood				+																									1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Bronchial, squamous cell carcinoma, metastatic, stomach												X																	1
Mediastinal, sarcoma, metastatic, stomach																													1
Mediastinal, squamous cell carcinoma, metastatic, stomach															X			X											3

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	322	350	366	368	379	388	389	392	393	406	413	417	423	428	429	435	437	437	442	444	445	452	452	455	458	461	465	470	471
Carcass ID Number	22201	21881	23331	19001	23991	20201	22441	22771	23631	20901	18111	23511	23001	21411	20771	18511	19811	20311	21111	18771	21611	21211	21151	22661	20661	20881	22001	20101	19021
Hematopoietic System (continued)																													
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach						X								X														X	
Mediastinal, squamous cell carcinoma, metastatic, stomach													X																
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach					X					X		X																	X
Thymus	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M
Squamous cell carcinoma, metastatic, stomach																													
Integumentary System																													
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																													
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle	+											+	+		+						+							+	
Sarcoma, metastatic, stomach															X														
Squamous cell carcinoma, metastatic, stomach												X	X								X							X	
Nervous System																													
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																													
Respiratory System																													
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																X	X												
Alveolar/bronchiolar adenoma, multiple																						X							
Hepatocellular carcinoma, metastatic, liver																										X			
Sarcoma, metastatic, stomach															X														
Squamous cell carcinoma, metastatic, stomach										X						X		X											
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	471	473	478	488	490	490	497	499	504	507	514	520	532	534	539	541	542	553	554	554	554	554	554	554	554	554	554	554	
Carcass ID Number	22251	22311	18311	23411	19111	23711	21011	21911	19611	20111	24011	18811	18911	22911	21311	21711	18611	19711	18211	18411	19411	19911	20411	20511	22811	23211	23811		**Total Tissues/ Tumors**
Hematopoietic System (continued)																													
Lymph node, mandibular	+	+	+	+	+	+	M	+	+	+	+	+	M	+	M	+	+	M	+	+	+	M	+	+	+	M	+		50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+		54
Squamous cell carcinoma, metastatic, stomach																		X						X					5
Mediastinal, squamous cell carcinoma, metastatic, stomach																													1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Squamous cell carcinoma, metastatic, stomach				X																									5
Thymus	+	+	+	+	+	+	M	M	+	+	+	+	+	+	M	M	+	M	+	+	+	+	+	M	+	+	+		46
Squamous cell carcinoma, metastatic, stomach						X																							1
Integumentary System																													
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M		
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		55
Musculoskeletal System																													
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Skeletal muscle								+										+						+					9
Sarcoma, metastatic, stomach																													1
Squamous cell carcinoma, metastatic, stomach								X										X						X					7
Nervous System																													
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Squamous cell carcinoma, metastatic, stomach																										X			1
Respiratory System																													
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Alveolar/bronchiolar adenoma						X											X						X						5
Alveolar/bronchiolar adenoma, multiple																													1
Hepatocellular carcinoma, metastatic, liver																													1
Sarcoma, metastatic, stomach																													1
Squamous cell carcinoma, metastatic, stomach				X				X										X											6
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	322	350	366	368	379	388	389	392	393	406	413	417	423	428	429	435	437	437	442	444	445	452	452	455	458	461	465	470	471
Carcass ID Number	221	181	331	901	391	021	241	271	361	091	811	351	301	141	071	851	981	031	111	871	161	121	151	261	061	081	201	001	921
Special Senses System																													
Eye		+																								+			+
Harderian gland																+						+	+		+	+	+		+
Adenoma																						X	X		X	X	X		X
Urinary System																													
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																													
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic	X																												

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	471	473	478	488	490	490	497	499	504	507	514	520	532	534	539	541	542	553	554	554	554	554	554	554	554	554	554	554	
Carcass ID Number	22251	22311	18311	23411	19111	23711	21011	21911	19611	20111	24011	18811	18911	22911	21311	21711	18611	19711	18211	18411	19411	19911	20411	20511	22811	23211	23811		**Total Tissues/ Tumors**
Special Senses System																													
Eye																													3
Harderian gland									+				+		+			+				+			+				13
Adenoma									X						X			X				X			X				11
Urinary System																													
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Systemic Lesions																													
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		56
Lymphoma malignant lymphocytic																													1

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Harderian Gland: Adenoma				
Overall rate[a]	1/60 (2%)	2/59 (3%)	10/60 (17%)	11/60 (18%)
Adjusted rate[b]	2.4%	6.5%	44.3%	49.2%
15-Month interim evaluation[c]	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
Terminal rate[d]	1/42 (2%)	0/18 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	729 (T)	639	505	452
Life table test[e]	P<0.001	P=0.323	P<0.001	P<0.001
Logistic regression test[e]	P=0.001	P=0.449	P=0.002	P=0.008
Cochran-Armitage test[e]	P=0.001			
Fisher exact test[e]		P=0.494	P=0.004	P=0.002
Liver: Hemangiosarcoma				
Overall rate	3/60 (5%)	0/59 (0%)	0/60 (0%)	0/60 (0%)
Adjusted rate	6.6%	0.0%	0.0%	0.0%
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
Terminal rate	1/42 (2%)	0/18 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	533	-[f]	-	-
Life table test	P=0.515N	P=0.196N	P=0.433N	P=0.740N
Logistic regression test	P=0.175N	P=0.118N	P=0.122N	P=0.162N
Cochran-Armitage test	P=0.134N			
Fisher exact test		P=0.125N	P=0.122N	P=0.122N
Liver: Hemangioma or Hemangiosarcoma				
Overall rate	3/60 (5%)	1/59 (2%)	0/60 (0%)	0/60 (0%)
Adjusted rate	6.6%	2.3%	0.0%	0.0%
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
Terminal rate	1/42 (2%)	0/18 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	533	541	-	-
Life table test	P=0.420N	P=0.416N	P=0.433N	P=0.740N
Logistic regression test	P=0.095N	P=0.293N	P=0.122N	P=0.162N
Cochran-Armitage test	P=0.097N			
Fisher exact test		P=0.316N	P=0.122N	P=0.122N
Liver: Hepatocellular Adenoma				
Overall rate	12/60 (20%)	18/59 (31%)	21/60 (35%)	31/60 (52%)
Adjusted rate	25.1%	61.9%	72.2%	100.0%
15-Month interim evaluation	1/8 (13%)	0/8 (0%)	0/6 (0%)	2/4 (50%)
Terminal rate	7/42 (17%)	9/18 (50%)	0/0 (0%)	0/0 (0%)
First incidence (days)	457 (I)	520	410	322
Life table test	P<0.001	P=0.003	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.073	P=0.028	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.134	P=0.051	P<0.001
Liver: Hepatocellular Carcinoma				
Overall rate	4/60 (7%)	11/59 (19%)	6/60 (10%)	3/60 (5%)
Adjusted rate	9.2%	40.6%	32.4%	15.6%
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	1/6 (17%)	0/4 (0%)
Terminal rate	3/42 (7%)	4/18 (22%)	0/0 (0%)	0/0 (0%)
First incidence (days)	592	577	457 (I)	389
Life table test	P<0.001	P=0.002	P=0.001	P=0.031
Logistic regression test	P=0.533	P=0.015	P=0.194	P=0.666
Cochran-Armitage test	P=0.113N			
Fisher exact test		P=0.044	P=0.372	P=0.500N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	14/60 (23%)	24/59 (41%)	25/60 (42%)	33/60 (55%)
Adjusted rate	29.3%	72.8%	82.9%	100.0%
15-Month interim evaluation	1/8 (13%)	0/8 (0%)	1/6 (17%)	2/4 (50%)
Terminal rate	9/42 (21%)	10/18 (56%)	0/0 (0%)	0/0 (0%)
First incidence (days)	457 (I)	520	410	322
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.008	P=0.007	P<0.001
Cochran-Armitage test	P=0.001			
Fisher exact test		P=0.033	P=0.025	P<0.001
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	7/60 (12%)	12/59 (20%)	3/60 (5%)	9/60 (15%)
Adjusted rate	15.9%	37.7%	10.4%	34.0%
15-Month interim evaluation	0/8 (0%)	1/8 (13%)	0/6 (0%)	3/4 (75%)
Terminal rate	6/42 (14%)	4/18 (22%)	0/0 (0%)	0/0 (0%)
First incidence (days)	458	424	388	435
Life table test	P<0.001	P=0.013	P=0.196	P<0.001
Logistic regression test	P=0.354	P=0.127	P=0.315N	P=0.280
Cochran-Armitage test	P=0.555			
Fisher exact test		P=0.149	P=0.161N	P=0.395
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	8/60 (13%)	12/59 (20%)	5/60 (8%)	9/60 (15%)
Adjusted rate	18.2%	37.7%	23.1%	34.0%
15-Month interim evaluation	0/8 (0%)	1/8 (13%)	0/6 (0%)	3/4 (75%)
Terminal rate	7/42 (17%)	4/18 (22%)	0/0 (0%)	0/0 (0%)
First incidence (days)	458	424	388	435
Life table test	P<0.001	P=0.021	P=0.020	P<0.001
Logistic regression test	P=0.347	P=0.182	P=0.616N	P=0.300
Cochran-Armitage test	P=0.496N			
Fisher exact test		P=0.219	P=0.279N	P=0.500
Stomach (Forestomach): Squamous Cell Papilloma				
Overall rate	3/60 (5%)	35/59 (59%)	25/60 (42%)	35/60 (58%)
Adjusted rate	6.7%	88.0%	83.7%	90.0%
15-Month interim evaluation	0/8 (0%)	7/8 (88%)	3/6 (50%)	2/4 (50%)
Terminal rate	2/42 (5%)	14/18 (78%)	0/0 (0%)	0/0 (0%)
First incidence (days)	486	457 (I)	445	322
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Stomach (Forestomach): Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	41/59 (69%)	54/60 (90%)	55/60 (92%)
Adjusted rate	0.0%	86.6%	100.0%	96.5%
15-Month interim evaluation	0/8 (0%)	1/8 (13%)	4/6 (67%)	4/4 (100%)
Terminal rate	0/42 (0%)	12/18 (67%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	424	385	350
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Stomach (Forestomach): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	3/60 (5%)	57/59 (97%)	57/60 (95%)	59/60 (98%)
Adjusted rate	6.7%	100.0%	100.0%	100.0%
15-Month interim evaluation	0/8 (0%)	7/8 (88%)	4/6 (67%)	4/4 (100%)
Terminal rate	2/42 (5%)	18/18 (100%)	0/0 (0%)	0/0 (0%)
First incidence (days)	486	424	385	322
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
All Organs: Hemangiosarcoma				
Overall rate	4/60 (7%)	0/59 (0%)	0/60 (0%)	0/60 (0%)
Adjusted rate	8.9%	0.0%	0.0%	0.0%
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
Terminal rate	2/42 (5%)	0/18 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	533	-	-	-
Life table test	P=0.478N	P=0.142N	P=0.433N	P=0.740N
Logistic regression test	P=0.153N	P=0.068N	P=0.096N	P=0.153N
Cochran-Armitage test	P=0.077N			
Fisher exact test		P=0.061N	P=0.059N	P=0.059N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rate	4/60 (7%)	2/59 (3%)	1/60 (2%)	0/60 (0%)
Adjusted rate	8.9%	6.0%	9.1%	0.0%
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
Terminal rate	2/42 (5%)	0/18 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	533	541	623	-
Life table test	P=0.674N	P=0.539N	P=0.659	P=0.740N
Logistic regression test	P=0.124N	P=0.345N	P=0.344N	P=0.153N
Cochran-Armitage test	P=0.052N			
Fisher exact test		P=0.348N	P=0.182N	P=0.059N
All Organs: Histiocytic Sarcoma and Malignant Lymphoma				
Overall rate	6/60 (10%)	5/59 (8%)	1/60 (2%)	1/60 (2%)
Adjusted rate	13.5%	20.9%	3.3%	1.7%
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
Terminal rate	4/42 (10%)	2/18 (11%)	0/0 (0%)	0/0 (0%)
First incidence (days)	495	620	540	322
Life table test	P=0.296	P=0.321	P=0.685	P=0.675
Logistic regression test	P=0.254N	P=0.614	P=0.211N	P=0.168N
Cochran-Armitage test	P=0.033N			
Fisher exact test		P=0.512N	P=0.057N	P=0.057N
All Organs: Malignant Lymphoma (Histiocytic, Lymphocytic, or Undifferentiated Cell Type)				
Overall rate	5/60 (8%)	4/59 (7%)	0/60 (0%)	1/60 (2%)
Adjusted rate	11.6%	18.5%	0.0%	1.7%
15-Month interim evaluation	0/8 (0%)	0/8 (0%)	0/6 (0%)	0/4 (0%)
Terminal rate	4/42 (10%)	2/18 (11%)	0/0 (0%)	0/0 (0%)
First incidence (days)	682	660	-	322
Life table test	P=0.155	P=0.318	-	P=0.503
Logistic regression test	P=0.670N	P=0.518	P=0.786N	P=0.517N
Cochran-Armitage test	P=0.062N			
Fisher exact test		P=0.511N	P=0.029N	P=0.103N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
All Organs: Benign Neoplasms				
Overall rate	20/60 (33%)	49/59 (83%)	46/60 (77%)	50/60 (83%)
Adjusted rate	41.2%	100.0%	100.0%	100.0%
15-Month interim evaluation	1/8 (13%)	7/8 (88%)	4/6 (67%)	3/4 (75%)
Terminal rate	14/42 (33%)	18/18 (100%)	0/0 (0%)	0/0 (0%)
First incidence (days)	457 (I)	424	388	322
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
All Organs: Malignant Neoplasms				
Overall rate	15/60 (25%)	44/59 (75%)	56/60 (93%)	58/60 (97%)
Adjusted rate	31.8%	89.6%	100.0%	96.7%
15-Month interim evaluation	0/8 (0%)	1/8 (13%)	4/6 (67%)	4/4 (100%)
Terminal rate	10/42 (24%)	13/18 (72%)	0/0 (0%)	0/0 (0%)
First incidence (days)	495	424	385	322
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
All Organs: Benign or Malignant Neoplasms				
Overall rate	30/60 (50%)	57/59 (97%)	59/60 (98%)	60/60 (100%)
Adjusted rate	58.7%	100.0%	100.0%	100.0%
15-Month interim evaluation	1/8 (13%)	7/8 (88%)	5/6 (83%)	4/4 (100%)
Terminal rate	21/42 (50%)	18/18 (100%)	0/0 (0%)	0/0 (0%)
First incidence (days)	457 (I)	424	385	322
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001

(T)Terminal sacrifice
(I)15-Month interim evaluation
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, epididymis, gallbladder, heart, kidney, larynx, liver, lung, nose, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] 15-Month interim evaluation began on day 457
[d] Observed incidence at terminal kill
[e] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by **N**.
[f] Not applicable; no neoplasms in animal group

TABLE C4a
Historical Incidence of Oral Cavity Neoplasms in Male B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls	
	Squamous Cell Papilloma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute		
2,4-Diaminophenol•2HCl	0/50	0/50
Tribromomethane	0/50	0/50
Phenylbutazone	0/50	0/50
Probenecid	0/50	0/50
Overall Historical Incidence		
Total	0/700	0/700

[a] Data as of 3 April 1991

TABLE C4b
Historical Incidence of Forestomach Neoplasms in Male B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Squamous Cell Papilloma	Squamous Cell Carcinoma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	2/50	0/50	2/50
Tribromomethane	0/50	0/50	0/50
Phenylbutazone	1/50	0/50	1/50
Probenecid	0/50	0/50	0/50
Overall Historical Incidence			
Total	19/700 (2.7%)	2/700 (0.3%)	21/700 (3.0%)
Standard deviation	3.7%	0.7%	3.9%
Range	0%-14%	0%-2%	0%-14%

[a] Data as of 3 April 1991

TABLE C4c
Historical Incidence of Liver Neoplasms in Male B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	11/50	5/50	15/50
Tribromomethane	11/50	7/50	16/50
Phenylbutazone	8/50	8/50	16/50
Probenecid	12/50	7/50	15/50
Overall Historical Incidence			
Total	162/699 (23.2%)	122/699 (17.5%)	261/699 (37.3%)
Standard deviation	11.7%	5.8%	11.6%
Range	4%-40%	10%-32%	14%-52%

[a] Data as of 3 April 1991

TABLE C4d
Historical Incidence of Harderian Gland Neoplasms in Male B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	1/50	1/50	2/50
Tribromomethane	2/50	0/50	2/50
Phenylbutazone	2/50	0/50	2/50
Probenecid	2/50	2/50	4/50
Overall Historical Incidence			
Total	40/700 (5.7%)	5/700 (0.7%)	44/700 (6.3%)
Standard deviation	4.4%	1.3%	4.2%
Range	0%-16%	0%-4%	0%-16%

[a] Data as of 3 April 1991

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	8	8	6	4
Early deaths				
Moribund	3	26	40	44
Natural deaths	7	7	4	3
Scheduled sacrifice			10	9
Survivors				
Terminal sacrifice	42	18		
Missexed		1		
Animals examined microscopically	60	59	60	60
15-Month Interim Evaluation				
Alimentary System				
Esophagus	(4)	(8)	(6)	(4)
Hyperplasia, basal cell				1 (25%)
Liver	(8)	(8)	(6)	(4)
Clear cell focus		1 (13%)		
Eosinophilic focus			1 (17%)	2 (50%)
Fatty change, diffuse		1 (13%)		
Necrosis	1 (13%)	1 (13%)	3 (50%)	
Stomach, forestomach	(8)	(8)	(6)	(4)
Hyperkeratosis		8 (100%)	6 (100%)	4 (100%)
Hyperplasia, basal cell			2 (33%)	2 (50%)
Hyperplasia, squamous		8 (100%)	5 (83%)	4 (100%)
Stomach, glandular	(8)	(7)	(6)	(4)
Hyperplasia			1 (17%)	1 (25%)
Cardiovascular System				
Heart	(8)	(8)	(6)	(4)
Embolus				1 (25%)
Endocrine System				
None				
General Body System				
None				
Genital System				
None				

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
15-Month Interim Evaluation (continued)				
Hematopoietic System				
Lymph node, mesenteric	(8)	(8)	(6)	(4)
Thrombus				1 (25%)
Spleen	(8)	(8)	(6)	(4)
Hematopoietic cell proliferation				2 (50%)
Integumentary System				
None				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Esophagus	(51)	(50)	(54)	(54)
Hyperkeratosis				2 (4%)
Gallbladder	(47)	(46)	(51)	(55)
Dilatation				1 (2%)
Hyperplasia				1 (2%)
Intestine large, cecum	(51)	(49)	(53)	(55)
Hyperplasia		1 (2%)		
Liver	(52)	(51)	(54)	(56)
Basophilic focus		7 (14%)	3 (6%)	5 (9%)
Clear cell focus			1 (2%)	
Cyst		1 (2%)		1 (2%)
Eosinophilic focus	2 (4%)	3 (6%)	8 (15%)	32 (57%)
Fatty change, focal	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Fibrosis				1 (2%)
Inflammation, acute			1 (2%)	
Mixed cell focus	2 (4%)	2 (4%)		
Necrosis	1 (2%)	2 (4%)	11 (20%)	8 (14%)

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Mesentery	(4)	(15)	(17)	(16)
Hemorrhage	1 (25%)			
Fat, mineralization			2 (12%)	
Fat, necrosis	1 (25%)	1 (7%)		
Pancreas	(52)	(50)	(53)	(55)
Acinus, hyperplasia			2 (4%)	1 (2%)
Stomach, forestomach	(52)	(51)	(54)	(56)
Hyperkeratosis	3 (6%)	27 (53%)	26 (48%)	40 (71%)
Hyperplasia, squamous	8 (15%)	29 (57%)	27 (50%)	34 (61%)
Inflammation, acute	1 (2%)			
Ulcer	5 (10%)	1 (2%)	1 (2%)	
Stomach, glandular	(52)	(51)	(53)	(56)
Hyperplasia		1 (2%)		
Inflammation, acute				1 (2%)
Mineralization		1 (2%)		
Necrosis				1 (2%)
Tongue	(2)	(1)	(1)	(3)
Mineralization	1 (50%)			
Cardiovascular System				
Heart	(52)	(51)	(54)	(56)
Mineralization		1 (2%)	2 (4%)	1 (2%)
Endocrine System				
Adrenal gland, cortex	(52)	(51)	(51)	(54)
Accessory adrenal cortical nodule				1 (2%)
Hypertrophy	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Islets, pancreatic	(52)	(50)	(53)	(55)
Hyperplasia			1 (2%)	
Thyroid gland	(50)	(51)	(54)	(56)
Follicular cell, hyperplasia	1 (2%)	2 (4%)		
General Body System				
None				
Genital System				
Preputial gland	(32)	(41)	(39)	(42)
Abscess			1 (3%)	
Dilatation	30 (94%)	39 (95%)	35 (90%)	28 (67%)
Prostate	(51)	(50)	(54)	(53)
Hyperplasia			2 (4%)	1 (2%)

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Hematopoietic System				
Lymph node	(52)	(51)	(54)	(56)
Bronchial, infiltration cellular, plasma cell			1 (2%)	
Bronchial, infiltration cellular, histiocyte			1 (2%)	
Iliac, infiltration cellular, plasma cell		1 (2%)		
Mediastinal, hematopoietic cell proliferation		2 (4%)	2 (4%)	1 (2%)
Mediastinal, infiltration cellular, plasma cell			2 (4%)	
Mediastinal, infiltration cellular, histiocyte		1 (2%)	2 (4%)	
Lymph node, mandibular	(50)	(49)	(51)	(50)
Infiltration cellular, plasma cell			1 (2%)	
Lymph node, mesenteric	(48)	(48)	(52)	(54)
Angiectasis	5 (10%)	9 (19%)	4 (8%)	4 (7%)
Hematopoietic cell proliferation		8 (17%)	8 (15%)	1 (2%)
Infiltration cellular, plasma cell			1 (2%)	
Necrosis			1 (2%)	
Spleen	(52)	(51)	(54)	(56)
Angiectasis	1 (2%)			
Depletion lymphoid				1 (2%)
Hematopoietic cell proliferation	4 (8%)	36 (71%)	46 (85%)	42 (75%)
Hemorrhage		1 (2%)		
Thymus	(47)	(40)	(47)	(46)
Epithelial cell, hyperplasia			1 (2%)	
Integumentary System				
Skin	(52)	(50)	(54)	(55)
Erosion		1 (2%)		
Musculoskeletal System				
None				
Nervous System				
Brain	(52)	(50)	(54)	(56)
Inflammation, acute			1 (2%)	
Respiratory System				
Lung	(52)	(51)	(54)	(56)
Edema	1 (2%)		1 (2%)	
Embolus tumor		1 (2%)		
Hemorrhage	3 (6%)		1 (2%)	1 (2%)
Hyperplasia			1 (2%)	
Infiltration cellular, histiocyte	2 (4%)	2 (4%)	2 (4%)	4 (7%)
Inflammation, acute		1 (2%)	3 (6%)	2 (4%)
Leukocytosis		3 (6%)	5 (9%)	2 (4%)
Alveolar epithelium, hyperplasia	1 (2%)	5 (10%)		2 (4%)
Bronchiole, hyperplasia		1 (2%)	3 (6%)	31 (55%)
Nose	(52)	(51)	(54)	(56)
Inflammation, acute			1 (2%)	4 (7%)

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Special Senses System				
Eye	(2)	(1)	(2)	(3)
Cornea, inflammation, acute	1 (50%)			
Cornea, necrosis	1 (50%)			
Harderian gland	(1)	(3)	(11)	(13)
Hyperplasia			1 (9%)	1 (8%)
Urinary System				
Kidney	(52)	(51)	(54)	(56)
Cyst		1 (2%)		
Nephropathy	4 (8%)	3 (6%)		
Renal tubule, regeneration	1 (2%)			
Urinary bladder	(52)	(50)	(53)	(56)
Calculus gross observation			1 (2%)	2 (4%)
Calculus micro observation only			1 (2%)	2 (4%)

[a] Number of animals examined microscopically at site and number of animals with lesion

APPENDIX D
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR GAVAGE STUDY OF 1,2,3-TRICHLOROPROPANE

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	9	5
Early deaths				
Accidental deaths			1	
Moribund	8	34	37	48
Natural deaths	1	3	4	1
Scheduled sacrifice			9	6
Survivors				
Terminal sacrifice	41	13		
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(10)	(9)	(5)
Hepatocellular adenoma	1 (10%)			1 (20%)
Hepatocellular adenoma, multiple			1 (11%)	4 (80%)
Squamous cell carcinoma, metastatic, stomach		1 (10%)		
Stomach	(10)	(10)	(9)	(5)
Papilloma squamous				1 (20%)
Stomach, forestomach	(10)	(10)	(9)	(5)
Papilloma squamous		3 (30%)		
Papilloma squamous, multiple		2 (20%)	9 (100%)	4 (80%)
Squamous cell carcinoma		1 (10%)	5 (56%)	2 (40%)
Squamous cell carcinoma, multiple			1 (11%)	
Cardiovascular System				
None				
Endocrine System				
Pituitary gland	(10)	(10)	(9)	(5)
Pars distalis, adenoma	1 (10%)			
General Body System				
None				
Genital System				
Uterus	(10)	(10)	(9)	(5)
Adenoma				1 (20%)
Polyp stromal			1 (11%)	1 (20%)
Endometrium, adenocarcinoma				2 (40%)
Hematopoietic System				
None				

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
15-Month Interim Evaluation (continued)				
Integumentary System				
Mammary gland	(10)	(10)	(9)	(5)
Adenocarcinoma				1 (20%)
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)	(10)	(9)	(5)
Alveolar/bronchiolar adenoma				1 (20%)
Special Senses System				
Harderian gland	(1)			
Adenoma	1 (100%)			
Urinary System				
None				
2-Year Study				
Alimentary System				
Gallbladder	(49)	(46)	(48)	(54)
Sarcoma, metastatic, uterus				1 (2%)
Squamous cell carcinoma, metastatic, stomach		5 (11%)	7 (15%)	1 (2%)
Intestine large	(49)	(50)	(50)	(55)
Anorectal junction, squamous cell carcinoma			1 (2%)	1 (2%)
Intestine large, cecum	(49)	(48)	(47)	(55)
Squamous cell carcinoma, metastatic, stomach				1 (2%)
Intestine small, duodenum	(49)	(46)	(48)	(55)
Intestine small, ileum	(49)	(49)	(50)	(55)
Intestine small, jejunum	(49)	(47)	(49)	(55)
Sarcoma			1 (2%)	
Squamous cell carcinoma, metastatic, stomach				1 (2%)
Liver	(50)	(50)	(51)	(55)
Hemangiosarcoma			1 (2%)	
Hepatocellular carcinoma	1 (2%)	3 (6%)		2 (4%)
Hepatocellular adenoma	4 (8%)	7 (14%)	4 (8%)	9 (16%)
Hepatocellular adenoma, multiple	2 (4%)	2 (4%)	4 (8%)	22 (40%)
Histiocytic sarcoma	2 (4%)	1 (2%)		
Sarcoma, metastatic, uncertain primary site				1 (2%)
Sarcoma, metastatic, uterus				1 (2%)
Squamous cell carcinoma, metastatic		1 (2%)	2 (4%)	
Squamous cell carcinoma, metastatic, stomach		23 (46%)	25 (49%)	14 (25%)

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Mesentery	(3)	(17)	(20)	(10)
Sarcoma, metastatic, skin	1 (33%)			
Sarcoma, metastatic, uncertain primary site				1 (10%)
Sarcoma, metastatic, uterus				1 (10%)
Squamous cell carcinoma, metastatic, stomach		16 (94%)	19 (95%)	7 (70%)
Pancreas	(49)	(50)	(51)	(55)
Sarcoma, metastatic, skin	1 (2%)			
Sarcoma, metastatic, uterus				1 (2%)
Squamous cell carcinoma, metastatic, stomach		17 (34%)	22 (43%)	8 (15%)
Pharynx	(1)		(1)	(5)
Squamous cell carcinoma			1 (100%)	1 (20%)
Palate, papilloma squamous	1 (100%)			
Palate, squamous cell carcinoma				4 (80%)
Salivary glands	(49)	(50)	(49)	(54)
Stomach, forestomach	(50)	(49)	(51)	(55)
Papilloma squamous		10 (20%)	14 (27%)	13 (24%)
Papilloma squamous, multiple		13 (27%)	4 (8%)	16 (29%)
Squamous cell carcinoma		29 (59%)	24 (47%)	24 (44%)
Squamous cell carcinoma, multiple		17 (35%)	25 (49%)	25 (45%)
Stomach, glandular	(49)	(50)	(50)	(54)
Tongue		(1)	(3)	(1)
Papilloma squamous			1 (33%)	
Cardiovascular System				
Heart	(50)	(50)	(51)	(55)
Endocrine System				
Adrenal gland, cortex	(50)	(47)	(49)	(54)
Adenoma				1 (2%)
Squamous cell carcinoma, metastatic, stomach		1 (2%)	1 (2%)	1 (2%)
Adrenal gland, medulla	(49)	(44)	(47)	(54)
Islets, pancreatic	(49)	(50)	(50)	(55)
Pituitary gland	(48)	(46)	(45)	(53)
Pars distalis, adenoma	3 (6%)	2 (4%)		
Pars intermedia, adenoma				1 (2%)
Thyroid gland	(49)	(49)	(49)	(54)
General Body System				
None				
Genital System				
Ovary	(49)	(50)	(48)	(53)
Adenoma				1 (2%)
Cystadenoma				1 (2%)
Hemangioma		1 (2%)		
Histiocytic sarcoma	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		9 (18%)	4 (8%)	3 (6%)
Teratoma malignant	1 (2%)			

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Genital System (continued)				
Oviduct	(47)	(48)	(50)	(52)
Squamous cell carcinoma, metastatic, stomach			1 (2%)	
Uterus	(50)	(50)	(51)	(54)
Histiocytic sarcoma	1 (2%)	1 (2%)		
Polyp stromal		2 (4%)	1 (2%)	6 (11%)
Sarcoma	1 (2%)			1 (2%)
Squamous cell carcinoma, metastatic, stomach		2 (4%)	2 (4%)	
Endometrium, adenocarcinoma		4 (8%)	3 (6%)	6 (11%)
Endometrium, adenoma		1 (2%)		3 (6%)
Hematopoietic System				
Bone marrow	(50)	(49)	(51)	(55)
Lymph node	(50)	(49)	(51)	(55)
Mediastinal, squamous cell carcinoma, metastatic, stomach		5 (10%)	8 (16%)	4 (7%)
Pancreatic, squamous cell carcinoma, metastatic, stomach		1 (2%)	1 (2%)	
Renal, squamous cell carcinoma, metastatic, stomach		1 (2%)		
Lymph node, mandibular	(48)	(47)	(48)	(52)
Squamous cell carcinoma, metastatic, stomach				1 (2%)
Lymph node, mesenteric	(48)	(45)	(50)	(53)
Histiocytic sarcoma	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		7 (16%)	16 (32%)	3 (6%)
Spleen	(49)	(50)	(51)	(54)
Hemangioma	1 (2%)			
Histiocytic sarcoma	1 (2%)			
Sarcoma, metastatic, uterus				1 (2%)
Squamous cell carcinoma, metastatic, stomach		6 (12%)	6 (12%)	4 (7%)
Thymus	(46)	(45)	(48)	(52)
Histiocytic sarcoma	1 (2%)			
Squamous cell carcinoma, metastatic, stomach		1 (2%)	2 (4%)	2 (4%)
Integumentary System				
Mammary gland	(44)	(35)	(50)	(54)
Adenoacanthoma			1 (2%)	2 (4%)
Adenocarcinoma		2 (6%)		
Skin	(50)	(50)	(51)	(55)
Basosquamous tumor benign				1 (2%)
Subcutaneous tissue, sarcoma	2 (4%)			
Musculoskeletal System				
Skeletal muscle	(2)	(11)	(15)	(5)
Hemangioma			1 (7%)	
Squamous cell carcinoma, metastatic, stomach		10 (91%)	15 (100%)	3 (60%)
Nervous System				
Brain	(49)	(49)	(51)	(55)

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Respiratory System				
Lung	(50)	(50)	(51)	(55)
Adenoacanthoma, metastatic, mammary gland			1 (2%)	1 (2%)
Alveolar/bronchiolar adenoma	3 (6%)	3 (6%)		9 (16%)
Alveolar/bronchiolar adenoma, multiple	1 (2%)			1 (2%)
Alveolar/bronchiolar carcinoma	3 (6%)			
Hepatocellular carcinoma, metastatic, liver		1 (2%)		
Histiocytic sarcoma		1 (2%)		
Squamous cell carcinoma, metastatic			2 (4%)	
Squamous cell carcinoma, metastatic, stomach		6 (12%)	9 (18%)	3 (5%)
Squamous cell carcinoma, metastatic, intestine large				1 (2%)
Mediastinum, squamous cell carcinoma, metastatic, stomach				1 (2%)
Special Senses System				
Harderian gland	(2)	(7)	(8)	(10)
Adenoma	2 (100%)	6 (86%)	5 (63%)	9 (90%)
Bilateral, adenoma			2 (25%)	1 (10%)
Urinary System				
Kidney	(49)	(50)	(51)	(55)
Histiocytic sarcoma	1 (2%)	1 (2%)		
Sarcoma, metastatic, uterus				1 (2%)
Squamous cell carcinoma, metastatic, stomach		1 (2%)	3 (6%)	
Urinary bladder	(49)	(48)	(51)	(52)
Squamous cell carcinoma, metastatic, stomach		1 (2%)	1 (2%)	
Systemic Lesions				
Multiple organs[b]	(50)	(50)	(51)	(55)
Histiocytic sarcoma	2 (4%)	1 (2%)		
Lymphoma malignant histiocytic	1 (2%)		2 (4%)	
Lymphoma malignant lymphocytic	2 (4%)	2 (4%)		2 (4%)
Lymphoma malignant mixed	1 (2%)			1 (2%)
Lymphoma malignant undifferentiated cell	11 (22%)	4 (8%)	1 (2%)	

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Neoplasm Summary				
Total animals with primary neoplasms[c]				
15-Month interim evaluation	3	6	9	5
2-Year study	36	48	50	55
Total primary neoplasms				
15-Month interim evaluation	3	6	17	18
2-Year study	42	109	96	163
Total animals with benign neoplasms				
15-Month interim evaluation	3	5	9	5
2-Year study	17	31	31	48
Total benign neoplasms				
15-Month interim evaluation	3	5	11	13
2-Year study	17	47	36	94
Total animals with malignant neoplasms				
15-Month interim evaluation		1	6	5
2-Year study	23	47	49	53
Total malignant neoplasms				
15-Month interim evaluation		1	6	5
2-Year study	25	62	60	69
Total animals with secondary neoplasms[d]				
15-Month interim evaluation		1		
2-Year study	1	27	36	28
Total secondary neoplasms				
15-Month interim evaluation		1		
2-Year study	2	115	147	67
Total animals with malignant neoplasms uncertain primary site				
2-Year study				1

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms
[d] Secondary neoplasms: metastatic neoplasms or neoplasms invasive to an adjacent organ

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control

Number of Days on Study	0 6 8	4 8 0	4 8 2	5 1 1	6 3 1	6 9 1	6 9 9	6 9 9	7 2 8	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	2 8 6 1	3 0 8 1	2 6 0 1	2 6 3 1	2 9 7 1	2 9 9 1	2 7 7 1	3 1 1 1	2 8 2 1	2 6 8 1	2 7 0 1	2 7 1 1	2 7 2 1	2 7 3 1	2 7 4 1	2 7 5 1	2 7 6 1	2 7 8 1	2 8 0 1	2 8 4 1	2 8 5 1	2 8 9 1	2 9 0 1	2 9 1 1	2 9 2 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma															X										
Hepatocellular adenoma																				X					
Hepatocellular adenoma, multiple																					X				
Histiocytic sarcoma		X																							
Mesentery				+				+															+		
Sarcoma, metastatic, skin								X																	
Pancreas	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, skin								X																	
Pharynx																									
Palate, papilloma squamous																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	M	M	+	M	+	+	+	+	+	+	M	+	M	+	+	M	+	+	+	+	+	M	+	+	+
Pituitary gland	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Thyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	2 9 3 1	2 9 8 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 1 1	2 6 2 1	2 6 4 1	2 6 5 1	2 6 6 1	2 6 7 1	2 6 9 1	2 8 7 1	3 0 0 1	3 0 2 1	3 0 3 1	3 0 4 1	3 0 5 1	3 0 6 1	3 0 7 1	3 0 9 1	3 1 2 1	3 1 3 1	3 1 4 1	3 1 5 1	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Hepatocellular carcinoma																										1	
Hepatocellular adenoma	X								X										X							4	
Hepatocellular adenoma, multiple																X										2	
Histiocytic sarcoma																					X					2	
Mesentery																										3	
Sarcoma, metastatic, skin																										1	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Sarcoma, metastatic, skin																										1	
Pharynx							+																			1	
Palate, papilloma squamous							X																			1	
Salivary glands	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Parathyroid gland	M	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	M	+	M	M	+	36	
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48	
Pars distalis, adenoma													X		X			X								3	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	0 6 8	4 8 0	4 8 2	5 1 1	6 3 1	6 9 1	6 9 9	6 9 9	7 2 8	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	2 8 6 1	3 0 8 1	2 6 0 1	2 6 3 1	2 9 7 1	2 9 9 1	2 7 7 1	3 1 1 1	2 8 2 1	2 6 8 1	2 7 0 1	2 7 1 1	2 7 2 1	2 7 3 1	2 7 4 1	2 7 5 1	2 7 6 1	2 7 8 1	2 8 0 1	2 8 4 1	2 8 5 1	2 8 9 1	2 9 0 1	2 9 1 1	2 9 2 1
General Body System																										
None																										
Genital System																										
Clitoral gland								+															+			
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma		X																								
Teratoma malignant	X																									
Oviduct	M	+	+	+	+	+	+	+	+	+	+		+	+	+	M	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma		X																								
Sarcoma																					X					
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										
Spleen	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																										
Histiocytic sarcoma																										
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										
Integumentary System																										
Mammary gland	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, sarcoma								X	X																	
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle												+														
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	2 9 3 1	2 9 8 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 1 1	2 6 2 1	2 6 4 1	2 6 5 1	2 6 6 1	2 6 7 1	2 6 9 1	2 8 7 1	3 0 0 1	3 0 2 1	3 0 3 1	3 0 4 1	3 0 5 1	3 0 6 1	3 0 7 1	3 0 9 1	3 1 2 1	3 1 3 1	3 1 4 1	3 1 5 1	**Total Tissues/ Tumors**	
General Body System																												
None																												
Genital System																												
Clitoral gland	+																									3		
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4 9		
Histiocytic sarcoma																										1		
Teratoma malignant																										1		
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4 7		
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0		
Histiocytic sarcoma																										1		
Sarcoma																										1		
Hematopoietic System																												
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0		
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0		
Lymph node, mandibular	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	4 8		
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4 8		
Histiocytic sarcoma																					X					1		
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4 9		
Hemangioma						X																				1		
Histiocytic sarcoma																					X					1		
Thymus	M	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	4 6		
Histiocytic sarcoma																					X					1		
Integumentary System																												
Mammary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	44		
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50		
Subcutaneous tissue, sarcoma																										2		
Musculoskeletal System																												
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0		
Skeletal muscle																				+						2		
Nervous System																												
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49		

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	0 6 8	4 8 0	4 8 2	5 1 1	6 3 1	6 9 1	6 9 9	6 9 9	7 2 8	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3	7 3 3
Carcass ID Number	2 8 6 1	3 0 8 1	2 6 0 1	2 6 3 1	2 9 7 1	2 9 9 1	2 7 7 1	3 1 1 1	2 8 2 1	2 6 8 1	2 7 0 1	2 7 1 1	2 7 2 1	2 7 3 1	2 7 4 1	2 7 5 1	2 7 6 1	2 7 8 1	2 8 0 1	2 8 4 1	2 8 5 1	2 8 9 1	2 9 0 1	2 9 1 1	2 9 2 1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																								X		
Alveolar/bronchiolar adenoma, multiple							X																			
Alveolar/bronchiolar carcinoma					X																					X
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Eye																+										
Harderian gland													+			+										
Adenoma													X			X										
Urinary System																										
Kidney	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										
Urinary bladder	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma		X																								
Lymphoma malignant histiocytic																										
Lymphoma malignant lymphocytic												X														
Lymphoma malignant mixed									X																	
Lymphoma malignant undifferentiated cell type						X							X	X			X									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: Vehicle Control (continued)

Number of Days on Study	7 3 3	7 3 3	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	7 3 4	
Carcass ID Number	2 9 3 1	2 9 8 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 1 1	2 6 2 1	2 6 4 1	2 6 5 1	2 6 6 1	2 6 7 1	2 6 9 1	2 8 7 1	3 0 0 1	3 0 0 2	3 0 3 1	3 0 4 1	3 0 5 1	3 0 6 1	3 0 7 1	3 0 9 1	3 1 2 1	3 1 3 1	3 1 4 1	3 1 5 1	**Total Tissues/ Tumors**
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma											X						X										3
Alveolar/bronchiolar adenoma, multiple																											1
Alveolar/bronchiolar carcinoma														X													3
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+		49
Special Senses System																											
Eye																											1
Harderian gland																											2
Adenoma																											2
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																					X						1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	4 9
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Histiocytic sarcoma																					X						2
Lymphoma malignant histiocytic		X																									1
Lymphoma malignant lymphocytic																				X							2
Lymphoma malignant mixed																											1
Lymphoma malignant undifferentiated cell type			X		X									X			X		X			X	X			11

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg

Number of Days on Study	160	207	414	448	516	540	557	558	566	571	574	580	582	583	587	600	601	603	607	609	623	624	629	634	643
Carcass ID Number	34211	35311	34401	36311	37211	34311	35511	32411	36011	37111	36711	35211	32711	34611	35511	32511	33211	33011	32111	32661	36611	31811	32811	32311	33911
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	M	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach				X		X																	X		
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	A	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma													X									X			
Hepatocellular adenoma						X							X												
Hepatocellular adenoma, multiple																									
Histiocytic sarcoma																X									
Squamous cell carcinoma, metastatic																							X		
Squamous cell carcinoma, metastatic, stomach			X	X		X	X			X	X	X		X	X		X			X	X	X			X
Mesentery				+		+	+			+		+			+		+			+	+		+		+
Squamous cell carcinoma, metastatic, stomach				X		X	X			X		X			X		X			X	X		X		X
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach				X		X	X			X		X		X	X		X						X	X	X
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous							X				X	X	X			X									
Papilloma squamous, multiple														X										X	
Squamous cell carcinoma			X	X	X	X	X	X		X	X	X	X	X	X				X	X	X				X
Squamous cell carcinoma, multiple									X							X	X	X				X	X	X	
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue													+												
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	653	671	676	680	687	687	693	698	705	719	721	728	733	733	733	733	733	733	733	733	733	733	733	733	733	
Carcass ID Number	319	359	365	331	354	362	337	356	349	369	331	358	320	322	329	341	366	345	370	351	355	361	368	370	374	**Total Tissues/ Tumors**
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	A	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	46
Squamous cell carcinoma, metastatic, stomach										X	X															5
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	A	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma														X												3
Hepatocellular adenoma					X					X					X	X									X	7
Hepatocellular adenoma, multiple																					X	X				2
Histiocytic sarcoma																										1
Squamous cell carcinoma, metastatic																										1
Squamous cell carcinoma, metastatic, stomach	X		X			X	X	X		X	X			X			X									23
Mesentery	+							+		+	+			+										+		17
Squamous cell carcinoma, metastatic, stomach	X							X		X	X			X												16
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach	X			X						X	X			X			X									17
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papilloma squamous					X		X			X					X							X				10
Papilloma squamous, multiple		X							X		X	X	X			X	X			X	X		X	X		13
Squamous cell carcinoma	X	X	X	X	X		X	X					X			X		X	X			X		X		29
Squamous cell carcinoma, multiple						X			X	X	X	X		X	X		X						X			X	17
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5 0
Tongue																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	160	207	414	448	516	540	557	558	566	571	574	580	582	583	587	600	601	603	607	609	623	624	629	634	643
Carcass ID Number	34211	35311	34011	36311	37211	34311	33511	32411	36011	37111	36711	35211	32711	34611	35511	32511	33211	33011	32111	32611	36611	31811	32811	32311	33911
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach				X																					
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	M	+	M	+	+	+	+	+	+	+	+	+	M	+	+	M	+	M	M	+	+	+	+	+	M
Pituitary gland	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+
General Body System																									
Tissue NOS																									
Genital System																									
Clitoral gland				+		+																			
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Squamous cell carcinoma, metastatic, stomach							X					X			X								X		X
Oviduct	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Polyp stromal																									X
Squamous cell carcinoma, metastatic, stomach							X					X													
Endometrium, adenocarcinoma																									
Endometrium, adenoma																									
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Mediastinal, squamous cell carcinoma, metastatic, stomach				X		X									X								X		
Pancreatic, squamous cell carcinoma, metastatic, stomach																									
Renal, squamous cell carcinoma, metastatic, stomach																									X

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	653	671	676	680	687	687	693	698	705	719	721	728	733	733	733	733	733	733	733	733	733	733	733	733	733	
Carcass ID Number	319	359	365	331	354	362	337	356	349	369	333	358	320	322	329	334	336	345	347	350	351	361	368	370	374	**Total Tissues/ Tumors**
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Endocrine System																										
Adrenal gland[a]	M	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adrenal gland, cortex[b]	M	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Squamous cell carcinoma, metastatic, stomach																										1
Adrenal gland, medulla	M	+	M	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	44
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	M	+	+	M	+	M	+	+	M	M	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	36
Pituitary gland[c]	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	46
Pars distalis, adenoma										X								X								2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
Tissue NOS																								+		1
Genital System																										
Clitoral gland		+						+																		4
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																			X							1
Squamous cell carcinoma, metastatic, stomach	X			X			X				X															9
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	48
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Polyp stromal																				X						2
Squamous cell carcinoma, metastatic, stomach																										2
Endometrium, adenocarcinoma								X			X									X		X				4
Endometrium, adenoma																		X								1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Mediastinal, squamous cell carcinoma, metastatic, stomach											X															5
Pancreatic, squamous cell carcinoma, metastatic, stomach																	X									1
Renal, squamous cell carcinoma, metastatic, stomach																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	160	207	414	448	516	540	557	558	566	571	574	580	582	583	587	600	601	603	607	609	623	624	629	634	643
Carcass ID Number	34211	35311	34011	36311	37211	34311	33511	32411	36001	37111	36711	35211	32711	34611	35511	32511	33211	33011	32111	32611	36611	31811	32811	32311	33911
Hematopoietic System (continued)																									
Lymph node, mandibular	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+
Squamous cell carcinoma, metastatic, stomach																									X
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach							X				X			X									X	X	
Thymus	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	M	M	+	+	+	M	+	+	+	+
Adenocarcinoma														X											
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle				+								+			+		+				+		+		+
Squamous cell carcinoma, metastatic, stomach				X								X			X		X				X		X		X
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve	+																								
Spinal cord	+																								
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma											X														
Hepatocellular carcinoma, metastatic, liver													X												
Histiocytic sarcoma																X									
Squamous cell carcinoma, metastatic, stomach							X				X									X	X				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	653	671	676	680	687	687	693	698	705	719	721	728	733	733	733	733	733	733	733	733	733	733	733	733	733	
Carcass ID Number	31911	35911	36511	33111	35411	36211	33711	35611	34911	36911	33311	35811	32011	32211	32911	33411	33611	34511	34711	35011	35111	35511	36111	36611	37011	37411	**Total Tissues/ Tumors**
Hematopoietic System (continued)																											
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	45
Squamous cell carcinoma, metastatic, stomach	X		X	X			X				X			X													7
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach								X																			6
Thymus	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Squamous cell carcinoma, metastatic, stomach						X																					1
Integumentary System																											
Mammary gland	+	+	M	M	+	M	M	+	+	+	+	M	+	+	M	M	+	M	M	+	+	+	M	+	+		35
Adenocarcinoma	X																										2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skeletal muscle	+								+	+	+																11
Squamous cell carcinoma, metastatic, stomach	X									X	X																10
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	49
Peripheral nerve																											1
Spinal cord																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma													X		X												3
Hepatocellular carcinoma, metastatic, liver																											1
Histiocytic sarcoma																											1
Squamous cell carcinoma, metastatic, stomach						X								X													6
Nose	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	160	207	414	448	516	540	557	558	566	571	574	580	582	583	587	600	601	603	607	609	623	624	629	634	643
Carcass ID Number	34211	35311	40401	46311	37211	43431	35151	32411	60101	71111	67611	52111	72711	46111	55151	25111	32111	30111	32111	26161	66161	18111	28111	23111	39111
Special Senses System																									
Eye																									
Harderian gland								+											+						
Adenoma								X											X						
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Squamous cell carcinoma, metastatic, stomach																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Squamous cell carcinoma, metastatic, stomach				X																					
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Lymphoma malignant lymphocytic																									
Lymphoma malignant undifferentiated cell type																									

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 6 mg/kg (continued)

Number of Days on Study	653	671	676	680	687	687	693	698	705	719	721	728	733	733	733	733	733	733	733	733	733	733	733	733	733	
Carcass ID Number	31911	35911	36511	36311	35411	36211	33711	35611	34911	36911	33311	35811	32011	32211	32911	33411	33611	34511	34711	35011	35511	35611	36811	37011	37411	**Total Tissues/ Tumors**
Special Senses System																										
Eye		+																								1
Harderian gland	+	+			+								+												+	7
Adenoma	X				X								X												X	6
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Squamous cell carcinoma, metastatic, stomach						X																				1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Squamous cell carcinoma, metastatic, stomach																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant lymphocytic									X								X									2
Lymphoma malignant undifferentiated cell type												X	X		X			X								4

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg

Number of Days on Study	0111	3112	3822	4441	4442	4446	4554	4558	4622	4655	4665	4667	4669	4673	4994	4994	5001	5022	5022	5022	5099	5111	5222	5233	5332	5440
Carcass ID Number	39611	38811	42441	37911	41311	42211	42911	39771	38711	38411	40811	39211	39011	41511	38511	43511	42811	37711	38111	38211	39911	40311	42011	41111	41911	40711
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	M	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																		X	X							
Intestine large	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Anorectal junction, squamous cell carcinoma																										
Intestine large, cecum	M	+	+	+	M	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	M	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	M	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma												X														
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																										
Hepatocellular adenoma							X																			
Hepatocellular adenoma, multiple																										
Squamous cell carcinoma, metastatic																									X	
Squamous cell carcinoma, metastatic, stomach							X	X	X					X	X		X	X		X		X		X		X
Mesentery			+						+						+			+	+					+	+	+
Squamous cell carcinoma, metastatic, stomach			X						X						X			X	X					X	X	X
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach									X				X	X	X			X	X	X		X		X		X
Pharynx																										
Squamous cell carcinoma																										
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous					X	X		X	X		X			X	X	X										
Papilloma squamous, multiple																					X		X			
Squamous cell carcinoma		X	X	X	X	X	X	X	X	X					X			X						X	X	
Squamous cell carcinoma, multiple												X	X	X		X	X		X	X	X	X	X			X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+
Tongue		+																								
Papilloma squamous																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	545	551	558	560	565	570	573	573	578	580	582	589	603	608	617	620	620	620	620	620	620	620	620	620	620		
Carcass ID Number	38611	42711	40111	37611	39111	40511	41711	43111	41011	43011	39511	40911	43311	41611	40011	38011	38311	38911	39311	40211	40611	41211	41411	42311	43411		**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Squamous cell carcinoma, metastatic, stomach					X	X			X		X							X									7
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Anorectal junction, squamous cell carcinoma								X																			1
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine large, rectum	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Sarcoma																											1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Hemangiosarcoma													X														1
Hepatocellular adenoma															X						X				X		4
Hepatocellular adenoma, multiple																X		X	X			X					4
Squamous cell carcinoma, metastatic			X																								2
Squamous cell carcinoma, metastatic, stomach	X				X		X		X		X		X	X	X	X	X	X	X		X		X				25
Mesentery			+		+	+	+		+	+	+						+	+			+	+		+			20
Squamous cell carcinoma, metastatic, stomach			X		X	X	X		X	X	X						X	X			X			X			19
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Squamous cell carcinoma, metastatic, stomach	X			X	X		X		X	X	X		X				X	X			X			X			22
Pharynx		+																									1
Squamous cell carcinoma		X																									1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+		49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Papilloma squamous					X				X		X									X		X	X				14
Papilloma squamous, multiple																								X	X		4
Squamous cell carcinoma	X	X		X		X					X	X			X			X	X	X				X			24
Squamous cell carcinoma, multiple			X		X		X	X	X	X			X	X		X	X				X	X	X		X		25
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Tongue									+										+								3
Papilloma squamous									X																		1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	0111	3122	3822	4441	4442	4446	4454	4458	4462	4465	4665	4667	4699	4773	4994	4994	5011	5022	5022	5022	5099	5111	5222	5233	5332	5440
Carcass ID Number	3961	3881	4241	3791	4131	4221	4291	3971	3871	3841	4081	3921	3901	4151	3851	4351	4281	3771	3811	3821	3991	4031	4201	4111	4191	4071
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach									X																	
Adrenal gland, medulla	+	+	+	+	+	+	+	+	M	+	A	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	M	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Thyroid gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																										
None																										
Genital System																										
Clitoral gland												+								+				+		
Ovary	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach													X													
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach									X																	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal		X																								
Squamous cell carcinoma, metastatic, stomach																										
Endometrium, adenocarcinoma																										
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, squamous cell carcinoma, metastatic, stomach																		X	X							X
Pancreatic, squamous cell carcinoma, metastatic, stomach																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	545	551	558	560	565	570	573	573	578	580	582	589	603	608	617	620	620	620	620	620	620	620	620	620	620	
Carcass ID Number	38611	42711	40111	37611	39111	40151	41171	43111	41101	43001	39511	40911	43311	41611	40011	38011	38311	38911	39311	40211	40061	41211	41411	42311	43411	**Total Tissues/ Tumors**
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell carcinoma, metastatic, stomach																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	M	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	M	M	+	+	+	+	42
Pituitary gland	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	45
Thyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
General Body System																										
None																										
Genital System																										
Clitoral gland			+																					+		5
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	48
Squamous cell carcinoma, metastatic, stomach					X				X								X									4
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Polyp stromal																										1
Squamous cell carcinoma, metastatic, stomach											X						X									2
Endometrium, adenocarcinoma											X					X						X				3
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Mediastinal, squamous cell carcinoma, metastatic, stomach					X		X		X		X							X								8
Pancreatic, squamous cell carcinoma, metastatic, stomach																					X					1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	0111	3112	3822	4441	4442	4446	4554	4558	4662	4665	4667	4669	4673	4694	4994	5001	5022	5022	5022	5099	5111	5122	5233	5332	5440
Carcass ID Number	3961	3881	4241	3791	4131	4221	4291	3971	3871	3841	4081	3921	3901	4151	3851	4351	4281	3771	3811	3821	3991	4031	4201	4111	4191	4071
Hematopoietic System (continued)																										
Lymph node, mandibular	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Squamous cell carcinoma, metastatic, stomach													X	X					X	X					X	X
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																		X								
Thymus	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoacanthoma																X										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																		+	+				+	+		
Hemangioma																										
Squamous cell carcinoma, metastatic, stomach																		X	X				X	X		
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoacanthoma, metastatic, mammary gland																X										
Squamous cell carcinoma, metastatic					X			X																		
Squamous cell carcinoma, metastatic, stomach														X			X		X							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Eye																										
Harderian gland																										
Adenoma																										
Bilateral, adenoma																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	545	551	558	560	565	570	573	573	578	580	582	589	603	608	617	620	620	620	620	620	620	620	620	620	620	620	
Carcass ID Number	38611	42711	40111	37611	39111	40151	41171	43111	41011	43011	39951	40911	43311	41611	40101	38301	38391	39331	40211	40611	41211	41411	42311	43411		**Total Tissues/ Tumors**
Hematopoietic System (continued)																											
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+		48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Squamous cell carcinoma, metastatic, stomach					X	X	X		X	X	X						X	X	X		X						16
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Squamous cell carcinoma, metastatic, stomach	X			X			X			X							X										6
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+		48
Squamous cell carcinoma, metastatic, stomach																	X	X									2
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+		50
Adenoacanthoma																											1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Skeletal muscle					+	+	+		+	+	+			+			+	+	+				+				15
Hemangioma														X													1
Squamous cell carcinoma, metastatic, stomach					X	X	X		X	X	X			X			X	X	X				X				15
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Adenoacanthoma, metastatic, mammary gland																											1
Squamous cell carcinoma, metastatic																											2
Squamous cell carcinoma, metastatic, stomach			X		X	X	X				X							X									9
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		51
Special Senses System																											
Eye							+	+									+				+		+				5
Harderian gland	+		+				+	+				+					+				+		+				8
Adenoma	X		X				X					X											X				5
Bilateral, adenoma								X													X						2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	0111	3112	3822	4441	4442	4446	4554	4558	4662	4665	4665	4667	4699	4773	4994	4994	5001	5022	5022	5022	5099	5111	5222	5233	5320	5440
Carcass ID Number	3961	3881	4241	3791	4131	4221	4291	3971	3871	3841	4081	3921	3901	4151	3851	4351	4281	3771	3811	3821	3991	4031	4201	4111	4191	4071
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																	X							X		
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																										
Lymphoma malignant undifferentiated cell type																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 20 mg/kg (continued)

Number of Days on Study	545	551	558	560	565	570	573	573	578	580	582	589	603	608	617	620	620	620	620	620	620	620	620	620	620	
Carcass ID Number	38611	42711	40111	37611	39111	40151	41771	43111	41101	43001	39511	40911	43131	41601	40011	38031	38391	38931	39031	40211	40061	41211	41411	42311	43411	**Total Tissues/ Tumors**
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Squamous cell carcinoma, metastatic, stomach			X																							3
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Squamous cell carcinoma, metastatic, stomach																	X									1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymphoma malignant histiocytic																			X						X	2
Lymphoma malignant undifferentiated cell type														X												1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg

Number of Days on Study	295	341	377	378	379	379	383	383	390	397	405	407	411	419	420	424	427	432	434	439	442	445	445	447	460	466	467	468	469
Carcass ID Number	45111	44611	47611	49311	48511	49511	43611	46311	48611	48711	48211	44311	45211	46011	49411	48311	49111	46511	45011	48411	44211	45711	46611	48111	47711	46911	47411	47811	46211
Alimentary System																													
Esophagus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uterus																					X								
Squamous cell carcinoma, metastatic, stomach																											X		
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Anorectal junction, squamous cell carcinoma							X																						
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																													
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	M	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																													
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																													
Hepatocellular adenoma															X		X			X		X							X
Hepatocellular adenoma, multiple																		X					X				X	X	
Sarcoma, metastatic, uncertain primary site												X																	
Sarcoma, metastatic, uterus																					X								
Squamous cell carcinoma, metastatic, stomach								X					X			X		X					X			X		X	X	X
Mesentery										+		+	+					+	+		+					+			
Sarcoma, metastatic, uncertain primary site												X																	
Sarcoma, metastatic, uterus																					X								
Squamous cell carcinoma, metastatic, stomach										X			X					X	X							X				
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uterus																					X								
Squamous cell carcinoma, metastatic, stomach										X																	X	X	
Pharynx																	+					+	+						
Squamous cell carcinoma																	X												
Palate, squamous cell carcinoma																						X	X						

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	469	469	473	473	473	480	480	487	487	490	491	494	496	498	501	504	505	506	508	508	511	511	511	511	511	
Carcass ID Number	47001	48811	44811	45311	45411	47111	47911	44511	49011	44011	45611	47411	49211	44911	45911	46111	47511	43911	44111	47211	43811	44411	46711	46811	47311	48891	**Total Tissues/ Tumors**
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Sarcoma, metastatic, uterus																											1
Squamous cell carcinoma, metastatic, stomach																											1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Anorectal junction, squamous cell carcinoma																											1
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Squamous cell carcinoma, metastatic, stomach					X																						1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Squamous cell carcinoma, metastatic, stomach					X																						1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Hepatocellular carcinoma												X			X												2
Hepatocellular adenoma													X				X		X	X							9
Hepatocellular adenoma, multiple	X		X	X		X		X	X	X	X	X		X	X	X		X			X	X	X		X	X	22
Sarcoma, metastatic, uncertain primary site																											1
Sarcoma, metastatic, uterus																											1
Squamous cell carcinoma, metastatic, stomach					X	X	X						X					X									14
Mesentery					+					+																	10
Sarcoma, metastatic, uncertain primary site																											1
Sarcoma, metastatic, uterus																											1
Squamous cell carcinoma, metastatic, stomach					X																						7
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Sarcoma, metastatic, uterus																											1
Squamous cell carcinoma, metastatic, stomach		X	X					X						X					X								8
Pharynx						+		+																			5
Squamous cell carcinoma																											1
Palate, squamous cell carcinoma						X		X																			4

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	295	341	377	378	379	379	383	383	390	397	405	407	411	419	420	424	427	432	434	439	442	445	445	447	460	466	467	468	469
Carcass ID Number	45111	44611	47611	49311	48511	49511	43611	46311	48611	48711	48211	44311	45211	46011	49411	48311	49111	46511	45011	48411	44211	45711	46611	48111	47711	46911	47111	47811	46211
Alimentary System (continued)																													
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous			X		X	X		X					X						X	X			X	X			X		
Papilloma squamous, multiple							X		X	X		X		X												X		X	
Squamous cell carcinoma	X		X	X	X	X	X	X		X	X	X	X		X	X	X	X	X		X	X		X	X	X			
Squamous cell carcinoma, multiple																							X				X	X	X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tongue																							+						
Cardiovascular System																													
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																													
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Adenoma																													
Squamous cell carcinoma, metastatic, stomach																													
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	M	+	M	M	M	M	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M
Pituitary gland	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars intermedia, adenoma																													
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																													
Tissue NOS																													
Genital System																													
Clitoral gland										M								+									+		
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+
Adenoma																													
Cystadenoma																													
Squamous cell carcinoma, metastatic, stomach													X														X		
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	M	+	+		+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal						X			X	X								X											
Sarcoma																					X								
Endometrium, adenocarcinoma																													
Endometrium, adenoma																													

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	469	469	473	473	473	480	480	487	487	490	491	494	496	498	501	504	505	506	508	508	511	511	511	511	511	511	
Carcass ID Number	47001	48081	44881	45311	45411	47111	47911	44501	49001	44001	45611	47411	49211	44911	45911	46111	47511	43911	44111	47211	43811	44411	46711	46811	47311	48911	**Total Tissues/ Tumors**
Alimentary System (continued)																											
Salivary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Papilloma squamous	X											X		X													13
Papilloma squamous, multiple								X		X					X				X			X	X	X	X	X	16
Squamous cell carcinoma					X			X							X												24
Squamous cell carcinoma, multiple	X	X	X	X		X	X		X		X	X	X	X		X	X	X	X	X	X		X	X	X	X	25
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	54
Tongue																											1
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Adenoma											X																1
Squamous cell carcinoma, metastatic, stomach								X																			1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Parathyroid gland	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	44
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Pars intermedia, adenoma																					X						1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
General Body System																											
Tissue NOS																							+				1
Genital System																											
Clitoral gland												+	+		+					+				+		+	8
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	53
Adenoma			X																								1
Cystadenoma																					X						1
Squamous cell carcinoma, metastatic, stomach								X																			3
Oviduct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	54
Polyp stromal				X																					X		6
Sarcoma																											1
Endometrium, adenocarcinoma								X							X					X		X		X		X	6
Endometrium, adenoma										X				X				X									3

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	295	341	377	378	379	379	383	383	390	397	405	407	411	419	420	424	427	432	434	439	442	445	445	447	460	466	467	468	469
Carcass ID Number	45111	44611	47611	49311	48511	49511	43611	46311	48611	48711	48211	44311	45211	46011	49411	48311	49111	46511	45011	48411	44211	45711	46611	48111	47711	46911	47111	47811	46211
Hematopoietic System																													
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, squamous cell carcinoma, metastatic, stomach										X			X						X						X				
Lymph node, mandibular	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																											X		
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach																X											X		
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uterus																					X								
Squamous cell carcinoma, metastatic, stomach			X															X											
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach													X														X		
Integumentary System																													
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoacanthoma		X																	X										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basosquamous tumor benign																													
Musculoskeletal System																													
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle										+				+													+		
Squamous cell carcinoma, metastatic, stomach										X																	X		
Nervous System																													
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	469	469	473	473	473	480	480	487	487	490	491	494	496	498	501	504	505	506	508	508	511	511	511	511	511	
Carcass ID Number	47001	48081	44881	45331	45411	47111	47991	44501	49001	44001	45611	47411	49211	44911	45991	46111	47551	43991	44121	47211	43811	44441	46711	46811	47331	48891	**Total Tissues/ Tumors**
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Mediastinal, squamous cell carcinoma, metastatic, stomach																											4
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Squamous cell carcinoma, metastatic, stomach																											1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	53
Squamous cell carcinoma, metastatic, stomach					X																						3
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	54
Sarcoma, metastatic, uterus																											1
Squamous cell carcinoma, metastatic, stomach				X												X											4
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	52
Squamous cell carcinoma, metastatic, stomach																											2
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	54
Adenoacanthoma																											2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Basosquamous tumor benign																							X				1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Skeletal muscle										+				+													5
Squamous cell carcinoma, metastatic, stomach														X													3
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	295	341	377	378	379	379	383	383	390	397	405	407	411	419	420	424	427	432	434	439	442	445	445	447	460	466	467	468	469
Carcass ID Number	45111	44611	47611	49311	48511	49511	43611	46311	48611	48711	48211	44311	45211	46011	49411	48311	49111	46511	45011	48411	44211	45711	46611	48111	47711	46911	47111	47811	46211
Respiratory System																													
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoacanthoma, metastatic, mammary gland		X																											
Alveolar/bronchiolar adenoma					X						X										X								
Alveolar/bronchiolar adenoma, multiple																													
Squamous cell carcinoma, metastatic, stomach																X									X				
Squamous cell carcinoma, metastatic, intestine large							X																						
Mediastinum, squamous cell carcinoma, metastatic, stomach																													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																													
Eye																												+	
Harderian gland																							+						
Adenoma																													
Bilateral, adenoma																							X						
Urinary System																													
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uterus																					X								
Urinary bladder	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																													
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic														X															
Lymphoma malignant mixed																													

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane: 60 mg/kg (continued)

Number of Days on Study	4 6 9	4 6 9	4 7 3	4 7 3	4 7 3	4 8 0	4 8 0	4 8 7	4 8 7	4 9 0	4 9 1	4 9 4	4 9 6	4 9 8	5 0 1	5 0 4	5 0 5	5 0 6	5 0 8	5 0 8	5 1 1	5 1 1	5 1 1	5 1 1	5 1 1	
Carcass ID Number	4 7 0 1	4 8 8 1	4 4 8 1	4 5 3 1	4 5 4 1	4 7 1 1	4 7 9 1	4 4 5 1	4 9 0 1	4 4 0 1	4 5 6 1	4 7 4 1	4 9 2 1	4 4 9 1	4 5 9 1	4 6 1 1	4 7 5 1	4 3 9 1	4 4 1 1	4 7 2 1	4 3 8 1	4 4 4 1	4 6 7 1	4 6 8 1	4 7 3 1	4 8 9 1	**Total Tissues/ Tumors**
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Adenoacanthoma, metastatic, mammary gland																										1
Alveolar/bronchiolar adenoma	X					X	X						X	X			X									9
Alveolar/bronchiolar adenoma, multiple												X														1
Squamous cell carcinoma, metastatic, stomach																X										3
Squamous cell carcinoma, metastatic, intestine large																										1
Mediastinum, squamous cell carcinoma, metastatic, stomach																			X							1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Special Senses System																										
Eye	+																									2
Harderian gland	+						+	+				+	+				+	+	+		+					10
Adenoma	X						X	X				X	X				X	X	X		X					9
Bilateral, adenoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Sarcoma, metastatic, uterus																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	52
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	55
Lymphoma malignant lymphocytic										X																2
Lymphoma malignant mixed				X																						1

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Harderian Gland: Adenoma				
Overall rate[a]	3/60 (5%)	6/60 (10%)	7/60 (12%)	10/60 (17%)
Adjusted rate[b]	6.5%	26.8%	39.0%	57.2%
15-Month interim evaluation[c]	1/10 (10%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate[d]	2/41 (5%)	2/13 (15%)	0/0 (0%)	0/0 (0%)
First incidence (days)	461 (I)	558	545	445
Life table test[e]	P<0.001	P=0.036	P<0.001	P<0.001
Logistic regression test[e]	P=0.004	P=0.191	P=0.077	P=0.060
Cochran-Armitage test[e]	P=0.040			
Fisher exact test[e]		P=0.245	P=0.161	P=0.037
Liver: Hepatocellular Adenoma				
Overall rate	7/60 (12%)	9/60 (15%)	9/60 (15%)	36/60 (60%)
Adjusted rate	16.1%	47.7%	65.0%	97.1%
15-Month interim evaluation	1/10 (10%)	0/10 (0%)	1/9 (11%)	5/5 (100%)
Terminal rate	6/41 (15%)	5/13 (38%)	0/0 (0%)	0/0 (0%)
First incidence (days)	461 (I)	540	454	420
Life table test	P<0.001	P=0.011	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.164	P=0.057	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.395	P=0.395	P<0.001
Liver: Hepatocellular Carcinoma				
Overall rate	1/60 (2%)	3/60 (5%)	0/60 (0%)	2/60 (3%)
Adjusted rate	2.4%	13.2%	0.0%	14.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	1/41 (2%)	1/13 (8%)	0/0 (0%)	0/0 (0%)
First incidence (days)	733 (T)	582	-[f]	494
Life table test	P<0.001	P=0.100	-	P=0.036
Logistic regression test	P=0.259	P=0.242	-	P=0.395
Cochran-Armitage test	P=0.577			
Fisher exact test		P=0.309	P=0.500N	P=0.500
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rate	8/60 (13%)	11/60 (18%)	9/60 (15%)	36/60 (60%)
Adjusted rate	18.5%	55.8%	65.0%	97.1%
15-Month interim evaluation	1/10 (10%)	0/10 (0%)	1/9 (11%)	5/5 (100%)
Terminal rate	7/41 (17%)	6/13 (46%)	0/0 (0%)	0/0 (0%)
First incidence (days)	461 (I)	540	454	420
Life table test	P<0.001	P=0.003	P<0.001	P<0.001
Logistic regression test	P<0.001	P=0.093	P=0.067	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.309	P=0.500	P<0.001
Lung: Alveolar/bronchiolar Adenoma				
Overall rate	4/60 (7%)	3/60 (5%)	0/60 (0%)	11/60 (18%)
Adjusted rate	9.4%	17.5%	0.0%	43.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	1/5 (20%)
Terminal rate	3/41 (7%)	2/13 (15%)	0/0 (0%)	0/0 (0%)
First incidence (days)	699	574	-	379
Life table test	P<0.001	P=0.314	-	P<0.001
Logistic regression test	P<0.001	P=0.585	P=0.939N	P=0.054
Cochran-Armitage test	P=0.002			
Fisher exact test		P=0.500N	P=0.059N	P=0.048

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Lung: Alveolar/bronchiolar Carcinoma				
Overall rate	3/60 (5%)	0/60 (0%)	0/60 (0%)	0/60 (0%)
Adjusted rate	6.9%	0.0%	0.0%	0.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	2/41 (5%)	0/13 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	631	-	-	-
Life table test	P=0.999N	P=0.324N	-	-
Logistic regression test	P=0.645N	P=0.181N	P=0.502N	P=0.794N
Cochran-Armitage test	P=0.135N			
Fisher exact test		P=0.122N	P=0.122N	P=0.122N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rate	7/60 (12%)	3/60 (5%)	0/60 (0%)	11/60 (18%)
Adjusted rate	16.1%	17.5%	0.0%	43.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	1/5 (20%)
Terminal rate	5/41 (12%)	2/13 (15%)	0/0 (0%)	0/0 (0%)
First incidence (days)	631	574	-	379
Life table test	P<0.001	P=0.588	-	P<0.001
Logistic regression test	P<0.001	P=0.363N	P=0.305N	P=0.103
Cochran-Armitage test	P=0.022			
Fisher exact test		P=0.161N	P=0.006N	P=0.222
Oral Cavity (Pharynx and Tongue): Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	0/60 (0%)	1/60 (2%)	5/60 (8%)
Adjusted rate	0.0%	0.0%	4.2%	16.3%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	0/41 (0%)	0/13 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	-	551	427
Life table test	P<0.001	-	P=0.370	P=0.006
Logistic regression test	P=0.008	-	P=0.552	P=0.128
Cochran-Armitage test	P=0.001			
Fisher exact test		-	P=0.500	P=0.029
Oral Cavity (Pharynx and Tongue): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	1/60 (2%)	0/60 (0%)	2/60 (3%)	5/60 (8%)
Adjusted rate	2.4%	0.0%	9.8%	16.3%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	1/41 (2%)	0/13 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	733 (T)	-	551	427
Life table test	P<0.001	P=0.728N	P=0.086	P=0.006
Logistic regression test	P=0.024	P=0.728N	P=0.365	P=0.212
Cochran-Armitage test	P=0.011			
Fisher exact test		P=0.500N	P=0.500	P=0.103
Pharynx: Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	0/60 (0%)	1/60 (2%)	5/60 (8%)
Adjusted rate	0.0%	0.0%	4.2%	16.3%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	0/41 (0%)	0/13 (0%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	-	551	427
Life table test	P<0.001	-	P=0.370	P=0.006
Logistic regression test	P=0.008	-	P=0.552	P=0.128
Cochran-Armitage test	P=0.001			
Fisher exact test		-	P=0.500	P=0.029

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Pituitary Gland (Pars Distalis or Unspecified Site): Adenoma				
Overall rate	4/58 (7%)	2/56 (4%)	0/54 (0%)	0/58 (0%)
Adjusted rate	9.1%	14.1%	0.0%	0.0%
15-Month interim evaluation	1/10 (10%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	3/41 (7%)	1/12 (8%)	0/0 (0%)	0/0 (0%)
First incidence (days)	463 (I)	719	-	-
Life table test	P=0.669N	P=0.568	P=0.521N	P=0.638N
Logistic regression test	P=0.339N	P=0.480N	P=0.135N	P=0.218N
Cochran-Armitage test	P=0.043N			
Fisher exact test		P=0.356N	P=0.068N	P=0.059N
Stomach (Forestomach): Squamous Cell Papilloma				
Overall rate	0/60 (0%)	28/60 (47%)	27/60 (45%)	33/60 (55%)
Adjusted rate	0.0%	84.8%	73.1%	94.1%
15-Month interim evaluation	0/10 (0%)	5/10 (50%)	9/9 (100%)	4/5 (80%)
Terminal rate	0/41 (0%)	9/13 (69%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	461 (I)	442	377
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Stomach (Forestomach): Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	47/60 (78%)	55/60 (92%)	51/60 (85%)
Adjusted rate	0.0%	95.9%	100.0%	97.9%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	6/9 (67%)	2/5 (40%)
Terminal rate	0/41 (0%)	11/13 (85%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	414	312	295
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Stomach (Forestomach): Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rate	0/60 (0%)	54/60 (90%)	59/60 (98%)	59/60 (98%)
Adjusted rate	0.0%	100.0%	100.0%	100.0%
15-Month interim evaluation	0/10 (0%)	6/10 (60%)	9/9 (100%)	5/5 (100%)
Terminal rate	0/41 (0%)	13/13 (100%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	414	312	295
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
Uterus: Stromal Polyp				
Overall rate	0/60 (0%)	2/60 (3%)	2/60 (3%)	7/60 (12%)
Adjusted rate	0.0%	11.2%	3.8%	28.6%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	1/9 (11%)	1/5 (20%)
Terminal rate	0/41 (0%)	1/13 (8%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	643	312	379
Life table test	P<0.001	P=0.083	P=0.228	P<0.001
Logistic regression test	P=0.023	P=0.165	P=0.378	P=0.074
Cochran-Armitage test	P=0.002			
Fisher exact test		P=0.248	P=0.248	P=0.006

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Uterus: Adenoma				
Overall rate	0/60 (0%)	1/60 (2%)	0/60 (0%)	4/60 (7%)
Adjusted rate	0.0%	7.7%	0.0%	25.0%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	1/5 (20%)
Terminal rate	0/41 (0%)	1/13 (8%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	733 (T)	-	461 (I)
Life table test	P<0.001	P=0.272	-	P=0.001
Logistic regression test	P=0.009	P=0.272	-	P=0.134
Cochran-Armitage test	P=0.011			
Fisher exact test		P=0.500	-	P=0.059
Uterus: Carcinoma				
Overall rate	0/60 (0%)	4/60 (7%)	3/60 (5%)	8/60 (13%)
Adjusted rate	0.0%	25.4%	25.3%	64.2%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	2/5 (40%)
Terminal rate	0/41 (0%)	2/13 (15%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	698	582	461 (I)
Life table test	P<0.001	P=0.002	P=0.003	P<0.001
Logistic regression test	P<0.001	P=0.007	P=0.050	P=0.017
Cochran-Armitage test	P=0.006			
Fisher exact test		P=0.059	P=0.122	P=0.003
Uterus: Adenoma or Carcinoma				
Overall rate	0/60 (0%)	5/60 (8%)	3/60 (5%)	11/60 (18%)
Adjusted rate	0.0%	32.2%	25.3%	72.4%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	2/5 (40%)
Terminal rate	0/41 (0%)	3/13 (23%)	0/0 (0%)	0/0 (0%)
First incidence (days)	-	698	582	461 (I)
Life table test	P<0.001	P<0.001	P=0.278	P<0.001
Logistic regression test	P<0.001	P=0.002	P=0.050	P=0.003
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.029	P=0.122	P<0.001
All Organs: Histiocytic Sarcoma and Malignant Lymphoma				
Overall rate	17/60 (28%)	7/60 (12%)	3/60 (5%)	3/60 (5%)
Adjusted rate	38.4%	41.2%	26.7%	11.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	14/41 (34%)	4/13 (31%)	0/0 (0%)	0/0 (0%)
First incidence (days)	480	600	608	419
Life table test	P<0.001	P=0.465	P=0.036	P=0.107
Logistic regression test	P=0.235	P=0.216N	P=0.588N	P=0.613N
Cochran-Armitage test	P=0.002N			
Fisher exact test		P=0.019N	P<0.001N	P<0.001N
All Organs: Malignant Lymphoma (Histiocytic, Lymphocytic, or Undifferentiated Cell Type)				
Overall rate	15/60 (25%)	6/60 (10%)	3/60 (5%)	3/60 (5%)
Adjusted rate	34.8%	39.5%	26.7%	11.7%
15-Month interim evaluation	0/10 (0%)	0/10 (0%)	0/9 (0%)	0/5 (0%)
Terminal rate	13/41 (32%)	4/13 (31%)	0/0 (0%)	0/0 (0%)
First incidence (days)	691	705	608	419
Life table test	P<0.001	P=0.426	P=0.002	P=0.036
Logistic regression test	P=0.031	P=0.558N	P=0.297	P=0.511
Cochran-Armitage test	P=0.006N			
Fisher exact test		P=0.026N	P=0.002N	P=0.002N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
All Organs: Benign Neoplasms				
Overall rate	20/60 (33%)	36/60 (60%)	40/60 (67%)	53/60 (88%)
Adjusted rate	43.5%	96.8%	96.7%	100.0%
15-Month interim evaluation	3/10 (30%)	5/10 (50%)	9/9 (100%)	5/5 (100%)
Terminal rate	16/41 (39%)	12/13 (92%)	0/0 (0%)	0/0 (0%)
First incidence (days)	461 (I)	461 (I)	312	377
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P=0.003	P<0.001	P<0.001
All Organs: Malignant Neoplasms				
Overall rate	23/60 (38%)	48/60 (80%)	55/60 (92%)	58/60 (97%)
Adjusted rate	48.5%	97.9%	100.0%	100.0%
15-Month interim evaluation	0/10 (0%)	1/10 (10%)	6/9 (67%)	5/5 (100%)
Terminal rate	17/41 (41%)	12/13 (92%)	0/0 (0%)	0/0 (0%)
First incidence (days)	68	414	312	295
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001
All Organs: Benign or Malignant Neoplasms				
Overall rate	39/60 (65%)	54/60 (90%)	59/60 (98%)	60/60 (100%)
Adjusted rate	76.2%	100.0%	100.0%	100.0%
15-Month interim evaluation	3/10 (30%)	6/10 (60%)	9/9 (100%)	5/5 (100%)
Terminal rate	29/41 (71%)	13/13 (100%)	0/0 (0%)	0/0 (0%)
First incidence (days)	68	414	312	295
Life table test	P<0.001	P<0.001	P<0.001	P<0.001
Logistic regression test	P<0.001	P<0.001	P<0.001	P<0.001
Cochran-Armitage test	P<0.001			
Fisher exact test		P<0.001	P<0.001	P<0.001

(T)Terminal sacrifice
(I)15-Month interim evaluation
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, gallbladder, heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, salivary gland, spleen, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] 15-Month interim evaluation began on day 461
[d] Observed incidence at terminal kill
[e] Beneath the "Vehicle Control" column are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by **N**.
[f] Not applicable; no neoplasms in animal group

TABLE D4a
Historical Incidence of Oral Cavity Neoplasms in Female B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls	
	Squamous Cell Papilloma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute		
2,4-Diaminophenol•2HCl	0/50	0/50
Tribromomethane	0/49	0/49
Phenylbutazone	0/50	0/50
Probenecid	0/49	0/49
Overall Historical Incidence		
Total	0/698	0/698

[a] Data as of 3 April 1991

TABLE D4b
Historical Incidence of Forestomach Neoplasms in Female B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Squamous Cell Papilloma	Squamous Cell Carcinoma	Squamous Cell Papilloma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	1/50	1/50	2/50
Tribromomethane	0/49	0/49	0/49
Phenylbutazone	3/50	2/50	5/50
Probenecid	3/49	0/49	3/49
Overall Historical Incidence			
Total	24/698 (3.4%)	3/698 (0.4%)	27/698 (3.9%)
Standard deviation	3.1%	1.2%	3.5%
Range	0%-10%	0%-4%	0%-10%

[a] Data as of 3 April 1991

TABLE D4c
Historical Incidence of Liver Neoplasms in Female B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute			
2,4-Diaminophenol•2HCl	3/50	1/50	4/50
Tribromomethane	3/49	1/49	4/49
Phenylbutazone	4/50	1/50	5/50
Probenecid	3/48	2/48	5/48
Overall Historical Incidence			
Total	59/697 (8.5%)	35/697 (5.0%)	88/697 (12.6%)
Standard deviation	6.6%	3.7%	8.0%
Range	2%-26%	2%-14%	2%-34%

[a] Data as of 3 April 1991

TABLE D4d
Historical Incidence of Harderian Gland Adenoma in Female B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls
Historical Incidence at EG&G Mason Research Institute	
2,4-Diaminophenol•2HCl	1/50
Tribromomethane	0/49
Phenylbutazone	1/50
Probenecid	0/49
Overall Historical Incidence	
Total	20/698 (2.9%)
Standard deviation	2.2%
Range	0%-6%

[a] Data as of 3 April 1991

TABLE D4e
Historical Incidence of Uterine Neoplasms in Female B6C3F$_1$ Mice Receiving Corn Oil Vehicle by Gavage[a]

Study	Incidence in Controls			
	Stromal Polyp	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at EG&G Mason Research Institute				
2,4-Diaminophenol•2HCl	0/50	0/50	0/50	0/50
Tribromomethane	1/49	0/49	0/49	0/49
Phenylbutazone	0/50	0/50	0/50	0/50
Probenecid	0/49	0/49	0/49	0/49
Overall Historical Incidence				
Total	11/698 (1.6%)	0/698	3/698 (0.4%)	3/698 (0.4%)
Standard deviation	2.0%		0.9%	0.9%
Range	0%-6%		0%-2%	0%-2%

[a] Data as of 3 April 1991

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane[a]

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	10	10	9	5
Early deaths				
Accidental deaths			1	
Moribund	8	34	37	48
Natural deaths	1	3	4	1
Scheduled sacrifice			9	6
Survivors				
Terminal sacrifice	41	13		
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(10)	(9)	(5)
Basophilic focus		1 (10%)		
Clear cell focus	1 (10%)			
Eosinophilic focus		1 (10%)	1 (11%)	5 (100%)
Stomach, forestomach	(10)	(10)	(9)	(5)
Hyperkeratosis	1 (10%)	10 (100%)	9 (100%)	5 (100%)
Hyperplasia, basal cell			1 (11%)	
Hyperplasia, squamous	1 (10%)	10 (100%)	9 (100%)	5 (100%)
Necrosis		1 (10%)	2 (22%)	
Stomach, glandular	(10)	(10)	(9)	(5)
Hyperplasia		4 (40%)	2 (22%)	1 (20%)
Cardiovascular System				
None				
Endocrine System				
Pituitary gland	(10)	(10)	(9)	(5)
Pars intermedia, hyperplasia				1 (20%)
General Body System				
None				
Genital System				
Ovary	(10)	(9)	(9)	(5)
Cyst	1 (10%)			
Degeneration, cystic		1 (11%)	1 (11%)	1 (20%)
Uterus	(10)	(10)	(9)	(5)
Endometrium, hyperplasia		3 (30%)	3 (33%)	5 (100%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
15-Month Interim Evaluation (continued)				
Hematopoietic System				
Spleen	(10)	(10)	(9)	(4)
Hematopoietic cell proliferation		1 (10%)		1 (25%)
Integumentary System				
None				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Esophagus	(50)	(50)	(51)	(54)
Hyperkeratosis				1 (2%)
Inflammation, acute			1 (2%)	
Liver	(50)	(50)	(51)	(55)
Basophilic focus	1 (2%)	3 (6%)	1 (2%)	
Clear cell focus		1 (2%)		1 (2%)
Cyst		1 (2%)		1 (2%)
Eosinophilic focus		6 (12%)	9 (18%)	33 (60%)
Eosinophilic focus, multiple				1 (2%)
Fatty change, diffuse	1 (2%)	1 (2%)		
Fatty change, focal			1 (2%)	1 (2%)
Fibrosis				1 (2%)
Granuloma		1 (2%)		
Hematopoietic cell proliferation				4 (7%)
Mixed cell focus	3 (6%)	1 (2%)	2 (4%)	2 (4%)
Necrosis	1 (2%)	6 (12%)	5 (10%)	10 (18%)
Thrombus		1 (2%)		
Mesentery	(3)	(17)	(20)	(10)
Fat, necrosis	2 (67%)	1 (6%)		

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Pancreas	(49)	(50)	(51)	(55)
Cyst	1 (2%)			
Acinus, hyperplasia			1 (2%)	2 (4%)
Duct, ectasia			1 (2%)	
Stomach, forestomach	(50)	(49)	(51)	(55)
Hyperkeratosis	4 (8%)	15 (31%)	14 (27%)	33 (60%)
Hyperplasia, squamous	10 (20%)	15 (31%)	14 (27%)	31 (56%)
Ulcer	2 (4%)			1 (2%)
Stomach, glandular	(49)	(50)	(50)	(54)
Hyperplasia	1 (2%)			
Inflammation, acute				1 (2%)
Tongue		(1)	(3)	(1)
Acanthosis			1 (33%)	
Cardiovascular System				
Heart	(50)	(50)	(51)	(55)
Cardiomyopathy	1 (2%)			
Mineralization		1 (2%)	2 (4%)	
Thrombus			1 (2%)	
Artery, inflammation, chronic active	1 (2%)			
Endocrine System				
Adrenal gland	(50)	(47)	(50)	(54)
Accessory adrenal cortical nodule				1 (2%)
Adrenal gland, cortex	(50)	(47)	(49)	(54)
Accessory adrenal cortical nodule		1 (2%)	1 (2%)	
Adrenal gland, medulla	(49)	(44)	(47)	(54)
Hyperplasia	1 (2%)			
Pituitary gland	(48)	(46)	(45)	(53)
Pars distalis, angiectasis	1 (2%)	1 (2%)		
Pars distalis, hyperplasia	12 (25%)	7 (15%)	2 (4%)	1 (2%)
Thyroid gland	(49)	(49)	(49)	(54)
Follicular cell, hyperplasia	8 (16%)	1 (2%)		
General Body System				
None				
Genital System				
Clitoral gland	(3)	(4)	(5)	(8)
Dilatation	2 (67%)	3 (75%)	5 (100%)	7 (88%)
Ovary	(49)	(50)	(48)	(53)
Abscess	1 (2%)		1 (2%)	
Angiectasis	1 (2%)			
Cyst	9 (18%)	9 (18%)	6 (13%)	9 (17%)
Hemorrhage	2 (4%)		1 (2%)	
Thrombus				1 (2%)

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Genital System (continued)				
Uterus	(50)	(50)	(51)	(54)
Abscess	1 (2%)			
Cyst			3 (6%)	
Dilatation	6 (12%)	6 (12%)		1 (2%)
Hemorrhage	1 (2%)			
Infiltration cellular, histiocyte				1 (2%)
Thrombus	1 (2%)			1 (2%)
Endometrium, hyperplasia	43 (86%)	38 (76%)	41 (80%)	52 (96%)
Hematopoietic System				
Lymph node	(50)	(49)	(51)	(55)
Lumbar, hematopoietic cell proliferation	1 (2%)	1 (2%)		
Mediastinal, hematopoietic cell proliferation			1 (2%)	
Mediastinal, infiltration cellular, plasma cell	1 (2%)	2 (4%)		1 (2%)
Mediastinal, infiltration cellular, histiocyte		1 (2%)	2 (4%)	
Pancreatic, infiltration cellular, plasma cell				1 (2%)
Renal, inflammation, granulomatous	1 (2%)			
Lymph node, mandibular	(48)	(47)	(48)	(52)
Hematopoietic cell proliferation			1 (2%)	
Infiltration cellular, plasma cell		1 (2%)		
Lymph node, mesenteric	(48)	(45)	(50)	(53)
Angiectasis		2 (4%)		
Hematopoietic cell proliferation	1 (2%)		1 (2%)	1 (2%)
Infiltration cellular, plasma cell				1 (2%)
Inflammation, granulomatous	1 (2%)			
Thrombus				1 (2%)
Spleen	(49)	(50)	(51)	(54)
Hematopoietic cell proliferation	8 (16%)	35 (70%)	45 (88%)	46 (85%)
Hemorrhage	1 (2%)			
Integumentary System				
Skin	(50)	(50)	(51)	(55)
Erosion		2 (4%)		
Musculoskeletal System				
None				
Nervous System				
None				

TABLE D5
Summary of the Incidence of Nonneoplastic Lesions in Female Mice at the 15-Month Interim Evaluation and in the 2-Year Gavage Study of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
2-Year Study (continued)				
Respiratory System				
Lung	(50)	(50)	(51)	(55)
Hemorrhage	3 (6%)	4 (8%)	2 (4%)	
Infiltration cellular, histiocyte	2 (4%)	3 (6%)		1 (2%)
Inflammation, acute		3 (6%)	6 (12%)	
Leukocytosis		1 (2%)	2 (4%)	
Alveolar epithelium, hyperplasia			2 (4%)	1 (2%)
Bronchiole, hyperplasia			3 (6%)	43 (78%)
Nose	(50)	(49)	(51)	(55)
Inflammation, acute	1 (2%)	1 (2%)	5 (10%)	2 (4%)
Special Senses System				
Harderian gland	(2)	(7)	(8)	(10)
Hyperplasia			1 (13%)	
Urinary System				
Kidney	(49)	(50)	(51)	(55)
Nephropathy		1 (2%)	2 (4%)	1 (2%)
Cortex, mineralization	1 (2%)	1 (2%)		
Papilla, mineralization			1 (2%)	
Renal tubule, pigmentation	2 (4%)	1 (2%)		

[a] Number of animals examined microscopically at site and number of animals with lesion

APPENDIX E
GENETIC TOXICOLOGY

GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST

Testing was performed as reported by Haworth *et al.* (1983). 1,2,3-Trichloropropane was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). It was incubated with the *Salmonella typhimurium* tester strains (TA97, TA98, TA100, TA1535, and TA1537) either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver) for 20 minutes at 37° C prior to the addition of soft agar supplemented with *l*-histidine and *d*-biotin, and subsequent plating on minimal glucose agar plates. Incubation continued for an additional 48 hours.

Each trial consisted of triplicate plates of concurrent positive and negative controls and of at least five doses of 1,2,3-trichloropropane. High dose was limited by toxicity. All negative assays were repeated and all positive assays were repeated under the conditions which elicited the positive response.

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

MOUSE LYMPHOMA PROTOCOL

The experimental protocol is presented in detail by Myhr *et al.* (1985). 1,2,3-Trichloropropane was supplied as a coded aliquot by Radian Corporation. The highest dose of 1,2,3-trichloropropane was determined by solubility or toxicity and did not exceed 50 µg/mL. L5178Y mouse lymphoma cells were maintained at 37° C as suspension cultures in Fischer's medium supplemented with 2 mM *l*-glutamine, 110 µg/mL sodium pyruvate, 0.05% pluronic F68, antibiotics, and heat-inactivated horse serum; normal cycling time was about 10 hours. To reduce the number of spontaneously occurring trifluorothymidine (TFT) resistant cells, subcultures were exposed once to medium containing THMG (thymidine, hypoxanthine, methotrexate, glycine) for 1 day, to THG for 1 day, and to normal medium for 3 to 5 days. For cloning, horse serum content was increased and Noble agar was added. Freshly prepared S9 metabolic activation factors were obtained from the livers of either Aroclor 1254-induced or noninduced Fischer 344 male rats.

All treatment levels within an experiment, including concurrent positive and solvent controls, were replicated. Treated cultures contained 6×10^6 cells in a 10 mL volume of medium. This volume included the S9 fraction in those experiments performed with metabolic activation. Incubation with 1,2,3-trichloropropane continued for 4 hours, at which time the medium plus 1,2,3-trichloropropane was removed and the cells were resuspended in 20 mL of fresh medium and incubated for an additional 48 hours to express the mutant phenotype. Cell density was monitored so that log phase growth was maintained. After the 48-hour expression period, 3×10^6 cells were plated in medium and soft agar supplemented with trifluorothymidine for selection of TFT-resistant cells ($TK^{-/-}$), and 600 cells were plated in nonselective medium and soft agar to determine cloning efficiency. Plates were incubated at 37° C in 5% CO_2 for 10 to 12 days. All data were evaluated statistically for both trend and peak response. Both responses had to be significant ($P<0.05$) for 1,2,3-trichloropropane to be considered capable of inducing TFT-resistance; a single significant response led to a "questionable" conclusion, and the absence of both a trend and a peak response resulted in a "negative" call.

Minimum criteria for accepting an experiment as valid and a detailed description of the statistical analysis and data evaluation are presented in Myhr *et al.* (1985). This assay is initially performed

without S9; since a clearly positive response was not obtained, the experiment was repeated with induced S9.

CHINESE HAMSTER OVARY CELL CYTOGENETICS ASSAYS

Testing was performed as reported by Galloway *et al*. (1987) and is presented briefly below. 1,2,3-Trichloropropane was sent to the laboratory as a coded aliquot from Radian Corporation. It was tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCEs) and chromosomal aberrations (Abs) both in the presence and absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least three doses of 1,2,3-trichloropropane; the high dose was limited by toxicity.

In the SCE test without S9, CHO cells were incubated for 25 hours with 1,2,3-trichloropropane in McCoy's 5A medium supplemented with 10% fetal bovine serum, *l*-glutamine (2 mM), and antibiotics. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 25 hours, the medium containing 1,2,3-trichloropropane was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2 to 3 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with 1,2,3-trichloropropane, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing BrdU and no 1,2,3-trichloropropane and incubation proceeded for an additional 25 to 26 hours, with Colcemid present for the final 2 hours. Harvesting and staining was the same as for cells treated without S9.

In the chromosome aberration test without S9, cells were incubated in McCoy's 5A medium with 1,2,3-trichloropropane for 8 hours; Colcemid was added and incubation continued for 2 to 3 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the Abs test with S9, cells were treated with 1,2,3-trichloropropane and S9 for 2 hours, after which the treatment medium was removed and the cells incubated for 8 to 9 hours in fresh medium, with Colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9.

Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind and those from a single test were read by the same person. For the SCE test, usually 50 second-division metaphase cells were scored for frequency of SCEs per cell from each dose level; 100 first-division metaphase cells were scored at each dose level for the Abs test unless numbers of Abs were extremely high or toxicity limited the available cells. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

Statistical analyses were conducted on both the slopes of the dose-response curves and the individual dose points. An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001. Chromosomal aberration data is presented as percentage of cells with aberrations. As with SCEs, both the dose-response curve and individual dose points were statistically analyzed. For a single trial, a statistically significant ($P<0.05$) difference for one dose point and a significant trend ($P<0.015$) were considered weak evidence for a positive response; significant differences for two or more doses indicated the trial was positive (Galloway *et al*., 1987).

RESULTS

1,2,3-Trichloropropane was tested for mutagenicity in *Salmonella typhimurium* by two laboratories using a preincubation protocol with and without Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9 (Table E1; Haworth *et al*., 1983). Mutagenic activity was observed in the presence of either species of S9 in strains TA97, TA100, and TA1535; for TA98, one laboratory reported increases in revertant colonies with either species of S9, and in the other laboratory, the mutagenic activity of 1,2,3-trichloropropane was observed only with induced hamster S9. No increase in revertants was observed with TA1537, with or without S9.

A positive response was obtained with 1,2,3-trichloropropane in the presence of Aroclor 1254-induced male Fisher rat liver S9 in the mouse lymphoma assay for induction of trifluorothymidine resistance in L5178Y cells; the lowest effective dose was 0.01 μL/mL (Table E2). Without S9, no induction of trifluorothymidine resistance was noted at doses below those which produced precipitation of 1,2,3-trichloropropane.

In cytogenetic tests with Chinese hamster ovary cells, 1,2,3-trichloropropane induced both sister chromatid exchanges (Table E3) and chromosomal aberrations (Table E4) in the presence of Aroclor 1254-induced male Sprague-Dawley rat liver S9; neither endpoint was significantly elevated in the absence of S9. In the single Abs trial without S9, an elevation in Abs was noted for the 943.7 μg/mL dose but the trend analysis was not significant and the call for this trial was therefore concluded to be questionable. Severe chemical-induced cytotoxicity reduced the number of scorable cells in this trial. In the Abs test with S9, the first trial was invalidated due to a lack of metaphase I cells available for analysis at two of the four doses tested. In trial 2, a strong induction of Abs was noted, along with marked cytotoxicity. The relationship, if any, between cytotoxicity and chromosomal aberrations has not been defined (Scott *et al.*, 1991). In the case of 1,2,3-trichloropropane, marked cytotoxicity occurred in all three Abs trials, yet a clear induction of Abs was noted in only one trial.

In conclusion, 1,2,3-trichloropropane demonstrated mutagenic activity in all of the *in vitro* assays conducted, and this mutagenic activity was dependent upon S9 activation.

TABLE E1
Mutagenicity of 1,2,3-Trichloropropane in *Salmonella typhimurium*[a]

Strain	Dose (μg/plate)	Revertants/plate[b] -S9	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
Study performed at SRI, International						
TA100						
	0	138 ± 11.8	179 ± 9.9	144 ± 4.7	158 ± 6.2	133 ± 4.3
	3	145 ± 21.0	267 ± 59.4	210 ± 26.1	141 ± 17.2	130 ± 1.9
	10	139 ± 5.6	458 ± 23.9	339 ± 18.6	180 ± 5.3	140 ± 6.5
	33	142 ± 14.6	492 ± 75.5	690 ± 24.3	211 ± 16.9	166 ± 9.4
	100	135 ± 22.0	816 ± 121.4	1,210 ± 44.4	344 ± 9.8	282 ± 12.8
	333	140 ± 7.0	1,005 ± 30.9	1,862 ± 50.8	652 ± 28.6	461 ± 37.9
Trial summary		Negative	Positive	Positive	Positive	Positive
Positive control[c]		352 ± 12.7	2,409 ± 23.4	1,121 ± 67.6	1,079 ± 36.4	688 ± 12.7
TA1535						
	0	12 ± 4.1	13 ± 0.0	10 ± 2.6	9 ± 2.7	5 ± 1.0
	1			41 ± 6.1		
	3	7 ± 0.9	47 ± 4.4	71 ± 10.0	10 ± 2.6	8 ± 0.9
	10	9 ± 1.5	98 ± 18.2	128 ± 20.5	11 ± 3.1	7 ± 1.2
	33	7 ± 1.5	209 ± 31.7	266 ± 46.1	31 ± 2.6	21 ± 4.8
	100	13 ± 0.6	422 ± 34.6	481 ± 44.6	73 ± 3.5	45 ± 7.9
	333	9 ± 0.3	734 ± 109.3		205 ± 7.0	80 ± 7.2
Trial summary		Negative	Positive	Positive	Positive	Positive
Positive control		294 ± 30.5	514 ± 7.3	179 ± 5.7	225 ± 18.5	103 ± 14.3
TA1537						
	0	5 ± 2.2	6 ± 0.6		6 ± 2.1	
	3	4 ± 0.9	7 ± 1.3		4 ± 0.9	
	10	4 ± 0.7	8 ± 0.3		4 ± 0.6	
	33	5 ± 1.8	8 ± 0.0		5 ± 1.0	
	100	6 ± 1.3	12 ± 2.4		6 ± 0.9	
	333	5 ± 1.3	7 ± 3.2		10 ± 2.2	
Trial summary		Negative	Negative		Negative	
Positive control		330 ± 31.5	657 ± 18.8		269 ± 5.2	
TA98						
	0	19 ± 1.5	26 ± 5.3	54 ± 2.2	26 ± 6.1	
	1			50 ± 5.8		
	3	15 ± 3.0	25 ± 0.7	65 ± 2.0	23 ± 2.7	
	33	18 ± 0.7	58 ± 3.8	70 ± 2.7	22 ± 1.3	
	100	21 ± 1.7	86 ± 12.4	100 ± 19.8	33 ± 2.6	
	333	16 ± 1.9	97 ± 19.9		38 ± 0.3	
Trial summary		Negative	Positive	Positive	Negative	
Positive control		793 ± 43.1	1,884 ± 71.5	395 ± 3.6	697 ± 40.5	

TABLE E1
Mutagenicity of 1,2,3-Trichloropropane in *Salmonella typhimurium* (continued)

Strain	Dose (μg/plate)	Revertants/plate -S9 Trial 1	-S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% hamster S9 Trial 3	+10% rat S9 Trial 1	+10% rat S9 Trial 2
Study performed at Microbiological Associates								
TA100								
	0	78 ± 6.5	106 ± 4.7	241 ± 21.1	81 ± 1.9	89 ± 3.8	93 ± 2.3	219 ± 1.0
	10	88 ± 1.2		527 ± 14.5	762 ± 29.7	728 ± 32.7	176 ± 3.0	
	33	94 ± 2.5	121 ± 2.5	1,008 ± 18.8	1,263 ± 20.0	1,122 ± 29.0	349 ± 10.2	380 ± 7.8
	100	86 ± 7.1	106 ± 4.2	1,628 ± 57.7	2,612 ± 269.1	2,728 ± 44.2	748 ± 27.5	700 ± 53.8
	333	87 ± 3.8	108 ± 2.7	2,292 ± 136.9	2,879 ± 87.3[d]	3,235 ± 210.9	1,518 ± 32.7	1,242 ± 54.3
	666	115 ± 4.0		Toxic	Toxic	148 ± 18.6[d]	1,924 ± 55.3	
	667		121 ± 4.5[d]					1,786 ± 24.2[d]
	1,000		Toxic					Toxic
Trial summary		Equivocal	Negative	Positive	Positive	Positive	Positive	Positive
Positive control		446 ± 27.0	410 ± 7.2	524 ± 17.9	355 ± 12.7	2,400 ± 65.0	509 ± 17.4	915 ± 26.9

Strain	Dose (μg/plate)	Revertants/plate -S9 Trial 1	-S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
TA1535							
	0	19 ± 2.4	21 ± 1.7	4 ± 0.6	8 ± 1.9	22 ± 2.3	47 ± 4.8
	10	14 ± 0.9		178 ± 6.7	159 ± 16.5	33 ± 1.9	
	33	17 ± 1.9	29 ± 5.5	364 ± 12.3	325 ± 5.9	107 ± 2.0	94 ± 4.7
	100	19 ± 3.2	24 ± 2.8	786 ± 32.8	720 ± 33.5	203 ± 7.9	203 ± 11.5
	333	20 ± 3.8	31 ± 2.3	1,286 ± 22.0[d]	1,340 ± 29.7	456 ± 22.6	415 ± 4.2
	666	22 ± 2.2		Toxic	Toxic	549 ± 38.7	
	667		23 ± 1.2[d]				544 ± 37.9[d]
	1,000		12 ± 0.5[d]				147 ± 20.4[d]
Trial summary		Negative	Negative	Positive	Positive	Positive	Positive
Positive control		280 ± 18.0	330 ± 18.8	59 ± 4.2	256 ± 8.7	239 ± 15.2	254 ± 11.9
TA97							
	0	74 ± 2.8	142 ± 4.4	108 ± 6.0	137 ± 3.0	111 ± 5.8	183 ± 20.5
	10	84 ± 4.2		211 ± 6.4	194 ± 6.5	133 ± 9.1	
	33	64 ± 8.5	177 ± 2.8	365 ± 5.0	319 ± 20.3	162 ± 8.4	233 ± 5.8
	100	78 ± 3.5	131 ± 12.2	779 ± 20.1	691 ± 24.7	219 ± 12.6	270 ± 7.2
	333	93 ± 2.5	160 ± 17.0	1,422 ± 50.3	358 ± 54.5[d]	408 ± 34.4	391 ± 7.3
	666	75 ± 2.6		270 ± 11.3[d]	Toxic	489 ± 5.0	
	667		99 ± 3.8[d]				520 ± 15.2
	1,000		97 ± 2.0[d]				518 ± 16.1
Trial summary		Negative	Negative	Positive	Positive	Positive	Positive
Positive control		105 ± 5.2	345 ± 10.0	521 ± 4.5	532 ± 10.6	1,411 ± 29.8	1,307 ± 28.3

TABLE E1
Mutagenicity of 1,2,3-Trichloropropane in *Salmonella typhimurium* (continued)

Strain	Dose (μg/plate)	Revertants/plate -S9 Trial 1	-S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
TA98							
	0	18 ± 4.6	22 ± 2.4	38 ± 1.2	59 ± 4.9	36 ± 6.2	38 ± 1.3
	10	19 ± 2.6		35 ± 0.3	59 ± 1.5	28 ± 3.5	
	33	17 ± 0.6	19 ± 1.9	53 ± 9.6	77 ± 12.5	34 ± 0.9	34 ± 2.3
	100	18 ± 3.8	24 ± 2.2	76 ± 5.1	82 ± 9.9	47 ± 5.2	59 ± 3.0
	333	13 ± 2.4	18 ± 2.0	193 ± 7.5[d]	191 ± 24.7	67 ± 3.2	68 ± 6.3
	666	14 ± 1.8		61 ± 8.7[d]		89 ± 10.9	
	667		22 ± 0.7		181 ± 8.7		91 ± 1.2
	1,000		Toxic				43 ± 3.1[d]
Trial summary		Negative	Negative	Positive	Positive	Positive	Positive
Positive control		189 ± 10.7	219 ± 11.5	2,226 ± 101.1	151 ± 11.0	263 ± 11.6	229 ± 11.3

[a] The detailed protocol for both *Salmonella* assays and the data from the SRI study are presented in Haworth *et al*. (1983). Cells and 1,2,3-trichloropropane or solvent (dimethylsulfoxide) were incubated in the absence of exogenous metabolic activation (-S9) or with Aroclor 1254-induced S9 from male Syrian hamster liver or male Sprague-Dawley rat liver. High dose was limited by toxicity. 0 μg/plate dose is the solvent control.
[b] Revertants are presented as mean ± standard error from three plates.
[c] 2-Aminoanthracene was used on all strains in the presence of S9. In the absence of metabolic activation, 4-nitro-*o*-phenylenediamine was tested on TA98, sodium azide was tested on TA100 and TA1535, and 9-aminoacridine was tested on TA1537 and TA97.
[d] Slight toxicity

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by 1,2,3-Trichloropropane[a]

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction[b]	Average Mutant Fraction[c]
-S9						
Trial 1						
Ethyl alcohol						
		87	106	162	62	
		99	103	166	56	
		83	79	142	57	
		103	112	201	65	60
Ethyl methanesulfonate						
		54	37	1,133	697	
	250	55	45	1,182	714	
		52	35	949	603	671*
1,2,3-Trichloropropane (μL/mL)						
	0.0078	100	119	168	56	
		78	92	155	66	
		81	90	166	68	64
	0.0156	102	117	130	42	
		97	111	142	49	
		93	102	171	62	51
	0.0313	86	108	137	53	
		69	87	229	111	
		92	111	138	50	71
	0.0625	80	89	123	51	
		84	98	114	46	
		79	76	135	57	51
	0.125	84	75	149	59	
		100	74	187	62	
		99	70	181	61	61
	0.25	86	49	159	62	
		90	29	196	73	67[d]
	0.5	Lethal				
		Lethal				
		Lethal				

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by 1,2,3-Trichloropropane (continued)

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
-S9 (continued)						
Trial 2						
Ethyl alcohol						
		97	83	148	51	
		83	92	113	45	
		76	92	115	50	
		117	133	127	36	46
Ethyl methanesulfonate						
		81	47	987	405	
	250	85	50	1,056	414	
		83	45	796	318	379*
1,2,3-Trichloropropane (μL/mL)						
	0.0156	95	89	105	37	
		70	85	61	29	
		72	90	81	37	34
	0.0313	65	68	70	36	
		96	75	92	32	
		68	59	96	47	38
	0.0625	106	77	129	41	
		72	62	82	38	
		85	70	129	50	43
	0.125	85	75	92	36	
		76	43	118	52	
		87	66	110	42	43
	0.25	99	37	97	33	
		74	25	109	49	
		90	31	111	41	41
	0.5	45	8	168	125	
		58	9	140	80	103*

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by 1,2,3-Trichloropropane (continued)

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
+S9[e]						
Trial 1						
Ethyl alcohol						
		76	81	95	41	
		108	108	111	34	
		116	107	125	36	
		83	104	78	31	36
Methylcholanthrene						
		91	77	512	189	
	2.5	79	63	587	248	
		89	76	621	233	223*
1,2,3-Trichloropropane (nL/mL)						
	1.56	76	98	59	26	
		94	111	91	32	
		69	106	80	38	32
	3.13	79	124	89	38	
		83	129	91	36	
		66	99	72	37	37
	6.25	77	130	81	35	
		99	124	105	35	
		96	115	122	42	38
	12.5	87	107	275	105	
		82	75	228	93	
		91	106	257	95	98*
	25	89	90	482	181	
		92	79	505	182	
		73	64	546	250	204*
	50	37	15	734	658	
		44	18	721	550	
		39	12	741	628	612*

TABLE E2
Induction of Trifluorothymidine Resistance in L5178Y Mouse Lymphoma Cells by 1,2,3-Trichloropropane (continued)

Compound	Concentration (μg/mL)	Cloning Efficiency (%)	Relative Total Growth (%)	Mutant Count	Mutant Fraction	Average Mutant Fraction
+S9 (continued)						
Trial 2						
Ethyl alcohol						
		72	90	56	26	
		77	97	71	31	
		67	114	66	33	30
Methylcholanthrene						
		77	84	329	143	
	2.5	83	92	321	129	136*
1,2,3-Trichloropropane (μL/mL)						
	0.01	52	65	79	51	
		55	78	73	44	
		60	87	85	47	48*
	0.02	52	70	169	109	
		55	74	161	98	
		67	70	173	86	97*
	0.03	55	57	225	136	
		59	59	294	166	
		78	89	166	71	124*
	0.04	55	41	464	280	
		56	37	546	328	
		71	47	353	165	258*
	0.05	45	25	532	393	
		57	31	524	307	
		49	24	499	338	346*
	0.06	32	8	436	452	
		36	10	578	543	
		59	26	574	325	440*

* Significant positive response ($P \leq 0.05$)

[a] Study performed at Litton Bionetics, Inc. The experimental protocol is presented in detail by Myhr *et al.* (1985). The highest dose of 1,2,3-trichloropropane was determined by solubility or toxicity and may not exceed 50 μg/mL. All doses are tested in triplicate; the average of the three tests is presented in the table. Cells (6×10^5/mL) were treated for 4 hours at 37° C in medium, washed, resuspended in medium, and incubated for 48 hours at 37° C. After expression, 3×10^6 cells were plated in medium and soft agar supplemented with trifluorothymidine for selection of cells that were mutant at the thymidine kinase (TK) locus, and 600 cells were plated in nonselective medium and soft agar to determine the cloning efficiency.

[b] Mutant fraction (frequency) is a ratio of the mutant count to the cloning efficiency, divided by 3 (to arrive at MF/10^6 cells treated).

[c] Mean from three replicate plates of approximately 10^6 cells each.

[d] Precipitate formed at this concentration.

[e] Tests conducted with metabolic activation were performed as described in [a] except that S9, prepared from the livers of Aroclor 1254-induced Fischer 344 rats, was added at the same time as 1,2,3-trichloropropane and/or solvent.

TABLE E3
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by 1,2,3-Trichloropropane[a]

Compound	Dose μg/mL	Total Cells	No. of Chromo-somes	No. of SCEs	SCEs/ Chromo-somes	SCEs/ Cell	Hrs in BrdU	Relative SCEs/ Chromosome (%)[b]
-S9								
Trial 1 Summary: Negative								
Dimethylsulfoxide		50	1,044	416	0.39	8.3	25.8	
Mitomycin-C	5.0	50	1,050	1,270	1.20	25.4	25.8	203.55
1,2,3-Trichloropropane	14.2	50	1,048	401	0.38	8.0	25.8	-3.97
	47.2	50	1,046	423	0.40	8.5	25.8	1.49
	141.7	50	1,047	420	0.40	8.4	25.8	0.67
								P=0.364[c]
+S9								
Trial 1 Summary: Weak positive								
Dimethylsulfoxide		50	1,036	411	0.39	8.2	25.8	
Cyclophosphamide	2.0	50	1,021	1,027	1.00	20.5	25.8	153.55
1,2,3-Trichloropropane	1.417	50	1,033	401	0.38	8.0	25.8	-2.15
	4.724	45	921	397	0.43	8.8	25.8	8.66
	14.170	50	1,027	530	0.51	10.6	25.8	30.08*
								P<0.001
+S9								
Trial 2 Summary: Positive								
Dimethylsulfoxide		50	1,043	469	0.44	9.4	25.5	
Cyclophosphamide	20.0	50	1,039	1,422	1.36	28.4	25.5	204.37
1,2,3-Trichloropropane	39.680	50	1,030	738	0.71	14.8	25.5	59.34*
	49.600	50	1,033	877	0.84	17.5	25.5	88.80*
	59.510	50	1,028	864	0.84	17.3	25.5	86.91*
								P<0.001

* Positive (P≥0.05)
[a] Study performed at Litton Bionetics, Inc. SCE = sister chromatid exchange; BrdU = bromodeoxyuridine. The protocol is presented in detail by Galloway *et al.* (1987); data published in Zeiger *et al.* (1987).
[b] SCEs/chromosome of culture exposed to 1,2,3-trichloropropane relative to those of culture exposed to solvent.
[c] Significance of relative SCEs/chromosome tested by the linear regression trend test vs. log of the dose

TABLE E4
Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by 1,2,3-Trichloropropane[a]

-S9					+S9				
Dose μg/mL	**Total Cells**	**No. of Abs**	**Abs/ Cell**	**Percent Cells w/Abs**	**Dose μg/mL**	**Total Cells**	**No. of Abs**	**Abs/ Cell**	**Percent Cells w/Abs**
Trial 1 - Harvest time: 10.5 hours Summary: Questionable					**Trial 1**) Harvest time: 10.8 hours Summary: Negative				
Dimethylsulfoxide					Dimethylsulfoxide				
	100	0	0.00	0.0		100	5	0.05	4.0
Mitomycin-C					Cyclophosphamide				
0.5	100	25	0.25	23.0	50.0	50	31	0.62	36.0
1,2,3-Trichloropropane					1,2,3-Trichloropropane				
870.3	100	3	0.03	3.0	69.4	0			
943.7	50	3	0.06	6.0*	75.1	100	6	0.06	6.0
1,020.2	50	0	0.00	0.0	79.4	100	5	0.05	4.0
1,076.9	100	0	0.00	0.0	90.7	0			
				P=0.711[b]					P=0.500
					Trial 2 - Harvest time: 20.0 hours[c] Summary: Positive				
					Dimethylsulfoxide				
						100	11	0.11	8.0
					Cyclophosphamide				
					10.0	50	36	0.72	52.0
					1,2,3-Trichloropropane				
					59.5	100	135	1.35	26.0*
					69.4	100	83	0.83	23.0*
					79.2	50	55	1.10	20.0*
									P=0.018

* Positive (P≥ 0.05)

[a] Study performed at Litton Bionetics, Inc. Abs = aberrations. A detailed presentation of the technique for detecting chromosomal aberrations is found in Galloway *et al*. (1987); data published in Zeiger *et al*. (1987).

[b] Significance of percent cells with aberrations tested by the linear regression trend test vs. log of the dose.

[c] Because of significant chemical-induced cell cycle delay, incubation time prior to addition of Colcemid was lengthened to provide sufficient metaphases at harvest.

APPENDIX F
ORGAN WEIGHTS
AND ORGAN-WEIGHT-TO-BODY-WEIGHT RATIOS

TABLE F1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 17-Week Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg
Male						
n	10	10	10	10	10	9
Necropsy body wt	361 ± 6	367 ± 7	351 ± 11	368 ± 4	308 ± 15**	279 ± 8**
Brain						
Absolute	2.02 ± 0.02	1.97 ± 0.03	1.94 ± 0.02	2.00 ± 0.01	1.94 ± 0.01*	1.92 ± 0.04**
Relative	5.61 ± 0.12	5.37 ± 0.10	5.57 ± 0.14	5.44 ± 0.05	6.44 ± 0.36*	6.99 ± 0.38**
Heart						
Absolute	1.04 ± 0.02	1.04 ± 0.05	0.93 ± 0.03	1.00 ± 0.01	0.90 ± 0.02**	0.82 ± 0.02**
Relative	2.89 ± 0.07	2.84 ± 0.16	2.66 ± 0.05	2.72 ± 0.03	3.00 ± 0.18	2.96 ± 0.07
R. Kidney						
Absolute	1.08 ± 0.02	1.09 ± 0.02	1.10 ± 0.03	1.24 ± 0.02**	1.13 ± 0.02**	1.28 ± 0.02**
Relative	3.00 ± 0.03	2.97 ± 0.04	3.14 ± 0.04	3.37 ± 0.03*	3.77 ± 0.24**	4.63 ± 0.16**
Liver						
Absolute	8.87 ± 0.14	9.82 ± 0.21**	9.72 ± 0.38**	11.20 ± 0.20**	10.93 ± 0.23**	12.07 ± 0.13**
Relative	24.6 ± 0.5	26.8 ± 0.4	27.6 ± 0.5	30.5 ± 0.7**	36.2 ± 1.9**	43.7 ± 1.6**
Lung						
Absolute	1.31 ± 0.03	1.28 ± 0.03	1.21 ± 0.03	1.34 ± 0.04	1.19 ± 0.02**	1.14 ± 0.02**
Relative	3.64 ± 0.08	3.49 ± 0.07	3.45 ± 0.06	3.64 ± 0.10	3.96 ± 0.26	4.11 ± 0.11*
R. Testis						
Absolute	1.53 ± 0.02	1.61 ± 0.04	1.48 ± 0.04	1.63 ± 0.03	1.54 ± 0.02[b]	1.52 ± 0.05
Relative	4.25 ± 0.04	4.39 ± 0.07	4.23 ± 0.13	4.43 ± 0.06	4.93 ± 0.28**[b]	5.47 ± 0.19**
Thymus						
Absolute	0.28 ± 0.01	0.24 ± 0.02	0.22 ± 0.01	0.25 ± 0.02	0.22 ± 0.02	0.27 ± 0.07
Relative	0.78 ± 0.03	0.64 ± 0.05	0.64 ± 0.04	0.69 ± 0.06	0.71 ± 0.06	0.96 ± 0.23
Female						
n	10	10	10	10	10	6
Necropsy body wt	200 ± 3	200 ± 4	210 ± 6	199 ± 4	193 ± 3	158 ± 6**
Brain						
Absolute	1.81 ± 0.02	1.80 ± 0.02	1.82 ± 0.02	1.82 ± 0.02	1.83 ± 0.05	1.72 ± 0.07[c]
Relative	9.07 ± 0.11	9.03 ± 0.21	8.73 ± 0.21	9.13 ± 0.15	9.50 ± 0.30	10.99 ± 0.44**[c]
Heart						
Absolute	0.67 ± 0.01	0.65 ± 0.01	0.67 ± 0.03	0.62 ± 0.02	0.66 ± 0.03	0.61 ± 0.07
Relative	3.34 ± 0.07	3.28 ± 0.09	3.20 ± 0.08	3.09 ± 0.06	3.41 ± 0.16	3.83 ± 0.31
R. Kidney						
Absolute	0.64 ± 0.01[b]	0.67 ± 0.03	0.71 ± 0.02	0.70 ± 0.02	0.80 ± 0.03**	0.71 ± 0.02**
Relative	3.16 ± 0.07[b]	3.37 ± 0.19	3.38 ± 0.06	3.49 ± 0.05	4.16 ± 0.17**	4.52 ± 0.19**
Liver						
Absolute	5.14 ± 0.10	5.49 ± 0.09	6.07 ± 0.16**	6.00 ± 0.09*	6.79 ± 0.17**	8.25 ± 0.20**
Relative	25.7 ± 0.4	27.5 ± 0.6	28.9 ± 0.4**	30.2 ± 0.6**	35.2 ± 0.8**	52.6 ± 2.3**
Lung						
Absolute	0.97 ± 0.03	0.97 ± 0.02	0.94 ± 0.03	0.93 ± 0.02	0.95 ± 0.05	0.80 ± 0.01**
Relative	4.85 ± 0.16	4.87 ± 0.13	4.47 ± 0.10	4.66 ± 0.07	4.90 ± 0.28	5.09 ± 0.15
Thymus						
Absolute	0.17 ± 0.01	0.19 ± 0.01	0.21 ± 0.02	0.20 ± 0.01	0.18 ± 0.01	0.22 ± 0.07
Relative	0.87 ± 0.04	0.97 ± 0.07	1.01 ± 0.07	1.00 ± 0.05	0.93 ± 0.05	1.37 ± 0.46

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error). No data collected from groups receiving 250 mg/kg due to 100% mortality.
[b] n=9
[c] n=5

TABLE F2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 15-Month Interim Evaluations in the 2-Year Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
n	10	10	10	8
Necropsy body wt	457 ± 8	473 ± 11	467 ± 10	458 ± 8
Brain				
Absolute	2.06 ± 0.02	2.08 ± 0.04	2.09 ± 0.02	2.06 ± 0.02
Relative	4.51 ± 0.08	4.40 ± 0.06	4.50 ± 0.08	4.50 ± 0.06
R. Kidney				
Absolute	1.35 ± 0.03	1.46 ± 0.04*	1.51 ± 0.03**	1.75 ± 0.05**
Relative	2.96 ± 0.04	3.09 ± 0.09	3.25 ± 0.05**	3.82 ± 0.05**
Liver				
Absolute	14.27 ± 0.37	15.63 ± 0.37*	16.80 ± 0.48**	18.23 ± 0.52**
Relative	31.2 ± 0.6	33.1 ± 0.7	36.0 ± 0.6**	39.8 ± 0.9**
Female				
n	10	10	8	8
Necropsy body wt	256 ± 6	288 ± 11*	260 ± 4	241 ± 7
Brain				
Absolute	1.89 ± 0.02	1.91 ± 0.03	1.91 ± 0.02	1.91 ± 0.03
Relative	7.40 ± 0.14	6.70 ± 0.24	7.34 ± 0.16	7.97 ± 0.22
R. Kidney				
Absolute	0.786 ± 0.015	0.839 ± 0.023	0.869 ± 0.019*	0.971 ± 0.034**
Relative	3.08 ± 0.07	2.93 ± 0.07	3.34 ± 0.06*	4.04 ± 0.12**
Liver				
Absolute	7.79 ± 0.13[b]	8.87 ± 0.31**	9.00 ± 0.28**	10.40 ± 0.37**
Relative	30.8 ± 0.8[b]	30.9 ± 0.6	34.6 ± 1.0**	43.2 ± 0.7**

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9

TABLE F3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 17-Week Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg	250 mg/kg
Male							
n	10	10	10	10	10	8	2
Necropsy body wt	26.6 ± 0.6	28.2 ± 0.6	28.0 ± 0.5	28.8 ± 0.5	27.4 ± 0.3	29.5 ± 1.1*	25.5 ± 0.5
Brain							
Absolute	0.454 ± 0.005	0.464 ± 0.006	0.446 ± 0.005	0.456 ± 0.003	0.440 ± 0.004	0.446 ± 0.006	0.435 ± 0.015
Relative	17.1 ± 0.3	16.5 ± 0.3	16.0 ± 0.2*	15.9 ± 0.3*	16.1 ± 0.1*	15.3 ± 0.6**	17.1 ± 0.9
Heart							
Absolute	0.166 ± 0.004	0.152 ± 0.005[b]	0.150 ± 0.003	0.160 ± 0.007	0.139 ± 0.006**	0.143 ± 0.008**	0.125 ± 0.005**
Relative	6.25 ± 0.16	5.36 ± 0.14**[b]	5.37 ± 0.13**	5.56 ± 0.22**	5.07 ± 0.19**	4.85 ± 0.27**	4.90 ± 0.10**
R. Kidney							
Absolute	0.232 ± 0.006	0.253 ± 0.007	0.248 ± 0.008	0.265 ± 0.008	0.215 ± 0.008	0.247 ± 0.011[c]	0.225 ± 0.005
Relative	8.75 ± 0.25	8.97 ± 0.15	8.85 ± 0.22	9.19 ± 0.14	7.86 ± 0.31	8.44 ± 0.58[c]	8.83 ± 0.37
Liver							
Absolute	1.06 ± 0.03	1.14 ± 0.04	1.09 ± 0.02	1.21 ± 0.03*	1.10 ± 0.03*	1.29 ± 0.04**	1.32 ± 0.00**
Relative	39.9 ± 1.0	40.3 ± 0.8	38.8 ± 0.6	42.0 ± 0.5	39.9 ± 0.8	44.0 ± 1.3**	51.8 ± 1.0**
Lung							
Absolute	0.178 ± 0.006	0.185 ± 0.008	0.198 ± 0.008	0.199 ± 0.008	0.166 ± 0.006	0.167 ± 0.008[c]	0.170 ± 0.000
Relative	6.73 ± 0.28	6.57 ± 0.27	7.08 ± 0.26	6.93 ± 0.30	6.05 ± 0.18	5.83 ± 0.24[c]	6.67 ± 0.13
R. Testis							
Absolute	0.110 ± 0.003	0.117 ± 0.004	0.123 ± 0.002	0.123 ± 0.003	0.114 ± 0.004	0.125 ± 0.009	0.099 ± 0.01
Relative	4.14 ± 0.08	4.15 ± 0.13	4.39 ± 0.12	4.28 ± 0.12	4.16 ± 0.14	4.25 ± 0.27	3.90 ± 0.82
Thymus[d]							
Absolute	24.90 ± 3.98	25.10 ± 2.54	23.20 ± 1.11	32.40 ± 3.63	18.70 ± 2.47	35.75 ± 4.04	29.00 ± 11.00
Relative	0.92 ± 0.14	0.89 ± 0.09	0.83 ± 0.04	1.13 ± 0.13	0.68 ± 0.09	1.22 ± 0.15	1.13 ± 0.41
Female							
n	10	10	7	10	9	9	6
Necropsy body wt	20.7 ± 0.6	20.6 ± 0.8	23.0 ± 0.6	21.3 ± 0.4	22.0 ± 0.9	23.0 ± 0.6	21.2 ± 0.9
Brain							
Absolute	0.485 ± 0.005	0.465 ± 0.008*	0.459 ± 0.004**[e]	0.457 ± 0.005**	0.463 ± 0.006**	0.460 ± 0.005**	0.437 ± 0.006**
Relative	23.6 ± 0.6	22.8 ± 0.8	20.0 ± 0.5**[e]	21.5 ± 0.3**	21.3 ± 0.8**	20.1 ± 0.4**	20.8 ± 0.7**
Heart							
Absolute	0.122 ± 0.004	0.122 ± 0.004	0.113 ± 0.007	0.105 ± 0.006	0.116 ± 0.004	0.110 ± 0.006	0.092 ± 0.006**
Relative	5.92 ± 0.17	5.98 ± 0.25	4.77 ± 0.40*	4.93 ± 0.28**	5.28 ± 0.16*	4.80 ± 0.27**	4.31 ± 0.12**
R. Kidney							
Absolute	0.170 ± 0.005	0.166 ± 0.007	0.164 ± 0.010	0.153 ± 0.005	0.160 ± 0.007	0.158 ± 0.005	0.148 ± 0.006*
Relative	8.23 ± 0.18	8.07 ± 0.17	6.86 ± 0.54**	7.18 ± 0.13**	7.31 ± 0.23**	6.87 ± 0.17**	7.04 ± 0.30**
Liver							
Absolute	0.898 ± 0.037	0.899 ± 0.035	0.938 ± 0.037	0.947 ± 0.016	0.994 ± 0.048	1.118 ± 0.029**	1.112 ± 0.053**
Relative	43.3 ± 1.1	43.7 ± 0.8	39.9 ± 1.8	44.5 ± 0.5	45.2 ± 0.8	48.7 ± 1.0**	52.7 ± 2.2**
Lung							
Absolute	0.181 ± 0.006[b]	0.178 ± 0.009[b]	0.173 ± 0.008[e]	0.166 ± 0.006	0.199 ± 0.022	0.181 ± 0.011	0.184 ± 0.015[f]
Relative	8.65 ± 0.26[b]	8.48 ± 0.39[b]	7.51 ± 0.34[e]	7.80 ± 0.26	9.33 ± 1.41	7.83 ± 0.29	9.08 ± 0.92[f]
Thymus[d]							
Absolute	27.89 ± 2.88[b]	28.70 ± 2.20	34.75 ± 2.48	27.60 ± 2.30	33.11 ± 3.39	28.78 ± 5.66	43.83 ± 2.90*
Relative	1.31 ± 0.13[b]	1.38 ± 0.07	1.52 ± 0.12	1.30 ± 0.10	1.54 ± 0.19	1.23 ± 0.23	2.09 ± 0.16**

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9 [c] n=7 [d] Weights are given in milligrams. [e] n=8 [f] n=5

TABLE F4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Month Interim Evaluations in the 2-Year Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Male				
n	10	9	8	5
Necropsy body wt	44.2 ± 1.0	45.0 ± 1.5	40.4 ± 1.8	38.4 ± 3.4*
Brain				
Absolute	0.463 ± 0.005	0.482 ± 0.006	0.462 ± 0.007	0.472 ± 0.010
Relative	10.5 ± 0.3	10.8 ± 0.4	11.6 ± 0.4	12.6 ± 1.0**
R. Kidney				
Absolute	0.353 ± 0.011	0.344 ± 0.019	0.314 ± 0.013	0.317 ± 0.022
Relative	8.00 ± 0.25	7.67 ± 0.41	7.81 ± 0.18	8.40 ± 0.59
Liver				
Absolute	1.72 ± 0.09	1.63 ± 0.08	1.76 ± 0.19	1.92 ± 0.14
Relative	38.9 ± 1.9	36.2 ± 1.5	44.6 ± 6.2	51.2 ± 4.8*
Female				
n	10	10	9	5
Necropsy body wt	43.6 ± 1.7	38.6 ± 1.1	42.1 ± 1.6	34.8 ± 2.0**
Brain				
Absolute	0.468 ± 0.005	0.467 ± 0.005	0.468 ± 0.005	0.467 ± 0.009
Relative	10.9 ± 0.4	12.2 ± 0.3	11.3 ± 0.5	13.6 ± 0.6**
R. Kidney				
Absolute	0.217 ± 0.006	0.203 ± 0.006	0.217 ± 0.006	0.210 ± 0.015
Relative	4.99 ± 0.09	5.27 ± 0.14	5.19 ± 0.14	6.02 ± 0.11**
Liver				
Absolute	1.49 ± 0.03	1.33 ± 0.03*	1.50 ± 0.04	1.69 ± 0.18
Relative	34.4 ± 0.8	34.7 ± 1.1	35.7 ± 0.6	48.3 ± 2.8**

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Organ and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).

APPENDIX G
HEMATOLOGY, CLINICAL CHEMISTRY, AND URINALYSIS RESULTS

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 8-Week Interim Evaluations in the 17-Week Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg
Male						
n	10	10	10	10	10	9
Hematology						
Hematocrit (%)	48.7 ± 0.8	48.3 ± 0.6	42.2 ± 0.6**	43.3 ± 0.6**	37.7 ± 0.7**	37.4 ± 0.6**
Hemoglobin (g/dL)	16.8 ± 0.2	16.8 ± 0.2	16.0 ± 0.2**	16.5 ± 0.2*	15.3 ± 0.2**	15.3 ± 0.1**
Erythrocytes (10^6/μL)	9.32 ± 0.10	9.28 ± 0.10	8.33 ± 0.11**	8.50 ± 0.11	7.57 ± 0.14**	7.60 ± 0.11**
Leukocytes (10^3/μL)	6.99 ± 0.29	7.45 ± 0.27	8.56 ± 0.37*	9.09 ± 0.31**	7.44 ± 0.45	6.40 ± 0.53
Segmented neutrophils (10^3/μL)	1.11 ± 0.09	1.26 ± 0.13	1.47 ± 0.16	1.79 ± 0.23	1.20 ± 0.17	0.92 ± 0.09
Lymphocytes (10^3/μL)	5.68 ± 0.26	5.93 ± 0.24	6.94 ± 0.27*	7.08 ± 0.23**	6.13 ± 0.41	5.38 ± 0.48
Monocytes (10^3/μL)	0.12 ± 0.02	0.16 ± 0.02	0.03 ± 0.02	0.11 ± 0.03	0.07 ± 0.03	0.09 ± 0.03
Eosinophils (10^3/μL)	0.06 ± 0.02	0.11 ± 0.04	0.08 ± 0.03	0.10 ± 0.04	0.04 ± 0.01	0.01 ± 0.01
Clinical Chemistry						
Blood urea nitrogen (mg/dL)	14.8 ± 0.4	18.0 ± 0.6	16.7 ± 0.4	16.4 ± 0.4	15.5 ± 0.2	14.9 ± 0.7
Creatinine (mg/dL)	0.58 ± 0.02	0.67 ± 0.02	0.55 ± 0.02	0.63 ± 0.02	0.59 ± 0.02	0.54 ± 0.08
Sodium (mEq/L)	145 ± 0	145 ± 0	145 ± 0	145 ± 0	143 ± 0**	143 ± 1**[c]
Potassium (mEq/L)	4.0 ± 0.1	4.0 ± 0.0	4.7 ± 0.5**	4.3 ± 0.1**	4.3 ± 0.1**	5.0 ± 0.3**[c]
Chloride (mEq/L)	99 ± 0	99 ± 0	101 ± 0**	98 ± 1[b]	99 ± 1	103 ± 1**[c]
Phosphorus (mg/dL)	7.2 ± 0.1	6.2 ± 0.2	7.7 ± 0.3	7.2 ± 0.1	7.1 ± 0.2	8.6 ± 0.7*
Total protein (g/dL)	6.4 ± 0.1	6.6 ± 0.1	6.7 ± 0.1*	6.6 ± 0.1	7.1 ± 0.1**	6.6 ± 0.1**[c]
Albumin (g/dL)	3.9 ± 0.1	4.1 ± 0.1*	4.0 ± 0.1	4.1 ± 0.1*	4.1 ± 0.1*	4.2 ± 0.1**[c]
Globulin (g/dL)	2.6 ± 0.1	2.5 ± 0.1	2.7 ± 0.1	2.5 ± 0.1	3.0 ± 0.1*	2.4 ± 0.1[d]
Albumin/globulin ratio	1.5 ± 0.1	1.6 ± 0.0	1.5 ± 0.0	1.7 ± 0.0	1.4 ± 0.0	1.7 ± 0.1[d]
Total bilirubin (mg/dL)	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.1 ± 0.0	0.3 ± 0.0**	0.3 ± 0.0**[d]
Alanine aminotransferase (IU/L)	31 ± 1	32 ± 1	33 ± 1[b]	32 ± 2	33 ± 1	38 ± 2*
Aspartate aminotransferase (IU/L)	65 ± 3	72 ± 1	76 ± 5	60 ± 3	58 ± 2	66 ± 9
Lactate dehydrogenase (IU/L)	485 ± 63	579 ± 27	683 ± 56	526 ± 65	598 ± 43	618 ± 110
Sorbitol dehydrogenase (IU/L)	8 ± 1	9 ± 1	13 ± 2**	8 ± 1	9 ± 1	11 ± 1**
Pseudocholinesterase (IU/L)	616 ± 12	636 ± 17	625 ± 15	561 ± 10**	601 ± 9	556 ± 16**
Urinalysis						
Specific gravity	1.053 ± 0.003	1.044 ± 0.004	1.039 ± 0.004*	1.037 ± 0.005*	1.064 ± 0.038**	1.034 ± 0.003**

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 8-Week Interim Evaluations in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg
Female						
Hematology						
n	10	10	10	10	10	9
Hematocrit (%)	46.7 ± 0.4	45.0 ± 0.4*	42.1 ± 0.5**	41.3 ± 0.7**	39.9 ± 0.5**	38.7 ± 0.8**
Hemoglobin (g/dL)	16.5 ± 0.2	16.4 ± 0.1	16.6 ± 0.2	16.4 ± 0.2	15.8 ± 0.1**	15.2 ± 0.2**
Erythrocytes (10^6/μL)	8.59 ± 0.08	8.31 ± 0.07*	7.77 ± 0.10**	7.60 ± 0.13**	7.39 ± 0.08**	7.60 ± 0.16**
Leukocytes (10^3/μL)	5.41 ± 0.25	5.73 ± 0.36	7.89 ± 0.45**	8.11 ± 0.34**	7.08 ± 0.35**	5.89 ± 0.40**
Segmented neutrophils (10^3/μL)	1.12 ± 0.11	1.17 ± 0.16	1.35 ± 0.14	1.77 ± 0.32	0.92 ± 0.16	2.01 ± 0.30
Lymphocytes (10^3/μL)	4.14 ± 0.24	4.39 ± 0.26	6.42 ± 0.35**	6.22 ± 0.19**	6.05 ± 0.30**	3.75 ± 0.37
Monocytes (10^3/μL)	0.04 ± 0.02	0.11 ± 0.02	0.02 ± 0.01	0.03 ± 0.02	0.06 ± 0.02	0.10 ± 0.03
Eosinophils (10^3/μL)	0.11 ± 0.03	0.06 ± 0.02	0.09 ± 0.02	0.08 ± 0.02	0.06 ± 0.02	0.03 ± 0.01*
Clinical Chemistry						
n	10	10	10	10	8	8
Blood urea nitrogen (mg/dL)	17.4 ± 0.2	17.1 ± 0.4	16.2 ± 0.5*	17.2 ± 0.7	13.4 ± 0.4**	15.9 ± 1.0**
Creatinine (mg/dL)	0.62 ± 0.01	0.66 ± 0.02	0.52 ± 0.01**	0.49 ± 0.04**	0.50 ± 0.02**	0.44 ± 0.05**
Sodium (mEq/L)	145 ± 0	145 ± 0	146 ± 0	144 ± 0	143 ± 0*	145 ± 2
Potassium (mEq/L)	4.2 ± 0.1	4.3 ± 0.1	4.3 ± 0.1	5.0 ± 0.5	4.5 ± 0.1*	5.2 ± 0.3**
Chloride (mEq/L)	99 ± 0	103 ± 0**	101 ± 1*	98 ± 1	103 ± 1**	107 ± 2**
Phosphorus (mg/dL)	7.1 ± 0.2	6.8 ± 0.3	7.2 ± 0.2	7.9 ± 0.3	7.1 ± 0.2	6.9 ± 0.2
Total protein (g/dL)	6.7 ± 0.1	6.5 ± 0.1	6.5 ± 0.1	6.4 ± 0.2	6.5 ± 0.1	6.9 ± 0.2
Albumin (g/dL)	4.1 ± 0.0	4.3 ± 0.0	4.2 ± 0.1	4.1 ± 0.1	4.1 ± 0.1	4.0 ± 0.1[e]
Globulin (g/dL)	2.6 ± 0.1	2.2 ± 0.0**	2.3 ± 0.1	2.3 ± 0.1	2.4 ± 0.0	3.0 ± 0.2[e]
Albumin/globulin ratio	1.6 ± 0.0	1.9 ± 0.0	1.8 ± 0.1	1.8 ± 0.1	1.7 ± 0.0	1.4 ± 0.1[e]
Total bilirubin (mg/dL)	0.2 ± 0.0	0.2 ± 0.0	0.1 ± 0.0	0.2 ± 0.0	0.3 ± 0.0**	0.5 ± 0.1**[e]
Alanine aminotransferase (IU/L)	22 ± 1	22 ± 1	23 ± 1	27 ± 2	27 ± 1*	286 ± 61**
Aspartate aminotransferase (IU/L)	63 ± 3	59 ± 2	66 ± 3	63 ± 3	61 ± 2	336 ± 70**
Lactate dehydrogenase (IU/L)	409 ± 60	360 ± 30	538 ± 40	430 ± 38	600 ± 48*	698 ± 82**
Sorbitol dehydrogenase (IU/L)	6 ± 1	6 ± 0[b]	6 ± 0	8 ± 1	8 ± 1	66 ± 12**
Pseudocholinesterase (IU/L)	3,777 ± 129	2,997 ± 86**	2,690 ± 154**	1,993 ± 211**	1,118 ± 68**	950 ± 51**
Urinalysis						
n	10	10	10	10	10	9
Specific gravity	1.037 ± 0.004	1.037 ± 0.004	1.034 ± 0.003	1.027 ± 0.003	1.021 ± 0.004**	1.029 ± 0.002*

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error; no data calculated for groups receiving 250 mg/kg due to 100% mortality.
[b] n=9
[c] n=8
[d] n=7

TABLE G2
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 17-Week Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg
Male						
n	10	10	10	10	10	9
Hematology						
Hematocrit (%)	46.0 ± 0.5	47.3 ± 0.6	45.2 ± 0.6	45.4 ± 0.7	41.4 ± 0.7**	38.2 ± 0.7**
Hemoglobin (g/dL)	15.9 ± 0.1	16.4 ± 0.2	15.9 ± 0.1	16.1 ± 0.2	15.3 ± 0.2*	15.6 ± 0.2
Erythrocytes (10^6/μL)	8.98 ± 0.09	9.18 ± 0.10	8.81 ± 0.10	8.97 ± 0.10	8.25 ± 0.13**	7.82 ± 0.11**
Leukocytes (10^3/μL)	5.90 ± 0.37	5.60 ± 0.24	5.77 ± 0.23	5.44 ± 0.22	5.92 ± 0.25	4.81 ± 0.16**
Segmented neutrophils (10^3/μL)	1.68 ± 0.16	1.78 ± 0.21	1.95 ± 0.16	1.16 ± 0.19*	1.21 ± 0.13*	1.45 ± 0.14
Lymphocytes (10^3/μL)	4.05 ± 0.31	3.75 ± 0.18	3.76 ± 0.21	4.11 ± 0.14	4.51 ± 0.28	3.21 ± 0.18
Monocytes (10^3/μL)	0.09 ± 0.03	0.01 ± 0.01	0.01 ± 0.01	0.11 ± 0.02	0.10 ± 0.02	0.08 ± 0.02
Eosinophils (10^3/μL)	0.08 ± 0.02	0.06 ± 0.02	0.04 ± 0.01	0.05 ± 0.01	0.09 ± 0.02	0.06 ± 0.02
Clinical Chemistry						
Blood urea nitrogen (mg/dL)	17.5 ± 0.7	18.0 ± 0.6	17.6 ± 0.7	17.6 ± 0.3	17.6 ± 0.4	13.8 ± 0.7**
Creatinine (mg/dL)	0.61 ± 0.01	0.58 ± 0.03	0.64 ± 0.04	0.64 ± 0.03	0.62 ± 0.03	0.60 ± 0.03
Sodium (mEq/L)	147 ± 0	145 ± 0**	145 ± 0**	145 ± 0**	145 ± 0**	144 ± 0**
Potassium (mEq/L)	4.2 ± 0.0	4.3 ± 0.1	4.3 ± 0.1	4.1 ± 0.1	4.3 ± 0.3	4.8 ± 0.3
Chloride (mEq/L)	100 ± 0	96 ± 0**	98 ± 0	97 ± 0*	99 ± 1	99 ± 1
Phosphorus (mg/dL)	6.5 ± 0.2	6.3 ± 0.1	6.0 ± 0.3	6.1 ± 0.3	6.9 ± 0.4	7.3 ± 0.7
Total protein (g/dL)	6.3 ± 0.1	6.3 ± 0.1	6.4 ± 0.1	7.1 ± 0.1**	6.9 ± 0.1**	6.6 ± 0.1**
Albumin (g/dL)	3.6 ± 0.0	3.7 ± 0.0*	3.9 ± 0.1**	4.1 ± 0.1**	4.0 ± 0.1**	3.9 ± 0.0**
Globulin (g/dL)	2.7 ± 0.1	2.6 ± 0.0	2.5 ± 0.0	3.0 ± 0.0	2.9 ± 0.1	2.6 ± 0.1
Albumin/globulin ratio	1.3 ± 0.0	1.5 ± 0.0*	1.5 ± 0.0**	1.4 ± 0.0	1.4 ± 0.1	1.5 ± 0.0**
Total bilirubin (mg/dL)	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
Alanine aminotransferase (IU/L)	39 ± 2	40 ± 2	39 ± 2	33 ± 1	37 ± 1	38 ± 2
Aspartate aminotransferase (IU/L)	93 ± 3	100 ± 4	83 ± 5	68 ± 2**	57 ± 2**	63 ± 4**
Lactate dehydrogenase (IU/L)	848 ± 57	1,132 ± 66	550 ± 46*	517 ± 87*	374 ± 45**	616 ± 68**
Sorbitol dehydrogenase (IU/L)	8 ± 0	8 ± 0	7 ± 1	7 ± 0	10 ± 0**	9 ± 1*
Pseudocholinesterase (IU/L)	707 ± 18	707 ± 15	656 ± 23	651 ± 9*	624 ± 17**	561 ± 13**
Urinalysis						
Specific gravity	1.060 ± 0.000	1.059 ± 0.001	1.053 ± 0.003*	1.042 ± 0.004**	1.058 ± 0.001**	1.036 ± 0.003**

TABLE G2
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg	63 mg/kg	125 mg/kg
Female						
Hematology						
n	10	10	10	10	10	6
Hematocrit (%)	45.9 ± 0.6	45.2 ± 0.4	44.3 ± 0.7	44.5 ± 0.5	40.2 ± 0.7**	41.2 ± 0.5**
Hemoglobin (g/dL)	16.3 ± 0.1	16.2 ± 0.1	15.6 ± 0.1**	15.8 ± 0.2*	15.3 ± 0.2**	15.4 ± 0.2**
Erythrocytes (10^6/μL)	8.49 ± 0.11	8.39 ± 0.05	8.19 ± 0.14*	8.43 ± 0.10	7.66 ± 0.14**	8.29 ± 0.11*
Leukocytes (10^3/μL)	5.07 ± 0.23	4.73 ± 0.11	4.74 ± 0.23	5.07 ± 0.23	5.10 ± 0.20	4.87 ± 0.24
Segmented neutrophils (10^3/μL)	1.48 ± 0.18	1.09 ± 0.09	1.59 ± 0.10	1.42 ± 0.20	1.34 ± 0.14	1.58 ± 0.07
Lymphocytes (10^3/μL)	3.42 ± 0.22	3.53 ± 0.14	3.09 ± 0.25	3.55 ± 0.12	3.61 ± 0.16	3.21 ± 0.20
Monocytes (10^3/μL)	0.07 ± 0.01	0.03 ± 0.02	0.00 ± 0.00**	0.05 ± 0.03	0.12 ± 0.02	0.06 ± 0.02
Eosinophils (10^3/μL)	0.06 ± 0.02	0.07 ± 0.02	0.05 ± 0.02	0.05 ± 0.01	0.02 ± 0.01	0.01 ± 0.01*
Clinical Chemistry						
n	10	10	10	10	10	5
Blood urea nitrogen (mg/dL)	18.0 ± 0.3	17.6 ± 0.5	17.1 ± 0.4	14.3 ± 0.4**	14.3 ± 0.6**	14.0 ± 0.6**
Creatinine (mg/dL)	0.61 ± 0.03	0.54 ± 0.02[b]	0.61 ± 0.03	0.59 ± 0.02	0.54 ± 0.02[b]	0.54 ± 0.02
Sodium (mEq/L)	146 ± 0	146 ± 1	144 ± 0**	144 ± 0**	145 ± 0*	145 ± 1
Potassium (mEq/L)	4.0 ± 0.1	4.0 ± 0.1	3.9 ± 0.1	4.0 ± 0.1	4.9 ± 0.5**	4.5 ± 0.2**
Chloride (mEq/L)	99 ± 0	99 ± 1	99 ± 1	102 ± 1	100 ± 1	99 ± 1
Phosphorus (mg/dL)	5.7 ± 0.2	5.8 ± 0.2	5.9 ± 0.3	4.7 ± 0.3	6.7 ± 0.3	5.6 ± 0.5
Total protein (g/dL)	6.7 ± 0.1	6.6 ± 0.1	6.4 ± 0.1*	6.3 ± 0.1**	6.3 ± 0.1**	7.0 ± 0.2
Albumin (g/dL)	4.0 ± 0.1	4.1 ± 0.1	4.0 ± 0.1	3.8 ± 0.1*	4.0 ± 0.1	3.8 ± 0.1*
Globulin (g/dL)	2.7 ± 0.0	2.5 ± 0.0	2.4 ± 0.0**	2.4 ± 0.1	2.3 ± 0.1**	3.2 ± 0.1
Albumin/globulin ratio	1.5 ± 0.0	1.7 ± 0.0	1.7 ± 0.0	1.6 ± 0.0	1.7 ± 0.0**	1.2 ± 0.0
Total bilirubin (mg/dL)	0.2 ± 0.0[b]	0.2 ± 0.0[b]	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.0[b]	0.3 ± 0.0
Alanine aminotransferase (IU/L)	31 ± 2	32 ± 2	34 ± 4	24 ± 1*	30 ± 2	108 ± 21*
Aspartate aminotransferase (IU/L)	82 ± 5	81 ± 6	64 ± 4*	66 ± 3	66 ± 4	144 ± 18
Lactate dehydrogenase (IU/L)	536 ± 37	478 ± 39	236 ± 31**	534 ± 64	480 ± 47	637 ± 46
Sorbitol dehydrogenase (IU/L)	6 ± 0	6 ± 1	5 ± 0	6 ± 0	8 ± 1	25 ± 5**
Pseudocholinesterase (IU/L)	3,954 ± 118	3,407 ± 126**	2,774 ± 124**	1,633 ± 90**	1,049 ± 67**	912 ± 10**
Urinalysis						
n	10	10	10	10	10	6
Specific gravity	1.058 ± 0.001	1.053 ± 0.004	1.059 ± 0.001	1.046 ± 0.005	1.042 ± 0.005*	1.037 ± 0.003**

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error; no data calculated for groups receiving 250 mg/kg due to 100% mortality.
[b] n=9

TABLE G3
Hematology and Clinical Chemistry Data for Rats at the 15-Month Interim Evaluations in the 2-Year Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Male				
Hematology				
n	10	10	9	8
Hematocrit (%)	46.4 ± 0.5	44.8 ± 0.3	46.0 ± 0.9	44.2 ± 0.5*
Hemoglobin (g/dL)	16.7 ± 0.2	16.1 ± 0.1**	16.6 ± 0.4	16.0 ± 0.2*
Erythrocytes (10^6/μL)	9.32 ± 0.11	9.09 ± 0.14	9.45 ± 0.18	9.09 ± 0.14
Mean cell volume (fL)	49.8 ± 0.6	49.3 ± 0.5	48.8 ± 0.4	48.6 ± 0.4
Mean cell hemoglobin (pg)	17.9 ± 0.2	17.8 ± 0.3	17.5 ± 0.1	17.6 ± 0.1
Mean cell hemoglobin concentration (g/dL)	36.0 ± 0.4	36.0 ± 0.3	36.0 ± 0.2	36.2 ± 0.2
Leukocytes (10^3/μL)	6.62 ± 0.24	7.61 ± 0.39	8.00 ± 0.61	9.14 ± 0.92**
Segmented neutrophils (10^3/μL)	1.71 ± 0.12	2.01 ± 0.23	2.67 ± 0.45	3.68 ± 0.97**
Lymphocytes (10^3/μL)	4.56 ± 0.28	5.34 ± 0.27	4.98 ± 0.24	5.03 ± 0.24
Monocytes (10^3/μL)	0.18 ± 0.05	0.14 ± 0.03	0.25 ± 0.04	0.25 ± 0.07
Eosinophils (10^3/μL)	0.15 ± 0.03	0.12 ± 0.02	0.09 ± 0.04	0.17 ± 0.04
Nucleated erythrocytes (10^3/μL)	0.04 ± 0.01	0.04 ± 0.01	0.06 ± 0.02	0.07 ± 0.04
Clinical Chemistry				
n	10	10	10	8
Alkaline phosphatase (IU/L)	208 ± 14	199 ± 11	206 ± 8	198 ± 16
Alanine aminotransferase (IU/L)	99 ± 11	91 ± 5	90 ± 11	68 ± 3*
Aspartate aminotransferase (IU/L)	160 ± 17	163 ± 11	138 ± 12	128 ± 18
Creatine kinase (U/L)	639 ± 99	602 ± 53	665 ± 47	665 ± 48
Lactate dehydrogenase (IU/L)	1,066 ± 125	1,253 ± 106	1,225 ± 93	1,200 ± 76
Sorbitol dehydrogenase (IU/L)	18 ± 2	19 ± 2	20 ± 3	18 ± 1
5-Nucleotidase (IU/L)	39.90 ± 1.52	40.00 ± 1.54	37.90 ± 0.84	34.63 ± 1.22*

TABLE G3
Hematology and Clinical Chemistry Data for Rats at the 15-Month Interim Evaluations in the 2-Year Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	3 mg/kg	10 mg/kg	30 mg/kg
Female				
Hematology				
n	10	9	7	8
Hematocrit (%)	43.4 ± 0.2	43.5 ± 0.7	43.1 ± 0.4	40.4 ± 1.3*
Hemoglobin (g/dL)	15.5 ± 0.1	15.6 ± 0.2	15.3 ± 0.1	14.5 ± 0.5
Erythrocytes (10^6/μL)	7.83 ± 0.06	7.89 ± 0.16	7.99 ± 0.08	7.39 ± 0.35
Mean cell volume (fL)	55.3 ± 0.3	55.2 ± 0.5	54.0 ± 0.2**	55.0 ± 1.2*
Mean cell hemoglobin (pg)	19.8 ± 0.1	19.8 ± 0.2	19.2 ± 0.2**	19.3 ± 0.3*[b]
Mean cell hemoglobin concentration (g/dL)	35.8 ± 0.1	35.9 ± 0.2	35.6 ± 0.3	35.9 ± 0.2
Leukocytes (10^3/μL)	4.23 ± 0.24	4.56 ± 0.28	4.47 ± 0.30	7.31 ± 0.73**
Segmented neutrophils (10^3/μL)	1.08 ± 0.06	1.22 ± 0.23	1.38 ± 0.20	3.36 ± 0.74**
Lymphocytes (10^3/μL)	3.02 ± 0.22	3.18 ± 0.14	2.88 ± 0.18	3.76 ± 0.20*
Monocytes (10^3/μL)	0.08 ± 0.02	0.11 ± 0.03	0.10 ± 0.03	0.11 ± 0.03
Eosinophils (10^3/μL)	0.04 ± 0.01	0.04 ± 0.01	0.10 ± 0.02*	0.06 ± 0.01
Nucleated erythrocytes (10^3/μL)	0.03 ± 0.01	0.13 ± 0.04*	0.10 ± 0.05	0.13 ± 0.03*
Clinical Chemistry				
n	10	10	8	8
Alkaline phosphatase (IU/L)	174 ± 11	201 ± 11	190 ± 23	198 ± 15
Alanine aminotransferase (IU/L)	58 ± 3	57 ± 3	65 ± 7	66 ± 10
Aspartate aminotransferase (IU/L)	108 ± 9	97 ± 8	110 ± 10	102 ± 9
Creatine kinase (U/L)	462 ± 56	484 ± 93	587 ± 71	384 ± 75
Lactate dehydrogenase (IU/L)	583 ± 82	750 ± 117	917 ± 95	632 ± 99
Sorbitol dehydrogenase (IU/L)	11 ± 1	12 ± 1	17 ± 4	16 ± 2
5-Nucleotidase (IU/L)	29.50 ± 1.19	30.60 ± 0.62	31.38 ± 1.36	31.50 ± 1.67

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error
[b] n=6

TABLE G4
Hematology, Clinical Chemistry, and Urinalysis Data for Mice at the 8-Week Interim Evaluations in the 17-Week Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg
Male				
Hematology				
n	10	10	9	9
Hematocrit (%)	47.4 ± 1.4	45.3 ± 1.6	46.9 ± 0.5	45.2 ± 1.4
Hemoglobin (g/dL)	16.1 ± 0.4	16.4 ± 0.5	16.4 ± 0.2	16.0 ± 0.3
Erythrocytes (10^6/μL)	9.60 ± 0.33	9.22 ± 0.35	9.64 ± 0.12	9.13 ± 0.32
Leukocytes (10^3/μL)	7.93 ± 0.63	6.18 ± 0.48	6.83 ± 0.34	5.02 ± 0.44**
Segmented neutrophils (10^3/μL)	1.71 ± 0.38	1.93 ± 0.54	1.82 ± 0.18	1.28 ± 0.19
Lymphocytes (10^3/μL)	5.70 ± 0.61	4.03 ± 0.32	4.72 ± 0.18	3.50 ± 0.28*
Monocytes (10^3/μL)	0.23 ± 0.04	0.10 ± 0.03*	0.11 ± 0.02	0.09 ± 0.03*
Eosinophils (10^3/μL)	0.27 ± 0.10	0.12 ± 0.04	0.19 ± 0.08	0.15 ± 0.06
Clinical Chemistry				
n	9	9	9	9
Blood urea nitrogen (mg/dL)	32.9 ± 5.9	29.1 ± 5.2	30.6 ± 5.9	19.9 ± 1.7
Creatinine (mg/dL)	0.39 ± 0.01	0.38 ± 0.04	0.40 ± 0.02	0.43 ± 0.02
Sodium (mEq/L)	174 ± 1[b]	172 ± 2*	166 ± 1**[c]	172 ± 3*[d]
Potassium (mEq/L)	5.0 ± 0.2[c]	5.3 ± 0.2	5.1 ± 0.2[c]	5.3 ± 0.2
Chloride (mEq/L)	135 ± 1	125 ± 2**	126 ± 1**[c]	130 ± 3
Phosphorus (mg/dL)	8.9 ± 0.4	7.8 ± 0.5	8.3 ± 0.6	7.1 ± 0.3**
Total protein (g/dL)	5.1 ± 0.1	5.0 ± 0.1	4.6 ± 0.1**	4.8 ± 0.1**
Albumin (g/dL)	2.9 ± 0.0	3.0 ± 0.0	2.9 ± 0.0	2.8 ± 0.1
Globulin (g/dL)	2.1 ± 0.0	2.0 ± 0.0	1.7 ± 0.1**	2.0 ± 0.0**
Albumin/globulin ratio	1.4 ± 0.0	1.5 ± 0.0	1.7 ± 0.0**	1.4 ± 0.0*
Total bilirubin (mg/dL)	0.1 ± 0.0[b]	0.2 ± 0.0	0.2 ± 0.0[c]	0.2 ± 0.0[c]
Alanine aminotransferase (IU/L)	40 ± 6	40 ± 6[e]	53 ± 11	24 ± 3[c]
Aspartate aminotransferase (IU/L)	91 ± 14[e]	94 ± 9[e]	93 ± 11	79 ± 9
Lactate dehydrogenase (IU/L)	315 ± 29	318 ± 20[e]	233 ± 22	278 ± 27
Sorbitol dehydrogenase (IU/L)	35 ± 3	34 ± 1[e]	28 ± 2	35 ± 5
Pseudocholinesterase (IU/L)	5,377 ± 233	5,427 ± 144[e]	4,872 ± 177	4,427 ± 146**
Urinalysis				
n	10	10	9	9
Specific gravity	1.020 ± 0.002	1.023 ± 0.003	1.022 ± 0.002	1.024 ± 0.002

TABLE G4
Hematology, Clinical Chemistry, and Urinalysis Data for Mice at the 8-Week Interim Evaluations in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	63 mg/kg	125 mg/kg	250 mg/kg
Male (continued)				
Hematology				
n	10	9	8	1[f]
Hematocrit (%)	47.4 ± 1.4	43.0 ± 1.0**	44.8 ± 0.6**	46.6
Hemoglobin (g/dL)	16.1 ± 0.4	15.4 ± 0.4	15.9 ± 0.2	16.9
Erythrocytes (10^6/µL)	9.60 ± 0.33	8.93 ± 0.19**	9.44 ± 0.11*	9.62
Leukocytes (10^3/µL)	7.93 ± 0.63	6.44 ± 0.45	7.60 ± 0.52	5.10
Segmented neutrophils (10^3/µL)	1.71 ± 0.38	1.82 ± 0.43	1.67 ± 0.23	1.33
Lymphocytes (10^3/µL)	5.70 ± 0.61	4.44 ± 0.40	5.69 ± 0.52	3.62
Monocytes (10^3/µL)	0.23 ± 0.04	0.08 ± 0.03**	0.19 ± 0.03	0.10
Eosinophils (10^3/µL)	0.27 ± 0.10	0.09 ± 0.03	0.05 ± 0.02*	0.05
Clinical Chemistry				
n	9	2	1[f]	1[f]
Blood urea nitrogen (mg/dL)	32.9 ± 5.9	17.8 ± 1.1*[g]	15.0	15.0
Creatinine (mg/dL)	0.39 ± 0.01	0.33 ± 0.03[h]	-[i]	-[i]
Sodium (mEq/L)	174 ± 1[b]	-[i]	174	-[i]
Potassium (mEq/L)	5.0 ± 0.2[c]	-[i]	9.9	-[i]
Chloride (mEq/L)	135 ± 1	141 ± 2	134	134
Phosphorus (mg/dL)	8.9 ± 0.4	7.3 ± 0.3[h]	9.0	7.0
Total protein (g/dL)	5.1 ± 0.1	5.0 ± 0.1[h]	4.8	5.3
Albumin (g/dL)	2.9 ± 0.0	3.1 ± 0.1	3.0	3.3
Globulin (g/dL)	2.1 ± 0.0	1.9 ± 0.1	1.8	2.0
Albumin/globulin ratio	1.4 ± 0.0	1.6 ± 0.1*	1.7	1.7
Total bilirubin (mg/dL)	0.1 ± 0.0[b]	-[i]	-[i]	-[i]
Alanine aminotransferase (IU/L)	40 ± 6	64 ± 24[j]	60 ± 11[b]	80
Aspartate aminotransferase (IU/L)	91 ± 14[e]	77 ± 13[b]	87 ± 18[h]	203
Lactate dehydrogenase (IU/L)	315 ± 29	402 ± 46[g]	498 ± 126[h]	749
Sorbitol dehydrogenase (IU/L)	35 ± 3	41 ± 5[g]	51 ± 5*[g]	85
Pseudocholinesterase (IU/L)	5,377 ± 233	4,711 ± 150*[d]	4,860 ± 137[g]	-[i]
Urinalysis				
n	10	9	8	1[f]
Specific gravity	1.020 ± 0.002	1.019 ± 0.002	1.020 ± 0.002	1.020

TABLE G4
Hematology, Clinical Chemistry, and Urinalysis Data for Mice at the 8-Week Interim Evaluations in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg
Female				
Hematology				
n	10	10	9	10
Hematocrit (%)	49.1 ± 0.4	43.4 ± 0.8**	48.0 ± 0.8	47.0 ± 0.7
Hemoglobin (g/dL)	16.5 ± 0.1	16.3 ± 0.2	16.7 ± 0.1	16.6 ± 0.2
Erythrocytes (10^6/μL)	9.94 ± 0.07	8.93 ± 0.17**	9.81 ± 0.14	9.56 ± 0.16
Leukocytes (10^3/μL)	4.70 ± 0.51	6.21 ± 0.74	4.86 ± 0.50	4.99 ± 0.66
Segmented neutrophils (10^3/μL)	0.56 ± 0.10	1.60 ± 0.56*	0.56 ± 0.11	1.22 ± 0.36
Lymphocytes (10^3/μL)	4.07 ± 0.43	4.42 ± 0.26	4.15 ± 0.40	3.51 ± 0.26
Monocytes (10^3/μL)	0.03 ± 0.01	0.04 ± 0.02	0.08 ± 0.02	0.08 ± 0.04
Eosinophils (10^3/μL)	0.05 ± 0.02	0.12 ± 0.02	0.06 ± 0.01	0.15 ± 0.06
Clinical Chemistry				
n	9	9	9	9
Blood urea nitrogen (mg/dL)	35.6 ± 3.6	24.1 ± 3.9*	19.7 ± 2.8**	16.1 ± 0.8**
Creatinine (mg/dL)	0.35 ± 0.04[c]	0.29 ± 0.04	0.36 ± 0.03	0.41 ± 0.01
Potassium (mEq/L)	4.5 ± 0.3[b]	5.2 ± 0.2[b]	5.1 ± 0.3	5.4 ± 0.5[j]
Chloride (mEq/L)	141 ± 1[g]	124 ± 4*	127 ± 1**	130 ± 2[j]
Phosphorus (mg/dL)	8.1 ± 0.6[c]	8.1 ± 0.6	7.3 ± 0.7	6.9 ± 0.3[c]
Total protein (g/dL)	5.0 ± 0.1[c]	4.9 ± 0.1	4.7 ± 0.1*	4.8 ± 0.1[c]
Albumin (g/dL)	3.3 ± 0.1[j]	3.3 ± 0.1	3.2 ± 0.1	3.2 ± 0.0*[c]
Globulin (g/dL)	1.8 ± 0.0[j]	1.6 ± 0.0	1.5 ± 0.0**	1.6 ± 0.0[c]
Albumin/globulin ratio	1.9 ± 0.0[j]	2.0 ± 0.0	2.1 ± 0.1	1.9 ± 0.0[c]
Alanine aminotransferase (IU/L)	63 ± 6	32 ± 4*[c]	29 ± 5**	27 ± 3**
Aspartate aminotransferase (IU/L)	194 ± 35	111 ± 19	87 ± 16*	90 ± 10**
Lactate dehydrogenase (IU/L)	413 ± 70	223 ± 31	154 ± 11**[c]	152 ± 15**
Sorbitol dehydrogenase (IU/L)	32 ± 3	25 ± 2	20 ± 2	22 ± 2
Pseudocholinesterase (IU/L)	6,526 ± 77[h]	-[i]	6,733 ± 182[c]	6,420 ± 64[d]
Urinalysis				
n	10	10	9	10
Specific gravity	1.015 ± 0.002	1.013 ± 0.002	1.016 ± 0.003	1.014 ± 0.001

TABLE G4
Hematology, Clinical Chemistry, and Urinalysis Data for Mice at the 8-Week Interim Evaluations in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	63 mg/kg	125 mg/kg	250 mg/kg
Female (continued)				
Hematology				
n	10	9	8	6
Hematocrit (%)	49.1 ± 0.4	47.8 ± 0.5	49.2 ± 1.2	45.3 ± 0.9*
Hemoglobin (g/dL)	16.5 ± 0.1	16.5 ± 0.2	17.1 ± 0.4	16.1 ± 0.3
Erythrocytes (10^6/μL)	9.94 ± 0.07	9.29 ± 0.47	9.90 ± 0.26	9.31 ± 0.19
Leukocytes (10^3/μL)	4.70 ± 0.51	4.77 ± 0.20	4.64 ± 0.32	5.92 ± 0.40
Segmented neutrophils (10^3/μL)	0.56 ± 0.10	0.84 ± 0.07	0.91 ± 0.13	0.77 ± 0.12
Lymphocytes (10^3/μL)	4.07 ± 0.43	3.78 ± 0.21	3.61 ± 0.23	4.98 ± 0.41
Monocytes (10^3/μL)	0.03 ± 0.01	0.06 ± 0.01	0.03 ± 0.02	0.07 ± 0.02
Eosinophils (10^3/μL)	0.05 ± 0.02	0.07 ± 0.01	0.09 ± 0.01	0.09 ± 0.05
Clinical Chemistry				
n	9	1[f]	1[f]	5
Blood urea nitrogen (mg/dL)	35.6 ± 3.6	15.0 ± 0.6**[h]	21.0	14.4 ± 1.1**
Creatinine (mg/dL)	0.35 ± 0.04[c]	0.35 ± 0.05[k]	-[i]	0.28 ± 0.03[g]
Potassium (mEq/L)	4.5 ± 0.3[b]	-[i]	-[i]	5.4[f]
Chloride (mEq/L)	141 ± 1[g]	133	-[i]	133 ± 3[h]
Phosphorus (mg/dL)	8.1 ± 0.6[c]	8.2 ± 0.3[h]	8.9	7.2 ± 0.5
Total protein (g/dL)	5.0 ± 0.1[c]	5.1 ± 0.1[h]	5.9	4.8 ± 0.1
Albumin (g/dL)	3.3 ± 0.1[j]	3.3	-[i]	3.1 ± 0.1*[g]
Globulin (g/dL)	1.8 ± 0.0[j]	1.7	-[i]	1.7 ± 0.1[g]
Albumin/globulin ratio	1.9 ± 0.0[j]	1.9	-[i]	1.8 ± 0.0[g]
Alanine aminotransferase (IU/L)	63 ± 6	35 ± 6[l]	54 ± 14[j]	45 ± 7[d]
Aspartate aminotransferase (IU/L)	194 ± 35	82 ± 10*[b]	128 ± 46[g]	76 ± 14**[d]
Lactate dehydrogenase (IU/L)	413 ± 70	348 ± 55[b]	832	462 ± 71
Sorbitol dehydrogenase (IU/L)	32 ± 3	33 ± 5[b]	37 ± 6[g]	45 ± 4
Pseudocholinesterase (IU/L)	6,526 ± 77[h]	-[i]	-[i]	-[i]
Urinalysis				
n	10	9	8	6
Specific gravity	1.015 ± 0.002	1.016 ± 0.006	1.009 ± 0.001*	1.012 ± 0.003

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error
[b] n=5
[c] n=8
[d] n=6
[e] n=10
[f] n=1; no standard error calculated due to high mortality in this group
[g] n=4
[h] n=3
[i] n=0; no data calculated due to 100% mortality in this group
[j] n=7
[k] n=2
[l] n=9

TABLE G5
Hematology, Clinical Chemistry, and Urinalysis Data for Mice in the 17-Week Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg
Male				
Hematology				
n	10	10	10	10
Hematocrit (%)	44.4 ± 1.2	41.5 ± 0.9	43.4 ± 0.4	43.4 ± 0.5
Hemoglobin (g/dL)	14.4 ± 0.4	14.7 ± 0.4	15.0 ± 0.2	15.2 ± 0.2
Erythrocytes (10^3/ L)	8.97 ± 0.30	8.53 ± 0.20	8.98 ± 0.08	8.90 ± 0.10
Leukocytes (10^3/ L)	9.07 ± 1.05	7.93 ± 1.03	3.19 ± 0.18**	5.73 ± 0.62
Segmented neutrophils (10^3/ L)	3.84 ± 0.73	4.77 ± 1.07	1.04 ± 0.11*	3.33 ± 0.59
Lymphocytes (10^3/ L)	4.92 ± 0.46	2.92 ± 0.47*	1.99 ± 0.10**	2.22 ± 0.20**
Monocytes (10^3/ L)	0.10 ± 0.03	0.07 ± 0.04	0.01 ± 0.01	0.06 ± 0.02
Eosinophils (10^3/ L)	0.17 ± 0.06	0.10 ± 0.05	0.13 ± 0.04	0.11 ± 0.04
Clinical Chemistry				
n	9	10	10	9
Blood urea nitrogen (mg/dL)	33.7 ± 6.1	18.1 ± 1.3**	18.1 ± 0.9**	17.6 ± 0.7**
Creatinine (mg/dL)	0.43 ± 0.04	0.36 ± 0.02*	0.34 ± 0.02*	0.33 ± 0.02**[b]
Sodium (mEq/L)	168 ± 1[c]	164 ± 0	165 ± 0	164 ± 2
Potassium (mEq/L)	7.0 ± 1.0[c]	4.7 ± 0.1*	4.7 ± 0.1*	4.6 ± 0.2**
Chloride (mEq/L)	134 ± 4[b]	122 ± 5	119 ± 4	123 ± 2
Phosphorus (mg/dL)	9.3 ± 0.7	7.1 ± 0.1	7.1 ± 0.3	6.4 ± 0.4*
Total protein (g/dL)	5.1 ± 0.1	4.8 ± 0.1	4.8 ± 0.1	4.5 ± 0.1**
Albumin (g/dL)	3.0 ± 0.1[b]	2.6 ± 0.1	2.8 ± 0.0	2.5 ± 0.1
Globulin (g/dL)	2.2 ± 0.1[b]	2.2 ± 0.1	2.1 ± 0.0	2.0 ± 0.0
Albumin/globulin ratio	1.4 ± 0.1[b]	1.2 ± 0.1	1.4 ± 0.0	1.3 ± 0.0
Total bilirubin (mg/dL)	0.2 ± 0.0[c]	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
Alanine aminotransferase (IU/L)	62 ± 12[d]	53 ± 11	57 ± 11	47 ± 8
Aspartate aminotransferase (IU/L)	132 ± 23[d]	66 ± 4*	71 ± 6	70 ± 7
Lactate dehydrogenase (IU/L)	516 ± 55	246 ± 22**	269 ± 24**	474 ± 81
Sorbitol dehydrogenase (IU/L)	48 ± 5[d]	26 ± 1**	28 ± 1*	39 ± 4
Pseudocholinesterase (IU/L)	5,495 ± 164[d]	5,158 ± 147	5,364 ± 158	4,735 ± 100
Urinalysis				
n	10	10	10	10
Specific gravity	1.019 ± 0.002	1.033 ± 0.004	1.037 ± 0.003**	1.031 ± 0.004

TABLE G5
Hematology, Clinical Chemistry, and Urinalysis Data for Mice in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	63 mg/kg	125 mg/kg	250 mg/kg
Male (continued)				
Hematology				
n	10	10	8	2
Hematocrit (%)	44.4 ± 1.2	43.6 ± 0.7	44.7 ± 1.0	44.2 ± 2.9
Hemoglobin (g/dL)	14.4 ± 0.4	15.4 ± 0.2*	16.1 ± 0.3**	16.1 ± 0.9
Erythrocytes (10^6/ L)	8.97 ± 0.30	8.95 ± 0.18	9.22 ± 0.22	9.27 ± 0.53
Leukocytes (10^3/ L)	9.07 ± 1.05	9.77 ± 1.48	8.88 ± 1.88	5.55 ± 1.75
Segmented neutrophils (10^3/ L)	3.84 ± 0.73	5.19 ± 1.31	5.71 ± 1.68	1.64 ± 0.92
Lymphocytes (10^3/ L)	4.92 ± 0.46	4.11 ± 0.43	2.57 ± 0.25*	3.75 ± 0.78
Monocytes (10^3/ L)	0.10 ± 0.03	0.22 ± 0.06	0.39 ± 0.16	0.04 ± 0.04
Eosinophils (10^3/ L)	0.17 ± 0.06	0.18 ± 0.05	0.12 ± 0.03	0.13 ± 0.09
Clinical Chemistry				
n	9	8	8	2
Blood urea nitrogen (mg/dL)	33.7 ± 6.1	23.6 ± 3.5*[e]	17.0 ± 1.1**[c]	16.0[f]
Creatinine (mg/dL)	0.43 ± 0.04	0.30 ± 0.03**[e]	0.24 ± 0.04**[c]	0.30 ± 0.00*
Sodium (mEq/L)	168 ± 1[c]	181 ± 1	178 ± 1[c]	180 ± 1
Potassium (mEq/L)	7.0 ± 1.0[c]	6.4 ± 0.3	5.8 ± 0.2[c]	5.1 ± 0.3
Chloride (mEq/L)	134 ± 4[b]	141 ± 3	138 ± 3	137 ± 2
Phosphorus (mg/dL)	9.3 ± 0.7	8.9 ± 0.6[e]	9.2 ± 1.2	7.7 ± 0.5
Total protein (g/dL)	5.1 ± 0.1	5.4 ± 0.1[e]	5.0 ± 0.1	5.4 ± 0.2
Albumin (g/dL)	3.0 ± 0.1[b]	3.1 ± 0.0	3.0 ± 0.1	3.4 ± 0.2
Globulin (g/dL)	2.2 ± 0.1[b]	2.3 ± 0.1	2.1 ± 0.1	2.1 ± 0.1
Albumin/globulin ratio	1.4 ± 0.1[b]	1.4 ± 0.0	1.5 ± 0.1	1.6 ± 0.0
Total bilirubin (mg/dL)	0.2 ± 0.0[c]	0.2 ± 0.0[c]	0.2 ± 0.1[c]	0.1 ± 0.0
Alanine aminotransferase (IU/L)	62 ± 12[d]	59 ± 14[d]	58 ± 6	93 ± 19
Aspartate aminotransferase (IU/L)	132 ± 23[d]	121 ± 21[d]	108 ± 9	88 ± 17
Lactate dehydrogenase (IU/L)	516 ± 55	374 ± 40[e]	339 ± 50	181 ± 22*
Sorbitol dehydrogenase (IU/L)	48 ± 5[d]	25 ± 2**[d]	36 ± 5	53 ± 2
Pseudocholinesterase (IU/L)	5,495 ± 164[d]	5,718 ± 138[d]	6,218 ± 161*	6,510 ± 24
Urinalysis				
n	10	10	8	2
Specific gravity	1.019 ± 0.002	1.032 ± 0.005	1.029 ± 0.006	1.017 ± 0.003

TABLE G5
Hematology, Clinical Chemistry, and Urinalysis Data for Mice in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	8 mg/kg	16 mg/kg	32 mg/kg
Female				
Hematology				
n	10	10	8	10
Hematocrit (%)	49.5 ± 0.7	49.0 ± 0.4	46.2 ± 0.9**	48.4 ± 0.6*
Hemoglobin (g/dL)	16.2 ± 0.2	16.3 ± 0.1	16.5 ± 0.2	16.4 ± 0.2
Erythrocytes (10^6/ L)	9.96 ± 0.12	10.06 ± 0.06	9.54 ± 0.21*	9.88 ± 0.09
Leukocytes (10^3/ L)	4.09 ± 0.33	4.18 ± 0.23	3.89 ± 0.39	5.03 ± 0.22
Segmented neutrophils (10^3/ L)	0.93 ± 0.14	0.97 ± 0.14	0.80 ± 0.15	1.51 ± 0.20
Lymphocytes (10^3/ L)	3.12 ± 0.21	3.14 ± 0.14	3.00 ± 0.25	3.38 ± 0.16
Monocytes (10^3/ L)	0.01 ± 0.01	0.01 ± 0.01	0.02 ± 0.01	0.04 ± 0.01
Eosinophils (10^3/ L)	0.09 ± 0.02	0.07 ± 0.02	0.11 ± 0.02	0.02 ± 0.01[g]
Clinical Chemistry				
n	8	9	8	9
Blood urea nitrogen (mg/dL)	14.6 ± 0.5	19.9 ± 1.8	13.5 ± 0.9	16.4 ± 0.7
Creatinine (mg/dL)	0.26 ± 0.03	0.39 ± 0.03*	0.31 ± 0.02[e]	0.31 ± 0.02
Sodium (mEq/L)	169 ± 2[c]	166 ± 1[c]	166 ± 1[h]	170 ± 1
Potassium (mEq/L)	5.1 ± 0.3[c]	4.5 ± 0.2[c]	5.1 ± 0.2[h]	4.7 ± 0.2
Chloride (mEq/L)	143 ± 3[c]	138 ± 3[b]	129 ± 5[i]	131 ± 2[d]
Phosphorus (mg/dL)	6.2 ± 0.4	7.9 ± 0.5*	5.6 ± 0.4[c]	5.9 ± 0.3
Total protein (g/dL)	4.8 ± 0.1	5.2 ± 0.2	4.7 ± 0.1[g]	4.8 ± 0.1
Albumin (g/dL)	3.1 ± 0.0	3.4 ± 0.1*	3.0 ± 0.0[g]	3.1 ± 0.0
Globulin (g/dL)	1.7 ± 0.1	1.8 ± 0.1	1.8 ± 0.1[g]	1.7 ± 0.0
Albumin/globulin ratio	1.8 ± 0.1	1.9 ± 0.1	1.7 ± 0.1[g]	1.8 ± 0.0
Total bilirubin (mg/dL)	0.3 ± 0.1[j]	0.3 ± 0.0[g]	0.2 ± 0.1[h]	0.2 ± 0.0[i]
Alanine aminotransferase (IU/L)	32 ± 4[e]	25 ± 4	32 ± 6	28 ± 3[d]
Aspartate aminotransferase (IU/L)	107 ± 22[d]	100 ± 19	72 ± 9	84 ± 8[d]
Lactate dehydrogenase (IU/L)	357 ± 46[d]	343 ± 25	185 ± 20**	166 ± 12**[d]
Sorbitol dehydrogenase (IU/L)	27 ± 2[d]	25 ± 1	19 ± 1	19 ± 1*[d]
Pseudocholinesterase (IU/L)	7,540 ± 162[d]	7,277 ± 185	7,011 ± 249	7,521 ± 184[d]
Urinalysis				
n	10	10	8	10
Specific gravity	1.015 ± 0.002	1.017 ± 0.002	1.021 ± 0.003	1.028 ± 0.003*

TABLE G5
Hematology, Clinical Chemistry, and Urinalysis Data for Mice in the 17-Week Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	63 mg/kg	125 mg/kg	250 mg/kg
Female (continued)				
Hematology				
n	10	10	9	6
Hematocrit (%)	49.5 ± 0.7	46.8 ± 2.0	45.1 ± 0.8**	46.3 ± 1.0**
Hemoglobin (g/dL)	16.2 ± 0.2	16.0 ± 0.5	15.8 ± 0.2	16.1 ± 0.3
Erythrocytes (10^6/ L)	9.96 ± 0.12	9.58 ± 0.39	9.32 ± 0.16**	9.50 ± 0.21*
Leukocytes (10^3/ L)	4.09 ± 0.33	5.73 ± 0.87	3.93 ± 0.18	4.57 ± 0.44
Segmented neutrophils (10^3/ L)	0.93 ± 0.14	1.63 ± 0.63	0.78 ± 0.11	1.17 ± 0.34
Lymphocytes (10^3/ L)	3.12 ± 0.21	3.87 ± 0.32	3.02 ± 0.11	3.32 ± 0.27
Monocytes (10^3/ L)	0.01 ± 0.01	0.14 ± 0.06**	0.02 ± 0.01	0.06 ± 0.04
Eosinophils (10^3/ L)	0.09 ± 0.02	-[k]	-[k]	-[k]
Clinical Chemistry				
n	8	8	9	5
Blood urea nitrogen (mg/dL)	14.6 ± 0.5	14.3 ± 1.5	13.6 ± 0.6	13.2 ± 0.4
Creatinine (mg/dL)	0.26 ± 0.03	0.29 ± 0.04	0.33 ± 0.02[b]	0.30 ± 0.03
Sodium (mEq/L)	169 ± 2[c]	176 ± 2*[j]	179 ± 2**[i]	184 ± 4*[h]
Potassium (mEq/L)	5.1 ± 0.3[c]	5.7 ± 0.3[j]	6.2 ± 0.7[i]	6.1 ± 0.5[h]
Chloride (mEq/L)	143 ± 3[c]	131 ± 6[c]	131 ± 11[g]	142 ± 7[i]
Phosphorus (mg/dL)	6.2 ± 0.4	6.5 ± 0.5[c]	10.7 ± 1.6**[c]	8.3 ± 0.3*[l]
Total protein (g/dL)	4.8 ± 0.1	5.3 ± 0.1*	4.8 ± 0.1[c]	5.2 ± 0.1[j]
Albumin (g/dL)	3.1 ± 0.0	3.4 ± 0.1**	3.3 ± 0.1*[b]	3.6 ± 0.1**[j]
Globulin (g/dL)	1.7 ± 0.1	1.9 ± 0.1	1.4 ± 0.1[c]	1.7 ± 0.1[j]
Albumin/globulin ratio	1.8 ± 0.1	1.8 ± 0.1	2.4 ± 0.2**[c]	2.1 ± 0.1*[j]
Total bilirubin (mg/dL)	0.3 ± 0.1[j]	0.2 ± 0.0[l]	0.1 ± 0.0*[l]	0.1[f]
Alanine aminotransferase (IU/L)	32 ± 4[e]	30 ± 6	35 ± 4	56 ± 7*[j]
Aspartate aminotransferase (IU/L)	107 ± 22[d]	78 ± 6	479 ± 10	117 ± 14
Lactate dehydrogenase (IU/L)	357 ± 46[d]	201 ± 34**	207 ± 35**	247 ± 24*
Sorbitol dehydrogenase (IU/L)	27 ± 2	21 ± 1	18 ± 2	43 ± 4
Pseudocholinesterase (IU/L)	7,540 ± 162[d]	7,612 ± 475[e]	7,125 ± 141[b]	7,733 ± 283
Urinalysis				
n	10	9	9	6
Specific gravity	1.015 ± 0.002	1.022 ± 0.005	1.020 ± 0.004	1.019 ± 0.005

* Significantly different (P 0.05) from the control group by Dunn's or Shirley's test
** P 0.01
[a] Mean ± standard error
[b] n=8
[c] n=7
[d] n=10
[e] n=9
[f] n=1; no standard error calculated due to high mortality
[g] n=6
[h] n=2
[i] n=5
[j] n=4
[k] n=0; no data calculated due to 100% mortality in this group
[l] n=3

TABLE G6
Hematology and Clinical Chemistry Data for Mice at the 15-Month Interim Evaluations in the 2-Year Gavage Studies of 1,2,3-Trichloropropane[a]

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Male				
Hematology				
n	9	9	8	5
Hematocrit (%)	44.8 ± 0.4	44.1 ± 0.5	42.4 ± 1.0*	40.1 ± 2.4**
Hemoglobin (g/dL)	15.4 ± 0.1	15.4 ± 0.2	14.9 ± 0.4	13.8 ± 0.8*
Erythrocytes (10^6/ L)	9.28 ± 0.05	9.46 ± 0.09	9.29 ± 0.26	8.36 ± 0.54
Mean cell volume (fL)	48.3 ± 0.4	46.7 ± 0.2**	45.9 ± 1.1**	48.4 ± 1.5
Mean cell hemoglobin (pg)	16.6 ± 0.1	16.2 ± 0.1	16.1 ± 0.4	16.5 ± 0.5
Mean cell hemoglobin concentration (g/dL)	34.4 ± 0.2	34.8 ± 0.3	35.2 ± 0.3	34.3 ± 0.2
Leukocytes (10^3/ L)	6.29 ± 0.37	4.49 ± 0.48	8.96 ± 3.17	22.38 ± 8.16
Segmented neutrophils (10^3/ L)	1.75 ± 0.30	1.64 ± 0.48	4.56 ± 2.27	16.99 ± 7.43
Lymphocytes (10^3/ L)	4.17 ± 0.35	2.65 ± 0.43	4.00 ± 0.84	4.63 ± 0.76
Monocytes (10^3/ L)	0.12 ± 0.04	0.04 ± 0.02	0.13 ± 0.05	0.10 ± 0.07
Eosinophils (10^3/ L)	0.25 ± 0.06	0.15 ± 0.03	0.27 ± 0.10	0.23 ± 0.08
Nucleated erythrocytes (10^3/ L)	0.04 ± 0.02	0.01 ± 0.01	0.01 ± 0.01	0.01 ± 0.01
Clinical Chemistry				
n	7	7	6	4
Alkaline phosphatase (IU/L)	45 ± 1[b]	51 ± 3[b]	45 ± 4	44 ± 6
Alanine aminotransferase (IU/L)	37 ± 4	32 ± 3	149 ± 56	79 ± 31
Aspartate aminotransferase (IU/L)	68 ± 4	79 ± 15	222 ± 101	107 ± 25
Creatine kinase (U/L)	96 ± 12[b]	132 ± 47	186 ± 47[c]	322 ± 84*
Lactate dehydrogenase (IU/L)	435 ± 34	348 ± 38	900 ± 221*	956 ± 354
Sorbitol dehydrogenase (IU/L)	32 ± 1	28 ± 2	30 ± 4	36 ± 2[d]
5-Nucleotidase (IU/L)	21.25 ± 0.92[b]	17.86 ± 1.08	21.60 ± 1.63[c]	27.75 ± 4.99

TABLE G6
Hematology and Clinical Chemistry Data for Mice at the 15-Month Interim Evaluations in the 2-Year Gavage Studies of 1,2,3-Trichloropropane (continued)

	Vehicle Control	6 mg/kg	20 mg/kg	60 mg/kg
Female				
Hematology				
n	10	10	9	5
Hematocrit (%)	45.4 ± 0.4	44.2 ± 0.9	43.6 ± 0.5*	40.4 ± 2.0**
Hemoglobin (g/dL)	15.9 ± 0.3	15.2 ± 0.3	14.9 ± 0.2**	14.0 ± 0.7**
Erythrocytes (10^6/ L)	9.57 ± 0.09	9.11 ± 0.42	9.09 ± 0.10**	8.32 ± 0.52**
Mean cell volume (fL)	47.3 ± 0.2	49.3 ± 2.2	48.0 ± 0.3	49.0 ± 1.1
Mean cell hemoglobin (pg)	16.6 ± 0.2	17.0 ± 0.7	16.4 ± 0.1	16.9 ± 0.3
Mean cell hemoglobin concentration (g/dL)	35.0 ± 0.4	34.5 ± 0.2	34.2 ± 0.2	34.7 ± 0.2
Leukocytes (10^3/ L)	4.89 ± 0.56	5.13 ± 0.48[e]	6.23 ± 0.65*	11.22 ± 1.26**
Segmented neutrophils (10^3/ L)	1.10 ± 0.14	1.40 ± 0.20[e]	2.30 ± 0.28**	5.14 ± 1.05**
Lymphocytes (10^3/ L)	3.61 ± 0.47	3.85 ± 0.41	3.68 ± 0.38	5.69 ± 0.44**
Monocytes (10^3/ L)	0.07 ± 0.01	0.06 ± 0.02[e]	0.10 ± 0.03	0.15 ± 0.02**
Eosinophils (10^3/ L)	0.12 ± 0.02	0.10 ± 0.02[e]	0.15 ± 0.05	0.19 ± 0.08
Nucleated erythrocytes (10^3/ L)	0.03 ± 0.01	0.01 ± 0.01	0.01 ± 0.01	0.02 ± 0.02
Clinical Chemistry				
n	10	9	9	5
Alkaline phosphatase (IU/L)	99 ± 8	118 ± 15[f]	105 ± 7	89 ± 10
Alanine aminotransferase (IU/L)	33 ± 4	24 ± 2	34 ± 7	38 ± 2
Aspartate aminotransferase (IU/L)	101 ± 18	67 ± 6	87 ± 8	79 ± 6
Creatine kinase (U/L)	70 ± 11	99 ± 19[f]	149 ± 35*	97 ± 20
Lactate dehydrogenase (IU/L)	432 ± 85	311 ± 29	474 ± 65	433 ± 98
Sorbitol dehydrogenase (IU/L)	22 ± 3[g]	22 ± 1[h]	24 ± 1[i]	38 ± 3*[d]
5-Nucleotidase (IU/L)	78.70 ± 4.38	75.44 ± 3.72	73.89 ± 2.86	66.40 ± 6.23

* Significantly different (P 0.05) from the control group by Dunn's or Shirley's test
** P 0.01
[a] Mean ± standard error
[b] n=8
[c] n=5
[d] n=3
[e] n=9
[f] n=10
[g] n=6
[h] n=7
[i] n=4

APPENDIX H
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION

CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

PROCUREMENT AND CHARACTERIZATION OF 1,2,3-TRICHLOROPROPANE

1,2,3-Trichloropropane was obtained from the Shell Chemical Company (Houston, TX) in one lot (JG32449), which was used throughout the 17-week and 2-year studies. The purity, elemental, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO), and confirmed by the study laboratories, Hazleton Laboratories America, (Vienna, VA) for the 17-week studies and EG&G Mason Research Institute (Worcester, MA) for the 2-year studies.

The study material, a clear, colorless, nonviscous liquid, was identified as 1,2,3-trichloropropane by physical properties and infrared, ultraviolet/visible, and nuclear magnetic resonance (NMR) spectroscopies. All spectra were consistent with those expected for the structure of 1,2,3-trichloropropane and were consistent with those in the literature (*Sadtler Standard Spectra*), as shown in Figures H1 and H2.

Purity of 1,2,3-trichloropropane (>99%) was determined by elemental analyses, Karl Fischer water analysis, titration, and gas chromatography. Titration of the acidic components was performed in methanol to the phenolphthalein endpoint using 0.01 N sodium hydroxide. Gas chromatography was performed with a flame ionization detector at 250° C in a nitrogen gas carrier with a 70 mL/minute flow rate. Two systems were used in the analyses, both using methylene chloride as a solvent:

System 1) 20% SP-2100/0.1% Carbowax 1500 on 100/120 mesh Supelcoport, oven temperature program of 50° C for 5 minutes, then 50° C to 170° C at 10° C/minute, and
System 2) 10% Carbowax 20M-TPA on 80/100 mesh Chromosorb W (AW), oven temperature program of 50° C for 5 minutes, then 50° C to 200° C at 10° C/minute.

Results of elemental analyses for carbon and hydrogen were slightly higher than the theoretical values; the result of the chloride analysis was slightly lower than the theoretical values. Karl Fischer water analysis indicated the presence of 0.066% ± 0.003% water. Titration indicated the free acid (HCl) content was 48 ± 2 ppm. Gas chromatography with System 1 indicated three impurities following the major peak, which had a combined area of 0.60% relative to the major peak area. With System 2, a group of unresolved impurities was indicated before the major peak and one impurity (less than 0.1% of the major peak area) followed the major peak. The combined area of these impurities was 0.88% of the major peak area. Impurities greater than 0.1% were identified as isomers of chlorohexane and chlorohexadiene by capillary gas chromatography/mass spectroscopy method. Isomeric configurations could not be deduced since standards were not available.

Stability studies on the bulk chemical used titration of the free acid component and gas chromatography (System 1) with an isothermal oven program of 100° C. The internal standard used was 0.2% n-octane (v/v) in methylene chloride. 1,2,3-Trichloropropane was stable as a bulk chemical when stored protected from light for 2 weeks at temperatures up to 60° C. During the 2-year studies, the bulk chemical was analyzed at least every 4 months and no degradation was detected.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared by mixing 1,2,3-trichloropropane, by weight, and corn oil, by volume, for the 17-day studies and on a weight-to-weight basis for the 2-year studies, to achieve the required concentrations (Table H1). The dose formulations were prepared weekly and stored in the dark at room temperature prior to administration.

Stability of a 20 mg/mL 1,2,3-trichloropropane in corn oil solution was determined by the analytical chemistry laboratory using gas chromatography (System 1) with a detector temperature of 200° C, a flow rate of 24 mL/minute, and an oven temperature program of 80° C for 2 minutes, increasing at 5° C/minute to 110° C, and remaining at 110° C for 4 minutes. n-Decane in hexane (0.3 mg/mL) was used as the internal standard. Stability of the formulation was confirmed after storage for 21 days in the dark at room temperature and at 5° C. Samples of the formulation stored for 3 hours open to air and exposed to light showed no significant degradation. Over the range of dose concentrations, the relative standard deviations were less than or equal to ± 0.7%.

Periodic analyses of the dose formulations of 1,2,3-trichloropropane were conducted by the study laboratories and the analytical chemistry laboratory using the gas chromatography method described previously. During the 17-week studies, the dose formulations from the mixing room were analyzed three times and those retained in the animal rooms were analyzed twice. Ninety-one percent of the samples were within 10% of the target concentrations (Tables H2 and H3). During the 2-year studies, the dose formulations from the mixing room were analyzed at 8-week intervals and those retained in the animal rooms were analyzed five times at approximately 5-month intervals (Table H4). Ninety-two percent of the samples were within 10% of the target concentrations. Referee analyses of dose formulations for rats and mice performed by the analytical chemistry laboratory were in good agreement with the results of the study laboratories (Table H5).

The corn oil vehicle (Duke's Corn Oil, lot number 80235 for the 17-week studies; Mazola Corn Oil, lot number MCOSG54-60 for the 2-year studies) was analyzed for peroxides monthly by titration with 0.005 N sodium thiosulfate. Periodic analyses of the corn oil vehicle by the study laboratory showed peroxide levels were less than 5 mEq/kg throughout the 17-week studies and less than 3 mEq/kg throughout the 2-year studies. All samples were below the 10 mEq/kg rancidity threshold.

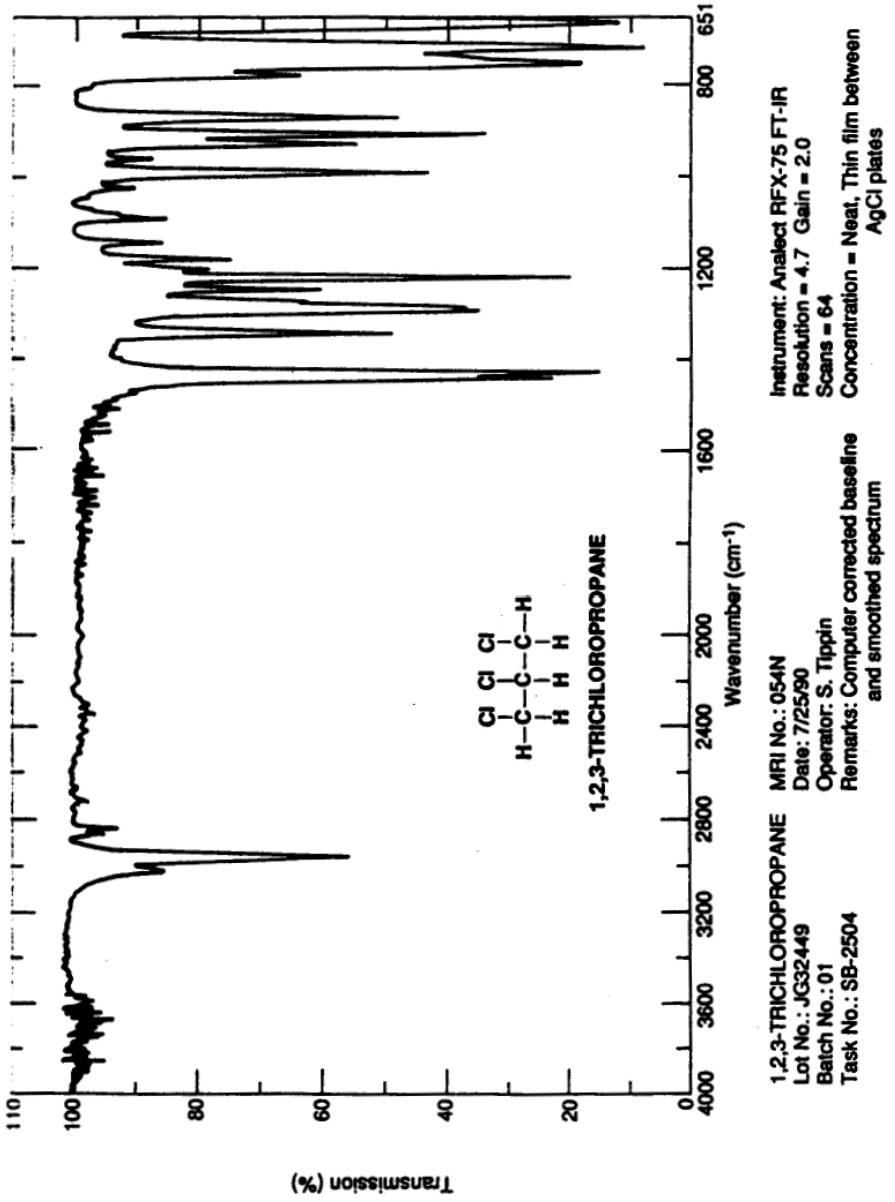

FIGURE H1
Infrared Absorption Spectrum of 1,2,3-Trichloropropane

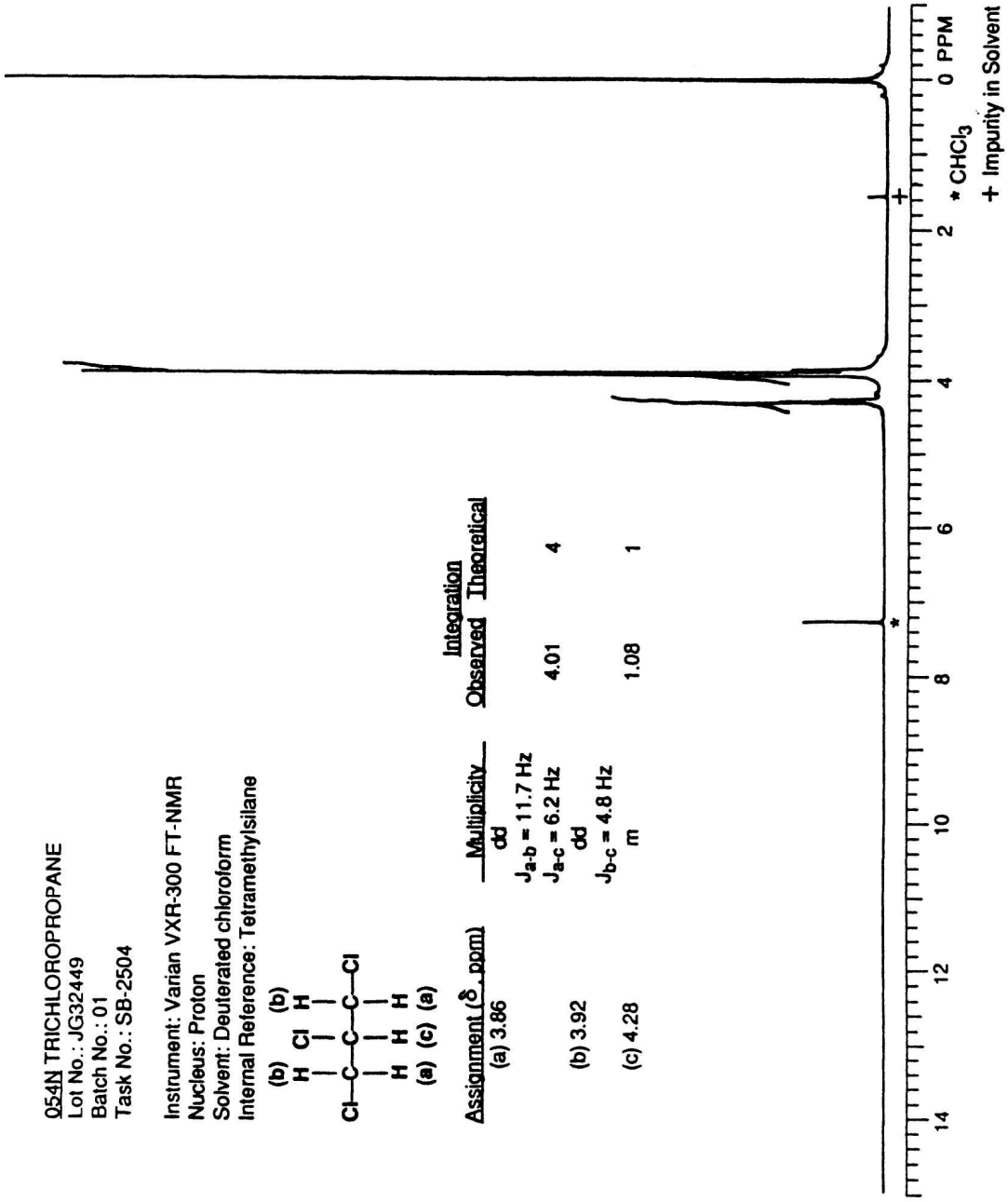

FIGURE H2
Nuclear Magnetic Resonance Spectrum of 1,2,3-Trichloropropane

TABLE H1
Preparation and Storage of Dose Formulations in the Gavage Studies of 1,2,3-Trichloropropane

17-Week Studies	2-Year Studies
Preparation 1,2,3-Trichloropropane was mixed with corn oil to obtain the appropriate concentrations. The dose formulations were mixed with a magnetic stirrer for 2 to 3 minutes before storage. Formulations were prepared weekly. Animals were dosed based on weekly average body weight of the dose group. Dosing volumes were 5 mL/kg body weight for rats and 10 mL/kg body weight for mice.	1,2,3-Trichloropropane was mixed with corn oil to obtain the appropriate concentrations. The dose formulations were mixed with a magnetic stirrer for 5 minutes before storage. Formulations were prepared weekly. Animals were dosed based on weekly average body weight of the dose group. Dosing volumes were 5 mL/kg body weight for rats and 10 mL/kg body weight for mice.
Lot JG32449	JG32449
Maximum Storage Time 7 days	3 weeks
Storage Conditions Dose solutions were stored in sealed, amber glass bottles at room temperature in the dark.	Dose solutions were stored in sealed, amber serum vials at 4° C in the dark.
Study Laboratory Hazleton Laboratories America (Vienna, PA)	EG&G Mason Research Institute (Worcester, MA)
Referee Laboratory Midwest Research Institute (Kansas City, MO)	Midwest Research Institute (Kansas City, MO)

TABLE H2
Results of Analysis of Dose Formulations for Rats in the 17-Week Gavage Studies of 1,2,3-Trichloropropane

Date Prepared	Date Analyzed	Target Concentration[a] (mg/mL)	Determined Concentration[b] (mg/mL)	Difference from Target (%)
18 February 1982	19 February 1982	1.6	1.58	-1
		3.2	3.14	-2
		6.4	6.12	-4
		12.6	12.4	-1
		25.0	23.79	-5
		50.0	47.94	-4
18 February 1982	4 March 1982[c]	1.6	1.55	-3
		3.2	3.28	+3
		6.4	6.28	-2
		12.6	12.26	-3
		25.0	24.48	-2
		50.0	52.16	+4
14 April 1982	16 April 1982	1.6	1.6	0
		3.2	3.1	-3
		6.4	6.34	-1
		12.6	12.2	-3
		25.0	24.32	-3
		50.0	46.8	-6
29 April 1982	12 May 1982	1.6	1.52	-5
		3.2	3.53	-4
		6.4	3.06	-4
		12.6	11.9	-6
		25.0	23.02	-8
23 June 1982	2 July 1982	1.6	1.5	-6

[a] Dosing volume = 5 mL/kg; 1.6 mg/mL = 8 mg/kg; 3.2 mg/mL = 16 mg/kg; 6.4 mg/mL = 32 mg/kg; 12.6 mg/mL = 63 mg/kg; 25.0 mg/mL = 125 mg/kg; 50.0 mg/mL = 250 mg/kg
[b] Results of duplicate analysis
[c] Animal room sample

TABLE H3
Results of Analysis of Dose Formulations for Mice in the 17-Week Gavage Studies of 1,2,3-Trichloropropane

Date Prepared	Date Analyzed	Target Concentration[a] (mg/mL)	Determined Concentration[b] (mg/mL)	Difference from Target (%)
18 March 1982	23 March 1982	0.8	0.8	-4
		1.6	1.6	-3
		3.2	2.9	-9
		6.3	6.1	-3
		12.5	12.3	-2
		25.0	23.5	-6
18 March 1982	9 April 1982[c]	0.8	0.8	-4
		1.6	1.5	-7
		3.2	3.1	-2
		6.3	6.2	-2
		12.5	10.7	-14
		25.0	24.0	-4
19 May 1982	21 May 1982	0.8	0.8	-1
		1.6	1.4	-10
		3.2	2.9	-9
		6.3	6.2	-1
		12.5	13.0	+3
		25.0	24.1	-3
24 May 1982	25 May 1982[d]	1.6	1.4	-15
26 May 1982	26 May 1982[e]	1.6	1.6	0
19 May 1982	3 June 1982	0.8	0.79	-1
		1.6	1.58	-1
		3.2	2.82	-12
		6.3	6.28	0
		12.5	12.93	+3
		25.0	24.55	-2
19 May 1982	8 June 1982[f]	3.2	2.90	-9
21 July 1982	22 July 1982	0.8	0.72	-11
		1.6	1.53	-4
		3.2	3.11	-3
		6.3	6.19	-2
		12.5	12.34	-1
		25.0	22.30	-11

[a] Dosing volume = 10 mL/kg; 0.8 mg/mL = 8 mg/kg; 1.6 mg/mL = 16 mg/kg; 3.2 mg/mL = 32 mg/kg; 6.3 mg/mL = 63 mg/kg; 12.5 mg/mL = 125 mg/kg; 25.0 mg/mL = 250 mg/kg
[b] Results of duplicate analysis
[c] Animal room sample
[d] First remix of 1.6 mg/mL concentration
[e] Second remix of 1.6 mg/mL concentration
[f] Remix of 3.2 mg/mL concentration

TABLE H4
Results of Analysis of Dose Formulations for Rats and Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

Date Prepared	Date Analyzed	Target Concentration[a] (mg/g)	Determined Concentration[b] (mg/g)	Difference from Target (%)
21 May 1985	22 May 1985	0.65	0.635	-2
		2.18	2.17	-1
		6.54	6.49	-1
21 May 1985	12 June 1985[c]	0.65	0.640	-2
		2.18	2.15	-1
		6.54	6.48	-1
16 July 1985	17 July 1985	0.65	0.552	-15[d]
		2.18	2.15	-1
		6.54	6.40	-2
10 September 1985	11 September 1985	0.65	0.722	+11
		2.18	0.945	-57
		6.54	5.75	-12
12 September 1985	12 September 1985[e]	0.65	0.610	-6
		2.18	2.13	-2
		6.54	6.33	-3
5 November 1985	6 November 1985	0.65	0.638	-2
		2.18	2.14	-2
		6.54	6.23	-5
5 November 1985	20 November 1985[c]	0.65	0.646	-1
		2.18	2.16	-1
		6.54	6.40	-2
7 January 1986	8 January 1986	0.65	0.632	-3
		2.18	2.16	-1
		6.54	6.51	0
25 February 1986	26 February 1986	0.65	0.661	+2
		2.18	2.15	-1
		6.54	6.38	-2
22 April 1986	24 April 1986	0.65	0.638	-2
		2.18	2.10	-4
		6.54	6.26	-4
22 April 1986	6 May 1986[c]	0.65	0.624	-4
		2.18	2.11	-3
		6.54	6.28	-4
17 June 1986	18 June 1986	0.65	0.654	+1
		2.18	2.17	0
		6.54	6.40	-2
13 August 1986	13 August 1986	0.65	0.655	+1
		2.18	2.13	-2
		6.54	6.42	-2

TABLE H4
Results of Analysis of Dose Formulations for Rats and Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane (continued)

Date Prepared	Date Analyzed	Target Concentration (mg/g)	Determined Concentration (mg/g)	Difference from Target (%)
7 October 1986	9 October 1986	0.65 2.18	0.633 2.12	-3 -3
7 October 1986	20 October 1986[c]	0.65 2.18	0.650 2.13	0 -2
2 December 1986	3 December 1986	0.65 2.18	0.646 2.15	-1 -1
27 January 1987	29 January 1987	0.65 2.18	0.647 2.11	-1 -3
24 March 1987	24 March 1987	0.65 2.18	0.631 2.11	-3 -3
24 March 1987	7 April 1987[c]	0.65 2.18	0.636 2.12	-2 -3
19 May 1987	19 May 1987	0.65 2.18	0.656 2.12	+1 -3

[a] Rats: Dosing volume = 5 mL/kg; 0.65 mg/g = 3 mg/kg; 2.18 mg/g = 10 mg/kg; 6.54 mg/g = 30 mg/kg;
Mice: Dosing volume = 10 mL/kg; 0.65 mg/g = 6 mg/kg; 2.18 mg/g = 20 mg/kg; 6.54 mg/g = 60 mg/kg
[b] Results of duplicate analysis
[c] Animal room sample
[d] Replaced and analyzed same day (17 July 1985) and found to be correct; 0.636 and 0.630 mg/g, which is within 3% of target.
[e] Remix

TABLE H5
Results of Referee Analysis of Dose Formulations for Rats and Mice in the 2-Year Gavage Studies of 1,2,3-Trichloropropane

Date Mixed	Target Concentration (mg/g)	Determined Concentration (mg/g)	
		Study Laboratory[a]	Referee Laboratory[b]
21 May 1985	0.65	0.635	0.632 ± 0.002
5 November 1985	2.18	2.14	2.14 ± 0.01
17 June 1986	6.54	6.40	6.26 ± 0.2
2 December 1986	0.65	0.646	0.645 ± 0.003
19 May 1987	2.18	2.12	2.12 ± 0.04

[a] Results of duplicate analysis
[b] Results of triplicate analysis

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

TABLE I1
Ingredients of NIH-07 Rat and Mouse Ration[a]

Ingredients[b]	Percent by Weight
Ground #2 yellow shelled corn	24.50
Ground hard winter wheat	23.00
Soybean meal (49% protein)	12.00
Fish meal (60% protein)	10.00
Wheat middlings	10.00
Dried skim milk	5.00
Alfalfa meal (dehydrated, 17% protein)	4.00
Corn gluten meal (60% protein)	3.00
Soy oil	2.50
Dried brewer's yeast	2.00
Dry molasses	1.50
Dicalcium phosphate	1.25
Ground limestone	0.50
Salt	0.50
Premixes (vitamin and mineral)	0.25

[a] NCI, 1976; NIH, 1978
[b] Ingredients were ground to pass through a U.S. Standard Screen No. 16 before being mixed.

TABLE I2
Vitamins and Minerals in NIH-07 Rat and Mouse Ration[a]

	Amount	Source
Vitamins		
A	5,500,000 IU	Stabilized vitamin A palmitate or acetate
D_3	4,600,000 IU	D-activated animal sterol
K_3	2.8 g	Menadione
d-α-Tocopheryl acetate	20,000 IU	
Choline	560.0 g	Choline chloride
Folic acid	2.2 g	
Niacin	30.0 g	
d-Pantothenic acid	18.0 g	*d*-Calcium pantothenate
Riboflavin	3.4 g	
Thiamine	10.0 g	Thiamine mononitrate
B_{12}	4,000 µg	
Pyridoxine	1.7 g	Pyridoxine hydrochloride
Biotin	140.0 mg	*d*-Biotin
Minerals		
Iron	120.0 g	Iron sulfate
Manganese	60.0 g	Manganous oxide
Zinc	16.0 g	Zinc oxide
Copper	4.0 g	Copper sulfate
Iodine	1.4 g	Calcium iodate
Cobalt	0.4 g	Cobalt carbonate

[a] Per ton (2,000 lb) of finished product

TABLE I3
Nutrient Composition of NIH-07 Rat and Mouse Ration

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	22.26 ± 0.51	21.3-23.2	22
Crude fat (% by weight)	5.51 ± 0.31	4.6-6.0	22
Crude fiber (% by weight)	3.55 ± 0.57	2.8-5.4	22
Ash (% by weight)	6.48 ± 1.01	2.4-7.9	22
Amino Acids (% of total diet)			
Arginine	1.308 ± 0.606	1.210-1.390	8
Cystine	0.306 ± 0.084	0.181-0.400	8
Glycine	1.150 ± 0.047	1.060-1.210	8
Histidine	0.576 ± 0.024	0.531-0.607	8
Isoleucine	0.917 ± 0.029	0.881-0.944	8
Leucine	1.946 ± 0.055	1.850-2.040	8
Lysine	1.270 ± 0.058	1.200-1.370	8
Methionine	0.448 ± 0.128	0.306-0.699	8
Phenylalanine	0.987 ± 0.140	0.665-1.110	8
Threonine	0.877 ± 0.042	0.824-0.940	8
Tryptophan	0.236 ± 0.176	0.107-0.671	8
Tyrosine	0.676 ± 0.105	0.564-0.794	8
Valine	1.103 ± 0.040	1.050-1.170	8
Essential Fatty Acids (% of total diet)			
Linoleic	2.393 ± 0.258	1.830-2.570	7
Linolenic	0.280 ± 0.040	0.210-0.320	7
Vitamins			
Vitamin A (IU/kg)	7,831 ± 3,946	4,500-19,000	22
Vitamin D (IU/kg)	4,450 ± 1,382	3,000-6,300	4
α-Tocopherol (ppm)	37.95 ± 9.406	22.50-48.90	8
Thiamine (ppm)	21.50 ± 1.47	12.0-25.0	22
Riboflavin (ppm)	7.92 ± 0.87	6.10-9.00	8
Niacin (ppm)	103.38 ± 26.59	65.0-150.0	8
Pantothenic acid (ppm)	29.54 ± 3.60	23.0-34.0	8
Pyridoxine (ppm)	9.55 ± 3.48	5.60-14.0	8
Folic acid (ppm)	2.25 ± 0.73	1.80-3.70	8
Biotin (ppm)	0.254 ± 0.042	0.19-0.32	8
Vitamin B_{12} (ppb)	38.45 ± 22.01	10.6-65.0	8
Choline (ppm)	3,089 ± 328.69	2,400-3,430	8
Minerals			
Calcium (%)	1.16 ± 0.12	0.90-1.40	22
Phosphorus (%)	0.93 ± 0.06	0.85-1.10	22
Potassium (%)	0.883 ± 0.078	0.772-0.971	6
Chloride (%)	0.526 ± 0.092	0.380-0.635	8
Sodium (%)	0.313 ± 0.390	0.258-0.371	8
Magnesium (%)	0.168 ± 0.010	0.151-0.181	8
Sulfur (%)	0.280 ± 0.064	0.208-0.420	8
Iron (ppm)	360.54 ± 100	255.0-523.0	8
Manganese (ppm)	91.97 ± 6.01	81.70-99.40	8
Zinc (ppm)	54.72 ± 5.67	46.10-64.50	8
Copper (ppm)	11.06 ± 2.50	8.090-15.39	8
Iodine (ppm)	3.37 ± 0.92	1.52-4.13	6
Chromium (ppm)	1.79 ± 0.36	1.04-2.09	8
Cobalt (ppm)	0.681 ± 0.14	0.490-0.780	4

TABLE I4
Contaminant Levels in NIH-07 Rat and Mouse Ration

	Mean ± Standard Deviation[a]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.67 ± 0.24	0.20-0.98	22
Cadmium (ppm)	<0.10		22
Lead (ppm)	0.39 ± 0.17	0.05-0.66	22
Mercury (ppm)[b]	0.05 ± 0.01	<0.05-0.08	22
Selenium (ppm)	0.36 ± 0.08	0.17-0.48	22
Aflatoxins (ppb)	<5.0		22
Nitrate nitrogen (ppm)	19.36 ± 8.27	2.90-19.0	22
Nitrite nitrogen (ppm)	0.28 ± 0.47	<0.10-2.10	22
BHA (ppm)[c]	2.32 ± 0.78	<2.00-5.00	22
BHT (ppm)[c]	1.18 ± 0.50	<1.00-3.00	22
Aerobic plate count (CFU/g)[d,e]	79,745 ± 71,847	3,900-280,000	20
Aerobic plate count (CFU/g)[f]	117,040 ± 140,898	3,900-570,000	22
Coliform (MPN/g)[g,h]	81 ± 103	<3.00-240	19
Coliform (MPN/g)[i]	133 ± 164	<3.00-460	22
E. coli (MPN/g)[j]	5.27 ± 8.53	<3.00-43.0	22
Total nitrosamines (ppb)[k]	7.32 ± 2.67	3.30-13.30	22
N-Nitrosodimethylamine (ppb)[k]	6.24 ± 2.52	3.00-13.00	22
N-Nitrosopyrrolidine (ppb)[k]	1.08 ± 1.12	0.30-4.30	22
Pesticides (ppm)			
α-BHC[l]	<0.01		22
β-BHC	<0.02		22
γ-BHC	<0.01		22
δ-BHC	<0.01		22
Heptachlor	<0.01		22
Aldrin	<0.01		22
Heptachlor epoxide	<0.01		22
DDE	<0.01		22
DDD	<0.01		22
DDT	<0.01		22
HCB	<0.01		22
Mirex	<0.01		22
Methoxychlor	<0.05		22
Dieldrin	<0.01		22
Endrin	<0.01		22
Telodrin	<0.01		22
Chlordane	<0.05		22
Toxaphene	<0.1		22
Estimated PCBs	<0.2		22
Ronnel	<0.01		22
Ethion	<0.02		22
Trithion	<0.05		22
Diazinon	<0.1		22
Methyl parathion	<0.02		22
Ethyl parathion	<0.02		22
Malathion[m]	0.27 ± 0.68	0.05-3.20	22
Endosulfan I	<0.01		22
Endosulfan II	<0.01		22
Endosulfan sulfate	<0.03		22

TABLE I4
Contaminant Levels in NIH-07 Rat and Mouse Ration (continued)

[a] For values less than the limit of detection, the detection limit is given for the mean.
[b] Two lots contained measurements greater than 0.05 ppm; lots milled 3 August 1986 and 4 December 1986 contained 0.08 ppm and 0.06 ppm, respectively.
[c] Sources of contamination: soy oil and fish meal
[d] CFU = colony forming unit
[e] Mean, standard deviation, and range exclude two high values obtained in lots milled 4 March 1985 and 10 April 1985; values excluded are 410,000 CFU/g and 570,000 CFU/g, respectively.
[f] Mean, standard deviation, and range include values given in [e].
[g] MPN = most probable number
[h] Mean, standard deviation, and range exclude the high value of 460 MPN/g obtained in lots milled 4 March 1985, 6 December 1985, and 19 January 1986.
[i] Includes the values given in [h]
[j] Mean, standard deviation, and range include one large value of 43 MPN/g obtained in lot milled 4 June 1986.
[k] All values were corrected for percent recovery.
[l] BHC = hexachlorocyclohexane or benzene hexachloride
[m] Ten lots contained more than 0.05 ppm, including one lot which contained 3.20 ppm milled on 7 May 1985.

APPENDIX J
SENTINEL ANIMAL PROGRAM

SENTINEL ANIMAL PROGRAM

METHODS

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

Serum samples were collected from randomly selected sentinel rats and mice during the 17-week and 2-year studies. Blood from each animal was collected from the retro-orbital sinus, allowed to clot, and the sera separated. Sera were diluted with physiologic saline solution on a 1:5 ratio and heated to 56° C for 30 minutes prior to shipping to Microbiological Associates (Bethesda, MD) for determination of antibody titers. The laboratory serology methods and the virus and mycoplasma agents for which testing was performed are listed below; the times during the studies at which blood was collected for serological testing are also listed.

Test and Method	Time of Analysis
Rats	
17-Week Studies	
Complement Fixation:	
RCV (rat coronavirus) and Sendai	Study termination
Hemagglutination Inhibition:	
PVM (pneumonia virus of mice), KRV (Kilham rat virus), and H-1 (Toolan's H-1 virus)	Study termination
2-Year Studies	
Hemagglutination Inhibition:	
KRV and H-1	6, 9, 10, 10.5, 11.5, 16.5, 18, 20, 21.5, 22, 22.5, and 24 months
ELISA	
RCV/SDA (rat coronavirus/sialodacryoadentis virus), PVM, Sendai, *Mycoplasma arthritidis*, and *Mycoplasma pulmonis*	6, 9, 10, 10.5, 11.5, 16.5, 18, 20, 21.5, 22, 22.5, and 24 months
Immunofluorescent Antibody:	
PVM	18 months
Sendai	24 months

Test and Method	Time of Analysis
Mice	
17-Week Studies	
Complement Fixation:	
Sendai, M. Ad. (mouse adenoma virus), and and LCM (lymphocytic choriomeningtis virus)	17 weeks
Hemagglutination Inhibition:	
PVM, Reo3 (Reo virus type 3), GDVII (mouse encephalomyelitis virus), Poly (Polyoma virus), MVM (minute virus of mice), and Ectro (Ectromelia virus)	17 weeks
ELISA:	
MHV (mouse hepatitis virus)	17 weeks
2-Year Studies	
Complement Fixation:	
LCM (lymphocytic choriomeningtis virus)	6, 10, 11, and 12 months
Hemagglutination Inhibition:	
K (papovavirus), Poly	6, 10, 11, 12, 18, and 24 months
MVM	6, 10, 11, 12, and 18 months
ELISA:	
MHV, PVM, Reo3, GDVII, Sendai, Ectro, M. Ad.	6, 10, 11, 12, and 18 months
Mycoplasma arthritidis and *Mycoplasma pulmonis*	6, 10, 11, 12, and 24 months
LCM and MVM	24 months
Immunofluorescent Antibody:	
EDIM (epizootic diarrhea of infant mice)	6, 10, 11, 12, 18 months, and 24 months
Reo3	10 and 11 months
LCM	18 months

Serology results are presented in Table J1.

TABLE J1
Murine Virus Antibody Determinations for Sentinel Rats and Mice in the 17-Week and 2-Year Gavage Studies of 1,2,3-Trichloropropane

	Interval	Number of Animals	Positive Serologic Reaction for
Rats			
17-Week Studies	17 weeks	9/9	None positive
2-Year Studies	6 months	10/10	None positive
	9 months	2/2	None positive
	10 months	2/2	None positive
	10.5 months	10/10	None positive
	11.5 months	10/10	None positive
	16.5 months	1/1	None positive
	18 months	1/11	PVM
	20 months	9/9	None positive
	21.5 months	2/2	None positive
	22 months	2/2	None positive
	22.5 months	1/1	None positive
	24 months	11/11	None positive
Mice			
17-Week Studies	17 weeks	7/7	None positive
2-Year Studies	6 months	11/11	None positive
	10 months	4/10	Reo3
	11 months	5/9	Reo3
		1/9	Possible *M. arthritidis*
	12 months	10/10	None positive
	18 months	2/2	None positive
	24 months	10/10	None positive

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TR No.	CHEMICAL
201	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Dermal)
206	1,2-Dibromo-3-chloropropane
207	Cytembena
208	FD & C Yellow No. 6
209	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Gavage)
210	1,2-Dibromoethane
211	C.I. Acid Orange 10
212	Di(2-ethylhexyl)adipate
213	Butyl Benzyl Phthalate
214	Caprolactam
215	Bisphenol A
216	11-Aminoundecanoic Acid
217	Di(2-Ethylhexyl)phthalate
219	2,6-Dichloro-p-phenylenediamine
220	C.I. Acid Red 14
221	Locust Bean Gum
222	C.I. Disperse Yellow 3
223	Eugenol
224	Tara Gum
225	D & C Red No. 9
226	C.I. Solvent Yellow 14
227	Gum Arabic
228	Vinylidene Chloride
229	Guar Gum
230	Agar
231	Stannous Chloride
232	Pentachloroethane
233	2-Biphenylamine Hydrochloride
234	Allyl Isothiocyanate
235	Zearalenone
236	*D*-Mannitol
237	1,1,1,2-Tetrachloroethane
238	Ziram
239	Bis(2-chloro-1-Methylethyl)ether
240	Propyl Gallate
242	Diallyl Phthalate (Mice)
243	Trichlorethylene (Rats and Mice)
244	Polybrominated Biphenyl Mixture
245	Melamine
246	Chrysotile Asbestos (Hamsters)
247	L-Ascorbic Acid
248	4,4′-Methylenedianiline Dihydrochloride
249	Amosite Asbestos (Hamsters)
250	Benzyl Acetate
251	2,4- & 2,6-Toluene Diisocyanate
252	Geranyl Acetate
253	Allyl Isovalerate
254	Dichloromethane (Methylene Chloride)
255	1,2-Dichlorobenzene
257	Diglycidyl Resorcinol Ether
259	Ethyl Acrylate
261	Chlorobenzene
263	1,2-Dichloropropane
266	Monuron
267	1,2-Propylene Oxide
269	Telone II® (1,3-Dichloropropene)
271	HC Blue No. 1
272	Propylene

TR No.	CHEMICAL
273	Trichloroethylene (Four Rat Strains)
274	Tris(2-ethylhexyl)phosphate
275	2-Chloroethanol
276	8-Hydroxyquinoline
277	Tremolite
278	2,6-Xylidine
279	Amosite Asbestos
280	Crocidolite Asbestos
281	HC Red No. 3
282	Chlorodibromomethane
284	Diallylphthalate (Rats)
285	C.I. Basic Red 9 Monohydrochloride
287	Dimethyl Hydrogen Phosphite
288	1,3-Butadiene
289	Benzene
291	Isophorone
293	HC Blue No. 2
294	Chlorinated Trisodium Phosphate
295	Chrysotile Asbestos (Rats)
296	Tetrakis(hydroxymethyl) phosphonium Sulfate & Tetrakis(hydroxymethyl) phosponium Chloride
298	Dimethyl Morpholinophosphoramidate
299	C.I. Disperse Blue 1
300	3-Chloro-2-methylpropene
301	*o*-Phenylphenol
303	4-Vinylcyclohexene
304	Chlorendic Acid
305	Chlorinated Paraffins (C_{23}, 43% chlorine)
306	Dichloromethane (Methylene Chloride)
307	Ephedrine Sulfate
308	Chlorinated Pariffins (C_{12}, 60% chlorine)
309	Decabromodiphenyl Oxide
310	Marine Diesel Fuel and JP-5 Navy Fuel
311	Tetrachloroethylene (Inhalation)
312	*n*-Butyl Chloride
313	Mirex
314	Methyl Methacrylate
315	Oxytetracycline Hydrochloride
316	1-Chloro-2-methylpropene
317	Chlorpheniramine Maleate
318	Ampicillin Trihydrate
319	1,4-Dichlorobenzene
320	Rotenone
321	Bromodichloromethane
322	Phenylephrine Hydrochloride
323	Dimethyl Methylphosphonate
324	Boric Acid
325	Pentachloronitrobenzene
326	Ethylene Oxide
327	Xylenes (Mixed)
328	Methyl Carbamate
329	1,2-Epoxybutane
330	4-Hexylresorcinol
331	Malonaldehyde, Sodium Salt
332	2-Mercaptobenzothiazole
333	*N*-Phenyl-2-naphthylamine
334	2-Amino-5-nitrophenol
335	C.I. Acid Orange 3

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TR No.	CHEMICAL
336	Penicillin VK
337	Nitrofurazone
338	Erythromycin Stearate
339	2-Amino-4-nitrophenol
340	Iodinated Glycerol
341	Nitrofurantoin
342	Dichlorvos
343	Benzyl Alcohol
344	Tetracycline Hydrochloride
345	Roxarsone
346	Chloroethane
347	D-Limonene
348	α-Methyldopa Sesquihydrate
349	Pentachlorophenol
350	Tribromomethane
351	*p*-Chloroaniline Hydrochloride
352	N-Methylolacrylamide
353	2,4-Dichlorophenol
354	Dimethoxane
355	Diphenhydramine Hydrochloride
356	Furosemide
357	Hydrochlorothiazide
358	Ochratoxin A
359	8-Methoxypsoralen
360	N,N-Dimethylaniline
361	Hexachloroethane
362	4-Vinyl-1-Cyclohexene Diepoxide
363	Bromoethane (Ethyl Bromide)
364	Rhodamine 6G (C.I. Basic Red 1)
365	Pentaerythritol Tetranitrate
366	Hydroquinone
367	Phenylbutazone
368	Nalidixic Acid
369	Alpha-Methylbenzyl Alcohol
370	Benzofuran
371	Toluene
372	3,3-Dimethoxybenzidine Dihydrochloride
373	Succinic Anhydride
374	Glycidol
375	Vinyl Toluene
376	Allyl Glycidyl Ether
377	*o*-Chlorobenzalmalononitrile
378	Benzaldehyde
379	2-Chloroacetophenone
380	Epinephrine Hydrochloride
381	*d*-Carvone
382	Furfural
385	Methyl Bromide
386	Tetranitromethane
387	Amphetamine Sulfate
388	Ethylene Thiourea
389	Sodium Azide
390	3,3′-Dimethylbenzidine Dihydrochloride
391	Tris(2-chloroethyl) Phosphate
392	Chlorinated Water and Chloraminated Water
393	Sodium Fluoride
394	Acetaminophen
395	Probenecid
396	Monochloroacetic Acid
397	C.I. Direct Blue 15
398	Polybrominated Biphenyls
399	Titanocene Dichloride
401	2,4-Diaminophenol Dihydrochloride
402	Furan
403	Resorcinol
404	5,5-Diphenylhydantoin
405	C.I. Acid Red 114
406	γ-Butyrolactone
407	C.I. Pigment Red 3
408	Mercuric Chloride
409	Quercetin
410	Naphthalene
411	C.I. Pigment Red 23
412	4,4-Diamino-2,2-Stilbenedisulfonic Acid
413	Ethylene Glycol
414	Pentachloroanisole
415	Polysorbate 80
416	*o*-Nitroanisole
417	*p*-Nitrophenol
418	*p*-Nitroaniline
419	HC Hellow 4
421	Talc
422	Coumarin
423	Dihydrocoumarin
427	Turmeric Oleoresin
431	Benzyl Acetate
434	1,3-Butadiene
443	Oxazepam

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