NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 228

CARCINOGENESIS BIOASSAY OF VINYLIDENE CHLORIDE

(CAS NO. 75-35-4)

IN F344 RATS AND B6C3F$_1$ MICE

(GAVAGE STUDY)

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

NATIONAL TOXICOLOGY PROGRAM

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

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

NTP Technical Report

on the

CARCINOGENESIS BIOASSAY

of

VINYLIDENE CHLORIDE

(CAS No. 75-35-4)

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

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park
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and
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NOTE TO THE READER

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

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

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room A-306, Landow Building, Bethesda, MD 20014 (301-496-1152) or at Research Triangle Park, North Carolina 27709 (919-541-3991).

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Single copies of this carcinogenesis bioassay 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.

TABLE OF CONTENTS

TABLES

Page

FIGURES

APPENDIXES

ABSTRACT

A subchronic and a chronic carcinogenesis study of vinylidene chloride (99% pure), a widely used chemical intermediate and monomer, were conducted in F344/N rats and B6C3F1/N mice. In subchronic studies, groups of 10 rats and 10 mice of either sex were administered vinylidene chloride in corn oil by gavage five times per week at 0, 5, 15, 40, 100, or 250 mg/kg body weight for 13 weeks. At the end of this study, representative tissues from these animals were subjected to histopathological examination. The liver was identified as a target organ for vinylidene chloride toxicity.

In the 104-week chronic exposure study, conducted primarily to determine possible carcinogenic potential of vinylidene chloride by the oral route, 50 F344/N rats and 50 B6C3F1/N mice of either sex were gavaged with vinylidene chloride suspended in corn oil at dose levels of 1 or 5 mg/kg (rats) and 2 or 10 mg/kg (mice). Groups of 50 rats and 50 mice of either sex received corn oil alone and served as vehicle controls.

Throughout most of the study, mean body weights of the dosed rats of either sex and high-dose female mice were comparable with those of the corresponding controls; the mean body weights of dosed male and low-dose female mice were slightly lower than those of the controls. The absence of compound-related effects on survival or clinical signs suggests that the rats and mice of either sex could have tolerated higher doses. While no significant differences in survival were observed for any group of rats, 12 control and 10 low-dose males were killed accidentally during week 82; this may have compromised the sensitivity of the male rat study.

The results of histopathological examination indicated an increased incidence of necrosis of the liver in high-dose male and low-dose female mice and chronic renal inflammation in high-dose rats of either sex.

The only observed significant ($P < 0.05$) increase in tumor incidence occurred in low-dose female mice: lymphoma (2/48, 9/49, 6/50) and lymphoma or leukemia (7/48, 15/49, 7/50). These increases were not considered to be related to vinylidene chloride administration because similar effects were not found in the high-dose female mice or in male mice or rats.

Under the conditions of this bioassay, vinylidene chloride administered by gavage was not carcinogenic for F344/N rats or B6C3F1/N mice of either sex. However, since the use of a maximum tolerated dose in this study has not been clearly demonstrated and since previously reported studies have shown that carcinogenicity is associated with inhalation exposure to vinylidene chloride, this study should not be taken as proof that the chemical is not a carcinogen.

CONTRIBUTORS

The bioassay of vinylidene chloride was conducted at Gulf South Research Institute, New Iberia, Louisiana, under a subcontract to Tracor Jitco, Inc., the prime contractor for the NCI/NTP Bioassay Program. The prechronic study was started in June 1976 and completed in January 1977; the chronic study was begun in June 1977 and completed in June 1979.

The bioassay was conducted under the supervision of Mr. R. J. Wheeler (1), principal investigator. Doses of the test chemical were selected by Drs. J. Robens (2,3) and C. Cueto (4). Drs. R. J. Brown (1) and E. Bernal (1), pathologists, directed the necropsies and performed the histopathologic evaluations. The pathology report and selected slides were evaluated by the NCI Pathology Working Group as described in Ward et al. (1978). The diagnoses represent a consensus of contracting pathologists and the NCI Pathology Working Group, with final approval by the NCI Pathology Working Group in August 1980.

Animal pathology tables and survival tables were compiled at EG&G Mason Research Institute, Rockville, Maryland (5). The statistical analyses were performed by Dr. J. R. Joiner (2) and Mr. J. Warner (2), using methods selected for the bioassay program by Dr. J. J. Gart (6). Chemicals were analyzed at Midwest Research Institute (7). Chemical reanalysis and analyses of chemical-vehicle mixtures were performed by Mr. S. M. Billedeau (1) and Mr. E. S. Collard (1).

This report was prepared at Tracor Jitco (2). Those responsible for the report at Tracor Jitco were Dr. C. Cueto, Director of the Bioassay Program; Dr. S. S. Olin, Associate Director; Dr. M. A. Stedham, pathologist; Dr. J. E. Tomaszewski, chemist; Dr. W. D. Theriault, reports manager; Dr. A. C. Jacobs, bioscience writer; and Ms. C. E. Dean, Technical Assistant.

The following scientists at NCI/NTP (8) were responsible for evaluating the bioassay experiment, interpreting the results, and reporting the findings: Dr. Rajendra S. Chhabra (Chemical Manager), Dr. J. Fielding Douglas, Dr. Charles K. Grieshaber, Dr. Larry Hart, Dr. Joseph Haseman, Dr. James Huff, Dr. Mary R. Kornreich, Dr. Ernest E. McConnell, Dr. James McCoy, Dr. John A. Moore, Dr. Sherman F. Stinson, Dr. Raymond Tennant, and Dr. Jerrold M. Ward.

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PEER REVIEW PANEL AND COMMENTS

On February 18, 1981, this carcinogenesis bioassay report on vinylidene chloride underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors, Technical Review Subcommittee and Associated Panel of Experts at an open meeting held in Building 31C, National Institutes of Health, Bethesda, Maryland. Members of the Subcommittee are: Drs. Margaret Hitchcock (Chairperson), Curtis Harper (principal reviewer) and Alice Whittemore. Members of the panel were: Drs. Norman Breslow, Joseph Highland, Frank Mirer, Sheldon Murphy, Svend Nielsen (principal reviewer), Bernard Schwetz, Roy Shore, James Swenberg and Gary Williams. (Drs. Norman Breslow and Alice Whittemore were not able to attend this meeting.)

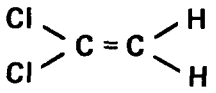
Dr. Harper, a principal reviewer, agreed that the compound was not carcinogenic in either rats or mice under the conditions of this bioassay. He felt, however, that the conclusion was too simply stated. Based on a review of the data from this study and previous positive findings for carcinogenicity of vinylidene chloride by other routes of exposure, he thought that both the abstract and conclusion statement should be revised to more accurately represent the risk that is potentially posed by this compound. He said there were a number of neoplasms which occurred at increased incidences which were not mentioned in the abstract, presumably because they did not meet the Bonferroni inequality criterion for overall significance. Included were pheochromocytomas, pancreatic islet-cell carcinomas, interstitial-cell tumors of the testes, and subcutaneous fibromas in male rats, and pituitary adenomas in female rats. Also noted were lymphomas or leukemia in low-dose female mice.

The other principal reviewer, Dr. Nielsen, agreed that under the conditions of the bioassay vinylidene chloride was not carcinogenic for rats and apparently not for mice, although the dose levels in female mice were less than optimal. He considered the data on weight gains in the 13-week study of female mice to be too variable to allow a reasonable determination of dose levels in the chronic study. He noted that low-dose female mice had a higher incidence of hepatic necrosis, a lower weight gain, and a lower survival rate than control or high-dose female mice.

Dr. Haseman (NTP) stated that the increased incidences of a number of tumors referred to by Dr. Harper were disregarded in the abstract not so much because of the Bonferroni criterion but because life table analyses indicated that the effects were not statistically significant. Also, this type of analysis aided in minimizing the impact of early accidental deaths of control and low-dose male rats. Drs. Shore and Harper requested that life table analyses be included in tabular form for those tumors where increased incidences were statistically significant by the Fisher exact test or by the Cochran-Armitage linear trend test but were not significant when life table analyses were used.

Dr. Harper moved that the report on the bioassay of vinylidene chloride be accepted contingent upon inclusion of a clarification of the data to explain how the maximal tolerated dose was chosen for the chronic mouse studies. Dr. Nielsen seconded the motion, and the bioassay report was approved unanimously (with one abstention) by the Peer Review Panel.

I. INTRODUCTION



VINYLIDENE CHLORIDE

CAS NO. 75-35-4

VINYLIDENE CHLORIDE

Vinylidene chloride (1,1-dichloroethylene; VDC; 1,1-DCE) CAS No. 75-35-4) is a volatile liquid used primarily as a chemical intermediate in the production of 1,1,1-trichloroethane and as a monomer in the production of copolymers of high vinylidene content. The production of this chemical in 1976 was 120-150 million kilograms (IARC, 1979; Chem. Eng. News, 1977). Current production figures for vinylidene chloride are not available (USITC, 1979).

The U.S. Food and Drug Administration has approved the use of vinylidene chloride copolymers in various products intended for use in contact with food (CFR, 1977). Vinylidene chloride-vinyl chloride copolymers are used mainly for food packaging films and coatings (e.g., household and industrial food wraps; laminations for cap liners and luncheon meat; shrink films for meat; and paper coatings for packaged potato chips, pretzels, cereals, and for cake mixes) (IARC, 1979). The industrial and household Saran® films contain residues of vinylidene chloride monomer (Birkel et al., 1977).

Vinylidene chloride-vinyl chloride copolymers are also used as laminations for packaged cosmetics, as coatings for steel piles and structures and for the interiors of ship tanks and railway tank cars, and as binders and coatings for magnetic, audio, video, and computer tapes (IARC, 1979).

Vinylidene chloride is mutagenic in Salmonella typhimurium TA 1530 and TA 100 after activation either by the 9,000-g liver supernatant from

phenobarbital treated male OF-1 mice (Bartsch et al., 1975) or by liver microsomes from rats pretreated with Aroclor 1254 (Simmon et al., 1977). VDC is also mutagenic in Salmonella typhimurium TA 1535 after activation by kidney and liver post-mitochondrial supernatant (S-9 mix) (Jones and Hathway, 1978b). Vinylidene chloride induced reverse mutations in Escherichia coli K12 in the presence of liver microsomes from mice pretreated with phenobarbital (Greim et al., 1975). VDC vapors caused dose-related toxicity in V79 hamster cells but were not mutagenic with or without liver S-9 activation (Devron and Kuroki, 1979). VDC induced both point mutation and mitotic gene conversion in Saccharomyces cerevisiae in suspension with metabolic activation and in the intrasanguineous host-mediated assay (Bronzetti et al., 1981). Vinylidene chloride was negative in dominant lethal tests in CD rats and CD-1 mice (Short et al., 1977a; and Anderson et al., 1977) and was not teratogenic in Sprague-Dawley rats (Murray et al., 1979).

In inhalation studies published while the present study was in progress, vinylidene chloride was reported to be carcinogenic for female Sprague-Dawley rats (producing mammary fibroadenomas or carcinomas) and for male Swiss mice (producing renal adenocarcinomas) (Maltoni et al. 1977; Norris, 1977). An increased incidence of lung, skin, and liver cell tumors in mice and the induction of hemangiosarcomas in both mice and rats were reported in another inhalation study (Lee et al., 1977). Vinylidene chloride was also found to be a skin tumor initiatior in Ha:ICR Swiss mice (Van Duuren et al., 1979). However, when vinylidene chloride was administered by gavage to male Swiss mice, to female BDIV rats, or to the progeny of female BDIV rats previously exposed in utero or when it was administered in drinking water to Sprague-Dawley rats, no carcinogenic effects were found (Maltoni et al. 1977; Norris, 1977; and Ponomarkov and Tomatis, 1980). Other studies have been conducted for which the final results have not yet been fully reported (Viola and Caputo, 1977; Rampy et al., 1978; Maltoni et al., 1977).

Vinylidene chloride was selected for testing by the Bioassay Program because of its widespread use and its structural relationship to vinyl chloride, a known human carcinogen (IARC, 1979). The objective of the present study was to determine the carcinogenic potential of vinylidene chloride in rats and mice by oral administration.

II. MATERIALS AND METHODS

A. Chemical

Vinylidene chloride (99% pure) was obtained in two batches from Dow Chemical Company (Freeport, TX). Lot No. UTLX83844 was used for the subchronic studies, and Lot No. V83848 was used for the chronic studies.

The results of purity and identity analyses performed at Midwest Research Institute (Appendix E) and at Gulf South Research Institute (Appendix F) were consistent with the assigned structure. Three minor impurities were identified in Lot No. UTLX83844 by vapor-phase chromatography and mass spectrometry: trans-dichloroethylene (0.1%); cis-dichloroethylene (less than 0.1%); and a stabilizer, the monomethylether of hydroquinone (MEHQ), present at a concentration of 0.05%. 1,1-Dichloroethane, 1,2-dichloroethane, trichloroethylene, and vinyl chloride were not detected; if present, the concentrations were less than 0.1%, 0.04%, 0.1%, and 0.01%, respectively. Two impurities in Lot No. V83848 were identified by vapor-phase chromatography: trans-dichloroethylene (0.15%) and MEHQ (0.02%).

Vinylidene chloride was stored under nitrogen in an amber glass bottle at -20°C. Lot No. V83848 was analyzed monthly at Gulf South, as described in Appendix F, and did not change in composition over the course of the study.

B. Dosage Preparation

Appropriate amounts of vinylidene chloride were weighed and then mixed with sufficient corn oil (Table 1) to give the desired concentration. Rats received a dose volume of 5 ml/kg and mice received 10 ml/kg. The vinylidene chloride - corn oil solutions were stored at 4°C for no longer than 7 days.

The stability of vinylidene chloride in corn oil was determined at Midwest Research Institute by analyzing methanol extracts of vinylidene chloride - corn oil mixtures that had been stored at room temperature (under nitrogen and in the dark) from 1 to 7 days. Amounts of the test chemical

Table 1. Source and Description of Materials Used for Dosage Preparation and Animal Maintenance

Item	Description	Source
Animal Meal	Wayne® Lab Blox	Allied Mills (Chicago, IL)
Cages	Polycarbonate	Lab Products, Inc. (Garfield, NJ)
Corn Oil	Lou Ana®	Paul A. Doerle Wholesale Co.
Filter Sheets	Disposable, nonwoven fiber	Lab Products, Inc. (Rochelle Park, NJ)
Bedding	Absorb Dri® hardwood chips	Lab Products, Inc. (Garfield, NJ)
Watering System	Edstrom Automatic	Edstrom Industries (Waterford, WI)

present were determined by vapor-phase chromatography (Appendix G). Vinylidene chloride at 1% w/v in corn oil was found to be stable for 7 days at room temperature.

Every 2 or 3 months, randomly selected batches of vinylidene chloride - corn oil were analyzed as described in Appendix H. The mean concentration (± standard deviation) of 12 samples, measured in duplicate and containing a theoretical level of 1 mg/ml, was 0.97 ± 0.053 mg/ml.

C. Animals

Four-week-old F344/N rats and B6C3F1/N mice were each obtained in single shipments from the NCI Frederick Cancer Research Center (Frederick, MD), observed for 5 weeks for the presence of parasites or other diseases, and then assigned to control or dosed groups according to a table of random numbers.

D. Animal Maintenance

Rats and mice were housed five per cage in solid bottom polycarbonate cages covered with spun bonded fiberglass filter sheets and supplied with hardwood chip bedding (Table 1). Cages and bedding were changed twice per week. Diets of Wayne® Lab Blox and tap water via an Edstrom automatic watering system were provided *ad libitum*. Feed hoppers were changed once per week.

Animal rooms were maintained at 23° ± 2°C and the relative humidity was 40%-70%. Incoming air was provided at a rate sufficient to give 10-12 changes of room air per hour. Fluorescent lighting was provided 12 hours per day.

All rats and mice were housed in the same room. No other chemicals were on test in that room.

E. Range-Finding and Repeated-Dose Studies

A single-dose range-finding study was conducted to determine the doses for the 14-day repeated-dose study (Table 2). Vinylidene chloride was diluted in corn oil and administered by gavage to groups of five males and five females of each species at each of the dose levels. The animals were observed for 14 days and then killed and necropsied on day 15.

One female rat receiving 500 mg/kg died. One male rat that received 10 mg/kg died after 7 days and two that received 1,000 mg/kg died within 48 hours.

All male mice receiving 500 or 1,000 mg/kg died. Among the female mice, 1/5 receiving 50 mg/kg, 3/5 receiving 500 mg/kg, and 5/5 receiving 1,000 mg/kg died.

Fourteen-day repeated-dose studies were conducted to determine the doses to be used in the 90-day studies. Groups of five males and five females of each species were administered vinylidene chloride in corn oil by gavage, daily for 14 days. Animals were weighed at 0, 7, and 14 days. On day 16, all survivors were killed and necropsied. Doses administered, survival, and mean body weights of the dosed and control groups are shown in Tables 3 and 4.

Four of 5 male rats receiving 1,000 mg/kg, 3/5 female rats receiving 500 mg/kg, and 3/5 female rats receiving 1,000 mg/kg died within 48 hours. All were hyporeactive. Weight gain of male rats receiving 500 mg/kg was depressed 28%; the only surviving male rat that received 1,000 mg/kg lost weight. A dose-related decrease in mean body weight gain was observed in female rats. Weight gain was depressed 62% and 129% in females receiving 500 or 1,000 mg/kg, respectively. Hemorrhagic necrosis of the liver was observed in all the rats that died.

All the mice receiving 500 mg/kg died. Before death, they exhibited hyporeactivity, a staggering gait, and rapid breathing. Hemorrhagic

Table 2. Dosage and Survival of Rats and Mice Administered a Single Dose of Vinylidene Chloride in Corn Oil by Gavage

	Dose (mg/kg)	Survival (a) Male	Survival (a) Female
Rats			
	0	5/5	5/5
	10	4/5	5/5
	50	5/5	5/5
	100	5/5	5/5
	500	5/5	4/5
	1,000	3/5	5/5
Mice			
	0	5/5	5/5
	10	5/5	5/5
	50	5/5	4/5
	100	5/5	5/5
	500	0/5	2/5
	1,000	0/5	0/5

a) Number surviving/number per group

Table 3. Dosage, Survival, and Mean Body Weights of Rats Administered Vinylidene Chloride by Gavage for 14 Days

Dose (mg/kg)	Survival(a)	Mean Body Weights (grams) Initial	Final	Change(b)	Weight Change Relative to Controls (%)(c)
Male					
0	5/5	116.8 ± 6.57	163.4 ± 6.79	46.6 ± 7.77	
10	5/5	110.6 ± 4.83	165.4 ± 9.24	54.8 ± 4.72	+ 17.6
50	5/5	112.0 ± 1.79	158.2 ± 4.39	46.2 ± 3.25	- 0.9
100	5/5	109.0 ± 4.68	151.8 ± 9.58	42.6 ± 9.11	- 8.6
500	5/5	114.0 ± 5.08	147.4 ± 2.25	33.4 ± 5.36	- 28.3
1,000	1/5	118.0 ± 0.00	114.0 ± 0.00	-4.0 ± 0.00	-108.6
Female					
0	5/5	94.6 ± 4.46	120.6 ± 8.62	26.0 ± 5.06	
10	5/5	97.2 ± 3.47	126.2 ± 1.56	29.0 ± 2.39	+ 11.5
50	5/5	97.0 ± 3.16	121.6 ± 3.33	24.6 ± 4.02	- 5.4
100	5/5	97.4 ± 2.48	120.4 ± 3.14	23.0 ± 1.79	- 11.5
500	2/5	102.0 ± 6.00	112.0 ±11.00	10.0 ± 5.00	- 61.5
1,000	2/5	100.5 ± 0.50	93.0 ± 7.00	-7.5 ± 6.50	-128.8

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study.
(b) Mean weight change of the survivors of the group ± standard error of the mean.
(c) Weight change of the dosed survivors relative to the survivors of the controls =

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

Table 4. Dosage, Survival, and Mean Body Weights of Mice Administered Vinylidene Chloride by Gavage for 14 Days

Dose (mg/kg)	Survival(a)	Mean Body Weights (grams) Initial	Final	Change(b)	Weight Change Relative to Controls (%)(c)
Male					
0	5/5	22.2 ± 0.37	24.8 ± 0.37	2.6 ± 0.40	
5	5/5	22.0 ± 0.32	23.4 ± 0.40	1.4 ± 0.40	- 46.2
10	5/5	23.0 ± 0.84	25.8 ± 0.86	2.8 ± 0.66	+ 7.7
50	5/5	22.2 ± 0.80	24.8 ± 0.97	2.6 ± 0.51	0.0
100	5/5	22.8 ± 0.37	24.0 ± 0.32	1.2 ± 0.20	- 53.8
500	0/5	(d)	(d)	(d)	
Female					
0	5/5	20.2 ± 0.20	21.6 ± 0.40	1.4 ± 0.40	
5	5/5	20.6 ± 0.40	21.2 ± 0.20	0.6 ± 0.40	- 57.1
10	5/5	20.4 ± 0.40	21.0 ± 0.63	0.6 ± 0.60	- 57.1
50	5/5	20.4 ± 0.24	21.0 ± 0.32	0.6 ± 0.24	- 57.1
100	5/5	21.0 ± 0.32	22.2 ± 0.49	1.2 ± 0.73	- 14.3
500	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) Weight change of the dosed survivors relative to the survivors of the controls =

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

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

necrosis of the liver was seen at necropsy. No compound-related histopathologic effects were observed in the mice.

F. Subchronic Studies

A 90-day subchronic study was conducted to determine the doses of vinylidene chloride to be used in the 2-year chronic study. Groups of 10 rats and 10 mice of either sex were administered vinylidene chloride in corn oil by gavage 5 times per week at 0, 5, 15, 40, 100, or 250 mg/kg body weight for 13 weeks. Vehicle control groups consisting of 10 males and 10 females of each species received corn oil alone. After 90 days, the rats and mice were killed using carbon dioxide and necropsied.

Representative tissues (see Section H) from rats and mice receiving 250 mg/kg, from mice receiving 100 mg/kg, and from control animals were examined microscopically. Livers from all other dosed groups were also examined. The doses administered, the survival of animals in each dosed group at the end of the study, and the mean body weights at week 13 are shown in Tables 5 and 6.

Rats: Three female rats receiving 250 mg/kg died during the first week. No other rats died. Weight gain was depressed 20% for male rats receiving 250 mg/kg compared with controls.

Severe centrilobular necrosis of the liver was observed in the 3 female rats that died. Minimal to moderate hepatocytomegaly was seen in the rest of the rats that received 250 mg/kg. Lesser degrees (minimal to mild) of hepatocytomegaly were seen in 6 of 10 male rats and 3 of 10 female rats that received 100 mg/kg. Various combinations of portal and subcapsular fibrosis, bile duct hyperplasia, pigmented macrophages, and hepatocellular atrophy were seen in all male rats (mild to severe in 9 of 10 and minimal in 1 of 10) and in 7 of 10 female rats (mild to moderate in 6 of 10 and minimal in 1 of 10) receiving 250 mg/kg. The rats receiving 100 mg/kg were affected to a much lesser degree, both in numbers and in severity. Foci of cytoplasmic change, primarily clear cell foci, (as defined under foci of cellular alteration of hepatocytes, Squire and Levitt, 1975) were seen in 3

of 10 males and 3 of 10 females receiving 250 mg/kg. Fatty metamorphosis or cytoplasmic vacuolization or both, usually in minimal or mild degrees of severity, occurred in the animals of most groups but had no distinct dose relationship (Table 7).

Original examination of the lesions in the rat livers placed more emphasis on the changes seen in the animals at the lower doses whereas a review interpreted these changes as being much less important. Thus, the doses of 1 and 5 mg/kg of body weight, which were selected for the chronic study and were originally based on hepatotoxic effects, were probably too low.

Table 5. Dosage, Survival, and Mean Body Weights of Rats Administered Vinylidene Chloride by Gavage for 13 Weeks

Dose (mg/kg)	Survival(a)	Mean Body Weights (grams) Initial	Final	Change	Weight Change Relative to Controls (%)(b)
Male					
0	10/10	118	316	+198	
5	10/10	115	307	+192	- 3
15	10/10	115	306	+191	- 4
40	10/10	119	302	+183	- 8
100	10/10	117	299	+182	- 8
250	10/10	117	276	+159	-20
Female					
0	10/10	95	200	+105	
5	10/10	93	193	+100	- 5
15	10/10	93	198	+105	0
40	10/10	97	194	+ 97	- 8
100	10/10	95	194	+ 99	- 6
250	7/10	97	190	+ 93	-11

(a) Number surviving/number per group
(b) Weight Change Relative to Controls =

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

Table 6. Dosage, Survival, and Mean Body Weights of Mice Administered Vinylidene Chloride by Gavage for 13 Weeks

Dose (mg/kg)	Survival(a)	Mean Body Weights (grams) Initial	Final	Change	Weight Change Relative to Controls (%)(b)
Male					
0	10/10	21	35	+14	
5	10/10	21	35	+14	0
15	10/10	21	34	+13	- 7
40	9/10	21	33	+12	-14
100	8/10	21	30	+ 9	-36
250	0/10	21	--	--	--
Female					
0	10/10	18	24	+ 6	
5	9/10	19	23	+ 4	-33
15	9/10	18	23	+ 5	-17
40	10/10	18	23	+ 5	-17
100	7/10	18	23	+ 5	-17
250	1/10	20	26	+ 6	0

(a) Number surviving/number per group

(b) Weight Change Relative to Controls =

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

Table 7. Incidence of Liver Lesions in Rats and Mice Administered Vinylidene Chloride by Gavage for 13 Weeks

Dose (mg/kg)	Controls		5		15		40		100		250	
Sex	M	F	M	F	M	F	M	F	M	F	M	F
Rats												
No. examined	9	10	10	10	10	10	10	10	10	10	10	10
Centrilobular necrosis	0	0	0	0	0	0	0	0	0	0	0	3
Fibrosis, pigmentation, bile duct hyperplasia, hepatocellular atrophy	0	0	0	0	0	0	0	0	3	4	10	7
Fatty metamorphosis	4	0	7	5	7	7	8	3	2	2	0	1
Hepatocytomegaly	0	0	0	0	0	0	1	0	6	3	10	7
Foci of cytoplasmic change (cellular alteration)	0	0	0	0	0	0	0	0	0	0	3	3
Mice												
No. examined	10	10	10	10	10	10	10	10	10	10	10	10
Cellular necrosis	0	0	0	0	0	0	0	0	2	2	5	5
Congestion	0	0	0	0	0	0	2	0	0	0	8	2
Necrosis, NOS	0	0	0	0	0	0	0	0	0	0	2	0
Cellular atypia	0	0	0	0	0	0	2	0	7	6	0	0
Fatty metamorphosis	0	0	0	1	2	0	2	2	0	0	0	0
Focal area of cellular alteration	0	0	1	0	0	0	0	0	0	0	0	0

Mice: All males receiving 250 mg/kg died within 24 hours; 9/10 females receiving 250 mg/kg died within 48 hours. Deaths occurred in 1/10 females receiving 5 mg/kg; 1/10 females receiving 15 mg/kg; 1/10 males receiving 40 mg/kg; and 2/10 males and 3/10 females receiving 100 mg/kg. A dose-related decrease in mean body weight gain was observed for male mice.

Centrilobular necrosis, hemorrhage, and congestion of the liver were observed in the males and females that died in the 250 mg/kg dose groups. Cellular atypia of the liver (less severe than that seen in the rats) was observed in 7/10 males and 6/10 females receiving 100 mg/kg but not in animals receiving 250 mg/kg. At 40, 15, and 5 mg/kg levels, severity of hepatic lesions was dose related. The incidence of hepatic lesions in males was dose related and was higher than that in females. The most frequently encountered change in mice exposed to 40 mg/kg or less was slight, sometimes moderate, fatty metamorphosis. Patchy foci of one or a few smaller cells with sparse cytoplasm were encountered much less frequently in mice than in rats.

Hepatic effects were considered to be minimal at 5 mg/kg, and doses selected for the mice for the chronic study were 2 and 10 mg/kg body weight.

G. Chronic Studies

The number of animals in test groups, doses administered, and durations of the chronic studies are shown in Table 8.

H. Clinical Examinations and Pathology

Mortality and morbidity checks were made twice daily and animals were weighed every 2 weeks. Animals that were moribund and those that survived to the end of the study were killed using carbon dioxide and necropsied.

Gross and microscopic examinations were performed on major tissues, major organs, and all gross lesions from killed animals and from animals found dead unless precluded in whole or in part by autolysis or cannibalization. Thus,

Table 8. Experimental Design of Chronic Vinylidene Chloride Gavage Studies in Rats and Mice

Test Group	Initial No. of Animals	Dose (a) (mg/kg)	Weeks on Study: Dosed	Weeks on Study: Not Dosed
Male Rats				
Vehicle-Control	50(b)	0	0	104
Low-Dose	50	1	104	0
High-Dose	50	5	104	0
Female Rats				
Vehicle-Control	50(b)	0	0	104
Low-Dose	50	1	104	0
High-Dose	50	5	104	0
Male Mice				
Vehicle-Control	50(b)	0	0	104
Low-Dose	50	2	104	0
High-Dose	50	10	104	0
Female Mice				
Vehicle-Control	50(b)	0	0	104
Low-Dose	50	2	104	0
High-Dose	50	10	104	0

(a) Doses were administered 5 times per week.
(b) Vehicle controls received corn oil alone.

The number of animals from which particular organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

The following were examined microscopically: skin, lungs and bronchi, trachea, bone and bone marrow, spleen, lymph nodes, heart, salivary gland, liver, pancreas, stomach, small intestine, large intestine, kidneys, urinary bladder, pituitary, adrenal, thyroid, parathyroid, mammary gland, prostate and seminal vesicles or uterus, testis or ovary, brain, thymus, larynx, and esophagus.

I. Data Recording and Statistical Analyses

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

Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time 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) extension of Cox's methods for testing for a dose-related trend. One-tailed P values have been reported for all tests except the departure from linearity test, which is reported only when its two-tailed P value is less than 0.05.

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 (numerator) to the number of animals in which that site is

examined (denominator). In most instances, the denominators include only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions prior to histological sampling (e.g., skin or mammary tumors) or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

The purpose of the statistical analyses of tumor incidence is to determine whether animals receiving the test chemical developed a significantly higher proportion of tumors than did the control animals. As part of these analyses, the one-tailed Fisher exact test (Cox, 1970) was used to compare the tumor incidence of a control group with that of a group of dosed animals at each level. When results for two dosed groups were compared simultaneously with those for a control group, a correction to ensure an overall significance level of 0.05 is made. The Bonferroni inequality criterion (Miller, 1966) requires that the P value for any comparison be less than or equal to 0.025. When this correction was used, it is discussed in the narrative section. It is not presented in the tables, where the Fisher exact P values are shown.

The Cochran-Armitage test for linear trend in proportions, with continuity correction (Armitage, 1971), was also used. Under the assumption of a linear trend, this test determines if the slope of the dose-response curve is different from zero at the one-tailed 0.05 level of significance. Unless otherwise noted, the direction of the significant trend is a positive dose relationship. This method also provides a two-tailed test of departure from linear trend.

A time-adjusted analysis was used. Deaths that occurred before the first tumor was observed were excluded by basing the statistical tests on animals that survived at least 52 weeks, unless a tumor was found at an anatomic site of interest before week 52. When such an early tumor was found, comparisons were based exclusively on animals that survived at least as long as the animal in which the first tumor was found. Once this reduced set of data was obtained, the standard procedures for analyses of the

incidence of tumors (Fisher exact tests, Cochran-Armitage tests, etc.) were followed.

Life table methods were used to analyze the incidence of tumors. These analyses included data from animals killed at the end of the study. Curves of the proportions surviving without an observed tumor were computed as in Saffiotti et al. (1972). The week during which an animal died naturally or was killed was entered as the time point of examination for tumors. The methods of Cox and of Tarone were used for the statistical tests of the groups. The statistical tests were one-tailed.

III. RESULTS - RATS

A. Body Weights and Clinical Signs (Rats)

Mean body weights of dosed and control rats of either sex were comparable throughout the study (Figure 1 and Table 9). No compound-related clinical signs were observed.

B. Survival (Rats)

Estimates of the probabilities of survival of male and female rats administered vinylidene chloride by gavage at the doses of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 2. While no significant differences in probability of survival were observed in any group of either sex of rats, 12 control and 10 low-dose males were accidentally killed during week 82 of the study as a result of a 5-hour temperature excursion to 37°C and 1 low-dose male was accidentally killed during the 42nd week. These animals were censored in the survival analysis but were examined histopathologically.

In male rats, 20/50 (40%) of the vehicle controls, 24/50 (48%) of the low-dose, and 37/50 (74%) of the high-dose group lived to the end of the study at 104 weeks. In female rats, 27/50 (54%) of the vehicle controls, 28/50 (56%) of the low-dose, and 29/50 (58%) of the high-dose group lived to the end of the study at 104 weeks.

The large number of accidental deaths in the control and low-dose male rats may have influenced the incidence of late appearing tumors in these groups.

C. Pathology (Rats)

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; Tables A3 and A4 give the survival and tumor status for each individual animal in the male and female rat studies, respectively.

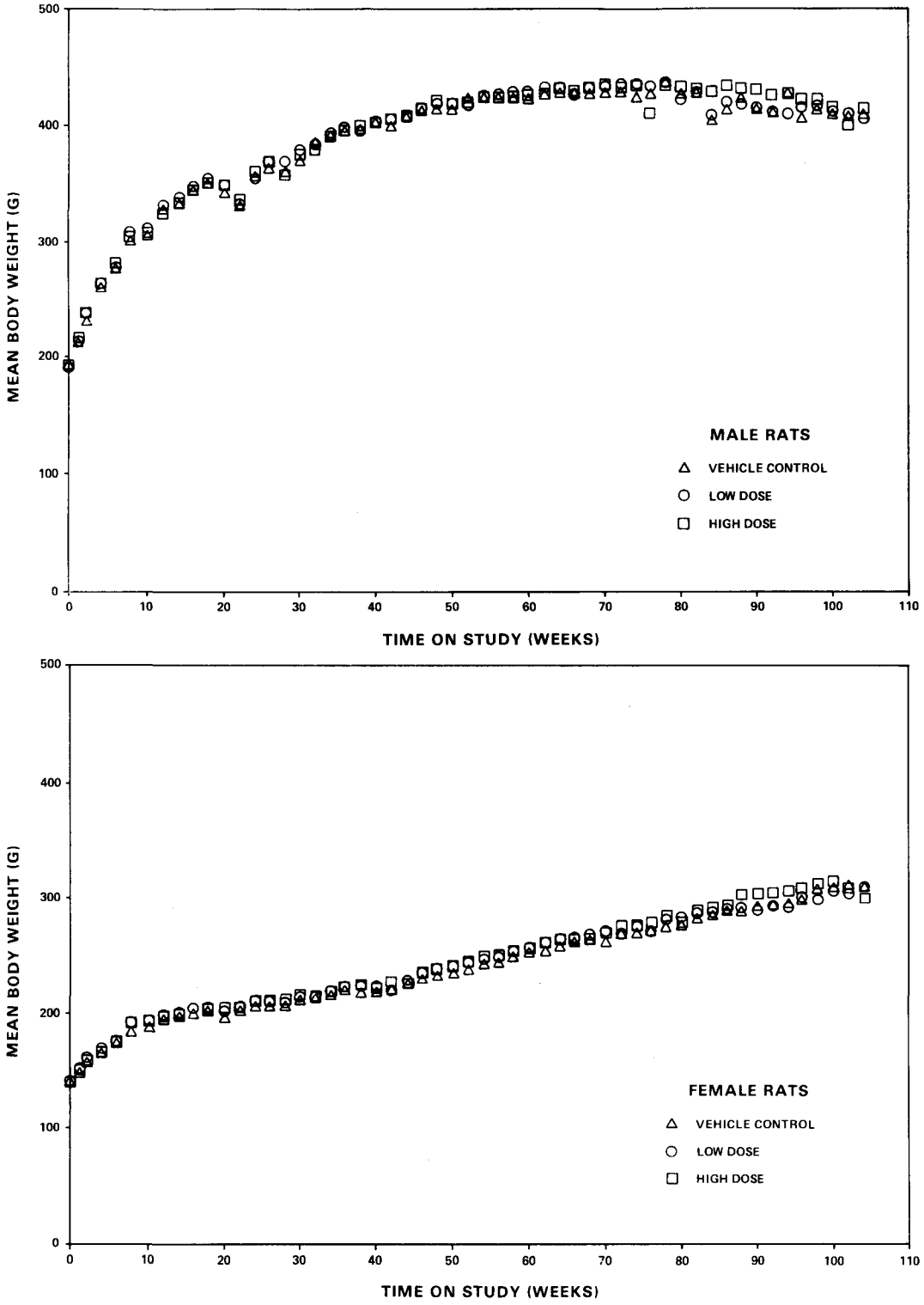


Figure 1. Growth Curves for Rats Administered Vinylidene Chloride by Gavage

Table 9. Mean Body Weight Change (Relative to Controls) of Rats Administered Vinylidene Chloride by Gavage

	Week No.	Mean Body Weight Change (grams) Control	Low Dose	High Dose	Weight Change Relative to Controls (a)(percent) Low Dose	High Dose
Male Rats	0	191(b)	190(b)	193(b)		
	1	20	23	24	+15	+20
	20	150	160	157	+ 7	+ 5
	40	210	214	210	+ 2	0
	60	230	239	233	+ 4	+ 1
	80	236	232	240	- 2	+ 2
	100	218	222	223	+ 2	+ 2
Female Rats	0	139(b)	140(b)	139(b)		
	1	10	12	12	+20	+20
	20	56	82	66	+46	+18
	40	79	84	83	+ 6	+ 5
	60	114	117	118	+ 3	+ 4
	80	143	147	150	+ 3	+ 5
	100	170	166	176	- 2	+ 4

(a) Weight Change Relative to Controls =

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

(b) Initial weight

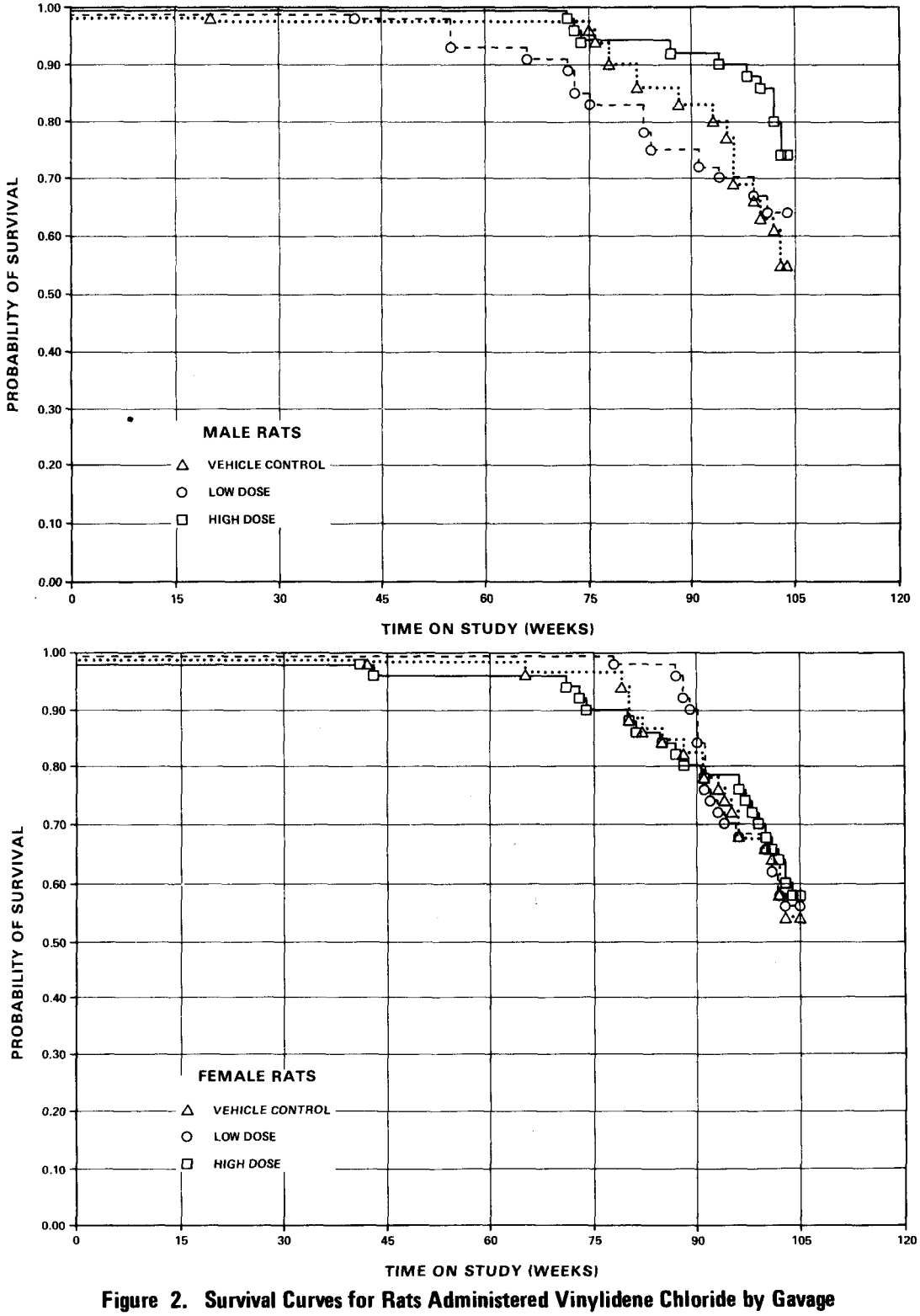


Figure 2. Survival Curves for Rats Administered Vinylidene Chloride by Gavage

Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2.

The tumors encountered were those commonly found in aging rats of this strain. They occurred in comparable numbers in test animals and controls and were not considered to be related to administration of the test compound (Goodman et al., 1979).

Several nonneoplastic lesions of possible significance were observed. The incidence of chronic inflammation of the kidney in both male and female rats was higher in high-dose animals than in controls (males: controls = 26/50, 52%; low-dose = 24/48, 50%; and high-dose = 43/48, 90%; females: controls = 3/49, 6%; low dose = 6/49, 12%; and high-dose = 9/44, 20%). Although the occurrence of chronic nephritis appears to be dose related, this lesion is common in aging rats.

D. Statistical Analyses of Results (Rats)

Tables 10 and 11 contain the results of Fisher's exact tests and Cochran-Armitage trend tests for those primary tumors whose incidence was 5% or greater in at least one of the three groups. Because of the many early deaths in the control and low-dose male rat groups, life table analyses of primary tumor incidence were also carried out. These procedures adjust for intercurrent mortality and thus minimize the influence of animals dying before the onset of late-appearing tumors. The results of these analyses are summarized in Table 12 for those tumors showing a significant increase by the "unadjusted" analyses reported in Tables 10 and 11.

Pheochromocytomas of the adrenal in male rats were observed in increased incidence in the high-dose group compared with the control group (6/50, 12% in the controls; 5/48, 10% in the low-dose; and 13/47, 28% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.010). The Fisher exact test between the high-dose group and the control group indicated a value of P=0.045. Analyses of these data by life table methods produced no statistically significant

results. The historical incidence of this tumor at this laboratory in untreated male F344 rats is 32/400 (8%), while the incidence in vehicle control (corn oil) male rats across the bioassay program is 13/125, 10.4%. In female rats, this tumor was not observed in statistically significant proportions.

Islet-cell adenomas or carcinomas of the pancreatic islets in male rats were observed in increased incidence in the high-dose group (4/49, 8% in the controls; 1/47, 2% in the low-dose; and 8/48, 17% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.025), but the Fisher exact tests were not significant. Analyses of these data by life table methods revealed no statistically significant results. These tumors have been observed in 18/400 (4.5%) of the untreated male rats at this laboratory and in 6/125 (4.8%) of the male vehicle control (corn oil) rats in the Bioassay Program. In female rats, this tumor was not observed in statistically significant proportions.

Interstitial-cell tumors of the testis were observed in increased incidence in the high-dose group compared with the control group (43/50, 86% in the controls; 39/47, 83% in the low-dose; and 47/48, 98% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.013). The Fisher exact test between the high-dose group and the control group indicated a value of P=0.034, but this high-dose effect is not statistically significant if age-adjusted analyses are used which eliminate those animals that died before 52 weeks (life table analyses are not appropriate for this tumor, since this lesion is not generally regarded as life-threatening). This tumor has been observed at incidences as high as 100% in untreated control groups at this laboratory.

Adenomas of the pituitary were observed in increased incidence in the high-dose female rats compared with the controls (16/48, 33% in the controls; 20/49, 41% in the low-dose; 24/43, 56% in the high-dose). The Cochran-Armitage test for linear trend was significant (P=0.017) and the Fisher exact

test between the high-dose and control groups was significant (P=0.026). The analysis of these data by life table methods revealed no statistically significant results. No significant differences are observed in the incidence of female rats with either adenomas or carcinomas of the pituitary. These tumors were not observed in statistically significant proportions in male rats.

Fibromas of the subcutaneous tissue were observed in increased incidence in the dosed groups of male rats compared with controls (0/50, 0% in the controls; 1/48, 2% in the low-dose; 4/48, 8% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.024), but the Fisher exact tests were not significant. Analyses of these data by life table methods revealed no statistically significant results. Fibromas of the skin have been observed in 58/2,230 (2.6%) of the untreated male F344 rats and in 5/125 (4%) of the male vehicle control F344 rats receiving corn oil by gavage in the bioassay program.

Leukemia (morphology unspecified) in female rats was observed in decreased incidence in the dosed groups compared with the controls (10/49, 20% in the controls; 3/50, 6% in the low-dose; 4/45, 9% in the high-dose). The Fisher exact test between the low-dose and control groups was significant in the negative direction (P=0.033). The Cochran-Armitage test for linear trend was not significant, but there was a departure from linear trend (P=0.041) due to the reduced incidence in the low-dose group compared with the high-dose and control group. Female rats with either lymphomas or leukemias of the hematopoietic system were observed in decreased proportions in the dosed groups compared with the controls (13/49, 27% in the controls; 7/50, 14% in the low-dose; 5/45, 11% in the high-dose). The Fisher exact test between the high-dose and control groups is significant in the negative direction (P=0.050). The incidence in the low-dose group was not significant. These tumors were not observed in statistically significant proportions in male rats.

Neoplastic nodules of the liver in female rats were observed in decreased incidence in dosed groups (4/49, 8% in the controls; 0/50, 0% in the low-dose; 0/45, 0% in the high-dose), but the Fisher exact tests were not significant. In male rats, liver tumors were not observed in statistically significant proportions.

All of the increased tumor incidences that were statistically significant by the Fisher exact test or by the Cochran-Armitage linear trend test were not significant when life table analyses were used. This difference occurs because life table analyses adjust for intercurrent mortality and thus they minimize the impact of animals dying before the onset of late-appearing tumors. This adjustment was particularly critical for the analyses of tumor incidences in male rats because 12 controls and 10 low-dose animals were accidentally killed during week 82 of the study.

Table 10. Analyses of the Incidence of Primary Tumors in Male Rats Administered Vinylidene Chloride by Gavage (a)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Subcutaneous Tissue:			
Fibroma (b)	0/50(0)	1/48(2)	4/48(8)
P Values (c),(d)	P=0.024	N.S.	N.S.
Relative Risk (e)		Infinite	Infinite
Lower Limit		0.056	0.966
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	99	94
Lung: Alveolar/Bronchiolar			
Adenoma or Carcinoma (b)	3/50(6)	2/47(4)	0/47(0)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.709	0.000
Lower Limit		0.061	0.000
Upper Limit		5.913	1.766
Weeks to First Observed Tumor	82	73	--
Hematopoietic System:			
Leukemia, NOS (b)	7/50(14)	4/48(8)	8/48(17)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.595	1.190
Lower Limit		0.136	0.409
Upper Limit		2.182	3.557
Weeks to First Observed Tumor	82	73	100

Table 10. Analyses of the Incidence of Primary Tumors in Male Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Hematopoietic System:			
Leukemia (b)	8/50(16)	4/48(8)	8/48(17)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.521	1.042
Lower Limit		0.122	0.370
Upper Limit		1.806	2.925
Weeks to First Observed Tumor	82	73	100
Liver: Neoplastic Nodule or			
Hepatocellular Carcinoma (b)	1/49(2)	3/48(6)	3/45(7)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		3.063	3.267
Lower Limit		0.257	0.274
Upper Limit		157.336	167.567
Weeks to First Observed Tumor	103	104	104
Pituitary: Adenoma, NOS (b)	7/49(14)	10/47(21)	10/44(23)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.489	1.591
Lower Limit		0.560	0.599
Upper Limit		4.225	4.490
Weeks to First Observed Tumor	75	66	102

Table 10. Analyses of the Incidence of Primary Tumors in Male Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Pituitary: Adenoma, NOS or Carcinoma, NOS (b)	7/49(14)	10/47(21)	11/44(25)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.489	1.750
Lower Limit		0.560	0.681
Upper Limit		4.225	4.482
Weeks to First Observed Tumor	75	66	102
Adrenal: Pheochromocytoma (b)	6/50(12)	5/48(10)	13/47(28)
P Values (c),(d)	P=0.010	N.S.	P=0.045
Relative Risk (e)		0.868	2.305
Lower Limit		0.224	0.897
Upper Limit		3.185	6.772
Weeks to First Observed Tumor	96	104	73
Thyroid: C-Cell Adenoma (b)	2/48(4)	1/46(2)	3/41(7)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.522	1.756
Lower Limit		0.009	0.211
Upper Limit		9.668	20.142
Weeks to First Observed Tumor	96	104	102

Table 10. Analyses of the Incidence of Primary Tumors in Male Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Thyroid: C-Cell Carcinoma (b)	4/48(8)	2/46(4)	3/41(7)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.522	0.878
Lower Limit		0.049	0.135
Upper Limit		3.449	4.877
Weeks to First Observed Tumor	104	104	102
Thyroid: C-Cell Adenoma or Carcinoma (b)	6/48(13)	3/46(7)	6/41(15)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.522	1.171
Lower Limit		0.089	0.338
Upper Limit		2.285	4.033
Weeks to First Observed Tumor	96	104	102
Pancreatic Islets: Islet-Cell Carcinoma (b)	4/49(8)	1/47(2)	6/48(13)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.261	1.531
Lower Limit		0.005	0.388
Upper Limit		2.507	6.946
Weeks to First Observed Tumor	96	104	104

Table 10. Analyses of the Incidence of Primary Tumors in Male Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Pancreatic Islets: Islet-Cell Adenoma or Carcinoma (b)	4/49(8)	1/47(2)	8/48(17)
P Values (c),(d)	P=0.025	N.S.	N.S.
Relative Risk (e)		0.261	2.042
Lower Limit		0.005	0.589
Upper Limit		2.507	8.659
Weeks to First Observed Tumor	96	104	104
Preputial Gland: Carcinoma, NOS (b)	3/50(6)	3/48(6)	1/48(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.042	0.347
Lower Limit		0.146	0.007
Upper Limit		7.419	4.143
Weeks to First Observed Tumor	76	72	104
Preputial Gland: Adenoma, NOS or Carcinoma, NOS (b)	3/50(6)	4/48(8)	1/48(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.389	0.347
Lower Limit		0.248	0.007
Upper Limit		9.031	4.143
Weeks to First Observed Tumor	76	72	104

Table 10. Analyses of the Incidence of Primary Tumors in Male Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Testis: Interstitial-Cell Tumor (b)	43/50(86)	39/47(83)	47/48(98)
P Values (c),(d)	P=0.013	N.S.	P=0.034
Relative Risk (e)		0.965	1.139
Lower Limit		0.808	0.992
Upper Limit		1.160	1.189
Weeks to First Observed Tumor	78	55	73
Prostate: Adenoma, NOS (b)	2/22(9)	2/35(6)	2/32(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.629	0.688
Lower Limit		0.049	0.054
Upper Limit		8.199	8.931
Weeks to First Observed Tumor	104	104	104

(a) Dosed groups received doses of 1 or 5 mg/kg by gavage.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the vehicle-control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.

Table 11. Analyses of the Incidence of Primary Tumors in Female Rats Administered Vinylidene Chloride by Gavage (a)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	4/49(8)	0/50(0)	1/45(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Departure from Linear Trend (e)	P=0.038		
Relative Risk (f)		0.000	0.272
Lower Limit		0.000	0.006
Upper Limit		1.057	2.615
Weeks to First Observed Tumor	95	--	104
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	4/49(8)	1/50(2)	1/45(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		0.245	0.272
Lower Limit		0.005	0.006
Upper Limit		2.362	2.615
Weeks to First Observed Tumor	95	104	104
Hematopoietic System: Leukemia, NOS (b)	10/49(20)	3/50(6)	4/45(9)
P Values (c),(d)	N.S.	P=0.033(N)	N.S.
Departure from Linear Trend (e)	P=0.041		
Relative Risk (f)		0.294	0.436
Lower Limit		0.055	0.107
Upper Limit		1.061	1.390
Weeks to First Observed Tumor	94	101	91

Table 11. Analyses of the Incidence of Primary Tumors in Female Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Hematopoietic System:			
All Leukemias (b)	10/49(20)	6/50(12)	5/45(11)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		0.588	0.544
Lower Limit		0.190	0.157
Upper Limit		1.642	1.603
Weeks to First Observed Tumor	94	88	74
Hematopoietic System:			
All Lymphomas (b)	3/49(6)	1/50(2)	0/45(0)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		0.327	0.000
Lower Limit		0.006	0.000
Upper Limit		3.903	1.805
Weeks to First Observed Tumor	82	102	--
Hematopoietic System:			
All Lymphomas or Leukemias (b)	13/49(27)	7/50(14)	5/45(11)
P Values (c),(d)	N.S.	N.S.	P=0.050(N)
Relative Risk (f)		0.528	0.419
Lower Limit		0.195	0.127
Upper Limit		1.295	1.140
Weeks to First Observed Tumor	82	88	74

Table 11. Analyses of the Incidence of Primary Tumors in Female Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Liver: Neoplastic Nodule (b)	4/49(8)	0/50(0)	0/45(0)
P Values (c),(d)	P=0.045(N)	N.S.	N.S.
Departure from Linear Trend (e)	P=0.030		
Relative Risk (f)		0.000	0.000
Lower Limit		0.000	0.000
Upper Limit		1.057	1.171
Weeks to First Observed Tumor	85	--	--
Pituitary: Adenoma, NOS (b)	16/48(33)	20/49(41)	24/43(56)
P Values (c),(d)	P=0.017	N.S.	P=0.026
Relative Risk (f)		1.224	1.674
Lower Limit		0.692	0.998
Upper Limit		2.197	2.820
Weeks to First Observed Tumor	65	78	71
Pituitary: Carcinoma, NOS (b)	3/48(6)	1/49(2)	0/43(0)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		0.327	0.000
Lower Limit		0.006	0.000
Upper Limit		3.898	1.848
Weeks to First Observed Tumor	101	104	--

Table 11. Analyses of the Incidence of Primary Tumors in Female Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Pituitary: Adenoma, NOS or Carcinoma, NOS (b)	19/48(40)	21/49(43)	24/43(56)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		1.083	1.410
Lower Limit		0.643	0.872
Upper Limit		1.834	2.265
Weeks to First Observed Tumor	65	78	71
Pituitary: Chromophobe Adenoma (b)	0/48(0)	2/49(4)	3/43(7)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		Infinite	Infinite
Lower Limit		0.290	0.673
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	101	103
Adrenal: Pheochromocytoma (b)	1/48(2)	2/50(4)	3/43(7)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		1.920	3.349
Lower Limit		0.103	0.281
Upper Limit		110.993	171.564
Weeks to First Observed Tumor	82	102	85

Table 11. Analyses of the Incidence of Primary Tumors in Female Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Thyroid: C-Cell Carcinoma (b)	4/47(9)	1/47(2)	4/44(9)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		0.250	1.068
Lower Limit		0.005	0.211
Upper Limit		2.404	5.393
Weeks to First Observed Tumor	104	104	104
Thyroid: C-Cell Adenoma or Carcinoma (b)	4/47(9)	2/47(4)	5/44(11)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		0.500	1.335
Lower Limit		0.047	0.307
Upper Limit		3.307	6.314
Weeks to First Observed Tumor	104	103	104
Thyroid: Follicular-Cell Adenoma or Carcinoma (b)	0/47(0)	1/47(2)	2/44(5)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		Infinite	Infinite
Lower Limit		0.054	0.317
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	104	96

Table 11. Analyses of the Incidence of Primary Tumors in Female Rats Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Mammary Gland: Fibroadenoma (b)	12/49(24)	14/50(28)	9/45(20)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		1.143	0.817
Lower Limit		0.549	0.336
Upper Limit		2.424	1.901
Weeks to First Observed Tumor	80	88	80
Uterus: Endometrial Stromal Polyp (b)	12/48(25)	9/49(18)	9/42(21)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (f)		0.735	0.857
Lower Limit		0.302	0.354
Upper Limit		1.719	1.982
Weeks to First Observed Tumor	82	91	85

(a) Dosed groups received doses of 1 or 5 mg/kg by gavage.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the vehicle-control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.
(f) The 95 percent confidence interval of the relative risk between each dosed group and the control group.

Table 12. Results of Life Table Analysis on Those Primary Tumors Showing Significant ($P<0.05$) Increases by "Unadjusted Analyses" (a) in the Two-Year Study of Vinylidene Chloride in Rats

Primary Tumor	Dose-Response Trend	Low Dose versus Controls	High Dose versus Controls
Male:			
Adrenal Pheochromocytoma	6/50 (b) (0.247) (c)	5/48 (b) (0.396N) (d)	13/47 (b) (0.422)
Pancreatic Islet-Cell Carcinoma or Adenoma	4/49 (0.249)	1/47 (0.149N)	8/48 (0.588)
Subcutaneous Fibroma	0/50 (0.114)	1/48 (0.508)	4/48 (0.162)
Female:			
Pituitary Adenoma	16/48 (0.112)	20/49 (0.305)	24/43 (0.104)

(a) "Unadjusted" analyses refer to the Cochran-Armitage test and the Fisher exact test, which do not account for survival differences among groups.
(b) Number of animals with tumors/number of animals examined for that site. The tumor incidences are given for control, low-dose, and high-dose groups.
(c) Probability (P) value in parentheses.
(d) An N after a probability value indicates a lower incidence in dosed groups than in controls.

IV. RESULTS - MICE

A. Body Weights and Clinical Signs (Mice)

Throughout most of the study, the mean body weights of dosed male mice were lower than those of the vehicle controls. Mean body weights of high-dose and control female mice were comparable (Figure 3 and Table 13). Mean body weights of low-dose mice of either sex were lower than those of the high-dose or vehicle-control mice. No compound-related clinical signs were observed.

B. Survival (Mice)

Estimates of the probabilities of survival of male and female mice administered vinylidene chloride by gavage at the doses of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 4. No significant differences in survival were observed between any group of male mice. A significant reduction in the survival of the low-dose group of female mice was observed when compared with the high-dose group.

In male mice, 33/50(66%) of the vehicle controls, 35/50 (70%) of the low-dose, and 36/50 (72%) of the high-dose group lived to the end of the study at 104 weeks. In female mice, 40/50 (80%) of the vehicle controls, 32/50 (64%) of the low-dose, and 42/50 (84%) of the high-dose group lived to the end of the study at 104 weeks.

C. Pathology (Mice)

Histopathologic findings on neoplasms in mice are summarized in Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status for each individual animal in the male and female mouse studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2.

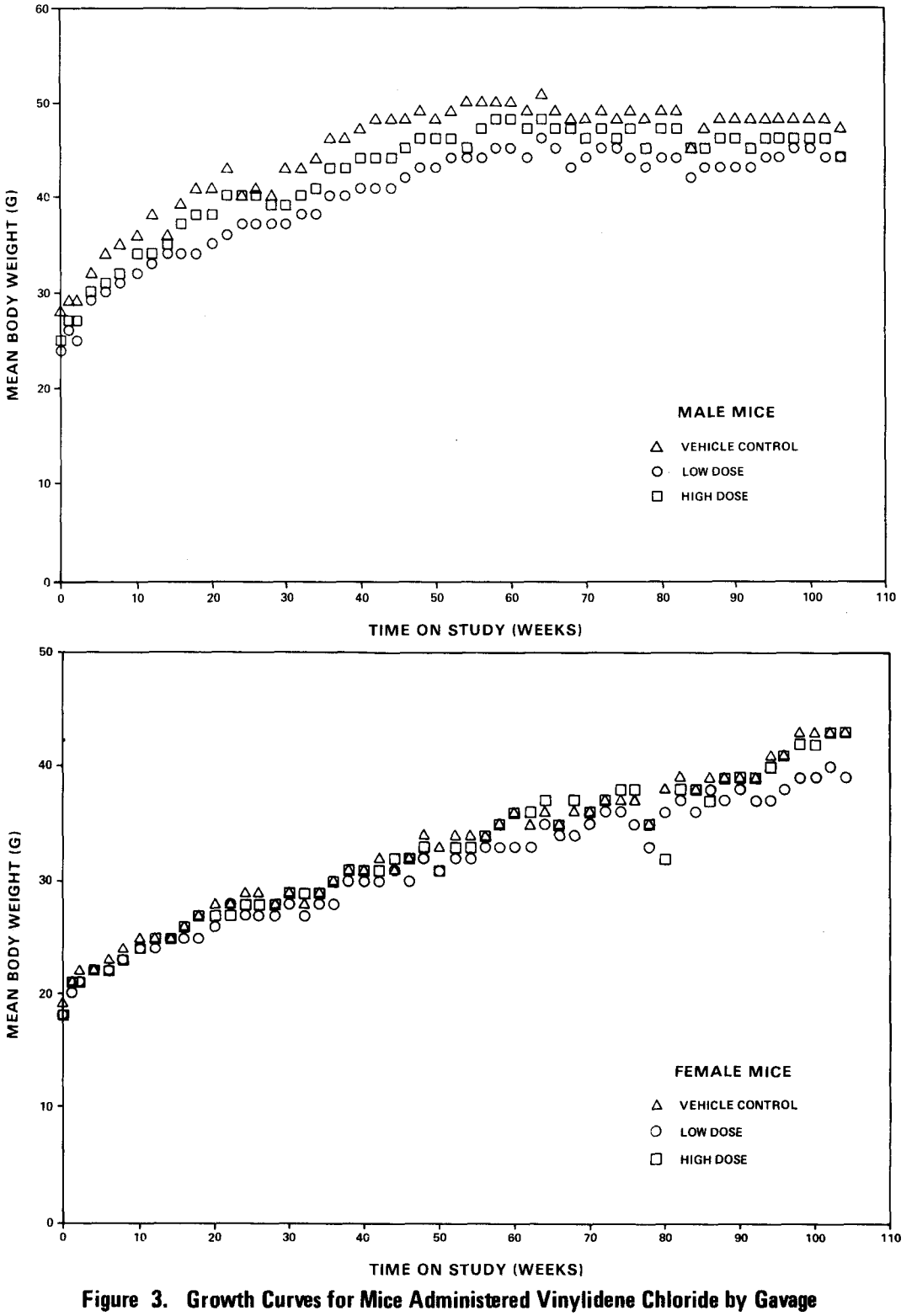


Figure 3. Growth Curves for Mice Administered Vinylidene Chloride by Gavage

Table 13. Mean Body Weight Change (Relative to Controls) of Mice Administered Vinylidene Chloride by Gavage

		Mean Body Weight Change (grams)			Weight Change Relative to Controls (a)(percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Male Mice	0	28(b)	24(b)	25(b)		
	1	1	2	2	+100	+100
	20	13	11	13	- 15	0
	40	19	17	19	- 20	0
	60	22	21	23	- 5	+ 5
	80	21	20	22	- 5	+ 5
	100	20	21	21	+ 5	+ 5
Female Mice	0	19(b)	18(b)	18(b)		
	1	2	2	3	0	+ 50
	20	9	8	9	- 11	0
	40	12	12	13	0	+ 8
	60	17	15	18	- 12	+ 6
	80	19	18	14	- 5	- 35
	100	24	21	24	- 13	0

(a) Weight Change Relative to Controls =

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

(b) Initial weight

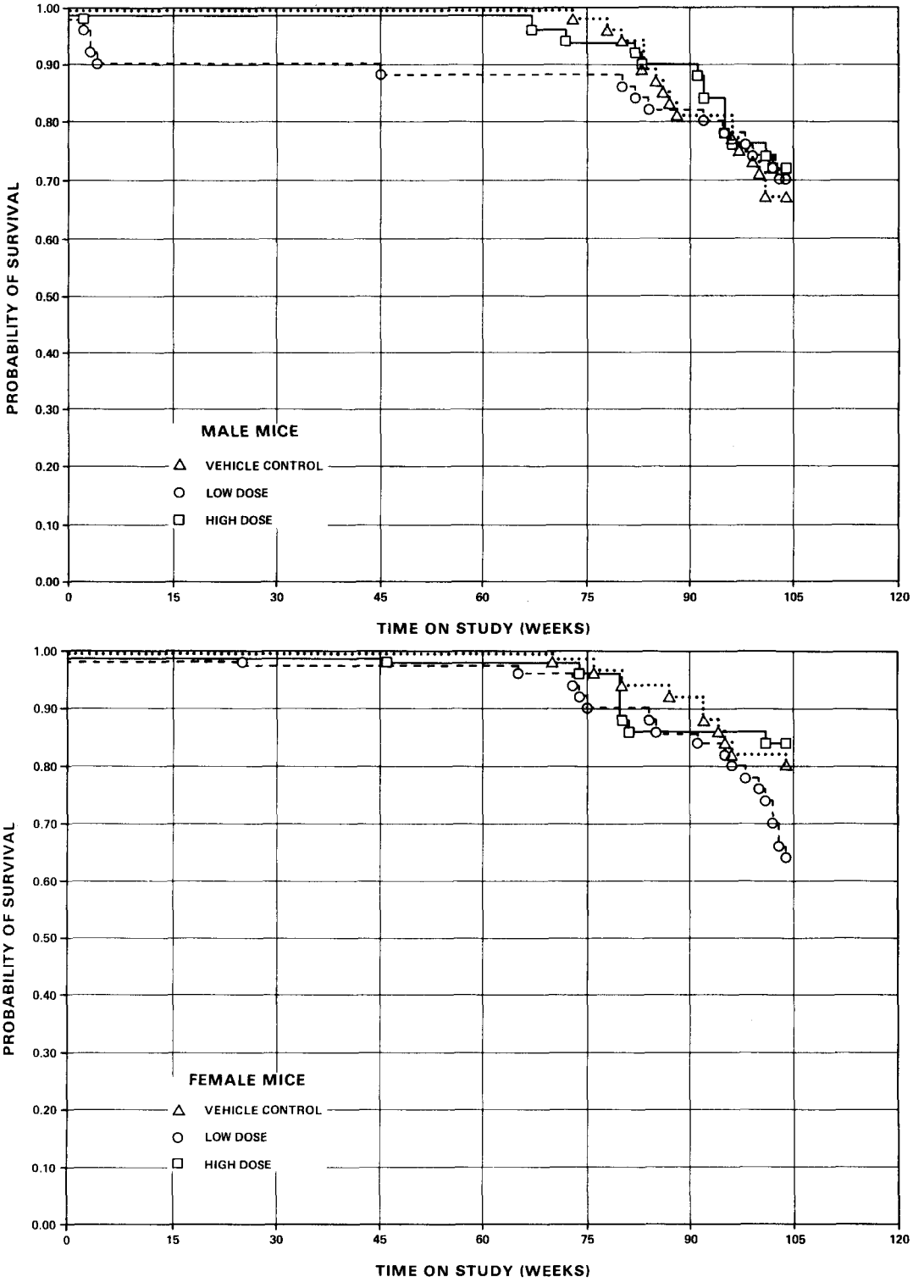


Figure 4. Survival Curves for Mice Administered Vinylidene Chloride by Gavage

Neoplastic lesions observed in the dosed mice were considered to be unrelated to administration of the test compound and within the usual incidence range seen in B6C3F1 control mice.

Necrosis of the liver (focal, multifocal, or diffuse) was observed more frequently in dosed mice than in controls (male controls, 1/46, 2%; low-dose 3/46, 7%; and high-dose, 7/49, 14%; female controls, 0/47, 0%; low-dose, 4/49, 8%; and high-dose, 1/49, 2%). The incidence of lung inflammation was slightly below that normally seen in 2-year-old B6C3F1 mice.

The results of the histopathologic examination indicated that, under the conditions of this bioassay, there was no evidence of carcinogenicity of vinylidene chloride in B6C3F1 mice.

D. Statistical Analyses of Results (Mice)

Tables 14 and 15 contain the statistical analyses of those primary tumors whose incidence was 5% or greater in at least one of the three groups.

Lymphomas of the hematopoietic system in female mice were observed in increased incidence in the low-dose group compared with the other two groups (2/48, 4% in the vehicle controls; 9/49, 18% in the low-dose; 6/50, 12% in the high dose). The Cochran-Armitage test for linear trend was not significant, but there was a departure from linear trend (P=0.033) due to the sharp increase of incidence in the low-dose group compared with the other two groups. The Fisher exact test between the low-dose group and the vehicle control group was significant (P=0.028). No significant incidence was observed in the high-dose group. When these data were analyzed by life table methods, the increased incidence of lymphomas in the low-dose group was statistically significant (P=0.012) but the incidence in the high-dose group and the dose-response trend were not significant. The incidence of lymphomas in female mice observed in this study (2/48, 4%) is less than the historical incidence for vehicle controls from all laboratories (31/315, 9.8%). Data are not yet available at this laboratory for other gavage

studies in which corn oil was used as the vehicle. In male mice, this tumor was not observed in statistically significant proportions.

Leukemia of the hematopoietic system in female mice was observed in decreased incidence in the high-dose group, compared with the controls (5/48, 10% in the controls; 7/49, 14% in the low-dose; and 1/50, 2% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.031), but the Fisher exact tests were not significant. In male mice, this tumor was not observed in statistically significant proportions.

Lymphomas or leukemia of the hematopoietic system in female mice were observed in increased incidence in the low-dose group compared with the vehicle controls (7/48, 15% in the controls; 15/49, 31% in the low-dose; 7/50, 14% in the high-dose). The Cochran-Armitage test for linear trend was not significant, but there was a departure from linear trend (P=0.029) due to the increase of incidence in the low-dose group. The Fisher exact test between the low-dose group and the vehicle controls was significant (P=0.05). No significant incidence was observed in the high-dose group. These tumors were not observed in statistically significant proportions in male mice.

Life table analyses (Table 16), using the death of an animal as the time point of examination for tumors, and time-adjusted tests, eliminating those animals that died before 52 weeks, did not materially affect the results reported in Tables 14 and 15.

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Administered Vinylidene Chloride by Gavage (a)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	3/46(7)	4/45(9)	4/46(9)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.363	1.333
Lower Limit		0.244	0.239
Upper Limit		8.829	8.645
Weeks to First Observed Tumor	82	80	82
Lung: Alveolar/Bronchiolar Carcinoma (b)	2/46(4)	1/45(2)	4/46(9)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.511	2.000
Lower Limit		0.009	0.303
Upper Limit		9.462	21.243
Weeks to First Observed Tumor	97	104	104
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	5/46(11)	5/45(11)	8/46(17)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.022	1.600
Lower Limit		0.252	0.501
Upper Limit		4.143	5.769
Weeks to First Observed Tumor	82	80	82

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Hematopoietic System:			
Lymphoma, Malignant, NOS (b)	6/47(13)	3/47(6)	7/50(14)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.500	1.097
Lower Limit		0.085	0.341
Upper Limit		2.191	3.671
Weeks to First Observed Tumor	85	99	92
Hematopoietic System:			
All Malignant Lymphomas (b)	6/47(13)	3/47(6)	8/50(16)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.500	1.253
Lower Limit		0.085	0.414
Upper Limit		2.191	4.065
Weeks to First Observed Tumor	85	99	92
Hematopoietic System:			
All Leukemias (b)	0/47(0)	3/47(6)	0/50(0)
P Values (c),(d)	N.S.	N.S.	N.S.
Departure from Linear Trend (f)	P=0.018		
Relative Risk (e)		Infinite	--
Lower Limit		0.603	--
Upper Limit		Infinite	--
Weeks to First Observed Tumor	--	82	--

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Hematopoietic System:			
All Lymphomas or Leukemias (b)	6/47(13)	6/47(13)	8/50(16)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.000	1.253
Lower Limit		0.288	0.414
Upper Limit		3.472	4.065
Weeks to First Observed Tumor	85	82	92
Circulatory System: Hemangioma (b)	1/47(2)	3/47(6)	2/50(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		3.000	1.880
Lower Limit		0.252	0.101
Upper Limit		154.015	108.696
Weeks to First Observed Tumor	104	99	104
Circulatory System: Hemangioma or Hemangiosarcoma (b)	2/47(4)	3/47(6)	4/50(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.500	1.880
Lower Limit		0.180	0.284
Upper Limit		17.287	20.027
Weeks to First Observed Tumor	88	99	96

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Liver: Hepatocellular Adenoma in the Absence of Carcinomas (b)	7/46(15)	4/46(9)	6/49(12)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.571	0.805
Lower Limit		0.131	0.241
Upper Limit		2.086	2.589
Weeks to First Observed Tumor	104	104	95
Liver: Hepatocellular Carcinoma (b)	8/46(17)	5/46(11)	9/49(18)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Matched Control) (e)		0.625	1.056
Lower Limit		0.173	0.397
Upper Limit		1.997	2.880
Weeks to First Observed Tumor	80	80	83
Liver: Hepatocellular Adenoma or Carcinoma (b)	15/46(33)	9/46(20)	15/49(31)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Matched Control) (e)		0.600	0.939
Lower Limit		0.259	0.486
Upper Limit		1.307	1.818
Weeks to First Observed Tumor	80	80	83

Table 14. Analyses of the Incidence of Primary Tumors in Male Mice Administered Vinylidene Chloride by Gavage (a)

(continued)

(a) Dosed groups received doses of 2 or 10 mg/kg by gavage.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the vehicle-control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Administered Vinylidene Chloride by Gavage (a)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	1/48(2)	1/45(2)	4/48(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.067	4.000
Lower Limit		0.014	0.416
Upper Limit		81.900	192.630
Weeks to First Observed Tumor	104	104	104
Hematopoietic System: All Leukemias (b)	5/48(10)	7/49(14)	1/50(2)
P Values (c),(d)	P=0.031(N)	N.S.	N.S.
Relative Risk (e)		1.371	0.192
Lower Limit		0.403	0.004
Upper Limit		5.119	1.630
Weeks to First Observed Tumor	70	91	74
Hematopoietic System: All Malignant Lymphomas (b)	2/48(4)	9/49(18)	6/50(12)
P Values (c),(d)	N.S.	P=0.028	N.S.
Departure from Linear Trend (f)	P=0.033		
Relative Risk (e)		4.408	2.880
Lower Limit		0.977	0.547
Upper Limit		40.199	28.073
Weeks to First Observed Tumor	104	100	104

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Hematopoietic System:			
All Lymphomas or Leukemias (b)	7/48(15)	15/49(31)	7/50(14)
P Values (c),(d)	N.S.	P=0.050	N.S.
Departure from Linear Trend (f)	P=0.029		
Relative Risk (e)		2.099	0.960
Lower Limit		0.891	0.311
Upper Limit		5.531	2.969
Weeks to First Observed Tumor	70	91	74
Liver: Hepatocellular Adenoma:			
in the Absence of Carcinoma (b)	2/47(4)	3/49(6)	2/49(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.439	0.959
Lower Limit		0.173	0.072
Upper Limit		16.604	12.769
Weeks to First Observed Tumor	104	104	104
Liver: Hepatocellular			
Adenoma or Carcinoma (b)	4/47(4)	3/49(6)	2/49(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.719	0.719
Lower Limit		0.111	0.111
Upper Limit		4.027	4.027
Weeks to First Observed Tumor	92	104	104

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Pituitary: Adenoma, NOS (b)	5/31(16)	6/32(19)	3/42(7)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.163	0.443
Lower Limit		0.330	0.074
Upper Limit		4.329	2.107
Weeks to First Observed Tumor	104	103	104
Pituitary: Adenoma, NOS or Carcinoma, NOS (b)	5/31(16)	7/32(22)	3/42(7)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		1.356	0.443
Lower Limit		0.417	0.074
Upper Limit		4.852	2.107
Weeks to First Observed Tumor	104	103	104
Mammary Gland: Fibroadenoma (b)	1/48(2)	1/49(2)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		0.980	2.880
Lower Limit		0.013	0.241
Upper Limit		75.342	148.076
Weeks to First Observed Tumor	87	85	104

Table 15. Analyses of the Incidence of Primary Tumors in Female Mice Administered Vinylidene Chloride by Gavage (a)

(continued)

Topography: Morphology	Vehicle Control	Low Dose	High Dose
Uterus: Endometrial Stromal Polyp (b)	0/46(0)	3/45(7)	2/47(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (e)		Infinite	Infinite
Lower Limit		0.617	0.290
Upper Limit		Infinite	Infinite
Weeks to First Observed Tumor	--	96	104

(a) Dosed groups received doses of 2 or 10 mg/kg by gavage.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the vehicle-control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicates a lower incidence in a dosed group than in a control group.
(e) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.
(f) The 95 percent confidence interval of the relative risk between each dosed group and the control group.

Table 16. Results of Life Table Analysis on Those Primary Tumors Showing Significant ($P<0.05$) Increases by "Unadjusted Analyses" (a) in the Two-Year Study of Vinylidene Chloride in Female Mice

Primary Tumor	Dose-Response Trend	Low Dose versus Controls	High Dose versus Controls
Lymphoma	2/48 (b) (0.449) (c)	9/49 (b) (0.012)	6/50 (b) (0.150)
Lymphoma or Leukemia	7/48 (0.231N) (d)	15/49 (0.037)	7/50 (0.581N)

(a) "Unadjusted" analyses refer to the Cochran-Armitage test and the Fisher exact test, which do not account for survival differences among groups.
(b) Number of animals with tumors/number of animals examined for that site. The tumor incidences are given for control, low-dose, and high-dose groups.
(c) Probability (P) value in parentheses.
(d) An N after a probability value indicates a lower incidence in dosed groups than in controls.

V. DISCUSSION

Throughout most of the chronic study, mean body weights of dosed rats of either sex and of high-dose female mice were comparable with those of the corresponding controls; the mean body weights of dosed male and low-dose female mice were slightly lower than those of the controls. In the subchronic study, the liver was identified as the target organ for vinylidene chloride-induced toxicity in both species; these observations supported the route selected for administering the chemical and the doses used for the chronic study. However, review of subchronic toxicity data and the absence of compound-related effects on survival or clinical signs in the chronic study suggest that mice and rats of both sexes could have tolerated higher doses of the chemical.

In the chronic studies, an increased incidence of necrosis of the liver in high-dose male mice and chronic renal inflammation in high-dose rats of either sex may have been related to administration of vinylidene chloride. Hepatoxic and/or nephrotoxic effects in rats and mice have been reported by others (Jenkins and Andersen, 1978; Reitz et al., 1980; and Prendergast et al., 1967).

There seems to be a great variation in the oral LD_{50} reported for vinylidene chloride: 1,510 mg/kg in adult Holtzman rats (Jenkins et al., 1972) and 217 mg/kg in male Alderly Park rats (Jones and Hathway, 1978a). A number of studies suggest that the toxicity of vinylidene chloride may be due to a reactive intermediate metabolite, possibly an epoxide, formed during *in vivo* microsomal metabolism of vinylidene chloride. Epoxides are detoxified *in vivo* by reaction with glutathione or by enzymic hydration. The epoxide hydrating pathways appear to play a minimal role in the metabolism of the reactive metabolite of vinylidene chloride. Vinylidene chloride causes increased toxicity in glutathione depleted animals, suggesting that the detoxication of this intermediate metabolite occurs mainly through conjugation with glutathione (Andersen and Jenkins, 1977, Andersen et al., 1978, 1979, 1980).

In the present study, there was little evidence that vinylidene chloride dosed groups had significantly increased tumor incidence relative to controls. The only observed significant ($P < 0.05$) increase in tumor incidence occurred in low-dose female mice: lymphoma (2/48, 9/49, 6/50) and lymphoma or leukemia (7/48, 15/49, 7/50). These increases were not considered to be related to vinylidene chloride administration because similar effects were not found in the high-dose female mice or for male mice or rats.

In previous studies, vinylidene chloride has been reported to be carcinogenic when administered by inhalation but not carcinogenic when administered orally. Renal adenocarcinomas were found in 24/150 male Swiss mice exposed to 25 ppm vinylidene chloride vapor for 4 hours per day for 52 weeks, compared with no such tumors in the controls; however, no carcinogenic effects were observed when vinylidene chloride (0.5 - 20 mg/kg) was administered by gavage for a similar period (Maltoni et al., 1977). An increased incidence of mammary fibroadenomas or carcinomas was found in female Sprague-Dawley rats exposed to 100 or 150 ppm vinylidene chloride in air for 4 hours daily for 52 weeks and then observed for an additional 41 weeks (Maltoni et al., 1977); but when male or female Sprague-Dawley rats were given drinking water containing 200 ppm vinylidene chloride for 2 years, no carcinogenic effects were found (Norris, 1977). In another study, an increased incidence of lung, skin, and liver cell tumors in mice and the induction of hemangiosarcomas in both mice and rats were reported (Lee at al., 1977). No carcinogenic effects were found when female BDIV rats were given 150 mg/kg vinylidene chloride in olive oil by gavage on day 17 of gestation and the offspring were given 50 mg/kg once per week for 100 weeks (Ponomarkov and Tomatis, 1980).

These studies and the present study indicate that the route of exposure may be one of the important factors influencing the expression of the carcinogenic potential of VDC in laboratory animals. The metabolism and pharmacokinetics of vinylidene chloride have been studied following inhalation exposue (McKenna et al. 1977, 1978a) or following oral administration (McKenna et al., 1978). Both routes of exposure show that vinylidene chloride is metabolized to an epoxide as an intermediate reactive metabolite.

Two major urinary metabolites were identified as N-acetyl-S-(2-hydroxyethyl) cysteine and thiodiglycolic acid, indicating a major pathway for detoxication of the reactive intermediate metabolites of vinylidene chloride is via conjugation with liver glutathione. Short et al. (1977b) have reported that mice are more susceptible to the toxic effects of vinylidene chloride than are rats. This could be because of increased ability for activation of vinylidene chloride to a reactive metabolite by mice compared to that observed in the rat (Reitz et al., 1980). The carcinogenic expression observed in inhalation studies and not by the oral route suggests that there may be qualitative and quantitative differences in the formation of reactive intermedite metabolite(s). Furthermore, these qualitative and quantitative differences in the formation of the reactive intermediate may be due to the differences in the bioavailability of the chemical to the target organ or macromolecule(s) between the oral and inhalation routes of exposure. Further metabolic and disposition studies should clarify the influence of route of exposure on vinylidene chloride's toxic and carcinogenic expression.

VI. CONCLUSION

Under the conditions of this bioassay, vinylidene chloride administered by gavage was not carcinogenic for F344/N rats or B6C3F1/N mice of either sex. However, since the use of a maximum tolerated dose in this study has not been clearly demonstrated and since previously reported studies have shown that carcinogenicity is associated with inhalation exposure to vinylidene chloride, this study should not be taken as proof that the chemical is not a carcinogen.

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Appendix A

Summary of the Incidence of Neoplasms in Rats Administered Vinylidene Chloride by Gavage

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS ADMINISTERED VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	48	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	48	48
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(48)	(48)
SQUAMOUS CELL CARCINOMA		1 (2%)	
KERATOACANTHOMA	1 (2%)		1 (2%)
*SUBCUT TISSUE	(50)	(48)	(48)
FIBROMA		1 (2%)	4 (8%)
LIPOMA			1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(47)	(47)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	1 (2%)	
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	1 (2%)	
OSTEOSARCOMA, METASTATIC			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(48)	(48)
LEUKEMIA,NOS	6 (12%)	4 (8%)	8 (17%)
MONOCYTIC LEUKEMIA	1 (2%)		
#SPLEEN	(50)	(47)	(48)
FIBROSARCOMA		1 (2%)	
#ADRENAL	(50)	(48)	(47)
LEUKEMIA,NOS	1 (2%)		
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(47)	(48)
HEMANGIOSARCOMA		1 (2%)	

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
*ORAL CAVITY	(50)	(48)	(48)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
#SALIVARY GLAND	(46)	(48)	(46)
ADENOMA, NOS		1 (2%)	
ADENOCARCINOMA, NOS	1 (2%)		
#LIVER	(49)	(48)	(45)
NEOPLASTIC NODULE	1 (2%)	1 (2%)	2 (4%)
HEPATOCELLULAR CARCINOMA		2 (4%)	1 (2%)
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(47)	(44)
CARCINOMA,NOS			1 (2%)
ADENOMA, NOS	7 (14%)	10 (21%)	10 (23%)
CHROMOPHOBE ADENOMA	1 (2%)		1 (2%)
CHROMOPHOBE CARCINOMA			1 (2%)
#ADRENAL	(50)	(48)	(47)
PHEOCHROMOCYTOMA	6 (12%)	5 (10%)	13 (28%)
GANGLIONEUROMA	1 (2%)		
#THYROID	(48)	(46)	(41)
PAPILLARY ADENOCARCINOMA	1 (2%)		1 (2%)
C-CELL ADENOMA	2 (4%)	1 (2%)	3 (7%)
C-CELL CARCINOMA	4 (8%)	2 (4%)	3 (7%)
#PANCREATIC ISLETS	(49)	(47)	(48)
ISLET-CELL ADENOMA			2 (4%)
ISLET-CELL CARCINOMA	4 (8%)	1 (2%)	6 (13%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(48)	(48)
FIBROMA			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
FIBROADENOMA	1 (2%)		1 (2%)
*PREPUTIAL GLAND	(50)	(48)	(48)
CARCINOMA,NOS	3 (6%)	3 (6%)	1 (2%)
ADENOMA, NOS		1 (2%)	
#PROSTATE	(22)	(35)	(32)
ADENOMA, NOS	2 (9%)	2 (6%)	2 (6%)
#TESTIS	(50)	(47)	(48)
INTERSTITIAL-CELL TUMOR	43 (86%)	39 (83%)	47 (98%)
NERVOUS SYSTEM			
#BRAIN	(50)	(48)	(47)
GLIOMA, NOS	1 (2%)		
ASTROCYTOMA			1 (2%)
SPECIAL SENSE ORGANS			
*EXTERNAL EAR	(50)	(48)	(48)
SEBACEOUS ADENOCARCINOMA		1 (2%)	
FIBROSARCOMA			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(48)	(48)
SARCOMA, NOS		1 (2%)	
FIBROSARCOMA			1 (2%)
*TUNICA VAGINALIS	(50)	(48)	(48)
MESOTHELIOMA, NOS		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(48)	(48)
MESOTHELIOMA, NOS	1 (2%)		1 (2%)

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	5	5
MORIBUND SACRIFICE	13	10	8
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED	12	11	
TERMINAL SACRIFICE	20	24	37
ANIMAL MISSING			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	47	42	48
TOTAL PRIMARY TUMORS	92	81	114
TOTAL ANIMALS WITH BENIGN TUMORS	46	40	48
TOTAL BENIGN TUMORS	67	61	86
TOTAL ANIMALS WITH MALIGNANT TUMORS	19	15	19
TOTAL MALIGNANT TUMORS	23	18	25
TOTAL ANIMALS WITH SECONDARY TUMORS#			1
TOTAL SECONDARY TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	2	3
TOTAL UNCERTAIN TUMORS	2	2	3
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 VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	45
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	45
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(49)	(50)	(45)
SEBACEOUS ADENOCARCINOMA	1 (2%)		
LIPOMA		1 (2%)	
NEURILEMOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(45)
CARCINOMA, NOS, METASTATIC		1 (2%)	
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	4 (8%)		1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(45)
MALIGNANT LYMPHOMA, NOS	1 (2%)	1 (2%)	
MALIG.LYMPHOMA, UNDIFFER-TYPE	1 (2%)		
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
LEUKEMIA,NOS	8 (16%)	3 (6%)	4 (9%)
UNDIFFERENTIATED LEUKEMIA		1 (2%)	
MYELOMONOCYTIC LEUKEMIA		1 (2%)	
LYMPHOCYTIC LEUKEMIA		1 (2%)	
MONOCYTIC LEUKEMIA			1 (2%)
#LIVER	(49)	(50)	(45)
LEUKEMIA,NOS	2 (4%)		
CIRCULATORY SYSTEM			
NONE			

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
*ORAL CAVITY	(49)	(50)	(45)
PAPILLOMA, NOS			1 (2%)
*TONGUE	(49)	(50)	(45)
SQUAMOUS CELL CARCINOMA			1 (2%)
#LIVER	(49)	(50)	(45)
NEOPLASTIC NODULE	4 (8%)		
#STOMACH	(47)	(48)	(42)
SQUAMOUS CELL CARCINOMA	1 (2%)		
#PYLORUS	(47)	(48)	(42)
ADENOCARCINOMA, NOS			1 (2%)
#CECUM	(43)	(43)	(42)
LIPOMA		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(49)	(49)	(44)
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
#URINARY BLADDER	(45)	(45)	(41)
TRANSITIONAL-CELL CARCINOMA		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(49)	(43)
CARCINOMA,NOS	3 (6%)	1 (2%)	
ADENOMA, NOS	16 (33%)	20 (41%)	24 (56%)
CHROMOPHOBE ADENOMA		2 (4%)	3 (7%)
#ADRENAL	(48)	(50)	(43)
CORTICAL ADENOMA	1 (2%)		
CORTICAL CARCINOMA		1 (2%)	
PHEOCHROMOCYTOMA	1 (2%)	2 (4%)	3 (7%)
#THYROID	(47)	(47)	(44)
FOLLICULAR-CELL ADENOMA			2 (5%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOLLICULAR-CELL CARCINOMA		1 (2%)	
C-CELL ADENOMA		1 (2%)	1 (2%)
C-CELL CARCINOMA	4 (9%)	1 (2%)	4 (9%)
#PANCREATIC ISLETS	(48)	(50)	(45)
ISLET-CELL CARCINOMA		1 (2%)	1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(45)
CARCINOMA,NOS		1 (2%)	
ADENOMA, NOS		1 (2%)	
ADENOCARCINOMA, NOS	1 (2%)	1 (2%)	1 (2%)
FIBROMA	1 (2%)		1 (2%)
FIBROADENOMA	12 (24%)	14 (28%)	9 (20%)
#UTERUS	(48)	(49)	(42)
PAPILLARY CARCINOMA			1 (2%)
PAPILLARY ADENOMA			1 (2%)
SARCOMA, NOS		1 (2%)	
ENDOMETRIAL STROMAL POLYP	12 (25%)	9 (18%)	9 (21%)
ENDOMETRIAL STROMAL SARCOMA	1 (2%)		1 (2%)
#OVARY	(47)	(49)	(44)
PAPILLOMA, NOS			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(49)	(50)	(45)
CARCINOMA, NOS, INVASIVE	1 (2%)		
ADENOMA, NOS	1 (2%)	1 (2%)	
GLIOMA, NOS			2 (4%)
#BRAIN STEM	(49)	(50)	(45)
ASTROCYTOMA	1 (2%)		
#PONS	(49)	(50)	(45)
ASTROCYTOMA	1 (2%)		
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL 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
BODY CAVITIES			
*ABDOMINAL CAVITY	(49)	(50)	(45)
ADENOCARCINOMA, NOS, METASTATIC			1 (2%)
*MESENTERY	(49)	(50)	(45)
ENDOMETRIAL STROMAL SARCOMA, MET			1 (2%)
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHə	4	7	13
MORIBUND SACRIFICE	19	15	8
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	27	28	29
ANIMAL MISSING			

ə 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	38	36
TOTAL PRIMARY TUMORS	78	70	73
TOTAL ANIMALS WITH BENIGN TUMORS	35	33	34
TOTAL BENIGN TUMORS	48	53	56
TOTAL ANIMALS WITH MALIGNANT TUMORS	23	17	15
TOTAL MALIGNANT TUMORS	26	17	17
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	1	2
TOTAL SECONDARY TUMORS	1	1	4
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	4		
TOTAL UNCERTAIN TUMORS	4		
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE A3.

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

VEHICLE CONTROL

ANIMAL NUMBER	0 0 1 2	0 0 2 3	0 0 3 4	0 0 4 8	0 0 5 1	0 0 6 2	0 0 7 4	0 0 8 5	0 0 9 4	0 1 0 4	0 1 1 2	0 1 2 0	0 1 1 4	0 1 3 1	0 1 4 4	0 1 5 2	0 1 6 6	0 1 7 9	0 1 8 9	0 1 9 4	0 2 0 4	0 2 1 6	0 2 2 3	0 2 3 4	0 2 4 1	0 2 5 4
WEEKS ON STUDY	0 8 2	0 8 2	0 8 2	0 8 8	1 0 0	1 0 8 2	1 0 4	1 0 7 5	1 0 4	1 0 4	1 0 2 0	1 0 4	1 0 4 1	1 0 4	1 0 4	1 0 8 2	1 0 9 6	1 0 9	1 0 4	1 0 4	1 0 9	1 0 4	1 0 9 3	1 0 4	1 0 4	1 0 4
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
KERATOACANTHOMA																	X									
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																										
ALVEOLAR/BRONCHIOLAR CARCINOMA																										
TRACHEA	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–
THYMUS	–	–	–	–	–	A	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																										
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA																									X	
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–
ADENOCARCINOMA, NOS													X													
LIVER	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																										
BILE DUCT	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	–	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	–	+	+	+	+	+	+	+	+	+	–	+	+	–	–	+	+	+	+	+	+	–	+	+	+	+
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS								X									X								X	
CHROMOPHOBE ADENOMA																								X		
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA														X			X	X								
GANGLIONEUROMA												X														
LEUKEMIA,NOS																										
THYROID	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	X	+	+	+	+	–	+	+	+
PAPILLARY ADENOCARCINOMA																										
C-CELL ADENOMA								X		X	X										X					
C-CELL CARCINOMA																										
PARATHYROID	–	+	+	–	+	+	+	+	+	–	–	+	+	–	–	+	+	–	+	+	+	–	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	X	+	X	+	+	+	+	+
ISLET-CELL CARCINOMA												X														
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	+	N	N	+	+	N	N	N	+	+	N	+	+	+	N	+	+	N	+	+	+	+
FIBROADENOMA																										
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X		X		X		X	X		X	X	X	X	X		X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	–	A	+	–	–	–	–	–	–	–	–	+	+	–	+	–	–	–	–	–	+	–
ADENOMA, NOS																			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	N
CARCINOMA,NOS																X										
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GLIOMA, 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	N
MESOTHELIOMA, NOS																										
LEUKEMIA,NOS					X											X							X		
MONOCYTIC LEUKEMIA																					X					

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

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

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

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	103	096	041	043	044	044	044	078	076	078	082	104	082	041	021	081	082	082	082	102	104	082	082	082	095	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
KERATOACANTHOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																X	X									2
ALVEOLAR/BRONCHIOLAR CARCINOMA		X																								1
TRACHEA	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	45
THYMUS	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
SQUAMOUS CELL PAPILLOMA																										1
SALIVARY GLAND	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ADENOCARCINOMA, NOS																										1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASTIC NODULE	X																									1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	-	-	+	+	41
SMALL INTESTINE	-	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	-	-	+	+	-	-	-	+	+	38
LARGE INTESTINE	-	+	+	+	+	+	+	-	+	+	-	+	-	+	+	-	-	-	+	+	-	-	-	+	+	35
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+	44
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS			X			X				X											X					7
CHROMOPHOBE ADENOMA																										1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA			X																	X					X	6
GANGLIONEUROMA																										1
LEUKEMIA,NOS																									X	1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PAPILLARY ADENOCARCINOMA																										1
C-CELL ADENOMA			X																							2
C-CELL CARCINOMA							X																			4
PARATHYROID	-	+	+	+	-	+	-	+	+	-	+	-	+	-	+	+	+	+	+	+	+	+	-	+	+	35
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ISLET-CELL CARCINOMA		X																								4
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	+	+	+	+	+	N	+	N	N	+	N	+	N	N	N	N	+	+	N	N	N	N	+	50
FIBROADENOMA		X																								1
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	43
PROSTATE	-	-	-	+	-	+	-	-	-	+	+	-	+	+	+	+	-	+	-	+	+	+	+	-	-	22
ADENOMA, NOS						X																				2
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											X						3
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GLIOMA, 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
MESOTHELIOMA, NOS																									X	1
LEUKEMIA,NOS	X			X																					X	6
MONOCYTIC LEUKEMIA																										1

* ANIMALS NECROPSIED

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

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

TABLE A3.

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

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	075	104	104	104	104	104	082	082	104	042	104	101	104	104	072	082	082	082	082	104	104	094	104	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																	X								
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																									
HEMANGIOSARCOMA																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									X
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
HEPATOCELLULAR CARCINOMA							X			X															
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	-	-	+	-	+	+	+	+	-	+	-	+	-	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	-	-	+	+	+	-	+	+	+	+	+	-	+	-	+	+	+	-	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS	X													X							X				
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA														X							X				
THYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA																									
C-CELL CARCINOMA																									
PARATHYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	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
PROSTATE	+	+	-	+	+	-	-	+	+	+	+	+	-	+	+	+	+	+	-	+	-	-	+	+	
ADENOMA, NOS																									
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N	N
CARCINOMA,NOS																	X						X		X
ADENOMA, NOS					X																				
SPECIAL SENSE ORGANS																									
EAR	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N	N	N	N	N
SEBACEOUS ADENOCARCINOMA														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
SARCOMA, NOS																									
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS		X																							

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

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

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

ANIMAL NUMBER	02 67	02 78	02 89	03 01	03 11	03 12	03 13	03 14	03 15	03 16	03 17	03 18	03 19	04 01	04 11	04 12	04 13	04 14	04 15	04 16	04 17	04 18	04 19	05 10	TOTAL
WEEKS ON STUDY	05 51	10 41	04 41	04 41	06 61	09 11	08 21	08 31	08 21	08 21	10 41	10 41	10 41	08 21	09 91	04 11	04 11	07 31	08 31	07 31	05 51	10 41	10 41	08 41	10 41	TISSUES TUMORS
INTEGUMENTARY SYSTEM																									
SKIN	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48*
SQUAMOUS CELL CARCINOMA							X																		1
SUBCUTANEOUS TISSUE	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48*
FIBROMA														X											1
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
ALVEOLAR/BRONCHIOLAR ADENOMA																									1
ALVEOLAR/BRONCHIOLAR CARCINOMA																	X								1
TRACHEA	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																									
BONE MARROW	A	+	+	+	+	+	+	-	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
SPLEEN	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
FIBROSARCOMA																								X	1
HEMANGIOSARCOMA																								X	1
LYMPH NODES	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
THYMUS	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	-	-	-	-	-	-	1
CIRCULATORY SYSTEM																									
HEART	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																									
SALIVARY GLAND	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48
ADENOMA, NOS																									1
LIVER	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48
NEOPLASTIC NODULE																								X	1
HEPATOCELLULAR CARCINOMA																									2
BILE DUCT	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48
GALLBLADDER & COMMON BILE DUCT	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	48*
PANCREAS	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
ESOPHAGUS	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
STOMACH	A	+	+	+	+	+	-	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	43
SMALL INTESTINE	A	+	+	+	-	+	-	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	38
LARGE INTESTINE	A	-	-	-	-	+	-	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	35
URINARY SYSTEM																									
KIDNEY	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48
URINARY BLADDER	A	+	+	+	+	+	+	+	+	+	+	-	+	-	+	A	+	-	+	+	+	+	+	+	42
ENDOCRINE SYSTEM																									
PITUITARY	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
ADENOMA, NOS					X					X			X	X	X							X		X		10
ADRENAL	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48
PHEOCHROMOCYTOMA			X												X							X				5
THYROID	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	46
C-CELL ADENOMA															X											1
C-CELL CARCINOMA			X																				X			2
PARATHYROID	A	+	+	-	+	+	+	-	+	+	-	+	+	+	+	A	-	+	+	-	+	+	-	+	39
PANCREATIC ISLETS	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
ISLET-CELL CARCINOMA																						X			1
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	A	+	+	+	N	N	N	N	N	N	+	+	+	N	+	+	A	+	N	N	N	+	N	N	+	48*
TESTIS	A	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	47
INTERSTITIAL-CELL TUMOR		X	X	X		X		X	X	X	X	X	X	X	X			X	X		X	X	X	X	X	39
PROSTATE	A	-	+	+	+	+	+	+	+	+	-	-	+	+	+	-	A	+	-	+	+	+	-	+	+	35
ADENOMA, NOS																						X			X	2
PREPUTIAL/CLITORAL GLAND	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	48*
CARCINOMA,NOS																										3
ADENOMA, NOS																										1
SPECIAL SENSE ORGANS																									
EAR	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	48*
SEBACEOUS ADENOCARCINOMA																									1
BODY CAVITIES																									
PERITONEUM	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	48*
SARCOMA, NOS					X																				1
TUNICA VAGINALIS	A	+	+	+	+	+	N	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	48*
MESOTHELIOMA, NOS														X											1
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	48*
LEUKEMIA,NOS													X				X							X	4

* ANIMALS NECROPSIED

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

TABLE A3.

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

HIGH 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	104	102	104	104	104	104	104	104	104	104	104	104	104	104	094	104	104	104	104	103	104	104	104	073	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
KERATOACANTHOMA																			X						
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA															X										
LIPOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
OSTEOSARCOMA, METASTATIC																							X		
TRACHEA	+	-	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
HEPATOCELLULAR CARCINOMA																									
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				
CHROMOPHOBE ADENOMA					X																	X			
CHROMOPHOBE CARCINOMA																									
ADRENAL	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA								X	X					X		X	X		X		X			X	
THYROID	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
PAPILLARY ADENOCARCINOMA						X																			
C-CELL ADENOMA																									
C-CELL CARCINOMA																									
PARATHYROID	-	-	+	-	-	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA										X															
ISLET-CELL CARCINOMA			X	X					X		X								X						
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	+	N	N	+	N	+	+	+	+	+	N	N	N	+	+	+	+	+	N	+	+	N	+
FIBROMA																									
FIBROADENOMA																		X							
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	-	+	-	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	
ADENOMA, NOS																								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						
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA	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	N
FIBROSARCOMA																									
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
FIBROSARCOMA																									
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
MESOTHELIOMA, NOS		X																							
LEUKEMIA,NOS																			X	X			X		

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	102	104	100	104	074	087	041	041	072	104	104	103	104	102	104	103	104	098	104	104	104	104	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	N	A	+	+	A	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	48✖
KERATOACANTHOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	N	A	+	+	A	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	48✖
FIBROMA				X							X							X								4
LIPOMA					X																					1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
OSTEOSARCOMA, METASTATIC																										1
TRACHEA	+	+	+	-	+	-	A	-	+	A	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	38
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
SPLEEN	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LYMPH NODES	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
THYMUS	-	-	-	-	-	-	A	-	-	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
LIVER	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
NEOPLASTIC NODULE																		X	X							2
HEPATOCELLULAR CARCINOMA																								X		1
BILE DUCT	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	A	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48✖
PANCREAS	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	-	+	-	A	+	+	A	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	43
STOMACH	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SMALL INTESTINE	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	44
LARGE INTESTINE	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	-	-	+	+	+	-	-	+	39
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY BLADDER	+	+	+	-	+	-	A	+	+	A	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	43
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	-	A	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	44
CARCINOMA,NOS												X														1
ADENOMA, NOS	X							X							X		X				X					10
CHROMOPHOBE ADENOMA																										1
CHROMOPHOBE CARCINOMA																										1
ADRENAL	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
PHEOCHROMOCYTOMA	X										X										X	X			X	13
THYROID	+	+	+	-	+	-	A	+	+	A	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	41
PAPILLARY ADENOCARCINOMA																										1
C-CELL ADENOMA		X							X					X												3
C-CELL CARCINOMA	X											X			X											3
PARATHYROID	+	+	-	-	+	-	A	+	+	A	-	-	-	+	-	+	-	+	-	+	+	+	+	+	+	32
PANCREATIC ISLETS	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ISLET-CELL ADENOMA			X																							2
ISLET-CELL CARCINOMA																								X		6
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	N	+	N	A	+	N	A	+	+	N	N	+	+	N	+	+	N	N	+	+	+	+	48✖
FIBROMA	X																									1
FIBROADENOMA																										1
TESTIS	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	47
PROSTATE	+	+	+	-	-	-	A	-	+	A	+	-	+	+	+	+	-	-	-	-	+	-	+	+	-	32
ADENOMA, NOS																								X		2
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	A	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48✖
CARCINOMA,NOS																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	-	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ASTROCYTOMA																										1
SPECIAL SENSE ORGANS																										
EAR	N	N	N	N	N	N	A	N	N	A	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	48✖
FIBROSARCOMA													X													1
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	A	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48✖
FIBROSARCOMA																				X						1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	A	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48✖
MESOTHELIOMA, NOS																										1
LEUKEMIA,NOS		X		X									X		X			X								8

✖ ANIMALS NECROPSIED

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

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

TABLE A4.

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

VEHICLE CONTROL

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	104	104	096	104	104	091	093	104	079	104	080	082	080	104	104	101	104	102	085	104	080	096	104	103	105
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
SEBACEOUS ADENOCARCINOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA				X																					
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	A	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	A	+	+	+	-
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
NEOPLASTIC NODULE														X					X						
LEUKEMIA,NOS																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
SQUAMOUS CELL CARCINOMA									X																
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+	+	+
CARCINOMA,NOS																X									
ADENOMA, NOS						X	X	X	X					X			X							X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA												X													
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
C-CELL CARCINOMA																									X
PARATHYROID	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	-	+	A	-	-	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	A	+	+	+	N
ADENOCARCINOMA, NOS					X																				
FIBROMA																		X							
FIBROADENOMA	X						X				X					X			X						
UTERUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
ENDOMETRIAL STROMAL POLYP	X			X		X						X													
ENDOMETRIAL STROMAL SARCOMA																									
OVARY	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
CARCINOMA, NOS, INVASIVE																X									
ADENOMA, NOS																								X	
ASTROCYTOMA																								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	A	N	N	N	N
MALIGNANT LYMPHOMA, NOS																						X			
MALIG.LYMPHOMA, UNDIFFER-TYPE												X													
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
LEUKEMIA,NOS	X		X											X	X					X					

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

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

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	095	103	104	102	104	102	104	104	104	091	104	104	094	042	104	100	104	104	104	104	104	065	104	104	088	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	49*
SEBACEOUS ADENOCARCINOMA																			X							1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA	X											X			X											4
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
THYMUS	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	2
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASTIC NODULE				X						X																4
LEUKEMIA,NOS															X	X										2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	+	45
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	47
SQUAMOUS CELL CARCINOMA																										1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	-	+	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-	+	-	+	+	-	+	+	+	+	43
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	45
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CARCINOMA,NOS												X												X		3
ADENOMA, NOS	X						X						X				X	X	X			X	X		X	16
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
CORTICAL ADENOMA		X																								1
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	47
C-CELL CARCINOMA							X	X																X		4
PARATHYROID	+	+	-	+	-	+	+	+	+	-	+	-	-	+	-	-	+	+	-	+	-	+	+	+	+	33
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	49*
ADENOCARCINOMA, NOS																										1
FIBROMA																										1
FIBROADENOMA				X	X	X			X						X						X			X		12
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOMETRIAL STROMAL POLYP							X		X	X			X			X				X	X		X			12
ENDOMETRIAL STROMAL SARCOMA		X																								1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA, NOS, INVASIVE																										1
ADENOMA, NOS																										1
ASTROCYTOMA	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	49*
MALIGNANT LYMPHOMA, NOS																										1
MALIG.LYMPHOMA, UNDIFFER-TYPE																										1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE				X																						1
LEUKEMIA,NOS	X	X											X													8

* ANIMALS NECROPSIED

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

TABLE A4.

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

LOW DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	092	104	100	104	104	104	087	091	104	078	104	090	101	091	102	104	104	088	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIPOMA										X															
NEURILEMOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, METASTATIC																									
ALVEOLAR/BRONCHIOLAR CARCINOMA																		X							
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+
LARGE INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
LIPOMA																X									
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-
TRANSITIONAL-CELL CARCINOMA																									
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
CARCINOMA,NOS																					X				
ADENOMA, NOS	X	X					X		X	X	X	X		X	X			X					X		X
CHROMOPHOBE ADENOMA													X												
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL CARCINOMA																									
PHEOCHROMOCYTOMA															X							X			
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
FOLLICULAR-CELL CARCINOMA																X									
C-CELL ADENOMA																									
C-CELL CARCINOMA																									
PARATHYROID	+	+	+	+	-	-	+	+	+	+	+	-	+	+	+	+	+	+	-	+	-	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS				X																					
ADENOCARCINOMA, NOS																									
FIBROADENOMA												X	X	X		X		X				X			
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
SARCOMA, NOS														X											
ENDOMETRIAL STROMAL POLYP																		X							
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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																									
LEUKEMIA,NOS				X									X												
UNDIFFERENTIATED LEUKEMIA																			X						
MYELOMONOCYTIC LEUKEMIA																									
LYMPHOCYTIC LEUKEMIA																									

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

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

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	103	091	102	104	093	090	041	011	090	104	104	104	088	089	104	104	104	096	104	091	104	104	094	104	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
LIPOMA																										1
NEURILEMOMA						X																				1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA, NOS, METASTATIC										X																1
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	45
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	46
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	-	+	+	-	+	-	+	43
LIPOMA																										1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	45
TRANSITIONAL-CELL CARCINOMA		X																								1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA,NOS																										1
ADENOMA, NOS		X			X				X	X	X												X	X	X	20
CHROMOPHOBE ADENOMA												X														2
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL CARCINOMA																									X	1
PHEOCHROMOCYTOMA																										2
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	47
FOLLICULAR-CELL CARCINOMA																										1
C-CELL ADENOMA		X																								1
C-CELL CARCINOMA																									X	1
PARATHYROID	+	+	+	+	+	-	+	+	+	-	-	+	+	+	-	+	+	+	+	-	-	+	+	+	+	39
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL CARCINOMA	X																									1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	50*
CARCINOMA,NOS										X																1
ADENOMA, NOS																										1
ADENOCARCINOMA, NOS																							X			1
FIBROADENOMA			X	X	X	X	X	X	X					X												14
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SARCOMA, NOS																										1
ENDOMETRIAL STROMAL POLYP		X	X			X			X			X						X		X				X		9
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	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																						1
LEUKEMIA,NOS											X															3
UNDIFFERENTIATED LEUKEMIA																										1
MYELOMONOCYTIC LEUKEMIA																										1
LYMPHOCYTIC LEUKEMIA																					X					1

* ANIMALS NECROPSIED

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

TABLE A4.

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

HIGH DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	104	104	097	104	104	104	096	073	104	043	099	104	104	104	098	102	103	074	081	104	103	091	104	104	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	X	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																									
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	-	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	-	+	+	-	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
THYMUS	-	-	-	-	-	-	+	A	-	A	-	-	-	-	-	A	-	+	-	-	-	+	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
ORAL CAVITY	N	N	N	N	N	N	N	A	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N
PAPILLOMA, NOS																									
SQUAMOUS CELL CARCINOMA																									
SALIVARY GLAND	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	A	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	-	+	+	-	+	+	+
STOMACH	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	-	+	+	-	+	+	+
ADENOCARCINOMA, NOS															X										
SMALL INTESTINE	+	+	-	+	+	+	+	A	+	A	+	+	-	+	+	A	+	+	-	+	+	-	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	A	+	A	+	+	-	+	+	A	+	+	+	+	+	-	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																					X				
URINARY BLADDER	+	+	+	+	+	+	+	A	+	A	+	+	-	+	+	A	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	-	+
ADENOMA, NOS		X	X	X	X				X		X			X	X				X						X
CHROMOPHOBE ADENOMA						X											X				X				
ADRENAL	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA		X																							
THYROID	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	-	+	+	+
FOLLICULAR-CELL ADENOMA							X																		
C-CELL ADENOMA														X											
C-CELL CARCINOMA				X																					
PARATHYROID	+	+	-	+	+	+	-	A	-	A	+	-	+	+	+	A	+	+	+	+	+	-	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	+	+	+	N	N	A	+	A	+	+	+	+	N	A	+	+	+	N	+	N	+	+	+
ADENOCARCINOMA, NOS																	X								
FIBROMA																	X								
FIBROADENOMA					X		X		X								X								X
UTERUS	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+
PAPILLARY CARCINOMA														X											
PAPILLARY ADENOMA																									
ENDOMETRIAL STROMAL POLYP											X						X								
ENDOMETRIAL STROMAL SARCOMA																							X		
OVARY	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
GLIOMA, NOS											X														
BODY CAVITIES																									
PERITONEUM	N	N	N	N	N	N	N	A	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS, METASTATIC																					X				
MESENTERY	N	N	N	N	N	N	N	A	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N
ENDOMETRIAL STROMAL SARCOMA, META																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	A	N	A	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS																						X			
MONOCYTIC LEUKEMIA																		X							

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

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

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	104	041	104	104	104	080	104	041	088	104	104	104	085	104	087	101	104	071	104	104	104	100	104	104	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
ADENOCARCINOMA, NOS, METASTATIC																										1
ALVEOLAR/BRONCHIOLAR ADENOMA																		X								1
TRACHEA	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	A	40
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
SPLEEN	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
LYMPH NODES	+	+	A	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	A	42
THYMUS	-	-	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	3
CIRCULATORY SYSTEM																										
HEART	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
DIGESTIVE SYSTEM																										
ORAL CAVITY	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	45*
PAPILLOMA, NOS																							X			1
SQUAMOUS CELL CARCINOMA																			X							1
SALIVARY GLAND	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
LIVER	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
BILE DUCT	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
GALLBLADDER & COMMON BILE DUCT	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	45*
PANCREAS	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
ESOPHAGUS	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	42
STOMACH	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	42
ADENOCARCINOMA, NOS																										1
SMALL INTESTINE	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	A	39
LARGE INTESTINE	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	A	42
URINARY SYSTEM																										
KIDNEY	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	44
ADENOCARCINOMA, NOS, METASTATIC																										1
URINARY BLADDER	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	A	41
ENDOCRINE SYSTEM																										
PITUITARY	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	43
ADENOMA, NOS	X	X			X			X				X	X	X		X	X	X	X		X	X		X		24
CHROMOPHOBE ADENOMA																										3
ADRENAL	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	A	43
PHEOCHROMOCYTOMA											X			X												3
THYROID	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	44
FOLLICULAR-CELL ADENOMA																					X					2
C-CELL ADENOMA																										1
C-CELL CARCINOMA	X										X							X								4
PARATHYROID	+	+	A	-	-	+	+	+	+	+	+	+	+	-	+	+	-	+	-	+	+	+	+	+	A	35
PANCREATIC ISLETS	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
ISLET-CELL CARCINOMA												X														1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	A	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	A	45*
ADENOCARCINOMA, NOS											X															1
FIBROMA																										1
FIBROADENOMA		X					X																X	X		9
UTERUS	+	+	A	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	42
PAPILLARY CARCINOMA																										1
PAPILLARY ADENOMA										X																1
ENDOMETRIAL STROMAL POLYP	X			X						X			X	X								X				9
ENDOMEIRIAL STROMAL SARCOMA																	X									1
OVARY	+	+	A	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	44
PAPILLOMA, NOS								X																		1
NERVOUS SYSTEM																										
BRAIN	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	45
GLIOMA, NOS																		X								2
BODY CAVITIES																										
PERITONEUM	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	45*
ADENOCARCINOMA, NOS, METASTATIC																										1
MESENTERY	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	45*
ENDOMETRIAL STROMAL SARCOMA, META																		X								1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	45*
LEUKEMIA,NOS				X	X								X													4
MONOCYTIC LEUKEMIA																										1

* ANIMALS NECROPSIED

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

Appendix B

Summary of the Incidence of Neoplasms in Mice
Administered Vinylidene Chloride by Gavage

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE ADMINISTERED VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	47	47	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	46	47	50
INTEGUMENTARY SYSTEM			
*SKIN	(47)	(47)	(50)
FIBROSARCOMA	1 (2%)		
NEUROFIBROSARCOMA	1 (2%)		
*SUBCUT TISSUE	(47)	(47)	(50)
SARCOMA, NOS			1 (2%)
FIBROSARCOMA		1 (2%)	
NEUROFIBROSARCOMA	1 (2%)		
NEURILEMOMA	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(46)	(45)	(46)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA	3 (7%)	4 (9%)	4 (9%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	2 (4%)	1 (2%)	4 (9%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(47)	(47)	(50)
MALIGNANT LYMPHOMA, NOS	5 (11%)	3 (6%)	6 (12%)
MONOCYTIC LEUKEMIA		1 (2%)	
#MESENTERIC L. NODE	(28)	(38)	(43)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
#LIVER	(46)	(46)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
LEUKEMIA,NOS		2 (4%)	
#SMALL INTESTINE	(36)	(41)	(39)
MALIGNANT LYMPHOMA, NOS			1 (3%)

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#SPLEEN	(45)	(45)	(48)
HEMANGIOMA	1 (2%)	2 (4%)	1 (2%)
#LIVER	(46)	(46)	(49)
HEMANGIOMA		1 (2%)	1 (2%)
HEMANGIOSARCOMA	1 (2%)		2 (4%)
DIGESTIVE SYSTEM			
#LIVER	(46)	(46)	(49)
HEPATOCELLULAR ADENOMA	7 (15%)	4 (9%)	6 (12%)
HEPATOCELLULAR CARCINOMA	8 (17%)	5 (11%)	9 (18%)
#STOMACH	(43)	(40)	(42)
SQUAMOUS CELL CARCINOMA			1 (2%)
#JEJUNUM	(36)	(41)	(39)
FIBROSARCOMA			1 (3%)
URINARY SYSTEM			
#KIDNEY	(45)	(46)	(46)
TUBULAR-CELL ADENOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(35)	(34)	(36)
CARCINOMA,NOS		1 (3%)	
ADENOMA, NOS	1 (3%)		
#ADRENAL	(41)	(43)	(47)
CORTICAL ADENOMA			1 (2%)
PHEOCHROMOCYTOMA	1 (2%)		2 (4%)
#THYROID	(41)	(45)	(46)
FOLLICULAR-CELL ADENOMA		2 (4%)	
#PANCREATIC ISLETS	(44)	(46)	(48)
ISLET-CELL ADENOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
NONE			

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(47)	(47)	(50)
ADENOMA, NOS	1 (2%)		
PAPILLARY ADENOMA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHS@	11	9	9
MORIBUND SACRIFICE	5	6	5
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED	1		
TERMINAL SACRIFICE	33	35	36
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	30	22	33
TOTAL PRIMARY TUMORS	37	27	42
TOTAL ANIMALS WITH BENIGN TUMORS	14	12	15
TOTAL BENIGN TUMORS	17	13	16
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	13	25
TOTAL MALIGNANT TUMORS	20	14	26
TOTAL ANIMALS WITH SECONDARY TUMORS#	1		
TOTAL SECONDARY TUMORS	1		
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE ADMINISTERED VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	49	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(48)	(49)	(50)
SARCOMA, NOS		1 (2%)	
FIBROUS HISTIOCYTOMA, MALIGNANT		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(48)	(45)	(48)
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)	1 (2%)	4 (8%)
OSTEOSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(48)	(49)	(50)
MALIGNANT LYMPHOMA, NOS		5 (10%)	2 (4%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE			1 (2%)
LEUKEMIA,NOS	3 (6%)	4 (8%)	
MONOCYTIC LEUKEMIA	2 (4%)	2 (4%)	1 (2%)
#SPLEEN	(46)	(47)	(46)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#MANDIBULAR L. NODE	(29)	(36)	(42)
MALIGNANT LYMPHOMA, NOS	1 (3%)		
#LIVER	(47)	(49)	(49)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
LEUKEMIA,NOS		1 (2%)	
#SMALL INTESTINE	(40)	(41)	(45)
MALIGNANT LYMPHOMA, NOS			1 (2%)
#JEJUNUM	(40)	(41)	(45)
MALIGNANT LYMPHOMA, NOS		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
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#ILEUM	(40)	(41)	(45)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#KIDNEY	(46)	(49)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		1 (2%)
CIRCULATORY SYSTEM			
#SPLEEN	(46)	(47)	(46)
HEMANGIOMA		2 (4%)	
#LYMPH NODE	(29)	(36)	(42)
LYMPHANGIOMA			1 (2%)
#LIVER	(47)	(49)	(49)
HEMANGIOMA			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(47)	(49)	(49)
HEPATOCELLULAR ADENOMA	2 (4%)	3 (6%)	2 (4%)
HEPATOCELLULAR CARCINOMA	2 (4%)		1 (2%)
#STOMACH	(43)	(43)	(42)
SQUAMOUS CELL CARCINOMA		1 (2%)	1 (2%)
ADENOMATOUS POLYP, NOS		1 (2%)	1 (2%)
#DUODENUM	(40)	(41)	(45)
ADENOMATOUS POLYP, NOS	1 (3%)		
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(31)	(32)	(42)
CARCINOMA,NOS		1 (3%)	
ADENOMA, NOS	5 (16%)	6 (19%)	3 (7%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#ADRENAL	(42)	(44)	(50)
PHEOCHROMOCYTOMA	2 (5%)	1 (2%)	1 (2%)
#THYROID	(41)	(45)	(43)
FOLLICULAR-CELL ADENOMA	2 (5%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(48)	(49)	(50)
FIBROADENOMA	1 (2%)	1 (2%)	3 (6%)
#UTERUS	(46)	(45)	(47)
LEIOMYOMA	1 (2%)		
ENDOMETRIAL STROMAL POLYP		3 (7%)	2 (4%)
#OVARY	(41)	(44)	(45)
ADENOMA, NOS		1 (2%)	
CYSTADENOMA, NOS			1 (2%)
TUBULAR ADENOMA		1 (2%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(48)	(49)	(50)
ADENOMA, NOS		2 (4%)	2 (4%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
*FEMUR	(48)	(49)	(50)
OSTEOSARCOMA		1 (2%)	
*SKELETAL MUSCLE	(48)	(49)	(50)
FIBROSARCOMA		1 (2%)	
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	11	4
MORIBUND SACRIFICE	5	7	4
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	40	32	42
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	23	33	21
TOTAL PRIMARY TUMORS	24	45	30
TOTAL ANIMALS WITH BENIGN TUMORS	15	22	15
TOTAL BENIGN TUMORS	15	23	21
TOTAL ANIMALS WITH MALIGNANT TUMORS	9	18	9
TOTAL MALIGNANT TUMORS	9	22	9
TOTAL ANIMALS WITH SECONDARY TUMORS#		1	
TOTAL SECONDARY TUMORS		1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE B3.

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

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	104	104	086	082	041	040	096	041	085	099	041	097	096	080	041	011	097	073	088	083	041	049	041	049	041
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	A	+	+	+	+	+	+
FIBROSARCOMA																			X						
NEUROFIBROSARCOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	A	+	+	+	+	+	+
NEUROFIBROSARCOMA							X																		
NEURILEMOMA	X																								
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									
ALVEOLAR/BRONCHIOLAR ADENOMA			X																						
ALVEOLAR/BRONCHIOLAR CARCINOMA		X										X													
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	A	+	+	A	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	A	+	+	A	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+
HEMANGIOMA	X																								
LYMPH NODES	–	+	+	–	+	+	+	+	+	+	–	+	+	–	–	A	+	–	A	+	+	–	+	+	
THYMUS	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	A	–	–	A	–	–	–	–	–	
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA		X																X				X	X		
HEPATOCELLULAR CARCINOMA								X					X	X						X					X
HEMANGIOSARCOMA																			X						
MALIGNANT LYMPHOMA, NOS																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	N	+	+	N	N	+	+	N	N	+	N	+	+	A	N	N	+	N	+	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	A	+	+	A	+	+	+	+	+	
ESOPHAGUS	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	A	+	+	A	+	+	+	+	+	
STOMACH	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	A	+	+	A	+	+	+	+	+	
SMALL INTESTINE	+	+	–	+	+	+	+	+	–	+	+	–	+	–	+	A	+	+	A	+	–	+	+	+	
LARGE INTESTINE	+	+	–	+	+	+	+	–	–	+	+	–	+	–	–	A	+	+	A	–	+	+	+	–	
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	
URINARY BLADDER	+	–	+	+	–	+	+	+	–	+	+	+	+	–	–	A	+	+	A	+	+	+	+	+	
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	–	+	+	+	+	+	+	–	+	–	A	+	+	A	+	+	+	+	+	–
ADENOMA, NOS																	X								
ADRENAL	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	A	+	+	A	+	+	+	+	+	
PHEOCHROMOCYTOMA	X																								
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	A	+	+	–	A	+	+	+	+	
PARATHYROID	–	–	–	+	–	+	–	+	–	+	–	–	+	+	+	A	–	+	–	A	–	–	–	–	
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	A	+	+	A	+	+	+	+	+	
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	N	N	+	N	N	N	N	N	N	N	N	N	N	N	+	N	N	A	N	N	N	N	N
TESTIS	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	–	
PROSTATE	–	–	+	+	–	+	+	+	–	+	–	+	–	+	+	A	+	+	A	+	+	+	–	+	
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	
ADENOMA, NOS																	X								
PAPILLARY ADENOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	
MALIGNANT LYMPHOMA, NOS									X																X

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

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

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

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	078	104	104	104	104	104	104	104	101	104	104	104	104	104	104	104	104	104	104	104	104	083	104	100	087	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47*
FIBROSARCOMA													X													1
NEUROFIBROSARCOMA																										1
SUBCUTANEOUS TISSUE	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47*
NEUROFIBROSARCOMA																										1
NEURILEMOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEPATOCELLULAR CARCINOMA, METASTA											X															1
ALVEOLAR/BRONCHIOLAR ADENOMA						X									X											3
ALVEOLAR/BRONCHIOLAR CARCINOMA																										2
TRACHEA	A	+	+	+	+	+	+	+	A	+	+	+	+	–	+	+	–	+	+	+	–	+	+	+	+	42
HEMATOPOIETIC SYSTEM																										
BONE MARROW	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	44
SPLEEN	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	45
HEMANGIOMA																										1
LYMPH NODES	A	–	–	–	–	+	–	+	A	–	+	–	–	+	+	–	–	+	–	+	+	+	+	+	+	28
THYMUS	A	–	–	–	–	–	–	–	A	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0
CIRCULATORY SYSTEM																										
HEART	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
DIGESTIVE SYSTEM																										
SALIVARY GLAND	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
LIVER	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEPATOCELLULAR ADENOMA														X		X		X								7
HEPATOCELLULAR CARCINOMA											X										X			X		8
HEMANGIOSARCOMA																										1
MALIGNANT LYMPHOMA, NOS		X																								1
BILE DUCT	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
GALLBLADDER & COMMON BILE DUCT	A	+	+	+	+	+	+	+	A	+	+	+	N	N	+	+	N	+	+	+	+	N	+	N	N	47*
PANCREAS	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+		44
ESOPHAGUS	A	+	+	+	+	+	–	+	A	+	+	+	–	–	+	+	–	+	+	+	–	+	+	+	+	39
STOMACH	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+		43
SMALL INTESTINE	A	+	–	+	+	+	+	+	A	+	+	–	+	+	+	+	–	+	+	+	–	+	–	+		36
LARGE INTESTINE	A	+	+	+	+	+	+	+	A	+	+	–	+	+	+	+	+	+	+	+	–	–	–	+		34
URINARY SYSTEM																										
KIDNEY	A	+	+	+	+	+	+	+	A	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	45
URINARY BLADDER	A	+	–	+	+	+	+	+	A	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+		38
ENDOCRINE SYSTEM																										
PITUITARY	A	–	–	+	+	–	–	+	A	–	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	35
ADENOMA, NOS																										1
ADRENAL	A	+	+	+	+	–	+	+	A	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	41
PHEOCHROMOCYTOMA																										1
THYROID	A	+	+	+	+	+	+	+	A	+	+	+	+	–	+	+	–	+	+	+	–	+	+	+	+	41
PARATHYROID	A	+	+	–	–	–	–	–	A	–	–	–	–	–	–	–	–	–	+	+	–	–	–	+	+	13
PANCREATIC ISLETS	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+		44
ISLET-CELL ADENOMA																			X							1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	A	N	N	+	+	+	+	N	A	+	N	N	N	N	+	N	N	+	+	+	N	+	+	N		47*
TESTIS	A	+	+	+	+	+	+	+	A	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	43
PROSTATE	A	–	+	+	+	+	–	+	A	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	36
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	A	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	47*
ADENOMA, NOS																										1
PAPILLARY ADENOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	A	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	47*
MALIGNANT LYMPHOMA, NOS			X																			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

TABLE B3.

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

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	104	104	104	104	092	104	082	104	084	104	104	104	095	104	104	099	104	104	104	104	104	104	103
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+
FIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																			X		X				
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
HEMANGIOMA																									
LYMPH NODES	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	-	-	+	+	+	+	+	+
THYMUS	+	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA				X																	X			X	
HEPATOCELLULAR CARCINOMA															X	X									X
HEMANGIOMA																		X							
LEUKEMIA,NOS									X							X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	+	+	N	N	+	+	N	+	+	+	+	N	+	+	+	+	+	+	N	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	-	+	-	+	-	+	+	+	-	+	+	+	+	+	+	-	+
STOMACH	+	+	-	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-
SMALL INTESTINE	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-
LARGE INTESTINE	+	-	-	+	+	+	+	+	-	+	-	-	+	+	+	+	+	-	+	-	+	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	-	+	-	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	-	-	+	+	+	+	+	-	+	+	-	-	+	+	+	+	+	+	-	+
CARCINOMA,NOS																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
FOLLICULAR-CELL ADENOMA																				X					
PARATHYROID	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	+	N	+	+	
TESTIS	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+
PROSTATE	+	+	+	-	+	+	-	+	-	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+
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						
MONOCYTIC LEUKEMIA											X														

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

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

TABLE 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
WEEKS ON STUDY	002	002	003	004	003	014	014	014	098	014	014	014	080	012	014	014	014	014	014	045	014	014	014	014	014	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	A	A	N	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47*
FIBROSARCOMA														X												1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	45
ALVEOLAR/BRONCHIOLAR ADENOMA								X					X													4
ALVEOLAR/BRONCHIOLAR CARCINOMA						X																				1
TRACHEA	A	A	+	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	A	A	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
SPLEEN	A	A	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
HEMANGIOMA							X																	X		2
LYMPH NODES	A	A	+	-	A	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	-	38
THYMUS	A	A	-	-	A	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
CIRCULATORY SYSTEM																										
HEART	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
DIGESTIVE SYSTEM																										
SALIVARY GLAND	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
LIVER	A	A	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEPATOCELLULAR ADENOMA																X										4
HEPATOCELLULAR CARCINOMA													X						X							5
HEMANGIOMA																										1
LEUKEMIA,NOS																										2
BILE DUCT	A	A	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
GALLBLADDER & COMMON BILE DUCT	A	A	N	N	A	+	+	+	+	+	+	+	N	+	+	+	N	+	+	N	+	+	+	+	+	47*
PANCREAS	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ESOPHAGUS	A	A	+	+	A	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	40
STOMACH	A	A	-	+	A	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	40
SMALL INTESTINE	A	A	-	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	41
LARGE INTESTINE	A	A	-	+	A	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	37
URINARY SYSTEM																										
KIDNEY	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
URINARY BLADDER	A	A	+	+	A	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	42
ENDOCRINE SYSTEM																										
PITUITARY	A	A	+	-	A	+	+	+	+	+	-	+	+	-	+	+	-	+	-	+	+	+	+	+	-	34
CARCINOMA,NOS																				X						1
ADRENAL	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	43
THYROID	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	45
FOLLICULAR-CELL ADENOMA																									X	2
PARATHYROID	A	A	+	+	A	-	-	+	-	+	-	-	-	+	-	-	+	+	+	-	+	+	-	-	-	13
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	A	A	N	N	A	+	+	N	N	N	N	+	N	N	+	N	N	N	N	N	N	+	+	N	+	47*
TESTIS	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
PROSTATE	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	40
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	A	A	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	47*
MALIGNANT LYMPHOMA, NOS																										3
MONOCYTIC LEUKEMIA																										1

* ANIMALS NECROPSIED

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

TABLE B3.

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

HIGH DOSE

ANIMAL NUMBER	00111	00201	00301	00401	00501	00601	00701	00801	00901	01001	01101	01201	01301	01401	01501	01601	01701	01801	01901	02101	02201	02301	02401	02501
WEEKS ON STUDY	10401	10401	10401	07201	10401	10401	10401	10401	10401	10401	10401	10401	10401	08201	10401	09601	09901	09201	10401	10401	10401	10401	08101	10401
INTEGUMENTARY SYSTEM																								
SUBCUTANEOUS TISSUE SARCOMA, NOS	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA ALVEOLAR/BRONCHIOLAR CARCINOMA	+	+	+	+	+	+	+ X	+	+	+	+	+	+ X	+ X	+ X	-	+	-	+	+	+ X	+	+	+
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN HEMANGIOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+
LYMPH NODES MALIG.LYMPHOMA, HISTIOCYTIC TYPE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	-	+	+
THYMUS	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
SALIVARY GLAND	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA HEMANGIOMA HEMANGIOSARCOMA	+	+	+	+	+	+ X	+	+	+ X	+ X	+ X	+	+	+	+	+	+ X	+	+	+	+	+	+ X	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	N	N	N	+	N	N	+	N	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	-	+	-	-	+	+	+	-	+
STOMACH SQUAMOUS CELL CARCINOMA	+	+	+	-	+	+	+	+	+	+	+	+	+	+ X	+	-	+	+	-	+	+	+	-	+
SMALL INTESTINE FIBROSARCOMA MALIGNANT LYMPHOMA, NOS	+	+	+	-	+	+	-	+	+	+	+ X	+	+	-	-	+	-	+	-	+	+	+	-	+
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-	+
URINARY SYSTEM																								
KIDNEY TUBULAR-CELL ADENOMA	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+
ENDOCRINE SYSTEM																								
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	-	+	-	+	-	-	-
ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+
PARATHYROID	+	-	-	-	-	+	-	+	-	-	+	-	-	-	-	-	-	+	-	-	+	-	+	-
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	N	+	+	N	+	N	+	+	N	+	+	+	N	N	+	N	N	N	+	N	+	+	N	+
TESTIS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N	N	N	N	N X	N	N	N	N	N

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

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	104	095	041	095	104	104	104	104	104	104	104	104	041	095	104	104	104	101	104	092	067	104	083	102	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	50*
SARCOMA, NOS																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+		46
ALVEOLAR/BRONCHIOLAR ADENOMA						X																				4
ALVEOLAR/BRONCHIOLAR CARCINOMA										X															X	4
TRACHEA	+	+	+	+	-	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	-	+	+		44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	-	+	+		47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+		48
HEMANGIOMA																										1
LYMPH NODES	+	+	+	-	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+		43
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																			X							1
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+		49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+		46
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+		49
HEPATOCELLULAR ADENOMA								X						X					X						X	6
HEPATOCELLULAR CARCINOMA		X									X					X		X				X				9
HEMANGIOMA																										1
HEMANGIOSARCOMA			X																							2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+		49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	+	+	+	N	+	+	+	N	+	+	+	N	+	+	+	N	N	N	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+		48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	-	+	+		41
STOMACH	+	-	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+		42
SQUAMOUS CELL CARCINOMA																										1
SMALL INTESTINE	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+		39
FIBROSARCOMA																										1
MALIGNANT LYMPHOMA, NOS								X																		1
LARGE INTESTINE	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+		42
URINARY SYSTEM																										
KIDNEY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+		46
TUBULAR-CELL ADENOMA																	X									1
URINARY BLADDER	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+		44
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	-	-	+		36
ADRENAL	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+		47
CORTICAL ADENOMA															X											1
PHEOCHROMOCYTOMA						X						X														2
THYROID	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+		46
PARATHYROID	-	+	-	+	-	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	+	+	-	+	+	15
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	N	N	+	+	+	+	+	+	+	+	N	N	+	+	+	N	+	N	N	+	N	N	N	50*
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	47
PROSTATE	+	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	-	+	+	40
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	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 B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF VINYLIDENE CHLORIDE

VEHICLE CONTROL

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	096	104	092	104	104	104	104	104	104	087	104	070	080	104	076	104	104	104	094	104	104	104	104	104	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	-	+	+	-	+	+	+	-	+	-	+	+	+	+	+	+	A	+	+	+	+	-	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	-	-	+	-	+	+	+	+	+	A	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	A	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	-	-	+	+	+	+	+	+	-	+	-	+	+	-	A	-	-	-	-	-	+	+	+
MALIGNANT LYMPHOMA, NOS																									
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																									
HEPATOCELLULAR CARCINOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	N	+	+	N	+	+	+	N	+	+	+	+	N	+	A	+	N	+	N	+	N	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
ESOPHAGUS	-	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	A	+	+	-	+	-	+	+	+
STOMACH	+	+	-	+	+	+	+	+	+	-	+	+	+	+	-	+	A	-	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	-	+	+	+	-	-	-	+	+	+	+	-	+	A	-	+	+	+	+	+	+	+
ADENOMATOUS POLYP, NOS																X									
LARGE INTESTINE	-	+	+	+	-	+	+	+	+	-	+	+	+	-	-	+	A	-	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
URINARY BLADDER	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	A	-	-	+	+	+	+	-	+
ENDOCRINE SYSTEM																									
PITUITARY	-	-	-	+	-	+	+	+	+	-	-	+	+	-	+	-	A	+	+	+	+	+	-	+	-
ADENOMA, NOS						X																		X	
ADRENAL	-	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	A	+	+	+	+	+	+	-	+
PHEOCHROMOCYTOMA																									X
THYROID	-	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	A	-	+	+	+	-	+	-	+
FOLLICULAR-CELL ADENOMA														X											
PARATHYROID	-	-	-	-	+	-	-	+	-	-	-	-	-	+	-	-	A	-	-	+	-	-	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	N	+	+	+	+	+	+	N	N	N	+	+	+	A	+	+	N	+	+	N	+	+
FIBROADENOMA										X															
UTERUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+	+	-	+	+	+	+	+
LEIOMYOMA				X																					
OVARY	-	+	-	-	+	+	+	+	+	-	+	+	+	+	-	-	A	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N
LEUKEMIA,NOS												X	X		X										
MONOCYTIC LEUKEMIA			X																	X					

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

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

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

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	095	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	092	104	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ALVEOLAR/BRONCHIOLAR ADENOMA															X											1
TRACHEA	+	A	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	40
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	A	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	44
SPLEEN	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	46
LYMPH NODES	+	A	+	+	-	+	-	+	+	+	-	-	+	-	+	+	-	+	-	+	+	-	+	+	-	29
MALIGNANT LYMPHOMA, NOS				X																						1
THYMUS	-	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0
CIRCULATORY SYSTEM																										
HEART	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEPATOCELLULAR ADENOMA	X													X												2
HEPATOCELLULAR CARCINOMA													X											X		2
BILE DUCT	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
GALLBLADDER & COMMON BILE DUCT	+	A	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	N	N	N	+	+	+	+	48*
PANCREAS	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	40
STOMACH	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	43
SMALL INTESTINE	+	A	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	40
ADENOMATOUS POLYP, NOS																										1
LARGE INTESTINE	+	A	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	+	+	+	+	+	+	+	+	39
URINARY SYSTEM																										
KIDNEY	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	46
MALIGNANT LYMPHOMA, NOS															X											1
URINARY BLADDER	+	A	-	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	40
ENDOCRINE SYSTEM																										
PITUITARY	-	A	+	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+	-	-	+	+	+	-	31
ADENOMA, NOS								X			X					X										5
ADRENAL	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	42
PHEOCHROMOCYTOMA																								X		2
THYROID	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
FOLLICULAR-CELL ADENOMA						X																				2
PARATHYROID	+	A	+	-	-	-	-	+	-	-	-	-	-	-	+	+	-	-	-	-	-	-	-	-	-	10
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	A	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	N	+	N	N	+	N	N	48*
FIBROADENOMA																										1
UTERUS	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
LEIOMYOMA																										1
OVARY	+	A	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	41
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	48*
LEUKEMIA,NOS																										3
MONOCYTIC LEUKEMIA																										2

* ANIMALS NECROPSIED

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF VINYLIDENE CHLORIDE

LOW DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	096	065	104	102	073	095	104	104	104	104	101	104	104	104	104	104	100	085	084	102	098	104	104	104	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N
SARCOMA, NOS																	X								
FIBROUS HISTIOCYTOMA, MALIGNANT																				X					
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	-
ALVEOLAR/BRONCHIOLAR ADENOMA																					X				
OSTEOSARCOMA, METASTATIC																									
TRACHEA	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+
HEMANGIOMA																							X		
MALIGNANT LYMPHOMA, NOS																									
LYMPH NODES	+	-	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	-	-	-	+	+	+	+	-
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA			X																						
MALIGNANT LYMPHOMA, NOS																									
LEUKEMIA,NOS							X																		
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	-
ESOPHAGUS	-	+	-	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+
SQUAMOUS CELL CARCINOMA					X																				
ADENOMATOUS POLYP, NOS																				X					
SMALL INTESTINE	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+
MALIGNANT LYMPHOMA, NOS			X				X																		
LARGE INTESTINE	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	-	-	+	-	-	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	-	-	+	+	-
CARCINOMA,NOS												X													
ADENOMA, NOS							X									X									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
PHEOCHROMOCYTOMA																									
THYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
FOLLICULAR-CELL ADENOMA						X																			
PARATHYROID	-	-	-	+	-	+	-	+	+	+	-	+	-	-	-	-	+	-	-	-	+	+	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	N	N	+	+	+	+	N	+	+	+	+	+	+	+	N	N	N	N	+	+	+
FIBROADENOMA																		X							
UTERUS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP	X			X																	X				
OVARY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
ADENOMA, NOS																									
TUBULAR ADENOMA												X													
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																						X		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																					X				
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
FIBROSARCOMA	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
MALIGNANT LYMPHOMA, NOS										X							X								X
LEUKEMIA,NOS	X					X															X				
MONOCYTIC LEUKEMIA											X														

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

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

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

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL
WEEKS ON STUDY	104	104	104	103	104	104	104	104	104	104	104	104	103	091	104	074	104	104	104	104	025	104	104	075	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	A	+	49*
SARCOMA, NOS																										1
FIBROUS HISTIOCYTOMA, MALIGNANT																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	45
ALVEOLAR/BRONCHIOLAR ADENOMA									X																	1
OSTEOSARCOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	-	A	+	44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	A	+	43
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	47
HEMANGIOMA										X						X										2
MALIGNANT LYMPHOMA, NOS																										1
LYMPH NODES	+	+	-	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	-	A	+	36
THYMUS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	0
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	A	+	45
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	49
HEPATOCELLULAR ADENOMA					X															X						3
MALIGNANT LYMPHOMA, NOS								X																		1
LEUKEMIA,NOS																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	N	+	N	+	+	A	+	49*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	45
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	A	+	43
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	A	+	43
SQUAMOUS CELL CARCINOMA																										1
ADENOMATOUS POLYP, NOS																										1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	-	+	-	+	+	A	+	41
MALIGNANT LYMPHOMA, NOS																										2
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	A	+	41
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	49
URINARY BLADDER	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	A	+	45
ENDOCRINE SYSTEM																										
PITUITARY	+	+	-	+	-	+	+	-	-	+	-	+	+	+	+	+	-	-	+	+	+	+	+	A	-	32
CARCINOMA,NOS																										1
ADENOMA, NOS	X			X								X										X				6
ADRENAL	+	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	A	+	44
PHEOCHROMOCYTOMA											X															1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	A	+	45
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	+	+	-	-	-	-	-	+	-	-	-	-	+	-	-	-	-	+	-	-	-	+	-	A	-	15
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	N	N	N	+	+	A	+	49*
FIBROADENOMA																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	A	+	45
ENDOMETRIAL STROMAL POLYP																										3
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	A	+	44
ADENOMA, NOS	X																									1
TUBULAR ADENOMA																										1
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	49*
ADENOMA, NOS																										2
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	A	N	49*
OSTEOSARCOMA																										1
MUSCLE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	A	N	49*
FIBROSARCOMA																										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	A	N	49*
MALIGNANT LYMPHOMA, NOS						X								X									X			5
LEUKEMIA,NOS																										4
MONOCYTIC LEUKEMIA													X													2

* ANIMALS NECROPSIED

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

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF VINYLIDENE CHLORIDE

HIGH DOSE

ANIMAL NUMBER	051	052	053	054	055	056	057	058	059	060	061	062	063	064	065	066	067	068	069	070	071	072	073	074	075
WEEKS ON STUDY	080	104	104	104	104	104	104	046	104	104	104	104	104	104	104	080	104	080	104	104	104	104	104	104	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	+	-	+	+	-	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
LYMPH NODES	-	+	+	-	+	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
LYMPHANGIOMA																									
THYMUS	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																									
HEPATOCELLULAR CARCINOMA																								X	
HEMANGIOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	+	+	+	+	N	+	N	+	+	+	+	N	N	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	-	+	-	+	+	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+
STOMACH	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
ADENOMATOUS POLYP, NOS																									
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
MALIGNANT LYMPHOMA, MIXED TYPE																						X			
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-
ADENOMA, NOS														X											
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																									
THYROID	+	+	-	+	+	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
PARATHYROID	-	-	-	+	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	+	-	+	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+
FIBROADENOMA				X																					
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
ENDOMETRIAL STROMAL POLYP		X																				X			
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CYSTADENOMA, NOS																									
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
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																					
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																					X				
MONOCYTIC LEUKEMIA																									

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

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

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

ANIMAL NUMBER	076	077	078	079	080	081	082	083	084	085	086	087	088	089	090	091	092	093	094	095	096	097	098	099	100	TOTAL
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	104	104	101	104	104	104	080	081	104	104	104	071	104	104	104	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
ALVEOLAR/BRONCHIOLAR ADENOMA	X		X				X			X																4
TRACHEA	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	42
HEMATOPOIETIC SYSTEM																										
BONE MARROW	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	46
LYMPH NODES	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	42
LYMPHANGIOMA										X																1
THYMUS	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	4
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA									X											X						2
HEPATOCELLULAR CARCINOMA																										1
HEMANGIOMA			X																							1
BILE DUCT	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	N	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	N	N	+	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	49
ESOPHAGUS	+	+	+	+	-	-	-	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	39
STOMACH	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	+	-	-	+	+	+	42
SQUAMOUS CELL CARCINOMA			X																							1
ADENOMATOUS POLYP, NOS								X																		1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	45
MALIGNANT LYMPHOMA, NOS															X											1
MALIGNANT LYMPHOMA, MIXED TYPE																										1
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	-	+	+	+	-	+	+	-	43
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIGNANT LYMPHOMA, NOS																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+	+	45
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	42
ADENOMA, NOS									X																X	3
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA																									X	1
THYROID	+	+	+	+	+	+	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
PARATHYROID	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	+	-	-	-	+	-	-	-	9
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	+	+	+	+	N	N	N	+	+	N	+	N	+	N	N	+	+	+	N	+	+	+	50*
FIBROADENOMA				X																			X			3
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	47
ENDOMETRIAL STROMAL POLYP																										2
OVARY	+	-	+	+	+	+	+	-	+	+	+	+	-	+	+	+	-	+	+	+	+	-	+	+	+	45
CYSTADENOMA, NOS	X																									1
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ADENOMA, NOS																			X				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*
MALIGNANT LYMPHOMA, NOS																						X				2
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																										1
MONOCYTIC LEUKEMIA																							X			1

* ANIMALS NECROPSIED

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

Appendix C

Summary of the Incidence of Nonneoplastic Lesions in Rats Administered Vinylidene Chloride by Gavage

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS ADMINISTERED VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	48	48
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	48	48
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(48)	(48)
HYPERKERATOSIS		1 (2%)	1 (2%)
ACANTHOSIS		1 (2%)	
RESPIRATORY SYSTEM			
#TRACHEAL CARTILAGE	(46)	(47)	(38)
MINERALIZATION		1 (2%)	
#LUNG	(50)	(47)	(47)
EMPHYSEMA, ALVEOLAR		1 (2%)	1 (2%)
EDEMA, NOS		1 (2%)	
HEMORRHAGE		2 (4%)	
INFLAMMATION, FOCAL	1 (2%)	1 (2%)	
INFLAMMATION, CHRONIC	11 (22%)	13 (28%)	21 (45%)
INFLAMMATION, GRANULOMATOUS	1 (2%)	1 (2%)	3 (6%)
HYPERPLASIA, ADENOMATOUS	1 (2%)		1 (2%)
METAPLASIA, SQUAMOUS		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MAMMARY GLAND	(50)	(48)	(48)
HYPERPLASIA, LYMPHOID		1 (2%)	
#BONE MARROW	(50)	(47)	(46)
HYPERPLASIA, NOS	1 (2%)		1 (2%)
HYPERPLASIA, RETICULUM CELL			1 (2%)
#SPLEEN	(50)	(47)	(48)
CYST, NOS		1 (2%)	
CONGESTION, NOS	1 (2%)		

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FIBROSIS		1 (2%)	2 (4%)
SCLEROSIS	2 (4%)	1 (2%)	1 (2%)
HEMOSIDEROSIS			1 (2%)
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, MESOTHELIAL			1 (2%)
HYPERPLASIA, LYMPHOID			1 (2%)
HEMATOPOIESIS	3 (6%)		
#LYMPH NODE	(45)	(47)	(44)
HYPERPLASIA, NOS			1 (2%)
#MESENTERIC L. NODE	(45)	(47)	(44)
PIGMENTATION, NOS	1 (2%)		
#LIVER	(49)	(48)	(45)
HEMATOPOIESIS		1 (2%)	
#COLON	(35)	(35)	(39)
HYPERPLASIA, LYMPHOID	1 (3%)	5 (14%)	4 (10%)
CIRCULATORY SYSTEM			
#LUNG	(50)	(47)	(47)
PERIARTERITIS		1 (2%)	
#HEART	(50)	(48)	(47)
THROMBOSIS, NOS	1 (2%)		
INFLAMMATION, NOS			1 (2%)
INFLAMMATION, CHRONIC	2 (4%)		4 (9%)
FIBROSIS	4 (8%)	8 (17%)	7 (15%)
FIBROSIS, FOCAL	4 (8%)	2 (4%)	4 (9%)
FIBROSIS, DIFFUSE			1 (2%)
DEGENERATION, NOS	9 (18%)	6 (13%)	4 (9%)
NECROSIS, NOS	4 (8%)	3 (6%)	2 (4%)
NECROSIS, FOCAL	1 (2%)		
#AURICULAR APPENDAGE	(50)	(48)	(47)
THROMBOSIS, NOS			3 (6%)
#MYOCARDIUM	(50)	(48)	(47)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
#ENDOCARDIUM	(50)	(48)	(47)
INFLAMMATION, NOS			1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*CORONARY ARTERY	(50)	(48)	(48)
INFLAMMATION, CHRONIC		1 (2%)	
HYPERTROPHY, NOS			1 (2%)
*PULMONARY ARTERY	(50)	(48)	(48)
HYPERTROPHY, NOS		1 (2%)	
#LIVER	(49)	(48)	(45)
ANEURYSM			1 (2%)
THROMBOSIS, NOS			1 (2%)
#PANCREAS	(49)	(47)	(48)
PERIARTERITIS	1 (2%)	1 (2%)	
#TESTIS	(50)	(47)	(48)
ARTERIOSCLEROSIS, NOS	2 (4%)		
DIGESTIVE SYSTEM			
*TONGUE	(50)	(48)	(48)
HYPERPLASIA, FOCAL			1 (2%)
#LIVER	(49)	(48)	(45)
EDEMA, NOS			1 (2%)
HEMORRHAGE			1 (2%)
INFLAMMATION, NOS			2 (4%)
INFLAMMATION, MULTIFOCAL		1 (2%)	
NECROSIS, DIFFUSE			1 (2%)
METAMORPHOSIS FATTY	6 (12%)	12 (25%)	6 (13%)
HYPERPLASIA, NODULAR	3 (6%)	3 (6%)	1 (2%)
HYPERPLASIA, FOCAL	5 (10%)	3 (6%)	3 (7%)
#LIVER/CENTRILOBULAR	(49)	(48)	(45)
NECROSIS, NOS			1 (2%)
#LIVER/PERIPORTAL	(49)	(48)	(45)
INFLAMMATION, CHRONIC	1 (2%)		
#LIVER/HEPATOCYTES	(49)	(48)	(45)
CYTOPLASMIC VACUOLIZATION	2 (4%)		
#BILE DUCT	(49)	(48)	(45)
HYPERPLASIA, NOS	7 (14%)	9 (19%)	7 (16%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PANCREAS	(49)	(47)	(48)
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
FIBROSIS		1 (2%)	
PIGMENTATION, NOS	1 (2%)		
ATROPHY, NOS	1 (2%)	1 (2%)	
ATROPHY, FOCAL	1 (2%)	8 (17%)	7 (15%)
#STOMACH	(41)	(43)	(47)
INFLAMMATION, NOS	1 (2%)		
ULCER, NOS	1 (2%)		
ULCER, PERFORATED		1 (2%)	
SCLEROSIS		1 (2%)	
HYPERPLASIA, EPITHELIAL		1 (2%)	
#DUODENUM	(38)	(38)	(44)
INFLAMMATION, CHRONIC			1 (2%)
#JEJUNUM	(38)	(38)	(44)
POLYP		1 (3%)	
#COLON	(35)	(35)	(39)
NEMATODIASIS		2 (6%)	
POLYP		1 (3%)	
URINARY SYSTEM			
#KIDNEY	(50)	(48)	(48)
MINERALIZATION		1 (2%)	
CYST, NOS			1 (2%)
GLOMERULONEPHRITIS, NOS		1 (2%)	
INFLAMMATION, CHRONIC	26 (52%)	24 (50%)	43 (90%)
PIGMENTATION, NOS	1 (2%)		
#KIDNEY/TUBULE	(50)	(48)	(48)
NECROSIS, FOCAL			1 (2%)
#URINARY BLADDER	(44)	(42)	(43)
HEMORRHAGE		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(47)	(44)
CYST, NOS		2 (4%)	3 (7%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEMORRHAGE	1 (2%)		
HYPERPLASIA, FOCAL	2 (4%)		
HYPERPLASIA, CYSTIC			1 (2%)
ANGIECTASIS	6 (12%)	6 (13%)	3 (7%)
#ADRENAL	(50)	(48)	(47)
NECROSIS, FOCAL			1 (2%)
METAMORPHOSIS FATTY	2 (4%)	1 (2%)	4 (9%)
HYPERPLASIA, FOCAL	1 (2%)		
ANGIECTASIS	2 (4%)	1 (2%)	3 (6%)
#ADRENAL CORTEX	(50)	(48)	(47)
HEMORRHAGE		1 (2%)	
CYTOPLASMIC VACUOLIZATION		1 (2%)	
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL			4 (9%)
#ADRENAL MEDULLA	(50)	(48)	(47)
HYPERPLASIA, FOCAL			1 (2%)
#THYROID	(48)	(46)	(41)
INFLAMMATION, CHRONIC		1 (2%)	
ATROPHY, NOS			1 (2%)
#THYROID FOLLICLE	(48)	(46)	(41)
ATROPHY, NOS	1 (2%)		
#PARATHYROID	(35)	(39)	(32)
CYST, NOS			1 (3%)
HYPERPLASIA, NOS		1 (3%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(48)	(48)
HYPERPLASIA, NOS	1 (2%)		2 (4%)
HYPERPLASIA, CYSTIC	1 (2%)	2 (4%)	3 (6%)
#PROSTATE	(22)	(35)	(32)
INFLAMMATION, ACUTE		1 (3%)	2 (6%)
INFLAMMATION, CHRONIC			2 (6%)
INFLAMMATION, GRANULOMATOUS			1 (3%)
HYPERPLASIA, CYSTIC			1 (3%)
*SEMINAL VESICLE	(50)	(48)	(48)
INFLAMMATION, CHRONIC			1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, PAPILLARY	1 (2%)		
HYPERPLASIA, CYSTIC			1 (2%)
#TESTIS	(50)	(47)	(48)
MINERALIZATION			1 (2%)
EDEMA, NOS			1 (2%)
ATROPHY, NOS	1 (2%)	2 (4%)	1 (2%)
HYPERPLASIA, INTERSTITIAL CELL	2 (4%)	2 (4%)	
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(48)	(47)
CONGESTION, NOS		1 (2%)	
HYPERPLASIA, NOS		1 (2%)	
#BRAIN	(50)	(48)	(47)
HEMORRHAGE		2 (4%)	
#CEREBELLUM	(50)	(48)	(47)
DEMYELINIZATION	3 (6%)		
#CEREBELLAR WHITE MAT	(50)	(48)	(47)
EXTRACELLULAR VACUOLE ALTERATION	1 (2%)		
SPECIAL SENSE ORGANS			
*EYE	(50)	(48)	(48)
MINERALIZATION			1 (2%)
CATARACT	1 (2%)	1 (2%)	2 (4%)
*EYE/CRYSTALLINE LENS	(50)	(48)	(48)
MINERALIZATION	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(48)	(48)
STEATITIS	1 (2%)	1 (2%)	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(48)	(48)
INFLAMMATION, CHRONIC		1 (2%)	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	1	1	
AUTO/NECROPSY/HISTO PERF	1		
AUTOLYSIS/NO NECROPSY		2	2

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

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS ADMINISTERED VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	45
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	50	45
INTEGUMENTARY SYSTEM			
*SKIN	(49)	(50)	(45)
INFLAMMATION, ACUTE FOCAL		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(45)
EMPHYSEMA, ALVEOLAR		1 (2%)	
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, FOCAL		1 (2%)	
INFLAMMATION, ACUTE		1 (2%)	
INFLAMMATION, CHRONIC	18 (37%)	15 (30%)	16 (36%)
INFLAMMATION, GRANULOMATOUS	5 (10%)	3 (6%)	6 (13%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	3 (6%)	2 (4%)
PERIVASCULAR CUFFING		1 (2%)	
HYPERPLASIA, ADENOMATOUS	1 (2%)	1 (2%)	
METAPLASIA, SQUAMOUS	1 (2%)		
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(50)	(45)
HYPOPLASIA, NOS	1 (2%)		
HYPERPLASIA, NOS		1 (2%)	1 (2%)
MYELOFIBROSIS			1 (2%)
HYPERPLASIA, RETICULUM CELL			1 (2%)
#SPLEEN	(49)	(50)	(45)
CONGESTION, NOS	1 (2%)		
HEMOSIDEROSIS	1 (2%)	1 (2%)	1 (2%)
LYMPHOID DEPLETION			1 (2%)
HYPERPLASIA, NODULAR	1 (2%)		
HYPERPLASIA, NOS		1 (2%)	

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, RETICULUM CELL			1 (2%)
HYPERPLASIA, LYMPHOID		1 (2%)	2 (4%)
#LYMPH NODE	(46)	(45)	(42)
HYPERPLASIA, LYMPHOID	1 (2%)		
#MANDIBULAR L. NODE	(46)	(45)	(42)
HYPERPLASIA, LYMPHOID		1 (2%)	
#LIVER	(49)	(50)	(45)
HEMATOPOIESIS		1 (2%)	1 (2%)
#PANCREAS	(48)	(50)	(45)
HYPERPLASIA, LYMPHOID			1 (2%)
#COLON	(43)	(43)	(42)
HYPERPLASIA, LYMPHOID		1 (2%)	1 (2%)
CIRCULATORY SYSTEM			
#HEART	(49)	(50)	(45)
THROMBOSIS, NOS		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)	2 (4%)	4 (9%)
FIBROSIS	3 (6%)	3 (6%)	3 (7%)
FIBROSIS, FOCAL	5 (10%)		
DEGENERATION, NOS	5 (10%)		1 (2%)
NECROSIS, NOS	3 (6%)	2 (4%)	2 (4%)
#AURICULAR APPENDAGE	(49)	(50)	(45)
THROMBOSIS, NOS		1 (2%)	1 (2%)
#LEFT AURICULAR APPEN	(49)	(50)	(45)
THROMBOSIS, NOS		1 (2%)	
#LEFT VENTRICLE	(49)	(50)	(45)
THROMBOSIS, NOS	1 (2%)		
#MYOCARDIUM	(49)	(50)	(45)
INFLAMMATION, INTERSTITIAL		1 (2%)	
*AORTA	(49)	(50)	(45)
INFLAMMATION, CHRONIC	1 (2%)		
#LIVER	(49)	(50)	(45)
THROMBOSIS, NOS			1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#ADRENAL	(48)	(50)	(43)
THROMBOSIS, NOS			1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(50)	(45)
SCLEROSIS			1 (2%)
ATROPHY, FOCAL			1 (2%)
#LIVER	(49)	(50)	(45)
MULTIPLE CYSTS		1 (2%)	
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
NECROSIS, FOCAL			1 (2%)
NECROSIS, DIFFUSE			2 (4%)
METAMORPHOSIS FATTY	3 (6%)		2 (4%)
BASOPHILIC CYTO CHANGE	2 (4%)		
FOCAL CELLULAR CHANGE	1 (2%)	1 (2%)	
HYPERPLASIA, NODULAR	5 (10%)	8 (16%)	2 (4%)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL	10 (20%)	18 (36%)	10 (22%)
#LIVER/CENTRILOBULAR	(49)	(50)	(45)
NECROSIS, COAGULATIVE			1 (2%)
#LIVER/PERIPORTAL	(49)	(50)	(45)
INFLAMMATION, CHRONIC		1 (2%)	
#LIVER/HEPATOCYTES	(49)	(50)	(45)
CYTOLOGIC ALTERATION, NOS	1 (2%)		
#BILE DUCT	(49)	(50)	(45)
HYPERPLASIA, NOS	2 (4%)		1 (2%)
#PANCREAS	(48)	(50)	(45)
METAMORPHOSIS FATTY	1 (2%)	1 (2%)	
ATROPHY, FOCAL			1 (2%)
#ESOPHAGUS	(45)	(49)	(42)
HYPERKERATOSIS			1 (2%)
#STOMACH	(47)	(48)	(42)
ULCER, NOS	1 (2%)		
DEGENERATION, CYSTIC		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
HYPERPLASIA, EPITHELIAL		1 (2%)	
#COLON	(43)	(43)	(42)
NEMATODIASIS	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(49)	(49)	(44)
MINERALIZATION		1 (2%)	
INFLAMMATION, NOS	1 (2%)		
INFLAMMATION, CHRONIC	3 (6%)	6 (12%)	9 (20%)
CALCINOSIS, NOS		1 (2%)	
#URINARY BLADDER	(45)	(45)	(41)
HYPERPLASIA, EPITHELIAL		3 (7%)	1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(49)	(43)
CYST, NOS	1 (2%)	1 (2%)	2 (5%)
MULTIPLE CYSTS	1 (2%)	2 (4%)	
EDEMA, NOS		2 (4%)	
EXTRACELLULAR VACUOLE ALTERATION	1 (2%)		
ATROPHY, FOCAL	1 (2%)		
HYPERPLASIA, NOS		1 (2%)	
ANGIECTASIS	15 (31%)	14 (29%)	9 (21%)
#ADRENAL	(48)	(50)	(43)
NECROSIS, DIFFUSE	1 (2%)		1 (2%)
METAMORPHOSIS FATTY	2 (4%)	3 (6%)	3 (7%)
ANGIECTASIS	1 (2%)	2 (4%)	
#ADRENAL CORTEX	(48)	(50)	(43)
METAMORPHOSIS FATTY	1 (2%)		
#ADRENAL MEDULLA	(48)	(50)	(43)
MINERALIZATION			1 (2%)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL			1 (2%)
#THYROID	(47)	(47)	(44)
INFLAMMATION, CHRONIC	1 (2%)		
ATROPHY, NOS			1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
GOITER	1 (2%)		
HYPERPLASIA, C-CELL	1 (2%)	1 (2%)	
#PARATHYROID	(33)	(39)	(35)
HYPERPLASIA, NOS			1 (3%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(45)
DILATATION/DUCTS	1 (2%)		
CYST, NOS	2 (4%)		1 (2%)
HYPERPLASIA, NOS	1 (2%)		2 (4%)
HYPERPLASIA, CYSTIC	5 (10%)	5 (10%)	3 (7%)
#UTERUS	(48)	(49)	(42)
DILATATION, NOS			1 (2%)
ATROPHY, DIFFUSE		1 (2%)	
HYPERPLASIA, STROMAL			2 (5%)
#CERVIX UTERI	(48)	(49)	(42)
HYPERPLASIA, STROMAL		1 (2%)	
#UTERUS/ENDOMETRIUM	(48)	(49)	(42)
CYST, NOS	3 (6%)	2 (4%)	1 (2%)
HYPERPLASIA, NOS			3 (7%)
HYPERPLASIA, CYSTIC	1 (2%)	5 (10%)	2 (5%)
#OVARY	(47)	(49)	(44)
CYST, NOS	1 (2%)		2 (5%)
FOLLICULAR CYST, NOS		3 (6%)	
MULTIPLE CYSTS		1 (2%)	
POLYCYSTIC OVARY		1 (2%)	
PAROVARIAN CYST			1 (2%)
HYPERTROPHY, NOS		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(49)	(50)	(45)
HYDROCEPHALUS, INTERNAL	1 (2%)		
CONGESTION, NOS		1 (2%)	
HEMORRHAGE	1 (2%)	1 (2%)	
#CEREBELLUM	(49)	(50)	(45)
DEMYELINIZATION	3 (6%)	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
#CEREBELLAR WHITE MAT	(49)	(50)	(45)
EXTRACELLULAR VACUOLE ALTERATION	8 (16%)	1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(49)	(50)	(45)
AGENESIS	1 (2%)		
CATARACT		2 (4%)	2 (4%)
*EYE/RETINA	(49)	(50)	(45)
ATROPHY, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*BONE	(49)	(50)	(45)
HEALED FRACTURE			1 (2%)
*COSTOCHONDRAL SYNCHO	(49)	(50)	(45)
NECROSIS, ASEPTIC		1 (2%)	
BODY CAVITIES			
*PERITONEUM	(49)	(50)	(45)
INFLAMMATION, FOCAL		1 (2%)	
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	1		1
AUTOLYSIS/NO NECROPSY	1		5

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

Appendix D

Summary of the Incidence of Nonneoplastic Lesions in Mice
Administered Vinylidene Chloride by Gavage

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE ADMINISTERED VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	47	47	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	46	47	50
INTEGUMENTARY SYSTEM			
*SKIN	(47)	(47)	(50)
INFLAMMATION, NOS		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(46)	(45)	(46)
HEMORRHAGE	1 (2%)	1 (2%)	
INFLAMMATION, NOS	1 (2%)		2 (4%)
INFLAMMATION, FOCAL		1 (2%)	
INFLAMMATION, DIFFUSE	1 (2%)		1 (2%)
INFLAMMATION, INTERSTITIAL		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
HEMOSIDEROSIS	1 (2%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
#SPLEEN	(45)	(45)	(48)
CONGESTION, NOS			1 (2%)
HYPERPLASIA, LYMPHOID	1 (2%)		3 (6%)
#LYMPH NODE	(28)	(38)	(43)
CONGESTION, NOS	1 (4%)	1 (3%)	
INFLAMMATION, NOS	1 (4%)		
NECROSIS, NOS	1 (4%)		
HYPERPLASIA, LYMPHOID			1 (2%)
#MESENTERIC L. NODE	(28)	(38)	(43)
CONGESTION, NOS	1 (4%)	2 (5%)	2 (5%)
HEMORRHAGE	2 (7%)	1 (3%)	
INFLAMMATION, NOS			1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NODULAR		1 (3%)	
HYPERPLASIA, LYMPHOID	1 (4%)		1 (2%)
#RENAL LYMPH NODE	(28)	(38)	(43)
INFLAMMATION, NOS			1 (2%)
#LIVER	(46)	(46)	(49)
HEMATOPOIESIS	1 (2%)		
#KIDNEY	(45)	(46)	(46)
HYPERPLASIA, LYMPHOID	1 (2%)	1 (2%)	
CIRCULATORY SYSTEM			
#HEART	(46)	(47)	(49)
FIBROSIS, FOCAL	1 (2%)		
#MYOCARDIUM	(46)	(47)	(49)
INFLAMMATION, FOCAL			1 (2%)
INFLAMMATION, INTERSTITIAL			1 (2%)
#LIVER	(46)	(46)	(49)
THROMBOSIS, NOS		1 (2%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(46)	(46)	(46)
INFLAMMATION, FOCAL			1 (2%)
#LIVER	(46)	(46)	(49)
HEMORRHAGE		1 (2%)	
INFLAMMATION, MULTIFOCAL	1 (2%)		3 (6%)
INFLAMMATION, DIFFUSE		2 (4%)	
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
NECROSIS, NOS			3 (6%)
NECROSIS, FOCAL		1 (2%)	3 (6%)
NECROSIS, DIFFUSE	1 (2%)	2 (4%)	1 (2%)
METAMORPHOSIS FATTY	4 (9%)	4 (9%)	5 (10%)
CLEAR-CELL CHANGE	2 (4%)		3 (6%)
CYTOLOGIC ALTERATION, NOS	3 (7%)		
#PANCREAS	(44)	(46)	(48)
DILATATION/DUCTS	1 (2%)	1 (2%)	1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
DEGENERATION, CYSTIC		1 (2%)	
NECROSIS, FOCAL			1 (2%)
#PANCREATIC ACINUS	(44)	(46)	(48)
NECROSIS, NOS			1 (2%)
ATROPHY, FOCAL	1 (2%)		
#STOMACH	(43)	(40)	(42)
INFLAMMATION, NOS			1 (2%)
PARASITISM			1 (2%)
METAPLASIA, SQUAMOUS	2 (5%)		
#JEJUNUM	(36)	(41)	(39)
PLASMA-CELL INFILTRATE			1 (3%)
URINARY SYSTEM			
#KIDNEY	(45)	(46)	(46)
INFLAMMATION, INTERSTITIAL		1 (2%)	
PYELONEPHRITIS, ACUTE	1 (2%)		
INFLAMMATION, CHRONIC		2 (4%)	
METAMORPHOSIS FATTY			1 (2%)
METAPLASIA, OSSEOUS			1 (2%)
#URINARY BLADDER	(38)	(42)	(44)
EDEMA, NOS		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(35)	(34)	(36)
CYST, NOS	1 (3%)		1 (3%)
#ADRENAL	(41)	(43)	(47)
CONGESTION, NOS	1 (2%)		
#ADRENAL CORTEX	(41)	(43)	(47)
HYPERPLASIA, FOCAL		1 (2%)	
#ADRENAL MEDULLA	(41)	(43)	(47)
HYPERPLASIA, NOS		1 (2%)	
#THYROID	(41)	(45)	(46)
ATROPHY, NOS		1 (2%)	

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PANCREATIC ISLETS	(44)	(46)	(48)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL			1 (2%)
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(47)	(47)	(50)
DEGENERATION, CYSTIC	1 (2%)		
METAPLASIA, SQUAMOUS	1 (2%)		
#PROSTATE	(36)	(40)	(40)
INFLAMMATION, ACUTE	1 (3%)		
*SEMINAL VESICLE	(47)	(47)	(50)
DILATATION, NOS		1 (2%)	1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(47)	(47)	(50)
CYST, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*STERNUM	(47)	(47)	(50)
EXOSTOSIS	1 (2%)		
BODY CAVITIES			
*ABDOMINAL CAVITY	(47)	(47)	(50)
NECROSIS, FAT			1 (2%)
*EPICARDIUM	(47)	(47)	(50)
INFLAMMATION, FOCAL		1 (2%)	
FIBROSIS, FOCAL	1 (2%)		
ALL OTHER SYSTEMS			
NONE			

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	10	14	6
AUTO/NECROPSY/NO HISTO	1		
AUTOLYSIS/NO NECROPSY	3	3	

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

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE ADMINISTERED VINYLIDENE CHLORIDE BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	48	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	48	49	50
INTEGUMENTARY SYSTEM			
*SKIN	(48)	(49)	(50)
ULCER, NOS		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG/BRONCHUS	(48)	(45)	(48)
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
#LUNG	(48)	(45)	(48)
INFLAMMATION, FOCAL		1 (2%)	
INFLAMMATION, CHRONIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(48)	(49)	(50)
HYPERPLASIA, LYMPHOID		1 (2%)	
#SPLEEN	(46)	(47)	(46)
CONGESTION, NOS		2 (4%)	1 (2%)
INFLAMMATION, NOS			1 (2%)
NECROSIS, DIFFUSE			1 (2%)
HYPERPLASIA, LYMPHOID	2 (4%)	5 (11%)	2 (4%)
#MESENTERIC L. NODE	(29)	(36)	(42)
INFLAMMATION, NOS	1 (3%)		1 (2%)
#LIVER	(47)	(49)	(49)
HEMATOPOIESIS			1 (2%)
#KIDNEY	(46)	(49)	(50)
HYPERPLASIA, LYMPHOID	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
#URINARY BLADDER	(40)	(45)	(45)
HYPERPLASIA, LYMPHOID	1 (3%)		
#THYMUS			(4)
NECROSIS, NOS			1 (25%)
CIRCULATORY SYSTEM			
#LUNG	(48)	(45)	(48)
EMBOLUS, SEPTIC		1 (2%)	
#MYOCARDIUM	(48)	(48)	(48)
INFECTION, BACTERIAL		1 (2%)	
#HEPATIC SINUSOID	(47)	(49)	(49)
CONGESTION, NOS	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(47)	(49)	(49)
HEMORRHAGE	1 (2%)		
INFLAMMATION, NOS			1 (2%)
INFLAMMATION, FOCAL			1 (2%)
INFLAMMATION, MULTIFOCAL		3 (6%)	
INFLAMMATION, GRANULOMATOUS		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	1 (2%)	
NECROSIS, FOCAL		2 (4%)	
NECROSIS, DIFFUSE		2 (4%)	1 (2%)
METAMORPHOSIS FATTY	5 (11%)	2 (4%)	3 (6%)
BASOPHILIC CYTO CHANGE	1 (2%)		
#BILE DUCT	(47)	(49)	(49)
INFLAMMATION, FOCAL	2 (4%)		
INFLAMMATION, CHRONIC			1 (2%)
#PANCREAS	(47)	(45)	(49)
DILATATION/DUCTS	1 (2%)	1 (2%)	2 (4%)
ATROPHY, NOS		2 (4%)	
#PANCREATIC ACINUS	(47)	(45)	(49)
ATROPHY, NOS			1 (2%)
#STOMACH	(43)	(43)	(42)
HYPERKERATOSIS		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
URINARY SYSTEM			
#KIDNEY	(46)	(49)	(50)
HYDRONEPHROSIS	1 (2%)		
INFLAMMATION, CHRONIC		1 (2%)	1 (2%)
METAPLASIA, OSSEOUS	1 (2%)		
#KIDNEY/CORTEX	(46)	(49)	(50)
ATROPHY, FOCAL	1 (2%)		
#KIDNEY/GLOMERULUS	(46)	(49)	(50)
AMYLOIDOSIS		1 (2%)	
#URINARY BLADDER	(40)	(45)	(45)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(31)	(32)	(42)
CONGESTION, NOS			1 (2%)
HYPERPLASIA, NOS	1 (3%)		
ANGIECTASIS	1 (3%)	1 (3%)	1 (2%)
#ADRENAL	(42)	(44)	(50)
NECROSIS, NOS		1 (2%)	
#THYROID	(41)	(45)	(43)
FOLLICULAR CYST, NOS			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(48)	(49)	(50)
HYPERPLASIA, CYSTIC	1 (2%)	2 (4%)	2 (4%)
#UTERUS	(46)	(45)	(47)
HYDROMETRA	1 (2%)	4 (9%)	
#UTERUS/ENDOMETRIUM	(46)	(45)	(47)
HYPERPLASIA, NOS			1 (2%)
HYPERPLASIA, CYSTIC	17 (37%)	16 (36%)	28 (60%)
#OVARY	(41)	(44)	(45)
CYST, NOS	2 (5%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOLLICULAR CYST, NOS	5 (12%)	2 (5%)	2 (4%)
MULTIPLE CYSTS		1 (2%)	
INFLAMMATION, NOS		1 (2%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(48)	(49)	(50)
FIBROSIS, FOCAL		1 (2%)	
ATROPHY, NOS		1 (2%)	
BODY CAVITIES			
*ABDOMINAL CAVITY	(48)	(49)	(50)
NECROSIS, FAT			1 (2%)
ALL OTHER SYSTEMS			
ADIPOSE TISSUE			
INFLAMMATION, GRANULOMATOUS		1	
NECROSIS, NOS		1	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	6	4	6
AUTOLYSIS/NO NECROPSY	2	1	

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

Appendix E

Analysis of Vinylidene Chloride
(Lot No. UTLX83844)
Midwest Research Institute

Appendix E

Analysis of Vinylidene Chloride (Lot No. UTLX83844)

A. BOILING POINT

Determined	Literature Values
b.p.: 30.9°C at 735.6mm	b.p.: 31.56°C at 760.00 mm (Hildenbrand et al., 1959)

B. DENSITY

Determined	Literature Values
d_{26}^{27}: 1.2033	d_{4}^{20}: 1.21293 (Stecher, 1968)
	d^{27}: 1.189 (Gallant, 1966)

C. REFRACTIVE INDEX

Determined	Literature Values
n_{D}^{20}: 1.4248	n_{D}^{20}: 1.4249 (Stecher, 1968)

D. VAPOR-PHASE CHROMATOGRAPHY

1. IMPURITY DETECTION

(a) SYSTEM 1

Instrument: Tracor MT 220
Detection: Flame ionization
Column: Chromosorb 102, 100/120; 1.8 m x 4 mm, glass
Inlet temperature: 200°C
Detector temperature: 275°C
Oven temperature program: 100°C, 5 min.; 100°-200°C at 10°C/min.
Compound concentration: Neat liquid
Results: Major peak and two impurities

Peak	Retention Time (min.)	Retention Time (relative to vinylidene chloride)	Area (relative to vinylidene chloride)
1	10.2	1.0	100
2	12.0	1.2	0.3
3	13.2	1.3	0.01

(a) SYSTEM 2

Instrument: Tracor MT 220
Detection: Flame ionization
Column: 10% Carbowax 20 M on 80/100 Chromosorb W AW
Inlet temperature: 200°C
Detector temperature: 275°C
Oven temperature program: 50°C, 10 min.; 50°-200°C at 10°C/min.
Compound concentration: Neat liquid
Results: Major peak and two impurities

Peak	Retention Time (min.)	Retention Time (relative to vinylidene chloride)	Area (relative to vinylidene chloride)
1	0.6	1.0	100
2	1.3	2.0	0.4
3	2.9	4.6	0.02

2. IDENTIFICATION AND QUANTIFICATION OF IMPURITIES

(a) SYSTEM 1 (vinyl chloride)

Instrument: Varian Aerograph 2400
Detection: Flame ionization
Column: Chromosorb 102, 60/80, 1.8 m x 2 mm I.D., stainless steel
Inlet temperature: 200°C
Detector temperature: 265°C
Oven temperature program: 70°C, isothermal
Compound concentration: Neat liquid

A gas syringe was used to take standard amounts of vinyl chloride at a concentration of 0.015 μg/ml from a vinyl chloride permeation tube flushed with nitrogen at a measured flow rate. Injections were made of 0.3, 0.4, and 0.5 ml aliquots from the permeation tube. Vinyl chloride had a retention time of 2.5±0.1 minutes and a response of 340±10 $cm^2/\mu g$. A 5 μl (4 mg) sample of vinylidene chloride was injected under the same conditions. This had a peak with a retention time of 2.3 minutes and an area of 5.1 cm^2.

Conclusion: The sample contains less than 0.01% vinyl chloride.

(b) SYSTEM 2 (1,1-dichlorethane, 1,2-dichloroethane, and trichloroethylene)

Instrument: Tracor MT 220
Detection: Flame ionization
Inlet temperature: 200°C

Detector temperature: 275°C
Oven temperature program: 125°C, 15 min.; 125°-150°C at 10°C/min.
Compound concentration: Neat liquid

Standards (1.6 μl) were injected containing 1,1 dichloroethane (0.1% v/v in 2,2,4-trimethylpentane), 1,2-dichloroethane (0.04% v/v in pentane), and trichloroethylene (0.01% v/v in pentane). The sample of vinylidene chloride injected under the same conditions contained no peaks at comparable retention times.

Conclusion: The sample contained less than 0.1% of 1,1-dichloroethane, 0.04% of 1,2-dichloroethane, and 0.01% trichloroethylene.

(c) SYSTEM 3 (Trans-dichloroethylene)

Instrument: Tracor MT 220
Detection: Flame ionization
Column: 10% Carbowax 20 M on 80/100 Chromosorb W AW
Inlet temperature: 200°C
Detector temperature: 265°C
Oven temperature program: 50°C, isothermal
Compound concentration: 10% v/v in o-dichlorobenzene
Results: Major peak and one impurity

Peak	Retention Time (min.)	Retention Time (relative to vinylidene chloride)	Area (relative to vinylidene chloride)
1	0.6	1.0	100
2	1.5	2.3	0.1

Peak No. 2 was enhanced when a small amount of trans-dichloroethylene was added to the sample. This peak was quantitated against a standard solution of trans-dichloroethylene (0.01% v/v in pentane).

Conclusion: Concentration of trans-dichloroethylene in the sample: 0.1%.

(d) SYSTEM 4 (monomethylether of hydroquinone)

Instrument: Tracor MT 220
Detection: Flame ionization
Column: 10% Carbowax 20 M on 80/100 Chromosorb W AW
Inlet temperature: 200°C
Detector temperature: 265°C
Oven temperature program: 200°C, isothermal
Compound concentration: 10% v/v in pentane

Results: Major peak was under the solvent front.
A minor peak was observed at 4.1 minutes, the same retention time as p-methoxyphenol (MEHQ, monomethylether of hydroquine). This peak was enhanced when spiked with MEHQ. The minor peak was quantitated against a p-methoxyphenol standard (0.007% in pentane).

Conclusion: Concentration of p-methoxyphenol (MEHQ) in the sample: 0.05%.

E. VAPOR-PHASE CHROMATOGRAPHY/MASS SPECTROMETRY

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

1. SYSTEM 1: IDENTIFICATION OF SAMPLE IMPURITIES

Vapor-phase chromatograph column: Chromosorb 102, 100/120, 1.8 m x 2 mm I.D., glass
Inlet temperature: 165°C
Oven temperature program: 16 min. at 100°C, then 100°-130°C at 10°C/min.
Results: Two minor peaks were observed in addition to the major peak. Chromatographic and mass frament data are contained in Tables E1 and E2.

TABLE E1. CHROMATOGRAPHIC DATA

Peak	Retention Time (min.)	Retention Time (Relative to Vinylidene Chloride)
1	6.0	1.0
2	11.2	1.9
3	16.4	2.7

TABLE E2. MASS FRAGMENTATION DATA

Peak	Mass	Percent of Base Peak	Percent of Base Peak (Normalized on Highest Peak)
2	61	100	100
	96	97	97
	98	73	73
	26	24	24
	63	52	52
	60	24	24
	25	6	6
	35	5	5
3	61	23	100
	96	13	56
	98	16	68
	26	4	18
	63	6	27
	60	3	14
	35	5	20
	25	< 1	< 4

Conclusion: Comparison with literature spectra (Eight Peak Index, 1970) indicated that the two impurity peaks had fragmentation peaks that matched in mass and intensity with those of the cis and trans isomers of dichloroethylene. Table E3 contains the literature spectra for these two compounds.

TABLE E3. LITERATURE SPECTRA OF THE DICHLOROETHYLENES
(Eight Peak Index, 1970)

	Mass	Percent of Base Peak
trans-dichloroethylene	61	100
	96	62
	98	40
	26	36
	63	32
	60	27
	25	17
	35	12
cis-dichloroethylene	61	100
	96	65
	98	41
	26	33
	63	32
	60	22
	35	20
	25	16

2. SYSTEM 2: DETECTION OF 1,1- AND 1,2-DICHLOROETHANE AND TRICHLOROETHYLENE IN THE VINYLIDENE CHLORIDE SAMPLE

The temperature program detailed in Section E1 was used. A standard was injected containing 0.1% v/v 1,1-dichloroethane, 0.04% v/v 1,2-dichloroethane, and 0.1% v/v trichloroethylene in pentane. Strong ion current monitor peaks were observed for each compound in the standard. The vinylidene sample injected under the same conditions contained no observable peaks at the same retention times. In addition, a computer search was conducted on the sample spectra for two ions characteristic of the mass spectra of each of the three possible impurities: 83, 85 for 1,1-dichloroethane; 62, 64 for 1,2-dichloroethane; and 130, 132 for trichloroethylene. No peaks in the sample spectra were observed with masses of 130, 132. Mass peaks of 62, 64, 83, and 85 with small intensities were observed only at a retention time of 6 minutes, which corresponds to vinylidene chloride. The retention times for the 1,1- and 1,2-dichloroethanes were 22 and 26.4 minutes, respectively.

Conclusion: The sample contains less than 0.1% 1,1-dichloroethane, less than 0.04% 1,2-dichloroethane, and less than 0.1% trichloroethylene.

F. SPECTRAL DATA

1. INFRARED

LITERATURE VALUES

Instrument: Beckman IR-12
Cell: 10 cm gas cell with sodium chloride windows
Results: See Figure 5

Consistent with literature spectrum (Sadtler Standard Spectra)

2. ULTRAVIOLET/VISIBLE

Instrument: Cary 118

λ max (nm)	ε
301	0.7
293.5	0.9
290	0.9
287.5(s)	0.9
284.5(s)	0.8

Solvent: n-Hexane
No absorbance between 350-800 nm at concentration of 10% v/v.

No literature values found

3. NUCLEAR MAGNETIC RESONANCE

Instrument: Varian HA-100
Solvent: Neat with added tetramethylsilane
Assignments: (see Figure 6)
(a) s, δ, 5.49 ppm
Integration Ratios: (a) 2.00

Consistent with literature spectrum (Sadtler Standard Spectra)

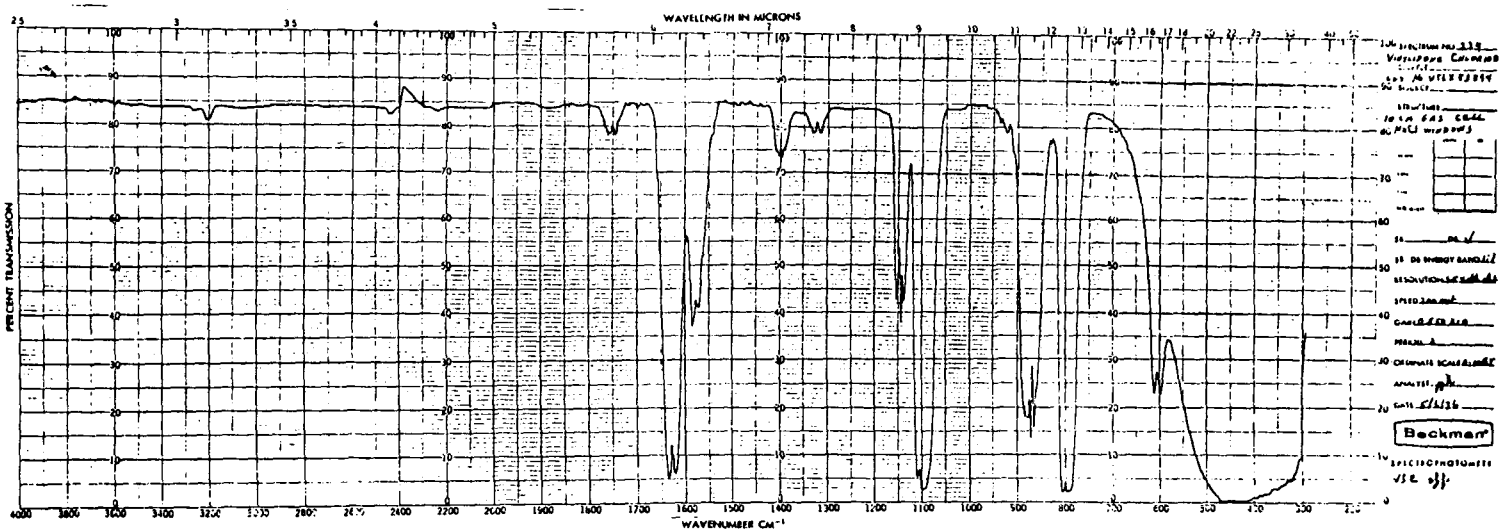

Figure 5. Infrared Absorption Spectrum of Vinylidene Chloride (Lot No. UTLX 83844)

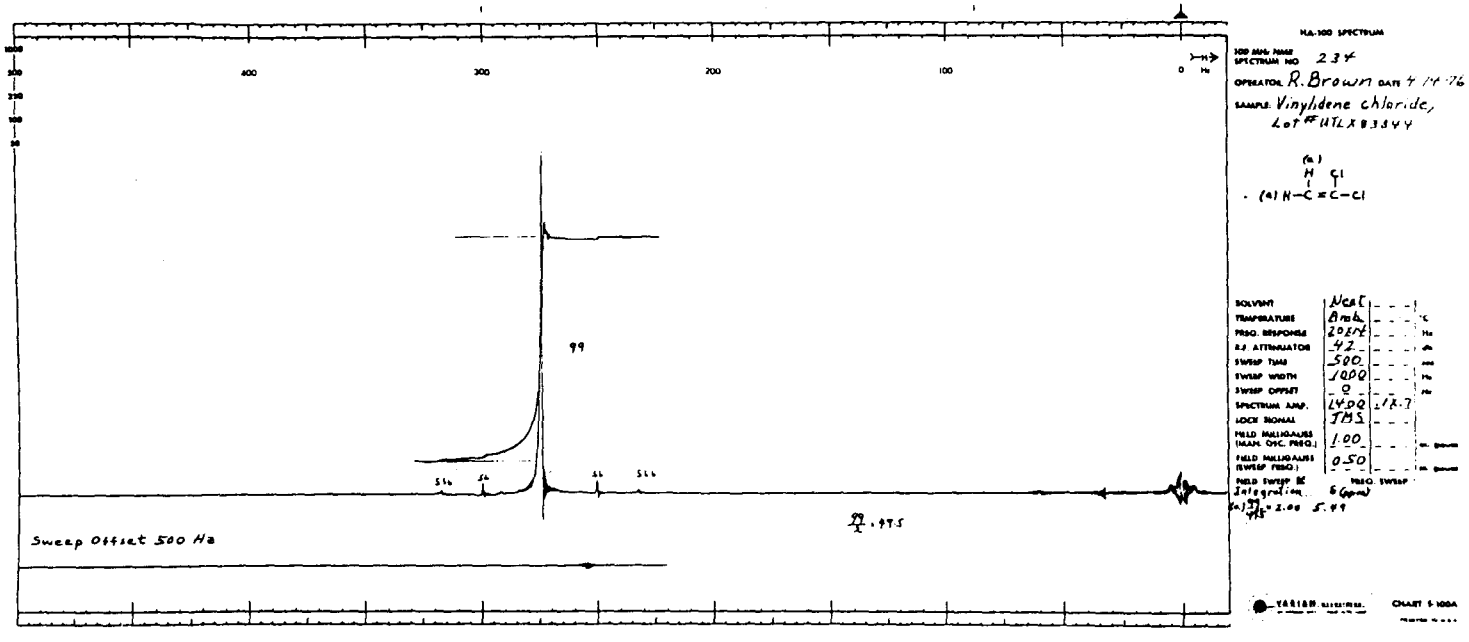

Figure 6. Nuclear Magnetic Resonance Spectrum of Vinylidene Chloride (Lot No. UTLX 83844)

Appendix F

Analysis of Vinylidene Chloride
(Lot No. V83848)
Gulf South Research Institute

APPENDIX F

Analysis of Vinylidene Chloride (Lot No. V83848)
Gulf South Research Institute

A. VAPOR-PHASE CHROMATOGRAPHY

1. Analysis: Volatiles present in addition to vinylidene chloride
   Instrument: MT-220
   Detector: Flame ionization
   Column: 10% Carbowax 20 M on 80/100 Chromosorb W AW
   Inlet temperature: 250°C
   Detector temperature: 250°C
   Oven temperature: 50°C
   Result: Major peak and one impurity

Peak	Retention Time (min.)	Retention Time (relative to vinylidene chloride)	Area (relative to vinylidene chloride)
1	2.25	1.00	100
2	4.15	1.84	0.9

A standard injection of a benzene solution containing 11.5 $\mu g/\mu l$ trans-dichloroethylene gave a peak at a retention time of 4.19 minutes. Addition of trans-dichloroethylene to the sample enhanced the peak at retention time of 4.15 minutes. The peak in the vinylidene chloride was quantitated against the standard injection of trans-dichloroethylene.

Conclusions: Trans-dichloroethylene was present in the sample of vinylidene chloride in a concentration of 0.154% by weight.

2. Analysis: Monomethylether of Hydroquinone (MEHQ Stabilizer)
   Instrument: MT-220
   Detector: Flame ionization
   Column: 10% Carbowax 20 M on 80/100 Chromosorb W AW, 9' x 1/4" o.d.: glass column
   Inlet temperature: 250°C
   Detector temperature: 250°C
   Oven temperature: 200°C isothermal
   Compound concentration: 3.57 $\mu g/\mu l$ in benzene

Results: The MEHQ stabilizer under these conditions had a retention time of 16.63 minutes. Liquid injections of vinylidene chloride contained a peak at 16.58 minutes.

Conclusions: The vinylidene chloride contained MEHQ in a concentration of 0.02% by weight.

B. SPECTRAL DATA

1. Infrared

Instrument
Cell: 10 cm gas cell
KBr windows
Results: see Figure 7

Consistent with the previous lot.

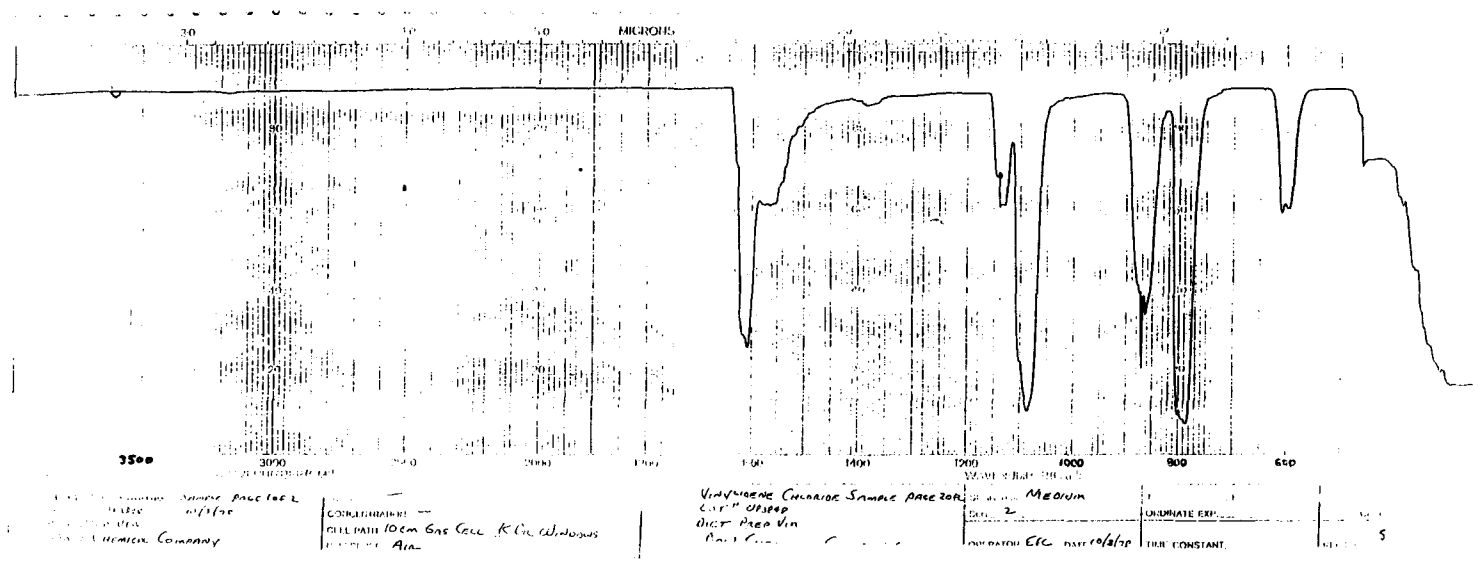

Figure 7. Infrared Absorption Spectrum of Vinylidene Chloride (Lot No. V83848)

Appendix G

Analysis of Vinylidene Chloride in Corn Oil for Stability
(Midwest Research Institute)

APPENDIX G

Analysis of Vinylidene Chloride in Corn Oil for Stability

SEVEN-DAY ROOM TEMPERATURE STABILITY STUDY OF CORN OIL SOLUTION

A. SAMPLE PREPARATION

A 1% (w/v) solution of vinylidene chloride in corn oil was prepared, for each day of the study, as follows: 10 ml of corn oil was transferred into a 50 ml Hypo-Vial, the vial was sealed, and a weighted amount (approximately 95 mg) of vinylidene chloride was added (vial weighed before and after addition) via a 100 μl syringe. The samples were shaken and then stored at room temperature (in the absence of light and under N_2) from 1 to 7 days.

B. EXTRACTION AND ANALYSIS

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

Instrument: Bendix 2500
Column: Chromosorb 102, 100/120 mesh, glass, 1.8 x 4 mm I.D.
Detection: Flame ionization
Oven temperature: 150°C, isothermal
Inlet temperature: 250°C
Detector temperature: 295°C
Retention time of test compound: 4.55 minutes

C. RESULTS

End of Day	Average % Compound (a)
1	0.99 ± 0.05
2	1.00 ± 0.05
3	1.01 ± 0.05
4	1.04 ± 0.05
5	1.06 ± 0.05
6	1.04 ± 0.05
7	1.02 ± 0.05

(a) Corrected for spiked recovery value of 72.0%.

D. CONCLUSION

Vinylidene chloride mixed in corn oil is stable for 7 days at room temperature in the dark under a nitrogen atmosphere.

Appendix H

Analysis of Vinylidene Chloride in Corn Oil (Gulf South Research Institute)

APPENDIX H

ANALYSIS OF VINYLIDENE CHLORIDE IN CORN OIL

A 1.0 μl sample of corn oil containing vinylidene chloride was diluted with n-butanol to a final volume of 10 ml. After shaking thoroughly, 4.0 μl aliquots for gas chromatography injections were used.

Reference standards were prepared by diluting pure vinylidene chloride (1.218 g/ml) by a factor of 1:2000 with n-butanol. This dilution yielded a concentration of 0.609 μg/μl, which was injected in 4 μl aliquots.

Instrument Parameters

Instrument: MT 220

Column: Carbowax 20 M

Temperatures: Detector: 285°C
Inlet: 245°C
Column: 50°C for 3 minutes then to 120° at 30°C/minute

Carrier gas: N_2

Flow: ~ 30 ml/min.

Retention time of vinylidene chloride: 1.5 minutes

Results: See Table H1.

Table H1. Analyses of Corn Oil Mixtures

Date Mixed (a)	Date Used (Week of)	Concentration (b) of Vinylidene Chloride for target concentration of 1.0 mg/ml	0.2 mg/ml
6/21/77	6/22/77	1.02	0.188
7/13/77	7/13/77	0.96	
8/27/77	8/27/77	0.99	
1/03/78	1/03/78	0.92	
3/29/78	3/29/78	0.90	
5/11/78	5/11/78	0.91	
7/13/78	7/13/78	1.0	
8/17/78	8/17/78	0.97	
10/20/78	10/20/78	1.02	
3/22/79	3/22/79	1.06	
Mean (mg/ml)		0.97	
Standard deviation		0.053	
Coefficient of variation		5.6	
Range (mg/ml)		0.90-1.06	
Number of samples		10	

a) June 22, 1977 was the start date for mice and for rats.
b) The data presented are the average of duplicate analyses.

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