NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 263

TOXICOLOGY AND CARCINOGENESIS STUDIES OF 1,2-DICHLOROPROPANE (Propylene Dichloride)

(CAS NO. 78-87-5)

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

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

NATIONAL TOXICOLOGY PROGRAM

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

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

Special Note: This Technical Report was peer reviewed in public session by the NTP Board of Scientific Counselors' Technical Reports Review Subcommittee on February 28 and June 29, 1983 [see pages 11 and 12]. Thereafter, the NTP adopted the policy that the experimental data and laboratory records from all NTP Toxicology and Carcinogenesis Studies not yet printed and distributed would be audited. [A summary of the data audit is presented in Appendix N.] Consequently, printing and distribution of this Technical Report have been delayed and the format differs from that of Technical Reports peer reviewed more recently.

NTP TECHNICAL REPORT
ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES OF 1,2-DICHLOROPROPANE (Propylene Dichloride)

(CAS NO. 78-87-5)

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

NATIONAL TOXICOLOGY PROGRAM
Box 12233
Research Triangle Park
North Carolina 27709

August 1986

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
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NOTE TO THE READER

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

Evidence of Carcinogenicity

Five categories of interpretative conclusions have been adopted for use in the Technical Reports series to specifically emphasize consistency and the concept of actual evidence of carcinogenicity. For each definitive study result (male rats, female rats, male mice, female mice) one of the following categories will be selected to describe the findings. These categories refer to the strength of the experimental evidence and not to either potency or mechanism.

- **Clear Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically-related increased incidence of malignant neoplasms, studies that exhibit a substantially increased incidence of benign neoplasms, or studies that exhibit an increased incidence of a combination of malignant and benign neoplasms where each increases with dose.
- **Some Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically-related increased incidence of benign neoplasms, studies that exhibit marginal increases in neoplasms of several organs/tissues, or studies that exhibit a slight increase in uncommon malignant or benign neoplasms.
- **Equivocal Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically-related marginal increase of neoplasms.
- **No Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing no chemically-related increases in malignant or benign neoplasms.
- **Inadequate Study of Carcinogenicity** demonstrates that because of major qualitative or quantitative limitations the studies cannot be interpreted as valid for showing either the presence or absence of a carcinogenic effect.

Additionally, the following concepts (as patterned from the International Agency for Research on Cancer Monographs) have been adopted by the NTP to give further clarification of these issues.

> The term *chemical carcinogenesis* generally means the induction by chemicals of neoplasms not usually observed, the earlier induction by chemicals of neoplasms that are commonly observed, or the induction by chemicals of more neoplasms than are usually found. Different mechanisms may be involved in these three situations. Etymologically, the term *carcinogenesis* means the induction of cancer, that is, of malignant neoplasms; however, the commonly accepted meaning is the induction of various types of neoplasms or of a combination of malignant and benign neoplasms. In the Technical Reports the words *tumor* and *neoplasm* are used interchangeably.

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

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in the report is encouraged to make this information known to the NTP. Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Studies should be directed to the National Toxicology Program, located at Research Triangle Park, NC 27709 (919-541-3991) or Room 835B, Westwood Towers, 5401 Westbard Ave., Bethesda, MD 20205 (301-496-1152).

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650). Single copies of this Technical Report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

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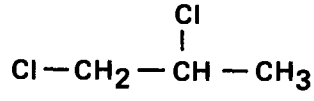

1,2-DICHLOROPROPANE

CAS NO. 78-87-5

$C_3H_6Cl_2$ Mol. Wt. 112.99

ABSTRACT

Carcinogenesis studies of 1,2-dichloropropane (propylene dichloride; >99% pure) were conducted by administering the chemical in corn oil by gavage to groups of 50 female F344/N rats and 50 male and 50 female B6C3F$_1$ mice at doses of 125 or 250 mg/kg body weight and to groups of 50 male F344/N rats at doses of 62 or 125 mg/kg body weight. Doses were administered five times per week for 103 weeks. Vehicle control groups of 50 rats and 50 mice of each sex received an equivalent amount of corn oil by gavage on the same dosing schedule.

Survival was reduced for high dose female rats ($P<0.001$) and for high dose female mice ($P<0.05$) relative to controls; 16/50 high dose female rats and 26/50 high dose female mice survived to the end of the experiment. Survival in the other groups was comparable to the control groups. In female mice, ovarian, uterine, or multiple organ infections may have contributed to the deaths of 5/11 vehicle control, 9/14 low dose, and 14/22 high dose animals that died before the end of the study. There was no evidence of an adverse effect on survival in male rats or in male mice.

Mean body weights of high dose male (-14%) and high dose female (-24%) rats were lower than those of the controls. Low dose rats and all groups of mice had mean body weights comparable to the controls.

High dose female rats had increased incidences of both clear-cell changes and necrosis of the liver; but there was no increase in the incidence of liver tumors in the female rats. There were no treatment-related effects observed in the male rats, other than decreased body weights.

Dose-related increases were observed for adenomas of the liver in both male (control, 7/50; low dose, 10/50; high dose, 17/50) and female (1/50, 5/50, 5/50) mice. The increase in the frequency of liver carcinomas supported the evidence that there was a neoplastic response in the mouse liver for both sexes (males: 11/50, 17/50, 16/50, females: 1/50, 3/50, 4/50). Hepatocytomegaly and hepatic necrosis were increased in male mice, but not in female mice.

A dose related increase in adenocarcinomas of the mammary gland was observed in female rats (control, 1/50; low dose, 2/50; high dose, 5/50) with the majority of these tumors being found at the end of the study (1/37, 3%; 2/43, 5%; 4/16, 25%). The incidence of mammary adenocarcinomas was increased when compared to the historical controls for this laboratory (3/150, 2.0%) and for all laboratories combined (11/895, 1.2%). Mammary fibroadenomas were decreased in the high dose treated female rats (15/50, 20/50, 7/50).

The mutagenic activity of 1,2-dichloropropane was marginal. The compound was tested in strains TA 100, TA 98, TA 1537, and TA 1535 of *Salmonella* in the presence or absence of S9 and no clearly positive response was obtained. Chromosomal aberration and sister chromatid exchange data showed that 1,2,-dichloropropane caused increases in both in the absence or presence of S9.

Under the conditions of these 2 year gavage studies, there was *no evidence of carcinogenicity** for male F344/N rats receiving 62 or 125 mg/kg. For female rats there was *equivocal evidence of carcinogenicity* in that 250 mg/kg 1,2-dichloropropane caused a marginally increased incidence of adenocarcinomas in the mammary gland; these borderline malignant lesions occurred concurrent with decreased survival and reduced body weight gain. There was *some evidence of carcinogenicity* for male and female B6C3F$_1$ mice exposed to 1,2-dichloropropane, as indicated by increased incidences of hepatocellular neoplasms, primarily adenomas.

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*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2.

CONTRIBUTORS

These studies of 1,2-dichloropropane were conducted at E.G. & G. Mason Research Institute under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The short-term phases of the studies were begun in May 1978. The 2-year studies in rats were begun in May 1979. The 2-year studies in mice were begun in April 1979.

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***Unable to attend 28 February 1983 meeting

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

On 28 February and on 29 June 1983, this technical report on 1,2-dichloropropane underwent peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The public review meetings began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina. The following precis represents the critiques made by the principal reviewers, as well as comments from and discussion by the Peer Review Panel, NTP staff, and attendees.

Peer Review Meeting of 28 February 1983

Dr. Friess, a principal reviewer for the report on the carcinogenesis studies of 1,2-dichloropropane, agreed with the conclusions in rats but questioned the conclusions in mice since there were significant increases in hepatocellular adenomas but not in carcinomas. Dr. J. Lamb, NTP, agreed that the evidence in mice was due mainly to benign liver lesions. However he emphasized that carcinomas of the liver in both male and female mice were numerically increased and that the combination of benign and malignant tumors increased the significant differences when compared to vehicle controls. Dr. Friess said that the genetic homogeneity of the parent C3H mice was less than optimum, and that the high doses were toxic for both female mice and rats, but neither finding would invalidate these studies.

As a second principal reviewer, Dr. Swenberg said that the conclusions are more equivocal than presented in the abstract since the increased weight loss and stress may be responsible for the increase in adenocarcinomas of the mammary gland. Dr. Lamb indicated he would search the literature for evidence of this possibility, and offered the observation that reduced body weight is often correlated with decreased incidences of mammary gland tumors. Dr. Swenberg stated that no mention is made in the discussion as to the possible consequences of the toxic doses and how this may have affected the results. Dr. Holland cautioned against continually belaboring the issue of maximally tolerable dose (MTD) but rather it should be considered in relation to the quality of the science and the quality of the experimental data. With regard to the mouse liver tumors, Dr. Swenberg said there was little question that there was an increase in adenomas; he asked that some discussion center on possible mechanisms. He opined that the report over-interpreted the data.

As a third principal reviewer, Dr. Beliczky said the mammary adenocarcinomas in female rats appear to be the major significant finding. Although increases in liver adenomas in mice were significant, he stated that combining liver adenomas and carcinomas was not realistic. [As stated by the NTP, combining liver tumors was considered appropriate since benign and malignant neoplasms may represent stages of a progression.] He said that assumptions and speculative judgment introduced into the discussion apparently make more of a case for carcinogenicity than just the mammary adenocarcinomas in female rats. More discussion was needed regarding mutagenic testing and screening for chromosome aberrations and sister chromatid exchanges. Dr. Beliczky said that doses selected were too high, survivorship was decreased, potential effects on genetic integrity were introduced into the study, and comparison with more potent chemical carcinogens was inappropriate.

Dr. Swenberg reiterated that the evidence was equivocal and at best there was probable or possible evidence for carcinogenicity. He requested a pathology reexamination of the mammary tumors. Dr. G. Boorman, NTP, said a review and grading would be done and included in the revised report. Dr. Moore said it would be useful to learn whether the study was appropriate for a carcinogenic interpretation based on the mammary tumors. Dr. Haseman pointed out that NTP historical control data on mammary adenocarcinomas indicate that these are rare and late-appearing tumors. Dr. Swenberg commented that tumors induced by known mammary carcinogens are early appearing (strain and species not specified). Dr. Scala mentioned two other possible factors which could influence interpretation of the data, one being an unacceptable degree of temperature fluctuation and the other being a mixing of species in the same animal room. Dr. Davis said sentinel animal data should be included.

Dr. Lamb said changes would be made in the abstract with regard to combining liver adenomas and carcinomas, including more discussion of the necrogenic activity of 1,2-dichloropropane; there would be a fuller discussion using literature references on how toxicity and possibly an altered nutritional state may relate to development of mammary tumors and for this experiment in female rats.

Dr. Swenberg moved that the technical report on the bioassay of 1,2-dichloropropane be deferred for revision. Dr. Friess seconded the motion and the report would be reconsidered at the next meeting of the Peer Review Panel.

Peer Review Meeting of 29 June 1983

Dr. Beliczky, a principal reviewer for the revised technical report on the carcinogenesis studies of 1,2-dichloropropane, agreed with the conclusions. In the new categories of evidence he considered the connotation of "some evidence" to be negative and said the "some" should be eliminated. He said that in retrospect, the selection of a more representative high dose might have resulted in more definitive conclusions. Further there was no question that 1,2-dichloropropane is toxic to the liver, and the judgment as to whether or not DCP is a complete animal carcinogen depends on its mechanism of action.

As a second principal reviewer, Dr. Swenberg agreed with the conclusions with minor rewording. He noted the experimental design was appropriate except for excessive toxicity in the high dose rats. He said mention should be made in the technical report that the animals had titers to pathogenic organisms even though the significance of the findings remains unknown. He submitted a computer search listing that contained references showing the influence of stress (both increase and decrease) on the incidence of mammary tumors. Where appropriate, these citations should be added to the technical report.

As a third principal reviewer, Dr. Freiss stated he agreed with the conclusions within the framework of the new categories for strength of evidence recently defined by the NTP (see the Note to the Reader). He expressed concern about the low survival in high dose female rats although he could accept the data as adjusted for survival by the life table and the incidental tumor tests.

In discussions from the floor, Dr. T. Torkelson, Dow Chemical USA, said the current draft was much improved over the February draft. In their opinion the mutagenesis data were overstated.

Dr. Davis said the dose-related increases in hematopoiesis in female rats and mice should be mentioned in the text, and, in general, significant nonneoplastic effects should be included in the abstract. Dr. Freiss asked whether NTP plans to focus more attention on chronic toxicity. Dr. Moore, NTP, said yes, but NTP had been limited until now by the uneven quality of the non-tumor data, and where acceptable to the Program these data will continue to be included.

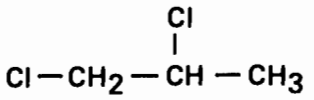
Dr. J. Lamb, NTP, said concerns about high mortality in female rats were reflected in the decision to describe the findings as equivocal evidence. DCP was a hepatotoxin but the conclusions were not dependent on whether one considers DCP to be a promoter. Dr. Moore said that since the liver was a target organ for neoplastic and nonneoplastic effects in mice the hepatotoxicity data would be included in the abstract.

There was considerable discussion as to what should be the minimum survival in animal groups for a study to be considered adequate. Dr. Hook noted there seemed to be a consensus on the Panel for development of guidelines in the area. Dr. Huff, NTP, said a draft working paper was in preparation. Dr. Swenberg said the new categories describing the strength of evidence for carcinogenicity should be displayed in the front of each technical report. [They are given in the Note to the Reader section of each technical report.]

Dr. Beliczky moved that the technical report on the carcinogenesis studies of 1,2-dichloropropane be accepted with modifications discussed and with inclusion of the definitions of the new categories. Dr. Swenberg seconded the motion and the technical report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION



1,2-DICHLOROPROPANE

CAS NO. 78-87-5

$C_3H_6Cl_2$ **Mol. Wt. 112.99**

1,2-Dichloropropane (propylene dichloride) is a chemical intermediate widely used in the production of tetrachloroethylene and carbon tetrachloride. It is an oil and fat solvent in certain furniture finishes, dry cleaning fluids, and paint removers and has been used to fumigate grain and soil and to control peach tree borers (Aviado, 1977; Fishbein, 1979; Spencer, 1973; Merck, 1976; Farm Chemical Handbook, 1977; Kirk-Othmer, 1981). Approximately 77 million pounds of 1,2-dichloropropane were produced in the United States in 1980 (USITC, 1981). The current 8-hour time-weighted-average concentration to which workers may be exposed is 75 ppm (USCFR, 1974).

An oral LD_{50} value of 2.19 g/kg has been reported for rats of unspecified strain or sex (Smyth et al., 1969). The 4-hour LC_{50} value is approximately 2,000 ppm for Sherman rats (Carpenter et al., 1949). Inhalation studies on the organ toxicity of 1,2-dichloropropane have used an exposure of 400 ppm 1,2-dichloropropane, seven hours a day, five days a week for 128 to 140 exposures. Of the 80 C3H mice that received just 37 exposures of 1,2-dichloropropane, including the exposure and the subsequent 7-month observation period, only three animals survived; multiple hepatomas were seen in the three treated but not in control mice but the 400 ppm exposure levels were clearly toxic. The inhalation exposures demonstrated that rats, guinea pigs, and dogs were less suceptible than mice to 1,2-dichloropropane toxicity; exposures of 400 ppm 1,2-dichloropropane produced no compound-related histologic effects in any of the three species and little treatment-related mortality was observed (Heppel et al., 1948).

1,2-Dichloropropane is hepatotoxic in laboratory animals (Heppel et al., 1948; Drew et al., 1978; Sidorenko et al.,1976), characterized by centrilobular necrosis and large increases in serum liver enzymes. Ingestion of cleaning solvent (50 ml) containing 1,2-dichloropropane by a man produced coma followed by delirium, irreversible shock, cardiac failure, and death (Larcan et al., 1977). Histopathological study indicated that this acute poisoning produced "centri- and mediolobular hepatic necrosis." However, other potential chemical components of this solvent were not described.

1,2-Dichloropropane is metabolized to a variety of metabolic products including certain intermediates which may be related to the toxicity of the compound. Administration of a single oral dose of 1 mg 1,2-dichloro[1-^{14}C]propane to strain E rats resulted in less than 7% of the dose being excreted in the feces; over 50% of the dose was excreted in the urine, and the remaining radioactivity (40%) was recovered in the expired air within 96 hours following dosing (Hutson et al., 1971). Approximately 1/2 (20%) of the expired dose was identified as carbon dioxide, with the remaining portion being other expired unidentified radiolabeled compounds. Some unmodified dichloropropane was excreted in the expired air in Sprague-Dawley rats, but not in the urine; dichloropropane oxidation yielded the mercapturic acid N-acetyl-S-(2-hydroxypropyl) cysteine (Jones and Gibson, 1980). Both 1-chloro-2-hydroxypropane and 1,2-epoxypropane are proposed intermediates in the metabolism to the mercapturic acid. The 1,2-epoxypropane can also be metabolized to propanediol which is further metabolized to pyruvate and enters the tricarboxylic acid cycle; carbon dioxide is released and then expired. Epoxypropane may also be conjugated with glutathione and excreted in the urine. Jones and Gibson (1980) further proposed that the 1-chloro-2-hydroxypropane may be metabolized to beta-chlorolactaldehyde and beta-chlorolactate.

Principe et al. (1981) tested DCP for mutagenic activity in *Salmonella* strains TA1535, TA1537, TA1538, TA98 and TA100 to a maximum of 11 mg/plate. The results indicated that DCP was marginally mutagenic in TA1535 and TA100 at 11 mg/plate. De Lorenzo et al. (1977) examined DCP mutagenicity in *Salmonella* strains TA1535, TA1978 and TA100 with and without S9 from Aroclor-1254-induced rat liver. Their results indicated that DCP at 10, 20, and 50 mg/plate caused a significantly increased mutant yield. Stolzenberg and Hines (1980) detected no mutagenic activity of DCP in strain TA100 up to 10 mg/plate; at 100 mg/plate, DCP completely inhibited bacterial growth. Principe et al. (1981) also reported that DCP (up to 1.1 mg/plate) failed to induce resistance to a low dose of streptomycin in *Streptomyces coelicolor*. These authors did find that DCP was mutagenic in *Aspergillus nidulans* and toxic at 4.4 mg/plate.

1,2-Dichloropropane (purity>99%) was tested because large amounts are produced annually and humans are exposed to the compound occupationally and may be exposed through commercial products. Also, no previous long-term studies on 1,2-dichloropropane were available and structurally-related chemicals (1,2-dichloroethane, NCI 1978c; 1,2-dibromoethane, NCI, 1978b, 1982a; 1,2-dibromo-3-chloropropane, NCI, 1978a, 1982b) were carcinogenic in rats and mice.

II. MATERIALS AND METHODS

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THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Study Design

Source and Specifications of Test Animals

Animal Maintenance

Clinical Examinations and Pathology

Data Recording and Statistical Methods

CHEMICAL ANALYSES

Reagent grade 1,2-dichloropropane was obtained from Fisher Scientific Company (St. Louis, MO) in one batch (Lot No. A7XB). Purity and identity analyses were conducted at Midwest Research Institute. Identity was verified by determining physical properties and spectral characteristics. Purity was determined by elemental analysis, titration of free acid, and gas chromatography (Appendix K).

Gas chromatographic analysis of Lot A7XB indicated an approximate purity of 99.4%. Toluene was identified as an impurity constituting 0.24% v/v of the compound by combined gas chromatography and mass spectrometry.

1,2-Dichloropropane was stored in the dark at 0° ± 5°C in brown glass bottles. Periodic reanalysis of the bulk chemical at Mason Research Institute by vapor-phase chromatography, titration of free-acid, and infrared spectroscopy indicated that no notable changes occurred throughout the study.

DOSE PREPARATION

Selected samples of 1,2-dichloropropane/corn oil mixtures were analyzed periodically (Appendix M). Results of chemical/vehicle analyses and of referee analyses at Midwest Research Institute indicated that the stock solutions were properly prepared.

1,2-Dichloropropane and corn oil were mixed to give the desired concentration based on a dosing volume of 3 ml/kg body weight (Table 1). 1,2-Dichloropropane in corn oil was found to be stable for at least 7 days at room temperature (Appendix L).

ANALYSIS OF 1,2-DICHLOROPROPANE IN CORN OIL

	Concentration of 1,2-Dichloropropane in Corn Oil for Target Concentration		
	21 mg/ml	42 mg/ml	83 mg/ml
Mean	20.0	41.6	83.1
Standard deviation	0.76	1.17	1.58
Coefficient of variation (%)	3.9	2.8	1.9
Range (mg/ml)	19.0-22.0	39.8-44.0	80.5-86.5
Number of samples	14	14	14

FOURTEEN-DAY STUDIES

No single-dose studies of dichloropropane were done in rats or mice.

For the 14-day studies, male and female F344/N rats and B6C3F$_1$ mice (C57BL/6N × C3H/HeN MTV-) were obtained from Harlan Industries and held for approximately 14 days before the studies began. The animals were approximately 6 weeks old when placed on study.

II. MATERIALS AND METHODS: THIRTEEN-WEEK STUDIES

Groups of five rats and five mice of each sex were administered 1,2-dichloropropane in corn oil by gavage at doses of 0, 125, 250, 500, 1,000, or 2,000 mg/kg. The doses were administered for 14 consecutive days and were followed by one day of observation.

Animals were housed five per cage and received water and feed *ad libitum*. Details of animal maintenance are presented in Table 1. The rats and mice were observed twice daily for mortality. Necropsies were performed on all animals.

THIRTEEN-WEEK STUDIES

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

Four- to five-week-old male and female F344/N rats were obtained from Harlan Industries and 10- to 11-week-old $B6C3F_1$ mice were obtained from Charles River Breeding Laboratories. Rats were observed for 18 days and mice for 33 days and then randomized by weight and assigned to test groups so that average cage weights were approximately equal for all animals of the same sex and species.

Rats and mice were housed five per cage and received water and feed *ad libitum* (Table 1). Groups of 10 rats of each sex were administered 1,2-dichloropropane in corn oil by gavage, 5 days per week for 13 weeks, at doses of 0, 60, 125, 250, 500, or 1,000 mg/kg. Groups of 10 mice of each sex were administered 0, 30, 60, 125, 250, or 500 mg/kg on the same schedule.

Animals were checked twice daily for mortality and signs of moribundity. Clinical signs were recorded daily. Those animals that were judged moribund were killed and necropsied. Each animal was given a weekly clinical examination, including palpation for tissue masses or swelling. Body weight data were collected weekly.

At the end of the 91-day studies, survivors were killed and necropsies were performed. The specimens examined histopathologically are listed in Table 1. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

TWO-YEAR STUDIES

Study Design

Groups of 50 female rats and groups of 50 male and female mice were administered 1,2-dichloropropane in corn oil by gavage, 5 days per week for 103 weeks, at doses of 0, 125, or 250 mg/kg. Groups of 50 male rats received doses of 0, 62, or 125 mg/kg on the same schedule.

Source and Specifications of Test Animals

Four- to six-week-old F344/N rats and hybrid $B6C3F_1$ ($C57BL/6N \times C3H/HeN\ MTV^-$) mice were obtained from Charles River Breeding Laboratories, observed for approximately 3 weeks, and then assigned to cages according to a table of random numbers. The cages were then assigned to dosed and control groups according to another table of random numbers.

A quality control skin grafting program has been in effect since early 1968 to monitor the genetic integrity of the inbred mice used to produce the hybrid $B6C3F_1$ test animal. In mid-1981, data were obtained that showed incompatibility between the NIH C3H reference colony and the C3H colony from a carcinogenesis studies program supplier. In August 1981, inbred parental lines of mice were further tested for genetic homogeneity via isozyme and protein electrophoregrams which demonstrate phenotype expressions of known genetic loci.

The C57BL/6 mice were homogeneous at all loci tested. Eighty-five percent of C3H mice monitored were variant at one to three loci, indicating some heterogeneity in the C3H line from this supplier. Nevertheless, the genome of this line is more homogeneous than those of randomly bred stocks.

Male mice from the C3H colony and female mice from the C57BL/6 colony were used as parents for the hybrid B6C3F$_1$ mice used in these studies. The influence of the potential genetic non-uniformity in the hybrid mice on the results of these studies is not known, but should not affect the validity of the studies since matched concurrent controls were included.

Animal Maintenance

Rats and mice were housed five per cage in polycarbonate cages covered with nonwoven polyester filter sheets (Table 1). Cages and bedding were replaced twice per week. Feed and water were available *ad libitum*.

The rats were housed in room 550 for quarantine from April 5, 1979 to April 30, 1979; the temperature range in that room was 21° to 23°C and the relative humidity was 30% to 74% during that time. Mice were housed in room 530 beginning March 27, 1979, along with rats beginning April 30, 1979 until February 2, 1981; the temperature in room 530 from March 27, 1981 to February 2, 1981 was in the range of 20° to 27°C 92% of the time. The high extreme was 28°C (May 11 and 12, 1979), the low extreme was 18°C (July 17, 1980; August 12, 14, 16, and 17, 1980; September 3 and 4, 1980). The relative humidity was in the range of 32% to 77% for 92% of the time. The high extreme was 80% (June 9, 1979) and the low extreme was 21% (January 21, 1980, February 24 and 25, 1980). The remaining animals were moved to room 550 for the last 3 months of the study (February 2, 1981 to May 26, 1981). The temperature in room 550 was 22° to 24°C for all readings; the relative humidity was 49% to 78% for all readings.

Clinical Examinations and Pathology

All animals were observed twice daily for mortality and moribundity. Clinical signs were recorded daily. Body weights were recorded once per week for the first 13 weeks and then monthly thereafter. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. Moribund animals and animals that survived to the end of the study were killed and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The tissues examined microscopically are listed in Table 1.

Necropsies were performed on all animals found dead and on those killed at the end of the study, unless precluded by autolysis or cannibalization. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

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

Data Recording and Statistical Methods

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

Survival Analyses—Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time that they died of other than natural causes or were found to be missing; animals dying from natural causes were not statistically censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) extensions of Cox's methods for testing for a dose-related trend. All reported P values for the survival analysis are two-sided.

Incidence Data—The incidence of neoplastic or nonneoplastic lesions has been given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators included only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

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

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

Incidental Analyses—The second method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "incidental"; i.e., they were merely observed at necropsy in animals dying of an unrelated cause. According to this approach, the proportions of animals found to have tumors in dosed and control groups were compared in each of five time intervals: 0-52 weeks, 53-78 weeks, 79-92 weeks, week 93 to the week before the terminal kill, and the terminal kill period. The denominators of these proportions were the number of animals actually necropsied during the time interval. The individual time interval comparisons were then combined by the previously described methods to obtain a single overall result. (See Peto et al., 1980, for the computational details of both methods.)

Trends and Pairwise Comparisons—In addition to these tests, one other set of statistical analyses was carried out and reported in the tables analyzing primary tumors: the Fisher exact test for pairwise comparisons and the Cochran-Armitage linear trend test for dose-response trends (Armitage, 1971; Gart et al., 1979). These tests were based on the overall proportion of tumor-bearing animals. All reported P values for the tumor incidence analyses are one-sided. For studies in which there is little effect of compound administration on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death.

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Animals and Animal Maintenance			
Species	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice
Animal Source	Harlan Industries, (Indianapolis, IN)	Rats: Harlan Industries Mice: Charles River, (Portage, MI)	Charles River
Time Held Before Start of Test	14 days	Rats: 18 days Mice: 33 days	Rats: 25 days Mice: 22 days
Age when placed on study	6 weeks	Rats: 7 to 8 weeks Mice: 15 weeks	7 to 9 weeks
Age when Killed	8 weeks	Rats: 20 to 21 weeks Mice: 28 weeks	111 to 113 weeks
Method of Animal Distribution	Animals distributed to cages on a weight basis	Same as 14-day study	Animals were assigned to cages and test groups according to table of random numbers
Feed	Ground Wayne Lab Blox®	Wayne Lab Blox® meal	Same as 13-week study
Bedding	Aspen Bed® hardwood chips	Same as 14-day study	Same as 14-day study
Water	Glass bottles with rubber stoppers and stainless steel sipper tubes; changed twice weekly	Edstrom automatic watering system (Edstrom Industries, Waterford, WI)	Same as 13 week study
Cages	Polycarbonate	Same as 14-day study	Same as 14-day study
Cage Filters	Non-woven fiber filter	Same as 14-day study	Same as 14-day study
Animals per Cage	Five	Five	Five
Animal Room Environment	Temperature and relative humidity not given. 12 hours of fluorescent light per day; 10 room air changes per hour	21°-27°C (mean temperature: 22°C);14%-79% relative humidity (mean: 41%); 12 hours of fluorescent light per day; 10 room air changes per hour	18°-28°C (mean temperature: 23°C); 20%-80% relative humidity; 12 hours of fluorescent light per day; 12 room air changes per hour
Other Chemicals on Test in Same Room	Not stated	None	None
Experimental Design			
Size of Test Group	5 males and 5 females of each species	10 males and 10 females of each species	50 males and 50 females of each species

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

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Experimental Design			
Dose	0, 125, 250, 500, 1,000, or 2,000 mg/kg body weight in corn oil by gavage (dose volume: 3 ml/kg body weight)	Rats: 0, 60, 125, 250, 500, or 1,000 mg/kg body weight in corn oil by gavage (dose volume: 3 ml/kg) Mice: 0, 30, 60, 125, 250, or 500 mg/kg body weight in corn oil by gavage (dose volume: 3 ml/kg)	Rats: female - 0, 125 or 250 mg/kg male - 0, 62, or 125 mg/kg body weight by gavage (dose volume: 3 ml/kg body weight) Mice: 0, 125, or 250 mg/kg body weight in corn oil by gavage (dose volume: 3 ml/kg body weight)
Duration of Dosing	14 consecutive days	13 weeks (5 days per week)	103 weeks (5 days per week)
Type and Frequency of Observations	Observed twice daily for clinical signs of toxicity; initial and final individual body weights recorded	Observed twice daily for clinical signs of toxicity; individual animal weights measured weekly	Observed twice daily for mortality and moribundity; weighed once weekly for first 13 weeks and then monthly thereafter
Necropsy and Histological Examination	Necropsies performed on all animals; no histopathologic examination performed	Necropsies performed on all animals; following tissues examined in control, 500, and 1,000 mg/kg groups of rats and in control and 500 mg/kg groups of mice: tissue masses, gross lesions, mandibular and mesenteric lymph nodes, mammary gland, salivary gland, sternebrae, thymus, trachea, lungs and bronchi, thyroid, parathyroid, esophagus, stomach, small intestine, colon, liver, pancreas, gall bladder (mice), spleen, kidneys, adrenal, urinary bladder, prostate/testes or ovaries/uterus, brain, pituitary, abnormal lymph nodes, spinal cord, and skin	Necropsies performed on all animals; following tissues examined in all groups: tissue masses, gross lesions, abnormal lymph nodes, mandibular and mesenteric lymph nodes, mammary gland, salivary gland, bone marrow, thymus, trachea, larynx, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, intestine, colon, liver, gall bladder (mice only), pancreas, spleen, kidneys, adrenals, urinary bladder, prostate/testes or ovaries/uterus, brain, pituitary, skin, costochondral junction

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

	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Chemical/Vehicle Mixture			
Preparation	1,2-Dichloropropane (99.4% pure) and corn oil were mixed in a ground glass stoppered graduate cylinder by manual inversion; lower doses were made by serial dilution of the high dose formulation	Same as 14-day study	1,2-Dichloropropane formulations were prepared with corn oil on a weight/volume basis
Maximum Storage Time	One week	One week	10 days
Storage Conditions	4°C in brown glass bottles, protected from light	4°C in brown glass bottles, protected from light	0°±5°C in brown glass bottles, protected from light

III. RESULTS

RATS

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

FOURTEEN-DAY STUDIES

All rats receiving 2,000 mg/kg died during the study (Table 2). Final mean body weight relative to controls was depressed 14% to 15% in the surviving high dose (1,000 mg/kg) groups of rats.

At necropsy the renal medullae were red in 4/5 males and 5/5 females receiving 2,000 mg/kg but not in rats receiving lower doses. However, histopathology was not performed on any tissues in the 14 day studies.

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

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weights Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
MALES					
0	5/5	114.0 ± 3.5	167.7 ± 6.2	53.7 ± 3.0	
125	4/5	113.7 ± 5.0	150.8 ± 4.9	37.1 ± 3.0	- 10
250	5/5	114.8 ± 3.0	150.2 ± 4.7	35.4 ± 2.6	- 10
500	5/5	114.6 ± 2.9	144.6 ± 5.1	30.0 ± 2.4	- 14
1000	5/5	114.7 ± 3.2	144.8 ± 5.1	30.1 ± 3.2	- 14
2000	0/5	*(d)*	*(d)*	*(d)*	
FEMALES					
0	5/5	94.8 ± 6.0	122.9 ± 8.2	28.1 ± 2.7	
125	5/5	97.5 ± 9.0	120.0 ± 7.9	22.5 ± 2.0	- 2
250	5/5	95.5 ± 4.9	116.3 ± 5.9	20.8 ± 1.2	- 5
500	5/5	96.6 ± 4.2	112.9 ± 5.4	16.3 ± 1.3	- 8
1000	5/5	95.3 ± 4.6	105.0 ± 4.8	9.7 ± 3.0	- 15
2000	0/5	*(d)*	*(d)*	*(d)*	

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

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

(c) Final weight of the dosed survivors relative to the survivors of the controls ◘

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

(d) No data are presented due to the 100% mortality in this group.

THIRTEEN-WEEK STUDIES

All male and female rats receiving 1,000 mg/kg and 5/10 males receiving 500 mg/kg died before the necropsy (Table 3). Final mean body weights relative to those of controls were depressed 16% in males and 8% in females that received 500 mg/kg.

The liver was the target of non-neoplastic lesions in the high dose rats from the 13 week study. Centrilobular congestion of the liver occurred in 5/10 males and 2/10 females receiving 1,000 mg/kg. Hepatic fatty changes and centrilobular necrosis were observed in 2/10 females receiving 1,000 mg/kg.

Doses of 62 and 125 mg/kg were set for males and 125 and 250 mg/kg for females in the 2-year studies based on the short-term studies and because of the concern about the cumulative adverse effects which had been observed in bioassays of other short-chain chlorinated hydrocarbons.

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

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weights Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
MALES					
0	10/10	135.7 ± 2.8	300.1 ± 7.8	164.4 ± 5.9	
60	10/10	136.6 ± 2.7	334.3 ± 7.7	197.7 ± 6.1	+ 11
125	10/10	135.0 ± 2.8	308.2 ± 8.3	173.2 ± 7.6	+ 3
250	10/10	136.4 ± 2.8	297.7 ± 4.0	161.3 ± 3.7	- 1
500	5/10	135.7 ± 4.9	252.4 ± 14.7	116.7 ± 12.8	- 16
1000	0/10	*(d)*	*(d)*	*(d)*	
FEMALES					
0	10/10	100.7 ± 2.1	188.2 ± 2.9	87.5 ± 2.2	
60	10/10	100.9 ± 1.9	191.5 ± 3.7	90.6 ± 2.5	+ 2
125	10/10	100.9 ± 1.7	191.2 ± 3.7	90.3 ± 2.8	+ 2
250	10/10	100.9 ± 2.2	183.7 ± 4.5	82.8 ± 3.4	- 2
500	10/10	101.0 ± 1.8	173.3 ± 3.0	72.3 ± 2.7	- 8
1000	0/10	*(d)*	*(d)*	*(d)*	

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

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

(c) Final weight of the dosed survivors relative to the survivors of the controls ◘

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

(d) No data are presented due to the 100% mortality in this group.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Throughout most of the study, mean body weights of dosed rats of each sex were lower than those of the controls (Figure 1, and Appendix E, Table E1). The depressions in mean body weights were dose related. Final body weights for low dose males and females were 5% less than control values, whereas the high dose male body weights were 14% lower and the high dose female body weights were decreased 24% compared to controls.

Survival

Estimates of the probabilities of survival of male and female rats administered 1,2-dichloropropane in corn oil at the doses of these studies, and those of the vehicle controls, are shown by Figure 2. The survival of high dose female rats was less than that observed for the vehicle controls and low dose group ($P<0.001$). The large numbers of females killed around the ninety-fourth week of the study were the result of both spontaneous deaths and of the sacrifice of moribund animals. No other significant differences in survival were observed.

Survival was adversely affected in the high dose female rats but not in the low dose female or male rats. In male rats, 39/50 (78%) of the vehicle controls, 42/50 (84%) of the low dose, and 41/50 (82%) of the high dose group lived to the end of the study at 105-108 weeks. In female rats, 37/50 (74%) of the vehicle controls, 43/50 (86%) of the low dose, and 16/50 (32%) of the high dose group lived to the end of the study. The survival incidences include one low dose male, one high dose male, one control female, and one low dose female that died during the termination of the study. For purposes of statistical analysis these animals have been pooled with those killed at the end of the study.

Pathology and Statistical Analyses of Results

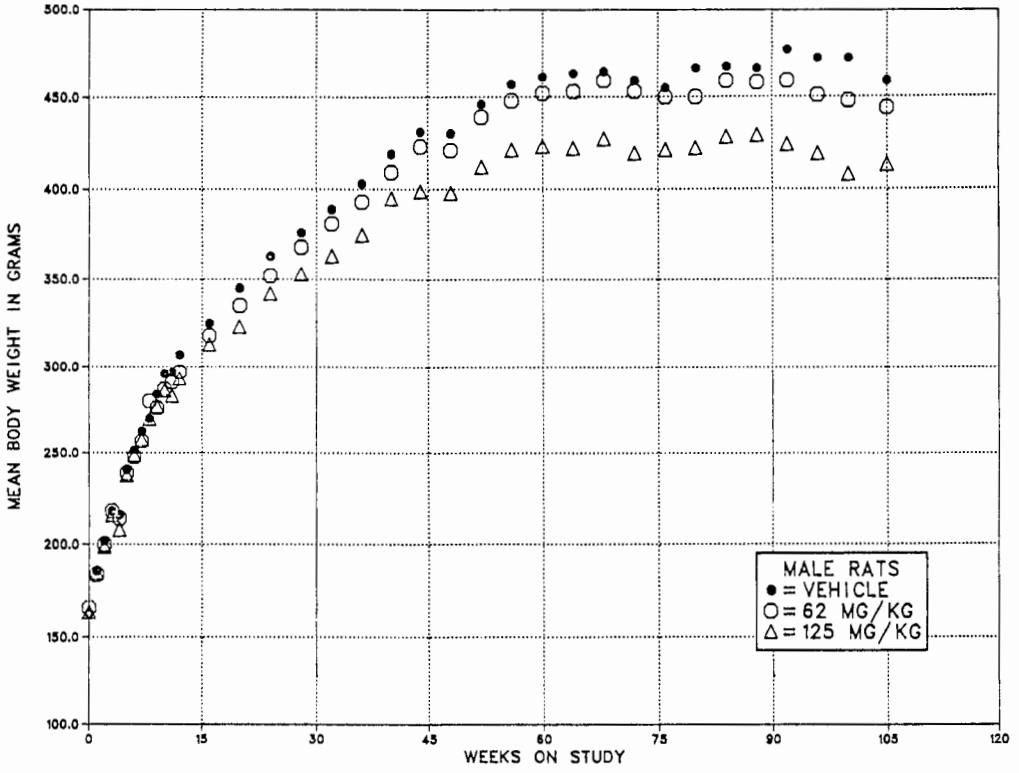
Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; Appendix Tables A3 and A4 give the survival and tumor status for individual male and female rats. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2. Historical incidences of selected tumors in control animals are listed in Appendix F. Appendix G, Tables G1 and G2, contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Data Recording and Statistical Methods) and Appendix G (footnotes).

Because of the reduced survival in high dose female rats, the statistical procedures that adjust for intercurrent mortality (life table and incidental tumor tests) were regarded as more meaningful than the "unadjusted" analysis in the evaluation of tumor incidence data in female rats.

Mammary Gland: Mammary gland hyperplasia was increased in the low dose female rats (controls, 10/50; low dose, 20/50) but, perhaps due to poor survival and the increased incidence of adenocarcinoma, there was only one high dose animal with mammary hyperplasia (1/50). Adenocarcinoma was increased in female rats with a significant positive trend, and the incidence in the high dose group was significantly higher than that in the vehicle controls (Table 4). The overall incidence of fibroadenomas occurred with a significant negative trend and decrease in the high dose group by the Cochran-Armitage test, but these decreases were not statistically significant when survival differences were taken into account (life table and incidental tumor tests). Neither tumor was observed in significant proportions in male rats.

Uterus: Endometrial stromal polyps occurred with a statistically significant positive trend (life table test; Table 5), but the incidence was not significantly increased in low or high dose groups.

Thyroid: Follicular cell carcinomas were found in two low dose female rats that were killed at the end of the study. These tumors were not seen in control or high dose females and were not significantly increased in the low dose group. The historical incidence of follicular cell carcinoma in controls is 1/150 (0.7%) from this laboratory and the interlaboratory value is only 2/859 (0.2%) (Appendix F, Table F6).



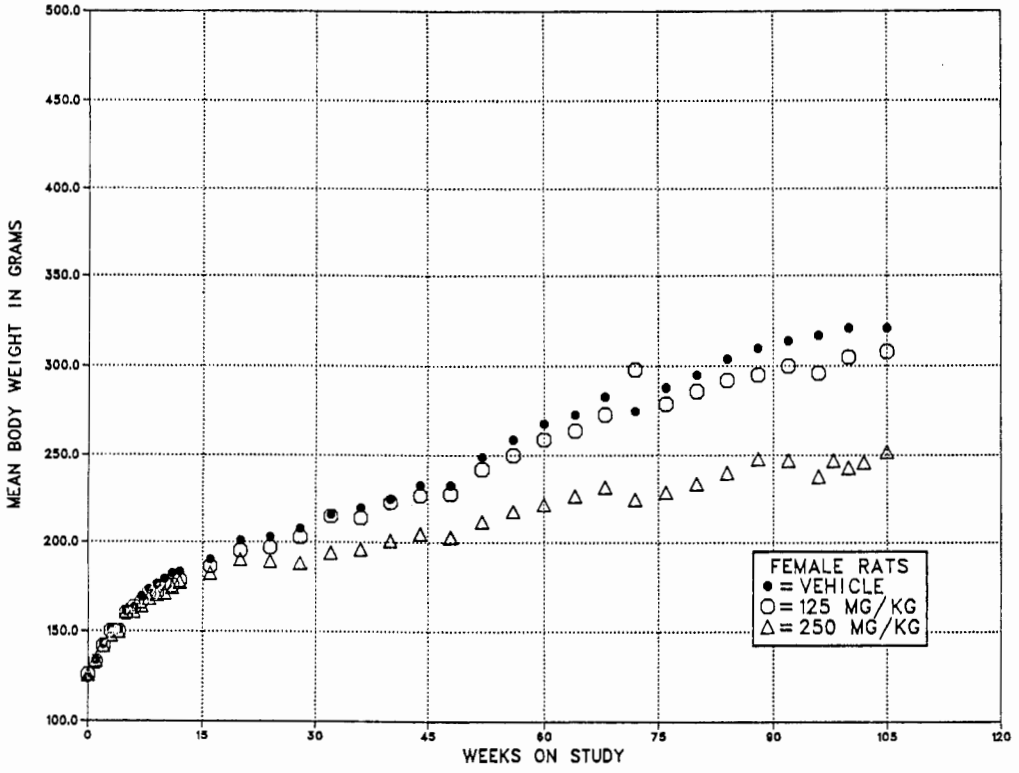
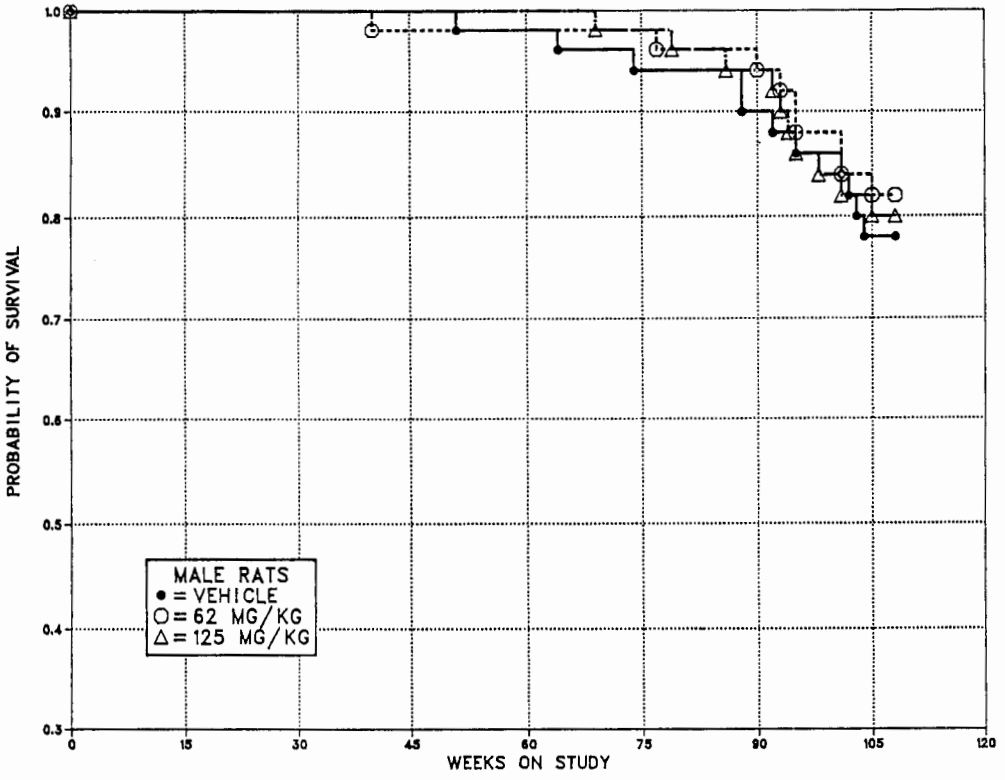


Figure 1. Growth Curves for Rats Administered 1,2-Dichloropropane by Gavage



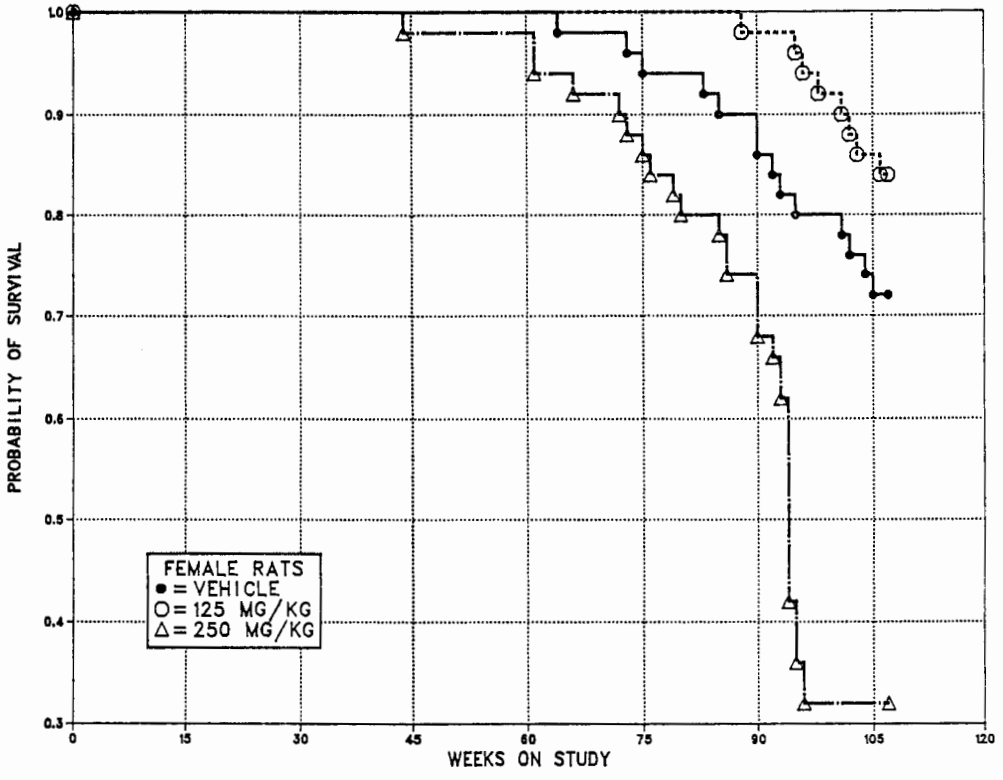


Figure 2. Survival Curves for Rats Administered 1,2-Dichloropropane by Gavage

TABLE 4. ANALYSIS OF MAMMARY GLAND TUMORS IN FEMALE RATS

	Vehicle Control	125 mg/kg	250 mg/kg
Adenocarcinoma			
Overall Rates	1/50 (2%)	2/50 (4%)	5/50 (10%)
Adjusted Rates	2.7%	4.7%	26.7%
Terminal Rates	1/37 (3%)	2/43 (5%)	4/16 (25%)
Life Table Test	P=0.005	P=0.552	P=0.012
Incidental Tumor Test	P=0.011	P=0.552	P=0.018
Cochran-Armitage Trend Test	P=0.060		
Fisher Exact Test		P=0.500	P=0.102
Fibroadenoma			
Overall Rates	15/50 (30%)	20/50 (40%)	7/50 (14%)
Adjusted Rates	39.4%	46.5%	37.0%
Terminal Rates	14/37 (38%)	20/43 (47%)	5/16 (31%)
Life Table Test	P=0.441	P=0.381	P=0.561
Incidental Tumor Test	P=0.490N	P=0.383	P=0.406N
Cochran-Armitage Trend Test	P=0.047N		
Fisher Exact Test		P=0.201	P=0.045N

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

	Vehicle Control	125 mg/kg	250 mg/kg
Endometrial Stromal Polyp			
Overall Rates	10/50 (20%)	17/49 (35%)	11/50 (22%)
Adjusted Rates	25.1%	37.5%	45.6%
Terminal Rates	8/37 (22%)	14/42 (33%)	6/16 (38%)
Life Table Test	P=0.024	P=0.174	P=0.051
Incidental Tumor Test	P=0.253	P=0.113	P=0.256
Cochran-Armitage Trend Test	P=0.454		
Fisher Exact Test		P=0.078	P=0.500

(a) One control female rat with an endometrial stromal polyp also had an endometrial stromal sarcoma; an endometrial stromal sarcoma was also observed in an additional low dose animal.

Stomach or Forestomach: Squamous cell papillomas were found in two high dose female rats. The lesions were not significantly increased compared to controls. Squamous cell papillomas or carcinomas have been observed in only 3/870 (0.3%) corn-oil dosed controls from this program and in 0/149 (0%) controls at this testing facility. (Appendix F, Table F3).

Liver: Nonneoplastic liver lesions were increased in female rats treated with 1,2-dichloropropane. Foci of clear cell change were found at an increased incidence in dosed female rats (vehicle controls: 3/50, 6%; low dose, 5/50, 10%; high dose, 11/50, 22%). Necrosis (focal and centrilobular combined) occurred at increased incidences in high dose females (vehicle control, 2/50, 4%; low dose, 1/50, 2%; high dose, 12/50, 24%). No increases in liver tumors were observed in male rats (control, 3/50, 6%; low dose, 3/50, 6%; high dose, 2/50, 4%) or in dosed female rats (1 neoplastic nodule in a control female).

Pancreas: Islet cell carcinomas occurred with a positive trend in male rats (Table 6). However, the incidence of adenomas was greatest in controls and the combined incidence of adenomas or carcinomas was not different among groups. These tumors were not observed in female rats. The historical rates for these lesions in males at this laboratory are 9/146 (6%) for adenomas and 4/146 (3%) for carcinomas. The interlaboratory rates in males for adenomas and carcinomas are 38/876 (4.3%) and 22/876 (2.5%) for adenomas and carcinomas, respectively (Appendix F, Table F9).

TABLE 6. ANALYSIS OF PANCREATIC ISLET CELL TUMORS IN MALE RATS

	Vehicle Control	62 mg/kg	125 mg/kg
Islet Cell Adenoma			
Overall Rates	4/48 (8%)	1/50 (2%)	3/50 (6%)
Adjusted Rates	10.5%	2.4%	6.9%
Terminal Rates	4/38 (11%)	1/42 (2%)	2/41 (5%)
Life Table Test	P=0.379N	P=0.151N	P=0.461N
Incidental Tumor Test	P=0.382N	P=0.151N	P=0.465N
Cochran-Armitage Trend Test	P=0.393N		
Fisher Exact Test		P=0.168N	P=0.477N
Islet Cell Carcinoma			
Overall Rates	0/48 (0%)	0/50 (0%)	3/50 (6%)
Adjusted Rates	0.0%	0.0%	7.3%
Terminal Rates	0/38 (0%)	0/42 (0%)	3/41 (7%)
Life Table Test	P=0.040	—	P=0.135
Incidental Tumor Test	P=0.040	—	P=0.135
Cochran-Armitage Trend Test	P=0.039		
Fisher Exact Test			P=0.129
Islet Cell Adenoma or Carcinoma			
Overall Rates	4/48 (8%)	1/50 (2%)	6/50 (12%)
Adjusted Rates	10.5%	2.4%	14.1%
Terminal Rates	4/38 (11%)	1/42 (2%)	5/41 (12%)
Life Table Test	P=0.316	P=0.151N	P=0.416
Incidental Tumor Test	P=0.314	P=0.151N	P=0.413
Cochran-Armitage Trend Test	P=0.301		
Fisher Exact Test		P=0.168N	P=0.397

Pituitary: The increased incidence of adenomas in low dose females was statistically significant by the Fisher exact test (Table 7). However, this increase was not statistically significant when survival differences were taken into account (life table and incidental tumor tests). The incidence of pituitary carcinomas was greater in the control female rats than in the low dose female rats. The combined incidences of adenomas and carcinomas were not significantly increased in the treated groups.

Adrenal Glands: Pheochromocytomas occurred in male rats with a negative trend (Table 8). No significant differences were observed between dosed and control groups for the combined incidence of pheochromocytoma or malignant pheochromocytoma.

Spleen: Hemosiderosis (control, 0/50, 0%; low dose, 0/50, 0%; high dose, 20/47, 43%) and hematopoiesis (control, 1/50, 2%; low dose, 1/50, 2%; high dose, 7/47, 15%) were seen at higher incidences in high dose female rats. Review of the slides for the incidence and severity of these lesions by NTP pathologists indicated that there may have been only a slight increase in hemosiderosis in the high dose female rats and no increase in hematopoiesis.

TABLE 7. ANALYSIS OF PITUITARY TUMORS IN FEMALE RATS

	Vehicle Control	125 mg/kg	250 mg/kg
Adenoma			
Overall Rates	16/49 (33%)	26/50 (52%)	10/46 (22%)
Adjusted Rates	40.6%	55.3%	46.9%
Terminal Rates	14/37 (38%)	22/43 (51%)	6/16 (38%)
Life Table Test	P=0.157	P=0.122	P=0.312
Incidental Tumor Test	P=0.453N	P=0.093	P=0.503N
Cochran-Armitage Trend Test	P=0.172N		
Fisher Exact Test		P=0.040	P=0.168N
Carcinoma			
Overall Rates	3/49 (6%)	2/50 (4%)	0/46 (0%)
Adjusted Rates	8.1%	4.7%	0.0%
Terminal Rates	3/37 (8%)	2/43 (5%)	0/16 (0%)
Life Table Test	P=0.183N	P=0.431N	P=0.301N
Incidental Tumor Test	P=0.183N	P=0.431N	P=0.301N
Cochran-Armitage Trend Test	P=0.089N		
Fisher Exact Test		P=0.490N	P=0.133N
Adenoma or Carcinoma			
Overall Rates	19/49 (39%)	28/50 (56%)	10/46 (22%)
Adjusted Rates	48.3%	59.6%	46.9%
Terminal Rates	17/37 (46%)	24/43 (56%)	6/16 (38%)
Life Table Test	P=0.292	P=0.187	P=0.484
Incidental Tumor Test	P=0.282N	P=0.151	P=0.323N
Cochran-Armitage Trend Test	P=0.062N		
Fisher Exact Test		P=0.065	P=0.057N

TABLE 8. ANALYSIS OF ADRENAL TUMORS IN MALE RATS

	Vehicle Control	62 mg/kg	125 mg/kg
Pheochromocytoma			
Overall Rates	11/50 (22%)	5/49 (10%)	5/50 (10%)
Adjusted Rates	28.2%	11.7%	11.8%
Terminal Rates	11/39 (28%)	4/41 (10%)	4/41 (10%)
Life Table Test	P=0.046N	P=0.069N	P=0.071N
Incidental Tumor Test	P=0.046N	P=0.071N	P=0.071N
Cochran-Armitage Trend Test	P=0.057N		
Fisher Exact Test		P=0.093N	P=0.086N
Pheochromocytoma or Pheochromocytoma, Malignant			
Overall Rates	11/50 (22%)	5/49 (10%)	7/50 (14%)
Adjusted Rates	28.2%	11.7%	16.6%
Terminal Rates	11/39 (28%)	4/41 (10%)	6/41 (15%)
Life Table Test	P=0.141N	P=0.069N	P=0.185N
Incidental Tumor Test	P=0.141N	P=0.071N	P=0.185N
Cochran-Armitage Trend Test	P=0.166N		
Fisher Exact Test		P=0.093N	P=0.218N

FOURTEEN-DAY STUDIES

All male mice receiving 1,000 or 2,000 mg/kg and all female mice receiving 2,000 mg/kg died (Table 9). Three of five males receiving 500 mg/kg and 4/5 females receiving 1,000 mg/kg also died. Mean body weights of surviving mice were not adversely affected by administration of 1,2-dichloropropane.

Renal medullae were red in all mice receiving 2,000 mg/kg, in 3/5 males receiving 500 mg/kg, in 3/5 females receiving 1,000 mg/kg and in 1/5 females in each of the 125, 250, and 500 mg/kg groups. No other compound-related effects were observed at necrospy. No histopathology was performed on any tissues in this study.

TABLE 9. SURVIVAL AND MEAN BODY WEIGHTS OF MICE ADMINISTERED 1,2-DICHLOROPROPANE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weights Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
MALES					
0	5/5	21.7 ± 0.6	24.6 ± 0.5	2.9 ± 0.5	
125	5/5	22.3 ± 0.3	25.6 ± 0.7	3.3 ± 0.5	+ 4.1
250	5/5	22.5 ± 0.4	25.6 ± 0.5	3.1 ± 0.2	+ 4.1
500	2/5	23.2 ± 0.0	27.7 ± 0.3	4.5 ± 0.3	+ 12.6
1000	0/5	*(d)*	*(d)*	*(d)*	
2000	0/5	*(d)*	*(d)*	*(d)*	
FEMALES					
0	5/5	18.1 ± 0.3	19.6 ± 0.5	1.5 ± 0.2	
125	5/5	18.4 ± 0.4	19.9 ± 0.3	1.5 ± 0.3	+ 1.5
250	5/5	18.3 ± 0.5	21.2 ± 0.7	2.9 ± 0.4	+ 8.2
500	5/5	18.5 ± 0.5	21.5 ± 0.4	3.0 ± 0.3	+ 9.7
1000	1/5	18.8 ± 0.0	21.7 ± 0.0	2.9 ± 0.0	+ 10.7
2000	0/5	*(d)*	*(d)*	*(d)*	

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

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

(c) Final weight of the dosed survivors relative to the survivors of the controls ◘

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

(d) No data is presented due to the 100% mortality in this group.

THIRTEEN-WEEK STUDIES

One male receiving 60 mg/kg died during the 1st week of the study, and a female receiving 500 mg/kg died during the 12th week. Mean body weight changes among males were not dose-related (Table 10). Body weights were depressed 4% to 5% for males that received 30 or 500 mg/kg and 3% to 4% for females that received 250 or 500 mg/kg compared to controls. No compound-related histopathologic effects were recorded.

The dosages selected for the 2-year studies were 125 and 250 mg/kg and the selection was based on the lack of mortality and marginal body weight differences in the 13-week studies.

TABLE 10 SURVIVAL AND MEAN BODY WEIGHTS OF MICE ADMINISTERED 1,2-DICHLOROPROPANE BY GAVAGE FOR 13 WEEKS

Dose (mg/kg)	Survival *(a)*	Mean Body Weights (grams)			Final Body Weights Relative to Controls *(c)* (Percent)
		Initial	Final	Change *(b)*	
MALES					
0	10/10	27.5 ± 0.5	36.1 ± 0.6	8.6 ± 0.3	
30	10/10	27.4 ± 0.5	34.5 ± 1.1	7.1 ± 0.8	- 4.4
60	9/10	27.5 ± 0.4	35.6 ± 0.5	8.1 ± 0.3	- 1.4
125	10/10	27.5 ± 0.4	35.7 ± 1.0	8.2 ± 0.7	- 1.1
250	10/10	27.2 ± 0.5	36.2 ± 0.7	9.0 ± 0.6	+ 0.3
500	10/10	27.1 ± 0.4	34.3 ± 0.6	7.2 ± 0.4	- 5.0
FEMALES					
0	10/10	21.8 ± 0.3	28.1 ± 0.9	6.3 ± 0.8	
30	10/10	21.6 ± 0.4	27.8 ± 0.6	6.2 ± 0.4	- 1.1
60	10/10	21.9 ± 0.4	28.0 ± 0.6	6.1 ± 0.7	- 0.4
125	10/10	22.0 ± 0.5	28.1 ± 0.8	6.1 ± 0.5	0
250	10/10	22.1 ± 0.5	27.2 ± 0.6	5.1 ± 0.4	- 3.2
500	9/10	22.0 ± 0.4	27.1 ± 0.6	5.1 ± 0.3	- 3.6

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

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

(c) Final weight of the dosed survivors relative to the survivors of the controls =

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

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of treated and vehicle control mice were comparable (Figure 3 and Appendix E, Table E2). No compound-related clinical signs were recorded.

Survival

Estimates of the probabilities of survival of male and female mice administered 1,2-dichloropropane in corn oil at the doses of these studies, and those of the vehicle controls, are shown in Figure 4. The survival of high dose female mice was less than that of the vehicle control group (P=0.035). In male mice, 35/50 (70%) of the vehicle controls, 33/50 (66%) of the low dose, and 35/50 (70%) of the high dose group lived to the termination period of the study at 105-107 weeks. In female mice, 35/50 (70%) of the vehicle controls, 29/50 (58%) of the low dose, and 26/50 (52%) of the high dose group lived to the termination period of the study at 105-107 weeks. The survival incidences include one control male, one low dose male, one control female, and two high dose females that died during the termination of the study. For statistical purposes, these animals have been pooled with those killed at the end of the study. The decreased survival of the female mice may have been in part related to infections. In female mice which died before the end of the study, 5/11 controls, 9/14 low dose, and 14/22 high dose females had inflammation of the reproductive tract.

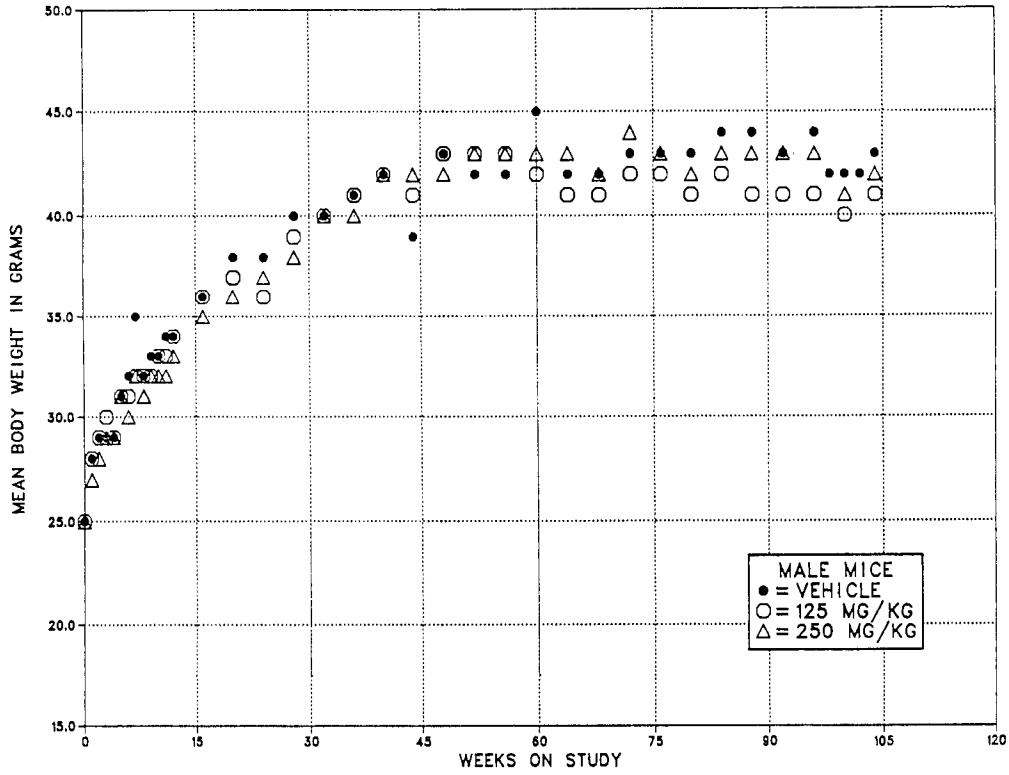
Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms in mice are summarized in Appendix B, Tables B1 and B2; Appendix Tables B3 and B4 give the survival and tumor status for individual male and female mice. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2. Historical incidences of tumors in control animals are listed in Appendix F. Appendix G, Tables G3 and G4, contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Data Recording and Statistical Methods) and Appendix G (footnotes).

Liver: 1,2-Dichloropropane caused nonneoplastic liver lesions in male mice. Hepatocytomegaly occurred at increased incidences in dosed male mice (vehicle control, 3/50, 6%; low dose, 5/49, 10%; high dose, 15/50, 30%). Hepatic necrosis (focal, NOS, and centrilobular combined) was increased in dosed males (vehicle controls, 2/50, 4%; low dose, 5/49, 10%; high dose, 10/50, 20%). These lesions did not occur at increased incidences in dosed female mice.

Liver tumors were increased in treated male and female mice. Liver adenomas occurred with positive trends in male and female mice. The tumor incidences in high dose males and in low and high dose females were significantly higher than those in the controls (Tables 11 and 12). The dosed animals had slightly higher incidences of carcinoma but they were not significantly increased. The historical incidence of liver adenomas in $B6C3F_1$ mice in the performing laboratory is 22/149, 14.7% for males and 8/148, 5.4% for females (Appendix F, Tables F1 and F2).

Thyroid: Two high dose female mice had follicular cell carcinomas. No follicular cell carcinomas were observed in the control or low dose female mice. The historical rate at this laboratory for carcinoma is 0/139 (0%), the interlaboratory rate is 3/818 (0.4%) (Appendix F, Table F7). The combined incidence of follicular cell adenomas or carcinomas in the high dose group was significantly higher than that in the controls but no adenomas or carcinomas were observed in the low dose female mice (Table 13). The historical incidence of thyroid follicular cell adenomas or carcinomas combined is 2/139 (1%) at this laboratory and the interlaboratory rate is 31/818 (3.8%) (Appendix F, Table F7). These tumors did not occur in male mice at statistically significant incidences; one male in the high dose group had follicular cell adenoma and another had follicular cell carcinoma.



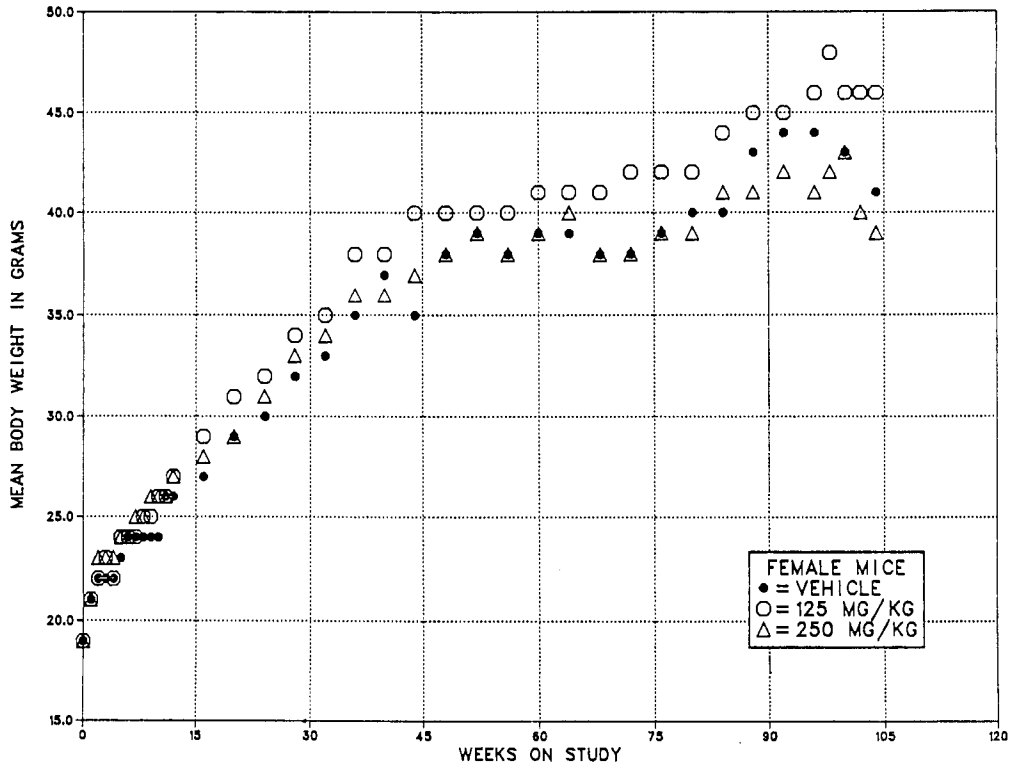


Figure 3. Growth Curves for Mice Administered 1,2-Dichloropropane by Gavage

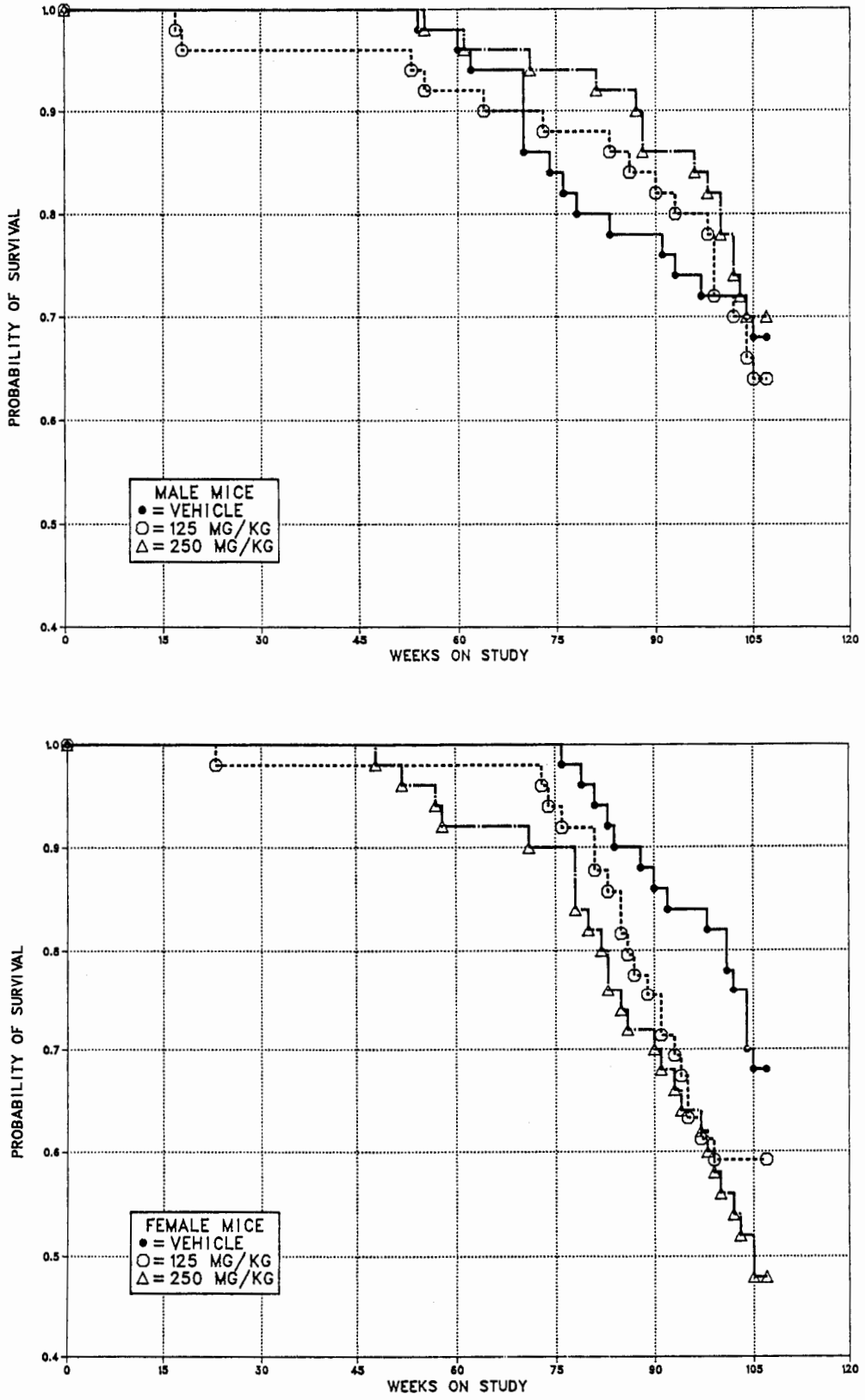


Figure 4. Survival Curves for Mice Administered 1,2-Dichloropropane by Gavage

TABLE 11. ANALYSIS OF LIVER TUMORS IN MALE MICE

	Vehicle Control	125 mg/kg	250 mg/kg
Adenoma			
Overall Rates	7/50 (14%)	10/50 (20%)	17/50 (34%)
Adjusted Rates	20.0%	28.8%	45.5%
Terminal Rates	7/35 (20%)	9/33 (27%)	15/35 (43%)
Life Table Test	P=0.011	P=0.248	P=0.017
Incidental Tumor Test	P=0.010	P=0.213	P=0.023
Cochran-Armitage Trend Test	P=0.012		
Fisher Exact Test		P=0.298	P=0.017
Carcinoma			
Overall Rates	11/50 (22%)	17/50 (34%)	16/50 (32%)
Adjusted Rates	28.1%	41.9%	37.3%
Terminal Rates	8/35 (23%)	10/33 (30%)	9/35 (26%)
Life Table Test	P=0.213	P=0.132	P=0.226
Incidental Tumor Test	P=0.358	P=0.226	P=0.337
Cochran-Armitage Trend Test	P=0.161		
Fisher Exact Test		P=0.133	P=0.184
Adenoma or Carcinoma			
Overall Rates	18/50 (36%)	26/50 (52%)	33/50 (66%)
Adjusted Rates	46.7%	62.9%	74.7%
Terminal Rates	15/35 (43%)	18/33 (55%)	24/35 (69%)
Life Table Test	P=0.006	P=0.069	P=0.007
Incidental Tumor Test	P=0.008	P=0.101	P=0.010
Cochran-Armitage Trend Test	P=0.002		
Fisher Exact Test		P=0.079	P=0.002

TABLE 12. ANALYSIS OF LIVER TUMORS IN FEMALE MICE

	Vehicle Control	125 mg/kg	250 mg/kg
Adenoma			
Overall Rates	1/50 (2%)	5/50 (10%)	5/50 (10%)
Adjusted Rates	2.9%	17.2%	19.2%
Terminal Rates	1/35 (3%)	5/29 (17%)	5/26 (19%)
Life Table Test	P=0.036	P=0.064	P=0.047
Incidental Tumor Test	P=0.036	P=0.064	P=0.047
Cochran-Armitage Trend Test	P=0.090		
Fisher Exact Test		P=0.102	P=0.102
Carcinoma			
Overall Rates	1/50 (2%)	3/50 (6%)	4/50 (8%)
Adjusted Rates	2.9%	9.7%	12.6%
Terminal Rates	1/35 (3%)	2/29 (7%)	2/26 (8%)
Life Table Test	P=0.080	P=0.238	P=0.117
Incidental Tumor Test	P=0.103	P=0.245	P=0.147
Cochran-Armitage Trend Test	P=0.133		
Fisher Exact Test		P=0.309	P=0.181
Adenoma or Carcinoma			
Overall Rates	2/50 (4%)	8/50 (16%)	9/50 (18%)
Adjusted Rates	5.7%	26.4%	30.8%
Terminal Rates	2/35 (6%)	7/29 (24%)	7/26 (27%)
Life Table Test	P=0.006	P=0.022	P=0.008
Incidental Tumor Test	P=0.008	P=0.023	P=0.010
Cochran-Armitage Trend Test	P=0.025		
Fisher Exact Test		P=0.046	P=0.026

TABLE 13. ANALYSIS OF FOLLICULAR CELL TUMORS OF THE THYROID IN FEMALE MICE

	Vehicle Control	125 mg/kg	250 mg/kg
Adenoma			
Overall Rates	1/48 (2%)	0/45 (0%)	3/46 (7%)*(a)*
Adjusted Rates	2.9%	0.0%	12.5%
Terminal Rates	1/34 (3%)	0/27 (0%)	3/24 (13%)
Life Table Test	P=0.110	P=0.546N	P=0.189
Incidental Tumor Test	P=0.110	P=0.546N	P=0.189
Cochran-Armitage Trend Test	P=0.168		
Fisher Exact Test		P=0.516N	P=0.292
Carcinoma			
Overall Rates	0/48 (0%)	0/45 (0%)	2/46 (4%)
Adjusted Rates	0.0%	0.0%	2.3%
Terminal Rates	0/34 (0%)	0/27 (0%)	2/24 (8%)
Life Table Test	P=0.065	*(b)*	P=0.165
Incidental Tumor Test	P=0.065	*(b)*	P=0.165
Cochran-Armitage Trend Test	P=0.093		
Fisher Exact Test		*(b)*	P=0.237
Adenoma or Carcinoma			
Overall Rates	1/48 (2%)	0/45 (0%)	5/46 (11%)
Adjusted Rates	2.9%	0.0%	20.8%
Terminal Rates	1/34 (3%)	0/27 (0%)	5/24 (21%)
Life Table Test	P=0.015	P=0.546N	P=0.040
Incidental Tumor Test	P=0.015	P=0.546N	P=0.040
Cochran-Armitage Trend Test	P=0.034		
Fisher Exact Test		P=0.516N	P=0.092

(a) Includes one animal with a cystadenoma, NOS.

(b) No statistical analyses were done because no tumors were observed in control or low dose groups.

Forestomach: Acanthosis of the surface epithelium in the forestomach occurred at increased incidences in high dose males and low and high dose females: males—vehicle control, 0/50; low dose, 0/48; high dose, 2/49, 4%; females—vehicle control, 0/50; low dose, 5/50, 10%; high dose, 4/50, 8%. Squamous cell papillomas occurred in dosed male and female mice: males—vehicle control, 0/50; low dose, 1/48, 2%; high dose, 3/49, 6%; females—vehicle control, 0/50; low dose, 2/50, 4%; high dose, 2/50, 4%. One high dose female mouse had a squamous cell carcinoma. The historical incidence for squamous cell papillomas at this laboratory is 0/146 for males and 0/147 for females; the interlaboratory rates are 2/855 (0.2% males) and 3/879 (0.3% females) (Appendix F, Tables F4 and F5).

Multiple Organs: Suppurative inflammation was found in the ovary, uterus, or multiple organs of 5/11 vehicle control, 9/14 low dose, and 14/22 high dose female mice that died before the end of the study.

Lung: Alveolar/bronchiolar adenomas and alveolar/bronchiolar adenomas or carcinomas (combined) occurred in female mice with statistically significant negative trends (Table 14). The incidence of adenomas in the low dose group was significantly lower than that of the controls. These tumors were not observed at significant incidences in male mice.

Integumentary System: Fibromas or fibrosarcomas of the subcutaneous tissue and fibromas or fibrosarcomas of the skin or subcutaneous tissue occurred with significant negative trends in male mice (Table 15). The incidences in the high dose group were significantly lower than those in the controls.

TABLE 14. ANALYSIS OF LUNG TUMORS IN FEMALE MICE

	Vehicle Control	125 mg/kg	250 mg/kg
Alveolar/Bronchiolar Adenoma			
Overall Rates	5/50 (10%)	0/50 (0%)	1/50 (2%)
Adjusted Rates	13.6%	0.0%	3.8%
Terminal Rates	4/35 (11%)	0/29 (0%)	1/26 (4%)
Life Table Test	P=0.073N	P=0.056N	P=0.189N
Incidental Tumor Test	P=0.061N	P=0.052N	P=0.162N
Cochran-Armitage Trend Test	P=0.037N		
Fisher Exact Test		P=0.028N	P=0.102N
Alveolar/Bronchiolar Carcinoma			
Overall Rates	1/50 (27%)	1/50 (2%)	0/50 (0%)
Adjusted Rates	2.9%	2.5%	0.0%
Terminal Rates	1/35 (3%)	0/29 (0%)	0/26 (0%)
Life Table Test	P=0.386N	P=0.726	P=0.559N
Incidental Tumor Test	P=0.348N	P=0.744N	P=0.559N
Cochran-Armitage Trend Test	P=0.331N		
Fisher Exact Test		P=0.753N	P=0.500N
Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates	6/50 (12%)	1/50 (2%)	1/50 (2%)
Adjusted Rates	16.4%	2.5%	3.8%
Terminal Rates	5/35 (14%)	0/29 (0%)	1/26 (4%)
Life Table Test	P=0.051N	P=0.100N	P=0.123N
Incidental Tumor Test	P=0.039N	P=0.079N	P=0.104N
Cochran-Armitage Trend Test	P=0.023N		
Fisher Exact Test		P=0.056N	P=0.056N

TABLE 15. ANALYSIS OF INTEGUMENTARY TUMORS IN MALE MICE

	Vehicle Control	125 mg/kg	250 mg/kg
Skin or Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Overall Rates	7/50 (14%)	4/50 (8%)	1/50 (2%)
Adjusted Rates	20.0%	12.1%	2.3%
Terminal Rates	7/35 (20%)	4/33 (12%)	0/35 (0%)
Life Table Test	P=0.021N	P=0.292N	P=0.031N
Incidental Tumor Test	P=0.016N	P=0.292N	P=0.021N
Cochran-Armitage Trend Test	P=0.021N		
Fisher Exact Test		P=0.262N	P=0.030N

IV. DISCUSSION AND CONCLUSIONS

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Short-term studies of 1,2-dichloropropane (DCP) used doses up to 2,000 mg/kg in rats and mice in the 14 day studies. Red renal medullae in both rats and mice were the only treatment related effects described in those studies. The kidney lesions were not examined histologically. Doses of 1,000 mg/kg for rats and 500 mg/kg for mice were selected as the high dose levels in the 13 week studies because of the mortality observed at higher dosages in the 14 day studies. Fatty changes and centrilobular congestion of the liver were observed in female rats at the highest dosage after 13 weeks exposure to DCP. No DCP-related lesions were observed in the male rats or in mice of either sex in the 13 week studies. Doses selected for the 2 year carcinogenesis studies were 62 and 125 mg/kg for the male rats and 125 and 250 mg/kg for the female rats and the male and female mice. Lower dosages were chosen for the male rats than for the female rats because of the greater mortality observed for males than for females during the 13 week studies. The high dose selected for female rats was considered to be toxic for the 2 year studies as reflected by reduced survival late in the study and lowered body weights. Only 16 female rats from the high dose group survived to the end of the 2 year studies.

Decreased survival in the dosed female mice was related to an increased incidence of reproductive tract infections in the animals which died before the end of the studies (control, 5/11; low dose, 9/14; high dose, 14/22). The infection-related deaths decreased the group sizes, especially for the treated groups; 26 high dose and 29 low dose female mice survived to the terminal sacrifice compared to 35 controls. Significant increases were observed in virus antibody titers for both rats and mice. The relationship of these increases to decreased survival, to non-neoplastic lesions, or to neoplastic lesions is unclear.

The principal target organ for DCP toxicity was the liver of rats and mice. Centrilobular congestion was seen in both male and female rats and fatty changes were observed in male rats receiving 1,000 mg/kg for 13 weeks. Clear cell changes and necrosis were increased in the livers of treated female rats in the 2 year studies. Hepatocytomegaly was increased in a dose-related manner in the male mice, but not in female mice.

Liver toxicity has been associated with DCP exposure in other investigations. DCP caused significant hepatic toxicity in laboratory animals whether administered orally or by inhalation (Heppel et al., 1948; Drew et al., 1978; Sidorenko et al., 1976; Belyaeva et al., 1977; Larcan et al., 1977). The nonneoplastic liver lesions have been identified as centrilobular necrosis in both humans (Larcan et al., 1977) and rats (Sidorenko et al., 1976). Similar centrilobular hepatic lesions have been observed with other short-chain halogenated hydrocarbons such as carbon tetrachloride, chloroform, trichloroethylene, 1,1,2-trichloroethane (Plaa, 1980), 1,2,3-trichloropropane, and perchloroethylene (Sidorenko et al., 1976). The liver zonal specificity of these compounds may be related to the relatively high concentrations of microsomal enzymes in that zone of the hepatic lobule which may activate the compounds to toxic intermediates (Plaa, 1980; Sidorenko et al., 1976). Hepatic enzyme changes have been identified in animals exposed to DCP. Inhalation of DCP by rats caused significant increases in the serum levels of glutamic oxaloacetic transaminase (Drew et al., 1978).

In the present study, neoplastic liver lesions were observed in B6C3F$_1$ mice. Oral exposure to DCP caused significant dose-related increases in the frequency of hepatocellular adenomas in both male and female B6C3F$_1$ mice (males: control, 7/50; low dose, 10/49; high dose, 16/50; females: 0/50, 4/50, 5/50). If the incidences of adenoma are combined with the incidences of carcinoma, the liver tumor incidences remain significantly higher than those in the controls. The increases in the frequency of liver carcinoma alone were not significant for dosed males and females versus controls but there was a numerical increase (males: 11/50, 16/49, 16/50; females: 1/50, 3/50, 4/50); this parallels the finding that DCP caused an increase in liver adenomas in male and female mice.

The concurrent control data for the incidence of liver neoplasia in these studies were essentially equal to the historical control data for this laboratory or for all laboratories combined (see Appendix F, Table F1). Despite the fact that there is some evidence of genetic heterogeneity of the C3H mouse strain used as the paternal stock for the B6C3F$_1$ mice for these studies, the impact of this variable on the usefulness of the historical control data should be considered in the total context of the evolution of the program (e.g., improved environmental controls, better quality control, more rigorous pathology, and improved control of nutrition). In these studies, as in other studies, the program relies first on the data from the concurrent controls, then on the

data derived from recent studies performed in the same laboratory using the same route of exposure, and finally on the control data from other laboratories using the same route of exposure.

To speculate about the mechanism by which 1,2-dichloropropane caused toxicity or increased the incidence of hepatocellular neoplasms in mice is beyond the scope of these carcinogenicity studies. Male $B6C3F_1$ mice have a high incidence of spontaneous benign liver tumors which can be further increased both by carcinogens, such as N-2-acetylaminofluorene and chlordane, and also by promoters, such as phenobarbital (Becker, 1982). Those studies have shown that promoting agents do not increase the incidence of liver adenomas in animals which do not have high incidences of spontaneous liver adenomas, like the C57Bl/6 mouse; carcinogen exposure was associated with increases in both benign and malignant liver tumors in mice, regardless of whether or not they developed the spontaneous liver tumors. In the present studies, DCP caused a significant increase in the incidence of hepatocellular adenomas in both male and female $B6C3F_1$ mice. The male, but not the female, has a high incidence of spontaneous liver tumors (historical control data at all laboratories combined, adenomas or carcinomas combined, males: 273/884, 30.9%; females: 67/978, 6.9%). Liver carcinomas alone were only slightly elevated but were not statistically increased, but considering the apparent inability of promoting agents to increase malignant liver tumor incidences (Becker, 1982), we cannot state whether DCP acts as a promoting agent.

There was a significant increase in the combined incidence of thyroid follicular cell tumors in the high dose female mice but no follicular cell tumors were observed in the low dose female mice. Neither follicular cell adenomas alone nor follicular cell carcinomas alone were significantly increased in the treated groups as compared to the controls. The historical incidence of thyroid follicular cell tumors in female mice is 2/139 (1%) at this laboratory (Appendix F, Table F7). Since deaths occurred earlier in the treated groups than in the controls and all follicular cell tumors occurred in animals sacrificed at the end of the study (control, 1/34; high dose, 5/24), the results of this study may underestimate the real incidence of thyroid tumors. We cannot be certain whether the thyroid lesions were related to the exposure to 1,2-dichloropropane or not.

Neoplastic lesions were not significantly increased in the male rats treated with DCP. In the female rats, the only neoplastic lesions which may have been treatment related were mammary gland adenocarcinomas (control, 1/50, 2%; low dose, 2/50, 4%; high dose, 5/50, 10%). The association between DCP exposure and this increase is strengthened by: 1) mammary gland adenocarcinomas are relatively uncommon neoplasms in female F344/N rats (the historical incidence in this laboratory is 3/150, 2%; and it is 11/895, 1.2% for all laboratories in this program; 2) the incidence of tumors was 4/16 (25%) for the high dose group female rats surviving to the end of the study; 3) lower body weights, if due to reduced food intake, would be expected to decrease the incidence of spontaneous mammary tumors (high dose animal body weights were decreased compared to controls). The relationship between DCP exposure and mammary adenocarcinomas is diminished by: 1) the 250 mg/kg dose level was toxic and may have compromised the responses of female rats' normal metabolic, immune or endocrine systems; 2) there was a decrease in the overall incidence of mammary fibroadenomas in the high dose female rats; 3) the adenocarcinomas were neither metastatic, anaplastic nor highly invasive; in fact, some pathologists have diagnosed these tumors as highly cellular fibroadenomas.

There are no known data which would associate the increase in mammary gland adenocarcinomas for the high dose female rats with the decreased body weight gain. In studies where feed intake or dietary fat intake are restricted with a subsequent decrease in body weight gain, there seems to be an inverse relationship with spontaneous tumor incidence (Wyndner, et al., 1981; Haseman, 1983). Altered endocrine status and elevated fat intake may play a role in mammary carcinogenesis. Prolactin can act as a promoter in breast cancer and prolactin secretion is increased in Sprague-Dawley rats fed high fat diets (Wyndner et al., 1981). Also, N-nitrosomethylurea induced mammary tumors were increased in F344 rats fed diets containing high levels of fat (Wyndner et al, 1981). These findings are consistent with a decrease, rather than an increase, in mammary tumorigenesis in a study like this one where body weight gain is reduced. There was a decrease in the overall incidence of mammary fibroadenomas in the high dose female rats, but not among those females which survived the full term of the study. There is no apparent association between nutritional status and the increase in mammary ade-

nocarcinomas in the high dose female rats, but the high dose toxicity may have affected other mechanisms resulting in the elevated incidence of mammary adenocarcinomas.

The mammary adenocarcinomas found in the female rats were characterized by a well-differentiated glandular pattern often containing cystic spaces filled with eosinophilic proteinaceous material. Cells lining the glands were single to multiple layered usually containing large clear cytoplasmic vacuoles. Nuclei were round to oval, and contained prominent nucleoli and some evidence of nuclear crowding. Mitotic figures were uncommon and evidence of invasion was minimal. Three of the five mammary adenocarcinomas in the high dose females were judged to be of low grade malignancy. There were no metastases or local invasion. While the tumors were cellular with little fibrous stroma, the cells showed orderly arrangement and little atypia. The morphological features are such that some pathologists would diagnose this as a highly cellular variant of a fibroadenoma or as an adenofibroma rather than adenocarcinoma. The biological potential of this morphological entity is not known.

The short chain halogenated hydrocarbons are widely used in agriculture and industry. The toxicity, carcinogenicity, and mutagenicity of the chemicals in this class varies widely (Van Duuren, 1977; Weisburger, 1977; Fishbein, 1979; IARC, 1979; Chu and Milman, 1981). The direct acting carcinogens in this class include the epoxides and the halo ethers; the indirect acting compounds (those requiring metabolic activation) may be metabolically activated to the ultimate carcinogen in tissues such as the liver, stomach, lung, or kidney (Van Duuren, 1977). Epoxide intermediates are demonstrated metabolites of trichloroethylene (epoxy-1,1,2-trichloroethane), allyl chloride (epichlorohydrin and glycialdehyde), and 1,2-dibromo-3-chloropropane (epichlorohydrin and glycialdehyde) (Van Duuren, 1977). Some of the halogenated hydrocarbons, such as 1,2-dibromomethane and 1,2-dichloroethane, are thought to be direct alkylating agents (Chu and Milman, 1981). DCP is reportedly metabolized to 1,2-epoxypropane (Jones and Gibson, 1980). DCP has not been shown to have any direct alkylating activity, while the metabolite 1,2-epoxypropane has been shown to be an alkylating agent (Jones and Gibson, 1980). The role of metabolic activation in DCP toxicity is not clear.

The mutagenic activity of 1,2-dichloropropane is marginal. This compound was tested in strains TA100, TA98, TA1537, and TA1535 of *Salmonella* (Appendix H) in the presence or absence of S9. No clearly positive response was obtained. In the absence of activation, there was a dose-related response in TA100 and in TA1535, with marginally positive responses at the highest doses tested (1 to 2 mg/plate). The potential for impurities to have caused the marginal, mutagenic response at these doses clouds the interpretation of these data. The dose-related response was not observed in TA100 or TA98 in the presence of S9 suggesting that the DCP or the impurity (if present) may be detoxified. These results agree with results reported by Principe et al. (1981) who tested up to 11 mg/plate, and by De Lorenzo et al. (1977) who tested doses between 10 and 50 mg/plate. De Lorenzo also observed a mutagenic response with DCP in strains TA100 and TA98 with S9, but only at these high dose levels. Stolzenberg and Hines (1980) reported no mutagenic activity of DCP up to 1.1 mg/plate and at 11 mg/plate their preparation was completely toxic. These authors also showed a wide variation in the mutagenic response of various halogenated propanes, with 1,2-dichloropropane eliciting one of the least mutagenic responses.

Chromosomal aberration and sister-chromatid exchange data showed that DCP was active in the absence or presence of S9 (Appendix H).

Conclusions: Under the conditions of these 2 year gavage studies, there was *no evidence of carcinogenicity** for male F344/N rats receiving 62 or 125 mg/kg. For female rats there was *equivocal evidence of carcinogenicity* in that 250 mg/kg 1,2-dichloropropane caused a marginally increased incidence of adenocarcinomas in the mammary gland; these borderline malignant lesions occurred concurrent with decreased survival and reduced body weight gain. There was *some evidence of carcinogenicity* for male and female $B6C3F_1$ mice exposed to 1,2-dichloropropane, as indicated by increased incidences of hepatocellular neoplasms, primarily adenomas.

* Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2.

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Ames, B.N.; McCann, J.; Yamasaki, E., Methods for detecting carcinogens and mutagens with the *Samonella*/mammalian-microsome mutagenicity test. Mutat. Res. 31:347-364; 1975.

Armitage, P., Statistical methods in medical research. New York: John Wiley & Sons, Inc.; 1971:362-365.

Aviado, D., Preclinical pharmacology and toxicology of halogenated solvents and propellants. Nat. Inst. Drug Abuse Res. Monograph Series. 15: 164-184; 1977.

Becker, F.F., Morphological classification of mouse liver tumors based on biological characteristics. Cancer Res. 42:3918-3923; 1982.

Berenblum, I., ed., Carcinogenicity testing: a report of the panel on carcinogenicity of the cancer research commission of UICC. Geneva: International Union Against Cancer, Vol. 2; 1969.

Belyaeva, N.; Bonashevskaya, B.; Marshak, T.; Brodskii, V., Investigation of the effect of certain chlorinated hydrocarbons on the composition of the hepatocyte population of the rat liver. Bull. Exp. Biol. 83:396-400; 1977.

Carpenter, C.; Smyth, H.; Pozzani, U., The assay of acute vapor toxicity, and the grading and interpretation of results on 96 chemical compounds. J. Ind. Hyg. Toxicol. 31: 343-346; 1949.

Chu, K.; Milman, H., Review of experimental carcinogenesis by compounds related to vinyl chloride. Environ. Health Perspect. 41:211-220; 1981.

Cox, D., Regression models and life tables. J.R. Stat. Soc. B34; 187-220; 1972.

De Lorenzo, F.; Degl'Innocenti, S.; Ruocco, A.; Silengo, L.; Cortese, R., Mutagenicity of pesticides containing 1,3-dichloropropane. Cancer Res. 37: 1915-1917; 1977.

Drew, R.; Patel, J.; Lin, F., Changes in serum enzymes in rats after inhalation of organic solvents singly and in combination. Toxicol. Appl. Pharmacol. 45:809-819; 1978.

E.G.& G. Mason, Unpublished study conducted at E.G.&G. Mason Research Institute, Rockville, MD in July 1980 with practical-grade 1,2-dichloropropane, Lot No. B7H22 (MCB Reagents, Gibbstown, NJ), S. Hayworth, principal investigator.

Eight peak index of mass spectra. First ed., Vol 1. Aldermaston, Reading, RG7PR, United Kingdom: Mass Spectrometry Data Center; 315.

Evans, H.J., Chromosomal aberrations produced by ionizing radiation. Internat. Rev. Cytology, 13:221-321; 1962.

Farm chemicals handbook, Willoughby, Ohio: Meister Publishing Co., 1977: D220.

Fishbein, L., Potential halogenated industrial carcinogenic and mutagenic chemicals III. Alkane halides, alkanols and ethers. Sci. Total Environ. 11: 223-257; 1979.

Gart, J.; Chu, K.; Tarone, R., Statistical issues in interpretation of chronic bioassay tests for carcinogenicity. J. Natl. Cancer Inst. 62(4):957; 1979.

Goto, K.; Maeda, S.; Kano, Y.; Sugimur, T., Factors involved in differential Giemsa-staining of sister chromatids. Chromosoma 66:351-359; 1978.

Hengler, W.C.; DePass, L.R., Ethyl acrylate: Lifetime dermal carcinogenesis study in C3H/HeJ male mice. Union Carbide Corp., Bushy Run Research Center. Project Report 45-513; 1982.

Heppel, L.; Highman, B.; Peake, E., Toxicology of 1,2-dichloropropane (propylene dichloride). IV. Effects of repeated exposures to a low concentration of the vapor. J. Ind. Hyg. Toxicol. 30: 189-191; 1948.

Hutson, D.; Moss, J.; Pickering, B., The excretion and retention of components of the soil fumigant D-D and their metabolites in the rat. Food Cosmet. Toxicol. 9: 677-680; 1971.

IARC, IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Some halogenated hydrocarbons, Vol. 20. Lyon, France: International Agency for Research on Cancer, 1979; 515-531.

Jones, A.; Gibson, J., 1,2-Dichloropropane: metabolism and fate in the rat. Xenobiotica 10(11): 835-846; 1980.

Kaplan, E.; Meier, P., Nonparametric estimation of incomplete observations. J. Amer. Stat. Assoc. 53:457-481; 1958.

Kirk-Othmer encyclopedia of chemical technology. New York: John Wiley & Sons, Inc.; 13: 466; 1981.

Larcan, A.; Lambert, H.; Laprevote, M.C.; Gustin, B., Acute poisoning induced by dichloropropane. Acta Pharmacol. Toxicol. (suppl.) 41:330; 1977.

Lawrence, W.H.; Bass, G.E.; Purcell, W.P.; Autian, J., Use of mathematical models in the study of structure-toxicity relationships of dental compounds. J. Dental Res. 51(part 2):526-535; 1972.

V. REFERENCES

Linhart, M.; Cooper, J.; Martin, R.; Page, N.; Peters, J., Carcinogenesis bioassay data system. Comp. Biomed. Res. 7:230-248; 1974.

Litton Bionetics, Inc. Mutagenicity evaluation of TD 79-278 in the mouse lymphoma forward mutation assay., LBI Project No. 20989, Genetics assay No. 4816, Kensington, MD, October 1980.

Mantel, N.; Haenszel, W., Statistical aspects of the analysis of data from retrospective studies of disease. J. Natl. Cancer Inst. 22:719-748; 1959.

Maronpot, R.R.; Boorman, G.A., Interpretation of rodent hepatocellular proliferative alterations and hepatocellular tumors in chemical safety assessment. Toxicol. Pathol. 10(2):71-80; 1982.

Merck Index, 9th ed., Rahway, New Jersey: Merck and Co., 1976; 7649.

Miller, R.R.; Ayres, J.A.; Rampy, L.W.; McKenna, M.J., Metabolism of acrylate esters in rat tissue homogenates. Fund. Appl. Toxicol. 1:410-414; 1981.

Miller, R.R.; Young, J.A.; Ayres, J.A.; Park, C.N., Ethyl acrylate: 27-month vapor inhalation study in rats. Dow Chemical Co. R and D Report HET-K-10118-(4G); 1982.

NCI, National Cancer Institute, Bioassay of dibromochloropropane (gavage study) for possible carcinogenicity, NCI TR 28, Department of Health, Education, and Welfare, Bethesda, Maryland, 1978a.

NCI, National Cancer Institute, Bioassay of 1,2-dibromoethane for potential carcinogenicity (gavage study), NCI TR 86, Department of Health, Education, and Welfare, Bethesda, Maryland, 1978b.

NCI, National Cancer Institute, Bioassay of 1,2-dichloroethane for possible carcinogenicity, NCI TR 55, Department of Health, Education, and Welfare, Bethesda, Maryland, 1978c.

Nemec, J.W.; Bauer, W. Jr., Acrylic acid & derivatives. In: Kirk-Othmer Encyclopedia of Chemical Technology 3rd Edition. Vol. 1, John Wiley & Sons, New York, pp 330-354.

NTP, National Toxicology Program, Carcinogenesis bioassay of 1,2-dibromoethane (inhalation study), NTP TR 210, Department of Health and Human Services, Research Triangle Park, North Carolina, 1982a.

NTP, National Toxicology Program, Carcinogenesis bioassay of 1,2-dibromo-3-chloropropane (inhalation study), NTP TR 206, Department of Health and Human Services, Research Triangle Park, North Carolina, 1982b.

Opdyke, D.L.J., Monographs on Fragrance Raw Materials. Ethyl acrylate. Food Cosmet. Toxicol. 13 Suppl.: 801-802; 1975.

Perry P.; Wolff, S., New Giemsa method for the differential staining of sister chromatids. Nature 251:156-158; 1974.

Peto, R.; Pike, M.; Day, N.; Gray, R.; Lee, R.; Parish, S.; Peto, J.; Richard, S.; Wahrendorf, J., Guidelines for simple, sensitive, significant tests for carcinogenic effects in long-term animal experiments. International Agency for Research Against Cancer. Monographs on the long-term and short-term screening assays for carcinogens: A critical appraisal. Geneva: World Health Organization. Supplement 2; 1980:311.

Plaa, G., Toxic responses to the liver. In: Cassarett and Doull's toxicology, ed. Doull, J.; Klaassen, C.; Amdur, M., 1980; 206-231.

Rosenthal, I. and J. M. Smith. 1982. Summary of latest findings from studies with ethyl acrylate. Letter to Dr. Donald Millar, Director of National Institute for Occupational Safety and Health from Industry Acrylate Testing Group. Sept. 24, 1982.

Sadtler Research Laboratories. Sadtler standard spectra. Philadelphia: Sadtler Research Laboratories; IR No. 3280; NMR No. 10492.

Sandmeyer, E.E.; Kirwin, C.J., Jr., Esters. In: Patty's Industrial Hygiene & Toxicology, 3rd Revised Edition, Volume 2A, John Wiley & Sons, New York, p. 2296.

Sidorenko, G.; Tsulaya, V.; Korenevskaya, E.; Bonashevka, T., Methodological approaches to the study of atmospheric pollutants as illustrated by chlorinated hydrocarbons. Environ. Health Perspec. 13:111-116; 1976.

Silver, E.H.; Murphy, S.D., Potentiation of acrylate ester toxicity by prior treatment with the carboxylesterase inhibitor triorthotolyl phosphate (TOTP). Toxicol. Appl. Pharmacol. 57:208-219; 1981.

Smyth, H.,; Carpenter, C.; Weil, C.; Pozzani, U.; Striegel, J.; Nycum, J., Range-finding toxicity data: List VII. Am. Ind. Hyg. Assoc. J. 30: 470; 1969.

Spencer, E., Guide to the chemicals used in crop protection. Sixth ed. London, Ontario: Research Institute of Western Ontario. Publication No. 1093. 1973: 436.

Stolzenberg,S.; Hine, C.; Mutagenicity of 2- and 3-carbon halogenated compounds in the *Salmonella*/mammalian-microsome test. Environ. Mutagen. 2:59-66; 1980.

V. REFERENCES

Tarone, R., Tests for trend in life table analysis. Biometrika. 62:679-682; 1975.

Terasima, T.; Tolmach, L., Changes in X-ray sensitivity of HeLa cells during the division cycle. Nature 190:1210-1211; 1961.

Treon, J.R.; Sigmon, H.; Wright, H.; Kitzmiller, K.V., The toxicity of methyl and ethyl acrylate. J. Ind. Hyg. Toxicol. 31:317-326; 1949.

Tucker, M.J., The effect of long-term food restriction on tumours in rodents. Int. J. Cancer 23:803-807, 1979.

USCFR, 29:1910.93; 1974.

USITC, United States International Trade Commission, Synthetic Organic Chemicals, United States Production and Sales 1980. USITC Publication 1189, U.S. Government Printing Office, Washington, D.C., 1981.

Van Duuren, B., Chemical structure, reactivity, and carcinogenicity of halohydrocarbons. Environ. Health Perspec. 21:17-23; 1977.

Ward, J.; Goodman, D.; Griesemer, R.; Hardisty, J.; Schueler, R.; Squire, R.; Strandberg, J., Quality assurance for pathology in rodent carcinogenesis tests. J. Environ. Path. Toxicol. 2:371-378; 1978.

Weast, R., Ed., Handbook of chemistry and physics. 57th ed. Cleveland, Ohio: Chemical Rubber Company Press. 1976-1977: C447.

Weisburger, E., Carcinogenicity studies on halogenated hydrocarbons. Environ. Health Perspec. 21:7-16; 1977.

Wyndner, E.L.; McCoy, G.D.; Reddy, B.S.; Cohen, L.; Hill, P.; Spingarn, N.E.; Weisburger, J.H., Nutrition and metabolic epidemiology of cancers of the oral cavity, esophagus, colon, breast, prostate, and stomach. In: Nutrition and Cancer: Etiology and Treatment, edited by G.R. Newell and N.M. Ellison, Raven Press, New York, 1981.

Yahagi, T.; Degawa, M.; Seino, Y.; Matsushima, T.; Nagao, M.; Sugimura, T.; Hashimoto, Y., Mutagenicity of carcinogenic azo dyes and their derivatives. Cancer Lett. 1:91-96; 1975.

APPENDIX A

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

TABLE A1.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	2 (4%)	3 (6%)	1 (2%)
SQUAMOUS CELL CARCINOMA	2 (4%)	2 (4%)	
ADNEXAL ADENOMA		1 (2%)	
KERATOACANTHOMA	2 (4%)	1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
SARCOMA, NOS			1 (2%)
FIBROMA	6 (12%)	6 (12%)	6 (12%)
FIBROSARCOMA	1 (2%)	1 (2%)	
LIPOMA			2 (4%)
#THYROID CAPSULE	(49)	(49)	(50)
FIBROUS HISTIOCYTOMA, MALIGNANT	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(50)
UNDIFFERENTIATED CARCINOMA METAS			1 (2%)
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)		1 (2%)
SEBACEOUS ADENOCARCINOMA, METAST		1 (2%)	
FIBROSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
MYELOMONOCYTIC LEUKEMIA	7 (14%)	6 (12%)	6 (12%)
MONOCYTIC LEUKEMIA	1 (2%)		

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#LYMPH NODE	(48)	(49)	(48)
SQUAMOUS CELL CARCINOMA, METASTA		1 (2%)	
#MANDIBULAR L. NODE	(48)	(49)	(48)
FIBROSARCOMA, METASTATIC		1 (2%)	
#LIVER	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(49)	(50)
HEMANGIOSARCOMA			1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(50)	(50)
ADENOCARCINOMA, NOS			1 (2%)
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	1 (2%)	1 (2%)	2 (4%)
HEPATOCELLULAR CARCINOMA	2 (4%)	2 (4%)	
PHEOCHROMOCYTOMA, METASTATIC			1 (2%)
#PANCREAS	(48)	(50)	(50)
ACINAR-CELL ADENOMA	1 (2%)	1 (2%)	1 (2%)
#FORESTOMACH	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
#COLON	(49)	(49)	(49)
ADENOMATOUS POLYP, NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
LIPOMA		1 (2%)	
#URINARY BLADDER	(49)	(47)	(49)
TRANSITIONAL-CELL PAPILLOMA			1 (2%)

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(48)	(47)
CARCINOMA,NOS	3 (6%)	3 (6%)	3 (6%)
ADENOMA, NOS	19 (38%)	12 (25%)	15 (32%)
#ADRENAL	(50)	(49)	(50)
CORTICAL ADENOMA	3 (6%)	2 (4%)	
PHEOCHROMOCYTOMA	11 (22%)	5 (10%)	5 (10%)
PHEOCHROMOCYTOMA, MALIGNANT			2 (4%)
GANGLIONEUROMA	1 (2%)		
#THYROID	(49)	(49)	(50)
FOLLICULAR-CELL CARCINOMA	1 (2%)		
C-CELL ADENOMA	1 (2%)	4 (8%)	
C-CELL CARCINOMA	1 (2%)		1 (2%)
#THYROID CAPSULE	(49)	(49)	(50)
SARCOMA, NOS	1 (2%)		
#PANCREATIC ISLETS	(48)	(50)	(50)
ISLET-CELL ADENOMA	4 (8%)	1 (2%)	3 (6%)
ISLET-CELL CARCINOMA			3 (6%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA		1 (2%)	2 (4%)
*PREPUCE	(50)	(50)	(50)
UNDIFFERENTIATED CARCINOMA			1 (2%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)	2 (4%)	4 (8%)
SQUAMOUS CELL CARCINOMA	1 (2%)		
ADENOMA, NOS			1 (2%)
#TESTIS	(50)	(47)	(50)
INTERSTITIAL-CELL TUMOR	45 (90%)	46 (98%)	46 (92%)
*SCROTUM	(50)	(50)	(50)
FIBROSARCOMA	1 (2%)		

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#CEREBRUM	(50)	(50)	(50)
ASTROCYTOMA			1 (2%)
#CEREBELLUM	(50)	(50)	(50)
ASTROCYTOMA	1 (2%)		
SPECIAL SENSE ORGANS			
*EXTERNAL EAR	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
*EAR CANAL	(50)	(50)	(50)
SEBACEOUS ADENOCARCINOMA		2 (4%)	
*ZYMBAL'S GLAND	(50)	(50)	(50)
SEBACEOUS ADENOCARCINOMA			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*BODY CAVITIES	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)		1 (2%)
*PERITONEUM	(50)	(50)	(50)
MESOTHELIOMA, NOS		1 (2%)	
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	2 (4%)	2 (4%)	2 (4%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
FIBROSARCOMA		1 (2%)	
LEIOMYOSARCOMA		1 (2%)	
TAIL			
FIBROSARCOMA	1		

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
AXILLA			
FIBROMA			1
LEG			
SARCOMA, NOS	1		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	5	3
MORIBUND SACRIFICE	6	4	7
SCHEDULED SACRIFICE	5		
TERMINAL SACRIFICE	34	41	40
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	49	48	49
TOTAL PRIMARY TUMORS	130	111	115
TOTAL ANIMALS WITH BENIGN TUMORS	48	47	48
TOTAL BENIGN TUMORS	98	85	85
TOTAL ANIMALS WITH MALIGNANT TUMORS	25	18	21
TOTAL MALIGNANT TUMORS	28	22	25
TOTAL ANIMALS WITH SECONDARY TUMORS#		3	3
TOTAL SECONDARY TUMORS		4	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	4	3	4
TOTAL UNCERTAIN TUMORS	4	4	5
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE A2.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
KERATOACANTHOMA	1 (2%)		1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
FIBROMA		2 (4%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(49)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)		
C-CELL CARCINOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
MALIG.LYMPHOMA, UNDIFFER-TYPE			1 (2%)
MYELOMONOCYTIC LEUKEMIA	9 (18%)	11 (22%)	5 (10%)
#BONE MARROW	(49)	(50)	(47)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	1 (2%)		
#STOMACH	(50)	(50)	(48)
SQUAMOUS CELL PAPILLOMA			1 (2%)
#FORESTOMACH	(50)	(50)	(48)
SQUAMOUS CELL PAPILLOMA			1 (2%)
URINARY SYSTEM			
NONE			

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(50)	(46)
CARCINOMA,NOS	3 (6%)	2 (4%)	
ADENOMA, NOS	16 (33%)	26 (52%)	10 (22%)
#ADRENAL	(49)	(50)	(50)
CORTICAL ADENOMA	5 (10%)	2 (4%)	4 (8%)
PHEOCHROMOCYTOMA	2 (4%)	3 (6%)	1 (2%)
GANGLIONEUROMA	1 (2%)		
#THYROID	(50)	(49)	(44)
FOLLICULAR-CELL CARCINOMA		2 (4%)	
C-CELL ADENOMA			1 (2%)
C-CELL CARCINOMA	1 (2%)	3 (6%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)	2 (4%)	5 (10%)
FIBROADENOMA	15 (30%)	20 (40%)	7 (14%)
*CLITORAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)		
#UTERUS	(50)	(49)	(50)
ADENOCARCINOMA, NOS			1 (2%)
LEIOMYOMA		2 (4%)	
LEIOMYOSARCOMA		1 (2%)	
ENDOMETRIAL STROMAL POLYP	10 (20%)	17 (35%)	11 (22%)
ENDOMETRIAL STROMAL SARCOMA	1 (2%)	1 (2%)	

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#OVARY	(49)	(50)	(50)
GRANULOSA-CELL TUMOR	1 (2%)		
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
ASTROCYTOMA			1 (2%)
#PONS	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV	1 (2%)		
SPECIAL SENSE ORGANS			
*EXTERNAL EAR	(50)	(50)	(50)
FIBROSARCOMA		1 (2%)	
*ZYMBAL'S GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	7	4	19
MORIBUND SACRIFICE	7	4	15
SCHEDULED SACRIFICE	5		
TERMINAL SACRIFICE	31	42	16
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	42	46	30
TOTAL PRIMARY TUMORS	72	95	51
TOTAL ANIMALS WITH BENIGN TUMORS	36	39	26
TOTAL BENIGN TUMORS	52	72	37
TOTAL ANIMALS WITH MALIGNANT TUMORS	16	21	13
TOTAL MALIGNANT TUMORS	18	23	14
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	1	
TOTAL SECONDARY TUMORS	1	1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2		
TOTAL UNCERTAIN TUMORS	2		
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

VEHICLE CONTROL

ANIMAL NUMBER	0012	0023	0034	0045	0056	0067	0078	0089	0090	0101	0112	0131	0142	0153	0165	0177	0188	0191	0201	0212	0225	0234	0245
WEEKS ON STUDY	107	074	103	107	071	082	107	107	105	088	107	092	107	107	107	095	107	107	107	107	081	105	107
INTEGUMENTARY SYSTEM																							
SKIN	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																							
SQUAMOUS CELL CARCINOMA																					X		
KERATOACANTHOMA																							
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA		X																					
FIBROMA						X										X							
FIBROSARCOMA				X																			
RESPIRATORY SYSTEM																							
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																							
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																							
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
THYMUS	-	+	+	+	+	-	+	+	+	-	-	-	+	-	-	+	+	+	+	-	+	+	+
CIRCULATORY SYSTEM																							
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																							
SALIVARY GLAND	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																							
HEPATOCELLULAR CARCINOMA																X							
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ACINAR-CELL ADENOMA																	X						
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																							
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																							
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																							
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS			X		X							X											
ADENOMA, NOS				X			X	X	X		X				X	X		X		X			X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																							X
PHEOCHROMOCYTOMA	X				X			X						X			X	X					
GANGLIONEUROMA								X															
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA														X									
C-CELL ADENOMA																			X				
C-CELL CARCINOMA																	X						
SARCOMA, NOS																	X						
FIBROUS HISTIOCYTOMA, MALIGNANT																							
PARATHYROID	+	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ISLET-CELL ADENOMA																	X						
REPRODUCTIVE SYSTEM																							
MAMMARY GLAND	N	N	N	N	+	N	N	+	N	+	N	+	N	N	N	+	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X			X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS																							
SQUAMOUS CELL CARCINOMA				X																			
NERVOUS SYSTEM																							
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																							
SPECIAL SENSE ORGANS																							
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+
SQUAMOUS CELL CARCINOMA																							X
BODY CAVITIES																							
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																X							
BODY CAVITIES	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS																							
ALL OTHER SYSTEMS																							
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MYELOMONOCYTIC LEUKEMIA							X						X	X					X				
MONOCYTIC LEUKEMIA										X													
TAIL																							
FIBROSARCOMA																	X						
LEG NOS																							
SARCOMA, NOS																							
SCROTUM NOS																							
FIBROSARCOMA															X								

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

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

ANIMAL NUMBER	026	027	028	029	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	108	064	107	104	108	101	108	108	108	108	105	108	108	108	108	108	103	104	108	108	108	108	108	108	
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
SQUAMOUS CELL PAPILLOMA					X																				2
SQUAMOUS CELL CARCINOMA			X					X								X			X						2
KERATOACANTHOMA																									2
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
SQUAMOUS CELL CARCINOMA																									1
FIBROMA					X					X							X						X		6
FIBROSARCOMA																									1
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA													X						X						2
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	49
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYMUS	+	+	-	+	-	-	+	+	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	35
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	49
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE									X																1
HEPATOCELLULAR CARCINOMA																		X							2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	■			48
ACINAR-CELL ADENOMA																									1
ESOPHAGUS	+	+	+	-	-	+	+	-	+	+	+	+	+	-	+	+	+	+	-	-	+	+	+	+	42
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL PAPILLOMA		X																							1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS																									3
ADENOMA, NOS					X								X	X	X			X	X		X	X			19
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA												X										X			3
PHEOCHROMOCYTOMA	X								X			X			X								X		11
GANGLIONEUROMA																									1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	49
FOLLICULAR-CELL CARCINOMA						X																			1
C-CELL ADENOMA																									1
C-CELL CARCINOMA																									1
SARCOMA, NOS																									1
FIBROUS HISTIOCYTOMA, MALIGNANT																									1
PARATHYROID	+	+	-	-	-	-	-	-	-	-	+	-	-	-	+	+	-	+	-	-	-	-	-	+	12
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	48
ISLET-CELL ADENOMA	X								X									X							4
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	+	N	N	+	N	N	N	50*
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	45
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
CARCINOMA,NOS										X															1
SQUAMOUS CELL CARCINOMA																									1
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	■	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA		X																							1
SPECIAL SENSE ORGANS																									
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA																									1
BODY CAVITIES																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
MESOTHELIOMA, NOS		X																							2
BODY CAVITIES	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MESOTHELIOMA, NOS						X																			1
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	H	N	N	N	N	N	N	N	N	N	M	N	N	N	N	N	M	N	N	N	N	50*
MYELOMONOCYTIC LEUKEMIA							X													X			X		7
MONOCYTIC LEUKEMIA																									1
TAIL																									
FIBROSARCOMA																									1
LEG NOS																									
SARCOMA, NOS				X																					1
SCROTUM NOS																									
FIBROSARCOMA																									1

* ANIMALS NECROPSIED

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	101	101	101	101	101	101	101	101	095	101	101	101	101	101	101	091	101	101	077	101	101	101	101	101	101
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA									X		X														
SQUAMOUS CELL CARCINOMA																									
ADNEXAL ADENOMA																									
KERATOACANTHOMA																								X	
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+
FIBROMA		X				X		X						X											X
FIBROSARCOMA							X																		
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SEBACEOUS ADENOCARCINOMA, METASTA									X																
FIBROSARCOMA, METASTATIC							X																		
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																									
FIBROSARCOMA, METASTATIC							X																		
THYMUS	+	+	+	+	+	-	-	+	-	+	+	+	+	+	+	-	-	+	+	+	+	+	+	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
HEPATOCELLULAR CARCINOMA														X											
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ACINAR-CELL ADENOMA																									
ESOPHAGUS	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMATOUS POLYP, NOS																	X								
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIPOMA				X																					
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+
CARCINOMA,NOS											X														
ADENOMA, NOS			X	X	X		X	X						X										X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA								X																	
PHEOCHROMOCYTOMA											X														
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA							X																X		
PARATHYROID	-	-	+	+	+	-	-	-	+	-	-	-	-	-	-	+	-	-	+	+	+	+	+	-	-
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	+	N	N	N	N	N	N	N	+	N	N	N	N	N	N	+	N	N	N	N	N	N	+
FIBROADENOMA																		X							
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS														X											
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
EAR	N	N	N	N	N	N	N	N	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SEBACEOUS ADENOCARCINOMA									X	X															
BODY CAVITIES																									
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+
MESOTHELIOMA, NOS					X																				
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROSARCOMA																	X								
LEIOMYOSARCOMA																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
MYELOMONOCYTIC LEUKEMIA																X			X					X	

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

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

ANIMAL NUMBER	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	TOTAL
WEEKS ON STUDY	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	1 0 5	0 4 0	0 9 5	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	0 9 3	1 0 7	1 0 7	1 0 7	1 0 7	1 0 7	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	50
SQUAMOUS CELL PAPILLOMA								X																		3
SQUAMOUS CELL CARCINOMA			X			X																				2
ADNEXAL ADENOMA																				X						1
KERATOACANTHOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	50
FIBROMA														X												6
FIBROSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SEBACEOUS ADENOCARCINOMA, METASTA																										1
FIBROSARCOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	49
SQUAMOUS CELL CARCINOMA, METASTAT					X																					1
FIBROSARCOMA, METASTATIC																										1
THYMUS	+	+	-	-	+	-	-	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	36
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																							X			1
HEPATOCELLULAR CARCINOMA											X															2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE									X																	1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ACINAR-CELL ADENOMA														X												1
ESOPHAGUS	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	-	+	+	-	+	+	+	42
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMATOUS POLYP, NOS																										1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIPOMA																										1
URINARY BLADDER	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	47
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CARCINOMA,NOS																			X			X				3
ADENOMA, NOS				X									X								X		X		X	12
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CORTICAL ADENOMA						X																				2
PHEOCHROMOCYTOMA			X				X													X			X			5
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-CELL ADENOMA														X				X								4
PARATHYROID	-	-	-	+	+	-	+	-	-	+	-	-	-	-	-	+	-	+	-	+	-	+	-	-	+	19
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA				X																						1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	+	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	50
FIBROADENOMA																										1
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	47
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X		X	X	X	X	X		X	X	X		X	X	X	X	X	46
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
CARCINOMA,NOS														X												2
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
SEBACEOUS ADENOCARCINOMA																										2
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MESOTHELIOMA, NOS																			X							1
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	N	+	+	+	+	50
MESOTHELIOMA, NOS																			X							2
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
FIBROSARCOMA																										1
LEIOMYOSARCOMA									X																	1
MALIG.LYMPHOMA, *HISTIOCYTIC TYPE*										X																1
MYELOMONOCYTIC LEUKEMIA												X										X			X	6

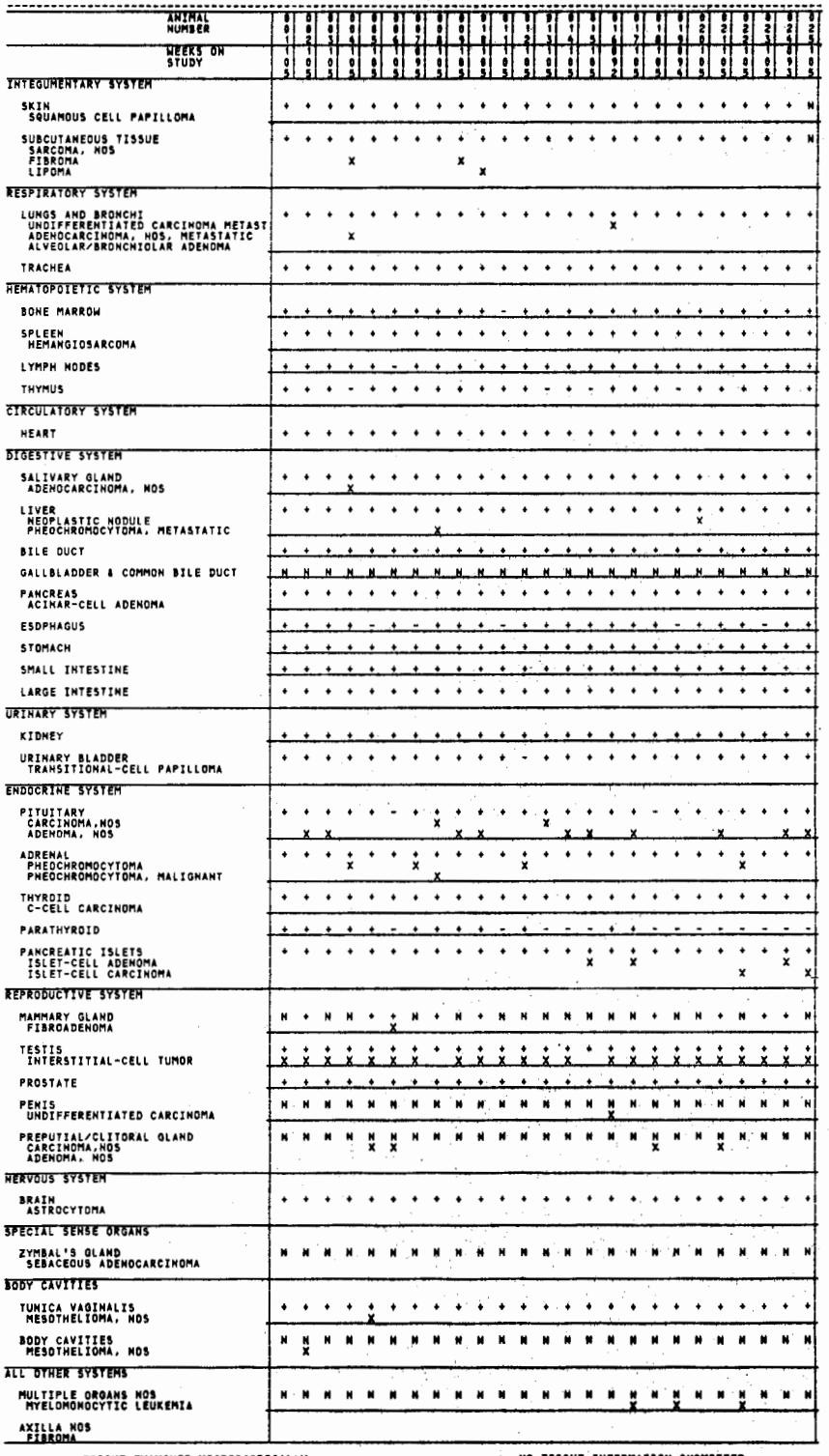
* ANIMALS NECROPSIED

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

HIGH DOSE



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

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

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50M
SQUAMOUS CELL PAPILLOMA	1
SUBCUTANEOUS TISSUE	50M
SARCOMA, NOS	1
FIBROMA	6
LIPOMA	2
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	50
UNDIFFERENTIATED CARCINOMA METAST	1
ADENOCARCINOMA, NOS, METASTATIC	1
ALVEOLAR/BRONCHIOLAR ADENOMA	1
TRACHEA	50
HEMATOPOIETIC SYSTEM	
BONE MARROW	48
SPLEEN	50
HEMANGIOSARCOMA	1
LYMPH NODES	48
THYMUS	40
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	50
ADENOCARCINOMA, NOS	1
LIVER	50
NEOPLASTIC NODULE	2
PHEOCHROMOCYTOMA, METASTATIC	1
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	50
ACINAR-CELL ADENOMA	1
ESOPHAGUS	46
STOMACH	50
SMALL INTESTINE	50
LARGE INTESTINE	49
URINARY SYSTEM	
KIDNEY	50
URINARY BLADDER	49
TRANSITIONAL-CELL PAPILLOMA	1
ENDOCRINE SYSTEM	
PITUITARY	47
CARCINOMA,NOS	3
ADENOMA, NOS	15
ADRENAL	50
PHEOCHROMOCYTOMA	5
PHEOCHROMOCYTOMA, MALIGNANT	2
THYROID	50
C-CELL CARCINOMA	1
PARATHYROID	19
PANCREATIC ISLETS	50
ISLET-CELL ADENOMA	3
ISLET-CELL CARCINOMA	3
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
FIBROADENOMA	2
TESTIS	50
INTERSTITIAL-CELL TUMOR	46
PROSTATE	49
PENIS	50M
UNDIFFERENTIATED CARCINOMA	1
PREPUTIAL/CLITORAL GLAND	50M
CARCINOMA,NOS	4
ADENOMA, NOS	1
NERVOUS SYSTEM	
BRAIN	50
ASTROCYTOMA	1
SPECIAL SENSE ORGANS	
ZYMBAL'S GLAND	50M
SEBACEOUS ADENOCARCINOMA	1
BODY CAVITIES	
TUNICA VAGINALIS	50M
MESOTHELIOMA, NOS	2
BODY CAVITIES	50M
MESOTHELIOMA, NOS	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
MYELOMONOCYTIC LEUKEMIA	6
AXILLA NOS	1
FIBROMA	

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

VEHICLE CONTROL

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025	0026	0027	0028	0029	0030	0031	0032	0033	0034	0035
WEEKS ON STUDY	073	107	107	090	095	097	105	115	107	107	071	107	107	093	107	095	064	085	097	071	107	107	107	107	095
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
KERATOACANTHOMA		X																							
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	-	-	-	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	●	+	+	+	+	●	+	+	+	+	●	+	+
NEOPLASTIC NODULE														X											
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS	X	X				X						X		X			X		X	X			X		
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA		X																		X	X				
PHEOCHROMOCYTOMA																									
GANGLIONEUROMA																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA																			X						
PARATHYROID	-	-	+	-	-	-	-	+	-	-	+	-	-	+	-	+	-	+	+	-	-	+	-	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	N	N	+	+	N	+	+	N	+	+	+	N	+	N	+	+	N	+	N	N	N	N
ADENOCARCINOMA, NOS		X																							
FIBROADENOMA		X	X				X		X	X			X		X		X		X	X					
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS		X																							
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP			X														X		X			X	X	X	X
ENDOMETRIAL STROMAL SARCOMA																								X	
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, INVASIVE																									
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS					X	X						X					X		X				X		
MYELOMONOCYTIC LEUKEMIA																									

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

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

ANIMAL NUMBER	0 2 6 4 1 0 7	0 2 7 1 1 0 7	0 2 8 1 1 0 7	0 2 9 1 1 0 7	0 3 0 1 1 0 7	0 3 1 1 1 0 7	0 3 2 0 0 8 5	0 3 3 0 0 9 2	0 3 6 1 1 0 7	0 3 5 1 1 0 7	0 3 6 1 1 0 5	0 3 7 1 1 0 1	0 3 8 1 1 0 2	0 3 9 0 0 8 3	0 4 0 1 1 0 7	0 4 1 1 1 0 7	0 4 2 0 0 7 5	0 4 3 1 1 0 7	0 4 4 1 1 0 4	0 4 5 1 1 0 8	0 4 6 1 1 0 9	0 4 7 1 1 0 7	0 4 8 1 1 0 7	0 4 9 1 1 0 7	0 5 0 1 1 0 7	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	50M
KERATOACANTHOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA									X													X				2
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	-	+	+	+	41
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	47
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
CARCINOMA, NOS					X										X									X		3
ADENOMA, NOS	X			X							X							X				X	X		X	16
ADRENAL	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CORTICAL ADENOMA			X			X																				5
PHEOCHROMOCYTOMA													X	X												2
GANGLIONEUROMA														X												1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL CARCINOMA																										1
PARATHYROID	-	-	-	+	-	-	-	+	-	-	+	+	-	-	-	+	-	-	-	+	-	~	+	+	+	18
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	+	+	N	+	+	+	+	N	+	+	N	+	+	N	N	N	+	+	+	+	+	+	50M
ADENOCARCINOMA, NOS																										1
FIBROADENOMA				X									X									X	X	X		15
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
CARCINOMA, NOS																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP	X				X								X													10
ENDOMETRIAL STROMAL SARCOMA																										1
OVARY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GRANULOSA-CELL TUMOR																							X			1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA, INVASIVE							X																			1
SPECIAL SENSE ORGANS																										
ZYMBAL'S GLAND	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL CARCINOMA							X																			1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIGNANT LYMPHOMA, NOS																		X								1
MYELOMONOCYTIC LEUKEMIA								X				X	X													9

M ANIMALS NECROPSIED

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

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

LOW DOSE

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0110	0111	0112	0113	0114	0115	0116	0117	0118	0119	0120	0121	0122	0123	0124	0125
WEEKS ON STUDY	106	106	106	106	095	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	096	106	106	106	106
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA								X														X			
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	■	+	+	+	■	+	+
C-CELL CARCINOMA, METASTATIC									X																
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	■	+	■	■	■	+	+	+	+	+	+	+	+	+	+	+	■	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	-	+	+	+	+	-	+	+	+	-	-	+	+	-	-	-	+	-	-	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS	X		X		X		X	X	X	X		X	X			X			X	X		X	X	X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA			X	X																X					
THYROID	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA															X								X		
C-CELL CARCINOMA									X																
PARATHYROID	-	+	-	-	+	+	-	-	+	-	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	N	N	+	+	N	+	+	+	+	+	N	+	+	+	N	+	+	N	+	+	N
ADENOCARCINOMA, NOS																							X		
FIBROADENOMA	X						X	X		X		X		X						X			X		
UTERUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOMA															X							X			
LEIOMYOSARCOMA																X									
ENDOMETRIAL STROMAL POLYP				X		X			X					X	X			X						X	X
ENDOMETRIAL STROMAL SARCOMA																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROSARCOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	M	N	N	M	N	M	N	N	N	N	N	N	M	M	N	N	N	N	M	N	N	M	N
MYELOMONOCYTIC LEUKEMIA			X			X		X							X						X				

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

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

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SUBCUTANEOUS TISSUE FIBROMA	50* 2
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI C-CELL CARCINOMA, METASTATIC	50 1
TRACHEA	50
HEMATOPOIETIC SYSTEM	
BONE MARROW	50
SPLEEN	50
LYMPH NODES	50
THYMUS	34
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	50
LIVER	50
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50*
PANCREAS	50
ESOPHAGUS	48
STOMACH	50
SMALL *INTESTINE*	50
LARGE INTESTINE	50
URINARY SYSTEM	
KIDNEY	50
URINARY BLADDER	50
ENDOCRINE SYSTEM	
PITUITARY CARCINOMA,NOS 2 ADENOMA, NOS 26	50
ADRENAL CORTICAL ADENOMA 2 *PHEOCHROMOCYTOMA* 3	50
THYROID FOLLICULAR-CELL CARCINOMA 2 C-CELL CARCINOMA 3	49
PARATHYROID	12
REPRODUCTIVE SYSTEM	
MAMMARY GLAND ADENOCARCINOMA, NOS 2 FIBROADENOMA 20	50*
UTERUS LEIOMYOMA 2 LEIOMYOSARCOMA 1 ENDOMETRIAL STROMAL POLYP 17 ENDOMETRIAL STROMAL SARCOMA 1	49
OVARY	50
NERVOUS SYSTEM	
BRAIN	50
SPECIAL SENSE ORGANS	
EAR FIBROSARCOMA 1	50*
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS MYELOMONOCYTIC LEUKEMIA 11	50*

* ANIMALS NECROPSIED

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	061	092	086	073	105	081	086	094	105	094	090	085	105	094	094	105	093	094	079	072	096	115	105	066	094
INTEGUMENTARY SYSTEM																									
SKIN KERATOACANTHOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW MALIG.LYMPHOMA, HISTIOCYTIC TYPE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	-	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH SQUAMOUS CELL PAPILLOMA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	●	+	+	+	+	+	+	+	+	+	+	+	●	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS	+	-	+	+	+	+	+ X	+	+	+	+	-	+	+	+	+	+ X	+	+	+	+ X	+	+ X	+	+
ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID C-CELL ADENOMA	+	+	+	+	+	-	+	+	+	-	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	+	-	-	-	-	+	-	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND ADENOCARCINOMA, NOS FIBROADENOMA	N	+ X	N	N	+	N	N	+	N	N	+	N	+ X	N	N	N	N	N	N	+	+	+ X X	+ X	N	N
UTERUS ADENOCARCINOMA, NOS ENDOMETRIAL STROMAL POLYP	+	+	+	+	+ X	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+ X	+ X	+	+	+	+	+
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN ASTROCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS MALIG.LYMPHOMA, UNDIFFER-TYPE MYELOMONOCYTIC LEUKEMIA	N X	N	N	N	N X	N	N	N	N X	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N

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

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

ANIMAL NUMBER / WEEKS ON STUDY	0216 071 6	0217 101 5	0218 061 7	0219 091 5	0301 091 5	0311 101 5	0312 101 5	0313 101 5	0314 091 3	0315 101 5	0316 101 4	0317 091 4	0318 071 5	0319 091 5	0320 101 5	0321 091 5	0322 101 5	0323 091 4	0324 091 5	0325 091 4	0326 091 6	0327 090 8	0328 101 5	0329 091 8	0330 101 5	0331 091 5	0332 101 5	0333 091 4	0334 101 5	0335 091 4	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM																															
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	50
KERATOACANTHOMA		X																													1
RESPIRATORY SYSTEM																															
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																															
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	47
MALIG.LYMPHOMA, HISTIOCYTIC TYPE						X																									1
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYMUS	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	~	+	-	+	-	-	+	-	-	+	-	-	+	-	-	38
CIRCULATORY SYSTEM																															
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																															
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-				46
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ESOPHAGUS	+	+	+	+	+	-	+	+	+	-	+	+	-	+	+	-	+	-	+	-	+	~	+	+	+	-	+	+			41
STOMACH	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SQUAMOUS CELL PAPILLOMA																		X				X									2
SMALL INTESTINE	+	+	+	+	■	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+				48
URINARY SYSTEM																															
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																															
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	46
ADENOMA, NOS					X	X	X										X							X		X					10
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA								X												X					X					X	4
PHEOCHROMOCYTOMA						X																									1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	~	+	+	-	+	+	+	+	+	+	+	+	+	44
C-CELL ADENOMA																															1
PARATHYROID	-	+	-	+	-	-	-	~	-	-	+	-	+	-	-	-	~	-	-	-	-	+	+	-	-	~					9
REPRODUCTIVE SYSTEM																															
MAMMARY GLAND	+	+	N	N	N	+	+	+	N	N	N	+	N	N	+	N	+	N	+	N	N	N	+	+	N	N					50
ADENOCARCINOMA, NOS	X					X	X																X			X					5
FIBROADENOMA															X				X							X					7
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				50
ADENOCARCINOMA, NOS																															1
ENDOMETRIAL STROMAL POLYP		X				X								X		X		X						X	X			X		11
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				50
NERVOUS SYSTEM																															
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+				50
ASTROCYTOMA		X																													1
ALL OTHER SYSTEMS																															
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MALIG.LYMPHOMA, UNDIFFER-TYPE																															1
MYELOMONOCYTIC LEUKEMIA			X																						X						5

■ ANIMALS NECROPSIED

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

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

APPENDIX B

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

TABLE B1.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
FIBROMA	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS			2 (4%)
FIBROMA	2 (4%)	1 (2%)	
FIBROSARCOMA	4 (8%)	3 (6%)	1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
HEPATOCELLULAR CARCINOMA, METAST		4 (8%)	4 (8%)
ALVEOLAR/BRONCHIOLAR ADENOMA	9 (18%)	8 (16%)	9 (18%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	3 (6%)		3 (6%)
TUBULAR-CELL ADENOCA, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	7 (14%)	8 (16%)	3 (6%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
MAST-CELL SARCOMA			1 (2%)
#MESENTERIC L. NODE	(42)	(45)	(42)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	1 (2%)
#LIVER	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		2 (4%)	2 (4%)
#PEYERS PATCH	(49)	(47)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)		

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#KIDNEY	(49)	(48)	(50)
MALIGNANT LYMPHOMA, NOS			1 (2%)
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
HEMANGIOSARCOMA		1 (2%)	1 (2%)
#SPLEEN	(48)	(47)	(49)
HEMANGIOSARCOMA			1 (2%)
*SKELETAL MUSCLE	(50)	(50)	(50)
HEMANGIOSARCOMA			1 (2%)
#HEART	(50)	(50)	(50)
TUBULAR-CELL ADENOCA, METASTATIC	1 (2%)		
#LIVER	(50)	(50)	(50)
HEMANGIOSARCOMA	2 (4%)	2 (4%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
BILE DUCT ADENOMA			1 (2%)
HEPATOCELLULAR ADENOMA	7 (14%)	10 (20%)	17 (34%)
HEPATOCELLULAR CARCINOMA	11 (22%)	17 (34%)	16 (32%)
#PANCREAS	(48)	(45)	(48)
ADENOCARCINOMA, NOS	1 (2%)		
#FORESTOMACH	(50)	(48)	(49)
SQUAMOUS CELL PAPILLOMA		1 (2%)	3 (6%)
*ANUS	(50)	(50)	(50)
SARCOMA, NOS			1 (2%)
URINARY SYSTEM			
#KIDNEY	(49)	(48)	(50)
TUBULAR-CELL ADENOCARCINOMA	1 (2%)		

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(43)	(42)	(47)
ADENOMA, NOS	1 (2%)		
#ADRENAL	(45)	(45)	(49)
CORTICAL ADENOMA	2 (4%)		
PHEOCHROMOCYTOMA		1 (2%)	1 (2%)
#THYROID	(47)	(45)	(45)
FOLLICULAR-CELL ADENOMA			1 (2%)
FOLLICULAR-CELL CARCINOMA			1 (2%)
#PANCREATIC ISLETS	(48)	(45)	(48)
ISLET-CELL ADENOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
#PROSTATE	(49)	(46)	(48)
PAPILLARY ADENOMA		1 (2%)	
#TESTIS	(49)	(48)	(50)
INTERSTITIAL-CELL TUMOR		1 (2%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)	2 (4%)	
PAPILLARY ADENOMA			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
ADENOCARCINOMA, NOS, METASTATIC	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	15	14	11
MORIBUND SACRIFICE	1	4	4
SCHEDULED SACRIFICE	5		
TERMINAL SACRIFICE	29	32	35
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	33	36	42
TOTAL PRIMARY TUMORS	54	60	69
TOTAL ANIMALS WITH BENIGN TUMORS	19	20	26
TOTAL BENIGN TUMORS	24	25	33
TOTAL ANIMALS WITH MALIGNANT TUMORS	23	29	28
TOTAL MALIGNANT TUMORS	30	35	36
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	4	4
TOTAL SECONDARY TUMORS	3	4	4

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

TABLE B2.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
SEBACEOUS ADENOMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS	1 (2%)		1 (2%)
FIBROSARCOMA		1 (2%)	2 (4%)
NEUROFIBROSARCOMA			1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
HEPATOCELLULAR CARCINOMA, METAST		1 (2%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	5 (10%)		1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	1 (2%)	
OSTEOSARCOMA, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	13 (26%)	13 (26%)	14 (28%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
#SPLEEN	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
#OVARY	(50)	(50)	(45)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(50)	(50)
HEMANGIOSARCOMA	2 (4%)		1 (2%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#HEART	(50)	(50)	(50)
SARCOMA, NOS		1 (2%)	
#LIVER	(50)	(50)	(50)
HEMANGIOSARCOMA	1 (2%)		
#UTERUS	(50)	(49)	(48)
HEMANGIOMA	1 (2%)	1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
HEPATOCELLULAR ADENOMA	1 (2%)	5 (10%)	5 (10%)
HEPATOCELLULAR CARCINOMA	1 (2%)	3 (6%)	4 (8%)
#FORESTOMACH	(50)	(50)	(50)
CARCINOMA IN SITU, NOS		1 (2%)	
SQUAMOUS CELL PAPILLOMA		2 (4%)	2 (4%)
SQUAMOUS CELL CARCINOMA			1 (2%)
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(38)	(45)	(44)
CARCINOMA, NOS	2 (5%)	1 (2%)	1 (2%)
ADENOMA, NOS	7 (18%)	8 (18%)	8 (18%)
#ADRENAL	(48)	(47)	(46)
CORTICAL ADENOMA	1 (2%)		
#THYROID	(48)	(45)	(46)
FOLLICULAR-CELL ADENOMA	1 (2%)		2 (4%)
FOLLICULAR-CELL CARCINOMA			2 (4%)
#THYROID FOLLICLE	(48)	(45)	(46)
CYSTADENOMA, NOS			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)	1 (2%)	

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MIXED TUMOR, MALIGNANT	1 (2%)		
*VAGINA	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA			1 (2%)
#UTERUS	(50)	(49)	(48)
ADENOCARCINOMA, NOS		1 (2%)	
LEIOMYOSARCOMA			1 (2%)
ENDOMETRIAL STROMAL POLYP			1 (2%)
#OVARY	(50)	(50)	(45)
GRANULOSA-CELL TUMOR		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
CARCINOMA, NOS, INVASIVE		1 (2%)	1 (2%)
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)		1 (2%)
*EAR	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
*EAR CANAL	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*LUMBAR VERTEBRA	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEPATOCELLULAR CARCINOMA, METAST		1 (2%)	
ALVEOLAR/BRONCHIOLAR CA, METASTA		1 (2%)	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	11	14	22
MORIBUND SACRIFICE	5	6	4
SCHEDULED SACRIFICE	5		
TERMINAL SACRIFICE	29	29	24
ACCIDENTALLY KILLED, NOS		1	
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	35	29	34
TOTAL PRIMARY TUMORS	43	44	51
TOTAL ANIMALS WITH BENIGN TUMORS	17	14	18
TOTAL BENIGN TUMORS	17	16	22
TOTAL ANIMALS WITH MALIGNANT TUMORS	24	20	28
TOTAL MALIGNANT TUMORS	26	27	29
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	4	3
TOTAL SECONDARY TUMORS	1	4	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT		1	
TOTAL UNCERTAIN TUMORS		1	

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	106	076	106	116	106	106	106	106	054	105	106	106	106	105	106	105	093	106	106	106	074	106	106	083	106
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+
FIBROMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+
FIBROMA				X																					
FIBROSARCOMA								X					X												
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA		X		X	X						X									X	X				
ALVEOLAR/BRONCHIOLAR CARCINOMA																			X						
TUBULAR-CELL ADENOCARCINOMA, META									X																
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	-	+	+	+	+	-	+	+	+	+	-	-	+	+	+	-	+	+	-	+	+	+
THYMUS	+	-	+	+	-	-	+	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA, META									X																
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA			X	X			X						X												
HEPATOCELLULAR CARCINOMA	X				X	X		X	X										X						
HEMANGIOSARCOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	N	N	+	N	N	+	N	+	+	+	N	N	+	N	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ADENOCARCINOMA, NOS						X																			
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS							X																		
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA									X																
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+
ADENOMA, NOS																									
ADRENAL	+	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
THYROID	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
PARATHYROID	+	-	-	-	-	+	-	+	-	-	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS								X																	
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS, METASTATIC							X																		
MALIGNANT LYMPHOMA, NOS		X			X													X	X			X	X		X

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

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

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 01	03 11	03 21	03 31	03 34	03 35	03 36	03 37	03 38	03 39	04 01	04 11	04 21	04 31	04 46	04 45	04 46	04 47	04 48	04 49	05 00	TOTAL TISSUES TUMORS
WEEKS ON STUDY	10 06	10 06	10 06	09 01	08 06	02 06	10 06	10 05	10 05	07 01	10 07	10 06	09 07	07 07	01 06	06 10	10 07	07 10	07 07	07 01	01 07	05 15	10 07	07 07	10 04	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA											X															1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA																							X			2
FIBROSARCOMA								X													X					4
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA	X	X							X																	9
ALVEOLAR/BRONCHIOLAR CARCINOMA	X																							X		3
TUBULAR-CELL ADENOCARCINOMA, META																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LYMPH NODES	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
THYMUS	-	-	+	-	+	-	+	-	-	+	+	+	-	-	-	-	-	+	-	-	-	+	-	+	-	15
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOCARCINOMA, META																										1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA	X							X													X					7
HEPATOCELLULAR CARCINOMA										X	X	X										X	X		X	11
HEMANGIOSARCOMA																							X		X	2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	N	N	+	+	N	50M
PANCREAS	+	+	+	-	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOCARCINOMA, NOS																										1
ESOPHAGUS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MALIGNANT LYMPHOMA, NOS																										1
LARGE INTESTINE	+	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	44
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TUBULAR-CELL ADENOCARCINOMA																										1
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	43
ADENOMA, NOS														X												1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	45
CORTICAL ADENOMA	X				X																					2
THYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
PARATHYROID	-	-	+	+	-	-	-	+	+	+	-	+	+	+	-	+	+	-	-	-	-	+	+	+	-	27
PANCREATIC ISLETS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ISLET-CELL ADENOMA																								X		1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOCARCINOMA, NOS, METASTATIC																										1
MALIGNANT LYMPHOMA, NOS																										7

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

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	106	106	106	118	106	106	106	106	106	106	106	106	099	106	105	106	041	106	099	090	106	106	106	106	102
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	+
FIBROMA									X																
FIBROSARCOMA										X				X											
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA			X														X								
ALVEOLAR/BRONCHIOLAR ADENOMA																		X				X			
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-
SPLEEN	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-
LYMPH NODES	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
THYMUS	-	+	-	+	-	-	+	+	+	+	-	+	+	-	+	-	-	-	-	-	+	+	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
HEPATOCELLULAR ADENOMA						X				X	X													X	
HEPATOCELLULAR CARCINOMA			X				X				X		X	X			X	X	X	X	X	X			X
HEMANGIOSARCOMA																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																		X							
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	N	+	+	N	+	+	+	+	+	+	N	+	N	+	N	+	+	+	+	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
SQUAMOUS CELL PAPILLOMA											X														
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	●	+	+	+	+	+	-	+	+	+	+	+	-
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	-	+	+	+	+	+	-
ADRENAL	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	-	+	+	+	+	+	-
PHEOCHROMOCYTOMA			X																						
THYROID	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
PARATHYROID	-	+	+	+	-	-	+	-	+	+	-	+	-	+	+	-	-	-	-	+	-	+	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
INTERSTITIAL-CELL TUMOR																									
PROSTATE	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	-
PAPILLARY ADENOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																						X			
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEMANGIOSARCOMA													X												
MALIGNANT LYMPHOMA, NOS																				X			X		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	106	085	106	099	055	073	017	106	066	066	066	086	093	104	066	066	051	066	098	066	064	066	066	066	066	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA																										1
FIBROSARCOMA								X																		3
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA													X													4
ALVEOLAR/BRONCHIOLAR ADENOMA			X					X	X											X				X	X	8
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	45
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									X	1
THYMUS	+	-	+	-	-	+	+	+	-	-	+	-	-	-	-	-	+	-	-	+	-	-	-	+	+	21
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA					X			X	X	X					X								X			10
HEPATOCELLULAR CARCINOMA			X									X								X			X			16
HEMANGIOSARCOMA												X											X			2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE				X																						1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	N	N	+	+	+	+	+	+	+	N	N	+	+	+	+	+	N	+	+	+	+	+	+	50M
PANCREAS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	45
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SQUAMOUS CELL PAPILLOMA																										1
SMALL INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	a	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+	44
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	-	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	42
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	45
PARATHYROID	-	-	-	-	+	+	-	+	+	-	-	+	+	-	+	+	+	+	-	-	-	+	-	+	+	26
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
INTERSTITIAL-CELL TUMOR														X												1
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
PAPILLARY ADENOMA																									X	1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																										2
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
HEMANGIOSARCOMA																										1
MALIGNANT LYMPHOMA, NOS		X			X									X	X		X				X					8
MALIG.LYMPHOMA, HISTIOCYTIC TYPE														X												1

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

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	105	105	105	104	088	105	105	105	061	105	071	081	105	103	105	105	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
FIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA				X			X						X												
ALVEOLAR/BRONCHIOLAR ADENOMA			X	X	X											X					X				X
ALVEOLAR/BRONCHIOLAR CARCINOMA																	X								
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA														X											
LYMPH NODES	+	+	+	-	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	-	+	+	+
MALIG.LYMPHOMA, HISTIOCYTIC TYPE								X																	
THYMUS	+	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	+	-	+	-	+	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	-	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT ADENOMA		X			X					X						X				X	X	X	X		
HEPATOCELLULAR ADENOMA				X			X	X				X	X	X	X	X		X		X					X
HEPATOCELLULAR CARCINOMA																X									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE											X														
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	N	+	N	+	+	N	+	+	+	N	N	+	N	N	+	N	+	N	+	+	N	N	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																X									
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RECTUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																									
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS				X																					
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA				X																					
THYROID	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA							X															X			
FOLLICULAR-CELL CARCINOMA																									
PARATHYROID	+	-	-	-	+	+	-	+	+	+	-	+	+	-	-	+	+	-	-	+	+	-	-	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLARY ADENOMA													X												
MUSCULOSKELETAL SYSTEM																									
MUSCLE	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N
HEMANGIOSARCOMA														X											
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEMANGIOSARCOMA																									
MALIGNANT LYMPHOMA, NOS								X													X			X	
MALIGNANT LYMPHOMA, MIXED TYPE																									
MAST-CELL SARCOMA						X																			

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

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

ANIMAL NUMBER	0026	0027	0028	0029	0030	0031	0032	0033	0034	0035	0036	0037	0038	0039	0040	0041	0042	0043	0044	0045	0046	0047	0048	0049	0050	TOTAL
WEEKS ON STUDY	098	055	055	055	055	055	000	055	055	055	055	055	096	055	055	012	055	055	010	012	088	055	055	055	087	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	+	+	50
SARCOMA, NOS														X		X										2
FIBROSARCOMA													X													1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																			X							4
ALVEOLAR/BRONCHIOLAR ADENOMA															X				X				X			9
ALVEOLAR/BRONCHIOLAR CARCINOMA											X													X		3
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMANGIOSARCOMA																										1
LYMPH NODES	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	42
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
THYMUS	+	-	-	+	-	+	-	-	-	+	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	12
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	●	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT ADENOMA																								X		1
HEPATOCELLULAR ADENOMA			X	X	X		X	X			X			X			X					X				16
HEPATOCELLULAR CARCINOMA	X														X			X	X		X					16
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									X	2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	N	N	N	+	+	+	+	N	+	+	N	+	+	N	+	+	+	+	+	+	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SQUAMOUS CELL PAPILLOMA																						X		X		3
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	49
RECTUM	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	50
SARCOMA, NOS																				X						1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIGNANT LYMPHOMA, NOS																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	49
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	-	+	45
FOLLICULAR-CELL ADENOMA																										1
FOLLICULAR-CELL CARCINOMA																										1
PARATHYROID	+	-	+	+	+	+	+	+	-	+	+	+	+	-	-	-	-	+	-	+	-	+	-	-	-	28
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
PAPILLARY ADENOMA																										1
MUSCULOSKELETAL SYSTEM																										
MUSCLE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
HEMANGIOSARCOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
HEMANGIOSARCOMA	X																									1
MALIGNANT LYMPHOMA, NOS																										3
MALIGNANT LYMPHOMA, MIXED TYPE																								X		1
MAST-CELL SARCOMA																										1

M ANIMALS NECROPSIED

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	083	017	117	107	098	084	107	107	107	107	105	107	107	107	107	107	105	092	111	161	104	114	105	107	107
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																					X				
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA			X							X									X						
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
OSTEOSARCOMA, METASTATIC																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA		X																							
MALIGNANT LYMPHOMA, NOS																									
LYMPH NODES	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
THYMUS	-	+	-	+	-	-	+	+	+	-	-	+	+	+	-	-	-	-	-	-	-	+	-	+	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																	X								
HEPATOCELLULAR CARCINOMA							X																		
HEMANGIOSARCOMA																	X								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	N	+	+	N	+	N	+	+	+	+	+	+	+	N	+	+
PANCREAS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+
CARCINOMA,NOS				X																					
ADENOMA, NOS												X			X						X			X	X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																							X		
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	-	-	-	+	+	-	+	+	+	-	+	-	+	+	-	+	+	+	-	+	-	+	-	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	N	+	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	+	N	N	
ADENOCARCINOMA, NOS																	X								
MIXED TUMOR, MALIGNANT																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA					X																				
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIG.LYMPHOMA, HISTIOCYTIC TYPE											X														
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS	X															X						X	X		

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

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

ANIMAL NUMBER	02616	02717	02818	02919	03011	03112	03213	03314	03415	03516	03617	03718	03819	03910	04011	04112	04213	04314	04415	04516	04617	04718	04819	04920	05020	TOTAL TISSUES TUMORS
WEEKS ON STUDY	107	107	105	107	107	105	101	081	107	104	079	107	107	107	107	107	107	102	105	107	090	107	107	107	088	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	N	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	N	+	+	+	+	+	+	+	+	+	50
SARCOMA, NOS													X													1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																					X					5
ALVEOLAR/BRONCHIOLAR CARCINOMA														X									X			1
OSTEOSARCOMA, METASTATIC														X												1
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA											X															2
MALIGNANT LYMPHOMA, NOS				X																						1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	46
THYMUS	+	+	-	-	+	+	-	-	-	-	+	-	-	+	-	-	+	-	+	-	-	+	+	+	-	21
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA																										1
HEMANGIOSARCOMA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	N	N	+	+	+	N	+	+	N	+	N	+	+	+	+	+	+	N	+	+	N	+	+	+	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	-	+	-	+	+	+	+	-	+	+	-	+	+	+	+	+	-	-	+	+	-	+	+	-	+	38
CARCINOMA,NOS					X																					2
ADENOMA, NOS									X				X													7
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	48
CORTICAL ADENOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	48
FOLLICULAR-CELL ADENOMA												X														1
PARATHYROID	+	-	+	-	+	-	-	+	+	-	-	-	-	+	+	+	+	+	-	-	+	+	+	-	+	29
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	+	N	N	N	+	N	N	N	+	N	+	N	N	N	N	N	N	+	N	+	N	50
ADENOCARCINOMA, NOS																										1
MIXED TUMOR, MALIGNANT					X																					1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOMA																										1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
ADENOMA, NOS						X																				1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MALIGNANT LYMPHOMA, NOS			X	X			X				X						X			X	X		X		X	13

* ANIMALS NECROPSIED

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	011	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	094	081	085	097	076	061	106	106	091	061	106	106	106	095	106	095	093	099	096	081	106	023	106	083	087
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA							X																		
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																X									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	-	+	-	+	+	-	+	+	+	+	+	-	+	-	+	-	+
THYMUS	-	-	-	-	-	+	-	-	-	-	+	+	+	-	+	-	-	-	+	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	-	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA										X															
HEPATOCELLULAR CARCINOMA								X								X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	+	+	+	N	+	+	+	N	+	N	N	+	+	N	+	+	N	+	+
PANCREAS	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA-IN-SITU, NOS						X																			
SQUAMOUS CELL PAPILLOMA																									
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS				X																					
ADENOMA, NOS																									
ADRENAL	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	-	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	-	+	+	+	+	+	+	-	-	+	+	-	-	-	-	+	-	+	+	-	-	-	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	+	N	+	N	N	N	N	N	+	N	N	+	N
ADENOCARCINOMA, NOS																									
UTERUS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS								X																	
HEMANGIOMA																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, INVASIVE				X																					
SPECIAL SENSE ORGANS																									
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																X									
MUSCULOSKELETAL SYSTEM																									
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEPATOCELLULAR CARCINOMA, METASTA																									
ALVEOLAR/BRONCHIOLAR CA, METASTAT																									
MALIGNANT LYMPHOMA, NOS	X	X		X				X						X				X							
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																					X				

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	106	106	073	006	003	106	106	106	106	074	106	106	085	006	089	091	086	061	006	106	106	106	106	106	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																										1
ALVEOLAR/BRONCHIOLAR CARCINOMA																	X									1
TRACHEA	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	-	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	41
THYMUS	-	-	-	-	-	+	+	-	+	-	+	+	-	+	-	-	-	+	+	-	+	+	+	+	-	18
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	●	+	+	+	+	+	+	+	50
SARCOMA, NOS	X																									1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
LIVER	+	+	+	+	+	+	+	+	+	■	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA				X														X				X	X			4
HEPATOCELLULAR CARCINOMA	X																									3
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	+	+	+	+	+	+	N	N	+	N	+	+	+	+	+	+	+	+	+	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	46
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA-IN-SITU, NOS																				X						1
SQUAMOUS CELL PAPILLOMA																									X	2
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-		45
CARCINOMA,NOS																										1
ADENOMA, NOS						X	X							X					X	X	X	X		X		8
ADRENAL	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
THYROID	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	45
PARATHYROID	-	-	-	-	-	+	+	-	-	+	+	-	+	-	-	+	-	-	-	-	-	-	-	-	+	20
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	+	N	N	H	+	N	N	N	N	N	N	N	N	N	N	N	N	+	N	+	N	N	50M
ADENOCARCINOMA, NOS								X																		1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOCARCINOMA, NOS																			X							1
HEMANGIOMA																										1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GRANULOSA-CELL TUMOR																				X						1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA, NOS, INVASIVE																										1
SPECIAL SENSE ORGANS																										
EAR	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL CARCINOMA							X																			2
MUSCULOSKELETAL SYSTEM																										
BONE	N	N	N	N	N	N	N	N	N	N	H	H	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
OSTEOSARCOMA				X																						1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
HEPATOCELLULAR CARCINOMA, METASTA	X																									1
ALVEOLAR/BRONCHIOLAR CA, METASTAT																	X									1
MALIGNANT LYMPHOMA, NOS	X			X			X			X			X	X	X											13
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1

M ANIMALS NECROPSIED

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR STUDY OF 1,2-DICHLOROPROPANE

HIGH DOSE

ANIMAL NUMBER	0011	0023	0035	0045	0055	0066	0077	0088	0095	0102	0111	0122	0133	0144	0155	0166	0177	0188	0199	0211	0222	0233	0244	0255
WEEKS ON STUDY	083	105	105	105	105	080	086	078	105	102	091	083	078	058	055	055	051	051	048	105	105	091	078	105	082
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SEBACEOUS ADENOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS			X																						
FIBROSARCOMA																									
NEUROFIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT													X												
ALVEOLAR/BRONCHIOLAR ADENOMA			X																						
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																									
LYMPH NODES	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	-	+	-	+	-	-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	-	-	+	+	
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																X		X							
HEPATOCELLULAR CARCINOMA																	X								X
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	N	+	+	+	+	N	+	+	+	+	+	+	N	N	+	+	+	N	+	+
PANCREAS	-	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+	-	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL PAPILLOMA																									
SQUAMOUS CELL CARCINOMA																									
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	-	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
CARCINOMA,NOS																				+					
ADENOMA, NOS															X			X		X		X			
ADRENAL	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+
THYROID	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA				X																					
FOLLICULAR-CELL CARCINOMA																						X			
CYSTADENOMA, NOS																									
PARATHYROID	-	+	-	+	-	-	-	+	+	-	-	-	+	-	+	-	+	+	-	-	+	-	+	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	+	N	N
VAGINA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA													X												
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOSARCOMA																									
ENDOMETRIAL STROMAL POLYP																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, INVASIVE																				+					
																				X					
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, METASTAT																									
MALIGNANT LYMPHOMA, NOS				X					X	X							X				X		X		

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

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

ANIMAL NUMBER	02626	02727	02828	02929	03030	03131	03232	03333	03434	03535	03636	03737	03838	03939	04040	04141	04242	04343	04444	04545	04646	04747	04848	04949	05050	TOTAL
WEEKS ON STUDY	06909	10951	09900	10551	09805	11105	10205	11405	10705	11005	11105	10805	11005	10905	10105	10705	10501	11001	10502	09404	11005	11003	11001	11005	10907	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	50
SEBACEOUS ADENOMA																									X	1
SUBCUTANEOUS TISSUE	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	50
SARCOMA, NOS																								X		1
FIBROSARCOMA												X														2
NEUROFIBROSARCOMA								X																		1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA, METASTAT																										1
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA																									X	1
LYMPH NODES	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	46
THYMUS	-	-	-	+	-	-	-	-	+	-	+	-	-	-	-	+	+	-	-	-	-	-	-	+	-	12
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	45
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA				X						X													X			3
HEPATOCELLULAR CARCINOMA									X						X											4
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	+	N	N	+	+	N	+	+	+	+	N	N	+	N	+	+	+	N	+	+	+	+	+	N	50
PANCREAS	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	43
ESOPHAGUS	+	+	+	-	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	43
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL PAPILLOMA					X																				X	2
SQUAMOUS CELL CARCINOMA																					X					1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	-	+	+	-	+	+	+	43
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	44
CARCINOMA,NOS																										1
ADENOMA, NOS				X			X	X										X						X		8
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	46
THYROID	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	46
FOLLICULAR-CELL ADENOMA																					X					2
FOLLICULAR-CELL CARCINOMA														X												2
CYSTADENOMA, NOS				X																						1
PARATHYROID	-	+	-	-	+	-	-	+	+	-	-	-	+	-	+	+	-	+	-	-	+	+	+	-	+	22
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	+	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
VAGINA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
SQUAMOUS CELL CARCINOMA																										1
UTERUS	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LEIOMYOSARCOMA																				X						1
ENDOMETRIAL STROMAL POLYP												X														1
OVARY	-	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	45
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA, NOS, INVASIVE																										1
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	M	N	N	N	N	N	N	50
ADENOMA, NOS		X																								1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	M	N	N	M	N	N	N	N	N	N	N	N	N	N	N	M	N	N	N	N	N	N	N	50
SQUAMOUS CELL CARCINOMA, METASTAT																					X					1
MALIGNANT LYMPHOMA, NOS	X	X			X		X						X		X			X						X		14

M ANIMALS NECROPSIED

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

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

APPENDIX C

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

TABLE C1.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST			1 (2%)
HEMORRHAGE			1 (2%)
ABSCESS, NOS	1 (2%)		
RESPIRATORY SYSTEM			
#TRACHEA	(49)	(49)	(50)
INFLAMMATION, CHRONIC			1 (2%)
HYPERPLASIA, PAPILLARY			1 (2%)
#LUNG	(49)	(50)	(50)
CONGESTION, NOS	1 (2%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)	2 (4%)	2 (4%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(50)	(49)	(50)
HEMOSIDEROSIS	2 (4%)		1 (2%)
HEMATOPOIESIS	1 (2%)	2 (4%)	1 (2%)
#LYMPH NODE	(48)	(49)	(48)
HYPERPLASIA, PLASMA CELL		1 (2%)	
#MANDIBULAR L. NODE	(48)	(49)	(48)
CYST, NOS	1 (2%)		
CONGESTION, NOS	1 (2%)		
HYPERPLASIA, PLASMA CELL		1 (2%)	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#MESENTERIC L. NODE	(48)	(49)	(48)
CYST, NOS	1 (2%)		1 (2%)
SCLEROSIS			1 (2%)
#RENAL LYMPH NODE	(48)	(49)	(48)
HEMOSIDEROSIS	1 (2%)		
#ADRENAL	(50)	(49)	(50)
HEMATOPOIESIS			1 (2%)
CIRCULATORY SYSTEM			
#HEART	(49)	(50)	(50)
FIBROSIS, DIFFUSE	1 (2%)		
#MYOCARDIUM	(49)	(50)	(50)
DEGENERATION, NOS	36 (73%)	25 (50%)	20 (40%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
NECROSIS, FOCAL		1 (2%)	
METAMORPHOSIS FATTY	35 (70%)	34 (68%)	26 (52%)
BASOPHILIC CYTO CHANGE	27 (54%)	13 (26%)	11 (22%)
GROUND-GLASS CYTO CHANGE	13 (26%)	11 (22%)	10 (20%)
FOCAL CELLULAR CHANGE	1 (2%)	2 (4%)	1 (2%)
CLEAR-CELL CHANGE	13 (26%)	15 (30%)	5 (10%)
HEPATOCYTOMEGALY	1 (2%)		
ANGIECTASIS	2 (4%)		1 (2%)
NODULAR REGENERATION		1 (2%)	
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
CONGESTION, NOS	1 (2%)		
NECROSIS, NOS			3 (6%)
ATROPHY, NOS	1 (2%)		
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	37 (74%)	32 (64%)	31 (62%)
#PANCREAS	(48)	(50)	(50)
ACCESSORY STRUCTURE			1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC		1 (2%)	
HYPERPLASIA, FOCAL		1 (2%)	
#PANCREATIC ACINUS	(48)	(50)	(50)
ATROPHY, NOS	1 (2%)		
ATROPHY, FOCAL	2 (4%)		2 (4%)
*JEJUNAL LUMEN	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		
#STOMACH	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL			1 (2%)
#FORESTOMACH	(50)	(50)	(50)
ULCER, NOS	1 (2%)		
INFLAMMATION, ACUTE		1 (2%)	
HYPERPLASIA, FOCAL			1 (2%)
HYPERPLASIA, DIFFUSE	1 (2%)		
HYPERPLASIA, BASAL CELL		2 (4%)	1 (2%)
#JEJUNUM	(49)	(50)	(50)
CYST, NOS			1 (2%)
#COLON	(49)	(49)	(49)
NEMATODIASIS	5 (10%)	6 (12%)	7 (14%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
CAST, NOS	1 (2%)		
HYDRONEPHROSIS			1 (2%)
NEPHROSIS, NOS	43 (86%)	43 (86%)	45 (90%)
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(48)	(47)
CYST, NOS	1 (2%)	2 (4%)	
HEMORRHAGIC CYST	1 (2%)		
HYPERTROPHY, FOCAL	1 (2%)		
HYPERPLASIA, FOCAL	2 (4%)	1 (2%)	1 (2%)
ANGIECTASIS	1 (2%)	1 (2%)	
#ADRENAL	(50)	(49)	(50)
DEGENERATION, LIPOID	1 (2%)		

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
METAMORPHOSIS FATTY		2 (4%)	
ANGIECTASIS		1 (2%)	
#ADRENAL CORTEX	(50)	(49)	(50)
CYST, NOS		1 (2%)	
DEGENERATION, NOS	6 (12%)	6 (12%)	2 (4%)
DEGENERATION, LIPOID			2 (4%)
METAMORPHOSIS FATTY		2 (4%)	1 (2%)
HYPERPLASIA, FOCAL	1 (2%)	1 (2%)	2 (4%)
#ADRENAL MEDULLA	(50)	(49)	(50)
HYPERPLASIA, FOCAL	4 (8%)	3 (6%)	3 (6%)
ANGIECTASIS	1 (2%)		
#THYROID	(49)	(49)	(50)
CYSTIC FOLLICLES	2 (4%)	2 (4%)	
HYPERPLASIA, C-CELL	4 (8%)	1 (2%)	2 (4%)
#PANCREATIC ISLETS	(48)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)	1 (2%)	1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
DILATATION/DUCTS			1 (2%)
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, CYSTIC	1 (2%)		1 (2%)
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	1 (2%)
HYPERPLASIA, NOS	1 (2%)		
#PROSTATE	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			2 (4%)
INFLAMMATION, ACUTE	4 (8%)	6 (12%)	1 (2%)
INFLAMMATION, ACUTE FOCAL	4 (8%)	2 (4%)	
INFLAMMATION, CHRONIC	2 (4%)		1 (2%)
FIBROSIS, FOCAL		1 (2%)	
#TESTIS	(50)	(47)	(50)
ATROPHY, NOS	3 (6%)	2 (4%)	2 (4%)
HYPERPLASIA, INTERSTITIAL CELL	5 (10%)	4 (9%)	5 (10%)
#TESTIS/TUBULE	(50)	(47)	(50)
DEGENERATION, NOS	2 (4%)	1 (2%)	2 (4%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*SCROTUM	(50)	(50)	(50)
NECROSIS, FAT		1 (2%)	
NERVOUS SYSTEM			
#CEREBRUM	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	2 (4%)		
ALL OTHER SYSTEMS			
ADIPOSE TISSUE			
NECROSIS, FAT		1	
OMENTUM			
NECROSIS, FAT	1		
SPECIAL MORPHOLOGY SUMMARY			
NONE			

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

TABLE C2.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
INFLAMMATION, ACUTE	2 (4%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(49)
INFLAMMATION, INTERSTITIAL	1 (2%)		1 (2%)
BRONCHOPNEUMONIA, ACUTE			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM		3 (6%)	2 (4%)
#LUNG/ALVEOLI	(50)	(50)	(49)
CALCULUS,UNKN GROSS OR MICRO		1 (2%)	
HEMATOPOIETIC SYSTEM			
#SPLEEN	(50)	(50)	(47)
HEMOSIDEROSIS			20 (43%)
HEMATOPOIESIS	1 (2%)	1 (2%)	7 (15%)
#MANDIBULAR L. NODE	(50)	(50)	(48)
HYPERPLASIA, PLASMA CELL	1 (2%)		
#PANCREATIC L.NODE	(50)	(50)	(48)
FIBROSIS			1 (2%)
#MESENTERIC L. NODE	(50)	(50)	(48)
CYST, NOS	1 (2%)	1 (2%)	
CIRCULATORY SYSTEM			
#MYOCARDIUM	(49)	(50)	(50)
DEGENERATION, NOS	12 (24%)	12 (24%)	13 (26%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NECROSIS, NOS			1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(50)	(46)
INFLAMMATION, ACUTE			1 (2%)
CYTOPLASMIC VACUOLIZATION			1 (2%)
#LIVER	(50)	(50)	(50)
NECROSIS, FOCAL	1 (2%)		3 (6%)
METAMORPHOSIS FATTY	10 (20%)	10 (20%)	5 (10%)
NUCLEAR ENLARGEMENT			1 (2%)
BASOPHILIC CYTO CHANGE	37 (74%)	39 (78%)	4 (8%)
GROUND-GLASS CYTO CHANGE	2 (4%)		
FOCAL CELLULAR CHANGE			1 (2%)
CLEAR-CELL CHANGE	3 (6%)	5 (10%)	11 (22%)
HEPATOCYTOMEGALY		1 (2%)	
ANGIECTASIS	2 (4%)	1 (2%)	
#PORTAL TRACT	(50)	(50)	(50)
SCLEROSIS			1 (2%)
FIBROSIS, FOCAL		1 (2%)	
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
CONGESTION, NOS			1 (2%)
NECROSIS, NOS	1 (2%)	1 (2%)	9 (18%)
METAMORPHOSIS FATTY			2 (4%)
#BILE DUCT	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)		
HYPERPLASIA, NOS	20 (40%)	8 (16%)	1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		
#PANCREAS	(49)	(50)	(46)
ECTOPIA			2 (4%)
#PANCREATIC ACINUS	(49)	(50)	(46)
ATROPHY, FOCAL		2 (4%)	
#ESOPHAGUS	(47)	(48)	(41)
POLYP		1 (2%)	
#GASTRIC MUCOSA	(50)	(50)	(48)
EROSION			1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NECROSIS, FOCAL	1 (2%)		1 (2%)
#FORESTOMACH	(50)	(50)	(48)
INFLAMMATION, ACUTE			1 (2%)
HYPERPLASIA, BASAL CELL	1 (2%)	1 (2%)	2 (4%)
#COLON	(48)	(50)	(48)
CONGENITAL MALFORMATION, NOS		1 (2%)	
NEMATODIASIS	8 (17%)	4 (8%)	1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
NEPHROSIS, NOS	11 (22%)	3 (6%)	3 (6%)
#KIDNEY/CORTEX	(50)	(50)	(50)
CYST, NOS		1 (2%)	
#KIDNEY/TUBULE	(50)	(50)	(50)
NECROSIS, NOS	1 (2%)		
HEMOSIDEROSIS	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(50)	(46)
CYST, NOS	9 (18%)	2 (4%)	3 (7%)
MULTILOCULAR CYST			1 (2%)
MULTIPLE CYSTS			2 (4%)
HEMORRHAGIC CYST	1 (2%)		
NECROSIS, FOCAL	1 (2%)		
HEMOSIDEROSIS		1 (2%)	
HYPERPLASIA, FOCAL	1 (2%)	2 (4%)	1 (2%)
#ADRENAL	(49)	(50)	(50)
CYST, NOS	1 (2%)		
NECROSIS, CORTICAL	1 (2%)		
CALCIFICATION, NOS	1 (2%)		
#ADRENAL CORTEX	(49)	(50)	(50)
HEMORRHAGIC CYST			1 (2%)
DEGENERATION, NOS	6 (12%)	12 (24%)	4 (8%)
DEGENERATION, LIPOID	1 (2%)		
NECROSIS, FOCAL		1 (2%)	3 (6%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
LIPOIDOSIS	1 (2%)		
HYPERPLASTIC NODULE		1 (2%)	
HYPERPLASIA, FOCAL	2 (4%)	3 (6%)	3 (6%)
#ADRENAL MEDULLA	(49)	(50)	(50)
NECROSIS, NOS	1 (2%)		
#THYROID	(50)	(49)	(44)
CYSTIC FOLLICLES		2 (4%)	
HYPERPLASIA, CYSTIC			1 (2%)
HYPERPLASIA, C-CELL	1 (2%)	2 (4%)	
#THYROID FOLLICLE	(50)	(49)	(44)
HYPERPLASIA, CYSTIC	1 (2%)		1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
HYPERPLASIA, NOS		6 (12%)	1 (2%)
HYPERPLASIA, CYSTIC	10 (20%)	14 (28%)	
*MAMMARY LOBULE	(50)	(50)	(50)
HYPERPLASIA, NOS		1 (2%)	
*CLITORAL GLAND	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
HYPERPLASIA, NOS			2 (4%)
#UTERUS	(50)	(49)	(50)
HEMORRHAGE	1 (2%)		
#UTERUS/ENDOMETRIUM	(50)	(49)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
HYPERPLASIA, CYSTIC	6 (12%)	8 (16%)	4 (8%)
#OVARY	(49)	(50)	(50)
CYST, NOS	4 (8%)	4 (8%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
NONE			

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)	2 (4%)	2 (4%)
ALL OTHER SYSTEMS			
TAIL			
INFLAMMATION, SUPPURATIVE		1	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED			2

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

APPENDIX D

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

TABLE D1.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)	1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		
INFLAMMATION, INTERSTITIAL			1 (2%)
PNEUMONIA INTERSTITIAL CHRONIC	1 (2%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)	1 (2%)	3 (6%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(48)	(47)	(49)
HYPERPLASIA, LYMPHOID		2 (4%)	1 (2%)
HEMATOPOIESIS	2 (4%)	3 (6%)	3 (6%)
#MEDIASTINAL L.NODE	(42)	(45)	(42)
HYPERPLASIA, LYMPHOID	1 (2%)		
#PANCREATIC L.NODE	(42)	(45)	(42)
INFLAMMATION, ACUTE	1 (2%)		
#MESENTERIC L. NODE	(42)	(45)	(42)
CONGESTION, NOS	10 (24%)	11 (24%)	2 (5%)
HEMORRHAGE		1 (2%)	

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, LYMPHOID	2 (5%)	1 (2%)	2 (5%)
HEMATOPOIESIS		1 (2%)	
#LIVER	(50)	(49)	(50)
HYPERPLASIA, RETICULUM CELL	1 (2%)		
#PEYER'S PATCH	(49)	(47)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)
#PERIRENAL TISSUE	(49)	(48)	(50)
HYPERPLASIA, LYMPHOID		1 (2%)	
CIRCULATORY SYSTEM			
#LUNG	(50)	(50)	(50)
THROMBOSIS, NOS			1 (2%)
PERIVASCULITIS	1 (2%)		
#HEART	(50)	(50)	(50)
CALCIFICATION, NOS	1 (2%)		
CALCIFICATION, FOCAL	1 (2%)		
#HEART/ATRIUM	(50)	(50)	(50)
THROMBOSIS, NOS		1 (2%)	
#MYOCARDIUM	(50)	(50)	(50)
NECROSIS, NOS	1 (2%)		
NECROSIS, FOCAL			1 (2%)
#CARDIAC VALVE	(50)	(50)	(50)
ENDOCARDITIS, BACTERIAL	2 (4%)	1 (2%)	
#OMENTUM	(50)	(48)	(49)
THROMBOSIS, NOS	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(50)
INFLAMMATION, CHRONIC	1 (2%)	2 (4%)	
NECROSIS, NOS		1 (2%)	2 (4%)
NECROSIS, FOCAL	1 (2%)	3 (6%)	6 (12%)
INFARCT HEMORRHAGIC			1 (2%)
METAMORPHOSIS FATTY	6 (12%)	6 (12%)	3 (6%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOCAL CELLULAR CHANGE	4 (8%)	1 (2%)	2 (4%)
HEPATOCYTOMEGALY	3 (6%)	5 (10%)	14 (28%)
ANGIECTASIS	1 (2%)		3 (6%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, NOS	1 (2%)	1 (2%)	2 (4%)
METAMORPHOSIS, FATTY	3 (6%)	3 (6%)	
HEPATOCYTOMEGALY			1 (2%)
#BILE DUCT	(50)	(50)	(50)
CYST, NOS	1 (2%)		
HYPERPLASIA, NOS	1 (2%)		
#PANCREAS	(48)	(45)	(48)
CYSTIC DUCTS	2 (4%)		
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)
#PANCREATIC ACINUS	(48)	(45)	(48)
ATROPHY, FOCAL		1 (2%)	
#PERIPANCREATIC TISSU	(48)	(45)	(48)
STEATITIS		1 (2%)	
NECROSIS, FAT		1 (2%)	
#GASTRIC MUCOSA	(50)	(48)	(49)
DILATATION, NOS		1 (2%)	
EROSION		1 (2%)	
#FORESTOMACH	(50)	(48)	(49)
INFLAMMATION, CHRONIC			1 (2%)
HYPERKERATOSIS			2 (4%)
ACANTHOSIS			2 (4%)
#ILEAL MUCOSA	(49)	(47)	(49)
NECROSIS, NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(49)	(48)	(50)
GLOMERULONEPHRITIS, CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL			1 (2%)
INFLAMMATION, GRANULOMATOUS			1 (2%)
SCLEROSIS	1 (2%)		
NEPHROSIS, NOS		1 (2%)	3 (6%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CALCIFICATION, NOS	1 (2%)		
#KIDNEY/TUBULE	(49)	(48)	(50)
NECROSIS, NOS	1 (2%)		
#KIDNEY/PELVIS	(49)	(48)	(50)
HYPERPLASIA, PAPILLARY			1 (2%)
#URINARY BLADDER	(49)	(48)	(50)
INFLAMMATION, ACUTE	1 (2%)		
#U.BLADDER/SEROSA	(49)	(48)	(50)
RETENTION OF CONTENT	1 (2%)		
ENDOCRINE SYSTEM			
#ANTERIOR PITUITARY	(43)	(42)	(47)
CYST, NOS			1 (2%)
#ADRENAL	(45)	(45)	(49)
DEGENERATION, NOS	1 (2%)		
#ADRENAL MEDULLA	(45)	(45)	(49)
HYPERPLASIA, FOCAL			1 (2%)
#THYROID	(47)	(45)	(45)
CYSTIC FOLLICLES			1 (2%)
HYPERPLASIA, CYSTIC			1 (2%)
HYPERPLASIA, FOLLICULAR-CELL		3 (7%)	3 (7%)
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(50)	(50)
DILATATION/DUCTS	1 (2%)		
*SEMINAL VESICLE	(50)	(50)	(50)
RETENTION OF CONTENT	1 (2%)		
HEMORRHAGE	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
*EPIDIDYMIS	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN/MENINGES	(49)	(50)	(50)
INFLAMMATION, ACUTE FOCAL	1 (2%)		
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
INFLAMMATION, ACUTE			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
NECROSIS, FAT		1 (2%)	
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
*PLEURA	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
*MESENTERY	(50)	(50)	(50)
RETENTION OF CONTENT	1 (2%)		
NECROSIS, FAT	1 (2%)		
ALL OTHER SYSTEMS			
ADIPOSE TISSUE			
HEMORRHAGE	1		
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	3	2	2

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

TABLE D2.

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

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
ABSCESS, NOS		1 (2%)	
RESPIRATORY SYSTEM			
#TRACHEA	(48)	(47)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#LUNG/BRONCHIOLE	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
#LUNG	(50)	(50)	(50)
BRONCHOPNEUMONIA, ACUTE		1 (2%)	
INFLAMMATION, ACUTE HEMORRHAGIC			2 (4%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)		1 (2%)
#LUNG/ALVEOLI	(50)	(50)	(50)
HISTIOCYTOSIS	1 (2%)		
HEMATOPOIETIC SYSTEM			
#SPLEEN	(50)	(50)	(50)
NECROSIS, NOS		1 (2%)	
HYPERPLASIA, LYMPHOID	1 (2%)	4 (8%)	1 (2%)
HEMATOPOIESIS	2 (4%)	8 (16%)	10 (20%)
ERYTHROPOIESIS			1 (2%)
#SPLENIC CAPSULE	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
#LYMPH NODE	(46)	(41)	(46)
HEMORRHAGIC CYST			1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, ACUTE		1 (2%)	
#MANDIBULAR L. NODE	(46)	(41)	(46)
HYPERPLASIA, PLASMA CELL	1 (2%)		1 (2%)
#MEDIASTINAL L. NODE	(46)	(41)	(46)
INFLAMMATION, ACUTE			2 (4%)
HYPERPLASIA, NOS			1 (2%)
HYPERPLASIA, PLASMA CELL	1 (2%)		3 (7%)
#LUMBAR LYMPH NODE	(46)	(41)	(46)
INFLAMMATION, ACUTE			1 (2%)
HYPERPLASIA, PLASMA CELL	1 (2%)	1 (2%)	
#MESENTERIC L. NODE	(46)	(41)	(46)
CONGESTION, NOS		2 (5%)	
INFLAMMATION, ACUTE		1 (2%)	
HYPERPLASIA, NOS			3 (7%)
HYPERPLASIA, LYMPHOID	1 (2%)	1 (2%)	
#RENAL LYMPH NODE	(46)	(41)	(46)
HYPERPLASIA, PLASMA CELL		1 (2%)	
#LIVER	(50)	(50)	(50)
HYPERPLASIA, RETICULUM CELL	2 (4%)		
HEMATOPOIESIS		6 (12%)	1 (2%)
#ADRENAL	(48)	(47)	(46)
HEMATOPOIESIS		2 (4%)	
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
#LUNG	(50)	(50)	(50)
PERIVASCULITIS	1 (2%)	1 (2%)	
#HEART/ATRIUM	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION, ACUTE FOCAL		1 (2%)	1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC DIFFUSE	1 (2%)		
#CARDIAC VALVE	(50)	(50)	(50)
ENDOCARDITIS, BACTERIAL	1 (2%)		
*CORONARY ARTERY	(50)	(50)	(50)
PERIVASCULITIS	1 (2%)		
#KIDNEY	(50)	(50)	(50)
PERIVASCULITIS		1 (2%)	
#U.BLADDER/SUBMUCOSA	(50)	(48)	(48)
PERIVASCULITIS		1 (2%)	
#UTERUS	(50)	(49)	(48)
THROMBUS, ORGANIZED	1 (2%)		
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(46)	(45)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
#LIVER	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
NECROSIS, NOS	1 (2%)		1 (2%)
NECROSIS, FOCAL		1 (2%)	
METAMORPHOSIS, FATTY	4 (8%)	4 (8%)	6 (12%)
FOCAL CELLULAR CHANGE		2 (4%)	
EOSINOPHILIC CYTO CHANGE	2 (4%)		
#HEPATIC CAPSULE	(50)	(50)	(50)
INFLAMMATION, ACUTE		1 (2%)	3 (6%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, NOS	1 (2%)		1 (2%)
METAMORPHOSIS, FATTY		1 (2%)	
#BILE DUCT	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		1 (2%)
HYPERPLASIA, NOS			1 (2%)
#PANCREAS	(48)	(47)	(43)
INFLAMMATION, SUPPURATIVE	1 (2%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC	1 (2%)	2 (4%)	1 (2%)
#PANCREATIC ACINUS	(48)	(47)	(43)
ATROPHY, NOS		1 (2%)	
ATROPHY, FOCAL	1 (2%)		
#GASTRIC MUCOSA	(50)	(50)	(50)
CALCIFICATION, NOS		1 (2%)	
#FORESTOMACH	(50)	(50)	(50)
ULCER, NOS			1 (2%)
INFLAMMATION, ACUTE FOCAL		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
HYPERKERATOSIS		2 (4%)	
ACANTHOSIS		5 (10%)	4 (8%)
#SMALL INTESTINE	(48)	(48)	(50)
INFLAMMATION, CHRONIC	1 (2%)		
#ILEUM	(48)	(48)	(50)
AMYLOIDOSIS			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
PYELONEPHRITIS, ACUTE		2 (4%)	
INFLAMMATION, CHRONIC		2 (4%)	3 (6%)
GLOMERULONEPHRITIS, CHRONIC		2 (4%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	
GLOMERULOSCLEROSIS, NOS		1 (2%)	1 (2%)
#KIDNEY/GLOMERULUS	(50)	(50)	(50)
AMYLOIDOSIS	1 (2%)	1 (2%)	1 (2%)
#KIDNEY/TUBULE	(50)	(50)	(50)
NECROSIS, NOS		1 (2%)	
#U.BLADDER/SUBMUCOSA	(50)	(48)	(48)
INFLAMMATION, CHRONIC	3 (6%)		
#U.BLADDER/SEROSA	(50)	(48)	(48)
INFLAMMATION, ACUTE		1 (2%)	
ENDOCRINE SYSTEM			
#ADRENAL	(48)	(47)	(46)
DEGENERATION, NOS	1 (2%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANGIECTASIS	1 (2%)		
#ADRENAL/CAPSULE	(48)	(47)	(46)
INFLAMMATION, ACUTE	1 (2%)		1 (2%)
HYPERPLASIA, NOS	1 (2%)		
#ADRENAL CORTEX	(48)	(47)	(46)
LIPOIDOSIS		1 (2%)	
#PERIADRENAL TISSUE	(48)	(47)	(46)
STEATITIS			1 (2%)
INFLAMMATION, ACUTE	1 (2%)	1 (2%)	
#THYROID	(48)	(45)	(46)
HYPERPLASIA, FOLLICULAR-CELL	5 (10%)	1 (2%)	3 (7%)
REPRODUCTIVE SYSTEM			
#UTERUS	(50)	(49)	(48)
INFLAMMATION, SUPPURATIVE		1 (2%)	
AMYLOIDOSIS		1 (2%)	
#UTERUS/ENDOMETRIUM	(50)	(49)	(48)
INFLAMMATION, SUPPURATIVE	6 (12%)	3 (6%)	6 (13%)
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
HYPERPLASIA, CYSTIC	35 (70%)	31 (63%)	23 (48%)
#OVARY	(50)	(50)	(45)
CYST, NOS	11 (22%)	13 (26%)	6 (13%)
HEMORRHAGIC CYST	1 (2%)		1 (2%)
INFLAMMATION, SUPPURATIVE	4 (8%)	10 (20%)	14 (31%)
ABSCESS, NOS	1 (2%)		
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
#CEREBRUM	(50)	(50)	(50)
MALACIA		1 (2%)	
SPECIAL SENSE ORGANS			
NONE			

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(50)	(50)
INFLAMMATION, ACUTE		1 (2%)	1 (2%)
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
INFLAMMATION, ACUTE	2 (4%)		
INFLAMMATION, CHRONIC			1 (2%)
*ABDOMINAL CAVITY	(50)	(50)	(50)
INFLAMMATION, ACUTE			2 (4%)
INFLAMMATION, CHRONIC		1 (2%)	
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)		3 (6%)
*PLEURA	(50)	(50)	(50)
INFLAMMATION, ACUTE FOCAL		1 (2%)	
*PERICARDIUM	(50)	(50)	(50)
INFLAMMATION, ACUTE FOCAL			1 (2%)
*MESENTERY	(50)	(50)	(50)
INFLAMMATION, ACUTE		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		
NECROSIS, FAT	2 (4%)		1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
INFLAMMATION, ACUTE		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
OMENTUM			
STEATITIS		1	
INFLAMMATION, ACUTE	2		3
ABSCESS, NOS	1		
INFLAMMATION, ACUTE/CHRONIC		1	
INFLAMMATION, CHRONIC			1
NECROSIS, FAT	1		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	1	1	

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

APPENDIX E

MEAN BODY WEIGHTS OF RATS AND MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS

TABLE E1. MEAN BODY WEIGHTS OF RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS

Weeks on Study	Vehicle Control		Low Dose			High Dose		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
0	163	50	166	101.8	50	164	100.6	50
1	186	50	184	98.9	50	185	99.5	50
2	202	50	200	99.0	50	199	98.5	50
3	218	50	218	100.0	50	216	99.1	50
4	216	50	214	99.1	50	208	96.3	50
5	241	50	239	99.2	50	238	98.8	50
6	252	50	248	98.4	50	249	98.8	50
7	263	50	257	97.7	50	258	98.1	50
8	270	50	280	103.7	50	270	100.0	50
9	284	50	276	97.2	50	277	97.5	50
10	296	50	287	97.0	50	286	96.6	50
11	297	50	291	98.0	50	283	95.3	50
12	307	50	297	96.7	50	293	95.4	50
16	325	50	318	97.8	50	313	96.3	50
20	345	50	335	97.1	50	323	93.6	50
24	363	50	352	97.0	50	342	94.2	50
28	376	50	368	97.9	50	353	93.9	50
32	389	50	381	97.9	50	363	93.3	50
36	403	50	393	97.5	50	375	93.1	50
40	419	50	409	97.6	50	395	94.3	50
44	431	50	423	98.1	49	399	92.6	50
48	430	50	421	97.9	49	398	92.6	50
52	446	49	439	98.4	49	412	92.4	50
56	457	49	448	98.0	49	421	92.1	50
60	461	49	452	98.0	49	423	91.8	50
64	463	49	453	97.8	49	422	91.1	50
68	464	48	459	98.9	49	427	92.0	50
72	459	48	453	98.7	49	419	91.3	49
76	455	47	450	98.9	49	421	92.5	49
80	466	47	450	96.6	48	422	90.6	48
84	467	47	459	98.3	48	428	91.6	48
88	466	47	458	98.3	48	429	92.1	47
92	477	44	459	96.2	47	424	88.9	47
96	472	43	451	95.6	44	419	88.8	43
100	472	43	448	94.9	44	408	86.4	43
105	459	39	444	96.7	42	413	90.0	41
FEMALE								
0	124	50	126	101.6	50	126	101.6	50
1	134	50	133	99.3	50	134	100.0	50
2	143	50	142	99.3	50	142	99.3	50
3	151	50	150	99.3	50	148	98.0	50
4	151	50	150	99.3	50	150	99.3	50
5	161	50	160	99.4	50	161	100.0	50
6	163	50	163	100.0	50	161	98.8	50
7	169	50	166	98.2	50	164	97.0	50
8	173	50	171	98.8	50	168	97.1	50
9	176	50	171	97.2	50	170	96.6	50
10	179	50	176	98.3	50	171	95.5	50
11	182	50	175	96.2	50	174	95.6	50
12	183	50	178	97.3	50	177	96.7	50
16	190	50	186	97.9	50	182	95.8	50
20	201	50	195	97.0	50	190	94.5	50
24	203	50	197	97.0	50	189	93.1	50
28	208	50	203	97.6	50	188	90.4	50
32	216	50	215	99.5	50	194	89.8	50
36	220	50	214	97.3	50	196	89.1	50
40	225	50	223	99.1	50	201	89.3	50
44	233	50	227	97.4	50	205	88.0	49
48	233	50	228	97.9	50	203	87.1	49
52	249	50	242	97.2	50	212	85.1	49
56	259	50	250	96.5	50	218	84.2	49
60	268	50	259	96.6	50	222	82.8	49
64	273	49	264	96.7	50	227	83.2	47
68	283	49	273	96.5	50	232	82.0	46
72	275	49	298	108.4	50	225	81.8	45
76	288	47	279	96.9	50	229	79.5	43
80	295	47	286	96.9	50	234	79.3	40
84	304	46	292	96.1	50	240	78.9	40
88	310	45	295	95.2	49	248	80.0	36
92	314	42	300	95.5	49	247	78.7	34
96	317	40	296	93.4	48	238	75.1	17
100	321	40	305	95.0	46	243	75.7	16
105	321	37	308	96.0	43	252	78.5	16

TABLE E2. MEAN BODY WEIGHTS OF MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS

Weeks on Study	Vehicle Control		Low Dose			High Dose		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
0	25	50	25	100.0	50	25	100.0	50
1	28	50	28	100.0	50	27	96.4	50
2	29	50	29	100.0	50	28	96.6	50
3	29	50	30	103.4	50	29	100.0	50
4	29	50	29	100.0	50	29	100.0	50
5	31	50	31	100.0	50	31	100.0	50
6	32	50	31	96.9	50	30	93.8	50
7	35	50	32	91.4	50	32	91.4	50
8	32	50	32	100.0	50	31	96.9	50
9	33	50	32	97.0	50	32	97.0	50
10	33	50	33	100.0	50	32	97.0	50
11	34	50	33	97.1	50	32	94.1	50
12	34	50	34	100.0	50	33	97.1	50
16	36	50	36	100.0	50	35	97.2	50
20	38	50	37	97.4	48	36	94.7	50
24	38	50	36	94.7	48	37	97.4	50
28	40	50	39	97.5	48	38	95.0	50
32	40	50	40	100.0	48	40	100.0	50
36	41	50	41	100.0	48	40	97.6	50
40	42	50	42	100.0	48	42	100.0	50
44	39	50	41	105.1	48	42	107.7	50
48	43	50	43	100.0	48	42	97.7	50
52	42	50	43	102.4	48	43	102.4	50
56	42	49	43	102.4	46	43	102.4	49
60	45	49	42	93.3	46	43	95.6	49
64	42	47	41	97.6	46	43	102.4	48
68	42	47	41	97.6	45	42	100.0	48
72	43	43	42	97.7	45	44	102.3	47
76	43	41	42	97.7	44	43	100.0	47
80	43	40	41	95.3	44	42	97.7	47
84	44	39	42	95.5	43	43	97.7	46
88	44	39	41	93.2	42	43	97.7	44
92	43	38	41	95.3	41	43	100.0	43
96	44	37	41	93.2	40	43	97.7	43
100	42	36	40	95.2	36	41	97.6	40
104	43	35	41	95.3	33	42	97.7	35
FEMALE								
0	19	50	19	100.0	50	19	100.0	50
1	21	50	21	100.0	50	21	100.0	50
2	22	50	22	100.0	50	23	104.5	50
3	22	50	23	104.5	49	23	104.5	50
4	22	50	22	100.0	49	23	104.5	50
5	23	50	24	104.3	49	24	104.3	50
6	24	50	24	100.0	49	24	100.0	50
7	24	50	24	100.0	49	25	104.2	50
8	24	50	25	104.2	49	25	104.2	50
9	24	50	25	104.2	49	26	108.3	50
10	24	50	26	108.3	49	26	108.3	50
11	26	50	26	100.0	49	26	100.0	50
12	26	50	27	103.8	49	27	103.8	50
16	27	50	29	107.4	49	28	103.7	50
20	29	50	31	106.9	49	29	100.0	50
24	30	50	32	106.7	48	31	103.3	50
28	32	50	34	106.3	48	33	103.1	50
32	33	50	35	106.1	48	34	103.0	50
36	35	50	38	108.6	48	36	102.9	50
40	37	50	38	102.7	48	36	97.3	50
44	35	50	40	114.3	48	37	105.7	50
48	38	50	40	105.3	48	38	100.0	49
52	39	50	40	102.6	48	39	100.0	48
56	38	50	40	105.3	48	38	100.0	48
60	39	50	41	105.1	48	39	100.0	46
64	39	50	41	105.1	48	40	102.6	46
68	38	50	41	107.9	48	38	100.0	46
72	38	50	42	110.5	48	38	100.0	45
76	39	49	42	107.7	45	39	100.0	45
80	40	48	42	105.0	45	39	97.5	42
84	40	45	44	110.0	42	41	102.5	38
88	43	44	45	104.7	38	41	95.3	36
92	44	43	45	102.3	35	42	95.5	34
96	44	42	46	104.5	31	41	93.2	32
100	43	41	46	107.0	29	43	100.0	28
104	41	38	46	112.2	29	39	95.1	26

APPENDIX F

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

TABLE F1. HISTORICAL INCIDENCE OF LIVER TUMORS IN MALE B6C3F1 MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Adenoma	Carcinoma	Adenoma or Carcinoma
RATES AT E.G. & G. MASON RESEARCH			
1,2-Dichloropropane	7/50 (14%)	11/50 (22%)	18/50 (36%)
Bis(2-Chloro-1-methylethyl) Ether	8/50 (16%)	5/50 (10%)	13/50 (26%)
Diglycidyl Resorcinol Ether	7/49 (14%)	7/49 (14%)	13/49 (26%)
Total	22/149 (14.7%)	23/149 (15.4%)	44/149 (29.5%)
SD *(b)*	1.15%	6.11%	5.77%
RATES AT NTP TESTING LABORATORIES *(c)*			
Total	101/884 (11.4%)	182/884 (20.6%)	273/884 (30.9%)
SD *(b)*	5.63%	7.59%	8.64%
Overall Historical Range			
High	10/48 (21%)	18/50 (36%)	23/50 (46%)
Low	0/50 (0%)	4/48 (8%)	7/50 (14%)

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total ▫ combined historical incidence from six laboratories: Battelle, Gulf South, Litton, Mason, Papanicolaou, and Southern.

TABLE F2. HISTORICAL INCIDENCE OF LIVER TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Adenoma	Carcinoma	Adenoma or Carcinoma
RATES AT E.G. & G. MASON RESEARCH			
1,2-Dichloropropane	0/50 (0%)	1/50 (2%)	1/50 (2%)
Bis(2-Chloro-1-methylethyl) Ether	5/50 (10%)	2/50 (4%)	7/50 (14%)
Diglycidyl Resorcinol Ether	3/48 (6%)	0/48 (0%)	3/48 (6%)
Total	8/148 (5.4%)	3/148 (2.0%)	11/148 (7.4%)
SD (b)	5.03%	2.00%	6.11%
RATES AT NTP TESTING LABORATORIES *(c)*			
Total	39/978 (4.0%)	29/978 (3.0%)	67/978 (6.9%)
SD *(b)*	2.45%	1.80%	3.26%
Overall Historical Range			
High	5/50 (10%)	3/49 (6%)	7/50 (14%)
Low	0/50 (0%)	0/50 (0%)	1/50 (2%)

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total = combined historical incidence from six laboratories: Battelle, Gulf South, Litton, Mason, Papanicolaou, and Southern.

TABLE F3. HISTORICAL INCIDENCE OF STOMACH TUMORS IN FEMALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Incidence	Site	Diagnosis
RATES AT E.G. & G. MASON RESEARCH			
1,2-Dichloropropane	0/50 (0%)	-	-
Diglycidyl Resorcinol Ether	0/49 (0%)	-	-
	0/50 (0%)		
Total	0/149 (0%)	-	-
SD *(b)*	0.00%		
RATES AT NTP TESTING LABORATORIES *(c)*			
Total	3/870 (0.3%)	*(d)*	*(d)*
SD *(b)*	0.77%		
Overall Historical Range			
High	1/47 (2%)		
Low	0/50 (0%)		

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total ▫ combined historical incidence from six laboratories: Battelle, Gulf South, Litton, Mason, Papanicolaou, and Southern.
(d) Tumor sites: stomach, NOS; forestomach. Individual tumor totals: 2 squamous cell papillomas; 1 squamous cell carcinoma.

TABLE F4. HISTORICAL INCIDENCE OF STOMACH TUMORS IN MALE B6C3F$_1$ MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Incidence	Site	Diagnosis
RATES AT E.G. & G. MASON RESEARCH			
1,2-Dichloropropane	0/50 (0%)	-	-
Bis(2-Chloro-1-methylethyl) Ether	0/49 (0%)	-	-
Diglycidyl Resorcinol Ether	0/47 (0%)	-	-
Total	0/146 (0%)	-	-
SD *(b)*	0.00%		
RATES AT NTP TESTING LABORATORIES *(c)*			
Total	2/855 (0.2%)	*(d)*	*(d)*
SD *(b)*	0.65%		
Overall Historical Range			
High	1/48 (2%)		
Low	0/50 (0%)		

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total = combined historical incidence from six laboratories: Battelle, Gulf South, Litton, Mason, Papanicolaou, and Southern.
(d) Tumor sites: stomach, NOS; forestomach. Individual tumor totals: 1 squamous cell papilloma; 1 squamous cell carcinoma.

TABLE F5. HISTORICAL INCIDENCE OF STOMACH TUMORS IN FEMALE B6C3F1 MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Incidence	Site	Diagnosis
RATES AT E.G. & G. MASON RESEARCH			
1,2-Dichloropropane	0/50 (0%)	—	—
Bis(2-Chloro-1-methylethyl) Ether	0/50 (0%)	—	—
Diglycidyl Resorcinol Ether	0/47 (0%)	—	—
Total	0/147 (0%)		
SD *(b)*	0.00%		
RATES AT NTP TESTING LABORATORIES *(c)*			
Total	3/879 (0.3%)	*(d)*	*(d)*
SD *(b)*	2.54%		
Overall Historical Range			
High	2/19 (11%)		
Low	0/50 (0%)		

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total ▫ combined historical incidence from six laboratories: Battelle, Gulf South, Litton, Mason, Papanicolaou, and Southern.
(d) Tumor sites: stomach, NOS; forestomach. Individual tumor totals: 3 squamous cell papillomas.

TABLE F6. HISTORICAL INCIDENCE OF THYROID FOLLICULAR CELL TUMORS IN FEMALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Adenoma	Carcinoma	Adenoma or Carcinoma
RATES AT E.G. & G. MASON RESEARCH			
1,2-Dichloropropane	0/50 (0%)	0/50 (0%)	0/50 (0%)
Diglycidyl Resorcinol Ether	1/50 (2%)	0/50 (0%)	1/50 (2%)
	0/50 (0%)	0/50 (0%)	0/50 (0%)
Total	1/150 (0.67%)	0/150 (0%)	1/150 (0.67%)
SD *(b)*	1.15%	0.00%	1.15%
RATES AT NTP TESTING LABORATORIES *(c)*			
Total	2/859 (0.2%)	2/859 (0.2%)	4/859 (0.5%)
SD *(b)*	0.65%	0.65%	0.86%
Overall Historical Range			
High	1/50 (2%)	1/50 (2%)	1/50 (2%)
Low	0/50 (0%)	0/50 (0%)	0/50 (0%)

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total= combined historical incidence from six laboratories: Battelle, Gulf South, Litton, Mason, Papanicolaou, and Southern.

TABLE F7. HISTORICAL INCIDENCE OF THYROID FOLLICULAR CELL TUMORS IN FEMALE B6C3F1 MICE RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Adenoma	Carcinoma	Adenoma or Carcinoma
RATES AT E.G. & G. MASON RESEARCH			
1,2-Dichloropropane	1/48 (2%)	0/48 (0%)	1/48 (2%)
Bis (2-Chloro-1-methylethyl) Ether	0/46 (0%)	0/46 (0%)	0/46 (0%)
Diglycidyl Resorcinol Ether	1/45 (2%)	0/45 (0%)	1/45 (2%)
Total (Mason)	2/139 (1%)	0/139 (0%)	2/139 (1%)
SD *(b)*	1.15%	0.00%	1.15%
RATES AT NTP TESTING LABORATORIES *(c)*			
Total	28/818 (3.4%)	3/818 (0.4%)	31/818 (3.8%)
SD *(b)*	2.88%	0.75%	2.84%
Overall Historical Range			
High	5/50 (10%)	1/45 (2%)	5/50 (10%)
Low	0/46 (0%)	0/50 (0%)	0/46 (0%)

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total = combined historical incidence from six laboratories: Battelle, Gulf South, Litton, Mason, Papanicolaou, and Southern.

TABLE F8. HISTORICAL INCIDENCE OF MAMMARY GLAND TUMORS IN FEMALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Adenocarcinoma (NOS)	Fibroadenoma
RATES AT E.G. & G. MASON RESEARCH		
1,2-Dichloropropane	1/50 (2%)	15/50 (30%)
Diglycidyl Resorcinol Ether	2/50 (4%)	18/50 (36%)
	0/50 (0%)	17/50 (34%
Total	3/150 (2%)	50/150 (33%)
SD *(b)*	2.00%	3.06%
RATES AT NTP TESTING LABORATORIES *(c)*		
Total	11/895 (1.2%)	203/895 (22.7%)
SD *(b)*	1.55%	9.79%
Overall Historical Range		
High	2/49 (4%)	18/50 (36%)
Low	0/50 (0%)	2/48 (4%)

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total = combined historical incidence from seven laboratories: Battelle, Gulf South, Hazleton, Litton, Mason, Papanicolaou, and Southern.

TABLE F9. HISTORICAL INCIDENCE OF PANCREATIC ISLET TUMORS IN MALE F344/N RATS RECEIVING CORN OIL BY GAVAGE *(a)*

Chemical	Islet Cell Adenoma	Islet Cell Carcinoma
RATES AT E.G. & G. MASON RESEARCH		
1,2-Dichloropropane	4/48 (8%)	0/48 (0%)
Diglycidyl Resorcinol Ether	2/49 (4%)	3/49 (6%)
	3/49 (6%)	1/49 (2%)
Total	9/146 (6.16%)	4/146 (2.74%)
SD *(b)*	2.00%	3.06%
RATES AT NTP TESTING LABORATORIES *(b)*		
Total	38/876 (4.3%)	22/876 (2.5%)
SD *(b)*	2.98%	2.53%
Overall Historical Range		
High	6/48 (12%)	4/49 (8%)
Low	0/50 (0%)	0/48 (0%)

(a) Data as of January 5, 1983 for studies of at least 104 weeks.
(b) Standard deviation.
(c) Total = combined historical incidence from seven laboratories: Battelle, Gulf South, Hazleton, Litton, Mason, Papanicolaou, and Southern.

APPENDIX G

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

TABLE G1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	62 mg/kg	125 mg/kg
Skin: Squamous Cell Papilloma			
Tumor Rates			
Overall *(a)*	2/50 (4%)	3/50 (6%)	1/50 (2%)
Adjusted *(b)*	5.1%	6.8%	2.4%
Terminal *(c)*	2/39 (5%)	2/42 (5%)	1/41 (2%)
Statistical Tests *(d)*			
Life Table	P=0.382N	P=0.531	P=0.483N
Incidental Tumor Test	P=0.383N	P=0.527	P=0.483N
Cochran-Armitage Trend Test	P=0.399N		
Fisher Exact Test		P=0.500	P=0.500N
Integumentary System: Squamous Cell Carcinoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	2/50 (4%)	0/50 (0%)
Adjusted *(b)*	7.1%	4.6%	0.0%
Terminal *(c)*	2/39 (5%)	1/42 (2%)	0/41 (0%)
Statistical Tests *(d)*			
Life Table	P=0.079N	P=0.476N	P=0.116N
Incidental Tumor Test	P=0.102N	P=0.540N	P=0.155N
Cochran-Armitage Trend Test	P=0.082N		
Fisher Exact Test		P=0.500N	P=0.121N
Integumentary System: Squamous Cell Papilloma or Carcinoma			
Tumor Rates			
Overall *(a)*	5/50 (10%)	5/50 (10%)	1/50 (2%)
Adjusted *(b)*	12.1%	11.2%	2.4%
Terminal *(c)*	4/39 (10%)	3/42 (7%)	1/41 (2%)
Statistical Tests *(d)*			
Life Table	P=0.084N	P=0.590N	P=0.095N
Incidental Tumor Test	P=0.098N	P=0.620	P=0.120N
Cochran-Armitage Trend Test	P=0.090N		
Fisher Exact Test		P=0.630	P=0.102N
Subcutaneous Tissue: Fibroma			
Tumor Rates			
Overall *(a)*	6/50 (12%)	6/50 (12%)	6/50 (12%)
Adjusted *(b)*	14.4%	14.3%	14.6%
Terminal *(c)*	4/39 (10%)	6/42 (14%)	6/41 (15%)
Statistical Tests *(d)*			
Life Table	P=0.531N	P=0.573N	P=0.591N
Incidental Tumor Test	P=0.529N	P=0.577N	P=0.591N
Cochran-Armitage Trend Test	P=0.562		
Fisher Exact Test		P=0.620	P=0.620
Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Tumor Rates			
Overall *(a)*	7/50 (14%)	7/50 (14%)	6/50 (12%)
Adjusted *(b)*	16.8%	16.7%	14.6%
Terminal *(c)*	5/39 (13%)	7/42 (17%)	6/41 (15%)
Statistical Tests *(d)*			
Life Table	P=0.408N	P=0.560N	P=0.469N
Incidental Tumor Test	P=0.407N	P=0.563N	P=0.468N
Cochran-Armitage Trend Test	P=0.442N		
Fisher Exact Test		P=0.613	P=0.500N

TABLE G1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	62 mg/kg	125 mg/kg
Hematopoietic System: Myelomonocytic Leukemia			
Tumor Rates			
Overall *(a)*	7/50 (14%)	6/50 (12%)	6/50 (12%)
Adjusted *(b)*	16.7%	13.2%	14.1%
Terminal *(c)*	5/39 (13%)	4/42 (10%)	5/41 (12%)
Statistical Tests *(d)*			
Life Table	P=0.413N	P=0.453N	P=0.471N
Incidental Tumor Test	P=0.444N	P=0.619	P=0.471N
Cochran-Armitage Trend Test	P=0.441N		
Fisher Exact Test		P=0.500N	P=0.500N
Hematopoietic System: Leukemia			
Tumor Rates			
Overall *(a)*	8/50 (16%)	6/50 (12%)	6/50 (12%)
Adjusted *(b)*	18.5%	13.2%	14.1%
Terminal *(c)*	5/39 (13%)	4/42 (10%)	5/41 (12%)
Statistical Tests *(d)*			
Life Table	P=0.308N	P=0.347N	P=0.364N
Incidental Tumor Test	P=0.334N	P=0.561N	P=0.360N
Cochran-Armitage Trend Test	P=0.330N		
Fisher Exact Test		P=0.387N	P=0.387N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(a)*	8/50 (16%)	8/50 (16%)	6/50 (12%)
Adjusted *(b)*	18.5%	17.3%	14.1%
Terminal *(c)*	5/39 (13%)	5/42 (12%)	5/41 (12%)
Statistical Tests *(d)*			
Life Table	P=0.313N	P=0.554N	P=0.364N
Incidental Tumor Test	P=0.338N	P=0.447	P=0.360N
Cochran-Armitage Trend Test	P=0.336N		
Fisher Exact Test		P=0.607	P=0.387N
Liver: Neoplastic Nodule or Carcinoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	3/50 (6%)	2/50 (4%)
Adjusted *(b)*	7.3%	7.1%	4.9%
Terminal *(c)*	2/39 (5%)	3/42 (7%)	2/41 (5%)
Statistical Tests *(d)*			
Life Table	P=0.392N	P=0.630N	P=0.482N
Incidental Tumor Test	P=0.392N	P=0.633N	P=0.482N
Cochran-Armitage Trend Test	P=0.412N		
Fisher Exact Test		P=0.661	P=0.500N
Pituitary: Adenoma			
Tumor Rates			
Overall *(a)*	19/50 (38%)	12/48 (25%)	15/47 (32%)
Adjusted *(b)*	47.4%	29.3%	36.9%
Terminal *(c)*	18/39 (46%)	12/41 (29%)	13/38 (34%)
Statistical Tests *(d)*			
Life Table	P=0.242N	P=0.065N	P=0.286N
Incidental Tumor Test	P=0.261N	P=0.065N	P=0.312N
Cochran-Armitage Trend Test	P=0.291N		
Fisher Exact Test		P=0.122N	P=0.340N

TABLE G1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	62 mg/kg	125 mg/kg
Pituitary: Carcinoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	3/48 (6%)	3/47 (6%)
Adjusted *(b)*	7.1%	7.3%	7.9%
Terminal *(c)*	1/39 (3%)	3/41 (7%)	3/38 (8%)
Statistical Tests *(d)*			
Life Table	P=0.576	P=0.640N	P=0.656
Incidental Tumor Test	P=0.572	P=0.518	P=0.653
Cochran-Armitage Trend Test	P=0.553		
Fisher Exact Test		P=0.641	P=0.631
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	22/50 (44%)	15/48 (31%)	18/47 (38%)
Adjusted *(b)*	52.2%	36.6%	44.5%
Terminal *(c)*	19/39 (49%)	15/41 (37%)	16/38 (42%)
Statistical Tests *(d)*			
Life Table	P=0.257N	P=0.074N	P=0.298N
Incidental Tumor Test	P=0.277N	P=0.104N	P=0.324N
Cochran-Armitage Trend Test	P=0.313N		
Fisher Exact Test		P=0.137N	P=0.358N
Adrenal: Cortical Adenoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	2/49 (4%)	0/50 (0%)
Adjusted *(b)*	7.7%	4.9%	0.0%
Terminal *(c)*	3/39 (8%)	2/41 (5%)	0/41 (0%)
Statistical Tests *(d)*			
Life Table	P=0.074N	P=0.477N	P=0.112N
Incidental Tumor Test	P=0.074N	P=0.477N	P=0.112N
Cochran-Armitage Trend Test	P=0.083N		
Fisher Exact Test		P=0.510N	P=0.121N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(a)*	11/50 (22%)	5/49 (10%)	5/50 (10%)
Adjusted *(b)*	28.2%	11.7%	11.8%
Terminal *(c)*	11/39 (28%)	4/41 (10%)	4/41 (10%)
Statistical Tests *(d)*			
Life Table	P=0.046N	P=0.069N	P=0.071N
Incidental Tumor Test	P=0.046N	P=0.071N	P=0.071N
Cochran-Armitage Trend Test	P=0.057N		
Fisher Exact Test		P=0.093N	P=0.086N
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant			
Tumor Rates			
Overall *(a)*	11/50 (22%)	5/49 (10%)	7/50 (14%)
Adjusted *(b)*	28.2%	11.7%	16.6%
Terminal *(c)*	11/39 (28%)	4/41 (10%)	6/41 (15%)
Statistical Tests *(d)*			
Life Table	P=0.141N	P=0.069N	P=0.185N
Incidental Tumor Test	P=0.141N	P=0.071N	P=0.185N
Cochran-Armitage Trend Test	P=0.166N		
Fisher Exact Test		P=0.093N	P=0.218N

TABLE G1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	62 mg/kg	125 mg/kg
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(a)*	1/49 (2%)	4/49 (8%)	0/50 (0%)
Adjusted *(b)*	2.6%	9.4%	0.0%
Terminal *(c)*	1/39 (3%)	3/41 (7%)	0/41 (0%)
Statistical Tests *(d)*			
Life Table	P=0.375N	P=0.195	P=0.490N
Incidental Tumor Test	P=0.374N	P=0.194	P=0.490N
Cochran-Armitage Trend Test	P=0.383N		
Fisher Exact Test		P=0.181	P=0.495N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	2/49 (4%)	4/49 (8%)	1/50 (2%)
Adjusted *(b)*	5.1%	9.4%	2.1%
Terminal *(c)*	2/39 (5%)	3/41 (7%)	0/41 (0%)
Statistical Tests *(d)*			
Life Table	P=0.391N	P=0.359	P=0.486N
Incidental Tumor Test	P=0.363N	P=0.358	P=0.442N
Cochran-Armitage Trend Test	P=0.396N		
Fisher Exact Test		P=0.339	P=0.492N
Pancreatic Islets: Islet Cell Adenoma			
Tumor Rates			
Overall *(a)*	4/48 (8%)	1/50 (2%)	3/50 (6%)
Adjusted *(b)*	10.5%	2.4%	6.9%
Terminal *(c)*	4/38 (11%)	1/42 (2%)	2/41 (5%)
Statistical Tests *(d)*			
Life Table	P=0.382N	P=0.151N	P=0.461N
Incidental Tumor Test	P=0.385N	P=0.151N	P=0.465N
Cochran-Armitage Trend Test	P=0.396N		
Fisher Exact Test		P=0.168N	P=0.477N
Pancreatic Islets: Islet Cell Carcinoma			
Tumor Rates			
Overall *(a)*	0/48 (0%)	0/50 (0%)	3/50 (6%)
Adjusted *(b)*	0.0%	0.0%	7.3%
Terminal *(c)*	0/38 (3%)	0/42 (0%)	3/41 (7%)
Statistical Tests *(d)*			
Life Table	P=0.040N	*(e)*	P=0.135
Incidental Tumor Test	P=0.040N	*(e)*	P=0.135
Cochran-Armitage Trend Test	P=0.039N		
Fisher Exact Test		*(e)*	P=0.129
Pancreatic Islets: Islet Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	4/48 (8%)	1/50 (2%)	6/50 (12%)
Adjusted *(b)*	10.5%	2.4%	14.1%
Terminal *(c)*	4/38 (11%)	1/42 (2%)	5/41 (12%)
Statistical Tests *(d)*			
Life Table	P=0.314N	P=0.151N	P=0.416
Incidental Tumor Test	P=0.312N	P=0.151N	P=0.413
Cochran-Armitage Trend Test	P=0.299N		
Fisher Exact Test		P=0.168N	P=0.397

TABLE G1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	62 mg/kg	125 mg/kg
Preputial Gland: Carcinoma			
Tumor Rates			
Overall *(a)*	2/50 (4%)	2/50 (4%)	4/50 (8%)
Adjusted *(b)*	5.1%	4.8%	9.8%
Terminal *(c)*	2/39 (5%)	2/42 (5%)	4/41 (10%)
Statistical Tests *(d)*			
Life Table	P=0.269	P=0.668N	P=0.360
Incidental Tumor Test	P=0.269	P=0.668N	P=0.360
Cochran-Armitage Trend Test	P=0.252		
Fisher Exact Test		P=0.691	P=0.339
Preputial Gland: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	2/50 (4%)	2/50 (4%)	5/50 (10%)
Adjusted *(b)*	5.1%	4.8%	12.2%
Terminal *(c)*	2/39 (5%)	2/42 (5%)	5/41 (12%)
Statistical Tests *(d)*			
Life Table	P=0.158	P=0.668N	P=0.236
Incidental Tumor Test	P=0.158	P=0.668N	P=0.236
Cochran-Armitage Trend Test	P=0.146		
Fisher Exact Test		P=0.691	P=0.218
Preputial Gland or Prepuce: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	2/50 (4%)	2/50 (4%)	6/50 (12%)
Adjusted *(b)*	5.1%	4.8%	14.1%
Terminal *(c)*	2/39 (5%)	2/42 (5%)	5/41 (12%)
Statistical Tests *(d)*			
Life Table	P=0.090	P=0.668N	P=0.152
Incidental Tumor Test	P=0.092	P=0.668N	P=0.151
Cochran-Armitage Trend Test	P=0.080		
Fisher Exact Test		P=0.691	P=0.134
Testis: Interstitial Cell Tumor			
Tumor Rates			
Overall *(a)*	45/50 (90%)	46/47 (98%)	46/50 (92%)
Adjusted *(b)*	93.7%	100.0%	95.8%
Terminal *(c)*	36/39 (92%)	40/40 (100%)	39/41 (95%)
Statistical Tests *(d)*			
Life Table	P=0.455N	P=0.576N	P=0.505N
Incidental Tumor Test	P=0.546N	P=0.093	P=0.616N
Cochran-Armitage Trend Test	P=0.425		
Fisher Exact Test		P=0.117	P=0.500
All Sites: Mesothelioma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	2/50 (4%)	3/50 (6%)
Adjusted *(b)*	6.7%	4.8%	7.3%
Terminal *(c)*	1/39 (3%)	2/42 (5%)	3/41 (7%)
Statistical Tests *(d)*			
Life Table	P=0.569N	P=0.476N	P=0.644N
Incidental Tumor Test	P=0.561	P=0.540N	P=0.626
Cochran-Armitage Trend Test	P=0.588		
Fisher Exact Test		P=0.500N	P=0.661

TABLE G1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	62 mg/kg	125 mg/kg

(a) Number of tumor bearing animals/number of animals examined at the site.

(b) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.

(c) Observed tumor incidence at terminal kill.

(d) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).

(e) Not significant; no tumors were observed in dosed or control groups.

TABLE G2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	125 mg/kg	250 mg/kg
Hematopoietic System: Myelomonocytic Leukemia			
Tumor Rates			
Overall *(a)*	9/50 (18%)	11/50 (22%)	5/50 (10%)
Adjusted *(b)*	21.1%	22.6%	19.3%
Terminal *(c)*	4/37 (11%)	6/43 (14%)	2/16 (13%)
Statistical Tests *(d)*			
Life Table	P=0.504	P=0.543	P=0.613
Incidental Tumor Test	P=0.051N	P=0.325	P=0.101N
Cochran-Armitage Trend Test	P=0.174N		
Fisher Exact Test		P=0.401	P=0.194N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(a)*	10/50 (20%)	11/50 (22%)	7/50 (14%)
Adjusted *(b)*	22.7%	22.6%	26.6%
Terminal *(c)*	4/37 (11%)	6/43 (14%)	3/16 (19%)
Statistical Tests *(d)*			
Life Table	P=0.373	P=0.545N	P=0.452
Incidental Tumor Test	P=0.076N	P=0.325	P=0.158N
Cochran-Armitage Trend Test	P=0.261N		
Fisher Exact Test		P=0.500	P=0.298N
Pituitary: Adenoma			
Tumor Rates			
Overall *(a)*	16/49 (33%)	26/50 (52%)	10/46 (22%)
Adjusted *(b)*	40.6%	55.3%	46.9%
Terminal *(c)*	14/37 (38%)	22/43 (51%)	6/16 (38%)
Statistical Tests *(d)*			
Life Table	P=0.157	P=0.122	P=0.312
Incidental Tumor Test	P=0.453N	P=0.093	P=0.503N
Cochran-Armitage Trend Test	P=0.172N		
Fisher Exact Test		P=0.040	P=0.168N
Pituitary: Carcinoma			
Tumor Rates			
Overall *(a)*	3/49 (6%)	2/50 (4%)	0/46 (0%)
Adjusted *(b)*	8.1%	4.7%	0.0%
Terminal *(c)*	3/37 (8%)	2/43 (5%)	0/16 (0%)
Statistical Tests *(d)*			
Life Table	P=0.183N	P=0.431N	P=0.301N
Incidental Tumor Test	P=0.183N	P=0.431N	P=0.301N
Cochran-Armitage Trend Test	P=0.089N		
Fisher Exact Test		P=0.490N	P=0.133N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	19/49 (39%)	28/50 (56%)	10/46 (22%)
Adjusted *(b)*	48.3%	59.6%	46.9%
Terminal *(c)*	17/37 (46%)	24/43 (56%)	6/16 (38%)
Statistical Tests *(d)*			
Life Table	P=0.292	P=0.187	P=0.484
Incidental Tumor Test	P=0.282N	P=0.151	P=0.323N
Cochran-Armitage Trend Test	P=0.062N		
Fisher Exact Test		P=0.065	P=0.057N

TABLE G2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	125 mg/kg	250 mg/kg
Adrenal: Cortical Adenoma			
Tumor Rates			
Overall *(a)*	5/49 (10%)	2/50 (4%)	4/50 (8%)
Adjusted *(b)*	13.9%	4.7%	14.7%
Terminal *(c)*	5/36 (14%)	2/43 (5%)	1/16 (6%)
Statistical Tests *(d)*			
Life Table	P=0.431	P=0.150N	P=0.402
Incidental Tumor Test	P=0.510N	P=0.150N	P=0.639N
Cochran-Armitage Trend Test	P=0.413N		
Fisher Exact Test		P=0.210N	P=0.487N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(a)*	2/49 (4%)	3/50 (6%)	1/50 (2%)
Adjusted *(b)*	4.6%	7.0%	6.2%
Terminal *(c)*	0/36 (0%)	3/43 (7%)	1/16 (6%)
Statistical Tests *(d)*			
Life Table	P=0.585	P=0.566	P=0.706N
Incidental Tumor Test	P=0.424N	P=0.442	P=0.388N
Cochran-Armitage Trend Test	P=0.391N		
Fisher Exact Test		P=0.509	P=0.492N
Thyroid: C-Cell Carcinoma			
Tumor Rates			
Overall *(a)*	1/50 (2%)	3/49 (6%)	0/44 (0%)
Adjusted *(b)*	2.7%	7.1%	0.0%
Terminal *(c)*	1/37 (3%)	3/42(7%)	0/14 (0%)
Statistical Tests *(d)*			
Life Table	P=0.639N	P=0.351	P=0.693N
Incidental Tumor Test	P=0.639N	P=0.351	P=0.693N
Cochran-Armitage Trend Test	P=0.418N		
Fisher Exact Test		P=0.301	P=0.532N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	1/50 (2%)	3/49 (6%)	1/44(2%)
Adjusted *(b)*	2.7%	7.1%	3.3%
Terminal *(c)*	1/37 (3%)	3/42 (7%)	0/14 (0%)
Statistical Tests *(d)*			
Life Table	P=0.356	P=0.351	P=0.616
Incidental Tumor Test	P=0.474	P=0.351	P=0.778N
Cochran-Armitage Trend Test	P=0.565		
Fisher Exact Test		P=0.301	P=0.720
Mammary Gland: Adenocarcinoma			
Tumor Rates			
Overall *(a)*	1/50 (2%)	2/50 (4%)	5/50 (10%)
Adjusted *(b)*	2.7%	4.7%	26.7%
Terminal *(c)*	1/37 (3%)	2/43 (5%)	4/16 (25%)
Statistical Tests *(d)*			
Life Table	P=0.005	P=0.552	P=0.012
Incidental Tumor Test	P=0.011	P=0.552	P=0.018
Cochran-Armitage Trend Test	P=0.060		
Fisher Exact Test		P=0.500	P=0.102

TABLE G2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	125 mg/kg	250 mg/kg
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(a)*	15/50 (30%)	20/50 (40%)	7/50 (14%)
Adjusted *(b)*	39.4%	46.5%	37.0%
Terminal *(c)*	14/37 (38%)	20/43 (47%)	5/16 (31%)
Statistical Tests *(d)*			
Life Table	P=0.441	P=0.381	P=0.561
Incidental Tumor Test	P=0.490N	P=0.383	P=0.406N
Cochran-Armitage Trend Test	P=0.047N		
Fisher Exact Test		P=0.201	P=0.045N
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(a)*	10/50 (20%)	17/49 (35%)	11/50 (22%)
Adjusted *(b)*	25.1%	37.5%	45.6%
Terminal *(c)*	8/37 (22%)	14/42 (33%)	6/16 (38%)
Statistical Tests *(d)*			
Life Table	P=0.024	P=0.174	P=0.051
Incidental Tumor Test	P=0.253	P=0.113	P=0.256
Cochran-Armitage Trend Test	P=0.454		
Fisher Exact Test		P=0.078	P=0.500
Uterus: Endometrial Stromal Polyp or Sarcoma			
Tumor Rates			
Overall *(a)*	10/50 (20%)	18/49 (37%)	11/50 (22%)
Adjusted *(b)*	25.1%	38.9%	45.6%
Terminal *(c)*	8/37 (22%)	14/42 (33%)	6/16 (38%)
Statistical Tests *(d)*			
Life Table	P=0.023	P=0.133	P=0.051
Incidental Tumor Test	P=0.291	P=0.079	P=0.256
Cochran-Armitage Trend Test	P=0.455		
Fisher Exact Test		P=0.052	P=0.500

(a) Number of tumor bearing animals/number of animals examined at the site.

(b) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.

(c) Observed tumor incidence at terminal kill.

(d) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).

TABLE G3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	125 mg/kg	250 mg/kg
Subcutaneous Tissue: Fibrosarcoma			
Tumor Rates			
Overall *(a)*	4/50 (8%)	3/50 (6%)	1/50 (2%)
Adjusted *(b)*	11.4%	9.1%	2.3%
Terminal *(c)*	4/35 (11%)	3/33 (9%)	0/35 (0%)
Statistical Tests *(d)*			
Life Table	P=0.130N	P=0.533N	P=0.172N
Incidental Tumor Test	P=0.108N	P=0.533N	P=0.127N
Cochran-Armitage Trend Test	P=0.133N		
Fisher Exact Test		P=0.500N	P=0.181N
Subcutaneous Tissue: All Sarcoma			
Tumor Rates			
Overall *(a)*	4/50 (8%)	3/50 (6%)	3/50 (6%)
Adjusted *(b)*	11.4%	9.1%	7.5%
Terminal *(c)*	4/35 (11%)	3/33 (9%)	1/35 (3%)
Statistical Tests *(d)*			
Life Table	P=0.410N	P=0.553N	P=0.482N
Incidental Tumor Test	P=0.338N	P=0.533N	P=0.357N
Cochran-Armitage Trend Test	P=0.421N		
Fisher Exact Test		P=0.500N	P=0.500N
Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Tumor Rates			
Overall *(a)*	6/50 (12%)	4/50 (8%)	1/50 (2%)
Adjusted *(b)*	17.1%	12.1%	2.3%
Terminal *(c)*	6/35 (17%)	4/33 (12%)	0/35 (0%)
Statistical Tests *(d)*			
Life Table	P=0.041N	P=0.405N	P=0.056N
Incidental Tumor Test	P=0.033N	P=0.405N	P=0.039N
Cochran-Armitage Trend Test	P=0.042N		
Fisher Exact Test		P=0.370N	P=0.056N
Skin or Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Tumor Rates			
Overall *(a)*	7/50 (14%)	4/50 (8%)	1/50 (2%)
Adjusted *(b)*	20.0%	12.1%	2.3%
Terminal *(c)*	7/35 (20%)	4/33 (12%)	0/35 (0%)
Statistical Tests *(d)*			
Life Table	P=0.021N	P=0.292N	P=0.031N
Incidental Tumor Test	P=0.016N	P=0.292N	P=0.021N
Cochran-Armitage Trend Test	P=0.021N		
Fisher Exact Test		P=0.262N	P=0.030N
***Lung*: Alveolar/Bronchiolar Adenoma**			
Tumor Rates			
Overall *(a)*	9/50 (18%)	8/50 (16%)	9/50 (18%)
Adjusted *(b)*	24.7%	23.2%	23.2%
Terminal *(c)*	8/35 (23%)	7/33 (21%)	6/35 (17%)
Statistical Tests *(d)*			
Life Table	P=0.533N	P=0.539N	P=0.582N
Incidental Tumor Test	P=0.489N	P=0.545N	P=0.531N
Cochran-Armitage Trend Test	P=0.553		
Fisher Exact Test		P=0.500N	P=0.602

TABLE G3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	125 mg/kg	250 mg/kg
Lung: Alveolar/Bronchiolar Carcinoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	0/50 (0%)	3/50 (6%)
Adjusted *(b)*	8.6%	0.0%	8.6%
Terminal *(c)*	3/35 (9%)	0/33 (0%)	3/35 (9%)
Statistical Tests *(d)*			
Life Table	P=0.600	P=0.131N	P=0.664
Incidental Tumor Test	P=0.600	P=0.131N	P=0.664
Cochran-Armitage Trend Test	P=0.601		
Fisher Exact Test		P=0.121N	P=0.661
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	11/50 (22%)	8/50 (16%)	12/50 (24%)
Adjusted *(b)*	30.3%	23.2%	31.1%
Terminal *(c)*	10/35 (29%)	7/33 (21%)	9/35 (26%)
Statistical Tests *(d)*			
Life Table	P=0.469	P=0.342N	P=0.518
Incidental Tumor Test	P=0.510	P=0.345N	P=0.568
Cochran-Armitage Trend Test	P=0.451		
Fisher Exact Test		P=0.306N	P=0.500
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Tumor Rates			
Overall *(a)*	0/50 (0%)	4/50 (8%)	3/50 (6%)
Adjusted *(b)*	0.0%	10.7%	7.5%
Terminal *(c)*	0/35 (0%)	2/33 (6%)	1/35 (3%)
Statistical Tests *(d)*			
Life Table	P=0.136	P=0.067	P=0.132
Incidental Tumor Test	P=0.143	P=0.122	P=0.094
Cochran-Armitage Trend Test	P=0.118		
Fisher Exact Test		P=0.059	P=0.121
Hematopoietic System: Lymphoma, All Malignant			
Tumor Rates			
Overall *(a)*	8/50 (16%)	11/50 (22%)	8/50 (16%)
Adjusted *(b)*	19.3%	25.5%	20.6%
Terminal *(c)*	3/35 (9%)	4/33 (12%)	5/35 (14%)
Statistical Tests *(d)*			
Life Table	P=0.512N	P=0.321	P=0.564N
Incidental Tumor Test	P=0.456	P=0.215	P=0.562
Cochran-Armitage Trend Test	P=0.552		
Fisher Exact Test		P=0.306	P=0.607
Circulatory System: Hemangiosarcoma			
Tumor Rates			
Overall *(a)*	2/50 (4%)	3/50 (6%)	2/50 (4%)
Adjusted *(b)*	5.6%	7.7%	5.2%
Terminal *(c)*	1/35 (3%)	1/33 (3%)	1/35 (3%)
Statistical Tests *(d)*			
Life Table	P=0.565N	P=0.503	P=0.679N
Incidental Tumor Test	P=0.399N	P=0.675N	P=0.520N
Cochran-Armitage Trend Test	P=0.594		
Fisher Exact Test		P=0.500	P=0.691

TABLE G3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	125 mg/kg	250 mg/kg
Liver: Adenoma			
Tumor Rates			
Overall *(a)*	7/50 (14%)	10/50 (20%)	17/50 (34%)
Adjusted *(b)*	20.0%	28.8%	45.5%
Terminal *(c)*	7/35 (20%)	9/33 (27%)	15/35 (43%)
Statistical Tests *(d)*			
Life Table	P=0.011	P=0.248	P=0.017
Incidental Tumor Test	P=0.010	P=0.213	P=0.023
Cochran-Armitage Trend Test	P=0.012		
Fisher Exact Test		P=0.298	P=0.017
Liver: Carcinoma			
Tumor Rates			
Overall *(a)*	11/50 (22%)	17/50 (34%)	16/50 (32%)
Adjusted *(b)*	28.1%	41.9%	37.3%
Terminal *(c)*	8/35 (23%)	10/33 (30%)	9/35 (26%)
Statistical Tests *(d)*			
Life Table	P=0.213	P=0.132	P=0.226
Incidental Tumor Test	P=0.358	P=0.226	P=0.337
Cochran-Armitage Trend Test	P=0.161		
Fisher Exact Test		P=0.133	P=0.184
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	18/50 (36%)	26/50 (52%)	33/50 (66%)
Adjusted *(b)*	46.7%	62.9%	74.7%
Terminal *(c)*	15/35 (43%)	18/33 (55%)	24/35 (69%)
Statistical Tests *(d)*			
Life Table	P=0.006	P=0.069	P=0.007
Incidental Tumor Test	P=0.008	P=0.101	P=0.010
Cochran-Armitage Trend Test	P=0.002		
Fisher Exact Test		P=0.079	P=0.002
Forestomach: Squamous Cell Papilloma			
Tumor Rates			
Overall *(a)*	0/50 (0%)	1/48 (2%)	3/49 (6%)
Adjusted *(b)*	0.0%	3.0%	8.6%
Terminal *(c)*	0/35 (0%)	1/33 (3%)	3/35 (9%)
Statistical Tests *(d)*			
Life Table	P=0.062	P=0.488	P=0.121
Incidental Tumor Test	P=0.062	P=0.488	P=0.121
Cochran-Armitage Trend Test	P=0.059		
Fisher Exact Test		P=0.490	P=0.117

(a) Number of tumor bearing animals/number of animals examined at the site.

(b) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.

(c) Observed tumor incidence at terminal kill.

(d) Beneath the control incidence are the P-values associated with the trend test. Beneath the dosed group incidence are the P-values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).

TABLE G4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS

	Vehicle Control	125 mg/kg	250 mg/kg
Subcutaneous Tissue: All Sarcomas			
Tumor Rates			
Overall *(a)*	1/50 (2%)	1/50 (2%)	4/50 (8%)
Adjusted *(b)*	2.9%	3.4%	15.4%
Terminal *(c)*	1/35 (3%)	1/29 (3%)	4/26 (15%)
Statistical Tests *(d)*			
Life Table	P=0.055	P=0.720	P=0.100
Incidental Tumor Test	P=0.055	P=0.720	P=0.100
Cochran-Armitage Trend Test	P=0.101		
Fisher Exact Test		P=0.753	P=0.181
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(a)*	5/50 (10%)	0/50 (0%)	1/50 (2%)
Adjusted *(b)*	13.6%	0.0%	3.8%
Terminal *(c)*	4/35 (11%)	0/29 (0%)	1/26 (4%)
Statistical Tests *(d)*			
Life Table	P=0.073N	P=0.056N	P=0.189N
Incidental Tumor Test	P=0.061N	P=0.052N	P=0.162N
Cochran-Armitage Trend Test	P=0.037N		
Fisher Exact Test		P=0.028N	P=0.102N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	6/50 (12%)	1/50 (2%)	1/50 (2%)
Adjusted *(b)*	16.4%	2.5%	3.8%
Terminal *(c)*	5/35 (14%)	0/29 (0%)	1/26 (4%)
Statistical Tests *(d)*			
Life Table	P=0.051N	P=0.100N	P=0.123N
Incidental Tumor Test	P=0.039N	P=0.079N	P=0.104N
Cochran-Armitage Trend Test	P=0.023N		
Fisher Exact Test		P=0.056N	P=0.056N
Hematopoietic System: Lymphoma, All Malignant			
Tumor Rates			
Overall *(a)*	15/50 (30%)	14/50 (28%)	14/50 (28%)
Adjusted *(b)*	39.1%	36.5%	41.8%
Terminal *(c)*	12/35 (34%)	6/29 (21%)	8/26 (31%)
Statistical Tests *(d)*			
Life Table	P=0.310	P=0.443	P=0.355
Incidental Tumor Test	P=0.497N	P=0.583N	P=0.570N
Cochran-Armitage Trend Test	P=0.456N		
Fisher Exact Test		P=0.500N	P=0.500N
Circulatory System: Hemangiosarcoma			
Tumor Rates			
Overall *(a)*	3/50 (6%)	0/50 (0%)	1/50 (2%)
Adjusted *(b)*	7.6%	0.0%	3.1%
Terminal *(c)*	2/35 (6%)	0/29 (0%)	0/26 (0%)
Statistical Tests *(d)*			
Life Table	P=0.241N	P=0.151N	P=0.401N
Incidental Tumor Test	P=0.196N	P=0.122N	P=0.336N
Cochran-Armitage Trend Test	P=0.176N		
Fisher Exact Test		P=0.121N	P=0.309N

TABLE G4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	125 mg/kg	250 mg/kg
Circulatory System: Hemangioma or Hemangiosarcoma			
Tumor Rates			
Overall *(a)*	4/50 (8%)	1/50 (2%)	1/50 (2%)
Adjusted *(b)*	9.8%	3.4%	3.1%
Terminal *(c)*	2/35 (6%)	1/29 (3%)	0/26 (0%)
Statistical Tests *(d)*			
Life Table	P=0.166N	P=0.247N	P=0.272N
Incidental Tumor Test	P=0.119N	P=0.204N	P=0.192N
Cochran-Armitage Trend Test	P=0.101N		
Fisher Exact Test		P=0.181N	P=0.181N
Liver: Adenoma			
Tumor Rates			
Overall *(a)*	1/50 (2%)	5/50 (10%)	5/50 (10%)
Adjusted *(b)*	2.9%	17.2%	19.2%
Terminal *(c)*	1/35 (3%)	5/29 (17%)	5/26 (19%)
Statistical Tests *(d)*			
Life Table	P=0.036	P=0.064	P=0.047
Incidental Tumor Test	P=0.036	P=0.064	P=0.047
Cochran-Armitage Trend Test	P=0.090		
Fisher Exact Test		P=0.102	P=0.102
Liver: Carcinoma			
Tumor Rates			
Overall *(a)*	1/50 (2%)	3/50 (6%)	4/50 (8%)
Adjusted *(b)*	2.9%	9.7%	12.6%
Terminal *(c)*	1/35 (3%)	2/29 (7%)	2/26 (8%)
Statistical Tests *(d)*			
Life Table	P=0.080	P=0.238	P=0.117
Incidental Tumor Test	P=0.103	P=0.245	P=0.147
Cochran-Armitage Trend Test	P=0.133		
Fisher Exact Test		P=0.309	P=0.181
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	2/50 (4%)	8/50 (16%)	9/50 (18%)
Adjusted *(b)*	5.7%	26.4%	30.8%
Terminal *(c)*	2/35 (6%)	7/29 (24%)	7/26 (27%)
Statistical Tests *(d)*			
Life Table	P=0.006	P=0.022	P=0.008
Incidental Tumor Test	P=0.008	P=0.023	P=0.010
Cochran-Armitage Trend Test	P=0.025		
Fisher Exact Test		P=0.046	P=0.026
Forestomach: Squamous Cell Papilloma or Carcinoma			
Tumor Rates			
Overall *(a)*	0/50 (0%)	2/50 (4%)	3/50 (6%)
Adjusted *(b)*	0.0%	6.9%	9.9%
Terminal *(c)*	0/35 (0%)	2/29 (7%)	1/26 (4%)
Statistical Tests *(d)*			
Life Table	P=0.051	P=0.198	P=0.078
Incidental Tumor Test	P=0.069	P=0.198	P=0.115
Cochran-Armitage Trend Test	P=0.082		
Fisher Exact Test		P=0.247	P=0.121

TABLE G4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE ADMINISTERED 1,2-DICHLOROPROPANE IN CORN OIL BY GAVAGE FOR TWO YEARS (Continued)

	Vehicle Control	125 mg/kg	250 mg/kg
Pituitary: Adenoma			
Tumor Rates			
Overall *(a)*	7/38 (18%)	8/45 (18%)	8/44 (18%)
Adjusted *(b)*	22.8%	32.0%	31.6%
Terminal *(c)*	6/29 (21%)	8/25 (32%)	7/24 (29%)
Statistical Tests *(d)*			
Life Table	P=0.271	P=0.365	P=0.323
Incidental Tumor Test	P=0.307	P=0.390	P=0.380
Cochran-Armitage Trend Test	P=0.547N		
Fisher Exact Test		P=0.581N	P=0.600N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	9/38 (24%)	9/45 (20%)	9/44 (20%)
Adjusted *(b)*	29.5%	34.2%	35.6%
Terminal *(c)*	8/29 (28%)	8/25 (32%)	8/24 (33%)
Statistical Tests *(d)*			
Life Table	P=0.353	P=0.449	P=0.406
Incidental Tumor Test	P=0.406	P=0.500	P=0.464
Cochran-Armitage Trend Test	P=0.417N		
Fisher Exact Test		P=0.443N	P=0.465N
Thyroid: Follicular Cell Adenoma			
Tumor Rates			
Overall *(a)*	1/48 (2%)	0/45 (0%)	3/46 (7%)
Adjusted *(b)*	2.9%	0.0%	12.5%
Terminal *(c)*	1/34 (3%)	0/27 (0%)	3/24 (13%)
Statistical Tests *(d)*			
Life Table	P=0.110	P=0.546N	P=0.189
Incidental Tumor Test	P=0.110	P=0.546N	P=0.189
Cochran-Armitage Trend Test	P=0.168		
Fisher Exact Test		P=0.516N	P=0.292
Thyroid: Follicular Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(a)*	1/48 (2%)	0/45 (0%)	5/46 (11%)*(e)*
Adjusted *(b)*	2.9%	0.0%	20.8%
Terminal *(c)*	1/34 (3%)	0/27 (0%)	5/24 (21%)
Statistical Tests *(d)*			
Life Table	P=0.015	P=0.546N	P=0.040
Incidental Tumor Test	P=0.015	P=0.546N	P=0.040
Cochran-Armitage Trend Test	P=0.034		
Fisher Exact Test		P=0.516N	P=0.092

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

APPENDIX H

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

APPENDIX H

A. METHODS FOR SALMONELLA/MICROSOME MUTAGENICITY TEST SYSTEM

1,2-Dichlorpropane was tested and evaluated blindly in each of four tester strains of *Salmonella typhimurium*, using a preincubation modification (Yahagi et al., 1975) of *Salmonella* assay (Ames et al, 1975). Strains of TA98 and TA1537 are more sensitive to chemicals that express frameshift mutagenic activity; strains TA100 and TA1535 are more sensitive to chemicals that cause base-pair substitutions. 1,2-Dichloropropane was dissolved in dimethyl sulfoxide (DMSO) and then added to the suspension culture. The mixture was then incubated with the tester strains in suspension culture (20 minutes at 37°C) prior to the addition of soft agar and plating for detection of induced mutants. Exogenous metabolic activation was provided by liver S-9 preparations from Arochlor-1254® induced rats and hamsters. Coded chemicals were tested at 5 doses (μg/ plate), in triplicate (A,B, and C), in each strain and were retested at least two weeks later.

B. RESULTS

See Table H1.

TABLE H1. MUTAGENICITY OF 1,2-DICHLOROPROPANE IN *SALMONELLA TYPHIMURIUM*

Strain	Dose (μg/plate)	Revertants/plate[a]		
		-S9	+S9 (rat)	+S9 (hamster)
TA100	0	135 ± 6.6	133 ± 4.4	123 ± 4.3
	33	125 ± 7.4	125 ± 4.4	109 ± 6.2
	100	143 ± 11.0	136 ± 6.9	137 ± 4.2
	333	152 ± 13.9	128 ± 4.1	114 ± 9.2
	1,000	196 ± 17.0	141 ± 5.5	120 ± 2.0
	2,000	153 ± 9.5	146 ± 8.0	118 ± 8.7
TA1535	0	28 ± 2.3	17 ± 1.3	12 ± 1.0
	33	30 ± 1.2	17 ± 2.3	15 ± 2.7
	100	31 ± 3.9	15 ± 1.0	12 ± 1.2
	333	34 ± 4.0	16 ± 2.5	17 ± 4.2
	1,000	54 ± 3.7	19 ± 2.9	19 ± 4.9
	2,000	54 ± 2.1	20 ± 1.7	18 ± 3.6
TA1537	0	7 ± 0.7	19 ± 2.1	15 ± 2.9
	33	11 ± 0.9	21 ± 2.9	18 ± 0.3
	100	11 ± 2.1	19 ± 2.1	18 ± 4.0
	333	11 ± 0.6	14 ± 1.5	15 ± 1.5
	1,000	11 ± 0.9	24 ± 3.2	16 ± 1.7
	2,000	12 ± 1.9	14 ± 1.5	16 ± 1.5
TA98	0	28 ± 0.9	37 ± 2.3	44 ± 3.0
	33	26 ± 0.9	43 ± 3.8	45 ± 4.3
	100	33 ± 3.5	45 ± 4.9	41 ± 2.3
	333	28 ± 2.2	43 ± 3.1	51 ± 8.7
	1,000	31 ± 3.2	35 ± 0.9	41 ± 2.9
	2,000	26 ± 0.9	36 ± 1.5	34 ± 1.2

[a] The S9 fractions were prepared from the livers of Aroclor-1254® -induced animals (male Sprague-Dawley rats and male Syrian hamsters). Cells and test compound or solvent (DMSO) were incubated for 20 min. at 37° C in the presence of either S9 or buffer (Yahagi et al., 1975). After the addition of soft agar, the contents of each tube were poured onto minimal medium, and the plates were incubated at 37° C for 48 hr. (Ames et al., 1975). The experiment was performed twice, each time in triplicate; because the results were similar, data from only one experiment are shown.

APPENDIX I

IN VITRO CYTOGENETIC TESTING

APPENDIX I

A. MATERIALS

1. Chinese Hamster Ovary Cells

Chinese hamster ovary cells (CHO) were obtained from Dr. S. Wolff at the Laboratory of Radiobiology, University of California Medical Centre, San Francisco, and were cloned in the laboratory of Dr. A. Bloom, Columbia University Medical Centre, New York. The cells have been designated CHO-W-B1. The cells were not used at passage levels of more than 15 after cloning and were thawed routinely from liquid nitrogen storage and maintained by transferring twice a week.

2. Medium and Cell Cultures

CHO cells were grown at 37°C in an atmosphere of 5% CO_2 in air, in McCoy's 5a medium supplemented with 10% fetal calf serum, (FCS) L-glutamine, penicillin and streptomycin. Cultures were set up 24 hours prior to treatment by seeding in 75 cm^2 plastic flasks in 10 ml of fresh medium. Cells were seeded at approximately $8x10^5$ per flask for SCE experiments, or up to 1.2×10^6 for aberration experiments.

A single culture was used for each dose level or control in both tests (with and without metabolic activation). Cultures were protected from light.

3. Metabolic Activation System

The *in vitro* metabolic activation system comprised rat liver enzymes and an energy-producing system necessary for their function (NADP and isocitric acid). The enzymes were contained in a preparation of liver microsomes (S9 fraction) from male rats treated previously with the alkylating agent Arochlor 1254 to induce enzymes capable of transforming chemicals to more active forms.

Liver S9 fraction (Litton biological Products, Inc.,) was retained frozen at -80°C until use. This S9 fraction was thawed immediately before use and added to a "core" reaction mixture to form the following activation system:

Component	Volume per Culture	Final Concentration per ml of Medium
Core	600 µl	
NADP (sodium salt)		2.4mg
Isocitric acid		4.5 mg
S9 fraction		
Liver homogenate	150 µl	15 µ

4. Test Compound and Controls

Immediately before use, a stock solution of the test compound was prepared in a suitable solvent such as culture medium, distilled water, dimethylsulfoxide, acetone, or absolute ethanol. Serial dilutions were prepared in the same solvent to achieve desired final concentrations by addition of 100 μl of test solution to each 10 ml culture, unless limited solubility required use of a larger volume.

Nothing was added to the negative controls, which contained simply cells and culture medium with or without the S9 fraction. Solvent controls contained the same concentration of solvent as the test cultures (usually 1%)

Known mutagenic and chromosome breaking agents were used:

Positive Control Compound	=/- S9 Fraction	Final Concentration For Aberration Test	Final Concentration For SCE Test
Triethylene-melamine	-	250-500 ng/ml	15 ng/ml
Cyclophosphamide	+	25-50 μg/ml	1.5-2.0 μg/ml

B. SOLUBILITY, TOXICITY, AND DOSE DETERMINATION

The approximate dose range is determined prior to cytogenetic testing.

1. Solubility Testing

Solvents tested in order of preference were medium, water, dimethylsulfoxide (DMSO), ethanol, and acetone.

a. Solids

A sample of the compound was weighed and an attempt made to prepare a stock solution at 500 mg/ml to obtain a maximum final concentration of 5 mg/ml in cultures. If sonication, mixing on a Vortex, or warming to about 37°C did not dissolve the compound, more solvent was added until a solution was obtained. From this maximum concentration a series of dilutions was made to achieve ten or eleven doses in a half-log series.

b. Liquids

Liquids were used "neat" to achieve a top dose of 10 μl/ml in cultures. Solubility or miscibility with solvents was tested as for solids, and a five-log range of concentrations in a half-log series was tested in the first trials.

2. Toxicity Testing

The toxicity test was incorporated into the first trial for each assay (SCE and aberrations). Cultures were exposed to a five-log range of concentrations of test compound. Immediately before fixation, the cultures were examined under the inverted microscope. The degree of confluency of the monolayer was noted, along with the occurrence of large, round healthy cells (mitotic) on the surface of the cell sheet or floating in the medium.

If no evidence of toxicity was found, only the top five or six dose levels were fixed. If there was toxicity, the highest dose likely to yield results was fixed in series with the five does levels below it.

C. ASSAY FOR SISTER CHROMATID EXCHANGE IN CHINESE HAMSTER OVARY CELLS

1. Objective

The objective of this in vitro assay was to evaluate the ability of a test compound or its metabolites to induce sister chromatid exchange (SCE) in Chinese hamster ovary (CHO) cells.

2. Rationale

The frequency of sister chromatid exchanges (SCEs) is a very sensitive indicator of exposure of the genetic material to chemical mutagens. The SCE test simply involved treating cultured cells with a test compound, growing the cells with 5-bromo-deoxyuridine (BrdU) for 2 cell cycles, and making chromosome preparations that were stained for detection of XCE.

3. Cell Treatment

a. Assay without the metabolic activation system

One day after culture initiation, the medium was replaced with fresh medium and cells were treated with test or control compounds for about 2 hours to allow some interaction with cells before addition of BrdU. BrdU was added (final concentration 10 μM) and incubation was continued for about 24 hours. The medium was then removed to allow an opportunity to wash off any test compound precipitate that might have interfered with cell fixation and to avoid harvest of cultures containing suspect compounds. Fresh medium containing BrdU (10 μM) and colcemid (final concentration 0.1 μg/ml) was added, and incubation was continued for 2 to 3 hours.

The total incubation time with test compound was thus about 26 hours, and total time with BrdU was also about 26 hours, beginning about 2 hours after addition of test compound.

b. Assay with the metabolic activation system

One day after culture initiation, medium was replaced with medium without fetal calf serum. Cells were incubated for two hours in the presence of the test or control compound and the S9 reaction mixture. The short incubation time was used because prolonged exposure to the S9 mixture is toxic to cells; also, enzyme activity is lost rapidly at 37°C. Serum was omitted to avoid the possible inactivation from the binding to serum proteins or short-lived, highly reactive intermediates produced by S9 enzymes. After the 2 hour exposure period, cells were washed at least twice with buffered saline, and complete culture medium containing 10% FCS and 10 μM BrdU was added. Cells were incubated for a further 26 hours, with colcemid (0.1 μg/ml) present for the final two to three hours of incubation.

c. Summary

	Incubation times from addition of test/control compound		
Type of Assay	**Test/Control Compound**	**BrdU**	**Colcemid**
With S9	0-2 hr.	2.5-28.5 hr.	26.5-28.5 hr.
Without S9	0-26 hr.	2.5-28.5 hr.	26.5-28.5 hr.

4. Cell Harvest and Fixation

a. Initial Harvest

Two to three hours after addition of colcemid, cells were collected by mitotic shake-off (Terasima and Tolmach, 1961) and treated for about 3 minutes at room temperature with hypotonic KCL (75 mM). Cells were then washed twice with fixative (3:1, methanol: glacial acetic acid, v/v), dropped on to slides, and air-dried.

b. Test for Cell Cycle Delay and Repeated Harvests

Because many compounds cause cell cycle delay, a technique was used for assessing this and necessary performing later harvests on the same cultures. After 2 to 3 hours incubation with colcemid, cells were harvested by mitotic shake-off and centrifuged to collect as a pellet. The supernatant medium could then be returned to appropriate flasks that were reincubated at 37°C. After fixation of cells, test slides were made and stained for 10 minutes in Hoechst 33258 (0.5 μg/ml in phosphate buffer, pH 6.8), rinsed in water, and mounted in the same buffer. These slides could be examined by fluorescence microscopy to assess the frequency of cells that had completed two cell cycles in BrdU. If there was significant delay, the same cultures could be harvested repeatedly until an adequate yield of cells showing complete differentiation between chromatids was obtained.

5. Staining and Scoring of Slides

Staining for detection of SCE was accomplished by a modified fluorescence plus Giemsa (FPG) technique (after Perry and Wolff, 1974 and Goto, et al., 1978). Slides were stained for 10 minutes with Hoechst 33258 (5 μg/ml) in phosphate buffer (pH 6.8), mounted in the same buffer and exposed at 55°-65°C to "black-light" from 15 Watt tubes for the amount of time required for differentiation between chromatids (about 5 minutes). Finally, slides were stained with 5% Giemsa for 5 to 20 minutes and air dried.

For control of bias, all slides were coded prior to scoring and scored "blind."

M2 cells were scored for the frequency of SCE per cell. Fifty cells were scored per dose from the top three dose levels fixed. If these were clearly negative or positive no further scoring was carried out. Lower doses were scored if necessary to establish a dose relation.

D. ASSAY FOR CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OVARY CELLS

1. Objective

The objective of this *in vitro* assay is to evaluate the ability of a test article to induce chromosome aberrations in Chinese hamster ovary (CHO) cells with or without an *in vitro* metabolic activation system.

2. Rationale

The objective is to establish whether the test article or its metabolites can interact with cells to induce gross chromosomal breaks, or changes in chromosome numbers. Chemically induced lesions may result in breaks in chromatin that are either repaired by the cell in such a way as to be undetectable, or can result in visible change. Aberrations are a consequence of failure or mistakes in repair processes that result in lack of rejoining of breaks, or rejoining in abnormal configurations (Evans, 1962).

Aberrations are examined when cells enter mitosis for the first time after chemical exposure, before they can be lost during the division process or converted into complex derivatives during subsequent cell cycles. For the CHO cells used here, most dividing cells examined 10 to 12 hours after treatment were in their first mitosis (M1 cells).

3. Cell Treatment

a. Assay Without the Metabolic Activation System

One day after culture initiation, the medium was replaced with fresh medium and cells were treated with test or control compounds for 8 to 10 hours. The medium was then removed, cultures were washed if any precipitate was evident, and the medium was replaced with fresh medium containing colcemid (0.1 μg/ml). After a further 2-3 hours of incubation cells were harvested by mitotic shake-off and fixed as described previously.

b. Assay With the Metabolic Activation System

One day after culture initiation, the medium was replaced with medium without fetal calf serum. Cells were incubated for two hours in the presence of the test or control compounds and the S9 reaction mixture. Cultures were then washed at least twice with buffered saline and incubation was continued for 8 to 10 hours. Colcemid was present for the last 2 to 3 hours of the incubation. Cells were harvested and fixed as above.

4. Staining and Scoring of Slides

Slides were stained in 5% Giemsa for 5 to 10 minutes. For control of bias, all slides were coded and scored blind. One hundred cells were scored for each dose.

TABLE I1. CYTOGENETIC EFFECTS OF 1,2-DICHLOROPROPANE IN CHINESE HAMSTER OVARY (CHO) CELLS

Sister Chromatic Exchanges *(a)*				Chromosome Aberrations *(b)*			
-S9		+S9		-S9		+S9	
μg/ml	SCE/Cell	μg/ml	SCE/Cell	μg/ml	Abs/100 Cells (% cells w/abs)	μg/ml	Abs/100 Cells (% cells w/abs)
DMSO (10 μl)	10.1	DMSO (10 μl)	9.1	DMSO (10 μl)	3 (3)	DMSO (10 μl)	> 4 (2)
112.7	12.6	112.7	10.7	1180	3 (3)	460	4 (2)
376.0	21.2	376.0	18.4	1370	16 (11)	660	17 (15)
1127.0	36.2	1127.0	22.1	1580	> 47 (26)	950	>16 (13)
Mitomycin C (0.01)	36.6	Cyclophos-phamide (1.5)	27.5	Mitomycin C (0.125)	>102 (50)	Cyclophos-phamide (50)	46 (24)

(a) In the absence of S9, CHO cells were incubated with test compound or solvent for 2 hr. at 37° C. Then BrdU was added and incubation continued for 24 hr. Cells were washed, fresh medium containing BrdU (10 μM) and colcemid (0.1 μg/ml) was added, and incubation was continued for 2-3 hr. Cells were then collected by mitotic shake-off, treated for 3 min. with KCl (75 mM), washed twice with fixative, and dropped onto slides and air-dried. Staining was by a modified technique (after Perry and Wolff, 1974; Goto *et al.*, 1978). In the presence of S9, cells were incubated with test compound or solvent for 2 hr. at 37° C. Then cells were washed, and medium contining 10 μM BrdU was added. Cells were incubated for a further 26 hr., with colcemid (0.1 μg/ml) present for the final 2-3 hr.

(b) In the absence of S9, CHO cells were incubated with test compound or solvent for 8-10 hr. at 37° C. Cells were then washed, and fresh medium containing colcemid (0.1 μg/ml) was added. After a further 2-3 hr. of incubation, cells were harvested by mitotic shake-off, fixed, and stained in 6% Giemsa. In the presence of S9, cells were incubated with test compound or solvent for 2 hr. at 37° C. Cells were then washed, medium was added, and incubation continued for 8-10 hr. Colcemid (0.1 μg/ml) was added for the last 2-3 hr. of incubation, then cells were harvested and fixed as above.

(c) S9 from the livers of Aroclor-1254®-induced male Sprague-Dawley rats.

		-S9	+S9
Conclusions:	SCE	+	+
	CA	+	+

APPENDIX J

NTP SENTINEL ANIMAL DATA

APPENDIX J

A. METHODS

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

Fifteen $B6C3F_1$ mice of both sexes and 15 F344/N rats of both sexes are selected at the time of randomization and allocation of the animals to the various study groups. Five animals of each designated sentinel group are killed at 6, 12, and 18 months on study. Data from animals surviving 24 months are collected from 5/50 randomly selected control animals of each sex and species. The blood from each animal is collected and clotted and the serum is separated. The serum is cooled on ice and shipped to Microbiological Associates' Comprehensive Animal Diagnostic Serice for determination of the viral titers. The following tests are performed:

	Hemagglutination Inhibition	Complement Fixation
Mice	PVM (Pneumonia Virus of Mice) Reo 3 (Reovirus, Type 1) GDVII (Strain of Murine Encephalomyelitis Virus) Poly (Polyoma Virus) Sendai (Sendai Virus) MVM (Minute Virus of Mice) Ectro (Infectious Ectromelia Virus of Mice)	M. Ad. LCM (Lymphocytic Choriomeningitis Virus of Mice)
Rats	PVM (Pneumonia Virus of Mice) Sendai (Sendai Virus) KRV (Kilham Rat Virus) H-1 (Toolan's H-1 Virus)	RCV (Rat Corona Virus)

B. RESULTS

See Tables J1 and J2.

TABLE J1. MURINE VIRUS ANTIBODY DETERMINATIONS FOR RATS IN THE TWO-YEAR STUDY

		Hemagglutination Inhibition				Complement Fixation	
Sample No.	Sex	PVM	KRV	H-1	Sendai	RCV	Sendai
SIX MONTHS							
1	M	80	—	—	—	—	—
2	M	80	—	—	—	—	—
3	M	80	320	—	—	—	—
4	M	80	160	—	—	—	—
5	M	80	—	—	—	—	—
1	F	80	—	—	—	—	—
2	F	80	160	—	—	—	—
3	F	80	—	—	—	—	—
4	F	80	320	—	—	—	—
5	F	80	—	—	—	—	—
TWELVE MONTHS							
6	M	40	—	—	—	—	80
7	M	80	40	—	—	—	80
8	M	80	—	—	—	10	40
9	M	*(a)*	*(a)*	*(a)*	—	*(a)*	*(a)*
10	M	40	40	—	—	—	40
6	F	80	—	—	—	40	80
7	F	80	—	—	—	—	80
8	F	80	—	—	—	10	40
9	F	80	—	—	—	20	40
10	F	80	—	—	—	10	80
EIGHTEEN MONTHS							
11	M	80	80	—	—	—	80
12	M	80	80	—	—	10	80
13	M	80	80	—	—	—	—
14	M	80	80	—	—	—	20
15	M	40	80	—	—	—	80
11	F	80	—	—	—	10	80
12	F	80	80	—	—	10	80
13	F	80	—	—	—	10	80
14	F	80	80	—	—	40	40
15	F	80	—	—	—	10	80
TWENTY-FOUR MONTHS							
9	M	80	80	—	20	—	—
21	M	40	—	—	10	—	—
24	M	80	—	—	—	—	—
37	M	80	80	—	—	—	—
43	M	40	40	—	—	—	—
25	F	80	80	—	10	—	—
19	F	80	—	—	20	20	—
36	F	80	—	—	—	*(b)*	—
7	F	80	—	—	—	—	—
8	F	80	80	—	20	40	—
Significant Titer		20	20	20	10	10	10

(a) Insufficient serum
(b) Anticomplimentary serum

TABLE J2. MURINE VIRUS ANTIBODY DETERMINATIONS FOR MICE IN THE TWO-YEAR STUDY*

Sample Number	Sex	Hemagglutination Inhibition							Complement Fixation			
		PVM	Reo 3	GDVII	Poly	MVM	Ec-tro	Sen-dai	Sen-dai	M. Ad	MHV	LCM
SIX MONTHS												
1	M	—	—	—	—	—	—	—	—	—	—	—
2	M	—	—	—	—	—	—	—	—	—	—	—
3	M	—	—	—	—	—	—	—	—	—	—	—
4	M	—	—	—	—	—	—	—	—	—	—	—
5	M	—	—	—	—	—	—	—	—	—	—	—
1	F	40	—	—	—	—	—	—	—	—	—	—
2	F	80	—	—	—	—	—	—	—	—	—	—
3	F	20	—	—	—	—	—	—	—	—	—	—
4	F	80	—	—	—	—	—	—	—	—	—	—
5	F	40	—	—	—	—	—	—	—	—	—	—
TWELVE MONTHS												
6	M	80	—	*(b)*	—	—	—	—	80	*(c)*	*(c)*	*(c)*
7	M	80	—	—	—	—	—	—	40	—	—	—
9	M	40	—	—	—	—	—	—	80	*(c)*	*(c)*	*(c)*
10	M	40	—	—	—	—	—	—	40	*(c)*	*(c)*	*(c)*
6	F	40	—	—	—	—	—	—	*(c)*	*(d)*	*(c)*	*(c)*
7	F	40	—	*(b)*	—	—	—	—	—	—	—	—
8	F	—	—	—	—	—	—	—	*(c)*	*(d)*	—	*(c)*
9	F	80	—	—	—	—	—	—	20	*(d)*	—	*(d)*
10	F	20	—	—	—	—	—	—	*(c)*	*(d)*	—	*(d)*
EIGHTEEN MONTHS												
11	M	80	—	—	—	—	—	—	—	—	—	—
12	M	—	—	—	—	—	—	—	—	—	—	—
13	M	20	—	—	—	—	—	—	—	—	*(c)*	—
15	M	—	—	—	—	—	—	—	*(c)*	—	*(c)*	*(c)*
11	F	—	—	—	—	—	—	—	*(c)*	—	*(c)*	*(c)*
12	F	—	—	—	—	—	—	—	*(c)*	—	*(c)*	*(c)*
13	F	*(a)*	—	—	—	—	—	—	40	—	*(c)*	*(a)*
14	F	—	—	—	—	—	—	—	—	—	—	—
15	F	—	—	—	—	—	—	—	—	—	—	—
TWENTY-FOUR MONTHS												
34	M	—	—	—	*(b)*	—	—	—	—	—	—	—
47	M	20	—	—	*(b)*	*(b)*	—	*(b)*	—	*(c)*	*(c)*	*(c)*
14	M	40	—	—	—	—	—	—	—	*(c)*	*(c)*	*(c)*
16	M	20	—	—	—	—	—	—	—	*(c)*	*(c)*	*(c)*
10	M	—	—	—	—	—	—	—	—	*(c)*	*(c)*	*(c)*
23	F	—	—	—	—	—	—	—	—	—	—	—
44	F	—	—	*(b)*	—	—	—	—	—	—	*(c)*	*(d)*
17	F	—	—	—	—	—	—	—	—	—	*(d)*	*(d)*
31	F	10	—	—	—	—	—	—	—	*(d)*	40	*(d)*
11	F	*(a)*	—	—	*(c)*	—	—	—	—	—	*(b)*	*(d)*
Significant Titer		20	20	20	20	20	20	—	10	10	10	10

(a) Insufficient serum
(b) Serum agglutinates red blood cells
(c) Anticomplimentary serum
(d) Serum reacts with control antigen

APPENDIX K

ANALYSIS OF 1,2-DICHLOROPROPANE
LOT NO. A7XB

APPENDIX K

A. ELEMENTAL ANALYSIS

Element	C	H	Cl
Theory	31.89	5.35	62.76
Determined	31.99	5.17	62.65
	32.14	5.21	62.84

B. WATER ANALYSIS (Karl Fisher)

<0.1%

C. TITRATION

Titration for acidic components with sodium hydroxide; 4 ± 1 ppm acidity (assumed to be HCl).

D. BOILING POINT

Determined	Literature Values
b.p.: 97.8 ± 0.2(δ)°C at 758 mm (visual, capillary boiling point)	b.p.: 96.37°C at 760 mm (Weast, 1976-1977)

E. INDEX OF REFRACTION

Determined	Literature Values
n_D^{20} : 1.4382	n_D^{20} : 1.4339 (Weast, 1976-1977)

F. DENSITY

Determined	Literature Values
d_{22}^{24} : 1.1481 g/ml	d_4^{20}: 1.1560 g/ml (Weast, 1976-1977)

G. VAPOR-PHASE CHROMATOGRAPHY

Instrument: Tracor MT 220
Detector: Flame ionization
Carrier gas: Nitrogen
Flow carrier gas: 70 cc/min

a. System 1

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm I.D., glass
Oven temperature program: 50°C, 5 min; 50°-170°C at 10°C/min
Inlet temperature: 170°C
Detector temperature: 230°C
Sample injected: 5 μl neat liquid diluted to 1% and 0.5% in pentane to quantitate major peak and check for overloading
Results: Major peak and six impurities. The largest impurity has an area 0.50% of the area of the major peak. The areas of the other impurities total less than 0.2% of the area of the major peak.

APPENDIX K

Peak	Retention Time (min)	Retention Time (Relative to 1,2,-Dichloropropane)	Area (Percent of 1,2,-Dichloropropane)
1	3.0	0.67	0.02
2	4.5	1.00	100
3	7.5	1.67	0.50
4	10.4	2.31	0.02
5	10.6	2.36	0.02
6	13.8	3.07	0.02
7	14.1	3.13	0.03

b. System 2

Column: 10% Carbowax 20 M-TPA on 80/100 Chromosorb W, AW, 1.8 m x 4 mm I.D., glass
Oven temperature program: 60°C, 5 min; 60°-200°C at 10°C/min
Inlet temperature: 180°C
Detector temperature: 250°C
Sample injected: 5 μl neat liquid diluted to 1% and 0.5% in hexanes to quantitate major peak and check for overloading
Results: Major peak and five impurities. The areas of the impurities total 0.1% of the area of the major peak.

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dichloropropane)	Area (Percent of 1,2-Dichloropropane)
1	6.6	1.00	100
2	8.9	1.35	0.02
3	9.3	1.41	0.02
4	12.1	1.83	0.04 } **shoulder
5	12.3	1.86	}
6	12.5	1.89	0.02 }

c. System 3 (as used by Mason for reanalysis)
Column: 0.1% SP-1000 on Carbopack C (Supelco), 6 ft x 1/4 in., I.D., glass
Oven temperature program: 70° - 200° at 6°C/mintemperature: 185°C
Detector temperature: 220°C
Sample injected: 0.5 μl of 1% solution in pentane
Results: Major peak and one impurity

Peak	Retention Time (min)	Retention Time (Relative to 1,2-Dichloropropane)	Area (Percent of 1,2-Dichloropropane)
1	6.1	1.00	100
2	15.3	2.51	0.50

APPENDIX K

H. IDENTIFICATION OF IMPURITY PEAK 3 IN SYSTEM 1

1. Vapor-Phase Chromatography/Mass Spectrometry

   a. Instrumental Parameters

   Instrument: Varian MAT CH 4B mass spectrometer interfaces via a Watson-Biemann helium separator to a Tracor MT 2000MF vapor-phase chromatograph. Data processed by a Varian 620/i computer.
   Vapor-phase chromatograph column: GP 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 2 mm I.D., glass
   Inlet temperature: 175° C
   Oven temperature program: 5 min at 50° C, then 50 to 170° C at 10° C/min
   Ionization voltage: 70 EV

1,2-Dichloropropane in n-pentane was injected (1 μl; 40 μg/μl) into the above system. The retention times, determined by the total ion current monitor, of the major component and the impurity were 3.1 and 6.3 minutes, respectively. Mass spectral data for the impurity peak are given below.

   b. Results

Mass	Spectrum Obtained for Impurity (Percent of Base Peak)	Literature Spectrum (Eight Peak Index) of Toluene (Percent of Base Peak)
91	100	100
92	69	65
65	8	11
39	8	9
63	3	6
51	4	5
93	3	5
45	3	4

2. Vapor-Phase Chromatography - Spiking

   a. Instrument Parameters

   Instrument: Varian 3740
   Detector: Flame ionization
   Carrier Gas: Nitrogen
   Carrier Gas Flow: 70 cc/min
   Column: GP 20% PS2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m x 4 mm I.D., glass.
   Inlet Temperature: 200° C
   Detector Temperature: 270° C
   Oven Temperature Program: 50° C, 5 min, 50° C to 170° C at 10° C/min

   b. Results: Toluene, when injected on the above system (6μl of 0.5% v/v solution of toluene in n-pentane) gave a peak with a retention time of 8.3 min. Injection of 1,2-dichloropropane (6μl, neat) under the same conditions gave an impurity peak with a retention time of 8.6 minutes. When a spike (a 1:1 mixture of the 1,2-dichloropropane and 0.5% v/v toluene in n-pentane) was injected, this peak was enhanced, yielding a single peak with a retention time of 8.5 minutes.

APPENDIX K

I. QUANTITATION OF TOLUENE IN 1,2-DICHLOROPROPANE BY VAPOR-PHASE CHROMATOGRAPHY

1. Instrument Parameters

Toluene was quantitated in 1,2-dichloropropane using the vapor-phase chromatographic system described in Section H-2-a except that the oven temperature was maintained at an isothermal temperature of 70° C.

2. Results

Toluene had a retention time of 5.5 minutes on this system. Injection of the spiked sample described in Section H-2-a yielded an enhanced peak under these conditions. Standards (0.25% v/v toluene in n-pentane, 5μl) were compared to neat injections of 1,2-dichloropropane (5μl) to quantitate the toluene.

Results: Percent toluene in 1,2-dichloropropane

0.24% ± 0.02 (δ) % v/v or 0.18% ± 0.01 (δ) % w/w

3. Conclusions

The impurity (peak 3; system 1; was identified to be toluene present at a concentration of 0.24% (v/v) or 0.18% (w/w).

J. SPECTRAL DATA

1. Infrared

Instrument: Beckman IR-12
Cell: Between silver chloride plates
Results: See Figure 5

Consistent with literature spectrum (Sadtler Standard Spectra)

2. Ultraviolet/Visible

No literature spectrum found

Instrument: Cary 118

λ max (nm)	ε x 10
268.5	6.01 ± 0.07 (δ)
264 shoulder	5.51 ± 0.04 (δ)
262	7.13 ± 0.04 (δ)
259 shoulder	6.25 ± 0.04 (δ)
256	5.67 ± 0.04 (δ)
249 shoulder	4.24 ± 0.04 (δ)
243	3.51 ± 0.03 (δ)

Solvent: Methanol

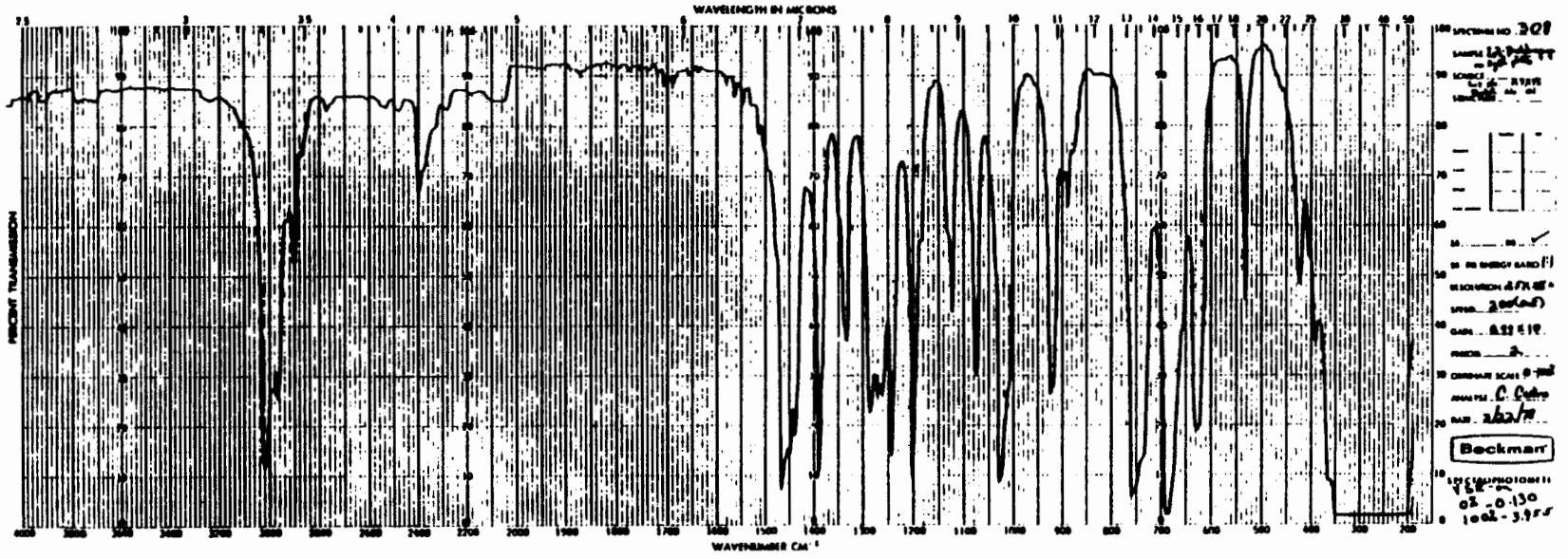

Figure 5. Infrared Absorption Spectrum of 1,2-Dichloropropane (Lot No. A7XB)

3. Nuclear Magnetic Resonance

Instrument: Varian EM-360-A

Consistent with literature spectrum (Sadtler standard spectra)

Solvent: Deuterated chloroform with internal tetramethylsilane

Assignments: (see Figure 6)

(a) d, δ 1.58 ppm, J_{ac} = 7 Hz;
(b) m, δ 3.35-3.80 ppm;
(c) m, δ 3.80-4.50 ppm;
(d) 7.20 ppm impurity

Integration Ratios:

(a) 3.05
(b) 1.79
(c) 1.17
(d) did not integrate

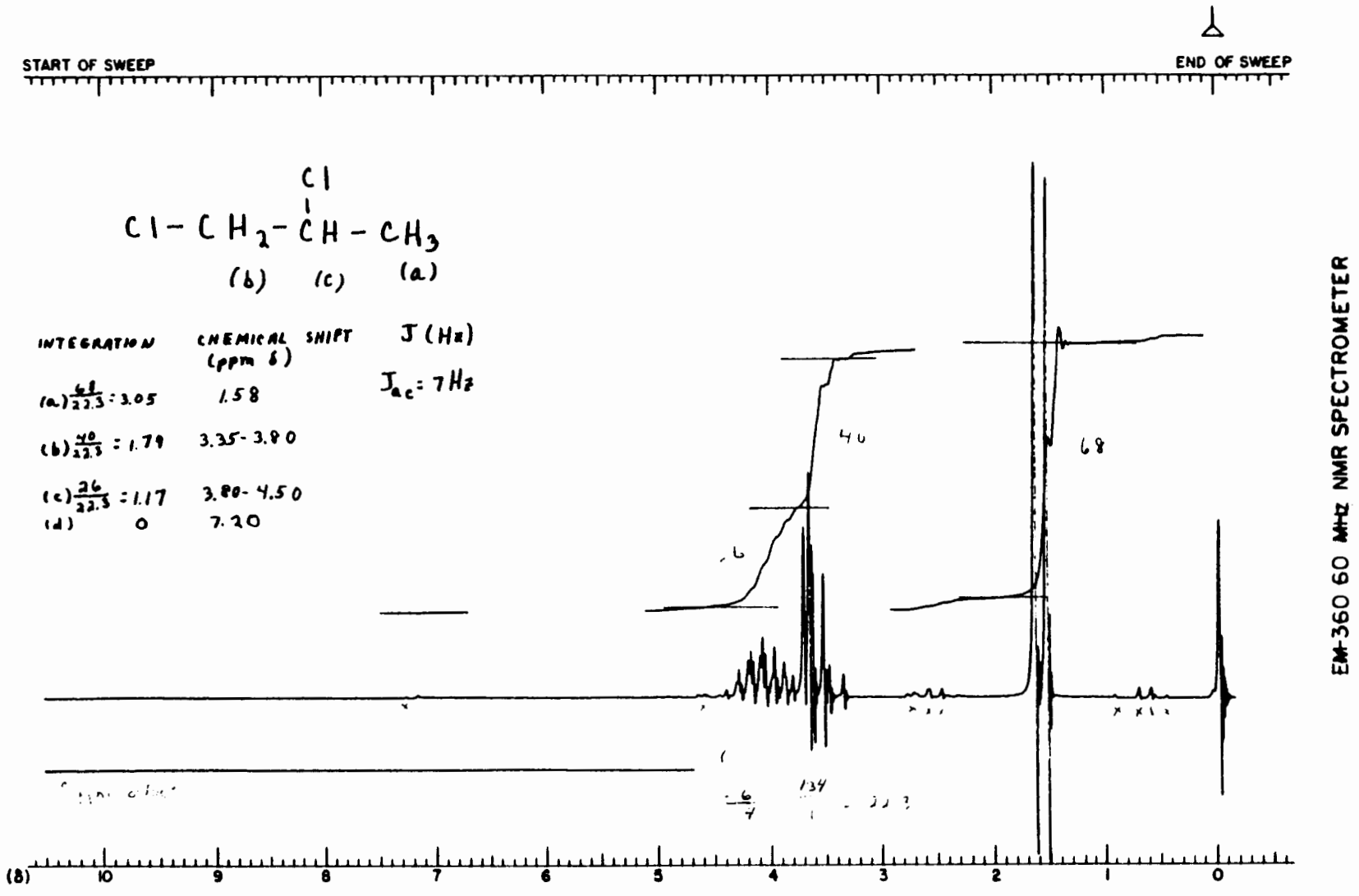

Figure 6. Nuclear Magnetic Resonance Spectrum of 1,2-Dichloropropane (Lot No. A7XB)

APPENDIX L

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

APPENDIX L

A. SAMPLE PREPARATION AND STORAGE

Two stock solutions of 1,2-dichloropropane in corn oil were prepared for each storage as follows: 2 ml (2.31 g) of the chemical was pipetted into each of two 60-ml septum vials containing 37.998 g and 38.000 g of corn oil, respectively, and the vials were sealed immediately (Microsep F-138 gas chromatography septa with Teflon® film facing, from Canton Biomedical Products, Inc.; aluminum crimp seals from Wheaton Scientific Company, Inc.). Each vial was manually shaken, agitated on a vortex mixer for 10 sec., and placed in an ultrasonic vibratory bath for 1 minute. These clear solutions were stored at room temperature (25°C) for 7 days with no effort made to protect them from light.

B. SAMPLE EXTRACTION AND ANALYSIS

At time-zero (just after preparation) and after storage for 1, 5, 6, and 7 days, the sample solutions were remixed on the vortex-mixer and ultrasonic vibratory bath as described in the preceding paragraph. The vials were unsealed, and two samples from each stock solution were removed (2.02 ± 0.01 g, accurately weighed). The stock solution vials were resealed and the samples were each placed in a clean 60-ml vial. Absolute methanol (20 ml, pipetted) containing 6.02 mg/ml of amyl alcohol was added to each sample vial, and these were sealed in turn. The methanol/amyl alcohol solution was prepared by weighing 3.01 g of amyl alcohol in a small vial on an analytical balance, quantitatively transferring it to a 500-ml volumetric flask with methanol, and diluting the solution to the volume mark with additional methanol.

The corn oil/methanol test samples were then mixed thoroughly by manual shaking, treatment by vortex mixer, and treatment by ultrasonic vibratory bath. After the layers had separated and the methanol phase had become clear, 5 ml of each methanol phase was placed in a small (8.5 ml) septum vial and sealed, for analysis by the gas chromatographic system described below:

Instrumental Parameters

Instrument: Bendix 2500
Column: 20% SP-2100/0.1% Carbowax 1500 on 100/120 mesh Supelcoport, 1.8 m x 4 mm I.D., glass
Detection: Flame ionization
Temperatures: Oven, 100°C isothermal; inlet, 150°C; detector, 225°C
Carrier gas: Nitrogen; flow rate, 30 cc/min
Retention time of test chemical: 1.5 min
Retention time of amyl alcohol reference: 2.2 min

C. QUALITY CONTROL PROCEDURES

Analysis was performed in duplicate, using amyl alcohol in methanol as an internal reference standard. Recovery studies (zero-time samples) were performed in duplicate at the same concentration level as the test samples, both at the start and at the end of the 7-day period. Gas chromatographic detector linearity was determined with standard solutions in methanol at 6.96, 4.64, and 2.32 mg/ml concentrations for the 1,2-dichloropropane, and 6.33, 4.22, and 2.11 mg/ml for the amyl alcohol reference. The least squares plot correlation coefficients were greater than 0.999 (i.e., approximately 1.0, linear) for both compounds.

D. RESULTS

Storage Time (Days)	Average Percent (w/w) Chemical Found in Chemical/ Vehicle Mixture *(a)*
1	5.7 ± 0.2 *(c)*
5	5.6 ± 0.2
6	5.5 ± 0.2
7	5.4 ± 0.2

(a) Zero-time recovery yield, 100% ± 4%. Theoretical concentration of chemical in corn oil, 5.75% ± 0.03%. The error values in this table are standard deviations obtained in the instrumental measurements of the test solutions, propagated by standard numerical methods in the calculation of the tabulated quantities.

E. CONCLUSION

1,2-Dichloropropane in corn oil solution of the 5.7% dose level is stable within experimental error when stored at room temperature (25°C) for 7 days.

APPENDIX M

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

APPENDIX M

Duplicate aliquots of 1 ml of the 21, 42, and 83 mg/ml formulations were extracted with 10, 25, and 50 ml, respectively, of methanol containing 2 mg/ml of n-amyl alcohol as an internal standard. Spiked corn oil standards samples at three concentrations, bracketing the range of sample concentrations, were prepared and extracted in the same manner to establish a calibration curve. Analyses of the supernatant solutions were by VPC-FID at 90° on a 6 ft. x 1/4 in. x 2 mm I.D., glass column packed with 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport.

Results of analyses are presented in Table M1.

TABLE M1. ANALYSIS OF 1,2-DICHLOROPROPANE IN CORN OIL

Date Mixed *(a)*	Analysis Date	Concentration (a) of 1,2-Dichloropropane in Corn Oil for Target Concentration		
		21 mg/ml	42 mg/ml	83 mg/ml
4/30/79	5/01/79	20.5	44.0	81.0
7/23/79	7/24/79	19.0	41.0	82.0
8/13/79	8/14/79	20.0	41.0	80.5
10/15/79	10/16/79	19.8	41.3	84.0
11/26/79	11/27/79	22.0 (20.8) *(b)*	41.0	84.5
1/28/80	1/29/80	22.0	43.3	85.0
1/30/80	1/30/80	20.0		
4/21/80	4/23/80	19.0	40.0	83.0
6/16/80	6/18/80	19.5	39.8 (42.8) *(b)*	83.2
7/21/80	7/24/80	20.8	42.5	82.3
9/15/80	9/16/80	19.5	41.0	83.0
11/17/80	11/18/80	20.0	42.0	82.0
1/17/80	1/20/81	20.0	41.6	82.8 (80.1) *(b)*
2/17/81	2/18/81	20.0	42.0	83.5
4/13/81	4/14/81	20.0	42.5 (41.7) *(b)*	86.5
Mean (mg/ml)		20.0	41.6	83.1
Standard deviation		0.76	1.17	1.58
Coefficient of variation %		3.9	2.8	1.9
Range (mg/ml)		19.0-22.0	39.8-44.0	80.5-86.5
Number of samples		14	14	14

(a) The data presented are the average of the results of duplicate analyses.
(b) Results of referee analysis at Midwest Research Institute

APPENDIX N

DATA AUDIT SUMMARY

DATA AUDIT SUMMARY

An audit was conducted on the archival data and pathology materials for the 2 year toxicology and carcinogenesis studies of 1,2-dichloropropane in rats and mice. The laboratory studies were conducted at EG&G Mason, Worcester, MA, under a subcontract with Tracor Jitco from the National Cancer Institute. The study was conducted from April 1979 to May 1982 and was initiated prior to the requirement of compliance to Good Laboratory Practices by NTP in October 1981. The audit was conducted Nov. 5-9, 1984, at the NTP Archives, Rockville, MD, and involved the following Dynamac personnel: C. Dippel, M. Phil.; F. Garner, D.V.M.; L. Keifer, Ph.D.; J. Konz, M.S.P.H.; J. Plautz, M.S.; R. Schueler, D.V.M.; and C. Sexsmith, B.S. Additional participants were: A. Grant (NTP), S. Corson (Pathology Associates, Inc.), and R. Joftes, (NTP). The complete audit report has been reviewed and approved by NTP personnel and is on file at NIEHS, Research Triangle Park, NC.

The audit consisted of an in-depth review of the data and pathology materials collected during the conduct of the study as well as review of the correspondence, laboratory final report, and draft Technical Report. For the in-life toxicology data, this review involved examination of 100% of the records on animal receipt and husbandry, mortality, environmental conditions, sentinel animals, and dosing. Body weight and clinical observation data for 10% of the animals were also reviewed. In the review of the chemistry data associated with the study, all of the records were examined pertaining to receipt and use of the chemical, analysis of the bulk chemical and dose solutions by the study laboratory, and characterization of the bulk chemical and analysis of the dose solutions by the referee laboratory. The audit of the pathology materials included review of 100% of the Individual Animal Data Records (IADRs) for correlation between gross and microscopic diagnosis and for clerical errors, examination of the wet tissues of 10% of the animals for unidentified lesions and animal identification, correlation of slides and tissue blocks for 6 of 10 animal groups, and verification of the pathology in the Technical Report on a 10% sample of the animals.

Several minor problems were noted in the study's documentation and conduct. Records of the quarantine and randomization of animals were not available for review and clinical observation data were limited by infrequent and nondetailed entries. No consistent record of mortalities was maintained in-life; IADRs were used as the primary record of mortality. Comparison of the available in-life records with the IADRs found several differences in recording cause of death. Review of the environmental data found that air temperature in the animal rooms was not well maintained during the study; many daily low temperatures were recorded as being under 70° F. No relationship was found between these periods and mortality. Review of the draft Technical Report found that all of the procedures, body weight data, and sentinel animal data have been accurately reported.

A review of all of the available chemistry data showed that the chemical was received, prepared into dosing mixtures, and reanalyzed as required. Data were not present for the corn oil peroxide analysis, the gas chromatographic analysis of the bulk chemical at the study laboratory, and exact use dates of the dose solutions; however, the lack of these data did not adversely affect achieving the objectives of the study.

The audit of the pathology materials revealed minor discrepancies in the labeling of bags and slides, and several slides were missing. Numerous discrepancies were noted between gross and microscopic diagnoses. Animal identification was acceptable in the majority of the animals checked. Potential tumors (enlargements, nodules, or masses with neoplastic diagnoses) in the target organ (liver) were noted in 7 mice. Potential tumors in nontarget organs were found in 26 mice and 27 rats. Untrimmed potential tumors in nontarget organs were noted only in the high dose male and female mouse groups and in the vehicle and low dose male and female rat groups. As a result of the audit the livers of all the mice were reexamined, and the results of these diagnoses are presented in the text and tables of the Technical Report. Additional adenomas were found in one high dose male mouse and in one control and one low dose female mouse; an additional carcinoma was found in one high dose male mouse. No gavage-related deaths were noted in the rats; 4 occurred in the mice.

Overall, the audit identified no problems that affected the interpretation of the studies. Those discussed in the audit report were adequately resolved or were determined not to affect the outcome of the study. In conclusion, the data examined in this audit are considered adequate to meet the objectives and conclusions of the study.

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