NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 272

TOXICOLOGY AND CARCINOGENESIS STUDIES OF PROPYLENE

(CAS NO. 115-07-1)

IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of 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 made up of four charter DHHS agencies: the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES OF PROPYLENE

(CAS NO. 115-07-1)

IN F344/N RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

NATIONAL TOXICOLOGY P[illegible]GRAM
P.O. Box 12233
Research Triangle Park, N[illegible]709

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U.S. DEPARTMENT OF HEALTH AND [illegible]IAN SERVICES
Public Health Servic[illegible]
National Institutes of He[illegible]

NOTE TO THE READER

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for testing in the NTP Carcinogenesis Program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical has the potential for hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

Five categories of interpretative conclusions were adopted for use in June 1983 in the Technical Reports series to specifically emphasize consistency and the concept of actual evidence of carcinogenicity. For each definitive study result (male rats, female rats, male mice, female mice), one of the following quintet will be selected to describe the findings. These categories refer to the strength of the experimental evidence and not to either potency or mechanism.

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

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

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

This study was initiated by the National Cancer Institute's Carcinogenesis Bioassay Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program. The studies described in this Technical Report have been conducted in compliance with NTP chemical health and safety requirements and must meet or exceed all applicable Federal, state, and local health and safety regulations. All NTP toxicology and carcinogenesis studies are subjected to a data audit before being presented for peer review.

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to identify any mistakes so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP. Comments and questions about the National Toxicology Program Technical Reports on Toxicology and Carcinogenesis Studies should be directed to Dr. J.E. Huff, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709 (919-541-3780).

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

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PROPYLENE

CAS NO. 115-07-1

C_3H_6 Mol. Wt. 42.08

ABSTRACT

Toxicology and carcinogenesis studies of propylene (greater than 99% pure) were conducted by exposing groups of 50 F344/N rats and 49 or 50 B6C3F$_1$ mice of each sex to propylene in air by inhalation at concentrations of 5,000 or 10,000 ppm, 6 hours per day, 5 days per week, for 103 weeks. Other groups of 50 rats and 50 mice of each sex in chambers received air only on the same schedule and served as chamber controls. The highest concentration of propylene that was considered safe for these studies was 10,000 ppm because of the risk of explosion that can occur at higher concentrations.

The survival of exposed and control rats and mice was comparable. Throughout most of the studies, mean body weights of exposed male and female rats were slightly lower (0%-5%) than those of the controls, but the decrements were not concentration related. After week 59 of the study, mean body weights of 10,000-ppm male mice were usually slightly lower (5%) than those of the controls, whereas those in other exposed groups of male and female mice were generally comparable with those of the controls. No compound-related adverse clinical signs were observed in either species.

An increased incidence of squamous metaplasia of the nasal cavity was observed in female rats exposed at the 5,000-ppm and 10,000-ppm concentrations (control, 0/49; low, 15/50; high, 6/50) and in male rats exposed at 5,000 ppm (2/50; 19/50; 7/50). Epithelial hyperplasia of the nasal cavity was increased in female rats exposed at the 10,000-ppm concentration (0/49; 4/50; 9/50); the incidences in male rats were 2/50, 2/50, and 5/50. Inflammation of the nasal cavity, characterized by an influx of lymphocytes, macrophages, and granulocytes into the submucosa and by granulocytes into the lumen, occurred at increased incidences in low concentration and high concentration male rats and in high concentration female rats. Chronic focal inflammation of the kidneys occurred at an increased incidence in low concentration and high concentration mice of each sex.

Hemangiosarcomas were found in one low dose male mouse (liver), two high dose male mice (spleen), and three high dose female mice (subcutis, spleen, and uterus). Hemangiomas were found in one low dose and in one high dose female mouse (liver). Vascular tumors were not found in control mice of either sex. The low incidences of vascular tumors and their occurrence in a variety of organs suggest that they are not related to administration of propylene.

The occurrence of uterine endometrial stromal polyps in female mice showed a positive trend ($P < 0.05$; 0/47; 0/47; 3/48); the incidence in the 10,000-ppm group was not significantly greater than that in the concurrent control group, but the incidence was higher than the mean historical control rate (22/2,411, 0.9%) and was within the range (0%-6%) observed in studies throughout the Carcinogenesis Program. The occurrence of endometrial stromal polyps in three high concentration female mice was not considered to be clearly related to exposure to propylene.

The incidence of male mice with alveolar/bronchiolar adenomas or carcinomas (combined) occurred with a negative trend ($P<0.05$; 16/50; 4/49; 7/50), and the reduced incidences in both exposed groups were less than ($P<0.05$) that in the control group. The control incidence of these tumors in an inhalation study conducted concurrently at the same laboratory was similar (15/50), suggesting a possible exposure-related decrease. The biologic significance of this decrease in male mice is difficult to assess; the incidences seen in these control and exposed animals are within the range of incidences (2%-34%; mean, 16.7%) observed in control male mice in other studies throughout the Carcinogenesis Program.

An audit of the experimental data was conducted for these carcinogenesis studies on propylene. No data discrepancies were found that influenced the final interpretations.

Under the conditions of these studies, there was *no evidence of carcinogenicity** in male and female F344/N rats or in male and female $B6C3F_1$ mice exposed to propylene by inhalation at concentrations of 5,000 or 10,000 ppm for 103 weeks. In the nasal cavity, propylene induced squamous metaplasia of the respiratory epithelium in male and female rats and epithelial hyperplasia in female rats.

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

CONTRIBUTORS

This NTP Technical Report on the Toxicology and Carcinogenesis Studies of Propylene is based on 2-year studies that began in October 1979 and ended in September 1981 at Battelle Pacific Northwest Laboratories. The 14-day and 14-week studies of propylene were conducted at Industrial Biotest Laboratories, Inc. (Northbrook, IL), in 1977.

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PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the draft Technical Report on propylene on June 29, 1983, are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity Panel members have five major responsibilities: (a) to ascertain that all relevant literature data have been adequately cited and interpreted, (b) to determine if the design and conditions of the NTP studies were appropriate, (c) to ensure that the Technical Report presents the experimental results and conclusions fully and clearly, (d) to judge the significance of the experimental results by scientific criteria, and (e) to assess the evaluation of the evidence of carcinogenicity and other observed toxic responses.

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SUMMARY OF PEER REVIEW COMMENTS ON THE CARCINOGENESIS STUDIES OF PROPYLENE

On June 29, 1983, the draft Technical Report on propylene received peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina. Members of the subcommittee were: Drs. Jerry Hook (Chairperson), Curtis Harper, and James Swenberg. Members of the Panel were: Mr. Louis Beliczky, and Drs. Devra Davis, Robert Elashoff, Seymour Friess, Michael Holland, Robert Scala, Tom Slaga, John Van Ryzin, Stan Vesselinovitch, and Mary Vore. Drs. Vesselinovitch and Vore were unable to attend the meeting.

Dr. Swenberg, a principal reviewer for the Technical Report on the carcinogenesis studies of propylene, agreed with the conclusions as written. He mentioned some changes regarding pathology descriptions and noted a few variations in inhalation exposures during the first year.

As a second principal reviewer, Dr. Scala agreed with the conclusions. He stated that because propylene is an explosive chemical more attention could have been given to safety considerations. He also felt that more discussion of toxicity, as contrasted with the lack of carcinogenicity, would have enhanced the report. Dr. J. Quest, NTP, indicated that toxicity findings were generally not observed in prechronic or long-term studies.

As a third principal reviewer, Mr. Beliczky also agreed with the conclusions and wondered whether the increased incidence of focal inflammation of the kidneys in mice might have been related to the use of propylene oxide in other studies in the same room and/or to biotransformation of propylene to the epoxide. Dr. Huff, NTP, stated that cross-contamination was highly unlikely, since chemical-specific chambers were used. Dr. Scala said there were ongoing studies using hemoglobin alkylation as a marker in humans exposed to propylene and propylene oxide. Dr. Quest said that the renal effects were increased in exposed groups but the biologic importance was unknown. Dr. Davis asked whether behavioral activities had been evaluated in view of the possible anesthetic effects at the high concentration. Dr. Quest replied that none was recorded or specifically requested.

Dr. Swenberg moved that the Technical Report on the carcinogenesis studies of propylene be accepted with the changes discussed. Dr. Scala seconded the motion, and the Technical Report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

Chemical Identification
Use
Production
Environmental Occurrence
Human Exposure
Toxicity
Carcinogenicity

I. INTRODUCTION

$H_2C = CH - CH_3$

PROPYLENE

CAS NO. 115-07-1

C_3H_6 Mol. Wt. 42.08

Chemical Identification

Propylene (propene, methylethylene, methylethene), an olefinic hydrocarbon, is a colorless gas under normal atmospheric conditions. It is produced commercially in industrial refinery operations that are involved in the generation of other hydrocarbon materials such as ethylene or gasoline. The available propylene is recovered from refinery off-gases by distillation procedures (Kirk-Othmer, 1978; MCA, 1974).

Use

Propylene is used as a starting material in the production of polypropylene plastics and various other chemicals, including acrylonitrile, isopropyl alcohol, propylene oxide, butyraldehyde, cumene, dodecane, nonene, and allyl chloride (IARC, 1979). The major derivatives are polypropylene (25%), acrylonitrile (15%), isopropyl alcohol (10%), and propylene oxide (10%) (Chem. & Eng. News, 1981). It is also a valuable feedstock chemical for the production of gasoline (Clayton and Clayton, 1982). Other miscellaneous applications include use as a starting material for polymerization reactions to form vinyl chloride copolymers and low-molecular-weight homopolymers that are used as additives in lubricating oils and in the manufacture of hydroquinone (IARC, 1979). The chemical is also used as an aerosol propellant or component (Clayton and Clayton, 1982). Propylene was studied for use as an anesthetic agent but was found to cause depression of heart function at the high concentrations required (60% or more by volume) (Price, 1975). The major end uses of propylene are in the production of fabricated plastics (50%) and fibers (15%) (Chem. & Eng. News, 1981).

Production

Large amounts of propylene are produced in the United States. In 1982, propylene ranked 14th in volume of all chemicals produced domestically, with a production of 12.30 billion pounds (Webber, 1983). Little propylene is exported; approximately 0.5 billion pounds were imported in 1981 (Chem. & Eng. News, 1981).

Environmental Occurrence

Propylene has been detected in the atmosphere of metropolitan areas (2.6-23.3 ppb) and rural areas (0.007-4.8 ppb) of the United States and Europe (Altshuller et al., 1971; Westberg et al., 1974; Landen and Perez, 1974; Cox et al., 1976; Leonard et al., 1976; Mayrsohn et al., 1977; Altwicker et al., 1980). Studies suggest that the higher levels found over metropolitan areas may be produced by engine exhaust emissions and industrial activity. Propylene has been detected in exhaust gases from diesel engines (1.0-6.7 ppm), gasoline engines (44.5 ppm), and jet engines (0.01-143.4 ppm) (Landen and Perez, 1974; Katzman and Libby, 1975). An atmospheric study conducted over Los Angeles found propylene levels in air to be highest during times of peak traffic activity (Altshuller et al., 1971). The contribution from industrial activity is suggested by a comparison of atmospheric concentrations over urban areas located near industrial complexes (10-100 ppb) and those over non-industrial and more rural areas (0.1-4.8 ppb) (Inoue et al., 1975; Cox et al., 1976). Propylene has also been shown to be released into the atmosphere as a volatile metabolite from germinating seeds of beans, corn, cotton, and peas (Vancura and Stotzky, 1976); and it has been found in the combustion products of

burning pine (50 ppm) (O'Mara, 1974). Propylene has been detected in samples of surface water from all the major oceans (0.1-16 nl/liter) (Swinnerton and Lamontagne, 1974). The presence of propylene in sea water appears to be related to biologic processes or photochemical reactions on organic matter.

Human Exposure

No threshold limit value for propylene has been established for the workplace (ACGIH, 1980). Its primary hazard in the workplace is flammability (flammable range, 2.0%-11.1% by volume in air) (Kirk-Othmer, 1968). No adverse effects have been reported in humans exposed at concentrations up to 20% of the lower flammability limit (4,000 ppm). Inhalation of propylene at higher concentrations may cause incoordination, drowsiness, an inability to concentrate, unconsciousness, and asphyxiation by exclusion of oxygen (MCA, 1974).

Toxicity

Little information is available on the mutagenic and short-term toxicologic effects of propylene in animals (IARC, 1979). Propylene was reported not to be mutagenic when tested with *Escherichia coli* (Clayton and Clayton, 1982). Two short-term toxicity studies have been performed in which only the liver was examined. Very slight to moderate fatty degeneration of the liver was reported in 3/13 white mice receiving 1-20 inhalation exposures (60-90 minutes duration) to 35% propylene. The propylene used was impure, however, and no control group was included (Reynolds, 1926). In a recent study, no hepatotoxic changes were seen in male Charles River COBS Sprague-Dawley rats exposed by inhalation to propylene for 4 hours at concentrations up to 65,000 ppm (Conolly and Osimitz, 1981). No pharmacokinetic or reproductive information is available for propylene (IARC, 1979).

Carcinogenicity

Two studies have examined propylene for carcinogenic activity. According to a preliminary report providing only limited information, Sprague-Dawley rats and Swiss mice were exposed to propylene by inhalation at concentrations of 200, 1,000, or 5,000 ppm for 7 hours per day, 5 days per week (C. Maltoni, personal communication to NTP, 1981). The exposure period lasted 24 months for rats and 18 months for mice. Propylene was reported not to cause a carcinogenic response in either species. In another study, which examined only the the effects of propylene on brain tissue in Sprague-Dawley rats, the 200-, 1,000-, or 5,000-ppm concentrations failed to produce brain tumors in animals exposed by inhalation 7 hours per day, 5 days per week for 104 weeks (Maltoni et al., 1982). Abbreviated results from both reports were made available to the NTP during the course of the present study; both reports may be part of the same study, but this has not been determined.

Propylene was studied because of the large amount produced, the widespread exposure of the population, the relative lack of toxicity and carcinogenicity information, and for comparison to the structurally related propylene oxide (NTP, 1985). A summary of the studies described in this Technical Report has been published (Toxicol. Appl. Pharmacol. 76:288-295, 1984).

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF PROPYLENE

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

FOURTEEN-DAY REPEATED-EXPOSURE STUDIES

FOURTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Study Design
Source and Specifications of Test Animals
Animal Maintenance
Clinical Examinations and Pathology
Statistical Methods

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF PROPYLENE

Propylene was obtained as polymerization grade material in three lots from Phillips Petroleum Company, Phillips, Texas. The chemical was received as a liquefied gas under its own vapor pressure in 28-gallon, low-pressure steel cylinders and was stored at or slightly below room temperature in the testing laboratory throughout the studies. Lot no. Y-458 was used for the 14-day and 14-week studies and for part of the 2-year studies. Lot nos. B-644 and B-887 were used for the rest of the 2-year studies.

The purity and identity of the lots were determined at Midwest Research Institute (Appendix G). The infrared spectra were consistent with the structure and with the literature spectra. Two gas chromatographic systems indicated a major peak and several minor impurities that did not exceed 0.3% of the total peak area.

Gas chromatographic analyses conducted at the testing laboratory during the 2-year studies indicated that the initial purity of the lots was 98.6%-99.7%. A major impurity, tentatively identified as propane by the manufacturer, was detected in each lot at a concentration of 0.3%-1.1%. The identity of the material was verified by infrared spectroscopy.

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

During the 2-year studies, propylene gas was metered to the exposure chambers and diluted in the chamber fresh-air inlets. The generation system is illustrated in Appendix H. The uniformity of the vapor concentration was periodically measured throughout the study.

Propylene concentrations in the exposure chambers were monitored by gas chromatography approximately 10 times during each 6-hour exposure period. Weekly and monthly chamber concentrations are presented in Appendix H. The exposure concentrations for the 2-year studies are summarized in Table 1.

TABLE 1. SUMMARY OF CHAMBER CONCENTRATIONS OF PROPYLENE DURING THE TWO-YEAR INHALATION STUDIES

Target Concentration (ppm)	Average Chamber Concentation (a) (ppm)	Total No. of Readings
MICE		
5,000	4,999 ± 285	5,440
10,000	9,957 ± 533	5,426
RATS		
5,000	4,985 ± 274	5,357
10,000	9,891 ± 515	5,332

(a) ± Standard deviation

Throughout the studies, samples taken from the chambers several times each day indicated that average daily chamber concentrations were usually within 5%-6% of the target concentrations. However, wider variations in exposures were observed during the first 40 weeks of the studies as compared with the remainder of the studies (Appendix H, Figures 8-11).

Atmospheric samples were obtained from the control and 10,000-ppm chambers during an exposure period during week 30 and were analyzed by gas chromatography. No peaks were observed in the air from the control chamber. Only those impurities present in the bulk propylene at the pretest analysis were observed in the air from the 10,000-ppm chamber.

FOURTEEN-DAY REPEATED-EXPOSURE STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Center and held for 14 days before the studies began. Groups of five males and five females of each species were exposed in a chamber to air containing 0, 625, 1,250, 2,500, 5,000, or 10,000 ppm propylene. Exposure occurred 6 hours per day, 5 days per week for 2 weeks.

The animals were housed individually and received water and feed ad libitum except during the exposure period, when only water was available. Details of animal maintenance are presented in Table 2.

Rats and mice were observed daily for mortality and were weighed on days 0, 5, 10, and 14. Necropsies were performed on all animals (Table 2).

FOURTEEN-WEEK STUDIES

Fourteen-week studies were conducted to evaluate the cumulative toxicity of propylene and to determine the concentrations to be used in the 2-year studies.

Weanling male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Center, observed for 8 days, and then assigned to test groups according to a table of random numbers. Rats and mice were housed individually in stainless steel mesh cages placed in stainless steel and glass chambers. Cages were replaced twice per week. Food and water were available ad libitum except during the exposure period, when only water was available. Further experimental details are summarized in Table 2.

Groups of 10 male and 10 female mice and 9-11 male and 9-11 female rats were exposed to air containing 0, 625, 1,250, 2,500, 5,000, or 10,000 ppm propylene, 6 hours per day, 5 days per week for 14 weeks. Initially, 10 rats of each sex were assigned to each concentration group but 2 males and 1 female were missexed.

Animals were checked daily for signs of moribundity and mortality; moribund animals were killed. Body weight data were collected weekly.

At the end of the 14-week studies, survivors were killed. Necropsies were performed on all animals. Tissues and groups examined are listed in Table 2.

TWO-YEAR STUDIES

Study Design

Groups of 50 male and 50 female rats and groups of 50 male and 49 (low concentration group only) or 50 female mice were exposed to air containing propylene at concentrations of 5,000 or 10,000 ppm, 6 hours per day, 5 days per week, for 103 weeks. (Initially, 50 female mice were assigned to the low concentration group; however, one missexed animal was found at week 86). Groups of 50 rats and 50 mice of each sex, serving as controls, were handled in the same manner as the test groups but were exposed in chambers to clean, dry air only.

Source and Specifications of Test Animals

The male and female F344/N rats and B6C3F$_1$ (C57BL/6N, female, × C3H/HeN MTV$^-$, male) mice used in this study were produced under strict barrier conditions at Charles River Breeding Laboratories under a contract to the Carcinogenesis Program. Breeding starts for the foundation colony at the production facility originated at the National Institutes of Health Repository. Animals shipped for testing were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. Animals were shipped to the testing laboratory at 4-5 weeks of age. The animals were quarantined at the testing facility for 5 weeks. Thereafter, a complete necropsy was performed on five animals of each sex to assess their health status. The rodents were placed on study at 9-10 weeks of age. The sentinel animal program is described in Appendix I.

A quality control skin grafting program has been in effect since early 1978 to monitor the genetic integrity of the inbred mice used to produce the hybrid B6C3F$_1$ test animal. In mid-1981, data were obtained that showed incompatibility between the NIH C3H reference colony and the C3H colony from a Program supplier. In August 1981, inbred parental lines of

TABLE 2. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF PROPYLENE

	Fourteen-Day Repeated-Exposure Studies (a)	Fourteen-Week Studies	Two-Year Studies
EXPERIMENTAL DESIGN			
Size of Test Groups	5 males and 5 females of each species	Rats--9-11 males and 9-11 females; mice--10 males and 10 females	50 males and 49 or 50 females of each species
Concentrations	0, 625, 1,250, 2,500, 5,000, or 10,000 ppm propylene via inhalation	0, 625, 1,250, 2,500, 5,000, or 10,000 ppm propylene via inhalation	0, 5,000, or 10,000 ppm propylene via inhalation
Date of First Exposure	3/4/77	5/27/77	10/29/79
Date of Last Exposure	3/17/77	Rats--9/1/77; mice--8/31/77	10/16/81
Duration of Exposures	6 h/d, 5 d/wk for 2 wk	6 h/d, 5 d /wk, for 14 wk	6 h/d, 5 d/wk for 103 wk
Type and Frequency of Observation	Observed 1 × d for signs of moribundity and mortality; weighed on d 0, 5, 10, and 14	Observed 1 × d for signs of moribundity and mortality; weighed on d 0, then 1 x wk	Observed 2 × d for signs of moribundity and mortality; clinically examined 1 × mo; weighed 1 × wk for 14 wk, then 1 × mo for 76 wk and biweekly thereafter
Necropsy and Histologic Examination	The following tissues were examined during necropsy of all animals: gross lesions, skin, mandibular lymph node, mammary gland, salivary gland, thigh muscle, sciatic nerve, sternebrae, vertebrae or femur including marrow, costochondral junction (rib), thymus, larynx and pharynx, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, duodenum, jejunum, ileum, colon, cecum, rectum, mesenteric lymph node, liver, gallbladder (mice), pancreas, spleen, kidneys and adrenal glands, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity and nasal turbinates, brain, pituitary gland, spinal cord, eyes	Necropsies performed on all animals; tissues examined: same as in 14-d study; histopath exam performed on all controls, high dose, and early death animals	Complete necropsy and histopath exam performed on all animals; tissues examined: gross lesions, skin, mandibular lymph node, mammary gland, sternebrae, vertebrae or femur including marrow, thymus, trachea (b), lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, colon, small intestine, liver (b), gallbladder (mice), pancreas, spleen, kidneys and adrenal glands (b), urinary bladder, prostate/testes (b) or ovaries/uterus (b), nasal cavity and nasal turbinates (c), brain (c), pituitary gland, and (if abnormal) spinal cord, eyes, and pharynx
ANIMALS AND ANIMAL MAINTENANCE			
Strain and Species	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice	F344/N rats; B6C3F$_1$ mice
Animal Source	Frederick Cancer Research Center (Frederick, MD)	Frederick Cancer Research Center (Frederick, MD)	Charles River Breeding Laboratories (Portage, MI)

TABLE 2. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF PROPYLENE (Continued)

	Fourteen-Day Repeated-Exposure Studies	Fourteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE (Continued)			
Testing Laboratory	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories
Time Held Before Test	14 d	8 d	35 d
Age When Placed on Study	Not available	Not available	9-10 wk
Age When Killed	--	--	113-115 wk
Necropsy Dates	3/17/77	Rats--9/1/77; mice--8/31/77	Rats--10/28/81; mice--10/30/81
Method of Animal Distribution	According to a table of random numbers	Same as 14-d repeated-exposure studies	Assigned to cages according to a table of randon numbers; cages then assigned to groups according to another table of random numbers
Feed	Wayne Lab-Blox® (Allied Mills, Inc., Chicago, IL); freely available except during inhalation exposure	Same as 14-d repeated-exposure studies	Same as 14-d repeated-exposure studies
Water	Provided ad libitum	Provided ad libitum	Tap water provided ad libitum through automatic watering system (Edstrom Industries, Waterford, WI)
Cages	Stainless steel mesh (Unifab Corp., Kalamazoo, MI)	Same as 14-d repeated-exposure studies	Stainless steel wire (Lab Products, Rochelle Pk, NJ)
Animals per Cage	1	1	1
Animal Room Environment	Fluorescent light 12 h/d; information on temperature, air changes and humidity not available	Same as 14-d repeated-exposure studies	Av temp--70° F during exposure, 75° F during nonexposure; rel humidity--54%-57%; fluorescent light 12 h/d; 20 room air changes/h; chamber environment: temp--78° ± 2° F (rats), 75° ± 2° F (mice); rel hum--57% ± 7% (rats), 9% ± 8% (mice)
Other Chemicals on Test in Same Room	1,3-Butadiene	1,3-Butadiene	Propylene oxide
CHEMISTRY			
Lot Numbers Used	Y-458	Y-458	Y-458, B-644, B-887
Date of Initial Use of Subsequent Lots	N/A	N/A	B-644 in June 1980; B-887 in March 1981
Supplier	Phillips Petroleum Co. (Phillips, TX)	Same as 14-d repeated-exposure studies	Same as 14-d repeated-exposure studies

TABLE 2. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF PROPYLENE (Continued)

	Fourteen-Day Repeated-Exposure Studies	Fourteen-Week Studies	Two-Year Studies
CHEMICAL/VEHICLE			
Preparation	Test material was metered into the chamber air supply so that it was well mixed with incoming air by turbulence	All test chambers received clean, dry chamber supply air, 24 h/d, at the top of each chamber; test material was metered into the chamber air supply so that it was well mixed with incoming air by turbulence; a dual-bank switching type manifold (Matheson Gas Products, Joliet, IL) provided a continuous supply of gas	Test material was delivered from its cylinder to the test chamber; then piped to a polyethylene hood containing a flow- limiting valve, two emergency shut-off valves, a pop-off valve and a pressure gauge; it was then piped to a second hood containing 4 metering valves that provided stable control of the gas flow rate and the chamber concentrations.

(a) No single-exposure studies were conducted.
(b) Two sections
(c) Three sections. For the nasal turbinate, three separate sections were examined: section one was at the level just caudal to the incisors; section two, midway between incisors and first molar; and the third section, at the middle of the second molar.

mice were further tested for genetic integrity via isozyme and protein electrophoretograms that demonstrate phenotype expressions of known genetic loci.

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

Male mice from the C3H colony and female mice from the C57BL/6 colony were used as parents for the hybrid B6C3F$_1$ mice used in this study. The influence of the potential genetic nonuniformity in the hybrid mice on the results is not known, but results of the studies are not affected because matched concurrent controls were included in each study.

Animal Maintenance

Rats and mice were housed individually. Food and water were available freely except during exposure periods, when only water was available. Details of animal maintenance are presented in Table 2.

Clinical Examinations and Pathology

All animals were observed twice daily for signs of moribundity or mortality. Clinical signs were recorded monthly. Individual animal body weights were recorded every week for the first 14 weeks, monthly from weeks 14 to 90, and biweekly from weeks 91 to 103. Mean body weights were calculated for each group. Examination of animals for palpable masses began 1 year after the study started and continued monthly thereafter. Moribund animals were killed, as were animals that survived to the end of the study. Necropsies were performed on all animals, including those found dead unless they were excessively autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that were placed on study in each group.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Tissues examined microscopically are listed in Table 2.

The nasal cavities were examined on three levels: just caudal to the incisor teeth, midway between the incisors and the first molar, and at the level of the middle of the second molar.

When the pathology examination was completed, the slides, individual animal data records, and summary tables were sent to an independent quality assurance laboratory. Individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10% of the animals were evaluated by a quality assurance pathologist. Slides of all target tissues and those about which the original and quality assurance pathologists disagreed were submitted to the Chairperson of the Pathology Working Group (PWG) for evaluation. Representative slides selected by the PWG Chairperson were reviewed by PWG pathologists, who reached a consensus and compared their findings with the original and quality assurance diagnoses. When diagnostic differences were found, the PWG sent the appropriate slides and comments to the original pathologist for review. This procedure has been described, in part, by Maronpot and Boorman (1982) and Boorman et al. (1985). The final diagnoses represent a consensus of contractor pathologists and the NTP Pathology Working Group.

Nonneoplastic lesions are not examined routinely by the quality assurance pathologist or the PWG. Certain nonneoplastic findings are reviewed by the quality assurance pathologist and the PWG if they are considered part of the toxic response to a chemical or if they are deemed of special interest.

Statistical Methods

Data Recording: 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, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

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

Calculation of Incidence Rates: The incidence of neoplastic or nonneoplastic lesions is given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators include only those animals for which the site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the number of animals on which necropsies were performed.

Analysis of Tumor Incidence: Three statistical methods are used to analyze tumor incidence data. The two that adjust for intercurrent mortality employ the classical method for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high dose and low dose groups with chamber controls and tests for overall dose-response trends.

For studies in which compound administration has little effect on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data depends on the extent to which the tumor under consideration is regarded as being the cause of death. All reported P values for tumor analyses are one-sided.

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

Incidental Tumor Analysis--The second method of analysis assumed that all tumors of a given type observed in animals that died before the end of the study were "incidental"; i.e., they were merely observed at necropsy in animals dying of an unrelated cause. According to this approach, the proportions of animals found to have tumors in dosed and control groups were compared in each of five time intervals: weeks 0-52, weeks 53-78, weeks 79-92, week 93 to the week before the terminal-kill period, and the terminal-kill period. The denominators of these proportions were the number of animals on which necropsies were actually performed during the time interval. The individual time interval comparisons were then combined by the previously described method to obtain a single overall result. (See Haseman, 1984, for the computational details of both methods.)

Unadjusted Analyses--Primarily, survival-adjusted methods are used to evaluate tumor incidence. In addition, the results of the Fisher exact test for pairwise comparisons and the Cochran-Armitage linear trend test (Armitage, 1971; Gart et al.,1979) are given in Appendix E. These two tests are based on the overall proportion of tumor-bearing animals and do not adjust for survival differences.

III. RESULTS

RATS

FOURTEEN-DAY REPEATED-EXPOSURE STUDIES

FOURTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

FOURTEEN-DAY REPEATED-EXPOSURE STUDIES

FOURTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

FOURTEEN-DAY REPEATED-EXPOSURE STUDIES

No rats died. Weight gains by exposed and control rats were comparable (Table 3). No compound-related effects, including changes of the nasal cavity, were recorded.

FOURTEEN-WEEK STUDIES

No rats died. The mean body weights of exposed male rats were 4%-12% higher than those of the controls throughout most of the study. Weight gains of exposed and control female rats were comparable (Table 4). No compound-related gross or microscopic pathologic effects (including changes of the nasal cavity) were recorded.

Even though no propylene-related toxicity was observed, concentrations of 5,000 and 10,000 ppm propylene were selected for rats in the 2-year studies. Concentrations higher than 10,000 ppm propylene could not be selected for male and female rats in the 2-year studies because of the risk of explosion.

TABLE 3. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-DAY REPEATED-EXPOSURE INHALATION STUDIES OF PROPYLENE

Concentration (a) (ppm)	Survival (b)	Mean Body Weight (grams) (c)		
		Initial	Final	Change
MALE				
0	5/5	160 ± 7	214 ± 6	+54 ± 3
625	5/5	159 ± 7	210 ± 8	+51 ± 2
1,250	5/5	163 ± 7	209 ± 6	+46 ± 2
2,500	5/5	164 ± 7	219 ± 8	+55 ± 4
5,000	5/5	162 ± 8	215 ± 7	+53 ± 4
10,000	5/5	169 ± 6	223 ± 5	+55 ± 1
FEMALE				
0	5/5	115 ± 3	139 ± 4	+24 ± 2
625	5/5	116 ± 4	143 ± 3	+26 ± 1
1,250	5/5	117 ± 3	140 ± 3	+23 ± 2
2,500	5/5	117 ± 4	144 ± 5	+27 ± 3
5,000	5/5	119 ± 3	149 ± 5	+30 ± 2
10,000	5/5	121 ± 3	144 ± 5	+23 ± 3

(a) Time-averaged mean
(b) Number surviving/number initially in the group
(c) Mean weight change of the survivors of the group ± standard error of the mean

TABLE 4. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-WEEK INHALATION STUDIES OF PROPYLENE

Concentration (ppm)	Survival(a)	Mean Body Weight (grams)			Final Weight Relative to Controls (percent)
		Initial	Final	Change(b)	
MALE					
0	10/10	79 ± 4	283 ± 6	+203 ± 5	
625	9/9	79 ± 4	300 ± 6	+221 ± 8	106
1,250	9/9	82 ± 4	311 ± 9	+230 ± 9	110
2,500	11/11	78 ± 4	299 ± 4	+221 ± 4	106
5,000	10/10	82 ± 3	317 ± 4	+235 ± 6	112
10,000	10/10	84 ± 4	294 ± 7	+211 ± 9	104
FEMALE					
0	10/10	60 ± 2	178 ± 3	+118 ± 4	
625	11/11	61 ± 3	172 ± 3	+111 ± 3	97
1,250	11/11	61 ± 3	172 ± 3	+111 ± 3	97
2,500	9/9	61 ± 2	175 ± 3	+114 ± 3	98
5,000	10/10	61 ± 2	176 ± 4	+115 ± 4	99
10,000	10/10	63 ± 2	180 ± 2	+117 ± 2	101

(a) Number surviving/number initially in the group
(b) Mean weight change of the group ± standard error of the mean

TWO-YEAR STUDIES

Body Weights and Clinical Signs

The mean body weights of exposed male and female rats were comparable to those of the controls throughout the study (Table 5 and Figure 1). The fluctuations in weight gain were not dose related. No compound-related clinical signs were recorded.

TABLE 5. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

Weeks on Study	Control		Low Dose			High Dose		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
1	195	50	203	104.1	50	203	104.1	50
2	218	50	224	102.8	50	223	102.3	50
3	236	50	243	103.0	50	240	101.7	50
4	251	50	251	100.0	50	253	100.8	50
6	277	50	276	99.6	50	276	99.6	50
7	289	50	286	99.0	50	285	98.6	50
8	299	50	296	99.0	50	295	98.7	50
9	308	50	305	99.0	50	304	98.7	50
10	319	50	316	99.1	50	315	98.7	50
11	320	50	319	99.7	50	317	99.1	50
12	323	50	321	99.4	50	322	99.7	50
13	328	50	325	99.1	50	325	99.1	50
14	333	50	331	99.4	50	333	100.0	50
18	358	50	350	97.8	50	354	98.9	50
21	369	50	362	98.1	50	356	96.5	50
25	385	50	380	98.7	50	379	98.4	50
30	395	50	393	99.5	50	389	98.5	50
34	395	50	391	99.0	50	394	99.7	50
39	402	50	406	101.0	50	396	98.5	50
43	426	50	416	97.7	50	417	97.9	50
47	431	50	428	99.3	50	426	98.8	50
52	438	50	445	101.6	50	440	100.5	50
55	449	50	449	100.0	50	436	97.1	49
59	456	50	455	99.8	50	446	97.8	49
64	460	50	465	101.1	50	466	101.3	48
68	460	48	460	100.0	50	453	98.5	48
72	450	48	451	100.2	50	446	99.1	48
77	448	48	429	95.8	49	444	99.1	47
81	453	48	442	97.6	48	440	97.1	47
86	454	47	444	97.8	48	445	98.0	47
90	440	46	444	100.9	46	438	99.5	46
92	453	44	441	97.4	45	441	97.4	46
94	457	42	445	97.4	41	444	97.2	46
96	451	40	442	98.0	40	438	97.1	46
98	452	39	440	97.3	38	437	96.7	45
100	442	36	446	100.9	35	443	100.2	40
102	452	33	447	98.9	34	443	98.0	37
FEMALE								
1	145	50	147	101.4	50	147	101.4	50
2	158	50	157	99.4	50	153	96.8	50
3	164	50	164	100.0	50	165	100.6	50
4	167	50	169	101.2	50	169	101.2	50
6	179	50	178	99.4	50	182	101.7	50
7	188	50	182	96.8	50	183	97.3	50
8	190	50	187	98.4	49	176	92.6	50
9	195	50	198	101.5	49	190	97.4	50
10	200	50	197	98.5	49	197	98.5	50
11	201	50	200	99.5	49	202	100.5	50
12	203	49	201	99.0	49	204	100.5	50
13	204	49	197	96.6	49	197	96.6	50
14	208	49	203	97.6	49	206	99.0	50
18	219	49	214	97.7	49	217	99.1	50
21	223	49	219	98.2	49	219	98.2	50
25	231	49	226	97.8	49	228	98.7	50
30	235	49	230	97.9	49	227	96.6	50
34	241	49	231	95.9	49	234	97.1	50
39	239	49	235	98.3	49	238	99.6	50
43	257	49	241	93.8	49	244	94.9	50
47	259	49	252	97.3	49	251	96.9	50
52	270	49	262	97.0	49	260	96.3	50
55	280	49	271	96.8	49	267	95.4	49
59	291	49	278	95.5	49	277	95.2	49
64	297	49	289	97.3	49	283	95.3	49
68	294	49	292	99.3	49	290	98.6	48
72	290	46	287	99.0	49	292	100.7	48
77	295	46	290	98.3	48	294	99.7	48
81	302	44	289	95.7	48	297	98.3	46
86	311	43	299	96.1	44	303	97.4	44
90	312	39	308	98.7	41	304	97.4	43
92	311	39	309	99.4	41	299	96.1	43
94	324	37	306	94.4	41	293	90.4	42
96	310	36	305	98.4	41	303	97.7	39
98	317	34	312	98.4	36	309	97.5	37
100	319	31	309	96.9	36	304	95.3	37
102	316	31	310	98.1	36	307	97.2	33

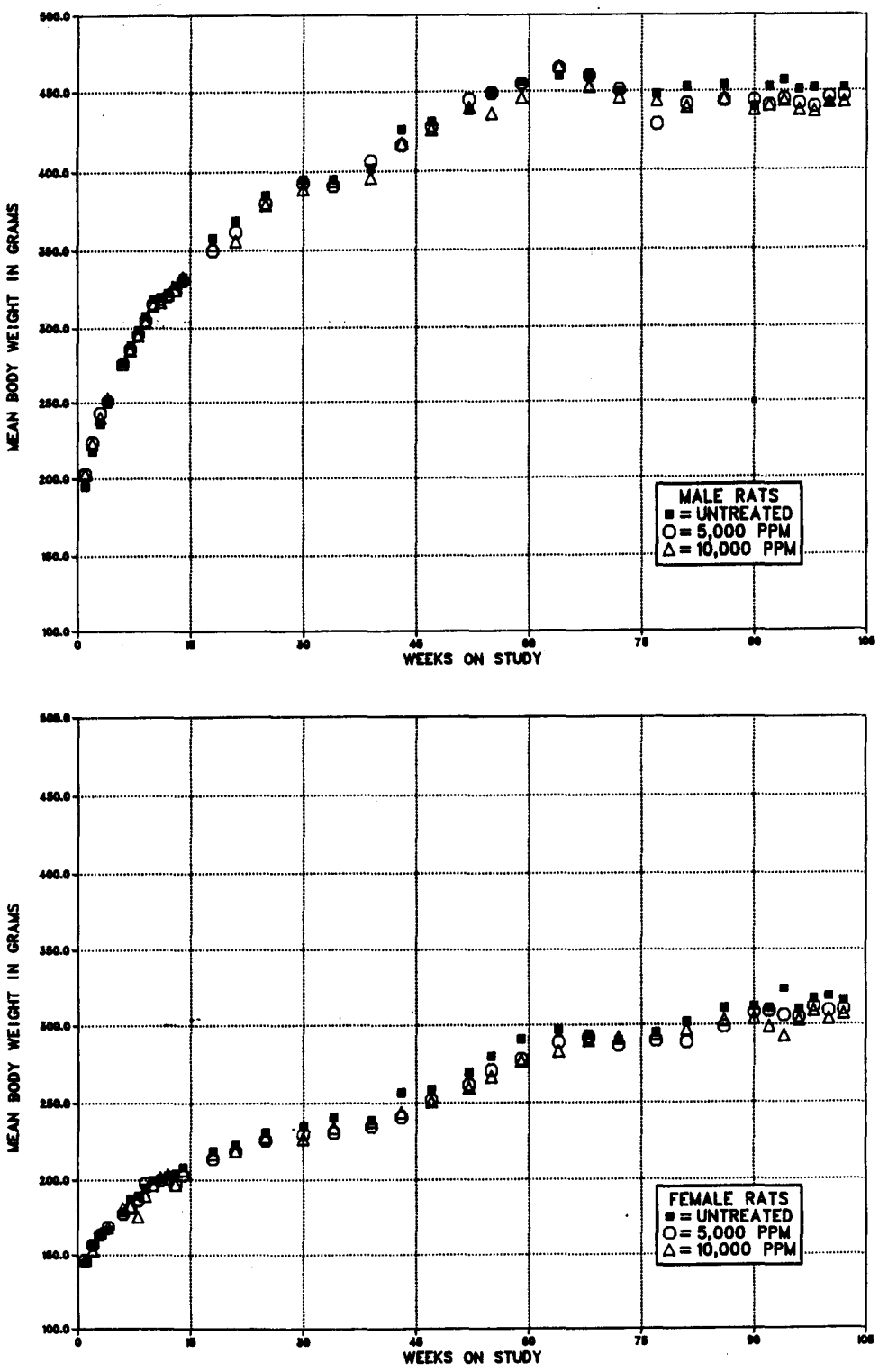

FIGURE 1. GROWTH CURVES FOR RATS EXPOSED TO PROPYLENE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female rats exposed to air containing propylene at the concentrations of these studies and those of the controls are shown in the Kaplan and Meier curves in Figure 2. No significant differences in survival were observed between any groups of either sex (Table 6).

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; Tables A3 and A4 give the survival and tumor status for individual male and female rats. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2. Appendix E, Tables E1 and E2, contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes). Historical incidences of tumors in control animals are listed in Appendix F.

TABLE 6. SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
Male (a)			
Animals initially in study	50	50	50
Natural deaths before termination (b)	17	17	13
Killed at termination	33	32	37
Died during termination period	0	1	0
Survival P values (c)	0.397	0.999	0.442
Female (a)			
Animals initially in study	50	50	50
Natural deaths before termination (b)	22	14	20
Accidentally killed	1	0	0
Killed at termination	26	36	30
Died during termination period	1	0	0
Survival P values (c)	0.641	0.160	0.684

(a) Terminal kill period: week 104
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

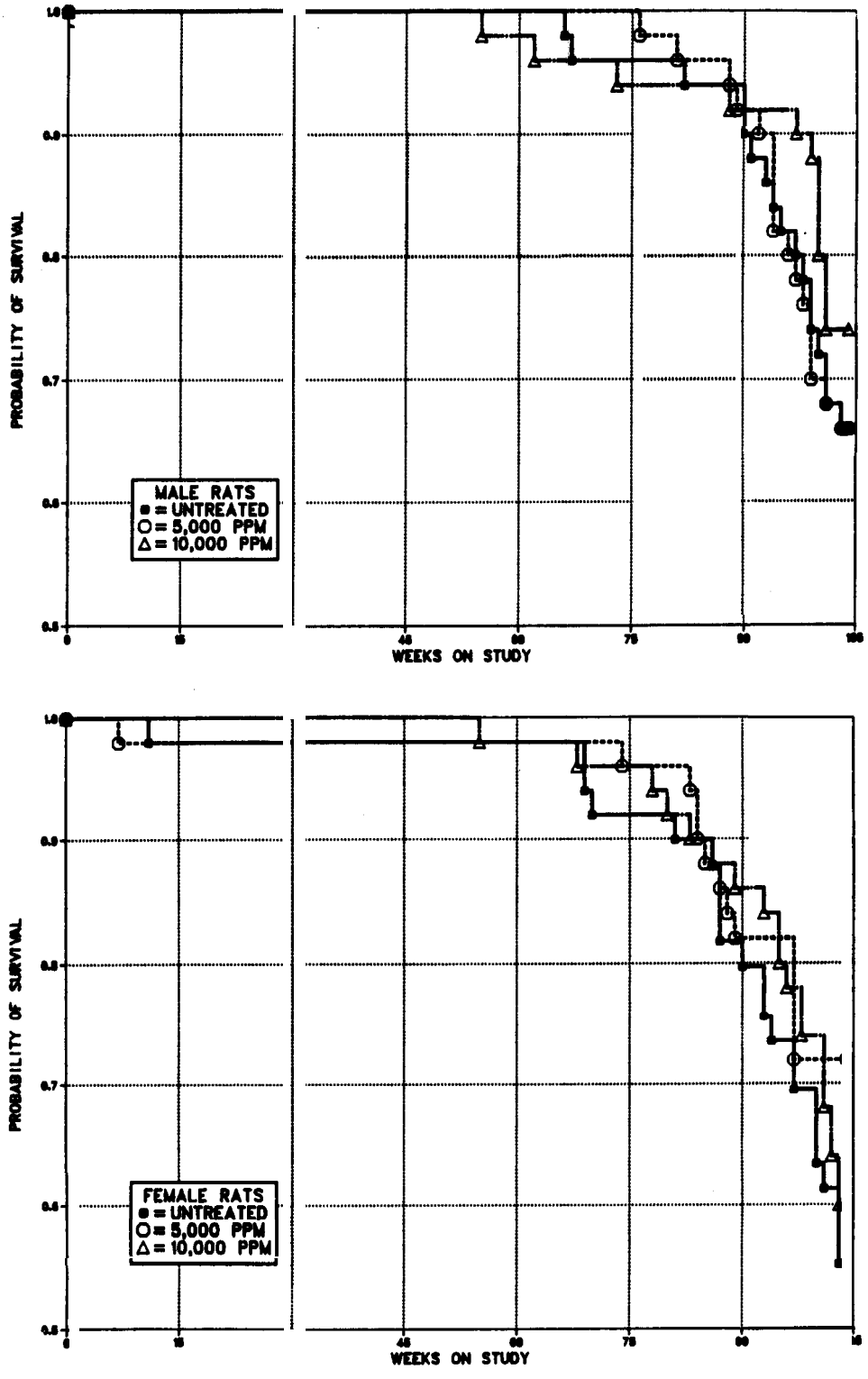

FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR RATS EXPOSED TO PROPYLENE BY INHALATION FOR TWO YEARS

Nasal Cavity: Squamous metaplasia occurred at increased incidences in exposed male rats (control, 2/50, 4%; low concentration, 19/50, 38%; high concentration, 7/50, 14%) and in exposed female rats (control, 0/49; low concentration, 15/50, 30%; high concentration, 6/50, 12%). The lesion was present in the first section taken at the level of the incisor teeth. The squamous metaplasia involved the respiratory epithelium just dorsal to the vomeronasal organ or on the lateral aspects of the nasal cavity.

Epithelial hyperplasia occurred at an increased incidence in female rats exposed to propylene at the high concentration (control, 0/49; low concentration, 4/50, 8%; high concentration, 9/50, 18%). A slightly increased incidence of epithelial hyperplasia occurred in male rats at the high concentration (control, 2/50, 4%; low concentration, 2/50, 4%; high concentration, 5/50, 10%). Inflammatory changes in the nasal cavity were found in both male and female rats (Table 7).

When the inflammatory lesion was characterized by a submucosal influx of lymphocytes and macrophages containing a few granulocytes, it was diagnosed as inflammation, not otherwise specified. This lesion was found to occur in male rats exposed to propylene at the low concentration. When the lesion was more severe, with granulocytes migrating through the epithelium and accumulating in the lumen, it was diagnosed as inflammation, suppurative. This lesion was found at an increased incidence in male and female rats exposed at the high concentration. The two diagnoses were combined because they appeared to represent the same inflammatory process and varied only by degree and by predominance of neutrophils. In combination, the nasal cavity lesions occurred at increased incidences in low concentration and high concentration male rats and in high concentration female rats. The lesions were more severe in the high concentration animals.

TABLE 7. INCIDENCES OF NASAL INFLAMMATORY CHANGES IN RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
MALE			
Inflammation, unspecified	4/50 (8%)	14/50 (28%)	5/50 (10%)
Inflammation, suppurative	7/50 (14%)	7/50 (14%)	14/50 (28%)
Inflammation, unspecified or suppurative	11/50 (22%)	21/50 (42%)	19/50 (38%)
FEMALE			
Inflammation, unspecified	0/49 (0%)	3/50 (6%)	2/50 (4%)
Inflammation, suppurative	8/49 (16%)	7/50 (14%)	11/50 (22%)
Inflammation, unspecified or suppurative	8/49 (16%)	10/50 (20%)	13/50 (26%)

Thyroid Gland: C-cell hyperplasia was found in exposed male and female rats at increased incidences (Table 8). C-cell adenomas and C-cell adenomas or carcinomas (combined) occurred in female rats with a significant negative trend.

The incidence of C-cell adenomas in the high concentration group was significantly lower than that in the controls. The incidences of C-cell adenomas or carcinomas (combined) in male rats were not significantly different in exposed and control groups.

TABLE 8. ANALYSIS OF THYROID GLAND LESIONS IN RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
MALE			
C-Cell Hyperplasia			
Overall Rates	4/45 (9%)	7/46 (15%)	9/47 (19%)
C-Cell Adenoma or Carcinoma			
Overall Rates	4/45 (9%)	1/46 (2%)	4/47 (9%)
FEMALE			
C-Cell Hyperplasia			
Overall Rates	2/39 (5%)	7/47 (15%)	6/47 (13%)
C-Cell Adenoma			
Overall Rates	5/39 (13%)	2/47 (4%)	0/47 (0%)
Adjusted Rates	15.6%	5.6%	0.0%
Terminal Rates	2/27 (7%)	2/36 (6%)	0/29 (0%)
Life Table Tests	P=0.013N	P=0.141N	P=0.031N
Incidental Tumor Tests	P=0.008N	P=0.239N	P=0.018N
C-Cell Adenoma or Carcinoma			
Overall Rates	6/39 (15%)	2/47 (4%)	2/47 (4%)
Adjusted Rates	19.0%	5.6%	6.9%
Terminal Rates	3/27 (11%)	2/36 (6%)	2/29 (7%)
Life Table Tests	P=0.064N	P=0.077N	P=0.120N
Incidental Tumor Tests	P=0.048N	P=0.135N	P=0.088N

FOURTEEN-DAY REPEATED-EXPOSURE STUDIES

All mice survived to the end of the exposure period. No compound-related effects, including changes of the nasal cavity, were recorded (Table 9).

FOURTEEN-WEEK STUDIES

One male exposed to propylene at 5,000 ppm was moribund on day 67 and was killed. One female exposed at 1,250 ppm died on day 35 (Table 10).

Differences in final mean body weights of exposed and control animals were less than 4% for males and less than 7% for females.

No compound-related gross or microscopic pathologic effects (including changes of the nasal cavity) were recorded. Even though no propylene-related toxicity was observed, concentrations of 5,000 and 10,000 ppm propylene were selected for male and female mice in the 2-year studies. These concentrations were selected because propylene at higher concentrations is an explosion hazard.

TABLE 9. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY REPEATED-EXPOSURE INHALATION STUDIES OF PROPYLENE

Concentration(a) (ppm)	Survival (b)	Mean Body Weight (grams) (c)		
		Initial	Final	Change
MALE				
0	5/5	22.8 ± 1.0	25.8 ± 0.6	+3.0 ± 1.0
625	5/5	23.2 ± 0.7	26.6 ± 0.7	+3.4 ± 0.7
1,250	5/5	23.6 ± 0.5	26.4 ± 0.2	+2.8 ± 0.4
2,500	5/5	23.4 ± 0.7	26.4 ± 0.6	+3.0 ± 0.3
5,000	5/5	23.4 ± 0.5	25.6 ± 0.7	+2.2 ± 0.9
10,000	5/5	24.0 ± 0.5	26.0 ± 1.0	+2.0 ± 1.5
FEMALE				
0	5/5	19.8 ± 0.6	23.6 ± 0.8	+3.8 ± 1.2
625	5/5	19.8 ± 0.7	22.2 ± 0.4	+2.4 ± 0.6
1,250	5/5	20.4 ± 0.5	23.2 ± 0.6	+2.8 ± 0.4
2,500	5/5	20.2 ± 0.7	21.8 ± 0.7	+1.6 ± 1.0
5,000	5/5	20.4 ± 0.5	21.2 ± 0.2	+0.8 ± 0.4
10,000	5/5	20.8 ± 0.4	22.6 ± 0.5	+1.8 ± 0.7

(a) Time-averaged mean
(b) Number surviving/number initially in the group
(c) Mean weight change of the group ± standard error of the mean

TABLE 10. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-WEEK INHALATION STUDIES OF PROPYLENE

Concentration (ppm)	Survival(a)	Mean Body Weight (grams)			Final Weight Relative to Controls (percent)
		Initial	Final	Change(b)	
MALE					
0	10/10	18.5 ± 0.5	30.7 ± 0.4	+12.2 ± 0.5	--
625	10/10	18.4 ± 0.4	30.5 ± 0.5	+12.1 ± 0.3	99.3
1,250	10/10	19.8 ± 0.5	31.7 ± 0.8	+11.9 ± 0.5	103.3
2,500	10/10	19.1 ± 0.9	30.8 ± 0.6	+11.7 ± 0.9	100.3
5,000	9/10	19.3 ± 0.6	31.0 ± 0.7	+11.7 ± 0.8	101.0
10,000	10/10	19.5 ± 0.5	30.9 ± 0.7	+11.4 ± 0.5	100.7
FEMALE					
0	10/10	14.9 ± 0.3	27.9 ± 0.4	+13.0 ± 0.3	--
625	10/10	15.8 ± 0.3	26.9 ± 0.6	+11.1 ± 0.4	96.4
1,250	9/10	16.0 ± 0.7	26.0 ± 0.7	+10.0 ± 0.7	93.2
2,500	10/10	16.7 ± 0.3	26.4 ± 0.5	+ 9.7 ± 0.3	94.6
5,000	10/10	15.7 ± 0.3	26.5 ± 0.5	+10.8 ± 0.3	95.0
10,000	10/10	16.3 ± 0.4	26.9 ± 0.5	+10.6 ± 0.3	96.4

(a) Number surviving/number initially in the group
(b) Mean weight change of the survivors of the group ± standard error of the mean

TWO-YEAR STUDIES

Body Weights and Clinical Signs

After week 59, mean body weights of high concentration male mice were approximately 5% lower than those of the controls (Table 11 and Figure 3). Throughout the study, mean body weights of low concentration and control male mice and of exposed and control female mice were comparable. No compound-related clinical signs were observed.

TABLE 11. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

Weeks on Study	Control		Low Dose			High Dose		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls)	No. of Survivors
MALE								
1	28	50	28	100.0	50	29	103.6	50
2	29	50	28	96.6	50	28	96.6	50
3	29	50	29	100.0	50	29	100.0	50
4	30	50	30	100.0	50	30	100.0	50
6	30	50	30	100.0	50	31	103.3	50
7	30	50	31	103.3	50	30	100.0	50
8	29	50	31	106.9	50	30	103.4	50
9	31	50	31	100.0	50	31	100.0	50
10	32	49	30	93.8	50	31	96.9	50
11	31	49	31	100.0	50	31	100.0	50
12	31	49	31	100.0	50	31	100.0	50
13	31	49	31	100.0	50	30	96.8	49
14	30	49	32	106.7	50	31	103.3	49
18	32	49	32	100.0	50	28	87.5	49
21	33	49	32	97.0	50	33	100.0	49
25	35	49	33	94.3	50	33	94.3	49
30	34	49	33	97.1	50	33	97.1	49
34	35	49	36	102.9	50	36	102.9	49
39	35	49	36	102.9	49	35	100.0	49
43	34	49	36	105.9	49	35	102.9	49
47	37	49	35	94.6	49	36	97.3	49
52	36	49	37	102.8	49	37	102.8	49
55	37	49	38	102.7	49	37	100.0	48
59	38	49	37	97.4	48	36	94.7	48
64	37	48	36	97.3	48	36	97.3	47
68	38	48	36	94.7	48	37	97.4	47
72	32	48	36	112.5	48	36	112.5	46
77	37	48	37	100.0	47	36	97.3	46
81	38	47	38	100.0	47	36	94.7	45
86	36	46	37	102.8	47	36	100.0	43
90	37	46	38	102.7	47	36	97.3	41
92	37	46	38	102.7	46	35	94.6	41
94	38	45	38	100.0	46	35	92.1	41
96	37	45	34	91.9	45	35	94.6	41
98	35	45	37	105.7	45	33	94.3	40
100	36	45	37	102.8	43	34	94.4	40
102	36	44	36	100.0	42	34	94.4	39
FEMALE								
1	22	50	23	104.5	50	23	104.5	50
2	23	50	28	121.7	49	23	100.0	50
3	23	50	24	104.3	49	24	104.3	50
4	25	50	24	96.0	49	24	96.0	50
6	25	50	26	104.0	49	26	104.0	50
7	24	50	26	108.3	49	27	112.5	50
8	25	50	26	104.0	49	26	104.0	50
9	26	50	26	100.0	48	27	103.8	50
10	26	49	27	103.8	48	27	103.8	50
11	26	49	26	100.0	48	26	100.0	50
12	27	49	28	103.7	48	26	96.3	50
13	26	49	25	96.2	48	26	100.0	50
14	26	49	28	107.7	48	27	103.8	49
18	28	49	29	103.6	47	26	92.9	49
21	28	49	28	100.0	47	26	92.9	49
25	29	49	28	96.6	46	28	96.6	49
30	28	46	29	103.6	46	28	100.0	47
34	30	46	30	100.0	46	29	96.7	47
39	30	46	31	103.3	46	30	100.0	47
43	30	44	30	100.0	46	30	100.0	47
47	30	44	27	90.0	45	31	103.3	47
52	30	44	31	103.3	45	31	103.3	47
55	30	43	32	106.7	45	30	100.0	46
59	32	43	31	96.9	45	31	96.9	46
64	31	42	32	103.2	45	32	103.2	45
68	32	42	32	100.0	45	32	100.0	44
72	31	42	31	100.0	44	31	100.0	44
77	31	42	31	100.0	42	32	103.2	43
81	34	42	33	97.1	42	32	94.1	42
86	31	40	32	103.2	38	30	96.8	41
90	32	37	32	100.0	37	31	96.9	39
92	31	36	34	109.7	35	32	103.2	39
94	33	36	34	103.0	35	33	100.0	38
96	33	35	33	100.0	34	33	100.0	38
98	29	33	33	113.8	33	32	110.3	38
100	31	33	32	103.2	33	32	103.2	38
102	31	33	33	106.5	33	31	100.0	36

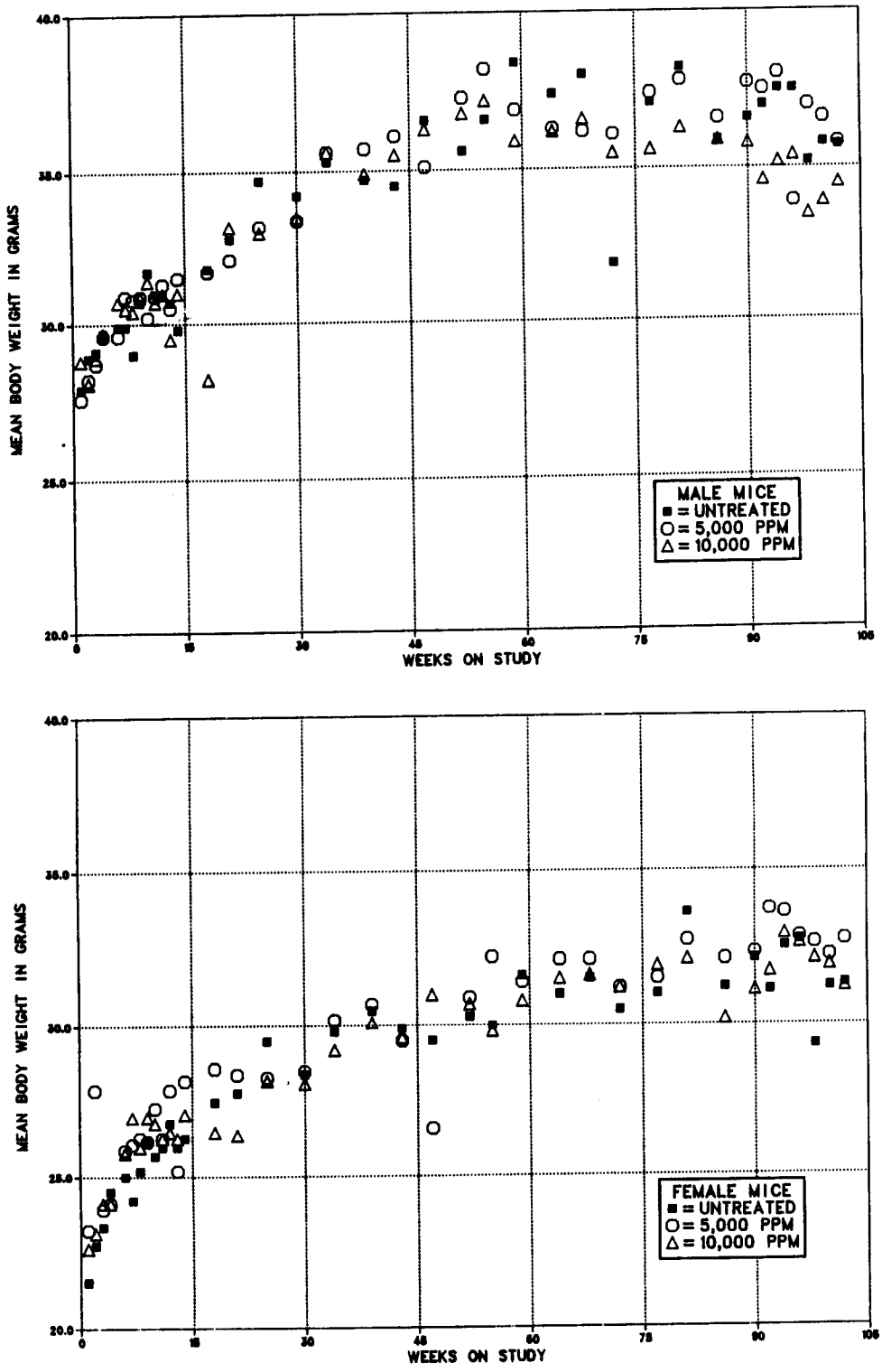

FIGURE 3. GROWTH CURVES FOR MICE EXPOSED TO PROPYLENE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female mice exposed to air containing propylene at the concentrations of this study are shown in Figure 4. No significant differences in survival were observed in the pairwise comparisons between any groups of either sex (Table 12).

Pathology and Statistical Analyses of Results

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 individual male and female mice. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2. Appendix E, Tables E3 and E4, contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes). Historical incidences of tumors in control animals are listed in Appendix F.

TABLE 12. SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
Male (a)			
Animals initially in study	50	50	50
Natural deaths before termination (b)	4	7	11
Accidentally killed	2	1	0
Killed at termination	44	42	38
Died during termination period	0	0	1
Survival P values (c)	0.067	0.542	0.099
Female (a)			
Animals initially in study	50	50	50
Natural deaths before termination (b)	16	16	14
Accidentally killed	1	0	0
Animals missexed	0	1	0
Killed at termination	33	32	34
Died during termination period	0	1	2
Survival P values (c)	0.848	0.946	0.910

(a) Terminal kill period: weeks 104-105
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

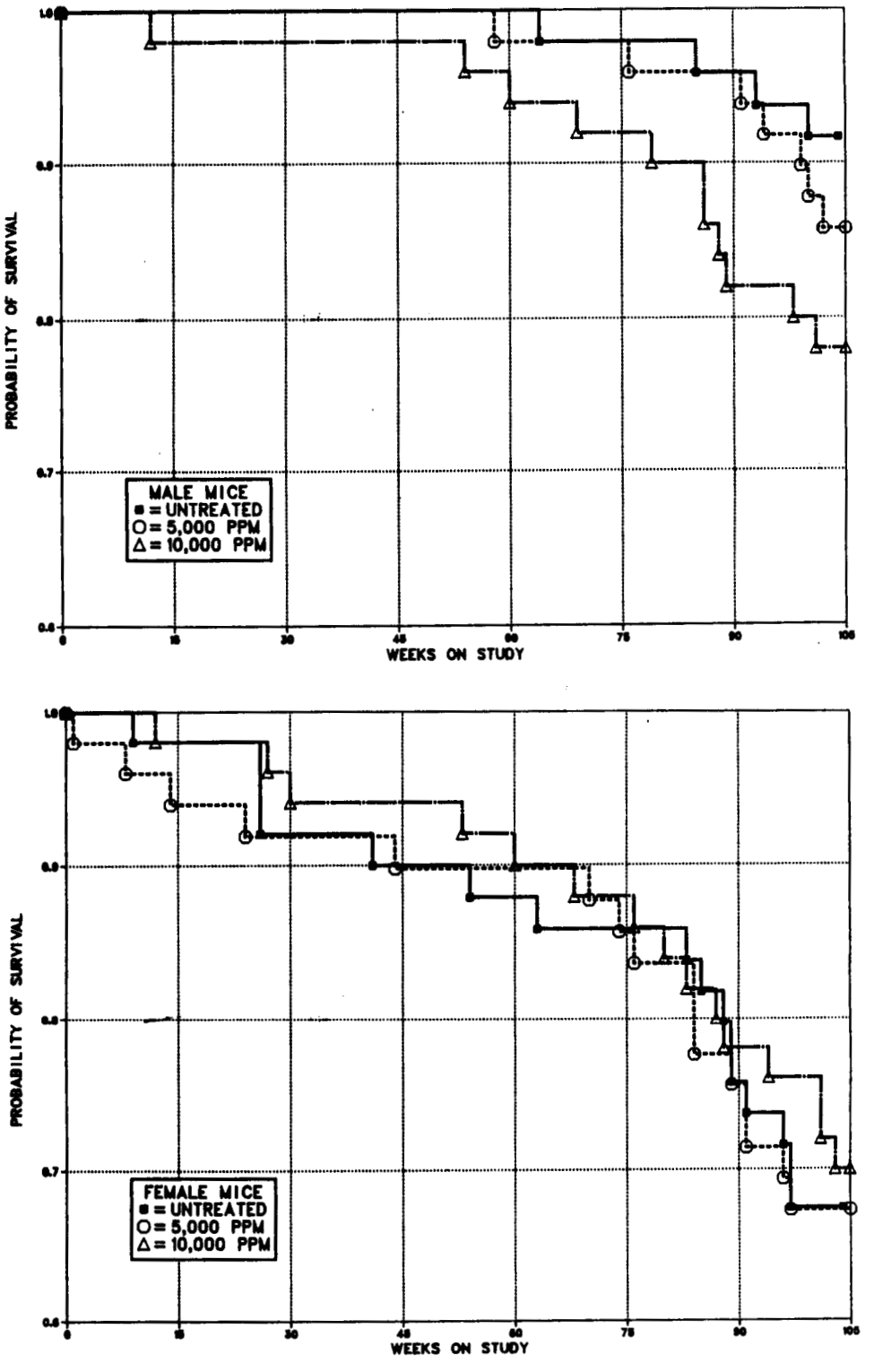

FIGURE 4. KAPLAN-MEIER SURVIVAL CURVES FOR MICE EXPOSED TO PROPYLENE BY INHALATION FOR TWO YEARS

Kidney: Chronic focal inflammation occurred at increased incidences in exposed mice: male--control, 0/50; low concentration, 17/49 (35%); high concentration, 9/49 (18%); female--control, 1/50, (2%); low concentration, 7/49, (14%); high concentration, 6/49, (12%). The renal lesion appeared to begin as a mild lymphocytic infiltrate around arcuate arteries and occasionaly extended to adjacent glomeruli. The involved glomeruli usually showed atrophy and mild fibrosis. The severity of the lesion was minimal and was similar in both control and exposed mice.

Lung: Compound-related nonneoplastic effects were not observed in male or female mice. The incidence of low concentration male mice with alveolar/bronchiolar carcinomas was significantly lower than in the controls (Table 13). Alveolar/bronchiolar adenomas or carcinomas (combined) occurred in male mice with a significant negative trend, and the incidences in the exposed groups were significantly lower than in the controls. The incidences of alveolar/bronchiolar adenomas or carcinomas (combined) in exposed female mice were not significantly different from those in the controls (control, 6/50, 12%; low, 4/49, 8%; high, 7/50, 14%).

TABLE 13. ANALYSIS OF LUNG TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
Alveolar/Bronchiolar Adenoma			
Overall Rates	7/50 (14%)	3/49 (6%)	3/50 (6%)
Adjusted Rates	15.9%	7.1%	7.7%
Terminal Rates	7/44 (16%)	3/42 (7%)	3/39 (8%)
Life Table Tests	P=0.143N	P=0.177N	P=0.210N
Incidental Tumor Tests	P=0.143N	P=0.177N	P=0.210N
Alveolar/Bronchiolar Carcinoma			
Overall Rates	9/50 (18%)	1/49 (2%)	4/50 (8%)
Adjusted Rates	19.9%	2.4%	10.3%
Terminal Rates	8/44 (18%)	1/42 (2%)	4/39 (10%)
Life Table Tests	P=0.086N	P=0.012N	P=0.167N
Incidental Tumor Tests	P=0.068N	P=0.009N	P=0.128N
Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates	16/50 (32%)	4/49 (8%)	7/50 (14%)
Adjusted Rates	35.4%	9.5%	17.9%
Terminal Rates	15/44 (34%)	4/42 (10%)	7/39 (18%)
Life Table Tests	P=0.025N	P=0.004N	P=0.055N
Incidental Tumor Tests	P=0.020N	P=0.003N	P=0.041N

Liver: Compound-related nonneoplastic effects were not observed in male or female mice. The incidence of low concentration male mice with adenomas was significantly lower than that in the controls, but the incidence of carcinomas in that group was slightly, although not significantly, higher than the control incidence (Table 14). The incidences of carcinomas and of adenomas or carcinomas (combined) in exposed male mice were not significantly different from those in the controls. Hepatocellular carcinomas were diagnosed in female mice (control, 2/50, 4%; low, 3/49, 6%; high, 5/49, 10%); no adenomas were observed.

TABLE 14. ANALYSIS OF LIVER TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
Adenoma			
Overall Rates	5/50 (10%)	0/49 (0%)	3/49 (6%)
Adjusted Rates	11.4%	0.0%	7.7%
Terminal Rates	5/44 (11%)	0/42 (0%)	3/39 (8%)
Life Table Tests	P=0.299N	P=0.038N	P=0.424N
Incidental Tumor Tests	P=0.299N	P=0.038N	P=0.424N
Carcinoma			
Overall Rates	9/50 (18%)	11/49 (22%)	12/49 (24%)
Adjusted Rates	19.9%	24.8%	28.1%
Terminal Rates	8/44 (18%)	9/42 (21%)	9/39 (23%)
Life Table Tests	P=0.192	P=0.365	P=0.229
Incidental Tumor Tests	P=0.324	P=0.397	P=0.369
Adenoma or Carcinoma			
Overall Rates	14/50 (28%)	11/49 (22%)	14/49 (29%)
Adjusted Rates	31.0%	24.8%	32.9%
Terminal Rates	13/44 (30%)	9/42 (21%)	11/39 (28%)
Life Table Tests	P=0.417	P=0.370N	P=0.453
Incidental Tumor Tests	P=0.512N	P=0.339N	P=0.567N

Circulatory System: Incidences of hemangiosarcomas and hemangiomas or hemangiosarcomas (combined) in female mice were increased significantly by all tests for trend, but the incidences in the high concentration group were not significantly higher than those in the controls (Table 15). These lesions were not site specific in female mice: hemangiosarcomas occurred in subcutaneous tissue, spleen, and uterus and hemangiomas occurred in the liver. The incidences of hemangiosarcomas in male mice did not differ significantly among exposed and control groups (control, 0/50; low, 1/49, 2%; high, 2/50, 4%); no hemangiomas were observed. In male mice, hemangiosarcomas occurred in the spleen and liver.

Uterus: Incidences of endometrial stromal polyps in female mice were significant by the trend tests; in pairwise comparisons, the incidences in the exposed groups were not significantly higher than the incidence in the controls (Table 16).

TABLE 15. ANALYSIS OF CIRCULATORY SYSTEM TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
Hemangiosarcoma			
Overall Rates	0/50 (0%)	0/49 (0%)	3/50 (6%)
Adjusted Rates	0.0%	0.0%	8.6%
Terminal Rates	0/33 (0%)	0/33 (0%)	3/35 (9%)
Life Table Tests	P=0.041	(a)	P=0.131
Incidental Tumor Tests	P=0.041	(a)	P=0.131
Hemangioma or Hemangiosarcoma			
Overall Rates	0/50 (0%)	1/49 (2%)	4/50 (8%)
Adjusted Rates	0.0%	2.7%	11.4%
Terminal Rates	0/33 (0%)	0/33 (0%)	4/35 (11%)
Life Table Tests	P=0.030	P=0.500	P=0.070
Incidental Tumor Tests	P=0.024	P=0.500	P=0.070

(a) No P value is presented because no tumors were observed in the 5,000-ppm and control groups.

TABLE 16. ANALYSIS OF ENDOMETRIAL STROMAL POLYPS OF THE UTERUS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Control	5,000 ppm	10,000 ppm
Overall Rates	0/47 (0%)	0/47 (0%)	3/48 (6%)
Adjusted Rates	0.0%	0.0%	8.6%
Terminal Rates	0/31 (0%)	0/33 (0%)	3/35 (9%)
Life Table Tests	P=0.044	(a)	P=0.143
Incidental Tumor Tests	P=0.044	(a)	P=0.143

(a) No P value is presented because no tumors were observed in the 5,000-ppm and control groups.

IV. DISCUSSION AND CONCLUSIONS

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Fourteen-day and 14-week studies were conducted to assess the toxicity of propylene in F344/N rats and B6C3F$_1$ mice at concentrations ranging from 625 to 10,000 ppm. No propylene-related toxic effects were observed. Inhalation toxicology and carcinogenesis studies of 2 years' duration were performed on F344/N rats and B6C3F$_1$ mice; exposure concentrations of 0 (chamber controls), 5,000, and 10,000 ppm were used. Concentrations greater than 10,000 ppm could not be safely tested in these studies because of the risk of explosion resulting from the flammability of the propylene/air mixtures (flammable range, 2.0%-11.1% by volume in air) (Kirk-Othmer, 1968).

In the 14-day and 14-week studies, propylene appeared to be nontoxic, since no compound-related deaths or clinical signs were observed. In addition, no gross or microscopic pathologic effects (including nasal cavity changes) were observed. A 4%-7% depression in final weight relative to the control weights occurred in female mice exposed to propylene for 14 weeks; these differences were not dose related. The only other short-term toxicologic data on propylene are from inhalation studies in which the liver was examined. Reynolds (1926) reported the occurrence of minimal fatty degeneration in the livers of 3/13 white mice that had received 1-20 exposures (60-90 minutes' duration) of 35% propylene. The proplyene used was impure, and no controls were included in the study. Conolly and Osimitz (1981) observed no hepatotoxic effects of inhaled propylene in Sprague-Dawley rats exposed to the chemical for 4 hours at concentrations up to 65,000 ppm. Thus, the results of these studies and the present study suggest a relative lack of toxicity of propylene in rodents exposed at concentrations up to 10,000 ppm for periods up to 14 weeks. These findings are consistent with available human data; except for central nervous system depression due apparently to exclusion of oxygen, no toxic effects were seen in workers exposed to propylene on a short-term basis in the workplace (MCA, 1974).

In the 2-year studies, neither concentration of propylene produced notable changes in weight gain, survival, or clinical signs in rats or mice. These results suggest that the 10,000-ppm concentration used in these studies may have been below the maximum concentration that could have been tolerated by male and female F344/N rats and B6C3F$_1$ mice; however, the use of higher concentrations was precluded due to concern over the flammability and explosivity of the gas.

Several nonneoplastic effects were observed in rats exposed to propylene in the 2-year studies. Squamous metaplasia of the respiratory epithelium of the nasal cavity occurred in female rats exposed to propylene at both concentrations and in male rats exposed at the high concentration. Inflammatory changes of the nasal cavity occurred in both male and female rats. The changes were characterized as unspecified inflammation and suppurative inflammation. The former lesion, consisting of a mild submucosal influx of lymphocytes, macrophages, and a few granulocytes, occurred in male rats exposed at the low concentration. The latter lesion was more severe and contained macrophages that migrated through the epithelium and accumulated in the lumen, occurring in male and female rats exposed at the high concentration. These two inflammatory lesions were combined numerically because they appeared to represent the same inflammatory process and varied only by degree and by the number of neutrophils. The combined incidence of these nasal cavity lesions was higher in male rats exposed at both concentrations and in female rats exposed at the high concentration than in controls. These changes may reflect local tissue responses to long-term inhalation exposure to propylene.

Chronic focal inflammation of the kidneys occurred at increased incidences in male and female mice exposed at both concentrations and appeared to be related to propylene exposure. The biologic relationship of the renal effect to propylene exposure is unknown.

The following discussion of neoplasms in F344/N rats and B6C3F$_1$ mice makes use of statistical comparisons between concurrent and exposed animals in the present study as well as with control animals from a concurrent inhalation study (propylene oxide) at the same laboratory or from feeding studies. Comparisons with propylene oxide were made because experimental conditions in both studies were similar. Comparisons with untreated controls from noninhalation studies as well as from other inhalation studies

were used because few inhalation studies have been conducted.

No evidence was found for a carcinogenic effect of propylene in rats. C-cell adenomas and C-cell adenomas or carcinomas (combined) of the thyroid gland occurred in female rats with a negative trend, and the incidence of C-cell adenomas in the high concentration group was significantly lower than that in the controls. The incidences in the controls (13%-15%) were higher than those observed in unexposed chamber control F344/N female rats in the propylene oxide inhalation study (C-cell adenomas, 1/45, 2.2%; C-cell adenomas or carcinomas, 2/45, 4.4%) (NTP, 1985) and in untreated control F344/N female rats in other studies (C-cell adenomas, 119/2,317, 5.1%; C-cell adenomas or carcinomas, 197/2,317, 8.5%). The incidences of C-cell hyperplasia occurred with a positive trend. In rats, C-cell hyperplasia, C-cell adenoma, and C-cell carcinoma appear to represent a continuous spectrum of progressive lesions. When hyperplasia, adenoma, and carcinoma are combined, the negative trend disappears. These comparisons suggest that the lower incidence of thyroid gland neoplasms is not related to administration of propylene.

In female mice, hemangiosarcomas alone or combined with hemangiomas occurred with positive trends; the incidences in both 10,000-ppm groups were not significantly higher than those in the controls or different from those observed in unexposed control $B6C3F_1$ female mice in the propylene oxide inhalation study conducted concurrently at this laboratory or in groups of untreated control $B6C3F_1$ female mice in other studies in this program. The three hemangiosarcomas and two hemangiomas were not site specific, occurring in the subcutaneous tissue, spleen, uterus, and liver. In the propylene oxide study (NTP, 1985), hemangiosarcomas and hemangiomas of the nasal cavity were related to chemical exposure; the vascular neoplasms at other sites were not considered to be related to propylene oxide administration. For these reasons, the neoplasms of the circulatory system in female mice are not considered to be related to exposure to propylene.

In contrast to the observations in rats, no compound-related nonneoplastic effects in the nasal cavity were observed in mice. The histopathologic procedures were identical for the two species of animals. This finding suggests that a species difference may exist between rats and mice in respiratory tract toxicity from propylene inhalation. The mechanism is unknown. Inhalation studies conducted with formaldehyde indicate that $B6C3F_1$ mice are better able to compensate, by reflex apnea, against inhalation of the gas than are F344 rats in response to sensory irritation of the nasal cavity. Chang et al. (1981, 1983) reported that $B6C3F_1$ mice responded to repeated inhalation exposures of formaldehyde with greater and more prolonged decreases in respiratory rate and minute volume than did F344 rats. In addition, the repeatedly exposed mice displayed more depressed baseline levels of respiratory minute volume than did the rats. This combination of factors resulted in a smaller intake of formaldehyde into the nasal cavity of the mice as compared with the rats, thereby providing a plausible explanation for less tissue damage and a smaller degree of respiratory tract toxicity. This species difference described for formaldehyde may also explain the observed difference in respiratory tract toxicity from propylene; however, this finding was not substantiated in the propylene oxide studies, where both nonneoplastic and neoplastic responses were observed in exposed mice (NTP, 1985).

Uterine endometrial stromal polyps occurred with a positive trend in female mice; the 6% incidence (3/48) of this lesion in the high concentration group was not significantly greater than that in the controls. The historical incidence of untreated control female $B6C3F_1$ mice with uterine endometrial stromal polyps is 22/2,411 (0.9%; range, 0%-6%). This marginally increased incidence of uterine endometrial stromal polyps in female mice is not considered to be clearly associated with exposure to propylene.

The incidences of exposed male mice with alveolar/bronchiolar adenomas or carcinomas occurred with a negative trend, and the incidences in both exposed groups were significantly less than those in the controls. The decreased

incidences of the combined pulmonary neoplasms did not appear to be concentration related. The incidence of these neoplasms in male mice may be exposure related, but decreased rates were not seen in the female mice or in the mice used in the propylene oxide studies (NTP, 1985). The incidences in the control and exposed groups in this study are within the range of incidences observed previously in untreated $B6C3F_1$ mice (Appendix F, Table F4). Therefore, the biologic significance of these reduced incidences is difficult to assess.

Hepatocellular adenomas were decreased marginally in the male mice exposed at 5,000 ppm but not in those exposed at 10,000 ppm. Because of this lack of an effect at the high concentration and since no significant differences were observed when the incidences of male mice with hepatocellular adenomas or with carcinomas were combined, the decreased incidence of hepatocellular adenomas in exposed male mice was considered to be unrelated to exposure to propylene.

The results of the present NTP studies in F344/N rats and $B6C3F_1$ mice appear to be similar to those obtained with Sprague-Dawley rats and Swiss mice (C. Maltoni, personal communication to NTP, 1981; Maltoni et al., 1982). In that study, inhalation of propylene at concentrations of 200, 1,000, or 5,000 ppm by mice for 18 months and rats for 24 months were not reported to produce a carcinogenic response.

Ethylene ($CH_2=CH_2$), another low-molecular-weight olefin structurally related to propylene, has been tested for carcinogenicity. Ethylene was administered by inhalation to male and female F344 rats at concentrations of 0, 300, 1,000, or 3,000 ppm for 6 hours per day, 5 days per week for 24 months. No carcinogenic responses were reported (CIIT, 1980).

Both propylene and ethylene contain double bonds that are capable of forming epoxides (Neal, 1980). In the case of ethylene, conversion to the epoxide form, ethylene oxide, has been demonstrated in male CBA mice following inhalation exposure (IARC, 1979). Transformation of ethylene, and presumably propylene as well, to an epoxide could be mediated by the cytochrome P-450 system (Neal, 1980). The epoxidated forms of both ethylene (i.e., ethylene oxide) and propylene (i.e., propylene oxide) have been tested for carcinogenic activity by the inhalation route of exposure, and both have been found to be carcinogenic in laboratory animals. Ethylene oxide produced peritoneal mesotheliomas in male F344 rats and mononuclear cell leukemia in female F344 rats, following inhalation exposure at concentrations up to 100 ppm for 2 years (Snellings et al., 1982); in another inhalation study, F344 rats exposed to ethylene oxide at 100 ppm developed mononuclear cell leukemia, peritoneal mesotheliomas, and mixed cell brain gliomas (Lynch et al., 1984). An inhalation study of ethylene oxide in $B6C3F_1$ mice is currently in progress in the NTP Carcinogenesis Program.

Propylene oxide has been tested in F344/N rats and $B6C3F_1$ mice in 2-year studies and was found to produce papillary adenomas of the nasal turbinates in rats and hemangiomas or hemangiosarcomas of the same tissue site in mice exposed at 400 ppm; inflammatory changes were found in the nasal epithelium for both species (NTP, 1985). Since studies indicate that neither propylene nor ethylene per se induces carcinogenic responses but their respective epoxidated forms do, epoxidation may not be the major biologic route of in vivo metabolism for these olefins. Styrene and styrene oxide are other examples (Huff, 1984).

Conclusions: Under the conditions of these studies, there was *no evidence of carcinogenicity** in male and female F344/N rats or in male and female $B6C3F_1$ mice exposed to propylene by inhalation at concentrations of 5,000 or 10,000 ppm for 103 weeks. In the nasal cavity, propylene induced squamous metaplasia of the respiratory epithelium in male and female rats and epithelial hyperplasia in female rats.

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

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	1 (2%)
BASAL-CELL TUMOR		1 (2%)	
KERATOACANTHOMA		1 (2%)	1 (2%)
SARCOMA, NOS			1 (2%)
FIBROMA	3 (6%)	1 (2%)	3 (6%)
FIBROSARCOMA		1 (2%)	1 (2%)
LIPOMA			1 (2%)
CARCINOSARCOMA	1 (2%)	1 (2%)	
OSTEOSARCOMA	1 (2%)		
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
#LUNG	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, INVASIV	1 (2%)		
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		
C-CELL CARCINOMA, METASTATIC	1 (2%)		
OSTEOSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
LEUKEMIA, MONONUCLEAR CELL	16 (32%)	13 (26%)	22 (44%)
#LYMPH NODE	(48)	(50)	(49)
CARCINOSARCOMA, INVASIVE		1 (2%)	
#MANDIBULAR L. NODE	(48)	(50)	(49)
OSTEOSARCOMA, METASTATIC		1 (2%)	
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
*MOUTH/ORAL MUCOSA	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
*TONGUE	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE		3 (6%)	3 (6%)
HEPATOCELLULAR CARCINOMA		1 (2%)	
#PANCREAS	(48)	(50)	(46)
ACINAR-CELL ADENOMA		1 (2%)	
#SMALL INTESTINE	(48)	(44)	(44)
ADENOCARCINOMA, NOS		1 (2%)	
#CECUM	(46)	(44)	(46)
ADENOCARCINOMA, NOS			1 (2%)
URINARY SYSTEM			
NONE			

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(48)	(47)
CARCINOMA, NOS		1 (2%)	
ADENOMA, NOS	12 (26%)	14 (29%)	16 (34%)
#ADRENAL	(50)	(50)	(49)
CORTICAL ADENOMA		1 (2%)	1 (2%)
CORTICAL CARCINOMA			1 (2%)
PHEOCHROMOCYTOMA	2 (4%)	5 (10%)	4 (8%)
PHEOCHROMOCYTOMA, MALIGNANT	2 (4%)		2 (4%)
GANGLIONEUROMA		1 (2%)	
#ADRENAL MEDULLA	(50)	(50)	(49)
PHEOCHROMOCYTOMA	1 (2%)	1 (2%)	1 (2%)
PHEOCHROMOCYTOMA, MALIGNANT			1 (2%)
#THYROID	(45)	(46)	(47)
FOLLICULAR-CELL ADENOMA	1 (2%)		2 (4%)
FOLLICULAR-CELL CARCINOMA	3 (7%)	2 (4%)	1 (2%)
C-CELL ADENOMA	2 (4%)	1 (2%)	3 (6%)
C-CELL CARCINOMA	2 (4%)		1 (2%)
#PANCREATIC ISLETS	(48)	(50)	(46)
ISLET-CELL ADENOMA	2 (4%)	1 (2%)	3 (7%)
ISLET-CELL CARCINOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
FIBROADENOMA		1 (2%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA, NOS		1 (2%)	2 (4%)
#TESTIS	(50)	(50)	(49)
INTERSTITIAL-CELL TUMOR	37 (74%)	36 (72%)	33 (67%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
CARCINOMA, NOS, INVASIVE		1 (2%)	
GRANULAR-CELL TUMOR, NOS			1 (2%)
GLIOMA, NOS		1 (2%)	
ASTROCYTOMA	1 (2%)		
SPECIAL SENSE ORGANS			
*EAR	(50)	(50)	(50)
NEUROFIBROSARCOMA		1 (2%)	
*ZYMBAL GLAND	(50)	(50)	(50)
CARCINOMA, NOS	1 (2%)		1 (2%)
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
*SKULL	(50)	(50)	(50)
OSTEOMA	1 (2%)		
BODY CAVITIES			
*THORACIC CAVITY	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
BODY CAVITIES (Continued)			
*PERITONEAL CAVITY	(50)	(50)	(50)
FIBROSARCOMA	1 (2%)		
MESOTHELIOMA, NOS	1 (2%)		
NEUROFIBROSARCOMA			1 (2%)
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	2 (4%)		3 (6%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
MESOTHELIOMA, NOS			1 (2%)
MESOTHELIOMA, MALIGNANT		2 (4%)	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	5	12	9
MORIBUND SACRIFICE	12	6	4
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	33	32	37
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	49	49	47
TOTAL PRIMARY TUMORS	96	98	112
TOTAL ANIMALS WITH BENIGN TUMORS	47	42	39
TOTAL BENIGN TUMORS	61	66	68
TOTAL ANIMALS WITH MALIGNANT TUMORS	25	25	32
TOTAL MALIGNANT TUMORS	32	29	36
TOTAL ANIMALS WITH SECONDARY TUMORS##	2	3	
TOTAL SECONDARY TUMORS	2	4	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	3	3	8
TOTAL UNCERTAIN TUMORS	3	3	8
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	49	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(49)	(50)	(50)
TRICHOEPITHELIOMA		1 (2%)	
FIBROMA	1 (2%)		
FIBROSARCOMA		1 (2%)	
LIPOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(48)	(50)
ALVEOLAR/BRONCHIOLAR ADENOMA		1 (2%)	1 (2%)
FIBROSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(49)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
LEUKEMIA, MONONUCLEAR CELL	13 (27%)	14 (28%)	15 (30%)
#LIVER	(48)	(48)	(49)
LEUKEMIA, MONONUCLEAR CELL			1 (2%)
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
*MOUTH/ORAL MUCOSA	(49)	(50)	(50)
SQUAMOUS CELL PAPILLOMA			1 (2%)
#LIVER	(48)	(48)	(49)
NEOPLASTIC NODULE			2 (4%)
*RECTUM	(49)	(50)	(50)
LEIOMYOSARCOMA		1 (2%)	
ENDOMETRIAL STROMAL SARCOMA, INV			1 (2%)
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(44)	(47)	(48)
CARCINOMA, NOS	1 (2%)	2 (4%)	
ADENOMA, NOS	18 (41%)	27 (57%)	21 (44%)
#ADRENAL	(47)	(46)	(47)
CORTICAL ADENOMA	1 (2%)		3 (6%)
PHEOCHROMOCYTOMA	1 (2%)	3 (7%)	1 (2%)
#THYROID	(39)	(47)	(47)
FOLLICULAR-CELL ADENOMA			1 (2%)
FOLLICULAR-CELL CARCINOMA	1 (3%)		1 (2%)
C-CELL ADENOMA	5 (13%)	2 (4%)	
C-CELL CARCINOMA	1 (3%)		2 (4%)
#PANCREATIC ISLETS	(44)	(46)	(47)
ISLET-CELL ADENOMA		1 (2%)	

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(50)
ADENOMA, NOS		1 (2%)	
ADENOCARCINOMA, NOS		1 (2%)	
FIBROADENOMA	9 (18%)	11 (22%)	6 (12%)
*CLITORAL GLAND	(49)	(50)	(50)
CARCINOMA, NOS		2 (4%)	
*VAGINA	(49)	(50)	(50)
ENDOMETRIAL STROMAL SARCOMA, INV		1	(2%)
#UTERUS	(46)	(47)	(49)
LEIOMYOSARCOMA			1 (2%)
ENDOMETRIAL STROMAL POLYP	3 (7%)	4 (9%)	4 (8%)
ENDOMETRIAL STROMAL SARCOMA	2 (4%)		2 (4%)
NERVOUS SYSTEM			
#BRAIN	(48)	(49)	(50)
CARCINOMA, NOS, INVASIVE		1 (2%)	
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*THORACIC CAVITY	(49)	(50)	(50)
LIPOMA			1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(50)	(50)
ENDOMETRIAL STROMAL SARCOMA, INV			1 (2%)
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	10	11	11
MORIBUND SACRIFICE	13	3	9
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	26	36	30
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA	1		
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF *PROPYLENE* (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	37	42	40
TOTAL PRIMARY TUMORS	57	73	63
TOTAL ANIMALS WITH BENIGN TUMORS	29	34	28
TOTAL BENIGN TUMORS	38	52	39
TOTAL ANIMALS WITH MALIGNANT TUMORS	19	19	21
TOTAL MALIGNANT TUMORS	19	21	22
TOTAL ANIMALS WITH SECONDARY TUMORS##		2	2
TOTAL SECONDARY TUMORS		2	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			2
TOTAL UNCERTAIN TUMORS			2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

• NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: CHAMBER CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	093	104	092	104	099	098	104	104	104	095	104	104	087	066	104	104	104	104	104	104	090	104	097	104
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																						X			
Carcinosarcoma																							X		
Osteosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, invasive															X										
Alveolar/bronchiolar carcinoma																									
C-cell carcinoma, metastatic																						X			
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	–	–	+	–	+	–	+	+	–	+	+	–	–	+	+	–	+	+	+	+	–	–	–
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS						X					X		X							X	X			X	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma					X													X				X			
Pheochromocytoma, malignant																									
Thyroid	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																						X			
Follicular cell carcinoma																		X							
C-cell adenoma																									
C-cell carcinoma			X																			X			
Parathyroid	–	+	+	–	–	+	+	–	+	–	+	+	+	–	+	+	+	–	+	+	+	–	+	+	+
Pancreatic islets	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma						X																			
REPRODUCTIVE SYSTEM																									
Mammary gland	+	N	+	N	+	N	+	+	+	N	N	+	+	N	N	+	N	+	+	N	+	N	+	N	+
Adenocarcinoma, NOS																									
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor	X	X	X				X	X	X	X		X	X	X		X	X		X		X	X	X		X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																									
SPECIAL SENSE ORGANS																									
Zymbal 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																									
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
Osteoma																									
BODY CAVITIES																									
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell carcinoma															X										
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															X										
Mesothelioma, NOS					X																				
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS												X													
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell		X	X	X			X		X			X					X							

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: : 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: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	0026	0027	0028	0029	0031	0032	0033	0034	0035	0036	0037	0038	0039	0040	0041	0042	0043	0044	0045	0046	0047	0048	0049	0050	TOTAL:
WEEKS ON STUDY	104	104	094	101	104	104	101	104	103	104	104	104	104	104	090	099	104	100	104	104	104	091	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma	X	X											X												3
Carcinosarcoma																									1
Osteosarcoma																									1
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, invasive																									1
Alveolar/bronchiolar carcinoma																					X				1
C-cell carcinoma, metastatic																									1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	49
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thymus	+	+	–	–	+	+	+	–	+	+	+	+	+	+	–	+	+	–	+	+	+	–	+	+	33
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	48
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	–	+	+	46
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																									
Pituitary	+	+	–	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	46
Adenoma, NOS													X			X		X	X		X			X	12
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma																									3
Pheochromocytoma, malignant					X								X												2
Thyroid	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	45
Follicular cell adenoma																									1
Follicular cell carcinoma												X	X												3
C-cell adenoma																	X	X							2
C-cell carcinoma																									2
Parathyroid	–	+	+	+	–	+	–	+	+	–	–	–	+	+	+	+	+	+	+	+	–	–	+	+	33
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Islet cell adenoma	X															X									2
Islet cell carcinoma																									1
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	N	N	+	N	N	+	N	N	+	+	N	+	+	+	+	N	+	N	+	N	N	*50
Adenocarcinoma, NOS																		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	37
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma			X																						1
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS										X															1
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	*50
Osteoma																	X								1
BODY CAVITIES																									
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Squamous cell carcinoma																									1
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Fibrosarcoma																									1
Mesothelioma, NOS																									1
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Mesothelioma, NOS						X																			2
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, *mononuclear cell*		X	X			X		X					X					X				X	X	X	16

* Animals Necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: LOW DOSE

ANIMAL NUMBER	0011	0012	0093	0044	0055	0066	0077	0088	0099	0110	0111	0122	0133	0144	0155	0166	0177	0188	0199	0200	0211	0222	0233	0244	0255
WEEKS ON STUDY	1004	1004	1004	0888	1004	1011	0776	0998	1004	1004	1004	1004	1004	1004	1004	0984	0889	1004	1004	1004	1004	1004	1004	0999	1004
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+
Squamous cell carcinoma																				X					
Basal cell tumor						X																			
Keratoacanthoma																									
Fibroma																X									
Fibrosarcoma																									
Carcinosarcoma																	X								
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasal cavity	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma																									
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	–	+	+	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinosarcoma, invasive																	X								
Osteosarcoma, metastatic																									
Thymus	+	+	+	+	–	+	–	+	–	+	–	+	+	+	+	+	–	–	–	+	+	+	+	–	
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
Squamous cell papilloma													X												
Squamous cell carcinoma																									
Salivary gland	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Neoplastic nodule												X		X	X										
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Acinar cell adenoma																									
Esophagus	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	
Small intestine	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	
Adenocarcinoma, NOS		X																							
Large intestine	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	–	
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Urinary bladder	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, NOS																		X							
Adenoma, NOS				X									X								X				
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Cortical adenoma																									
Pheochromocytoma													X			X					X				
Ganglioneuroma															X										
Thyroid	+	–	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma														X							X				
C-cell adenoma															X										
Parathyroid	–	–	–	+	–	–	–	+	+	–	+	–	–	+	+	+	+	–	+	–	+	+	+	–	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	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	
Prostate	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																		X							
Glioma, NOS																					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
Neurofibrosarcoma																									
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																	
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, malignant																									
Leukemia, mononuclear cell							X		X				X						X	X				X	

+ : **Tissue Examined Microscopically**
– : **Required Tissue Not Examined Microscopically**
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: *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: LOW DOSE (Continued)

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	099	104	104	104	104	094	104	104	104	104	099	104	104	103	104	094	104	104	104	096	092	104	097	104	104	
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	*50
Squamous cell carcinoma																										1
Basal cell tumor																										1
Keratoacanthoma							X																			1
Fibroma																										1
Fibrosarcoma					X																					1
Carcinosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic																X										1
Trachea	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Nasal cavity	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Osteosarcoma																X										1
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	45
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinosarcoma, invasive																										1
Osteosarcoma, metastatic																X										1
Thymus	+	–	+	–	+	–	+	–	+	+	–	+	+	–	–	+	+	–	+	+	+	–	–	–	+	31
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
Squamous cell carcinoma																				X						1
Salivary gland	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule																										3
Hepatocellular carcinoma										X																1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell adenoma																		X								1
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Small intestine	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	44
Adenocarcinoma, NOS																										1
Large intestine	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	48
Carcinoma, NOS																										1
Adenoma, NOS		X		X	X	X		X	X						X		X			X		X		X	14
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma																					X					1
Pheochromocytoma					X											X								X		6
Ganglioneuroma																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	46
Follicular cell carcinoma																										2
C-cell adenoma																										1
Parathyroid	+	+	+	+	+	+	+	+	+	–	–	+	+	+	–	+	–	+	+	+	–	–	–	+	+	31
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islet cell adenoma																				X						1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	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	36
Prostate	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	45
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS												X														1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS, invasive																										1
Glioma, NOS																										1
SPECIAL SENSE ORGANS																										
Ear	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	*50
Neurofibrosarcoma																	X									1
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	*50
Osteosarcoma																										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, malignant				X										X												2
Leukemia, mononuclear cell	X										X		X	X					X	X			X			13

* Animals Necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	101	104	055	101	104	104	104	104	104	100	104	104	104	090	104	104	104	104	104	097	104	088	104	100
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma														X											
Keratoacanthoma																									
Sarcoma, NOS										X															
Fibroma																									
Fibrosarcoma																									
Lipoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	–	–	+	+	+	+	+	+	+	+	–	+	+	–	–	–	+	+	+	–	–	+	+	+	–
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule										X															
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	–	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Small intestine	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	–	+	–
Large intestine	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–
Adenocarcinoma, NOS																			X						
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS		X	X			X										X		X		X					
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Cortical adenoma																									
Cortical carcinoma																									
Pheochromocytoma													X	X											
Pheochromocytoma, malignant				X				X																	
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Follicular cell adenoma																			X			X			
Follicular cell carcinoma															X										
C-cell adenoma			X																						
C-cell carcinoma																									
Parathyroid	+	+	+	–	–	+	–	+	–	+	+	–	+	–	–	+	+	+	+	–	+	+	+	+	–
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	–	+	+	+	+
Islet cell adenoma																				X					
REPRODUCTIVE SYSTEM																									
Mammary gland	+	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	
Prostate	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granular cell tumor, NOS																									
SPECIAL SENSE ORGANS																									
Zymbal 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
Carcinoma, NOS					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
Neurofibrosarcoma																							X		
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+
Mesothelioma, NOS														X											
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, NOS																									
Leukemia, mononuclear cell		X	X			X					X		X							X	X		X		X

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: HIGH DOSE (Continued)

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	099	104	104	104	104	062	104	104	104	104	104	100	104	104	104	073	104	104	104	104	104	101	104	104	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	*50	
Squamous cell carcinoma																						X			1	
Keratoacanthoma																									1	
Sarcoma, NOS																									1	
Fibroma						X			X						X										3	
Fibrosarcoma				X																					1	
Lipoma										X															1	
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Trachea	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	46	
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	48	
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	49	
Thymus	–	–	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	–	+	+	36	
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	47	
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Neoplastic nodule						X									X										3	
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50	
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	46	
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	–	+	+	47	
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48	
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	44	
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	46	
Adenocarcinoma, NOS																									1	
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47	
Adenoma, NOS						X			X			X	X		X					X	X	X		X	X	16	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Cortical adenoma																								X	1	
Cortical carcinoma									X																1	
Pheochromocytoma					X					X						X									5	
Pheochromocytoma, malignant															X										3	
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	47	
Follicular cell adenoma																									2	
Follicular cell carcinoma																									1	
C-cell adenoma										X														X	3	
C-cell carcinoma						X																			1	
Parathyroid	+	+	+	+	+	+	+	+	+	–	+	+	–	+	–	–	+	+	+	+	+	–	–	+	35	
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	46	
Islet cell adenoma											X								X						3	
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	N	+	N	+	+	+	+	N	+	N	N	N	+	N	+	+	N	+	N	+	N	+	*50	
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49	
Interstitial cell tumor	X	X	X	X	X	X		X	X	X	X	X			X	X		X	X		X			X	X	33	
Prostate	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45	
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50	
Carcinoma, NOS	X			X																					2	
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50	
Granular cell tumor, NOS																							X		1	
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50	
Carcinoma, NOS																									1	
BODY CAVITIES																										
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50	
Neurofibrosarcoma																									1	
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50	
Mesothelioma, NOS												X						X							3	
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	*50	
Mesothelioma, NOS									X																1	
Leukemia, mononuclear cell		X	X	X					X	X	X	X	X			X		X			X		X	X	22	

*Animals Necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: CHAMBER CONTROL

ANIMAL NUMBER	0001	0002	0003	0004	0005	0006	0007	0008	0009	0010	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025
WEEKS ON STUDY	1004	1004	0993	1004	0997	1004	1007	0704	1004	1004	1004	1004	0993	1004	1004	1004	1004	1004	1004	1004	0880	0871	1003	0997	0669
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	N	+	+
Fibroma																							X		
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	B	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	B	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Thymus	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	B	+	+	–	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	–	B	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	B	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	–
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	B	+	+	–	–
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	B	+	+	–	–
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	B	+	+	+	+
Urinary bladder	+	+	+	–	+	–	–	+	–	+	+	+	–	+	+	+	+	+	+	–	B	+	+	–	–
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	B	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS	X		X					X			X			X	X	X	X					X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
Cortical adenoma																				X					
Pheochromocytoma																									
Thyroid	+	+	+	+	–	+	+	–	+	+	+	+	–	+	+	+	+	+	+	–	B	+	+	–	–
Follicular cell carcinoma	X																								
C-cell adenoma							X																X		
C-cell carcinoma		X																							
Parathyroid	–	+	+	+	–	+	+	–	+	+	–	+	–	+	–	–	+	+	–	+	B	+	+	+	–
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	B	+	+	N	N
Fibroadenoma					X										X								X		
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	B	+	+	–	+
Endometrial stromal polyp																									
Endometrial stromal sarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	B	+	+	+	–
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	B	+	+	+	+
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	B	N	N	N	N
Malignant lymphoma, NOS																									X
Leukemia, mononuclear cell					X		X							X					X			X			

\+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	0026	0027	0028	0029	0030	0031	0032	0033	0034	0035	0036	0037	0038	0039	0040	0041	0042	0043	0044	0045	0046	0047	0048	0049	0050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	1003	1004	0609	0804	0871	1000	1004	0871	1111	0811	1003	0861	1004	1004	0904	1004	1004	1004	1004	1004	1004	1004	1001	0904	1004	
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*49
Sarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Trachea	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	46
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	45
Spleen	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	46
Lymph nodes	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thymus	+	+	–	+	+	–	–	–	+	–	+	+	+	–	–	+	–	+	+	+	+	–	–	+		36
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Bile duct	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Pancreas	+	+	+	–	+	+	–	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Small intestine	+	+	+	–	+	–	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	41
Large intestine	+	+	+	–	+	–	–	+	+	–	–	+	+	+	+	+	+	+	+	+	+	–	+	+		40
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		47
Urinary bladder	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	+			38
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	–	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Carcinoma, NOS																X										1
Adenoma, NOS	X						X	X			X			X	X		X			X			X			18
Adrenal	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		47
Cortical adenoma																										1
Pheochromocytoma																X										1
Thyroid	+	+	+	–	+	–	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+		39
Follicular cell carcinoma																										1
C-cell adenoma								X			X						X									5
C-cell carcinoma																										1
Parathyroid	+	+	+	–	–	–	+	+	+	–	+	+	+	–	+	+	+	–	+	–	–	+	+	+		32
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	+	+	+	N	+	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	*49
Fibroadenoma	X						X		X					X				X	X							9
Uterus	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Endometrial stromal polyp		X	X																						X	3
Endometrial stromal sarcoma						X								X												2
Ovary	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ALL OTHER SYSTEMS																										
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Malignant lymphoma, NOS																										1
Leukemia, mononuclear cell	X			X			X				X		X			X			X					X		13

* Animals Necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: LOW DOSE

ANIMAL NUMBER	0001	0002	0003	0004	0005	0006	0007	0008	0009	0010	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025
WEEKS ON STUDY	104	084	084	104	097	104	104	104	104	074	104	104	104	104	104	097	087	104	104	104	104	104	104	104	089
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+
Trichoepithelioma								X																	
Fibrosarcoma																	X								
Lipoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Fibrosarcoma, metastatic																	X								
Trachea	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	A	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+	+
Thymus	+	+	–	+	A	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Bile duct	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–
Esophagus	–	+	+	+	A	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–
Large intestine	+	–	+	+	A	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–
Rectum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leiomyosarcoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	A	+	+	+	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS						X																			
Adenoma, NOS	X	X		X			X			X			X	X						X	X	X	X	X	
Adrenal	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Pheochromocytoma	X																								
Thyroid	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
C-cell adenoma													X											X	
Parathyroid	+	–	+	+	A	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic islets	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	N	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N
Adenoma, NOS																						X			
Adenocarcinoma, NOS																								X	
Fibroadenoma		X										X	X		X		X		X		X		X		
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																							X		
Uterus	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal polyp				X																					
Ovary	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive																									
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell			X	X					X	X		X	X												X

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: LOW DOSE (Continued)

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	083	097	104	088	104	097	104	104	104	104	085	104	104	104	104	104	104	104	104	104	097	097	104	104	104	
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	N	N	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	*50
Trichoepithelioma																										1
Fibrosarcoma																										1
Lipoma																			X							1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Alveolar/bronchiolar adenoma															X											1
Fibrosarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+		47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	45
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		46
Thymus	–	–	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+		42
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	45
Stomach	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	46
Small intestine	+	–	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	43
Large intestine	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	42
Rectum	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leiomyosarcoma								X																		1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	46
Urinary bladder	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	43
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Carcinoma, NOS										X																2
Adenoma, NOS	X		X			X			X		X	X	X	X	X			X	X	X		X	X		X	27
Adrenal	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	46
Pheochromocytoma															X										X	3
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+		47
C-cell adenoma																										2
Parathyroid	–	–	–	–	+	+	+	–	+	+	–	–	–	–	–	+	–	+	+	–	+	–	–	–		30
Pancreatic islets	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Islet cell adenoma	X																									1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	+	+	N	+	+	+	+	+	+	+	N	N	+	N	N	+	N	+	+	+	+	+	+	*50
Adenoma, NOS																										1
Adenocarcinoma, NOS																										1
Fibroadenoma												X									X				X	11
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS												X														2
Uterus	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	47
Endometrial stromal polyp								X				X								X						4
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS, invasive										X																1
ALL OTHER SYSTEMS																										
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell				X		X				X	X	X					X			X						14

* Animals Necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: HIGH DOSE

ANIMAL NUMBER	0001	0002	0003	0004	0005	0006	0007	0008	0009	0010	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025
WEEKS ON STUDY	104	104	093	104	104	104	104	104	095	104	104	101	101	080	055	104	086	102	103	104	104	104	103	104	104
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																				X					
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+
Spleen	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	−	+	+	+	+	+	+	−	−	+	+	+	+	+	+	−	+	+	−	+
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
Squamous cell papilloma																						X			
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule											X														
Leukemia, mononuclear cell																									
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	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+
Rectum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N
Endometrial stromal sarcoma, invas															X										
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
Urinary bladder	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
Adenoma, NOS	X	X		X			X		X		X								X		X	X	X		X
Adrenal	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
Cortical adenoma																									
Pheochromocytoma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	−	−	+
Follicular cell adenoma																						X			
Follicular cell carcinoma																									
C-cell carcinoma								X													X				
Parathyroid	+	−	−	−	+	+	−	+	+	+	−	−	−	−	−	−	+	+	+	+	+	−	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	N	+	N	N	+	N	+	+	+	+	N	+	+	+	+
Fibroadenoma	X			X																			X		
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Endometrial stromal sarcoma, invas																X									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
Leiomyosarcoma																									X
Endometrial stromal polyp								X																	
Endometrial stromal sarcoma																X			X						
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																									
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Lipoma																									
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
Endometrial stromal sarcoma, invas																			X						
Leukemia, mononuclear cell							X	X				X	X	X			X			X			X		

\+ : Tissue Examined Microscopically
− : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: : 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: HIGH DOSE (Continued)

ANIMAL NUMBER	0226	0227	0228	0229	0330	0331	0332	0333	0334	0335	0336	0337	0338	0339	0440	0441	0442	0443	0444	0445	0446	0447	0448	0449	0550	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	1004	1004	1004	1004	1004	1004	0883	0889	1004	0983	1002	1004	1004	1004	0998	0996	1004	1004	1004	0787	1001	1004	0995	0968	0768	
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+		47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	–	+	+	+	+	–	+	+	+	+	–	–	+	+	+	+	+	–	+	+		42
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Thymus	+	+	+	+	+	+	–	+	+	–	+	+	–	+	–	+	+	+	+	+	+	+	+	–		40
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		*50
Squamous cell papilloma																										1
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Liver	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Neoplastic nodule			X																							2
Leukemia, mononuclear cell																								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		*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+		47
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	~	+	+	+	+	+	+	+	+	+		47
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	~	+	+	+	+	+	+	+	+	+		47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	~	–	+	+	+	+	+	+	+	+		45
Rectum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		*50
Endometrial stromal sarcoma, invas																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Urinary bladder	+	–	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+		44
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+		48
Adenoma, NOS					X		X		X	X	X					X	X		X				X	X		21
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+		47
Cortical adenoma									X			X					X									3
Pheochromocytoma										X																1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Follicular cell adenoma																										1
Follicular cell carcinoma																						X				1
C-cell carcinoma																										2
Parathyroid	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+		35
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+		*50
Fibroadenoma				X					X	X																6
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		*50
Endometrial stromal sarcoma, invas																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Leiomyosarcoma																										1
Endometrial stromal polyp		X	X	X																						4
Endometrial stromal sarcoma																										2
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
BODY CAVITIES																										
Pleura	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		*50
Lipoma																								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		*50
Endometrial stromal sarcoma, invas																										1
Leukemia, mononuclear cell			X				X			X			X		X	X				X						15

*Animals Necropsied

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(49)	(50)
FIBROSARCOMA		1 (2%)	
MYXOSARCOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(49)	(50)
HEPATOCELLULAR CARCINOMA, METAST	2 (4%)	1 (2%)	1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	7 (14%)	3 (6%)	3 (6%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	9 (18%)	1 (2%)	4 (8%)
FIBROSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(50)
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)	1 (2%)	1 (2%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	3 (6%)	4 (8%)	3 (6%)
MAST-CELL SARCOMA	1 (2%)		
#SPLEEN	(49)	(49)	(49)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)	1 (2%)	2 (4%)
#MESENTERIC L. NODE	(48)	(46)	(48)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
#SMALL INTESTINE	(44)	(43)	(44)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
CIRCULATORY SYSTEM			
#SPLEEN	(49)	(49)	(49)
HEMANGIOSARCOMA			2 (4%)
#LIVER	(50)	(49)	(49)
HEMANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEPATOCELLULAR ADENOMA	5 (10%)		3 (6%)
HEPATOCELLULAR CARCINOMA	9 (18%)	11 (22%)	12 (24%)
#STOMACH	(49)	(46)	(49)
LEIOMYOSARCOMA	1 (2%)		
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY INTERMEDIA	(48)	(43)	(49)
ADENOMA, NOS			1 (2%)
#ADRENAL	(46)	(48)	(48)
CORTICAL ADENOMA	1 (2%)	1 (2%)	
#ADRENAL/CAPSULE	(46)	(48)	(48)
ADENOMA, NOS	1 (2%)	1 (2%)	2 (4%)
#THYROID	(48)	(48)	(48)
FOLLICULAR-CELL ADENOMA		1 (2%)	1 (2%)
FOLLICULAR-CELL CARCINOMA	1 (2%)	1 (2%)	1 (2%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
#TESTIS	(50)	(48)	(49)
INTERSTITIAL-CELL TUMOR	2 (4%)		
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(49)	(50)
PAPILLARY CYSTADENOMA, NOS	2 (4%)	1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(49)	(50)
SARCOMA, NOS	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	4	6	11
MORIBUND SACRIFICE		1	1
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	44	42	38
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS	2	1	
ANIMAL MISSING			
ANIMAL MISSEXED			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	37	25	28
TOTAL PRIMARY TUMORS	45	30	37
TOTAL ANIMALS WITH BENIGN TUMORS	16	5	9
TOTAL BENIGN TUMORS	18	7	11
TOTAL ANIMALS WITH MALIGNANT TUMORS	24	21	21
TOTAL MALIGNANT TUMORS	27	23	26
TOTAL ANIMALS WITH SECONDARY TUMORS##	2	2	1
TOTAL SECONDARY TUMORS	2	2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(49)	(50)
SARCOMA, NOS			1 (2%)
FIBROSARCOMA		1 (2%)	1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(49)	(50)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA	6 (12%)	4 (8%)	6 (12%)
ALVEOLAR/BRONCHIOLAR CARCINOMA			2 (4%)
ADENOCA/SQUAM METAPLASIA, METAST		1 (2%)	
PHEOCHROMOCYTOMA, METASTATIC		1 (2%)	
FIBROSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(50)
MALIGNANT LYMPHOMA, NOS		1 (2%)	1 (2%)
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	4 (8%)	3 (6%)	6 (12%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	11 (22%)	6 (12%)	14 (28%)
MALIGNANT LYMPHOMA, MIXED TYPE	1 (2%)		1 (2%)
#SPLEEN	(47)	(48)	(46)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE		4 (8%)	
#LYMPH NODE	(50)	(46)	(49)
LEIOMYOSARCOMA, METASTATIC			1 (2%)
#KIDNEY	(50)	(49)	(49)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
CIRCULATORY SYSTEM			
*SUBCUT TISSUE	(50)	(49)	(50)
HEMANGIOSARCOMA			1 (2%)
#SPLEEN	(47)	(48)	(46)
HEMANGIOSARCOMA			1 (2%)
#LIVER	(50)	(49)	(49)
HEMANGIOMA		1 (2%)	1 (2%)
#UTERUS	(47)	(47)	(48)
HEMANGIOSARCOMA			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEPATOCELLULAR CARCINOMA	2 (4%)	3 (6%)	5 (10%)
#ESOPHAGUS	(47)	(45)	(44)
NEUROFIBROMA		1 (2%)	
URINARY SYSTEM			
NONE			

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(41)	(44)	(44)
ADENOMA, NOS	2 (5%)	2 (5%)	1 (2%)
CHROMOPHOBE ADENOMA	11 (27%)	9 (20%)	9 (20%)
CHROMOPHOBE CARCINOMA	4 (9%)	3 (7%)	
#ADRENAL	(45)	(48)	(48)
PHEOCHROMOCYTOMA, MALIGNANT		1 (2%)	
#ADRENAL/CAPSULE	(45)	(48)	(48)
ADENOMA, NOS		1 (2%)	
#THYROID	(45)	(48)	(47)
FOLLICULAR-CELL ADENOMA	4 (9%)	2 (4%)	5 (11%)
FOLLICULAR-CELL CARCINOMA		1 (2%)	
#PANCREATIC ISLETS	(46)	(44)	(43)
ISLET-CELL ADENOMA	1 (2%)		1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(49)	(50)
ADENOCARCINOMA, NOS	2 (4%)	2 (4%)	
ADENOCA/SQUAMOUS METAPLASIA		1 (2%)	
#VAGINA	(50)	(49)	(50)
FIBROMA			1 (2%)
#UTERUS	(47)	(47)	(48)
LEIOMYOSARCOMA	1 (2%)	1 (2%)	2 (4%)
ENDOMETRIAL STROMAL POLYP			3 (6%)
#OVARY	(45)	(48)	(47)
CYSTADENOMA, NOS			1 (2%)
GRANULOSA-CELL TUMOR			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(50)	(49)	(50)
CHROMOPHOBE CARCINOMA, INVASIVE		1 (2%)	
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(49)	(50)
PAPILLARY CYSTADENOMA, NOS		1 (2%)	1 (2%)
PAPILLARY CYSTADENOCARCINOMA, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	14	13	13
MORIBUND SACRIFICE	2	4	3
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	33	32	34
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS	1		
ANIMAL MISSING			
ANIMAL MISSEXED		1	
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	31	35	39
TOTAL PRIMARY TUMORS	45	49	71
TOTAL ANIMALS WITH BENIGN TUMORS	18	17	16
TOTAL BENIGN TUMORS	24	21	29
TOTAL ANIMALS WITH MALIGNANT TUMORS	21	25	32
TOTAL MALIGNANT TUMORS	21	28	41
TOTAL ANIMALS WITH SECONDARY TUMORS##	1	4	1
TOTAL SECONDARY TUMORS	1	4	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			1
TOTAL UNCERTAIN TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: CHAMBER CONTROL

ANIMAL NUMBER	0001	0002	0003	0004	0005	0006	0007	0008	0009	0010	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025
WEEKS ON STUDY	104	085	104	104	104	104	104	104	104	093	104	104	080	104	104	104	104	104	104	104	099	104	104	104	104
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																								X	
Alveolar/bronchiolar adenoma	X							X	X																
Alveolar/bronchiolar carcinoma						X									X	X						X			
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Malig. lymphoma, histiocytic type																	X								
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+
Thymus	+	+	–	–	–	–	+	+	–	–	–	+	–	–	+	+	+	–	+	–	–	+	+	–	–
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma												X						X							X
Hepatocellular carcinoma				X					X				X										X	X	
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	N	+	+	+	N	+	+	N	N	N	+	+	N	N	N	+	N	+	N	N	N	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Leiomyosarcoma										X															
Small intestine	+	–	+	+	–	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Large intestine	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Cortical adenoma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+
Follicular cell carcinoma			X																						
Parathyroid	–	–	–	–	+	–	–	+	+	–	–	+	+	–	+	+	+	–	+	+	–	+	–	–	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor									X																
Prostate	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	–	–	+	+	–	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papillary cystadenoma, NOS					X																				
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS		X																							
Malig. lymphoma, lymphocytic type															X										
Malig. lymphoma, histiocytic type	X			-																					
Mast cell sarcoma																									

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: CHAMBER CONTROL (Continued)

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	104	104	104	104	104	100	104	104	104	104	104	104	104	104	104	104	104	104	104	104	104	064	104	104	TISSUES TUMORS
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic													X													2
Alveolar/bronchiolar adenoma						X			X		X					X										7
Alveolar/bronchiolar carcinoma								X				X						X	X				X			9
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Malig. lymphoma, histiocytic type																										1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thymus	–	–	+	+	+	+	–	+	+	+	–	+	–	–	+	–	+	+	+	+	+	+	–	–	+	27
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																X								X		5
Hepatocellular carcinoma													X	X						X	X					9
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	N	+	N	+	+	+	+	+	+	+	+	+	N	+	N	N	+	N	N	N	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leiomyosarcoma																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	46
Adenoma, NOS																	X									1
Cortical adenoma													X													1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	48
Follicular cell carcinoma																										1
Parathyroid	–	+	+	+	–	+	–	–	+	–	–	–	–	+	–	–	–	+	+	–	+	–	+	–	+	23
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell tumor	X																									2
Prostate	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	–	+	+	–		41
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Papillary cystadenoma, NOS					X																					2
ALL OTHER SYSTEMS																										
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Sarcoma, NOS																										1
Malig. lymphoma, lymphocytic type																										1
Malig. lymphoma, histiocytic type							X								X											3
Mast cell sarcoma																				X						1

* Animals Necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: 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	105	105	105	105	094	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																									
Myxosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																									
Alveolar/bronchiolar adenoma	X		X																						X
Alveolar/bronchiolar carcinoma																									
Fibrosarcoma, metastatic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malig. lymphoma, histiocytic type																									
Lymph nodes	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malig. lymphoma, histiocytic type																									
Thymus	–	+	–	+	–	+	+	–	+	+	+	+	–	+	+	+	–	+	–	+	+	+	–	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma	X	X		X										X			X			X			X		
Hemangiosarcoma					X																				
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	+	N	N	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	–	+	–	–	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	–	+	+	+	–	+	–	+	–	+	+	–	+	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Cortical adenoma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									X
Follicular cell carcinoma																									
Parathyroid	+	–	+	–	+	–	+	+	+	+	–	–	+	+	–	+	+	–	–	–	–	+	–	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papillary cystadenoma, NOS													X												
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malig. lymphoma, lymphocytic type																									
Malig. lymphoma, histiocytic type		X																					X		

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: LOW DOSE (Continued)

ANIMAL NUMBER	0262	0271	0289	0290	0301	0312	0334	0335	0336	0337	0338	0339	0340	0411	0412	0413	0414	0415	0416	0417	0418	0419	0550	TOTAL:
WEEKS ON STUDY	0366	1055	1055	1055	1055	0767	1055	1055	1055	0700	1055	0999	1055	0588	1058	1059	1059	1059	0991	1005	1059	1059	1050	TISSUES TUMORS
INTEGUMENTARY SYSTEM																								
Subcutaneous tissue	B	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	*49
Fibroma																			X					1
Myxosarcoma																						X		1
RESPIRATORY SYSTEM																								
Lungs and bronchi	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma, metastatic						X																		1
Alveolar/bronchiolar adenoma																								3
Alveolar/bronchiolar carcinoma											X													1
Fibrosarcoma, metastatic																			X					1
Trachea	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																								
Bone marrow	B	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	48
Spleen	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Malig. lymphoma, histiocytic type															X									1
Lymph nodes	B	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	46
Malig. lymphoma, histiocytic type		X																						1
Thymus	B	–	–	+	+	–	+	+	–	+	+	+	–	+	+	+	+	+	–	–	–	+	+	–	+	32
CIRCULATORY SYSTEM																								
Heart	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																								
Salivary gland	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	48
Liver	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma						X		X			X									X				11
Hemangiosarcoma																								1
Bile duct	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	B	+	+	+	+	N	+	N	+	+	N	+	N	+	N	+	+	+	+	N	+	+	+	N	*49
Pancreas	B	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+	46
Esophagus	B	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+	41
Stomach	B	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	–	+	+	+	+	46
Small intestine	B	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	–	+	+	–	+	+	+	+	43
Large intestine	B	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	45
URINARY SYSTEM																								
Kidney	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																								
Pituitary	B	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Adrenal	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	48
Adenoma, NOS																X								1
Cortical adenoma																X								1
Thyroid	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Follicular cell adenoma																								1
Follicular cell carcinoma			X																					1
Parathyroid	B	+	+	+	–	+	–	–	+	+	–	–	+	–	+	–	–	–	+	–	–	–	+	–	–	24
REPRODUCTIVE SYSTEM																								
Mammary gland	B	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Testis	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	48
Prostate	B	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	46
NERVOUS SYSTEM																								
Brain	B	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																								
Harderian gland	B	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Papillary cystadenoma, NOS																								1
ALL OTHER SYSTEMS																								
Multiple organs NOS	B	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Malig. lymphoma, lymphocytic type														X										1
Malig. lymphoma, histiocytic type											X	X												4

* Animals Necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: HIGH DOSE

ANIMAL NUMBER	0001	0002	0003	0004	0005	0006	0007	0008	0009	0010	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025
WEEKS ON STUDY	098	105	105	086	105	105	105	105	105	086	105	088	105	105	105	105	105	105	105	105	105	105	105	105	105
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic															X										
Alveolar/bronchiolar adenoma		X																							
Alveolar/bronchiolar carcinoma							X	X																	X
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma								X																	
Malig. lymphoma, histiocytic type										X															
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	−	+	+	−	−	−	−	+	−	−	−	−	+	+	−	+	+	+	+	−	+	−	−	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma						X															X				
Hepatocellular carcinoma									X	X	X	X			X			X		X					X
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	+	N	N	+	+	+	+	N	N	N	+	+	+	+	N	N	+	N	N	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	−	+	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Malig. lymphoma, histiocytic type																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Adenoma, NOS																									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS														X											
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
Parathyroid	−	+	−	+	+	+	+	+	−	+	−	+	+	−	+	+	−	−	−	+	−	+	−	+	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORG																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papillary cystadenoma, 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
Malig. lymphoma, lymphocytic type				X																					
Malig. lymphoma, histiocytic type	X																								

\+ : Tissue Examined Microscopically
− : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: HIGH DOSE (Continued)

ANIMAL NUMBER	0262	0271	0288	0299	0300	0311	0322	0333	0344	0355	0366	0377	0388	0399	0401	0411	0422	0433	0444	0455	0466	0477	0488	0499	0500	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	1005	1005	1005	1005	1005	1005	1005	0898	1005	1005	1005	0954	1005	1005	0779	1005	0669	1011	1005	1004	1005	0601	0102	1005		
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma			X																			X				3
Alveolar/bronchiolar carcinoma	X																									4
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	49
Hemangiosarcoma		X																								2
Malig. lymphoma, histiocytic type																		X								2
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	48
Thymus	–	–	+	+	+	+	+	–	–	+	+	+	+	+	+	–	+	+	–	+	–	+	–	–	–	27
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	49
Hepatocellular adenoma			X																							3
Hepatocellular carcinoma		X	X													X									X	12
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	+	N	+	+	+	N	N	N	+	+	+	+	N	+	+	N	N	+	N	N	+	N	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+		48
Esophagus	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	47
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	44
Malig. lymphoma, histiocytic type																	X									1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	–	+	–	+	+	+	+		45
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS		X																								1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	48
Adenoma, NOS										X																2
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	48
Follicular cell adenoma										X																1
Follicular cell carcinoma																	X									1
Parathyroid	+	–	–	–	–	+	+	–	–	–	+	–	+	+	+	–	+	+	+	+	–	+	–	+	–	27
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	49
Prostate	+	–	–	+	+	+	+	+	–	+	+	–	–	+	+	+	+	+	–	+	+	+	+	–	+	42
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Papillary cystadenoma, 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
Malig. lymphoma, lymphocytic type																										1
Malig. lymphoma, histiocytic type								X	X																	3

*Animals Necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: CHAMBER CONTROL

ANIMAL NUMBER	00101	00102	00103	00104	00105	00106	00107	00108	00109	00111	00112	00113	00114	00115	00116	00117	00118	00119	00201	00221	00222	00223	00224	00225
WEEKS ON STUDY	08303	10414	10414	02606	10404	10404	10404	10404	10404	10404	10404	10404	10404	09707	10404	10404	10404	10404	10404	02606	10404	08501	04101	10404
RESPIRATORY SYSTEM																								
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma, metastatic																								
Alveolar/bronchiolar adenoma								X								X	X						
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	–	+	+	–	+	+	+	+	–	+	+	–	+	+	+	+	+	–	+	–	+
CIRCULATORY SYSTEM																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma							X																	
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	+	N	+	+	N	+	+	N	+	+	N	+	N	+	+	+	+	+	N	+	N	N	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	–	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	–	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																								
Pituitary	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	–	+	+	+
Adenoma, NOS														X										
Chromophobe adenoma					X					X	X	X	X				X					X		
Adrenal	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma											X							X						
Parathyroid	–	–	–	–	+	–	–	–	–	–	+	+	–	–	–	–	–	–	+	+	–	–	+	–	–
Pancreatic islet	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+
Islet cell adenoma																								
REPRODUCTIVE SYSTEM																								
Mammary gland	N	+	+	+	+	+	+	+	N	+	N	N	+	+	N	+	+	+	+	N	+	N	N	+
Adenocarcinoma, NOS																X								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																								
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+
NERVOUS SYSTEM																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																								
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malig. lymphoma, lymphocytic type						X				X	X													
Malig. lymphoma, histiocytic type			X						X								X		X			X		
Malignant lymphoma, mixed type														X										

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: : No Tissue Information Submitted
C : Necropsy, No Histology Due To Protocol
A : Autolysis
M : Animals Missing
B : No Necropsy Performed

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	063	089	104	104	104	043	104	104	104	026	104	096	088	104	054	104	091	089	104	097	104	009	104	104		
RESPIRATORY SYSTEM																										
Lungs and bronchi	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma, metastatic	X																									1
Alveolar/bronchiolar adenoma	X													X					X							6
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	47
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	-	+	+	-	+	-	+	+	-	+	+	+	-	-	+	-	+	+	+	+	-	A	-	+	34
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma	X																									2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	N	+	+	+	+	+	N	+	N	N	+	+	N	+	+	N	+	+	N	N	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	A	+	+	46
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	47
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	49
Small intestine	+	+	+	+	+	+	-	+	+	-	+	-	-	+	+	+	+	-	+	+	+	+	A	+	+	40
Large intestine	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	-	-	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	41
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	-	+	+	+	-	+	-	+	+	+	+	+	+	+	-	+	+	A	+	+	41
Adenoma, NOS																X										2
Chromophobe adenoma					X		X												X		X					11
Adrenal	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	A	+	+	45
Thyroid	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	-	45
Follicular cell adenoma														X		X										4
Parathyroid	-	-	+	+	-	-	-	+	-	+	-	+	+	-	+	-	+	-	-	-	-	-	A	-	-	14
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	A	+	+	46
ISlet cell adenoma																		X								1
REPRODUCTIVE SYSTEM *																										
Mammary gland	+	+	+	N	N	+	+	+	+	N	+	N	N	N	N	+	+	+	+	+	+	N	N	+	+	*50
Adenocarcinoma, NOS																					X					2
Uterus	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Leiomyosarcoma													X													1
Ovary	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	45
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malig. lymphoma, lymphocytic type											X															4
Malig. lymphoma, histiocytic type									X			X		X			X	X				X				11
Malignant lymphoma, mixed type																										1

* Animals Necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: LOW DOSE

ANIMAL NUMBER	0012	0091	0053	0864	0705	1056	1047	1058	1059	1051	1052	1053	1054	0975	0446	1056	0996	0841	0201	0841	1055	1055	1058
WEEKS ON STUDY	084	091	105	086	070	105	104	105	105	105	105	105	105	097	044	105	096	084	001	084	105	105	108
INTEGUMENTARY SYSTEM																							
Subcutaneous tissue	+	+	+	–	+	+	N	+	+	+	+	+	+	+	N	+	+	N	N	+	+	+	+
Fibrosarcoma															X								
RESPIRATORY SYSTEM																							
Lungs and bronchi	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma			X											X							X		
Adenoca/Squam metaplasia, metastatic																	X						
Pheochromocytoma, metastatic							X																
Fibrosarcoma, metastatic														X									
Trachea	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																							
Bone marrow	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+
Malig. lymphoma, histiocytic type			X			X																	
Lymph nodes	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Thymus	–	–	+	–	–	–	–	+	+	+	–	+	+	–	+	+	–	–	–	+	+	+	+
CIRCULATORY SYSTEM																							
Heart	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																							
Salivary gland	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																							
Hemangioma																							
Bile duct	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	N	–	N	+	N	+	N	+	+	N	+	+	N	N	+	N	+	N	N	+	+
Pancreas	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+
Esophagus	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Neurofibroma																							
Stomach	+	+	+	–	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Small intestine	+	+	+	–	–	+	–	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+
Large intestine	+	+	+	–	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																							
Kidney	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	A
ENDOCRINE SYSTEM																							
Pituitary	+	+	+	–	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	A
Adenoma, NOS												X											
Chromophobe adenoma							X	X								X							
Chromophobe carcinoma		X				X				X													
Adrenal	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																							
Pheochromocytoma, malignant							X																
Thyroid	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma											X												
Follicular cell carcinoma												X											
Parathyroid	+	+	+	–	–	+	–	–	–	+	–	–	–	+	–	–	+	–	+	–	–	+	–	A
REPRODUCTIVE SYSTEM																							
Mammary gland	+	+	+	–	+	+	N	+	+	+	+	+	+	+	N	N	+	+	N	N	+	+	+	N	+
Adenocarcinoma, NOS																							
Adenoca/squamous metaplasia																		X					
Uterus	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Leiomyosarcoma					X																		
Ovary	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
NERVOUS SYSTEM																							
Brain	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Chromophobe carcinoma, invasive		X																					
SPECIAL SENSE ORGANS																							
Harderian gland	N	N	N	–	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papillary cystadenoma, 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
Malignant lymphoma, NOS																							
Malig. lymphoma, lymphocytic type															X			X					
Malig. lymphoma, histiocytic type												X								X		X	

+ : Tissue Examined Microscopically
– : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: LOW DOSE (Continued)

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	105	105	105	105	024	105	014	105	105	105	105	105	105	105	105	091	105	089	105	076	074	105	105	105	105	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	N	+	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	*49
Fibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma								X																		4
Adenoca/squam metaplasia, metastatic																										1
Pheochromocytoma, metastatic																										1
Fibrosarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+		47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Malig. lymphoma, histiocytic type				X											X											4
Lymph nodes	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		46
Thymus	+	+	+	+	–	–	+	+	–	+	+	+	–	–	+	–	–	–	+	–	+	+	–	–		28
CIRCULATORY SYSTEM																										
Heart	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Hepatocellular carcinoma	X							X	X																	3
Hemangioma																X										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Gallbladder & common bile duct	+	N	+	+	N	+	+	+	+	+	+	+	+	N	+	N	N	N	+	N	N	+	+	+		*49
Pancreas	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+		44
Esophagus	–	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+		45
Neurofibroma						X																				1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Small intestine	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+		41
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+		45
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Urinary bladder	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+		43
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+		44
Adenoma, NOS											X															2
Chromophobe adenoma	X	X				X		X	X							X										9
Chromophobe carcinoma																								X		4
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Adenoma, NOS				X																						1
Pheochromocytoma, malignant																										1
Thyroid	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Follicular cell adenoma																X										2
Follicular cell carcinoma																										1
Parathyroid	–	+	–	+	–	+	–	–	–	–	+	+	+	–	+	+	–	+	+	–	–	–	–	+	–	21
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	+	+	N	+	+	+	+	+	+	+	N	+	N	+	+	+	+	+	N	+	+	+	+	*49
Adenocarcinoma, NOS	X																							X		2
Adenoca/squamous metaplasia																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	47
Leiomyosarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Chromophobe carcinoma, invasive																										1
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*49
Papillary cystadenoma, 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	*49
Malignant lymphoma, NOS																			X							1
Malig. lymphoma, lymphocytic type																				X						3
Malig. lymphoma, histiocytic type												X					X				X					6

* Animals Necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE: HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	105	105	088	012	105	105	027	053	105	087	105	105	105	105	105	105	105	030	105	105	105	105	105	105	103
INTEGUMENTARY SYSTEM																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+
Sarcoma, NOS																	X								
Fibrosarcoma	-																								
Hemangiosarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma										X										X		X			
Alveolar/bronchiolar carcinoma																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Spleen	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Hemangiosarcoma																						X			
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
Leiomyosarcoma, metastatic								X																	
Thymus	+	-	-	-	+	+	+	-	+	-	+	-	+	+	+	+	-	-	-	+	-	+	+	+	-
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Hepatocellular carcinoma												X	X											X	
Hemangioma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Gallbladder & common bile duct	+	+	+	N	+	+	+	+	+	+	+	N	+	+	N	+	+	N	N	+	N	+	N	+	N
Pancreas	+	+	+	+	+	+	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Esophagus	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Large intestine	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Malig. lymphoma, histiocytic type													X												
Urinary bladder	+	+	-	+	+	+	-	+	+	+	+	-	+	-	+	+	-	+	+	+	+	+	+	+	-
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS											X														
Chromophobe adenoma										X							X			X		X		X
Chromophobe carcinoma																X									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Thyroid	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma												X								X					
Parathyroid	-	+	-	-	-	+	+	-	-	+	+	+	+	+	-	-	+	-	-	-	-	+	-	-	+
Pancreatic islets	+	+	+	+	+	+	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	N	N	+	+	N	+	+	N	+	+	+	+	+	N	N	+	N	N	+	+	N	
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Fibroma												X													
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Leiomyosarcoma								X													X				
Endometrial stromal polyp												X											X		
Hemangiosarcoma																	X								
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Cystadenoma, NOS																					X				
Granulosa cell tumor																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papillary cystadenoma, NOS																									
Papillary cystadenocarcinoma, NOS						X																			
ALL OTHER SYSTEMS																									
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS																									
Malig. lymphoma, lymphocytic type			X	X											X									X	X
Malig. lymphoma, histiocytic type									X					X		X	X		X		X				
Malignant lymphoma, mixed type											X														

+ : Tissue Examined Microscopically
- : Required Tissue Not Examined Microscopically
X : Tumor Incidence
N : Necropsy, No Autolysis, No Microscopic Examination
S : Animal Missexed
: 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: HIGH DOSE (Continued)

ANIMAL NUMBER	0262	0272	0282	0299	0300	0311	0325	0333	0344	0355	0361	0371	0388	0399	0401	0411	0423	0434	0445	0456	0467	0478	0489	0490	0500	TOTAL:
WEEKS ON STUDY	1005	1005	1005	1005	1005	1011	1005	0766	1005	1005	1001	1005	0883	1005	1005	1005	1005	1005	0606	0688	0944	1005	1005	1004	0880	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Subcutaneous tissue	+	+	+	+	+	+	N	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																										1
Fibrosarcoma						X																				1
Hemangiosarcoma																							X			1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma										X					X	X										6
Alveolar/bronchiolar carcinoma										X	X															2
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Hemangiosarcoma																										1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leiomyosarcoma, metastatic																										1
Thymus	+	+	+	+	–	–	–	+	+	+	–	–	–	–	–	–	–	–	+	+	–	+	+	+	–	26
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hepatocellular carcinoma							X																X			5
Hemangioma															X											1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	+	+	+	N	+	+	+	+	N	+	N	+	+	+	+	+	+	N	N	+	+	N	N	*50
Pancreas	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	43
Esophagus	+	+	+	+	+	+	+	–	–	–	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	44
Stomach	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Small intestine	+	+	+	+	+	–	+	–	+	+	–	+	–	+	+	+	+	+	–	–	+	+	–	+	+	42
Large intestine	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	–	+	+	+	+	+	+	+	+	–	42
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Malig. lymphoma, histiocytic type																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
ENDOCRINE SYSTEM																										
Pituitary	–	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	–	+	+	+	+	44
Adenoma, NOS																										1
Chromophobe adenoma				X	X											X							X			9
Chromophobe carcinoma		X																							X	3
Adrenal	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	47
Follicular cell adenoma		X							X	X																5
Parathyroid	+	–	–	–	+	–	–	+	–	–	+	–	+	–	+	–	–	–	–	–	+	–	–	–	–	18
Pancreatic islets	+	+	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	43
Islet cell adenoma									X																	1
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	+	N	+	+	+	N	+	+	N	+	+	+	+	+	+	N	+	+	+	+	N	+	N	*50
Vagina	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Fibroma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leiomyosarcoma																										2
Endometrial stromal polyp				X																						3
Hemangiosarcoma																										1
Ovary	+	+	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	47
Cystadenoma, NOS																										1
Granulosa cell tumor									X								-									1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Harderian gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Papillary cystadenoma, NOS																						X				1
Papillary cystadenocarcinoma, NOS																										1
ALL OTHER SYSTEMS																										
Multiple organs NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS													X													1
Malig. lymphoma, lymphocytic type																				X						6
Malig. lymphoma, histiocytic type			X					X		X					X				X		X			X	X	14
Malignant lymphoma, mixed type																										1

* Animals Necropsied

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
ACANTHOSIS		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	2 (4%)		1 (2%)
INFLAMMATION, SUPPURATIVE	2 (4%)		
INFLAMMATION, CHRONIC FOCAL			1 (2%)
NECROSIS, FAT			2 (4%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
FOREIGN BODY, NOS	1 (2%)	2 (4%)	2 (4%)
INFLAMMATION, NOS	4 (8%)	14 (28%)	5 (10%)
INFLAMMATION, SUPPURATIVE	7 (14%)	7 (14%)	14 (28%)
GRANULATION, TISSUE			1 (2%)
DEGENERATION, NOS			2 (4%)
HYPERPLASIA, EPITHELIAL	2 (4%)	2 (4%)	5 (10%)
METAPLASIA, SQUAMOUS	2 (4%)	19 (38%)	7 (14%)
*LARYNX	(50)	(50)	(50)
INFLAMMATION, NOS		7 (14%)	
INFLAMMATION, SUPPURATIVE	9 (18%)	7 (14%)	9 (18%)
METAPLASIA, SQUAMOUS		1 (2%)	
#TRACHEA	(49)	(49)	(46)
INFLAMMATION, NOS	1 (2%)	9 (18%)	2 (4%)
INFLAMMATION, SUPPURATIVE	2 (4%)		
HYPERPLASIA, EPITHELIAL	1 (2%)	1 (2%)	
METAPLASIA, SQUAMOUS		3 (6%)	3 (7%)
#LUNG/BRONCHIOLE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	2 (4%)		1 (2%)
HYPERPLASIA, EPITHELIAL	1 (2%)	2 (4%)	
POLYP, INFLAMMATORY		1 (2%)	
#LUNG	(50)	(50)	(50)
FOREIGN BODY, NOS			1 (2%)
CONGESTION, NOS	3 (6%)	4 (8%)	3 (6%)
HEMORRHAGE	2 (4%)	2 (4%)	4 (8%)
INFLAMMATION, INTERSTITIAL	2 (4%)		1 (2%)
BRONCHOPNEUMONIA, ACUTE			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, GRANULOMATOUS		1 (2%)	1 (2%)
PIGMENTATION, NOS			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	3 (6%)	4 (8%)	6 (12%)
METAPLASIA, OSSEOUS			2 (4%)
#LUNG/ALVEOLI	(50)	(50)	(50)
HISTIOCYTOSIS	1 (2%)	1 (2%)	3 (6%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(48)	(45)	(48)
FIBROSIS	1 (2%)		2 (4%)
#SPLEEN	(50)	(50)	(50)
HEMORRHAGE			1 (2%)
FIBROSIS			3 (6%)
FIBROSIS, FOCAL	1 (2%)	1 (2%)	2 (4%)
NECROSIS, FOCAL	1 (2%)		

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM			
#SPLEEN (Continued)	(50)	(50)	(50)
PIGMENTATION, NOS		1 (2%)	
HEMOSIDEROSIS	2 (4%)		1 (2%)
HYPERPLASIA, LYMPHOID		2 (4%)	
HEMATOPOIESIS	4 (8%)	3 (6%)	1 (2%)
HEMATOPOIESIS	4 (8%)	3 (6%)	1 (2%)
#LYMPH NODE	(48)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC	10 (21%)	2 (4%)	6 (12%)
PIGMENTATION, NOS		1 (2%)	
HYPERPLASIA, NOS	1 (2%)	13 (26%)	7 (14%)
#LUNG	(50)	(50)	(50)
LEUKOCYTOSIS, NOS		2 (4%)	1 (2%)
HYPERPLASIA, LYMPHOID		7 (14%)	1 (2%)
HEMATOPOIESIS	1 (2%)		
#LIVER	(50)	(50)	(50)
LEUKOCYTOSIS, NOS			1 (2%)
HEMATOPOIESIS	2 (4%)	1 (2%)	
#ADRENAL	(50)	(50)	(49)
HEMATOPOIESIS	1 (2%)		1 (2%)
#THYMUS	(33)	(31)	(36)
DEGENERATION, CYSTIC		1 (3%)	
ATROPHY, NOS	1 (3%)		1 (3%)
HYPERPLASIA, EPITHELIAL	1 (3%)		
CIRCULATORY SYSTEM			
#LYMPH NODE	(48)	(50)	(49)
LYMPHANGIECTASIS		1 (2%)	1 (2%)
*NASAL CAVITY	(50)	(50)	(50)
THROMBOSIS, NOS		2 (4%)	1 (2%)
#HEART	(50)	(50)	(50)
THROMBUS, MURAL		1 (2%)	2 (4%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	2 (4%)	1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
FIBROSIS	24 (48%)	34 (68%)	34 (68%)
DEGENERATION, NOS	1 (2%)		1 (2%)
HEMOSIDEROSIS	1 (2%)		
#CARDIAC VALVE	(50)	(50)	(50)
THROMBOSIS, NOS			1 (2%)
INFLAMMATION, NOS			1 (2%)
*BLOOD VESSEL	(50)	(50)	(50)
THROMBOSIS, NOS			2 (4%)
INFLAMMATION, NOS			3 (6%)
*PALATE	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		
#KIDNEY	(50)	(50)	(49)
THROMBOSIS, NOS			1 (2%)
DIGESTIVE SYSTEM			
*TOOTH	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	3 (6%)		
#SALIVARY GLAND	(48)	(47)	(47)
INFLAMMATION, NOS	1 (2%)		
ATROPHY, NOS	1 (2%)	1 (2%)	2 (4%)
HYPERPLASIA, DIFFUSE			1 (2%)
#LIVER	(50)	(50)	(50)
CONGESTION, NOS		1 (2%)	2 (4%)
INFLAMMATION, FOCAL		1 (2%)	
INFLAMMATION GRANULOMATOUS FOCAL		1 (2%)	

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
#LIVER (Continued)	(50)	(50)	(50)
DEGENERATION, NOS	2 (4%)	4 (8%)	2 (4%)
DEGENERATION, CYSTIC		2 (4%)	1 (2%)
DEGENERATION, LIPOID	17 (34%)	15 (30%)	19 (38%)
NECROSIS, NOS		2 (4%)	1 (2%)
NECROSIS, FOCAL	2 (4%)	2 (4%)	3 (6%)
NECROSIS, CENTRAL	1 (2%)	2 (4%)	
CYTOPLASMIC CHANGE, NOS		1 (2%)	
BASOPHILIC CYTO CHANGE	26 (52%)	26 (52%)	22 (44%)
FOCAL CELLULAR CHANGE		1 (2%)	
EOSINOPHILIC CYTO CHANGE	4 (8%)	2 (4%)	6 (12%)
ANGIECTASIS	1 (2%)	5 (10%)	2 (4%)
REGENERATION, NOS			1 (2%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
DEGENERATION, NOS	2 (4%)	2 (4%)	3 (6%)
#LIVER/PERIPORTAL	(50)	(50)	(50)
FIBROSIS			2 (4%)
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	47 (94%)	44 (88%)	39 (78%)
#PANCREAS	(48)	(50)	(46)
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
ATROPHY, FOCAL	6 (13%)	11 (22%)	1 (2%)
ATROPHY, DIFFUSE	7 (15%)	2 (4%)	3 (7%)
HYPERPLASIA, FOCAL		1 (2%)	
#PANCREATIC ACINUS	(48)	(50)	(46)
FOCAL CELLULAR CHANGE		2 (4%)	
HYPERPLASIA, FOCAL		1 (2%)	
#STOMACH	(50)	(47)	(48)
INFLAMMATION, NOS	2 (4%)		
ULCER, NOS	1 (2%)	1 (2%)	
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
EROSION	1 (2%)		
HYPERPLASIA, EPITHELIAL	10 (20%)	6 (13%)	2 (4%)
HYPERKERATOSIS	1 (2%)		
#COLON	(46)	(44)	(46)
PARASITISM	4 (9%)	2 (5%)	4 (9%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
MINERALIZATION			4 (8%)
HYDRONEPHROSIS	1 (2%)		
PYELONEPHRITIS, ACUTE	1 (2%)	2 (4%)	
NEPHROPATHY	48 (96%)	44 (88%)	45 (92%)
NEPHROSIS, NOS		2 (4%)	
INFARCT, NOS			1 (2%)
LIPOIDOSIS	1 (2%)		
PIGMENTATION, NOS	1 (2%)		
#KIDNEY/TUBULE	(50)	(50)	(49)
MINERALIZATION	1 (2%)		
PIGMENTATION, NOS	48 (96%)	46 (92%)	47 (96%)
#KIDNEY/PELVIS	(50)	(50)	(49)
MINERALIZATION		2 (4%)	1 (2%)
NECROSIS, NOS		1 (2%)	
HYPERPLASIA, EPITHELIAL	1 (2%)	1 (2%)	
#URINARY BLADDER	(50)	(47)	(49)
CALCULUS, GROSS OBSERVATION ONLY		1 (2%)	
INFLAMMATION, SUPPURATIVE	1 (2%)	1 (2%)	
HYPERPLASIA, EPITHELIAL	1 (2%)	1 (2%)	1 (2%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
URINARY SYSTEM (Continued)			
#U. BLADDER/MUCOSA	(50)	(47)	(49)
HYPERPLASIA, NOS	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(48)	(47)
CYST, NOS	8 (17%)	2 (4%)	2 (4%)
HEMORRHAGE			2 (4%)
HYPERPLASIA, FOCAL	15 (33%)	12 (25%)	6 (13%)
ANGIECTASIS		1 (2%)	
#PITUITARY POSTERIOR	(46)	(48)	(47)
EMBRYONAL REST		1 (2%)	
#ADRENAL	(50)	(50)	(49)
HEMORRHAGE		1 (2%)	
DEGENERATION, CYSTIC		1 (2%)	
DEGENERATION, LIPOID	14 (28%)	11 (22%)	12 (24%)
NECROSIS, NOS		1 (2%)	1 (2%)
ANGIECTASIS	1 (2%)		
#ADRENAL CORTEX	(50)	(50)	(49)
DEGENERATION, LIPOID		1 (2%)	
HYPERPLASIA, FOCAL	9 (18%)	9 (18%)	12 (24%)
#ADRENAL MEDULLA	(50)	(50)	(49)
HYPERPLASIA, NOS	2 (4%)	3 (6%)	3 (6%)
#THYROID	(45)	(46)	(47)
CYST, NOS		1 (2%)	
HEMORRHAGE	1 (2%)		
HYPERPLASIA, EPITHELIAL			1 (2%)
HYPERPLASIA, C-CELL	4 (9%)	7 (15%)	9 (19%)
#THYROID FOLLICLE	(45)	(46)	(47)
HYPERPLASIA, CYSTIC			1 (2%)
#PARATHYROID	(33)	(31)	(35)
HYPERPLASIA, FOCAL			1 (3%)
#PANCREATIC ISLETS	(48)	(50)	(46)
HYPERPLASIA, NOS		1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	2 (4%)		
HYPERPLASIA, NOS	18 (36%)	26 (52%)	27 (54%)
*PREPUCE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
ABSCESS, NOS	1 (2%)		
HYPERPLASIA, EPITHELIAL	1 (2%)		
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)	1 (2%)	
#PROSTATE	(49)	(45)	(45)
INFLAMMATION, NOS	3 (6%)	1 (2%)	
INFLAMMATION, SUPPURATIVE	13 (27%)	9 (20%)	2 (4%)
HYPERPLASIA, NOS	2 (4%)	1 (2%)	1 (2%)
HYPERPLASIA, FOCAL	4 (8%)	5 (11%)	2 (4%)
*SEMINAL VESICLE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	6 (12%)	15 (30%)	12 (24%)
#TESTIS	(50)	(50)	(49)
MINERALIZATION	21 (42%)	14 (28%)	21 (43%)
ATROPHY, NOS	38 (76%)	38 (76%)	38 (78%)
HYPERPLASIA, INTERSTITIAL CELL	6 (12%)	9 (18%)	6 (12%)
HYPERPLASIA, MESOTHELIAL			1 (2%)
*EPIDIDYMIS	(50)	(50)	(50)
GRANULOMA, SPERMATIC		1 (2%)	2 (4%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
HEMORRHAGE	5 (10%)	4 (8%)	7 (14%)
PERIVASCULAR CUFFING	1 (2%)		
NECROSIS, FOCAL	3 (6%)	3 (6%)	1 (2%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
*EYE/LACRIMAL GLAND	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
*NASOLACRIMAL DUCT	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	12 (24%)	5 (10%)	9 (18%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERITONEAL CAVITY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
HYPERPLASIA, NOS			1 (2%)
ADIPOSE TISSUE			
MINERALIZATION		1	
SPECIAL MORPHOLOGY SUMMARY			
NONE			

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

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	49	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	49	49	50
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
*NASAL CAVITY	(49)	(50)	(50)
FOREIGN BODY, NOS		1 (2%)	2 (4%)
INFLAMMATION, NOS		3 (6%)	2 (4%)
INFLAMMATION, SUPPURATIVE	8 (16%)	7 (14%)	11 (22%)
HYPERPLASIA, EPITHELIAL		4 (8%)	9 (18%)
METAPLASIA, NOS			1 (2%)
METAPLASIA, SQUAMOUS		15 (30%)	6 (12%)
*LARYNX	(49)	(50)	(50)
INFLAMMATION, NOS	1 (2%)	4 (8%)	8 (16%)
INFLAMMATION, SUPPURATIVE	7 (14%)	5 (10%)	8 (16%)
METAPLASIA, SQUAMOUS		1 (2%)	1 (2%)
#TRACHEA	(46)	(47)	(47)
INFLAMMATION, NOS	2 (4%)	2 (4%)	4 (9%)
METAPLASIA, SQUAMOUS			1 (2%)
#LUNG/BRONCHIOLE	(49)	(48)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
HYPERPLASIA, EPITHELIAL	2 (4%)		
#LUNG	(49)	(48)	(50)
EMPHYSEMA, NOS		1 (2%)	
CONGESTION, NOS	3 (6%)	7 (15%)	7 (14%)
EDEMA, NOS	1 (2%)		
HEMORRHAGE	6 (12%)	1 (2%)	3 (6%)
INFLAMMATION, INTERSTITIAL	2 (4%)	1 (2%)	2 (4%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	1 (2%)	
INFLAMMATION, GRANULOMATOUS		1 (2%)	1 (2%)
GRANULOMA, FOREIGN BODY	2 (4%)		
FIBROSIS, FOCAL	2 (4%)		1 (2%)
NECROSIS, FOCAL		1 (2%)	
PIGMENTATION, NOS	1 (2%)		2 (4%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	3 (6%)	3 (6%)	3 (6%)
#LUNG/ALVEOLI	(49)	(48)	(50)
HISTIOCYTOSIS	2 (4%)	4 (8%)	3 (6%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(45)	(45)	(42)
FIBROSIS	1 (2%)		3 (7%)
HISTIOCYTOSIS	1 (2%)		
#SPLEEN	(46)	(48)	(48)
HEMORRHAGE		1 (2%)	
FIBROSIS	1 (2%)		
FIBROSIS, FOCAL		1 (2%)	
PIGMENTATION, NOS	1 (2%)	2 (4%)	1 (2%)
HEMOSIDEROSIS		1 (2%)	
ATROPHY, NOS	1 (2%)		
HEMATOPOIESIS	3 (7%)	2 (4%)	4 (8%)
#SPLENIC CAPSULE	(46)	(48)	(48)
NECROSIS, FOCAL	1 (2%)		

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#LYMPH NODE	(48)	(46)	(49)
CONGESTION, NOS			2 (4%)
INFLAMMATION, ACUTE/CHRONIC	6 (13%)	4 (9%)	9 (18%)
FIBROSIS			1 (2%)
NECROSIS, NOS			1 (2%)
HYPERPLASIA, NOS		10 (22%)	2 (4%)
ERYTHROPHAGOCYTOSIS	2 (4%)		1 (2%)
HEMATOPOIESIS	2 (4%)		1 (2%)
#LUNG	(49)	(48)	(50)
LEUKOCYTOSIS, NOS			3 (6%)
HYPERPLASIA, LYMPHOID	1 (2%)	3 (6%)	2 (4%)
#LIVER	(48)	(48)	(49)
LEUKOCYTOSIS, NOS	2 (4%)	1 (2%)	
HEMATOPOIESIS	1 (2%)	1 (2%)	2 (4%)
#THYMUS	(36)	(42)	(40)
DEGENERATION, CYSTIC			2 (5%)
ATROPHY, NOS	2 (6%)		1 (3%)
HYPERPLASIA, EPITHELIAL		1 (2%)	
CIRCULATORY SYSTEM			
#LYMPH NODE	(48)	(46)	(49)
LYMPHANGIECTASIS			1 (2%)
*NASAL CAVITY	(49)	(50)	(50)
THROMBOSIS, NOS	1 (2%)	1 (2%)	3 (6%)
#LUNG	(49)	(48)	(50)
THROMBOSIS, NOS			1 (2%)
#HEART	(49)	(49)	(50)
DILATATION, NOS			1 (2%)
THROMBOSIS, NOS	1 (2%)		
THROMBUS, MURAL		1 (2%)	4 (8%)
INFLAMMATION, ACUTE/CHRONIC	2 (4%)		3 (6%)
INFLAMMATION, CHRONIC		1 (2%)	
FIBROSIS	3 (6%)	14 (29%)	11 (22%)
DEGENERATION, NOS		1 (2%)	1 (2%)
#CARDIAC VALVE	(49)	(49)	(50)
THROMBOSIS, NOS		1 (2%)	
INFLAMMATION, NOS		1 (2%)	
*BLOOD VESSEL	(49)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
DIGESTIVE SYSTEM			
*PALATE	(49)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
HYPERPLASIA, EPITHELIAL			1 (2%)
#SALIVARY GLAND	(44)	(47)	(50)
ATROPHY, NOS		1 (2%)	
#LIVER	(48)	(48)	(49)
CONGESTION, NOS			1 (2%)
INFLAMMATION, FOCAL	1 (2%)	4 (8%)	3 (6%)
DEGENERATION, NOS	3 (6%)	3 (6%)	7 (14%)
DEGENERATION, CYSTIC			1 (2%)
DEGENERATION, LIPOID	6 (13%)	10 (21%)	7 (14%)
NECROSIS, NOS			3 (6%)
NECROSIS, FOCAL	3 (6%)	7 (15%)	1 (2%)
NECROSIS, CENTRAL	2 (4%)		3 (6%)
PIGMENTATION, NOS			2 (4%)
BASOPHILIC CYTO CHANGE	32 (67%)	28 (58%)	25 (51%)
EOSINOPHILIC CYTO CHANGE	1 (2%)	1 (2%)	
CLEAR-CELL CHANGE	1 (2%)		
ANGIECTASIS	1 (2%)		1 (2%)
REGENERATION, NOS		1 (2%)	
#LIVER/CENTRILOBULAR	(48)	(48)	(49)
DEGENERATION, NOS	5 (10%)		4 (8%)
#BILE DUCT	(48)	(48)	(49)
HYPERPLASIA, NOS	12 (25%)	18 (38%)	12 (24%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#PANCREAS	(44)	(46)	(47)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
ATROPHY, FOCAL	1 (2%)	2 (4%)	4 (9%)
ATROPHY, DIFFUSE		2 (4%)	
#STOMACH	(48)	(46)	(47)
HEMORRHAGE	1 (2%)		
INFLAMMATION, NOS	2 (4%)		2 (4%)
ULCER, NOS		1 (2%)	1 (2%)
INFLAMMATION, SUPPURATIVE	2 (4%)		1 (2%)
EROSION	2 (4%)		
HYPERPLASIA, EPITHELIAL	7 (15%)	3 (7%)	10 (21%)
#COLON	(40)	(42)	(45)
INFLAMMATION, SUPPURATIVE			1 (2%)
PARASITISM	3 (8%)	4 (10%)	
URINARY SYSTEM			
#KIDNEY	(47)	(46)	(48)
HYDRONEPHROSIS			1 (2%)
NEPHROPATHY	42 (89%)	37 (80%)	41 (85%)
NEPHROSIS, NOS	2 (4%)	1 (2%)	1 (2%)
PIGMENTATION, NOS			1 (2%)
#KIDNEY/TUBULE	(47)	(46)	(48)
PIGMENTATION, NOS	40 (85%)	43 (93%)	46 (96%)
#KIDNEY/PELVIS	(47)	(46)	(48)
MINERALIZATION	6 (13%)	11 (24%)	9 (19%)
#URINARY BLADDER	(38)	(43)	(44)
INFLAMMATION, SUPPURATIVE		1 (2%)	
HYPERPLASIA, EPITHELIAL		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(44)	(47)	(48)
CYST, NOS	2 (5%)	4 (9%)	11 (23%)
HEMORRHAGE		1 (2%)	
PIGMENTATION, NOS	1 (2%)	1 (2%)	
HYPERPLASIA, NOS			1 (2%)
HYPERPLASIA, FOCAL	7 (16%)	2 (4%)	8 (17%)
ANGIECTASIS	6 (14%)	3 (6%)	3 (6%)
#ADRENAL	(47)	(46)	(47)
CONGESTION, NOS	1 (2%)		
DEGENERATION, CYSTIC	1 (2%)		
DEGENERATION, LIPOID	4 (9%)	13 (28%)	8 (17%)
PIGMENTATION, NOS	1 (2%)		1 (2%)
ANGIECTASIS		1 (2%)	2 (4%)
#ADRENAL CORTEX	(47)	(46)	(47)
DEGENERATION, LIPOID	5 (11%)		1 (2%)
NECROSIS, NOS			1 (2%)
HYPERPLASIA, NOS	2 (4%)		
HYPERPLASIA, FOCAL	9 (19%)	15 (33%)	15 (32%)
#ADRENAL MEDULLA	(47)	(46)	(47)
HYPERPLASIA, NOS	1 (2%)	1 (2%)	2 (4%)
#THYROID	(39)	(47)	(47)
HYPERPLASIA, C-CELL	2 (5%)	7 (15%)	6 (13%)
HYPERPLASIA, FOLLICULAR-CELL			1 (2%)
#PARATHYROID	(32)	(30)	(35)
HYPERPLASIA, NOS			1 (3%)
#PANCREATIC ISLETS	(44)	(46)	(47)
HYPERPLASIA, NOS			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(49)	(50)	(50)
GALACTOCELE	3 (6%)	3 (6%)	7 (14%)
HYPERPLASIA, NOS	28 (57%)	30 (60%)	25 (50%)
#UTERUS	(46)	(47)	(49)
DILATATION, NOS			1 (2%)
HEMORRHAGE	1 (2%)		
INFLAMMATION, SUPPURATIVE		1 (2%)	3 (6%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM (Continued)			
#CERVIX UTERI	(46)	(47)	(49)
INFLAMMATION, SUPPURATIVE	2 (4%)		
#UTERUS/ENDOMETRIUM	(46)	(47)	(49)
CYST, NOS	1 (2%)		
HYPERPLASIA, NOS		6 (13%)	4 (8%)
HYPERPLASIA, CYSTIC	6 (13%)	3 (6%)	4 (8%)
#OVARY	(45)	(48)	(50)
CYST, NOS	4 (9%)	5 (10%)	3 (6%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
ATROPHY, NOS	12 (27%)	7 (15%)	9 (18%)
NERVOUS SYSTEM			
#BRAIN	(48)	(49)	(50)
HEMORRHAGE	4 (8%)	2 (4%)	3 (6%)
GLIOSIS			1 (2%)
NECROSIS, FOCAL	2 (4%)	1 (2%)	
MALACIA			1 (2%)
PIGMENTATION, NOS			1 (2%)
SPECIAL SENSE ORGANS			
*EYE	(49)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
SYNECHIA, ANTERIOR	1 (2%)		
SYNECHIA, POSTERIOR	1 (2%)		
RETINOPATHY	2 (4%)		
*EYE/CRYSTALLINE LENS	(49)	(50)	(50)
MINERALIZATION	3 (6%)		
*EYE/LACRIMAL GLAND	(49)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
PIGMENTATION, NOS	1 (2%)		
*NASOLACRIMAL DUCT	(49)	(50)	(50)
INFLAMMATION, SUPPURATIVE	7 (14%)	4 (8%)	4 (8%)
MUSCULOSKELETAL SYSTEM			
*BONE	(49)	(50)	(50)
FIBROUS OSTEODYSTROPHY			1 (2%)
BODY CAVITIES			
*PERITONEAL CAVITY	(49)	(50)	(50)
NECROSIS, FAT	2 (4%)		1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(49)	(50)	(50)
MINERALIZATION			1 (2%)
SPECIAL MORPHOLOGY SUMMARY			
ACCIDENTAL DEATH	1		
AUTO/NECROPSY/NO HISTO		1	

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

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(49)	(50)
ABSCESS, NOS		1 (2%)	
INFLAMMATION, CHRONIC	3 (6%)		
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(49)	(50)
HEMORRHAGE	24 (48%)	9 (18%)	16 (32%)
INFLAMMATION, ACUTE	2 (4%)		1 (2%)
INFLAMMATION, ACUTE SEROUS	6 (12%)	14 (29%)	5 (10%)
#TRACHEA	(50)	(49)	(49)
HEMORRHAGE			1 (2%)
#LUNG/BRONCHIOLE	(50)	(49)	(50)
INFLAMMATION, ACUTE			1 (2%)
#LUNG	(50)	(49)	(50)
ATELECTASIS		2 (4%)	
CONGESTION, NOS		6 (12%)	3 (6%)
HEMORRHAGE	4 (8%)	1 (2%)	3 (6%)
INFLAMMATION, INTERSTITIAL	7 (14%)	1 (2%)	3 (6%)
INFLAMMATION, CHRONIC FOCAL		2 (4%)	
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)		
METAPLASIA, OSSEOUS			1 (2%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(49)	(49)	(49)
HEMORRHAGE			1 (2%)
ATROPHY, NOS			2 (4%)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, LYMPHOID			1 (2%)
HEMATOPOIESIS	2 (4%)	5 (10%)	4 (8%)
#LYMPH NODE	(48)	(46)	(48)
HEMOSIDEROSIS	1 (2%)		
#BRONCHIAL LYMPH NODE	(48)	(46)	(48)
CONGESTION, NOS	1 (2%)		
HEMORRHAGE	1 (2%)		
INFLAMMATION, CHRONIC			1 (2%)
HYPERPLASIA, NOS	1 (2%)		
#MESENTERIC L. NODE	(48)	(46)	(48)
CONGESTION, NOS		10 (22%)	6 (13%)
#RENAL LYMPH NODE	(48)	(46)	(48)
CONGESTION, NOS		1 (2%)	2 (4%)
EDEMA, NOS	1 (2%)		
HEMORRHAGE	1 (2%)		
#LIVER	(50)	(49)	(49)
LEUKEMOID REACTION	1 (2%)		2 (4%)
HEMATOPOIESIS		1 (2%)	
#THYMUS	(27)	(32)	(27)
CYST, NOS			2 (7%)
CIRCULATORY SYSTEM			
#HEART	(49)	(49)	(49)
THROMBUS, MURAL			1 (2%)
INFLAMMATION, ACUTE			1 (2%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(48)	(50)
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)
#LIVER	(50)	(49)	(49)
INFLAMMATION, CHRONIC FOCAL			2 (4%)
FIBROSIS, FOCAL		1 (2%)	
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL	2 (4%)	1 (2%)	1 (2%)
INFARCT, NOS		4 (8%)	
METAMORPHOSIS FATTY	10 (20%)		2 (4%)
#PANCREAS	(49)	(46)	(48)
ATROPHY, NOS	1 (2%)		
ATROPHY, FOCAL		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(49)
MINERALIZATION			1 (2%)
CAST, NOS			1 (2%)
CYST, NOS	5 (10%)		2 (4%)
HEMORRHAGE	1 (2%)		
PYELONEPHRITIS, NOS			1 (2%)
PYELONEPHRITIS, FOCAL	1 (2%)		
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
INFLAMMATION, ACUTE FOCAL			1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC FOCAL		17 (35%)	9 (18%)
REGENERATION, NOS	1 (2%)		
#KIDNEY/CORTEX	(50)	(49)	(49)
CYST, NOS	1 (2%)		
#URINARY BLADDER	(50)	(49)	(47)
INFLAMMATION, ACUTE			1 (2%)
ENDOCRINE SYSTEM			
#ADRENAL	(46)	(48)	(48)
CYST, NOS	1 (2%)		
FIBROSIS, FOCAL	1 (2%)		
METAMORPHOSIS FATTY	1 (2%)		
#THYROID	(48)	(48)	(48)
FOLLICULAR CYST, NOS	2 (4%)		2 (4%)
HYPERPLASIA, FOLLICULAR-CELL	1 (2%)		
#PARATHYROID	(23)	(24)	(27)
CYST, NOS			1 (4%)
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(49)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		1 (2%)
ABSCESS, NOS		3 (6%)	
INFLAMMATION, CHRONIC	2 (4%)		
#PROSTATE	(41)	(46)	(42)
INFLAMMATION, ACUTE			2 (5%)
#TESTIS	(50)	(48)	(49)
MINERALIZATION	1 (2%)		
INFLAMMATION, ACUTE FOCAL	1 (2%)		
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
ATROPHY, NOS	2 (4%)		7 (14%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN	(50)	(49)	(50)
HEMORRHAGE			1 (2%)
CORPORA AMYLACEA	35 (70%)	32 (65%)	25 (50%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(49)	(50)
MICROPHTHALMIA		1 (2%)	
INFLAMMATION, ACUTE	1 (2%)		
CATARACT	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(49)	(50)
FIBROUS OSTEODYSTROPHY	1 (2%)		
BODY CAVITIES			
*PERITONEUM	(50)	(49)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
NECROSIS, FAT	1 (2%)		
*MESENTERY	(50)	(49)	(50)
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
NECROSIS, FAT		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(49)	(50)
HEMORRHAGE	1 (2%)		
SPECIAL MORPHOLOGY SUMMARY			
ACCIDENTAL DEATH		1	

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

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(50)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION, ACUTE FOCAL		1 (2%)	
ATROPHY, NOS	1 (2%)		
*SUBCUT TISSUE	(50)	(49)	(50)
MINERALIZATION			1 (2%)
STEATITIS			1 (2%)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
INFARCT, NOS			1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(49)	(50)
HEMORRHAGE	20 (40%)	10 (20%)	19 (38%)
INFLAMMATION, ACUTE		7 (14%)	2 (4%)
INFLAMMATION, ACUTE SEROUS	14 (28%)	12 (24%)	9 (18%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
NECROSIS, NOS		1 (2%)	
METAPLASIA, SQUAMOUS		1 (2%)	
*LARYNX	(50)	(49)	(50)
HEMORRHAGE		1 (2%)	
#TRACHEA	(49)	(49)	(50)
HEMORRHAGE		2 (4%)	
#LUNG	(50)	(49)	(50)
CONGESTION, NOS	2 (4%)	3 (6%)	4 (8%)
HEMORRHAGE	2 (4%)	1 (2%)	3 (6%)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)	2 (4%)	1 (2%)
INFLAMMATION, INTERSTITIAL	2 (4%)		3 (6%)
INFLAMMATION, ACUTE	1 (2%)		
INFLAMMATION, GRANULOMATOUS	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(50)
LEUKEMOID REACTION		1 (2%)	
#BONE MARROW	(50)	(47)	(48)
PIGMENTATION, NOS		1 (2%)	
#SPLEEN	(47)	(48)	(46)
CONGESTION, NOS	1 (2%)		1 (2%)
EDEMA, NOS	1 (2%)		
HEMORRHAGE		1 (2%)	
HEMOSIDEROSIS	1 (2%)	1 (2%)	
ATROPHY, NOS			1 (2%)
ANGIECTASIS		1 (2%)	
HEMATOPOIESIS	2 (4%)	5 (10%)	8 (17%)
#LYMPH NODE	(50)	(46)	(49)
INFLAMMATION, ACUTE			1 (2%)
#MANDIBULAR L. NODE	(50)	(46)	(49)
CYST, NOS	1 (2%)		
HEMOSIDEROSIS	1 (2%)		
HYPERPLASIA, NOS		1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#BRONCHIAL LYMPH NODE	(50)	(46)	(49)
CONGESTION, NOS			1 (2%)
EDEMA, NOS	1 (2%)		
HEMORRHAGE	1 (2%)		
INFLAMMATION, ACUTE		1 (2%)	
CHOLESTEROL DEPOSIT	1 (2%)		
#MESENTERIC L. NODE	(50)	(46)	(49)
CONGESTION, NOS		2 (4%)	1 (2%)
EDEMA, NOS	1 (2%)		
INFLAMMATION, ACUTE		1 (2%)	
ABSCESS, NOS	1 (2%)		
#RENAL LYMPH NODE	(50)	(46)	(49)
EDEMA, NOS	1 (2%)		
HYPERPLASIA, NOS			1 (2%)
#LIVER	(50)	(49)	(49)
LEUKEMOID REACTION	2 (4%)	2 (4%)	1 (2%)
HYPERPLASIA, LYMPHOID	1 (2%)		
HEMATOPOIESIS			2 (4%)
CIRCULATORY SYSTEM			
#HEART	(50)	(48)	(50)
THROMBUS, MURAL			1 (2%)
NECROSIS, NOS	1 (2%)		
#HEART/ATRIUM	(50)	(48)	(50)
THROMBOSIS, NOS	2 (4%)		
#CARDIAC VALVE	(50)	(48)	(50)
MELANIN	1 (2%)		
#LIVER	(50)	(49)	(49)
THROMBOSIS, NOS	1 (2%)	2 (4%)	1 (2%)
#UTERUS	(47)	(47)	(48)
LYMPHANGIECTASIS		1 (2%)	
THROMBOSIS, NOS	1 (2%)	1 (2%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(48)	(48)
INFLAMMATION, CHRONIC FOCAL	2 (4%)		
ATROPHY, NOS		1 (2%)	
#LIVER	(50)	(49)	(49)
INFLAMMATION, FOCAL	1 (2%)		
INFLAMMATION, CHRONIC	5 (10%)	1 (2%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL		3 (6%)	7 (14%)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
FIBROSIS	1 (2%)		2 (4%)
NECROSIS, NOS	2 (4%)	1 (2%)	2 (4%)
NECROSIS, FOCAL		2 (4%)	2 (4%)
METAMORPHOSIS FATTY	1 (2%)	3 (6%)	2 (4%)
PIGMENTATION, NOS	1 (2%)		
CYTOPLASMIC VACUOLIZATION		1 (2%)	
CLEAR-CELL CHANGE	1 (2%)		
#LIVER/CENTRILOBULAR	(50)	(49)	(49)
DEGENERATION, NOS	1 (2%)		
#BILE DUCT	(50)	(49)	(49)
INFLAMMATION, NOS			1 (2%)
#PANCREAS	(46)	(44)	(43)
DILATATION/DUCTS	1 (2%)		
CYSTIC DUCTS			1 (2%)
AMYLOIDOSIS	1 (2%)		
ATROPHY, NOS			2 (5%)
#LARGE INTESTINE	(48)	(45)	(42)
INFLAMMATION, ACUTE	1 (2%)		

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(49)
CAST, NOS			1 (2%)
CYST, NOS		2 (4%)	
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	7 (14%)	6 (12%)
NEPHROPATHY		1 (2%)	
DEGENERATION, HYALINE		1 (2%)	2 (4%)
METAPLASIA, OSSEOUS	1 (2%)		
#KIDNEY/GLOMERULUS	(50)	(49)	(49)
INFLAMMATION, NOS			1 (2%)
AMYLOIDOSIS			1 (2%)
#KIDNEY/TUBULE	(50)	(49)	(49)
DEGENERATION, NOS		1 (2%)	
NECROSIS, FOCAL		1 (2%)	
#URINARY BLADDER	(41)	(43)	(43)
INFLAMMATION, ACUTE	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(41)	(44)	(44)
HEMORRHAGIC CYST			1 (2%)
FIBROSIS			1 (2%)
#ADRENAL	(45)	(48)	(48)
METAMORPHOSIS FATTY		1 (2%)	
#THYROID	(45)	(48)	(47)
ULTIMOBRANCHIAL CYST	1 (2%)		
CYST, NOS	1 (2%)		
FOLLICULAR CYST, NOS			6 (13%)
INFLAMMATION, ACUTE	1 (2%)		
#PANCREATIC ISLETS	(46)	(44)	(43)
HYPERPLASIA, NOS			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(49)	(50)
DILATATION/DUCTS		1 (2%)	
GALACTOCELE	1 (2%)		
CYST, NOS	2 (4%)		1 (2%)
HYPERPLASIA, NOS		1 (2%)	
#UTERUS	(47)	(47)	(48)
MINERALIZATION	1 (2%)	1 (2%)	
MUCOCELE	1 (2%)		
HYDROMETRA		1 (2%)	
CYST, NOS	36 (77%)	31 (66%)	38 (79%)
HEMORRHAGE		1 (2%)	
HEMORRHAGIC CYST	1 (2%)		1 (2%)
INFLAMMATION, ACUTE	1 (2%)	2 (4%)	2 (4%)
INFLAMMATION, ACUTE FOCAL			1 (2%)
FIBROSIS		1 (2%)	
FIBROSIS, FOCAL		1 (2%)	
HYPERPLASIA, STROMAL	1 (2%)		
#UTERUS/ENDOMETRIUM	(47)	(47)	(48)
HYPERPLASIA, CYSTIC		1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	CONTROL (CHAM)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM (Continued)			
#OVARY	(45)	(48)	(47)
CYST, NOS	9 (20%)	11 (23%)	7 (15%)
HEMORRHAGIC CYST	8 (18%)	2 (4%)	11 (23%)
ABSCESS, NOS	1 (2%)		
INFLAMMATION, CHRONIC			1 (2%)
HEMOSIDEROSIS	1 (2%)		
ATROPHY, NOS		1 (2%)	1 (2%)
NERVOUS SYSTEM			
*CHOROID PLEXUS	(50)	(49)	(50)
INFLAMMATION, ACUTE	1 (2%)		
#BRAIN	(50)	(49)	(50)
HEMORRHAGE	1 (2%)		1 (2%)
CORPORA AMYLACEA	30 (60%)	17 (35%)	21 (42%)
FIBROUS OSTEODYSTROPHY		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(50)	(49)	(50)
AGENESIS			1 (2%)
CATARACT			1 (2%)
PHTHISIS BULBI		1 (2%)	
*EYE/CORNEA	(50)	(49)	(50)
MINERALIZATION			1 (2%)
*EYE/CRYSTALLINE LENS	(50)	(49)	(50)
MINERALIZATION		1 (2%)	
*HARDERIAN GLAND	(50)	(49)	(50)
FIBROSIS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(49)	(50)
FIBROUS OSTEODYSTROPHY	43 (86%)	38 (78%)	40 (80%)
BODY CAVITIES			
*PERITONEUM	(50)	(49)	(50)
INFLAMMATION, NOS	2 (4%)		
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	2	1	
ANIMAL MIS-SEXED/NO NECROPSY		1	
AUTO/NECROPSY/HISTO PERF	1	1	

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

APPENDIX E

ANALYSES OF PRIMARY TUMORS IN RATS AND MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Chamber Control	5,000 ppm	10,000 ppm
Subcutaneous Tissue: Fibroma			
Overall Rates (a)	3/50 (6%)	1/50 (2%)	3/50 (6%)
Adjusted Rates (b)	9.1%	2.2%	8.1%
Terminal Rates (c)	3/33 (9%)	0/33 (0%)	3/37 (8%)
Life Table Tests (d)	P=0.546N	P=0.302N	P=0.610N
Incidental Tumor Tests (d)	P=0.562N	P=0.299N	P=0.610N
Cochran-Armitage Trend Test (d)	P=0.594		
Fisher Exact Tests		P=0.309N	P=0.661
Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Overall Rates (a)	3/50 (6%)	2/50 (4%)	4/50 (8%)
Adjusted Rates (b)	9.1%	5.2%	10.8%
Terminal Rates (c)	3/33 (9%)	1/33 (3%)	4/37 (11%)
Life Table Tests (d)	P=0.472	P=0.496N	P=0.563
Incidental Tumor Tests (d)	P=0.458	P=0.492N	P=0.563
Cochran-Armitage Trend Test (d)	P=0.417		
Fisher Exact Tests		P=0.500N	P=0.500
Hematopoietic System: Mononuclear Cell Leukemia			
Overall Rates (a)	16/50 (32%)	13/50 (26%)	22/50 (44%)
Adjusted Rates (b)	39.6%	29.9%	48.2%
Terminal Rates (c)	10/33 (30%)	4/33 (12%)	14/37 (38%)
Life Table Tests (d)	P=0.246	P=0.346N	P=0.290
Incidental Tumor Tests (d)	P=0.081	P=0.317N	P=0.097
Cochran-Armitage Trend Test (d)	P=0.123		
Fisher Exact Tests		P=0.330N	P=0.151
Liver: Neoplastic Nodule			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	0.0%	9.1%	8.1%
Terminal Rates (c)	0/33 (0%)	3/33 (9%)	3/37 (8%)
Life Table Tests (d)	P=0.125	P=0.120	P=0.142
Incidental Tumor Tests (d)	P=0.125	P=0.120	P=0.142
Cochran-Armitage Trend Test (d)	P=0.101		
Fisher Exact Tests		P=0.121	P=0.121
Liver: Neoplastic Nodule or Carcinoma			
Overall Rates (a)	0/50 (0%)	4/50 (8%)	3/50 (6%)
Adjusted Rates (b)	0.0%	11.5%	8.1%
Terminal Rates (c)	0/33 (0%)	3/33 (9%)	3/37 (8%)
Life Table Tests (d)	P=0.149	P=0.064	P=0.142
Incidental Tumor Tests (d)	P=0.136	P=0.067	P=0.142
Cochran-Armitage Trend Test (d)	P=0.118		
Fisher Exact Tests		P=0.059	P=0.121
Pituitary: Adenoma			
Overall Rates (a)	12/46 (26%)	14/48 (29%)	16/47 (34%)
Adjusted Rates (b)	31.6%	38.7%	44.0%
Terminal Rates (c)	7/31 (23%)	11/32 (34%)	14/34 (41%)
Life Table Tests (d)	P=0.319	P=0.436	P=0.361
Incidental Tumor Tests (d)	P=0.222	P=0.485	P=0.259
Cochran-Armitage Trend Test (d)	P=0.234		
Fisher Exact Tests		P=0.459	P=0.271
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	12/46 (26%)	15/48 (31%)	16/47 (34%)
Adjusted Rates (b)	31.6%	41.6%	44.0%
Terminal Rates (c)	7/31 (23%)	12/32 (38%)	14/34 (41%)
Life Table Tests (d)	P=0.322	P=0.355	P=0.361
Incidental Tumor Tests (d)	P=0.226	P=0.397	P=0.259
Cochran-Armitage Trend Test (d)	P=0.236		
Fisher Exact Tests		P=0.373	P=0.271

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	Chamber Control	5,000 ppm	10,000 ppm
Adrenal: Pheochromocytoma			
Overall Rates (a)	3/50 (6%)	6/50 (12%)	5/49 (10%)
Adjusted Rates (b)	8.1%	16.0%	13.5%
Terminal Rates (c)	2/33 (6%)	4/33 (12%)	5/37 (14%)
Life Table Tests (d)	P=0.363	P=0.250	P=0.411
Incidental Tumor Tests (d)	P=0.290	P=0.255	P=0.325
Cochran-Armitage Trend Test (d)	P=0.291		
Fisher Exact Tests		P=0.243	P=0.346
Adrenal: Pheochromocytoma, Malignant			
Overall Rates (a)	2/50 (4%)	0/50 (0%)	3/49 (6%)
Adjusted Rates (b)	6.1%	0.0%	7.3%
Terminal Rates (c)	2/33 (6%)	0/33 (0%)	2/37 (5%)
Life Table Tests (d)	P=0.425	P=0.238N	P=0.541
Incidental Tumor Tests (d)	P=0.462	P=0.238N	P=0.578
Cochran-Armitage Trend Test (d)	P=0.383		
Fisher Exact Tests		P=0.247N	P=0.490
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant			
Overall Rates (a)	5/50 (10%)	6/50 (12%)	8/49 (16%)
Adjusted Rates (b)	14.0%	16.0%	20.5%
Terminal Rates (c)	4/33 (12%)	4/33 (12%)	7/37 (19%)
Life Table Tests (d)	P=0.289	P=0.504	P=0.341
Incidental Tumor Tests (d)	P=0.248	P=0.511	P=0.296
Cochran-Armitage Trend Test (d)	P=0.214		
Fisher Exact Tests		P=0.500	P=0.264
Thyroid: Follicular Cell Carcinoma			
Overall Rates (a)	3/45 (7%)	2/46 (4%)	1/47 (2%)
Adjusted Rates (b)	10.0%	6.3%	2.3%
Terminal Rates (c)	3/30 (10%)	2/32 (6%)	0/37 (0%)
Life Table Tests (d)	P=0.168N	P=0.470N	P=0.240N
Incidental Tumor Tests (d)	P=0.192N	P=0.470N	P=0.293N
Cochran-Armitage Trend Test (d)	P=0.209N		
Fisher Exact Tests		P=0.489N	P=0.292N
Thyroid: Follicular Cell Adenoma or Carcinoma			
Overall Rates (a)	4/45 (9%)	2/46 (4%)	3/47 (6%)
Adjusted Rates (b)	11.9%	6.3%	7.6%
Terminal Rates (c)	3/30 (10%)	2/32 (6%)	2/37 (5%)
Life Table Tests (d)	P=0.333N	P=0.314N	P=0.410N
Incidental Tumor Tests (d)	P=0.400N	P=0.292N	P=0.536N
Cochran-Armitage Trend Test (d)	P=0.395N		
Fisher Exact Tests		P=0.328N	P=0.475N
Thyroid: C-Cell Adenoma			
Overall Rates (a)	2/45 (4%)	1/46 (2%)	3/47 (6%)
Adjusted Rates (b)	5.9%	3.1%	8.1%
Terminal Rates (c)	1/30 (3%)	1/32 (3%)	3/37 (8%)
Life Table Tests (d)	P=0.481	P=0.491N	P=0.589
Incidental Tumor Tests (d)	P=0.439	P=0.485N	P=0.531
Cochran-Armitage Trend Test (d)	P=0.416		
Fisher Exact Tests		P=0.492N	P=0.521
Thyroid: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	4/45 (9%)	1/46 (2%)	4/47 (9%)
Adjusted Rates (b)	11.1%	3.1%	10.8%
Terminal Rates (c)	2/30 (7%)	1/32 (3%)	4/37 (11%)
Life Table Tests (d)	P=0.493N	P=0.176N	P=0.545N
Incidental Tumor Tests (d)	P=0.570N	P=0.155N	P=0.628
Cochran-Armitage Trend Test (d)	P=0.562N		
Fisher Exact Tests		P=0.174N	P=0.618N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	Chamber Control	5,000 ppm	10,000 ppm
Pancreatic Islets: Islet Cell Adenoma			
Overall Rates (a)	2/48 (4%)	1/50 (2%)	3/46 (7%)
Adjusted Rates (b)	5.5%	2.4%	8.6%
Terminal Rates (c)	1/33 (3%)	0/33 (0%)	3/35 (9%)
Life Table Tests (d)	P=0.434	P=0.503N	P=0.534
Incidental Tumor Tests (d)	P=0.361	P=0.480N	P=0.481
Cochran-Armitage Trend Test (d)	P=0.382		
Fisher Exact Tests		P=0.485N	P=0.480
Pancreatic Islets: Islet Cell Adenoma or Carcinoma			
Overall Rates (a)	3/48 (6%)	1/50 (2%)	3/46 (7%)
Adjusted Rates (b)	8.0%	2.4%	8.6%
Terminal Rates (c)	1/33 (3%)	0/33 (0%)	3/35 (9%)
Life Table Tests (d)	P=0.552N	P=0.313N	P=0.621N
Incidental Tumor Tests (d)	P=0.535	P=0.279N	P=0.612
Cochran-Armitage Trend Test (d)	P=0.577		
Fisher Exact Tests		P=0.293N	P=0.641
Testis: Interstitial Cell Tumor			
Overall Rates (a)	37/50 (74%)	36/50 (72%)	33/49 (67%)
Adjusted Rates (b)	83.8%	83.7%	82.4%
Terminal Rates (c)	26/33 (79%)	26/33 (79%)	30/37 (81%)
Life Table Tests (d)	P=0.079N	P=0.504N	P=0.090N
Incidental Tumor Tests (d)	P=0.176N	P=0.463N	P=0.239N
Cochran-Armitage Trend Test (d)	P=0.268N		
Fisher Exact Tests		P=0.500N	P=0.307N
Tunica Vaginalis: Mesothelioma			
Overall Rates (a)	2/50 (4%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	6.1%	0.0%	8.1%
Terminal Rates (c)	2/33 (6%)	0/33 (0%)	3/37 (8%)
Life Table Tests (d)	P=0.433	P=0.238N	P=0.552
Incidental Tumor Tests (d)	P=0.433	P=0.238N	P=0.552
Cochran-Armitage Trend Test (d)	P=0.390		
Fisher Exact Tests		P=0.248N	P=0.500
All Sites: Mesothelioma			
Overall Rates (a)	3/50 (6%)	2/50 (4%)	4/50 (8%)
Adjusted Rates (b)	9.1%	5.9%	10.8%
Terminal Rates (c)	3/33 (9%)	1/33 (3%)	4/37 (11%)
Life Table Tests (d)	P=0.473	P=0.500N	P=0.563
Incidental Tumor Tests (d)	P=0.458	P=0.492N	P=0.563
Cochran-Armitage Trend Test (d)	P=0.417		
Fisher Exact Tests		P=0.500N	P=0.500

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

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Chamber Control	5,000 ppm	10,000 ppm
Hematopoietic System: Mononuclear Cell Leukemia			
Overall Rates (a)	13/49 (27%)	14/50 (28%)	16/50 (32%)
Adjusted Rates (b)	30.8%	32.2%	36.2%
Terminal Rates (c)	2/27 (7%)	8/36 (22%)	4/30 (13%)
Life Table Tests (d)	P=0.394	P=0.502N	P=0.437
Incidental Tumor Tests (d)	P=0.248	P=0.325	P=0.261
Cochran-Armitage Trend Test (d)	P=0.312		
Fisher Exact Tests		P=0.525	P=0.353
Pituitary: Adenoma			
Overall Rates (a)	18/44 (41%)	27/47 (57%)	21/48 (44%)
Adjusted Rates (b)	50.5%	66.9%	56.7%
Terminal Rates (c)	10/26 (38%)	21/34 (62%)	14/29 (48%)
Life Table Tests (d)	P=0.464N	P=0.270	P=0.494
Incidental Tumor Tests (d)	P=0.455N	P=0.077	P=0.477
Cochran-Armitage Trend Test (d)	P=0.450N		
Fisher Exact Tests		P=0.086	P=0.475
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	19/44 (43%)	29/47 (62%)	21/48 (44%)
Adjusted Rates (b)	53.6%	72.0%	56.7%
Terminal Rates (c)	11/26 (42%)	23/34 (68%)	14/29 (48%)
Life Table Tests (d)	P=0.529N	P=0.233	P=0.572
Incidental Tumor Tests (d)	P=0.537N	P=0.060	P=0.564
Cochran-Armitage Trend Test (d)	P=0.540N		
Fisher Exact Tests		P=0.059	P=0.562
Adrenal: Cortical Adenoma			
Overall Rates (a)	1/47 (2%)	0/46 (0%)	3/47 (6%)
Adjusted Rates (b)	3.0%	0.0%	9.1%
Terminal Rates (c)	0/27 (0%)	0/36 (0%)	2/30 (7%)
Life Table Tests (d)	P=0.196	P=0.483N	P=0.347
Incidental Tumor Tests (d)	P=0.204	P=0.923N	P=0.324
Cochran-Armitage Trend Test (d)	P=0.177		
Fisher Exact Tests		P=0.505N	P=0.308
Adrenal: Pheochromocytoma			
Overall Rates (a)	1/47 (2%)	3/46 (7%)	1/47 (2%)
Adjusted Rates (b)	3.7%	8.3%	2.9%
Terminal Rates (c)	1/27 (4%)	3/36 (8%)	0/30 (0%)
Life Table Tests (d)	P=0.576N	P=0.412	P=0.735N
Incidental Tumor Tests (d)	P=0.581N	P=0.412	P=0.749N
Cochran-Armitage Trend Test (d)	P=0.609		
Fisher Exact Tests		P=0.300	P=0.753
Thyroid: C-Cell Adenoma			
Overall Rates (a)	5/39 (13%)	2/47 (4%)	0/47 (0%)
Adjusted Rates (b)	15.6%	5.6%	0.0%
Terminal Rates (c)	2/27 (7%)	2/36 (6%)	0/29 (0%)
Life Table Tests (d)	P=0.013N	P=0.141N	P=0.031N
Incidental Tumor Tests (d)	P=0.008N	P=0.239N	P=0.018N
Cochran-Armitage Trend Test (d)	P=0.009N		
Fisher Exact Tests		P=0.147N	P=0.017N
Thyroid: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	6/39 (15%)	2/47 (4%)	2/47 (4%)
Adjusted Rates (b)	19.0%	5.6%	6.9%
Terminal Rates (c)	3/27 (11%)	2/36 (6%)	2/29 (7%)
Life Table Tests (d)	P=0.064N	P=0.077N	P=0.120N
Incidental Tumor Tests (d)	P=0.048N	P=0.135N	P=0.088N
Cochran-Armitage Trend Test (d)	P=0.046N		
Fisher Exact Tests		P=0.081N	P=0.081N

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	Chamber Control	5,000 ppm	10,000 ppm
Mammary Gland: Fibroadenoma			
Overall Rates (a)	9/49 (18%)	11/50 (22%)	6/50 (12%)
Adjusted Rates (b)	25.9%	28.3%	17.5%
Terminal Rates (c)	3/27 (11%)	9/36 (25%)	4/30 (13%)
Life Table Tests (d)	P=0.199N	P=0.587N	P=0.238N
Incidental Tumor Tests (d)	P=0.222N	P=0.388	P=0.244N
Cochran-Armitage Trend Test (d)	P=0.239N		
Fisher Exact Tests		P=0.421	P=0.274N
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	3/46 (7%)	4/47 (9%)	4/49 (8%)
Adjusted Rates (b)	11.1%	11.1%	13.3%
Terminal Rates (c)	3/27 (11%)	4/36 (11%)	4/30 (13%)
Life Table Tests (d)	P=0.476	P=0.656	P=0.559
Incidental Tumor Tests (d)	P=0.476	P=0.656	P=0.559
Cochran-Armitage Trend Test (d)	P=0.459		
Fisher Exact Tests		P=0.512	P=0.536
Uterus: Endometrial Stromal Polyp or Sarcoma			
Overall Rates (a)	5/46 (11%)	4/47 (9%)	6/49 (12%)
Adjusted Rates (b)	16.8%	11.1%	17.6%
Terminal Rates (c)	4/27 (15%)	4/36 (11%)	4/30 (13%)
Life Table Tests (d)	P=0.492	P=0.341N	P=0.564
Incidental Tumor Tests (d)	P=0.480	P=0.333N	P=0.539
Cochran-Armitage Trend Test (d)	P=0.476		
Fisher Exact Tests		P=0.486N	P=0.545

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

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Chamber Control	5,000 ppm	10,000 ppm
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	7/50 (14%)	3/49 (6%)	3/50 (6%)
Adjusted Rates (b)	15.9%	7.1%	7.7%
Terminal Rates (c)	7/44 (16%)	3/42 (7%)	3/39 (8%)
Life Table Tests (d)	P=0.143N	P=0.177N	P=0.210N
Incidental Tumor Tests (d)	P=0.143N	P=0.177N	P=0.210N
Cochran-Armitage Trend Test (d)	P=0.107N		
Fisher Exact Tests		P=0.167N	P=0.159N
Lung: Alveolar/Bronchiolar Carcinoma			
Overall Rates (a)	9/50 (18%)	1/49 (2%)	4/50 (8%)
Adjusted Rates (b)	19.9%	2.4%	10.3%
Terminal Rates (c)	8/44 (18%)	1/42 (2%)	4/39 (10%)
Life Table Tests (d)	P=0.086N	P=0.012N	P=0.167N
Incidental Tumor Tests (d)	P=0.068N	P=0.009N	P=0.128N
Cochran-Armitage Trend Test (d)	P=0.062N		
Fisher Exact Tests		P=0.009N	P=0.117N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	16/50 (32%)	4/49 (8%)	7/50 (14%)
Adjusted Rates (b)	35.4%	9.5%	17.9%
Terminal Rates (c)	15/44 (34%)	4/42 (10%)	7/39 (18%)
Life Table Tests (d)	P=0.025N	P=0.004N	P=0.055N
Incidental Tumor Tests (d)	P=0.020N	P=0.003N	P=0.041N
Cochran-Armitage Trend Test (d)	P=0.014N		
Fisher Exact Tests		P=0.003N	P=0.028N
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Overall Rates (a)	4/50 (8%)	6/49 (12%)	6/50 (12%)
Adjusted Rates (b)	8.9%	13.9%	13.5%
Terminal Rates (c)	3/44 (7%)	5/42 (12%)	2/39 (5%)
Life Table Tests (d)	P=0.259	P=0.348	P=0.318
Incidental Tumor Tests (d)	P=0.393	P=0.430	P=0.508
Cochran-Armitage Trend Test (d)	P=0.314		
Fisher Exact Tests		P=0.357	P=0.370
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	5/50 (10%)	7/49 (14%)	7/50 (14%)
Adjusted Rates (b)	11.1%	15.6%	15.5%
Terminal Rates (c)	4/44 (9%)	5/42 (12%)	2/39 (5%)
Life Table Tests (d)	P=0.271	P=0.357	P=0.325
Incidental Tumor Tests (d)	P=0.482	P=0.474	P=0.555
Cochran-Armitage Trend Test (d)	P=0.326		
Fisher Exact Tests		P=0.365	P=0.380
Liver: Adenoma			
Overall Rates (a)	5/50 (10%)	0/49 (0%)	3/49 (6%)
Adjusted Rates (b)	11.4%	0.0%	7.7%
Terminal Rates (c)	5/44 (11%)	0/42 (0%)	3/39 (8%)
Life Table Tests (d)	P=0.299N	P=0.038N	P=0.424N
Incidental Tumor Tests (d)	P=0.299N	P=0.038N	P=0.424N
Cochran-Armitage Trend Test (d)	P=0.260N		
Fisher Exact Tests		P=0.030N	P=0.369N
Liver: Carcinoma			
Overall Rates (a)	9/50 (18%)	11/49 (22%)	12/49 (24%)
Adjusted Rates (b)	19.9%	24.8%	28.1%
Terminal Rates (c)	8/44 (18%)	9/42 (21%)	9/39 (23%)
Life Table Tests (d)	P=0.192	P=0.365	P=0.229
Incidental Tumor Tests (d)	P=0.324	P=0.397	P=0.369
Cochran-Armitage Trend Test (d)	P=0.254		
Fisher Exact Tests		P=0.382	P=0.294

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	Chamber Control	5,000 ppm	10,000 ppm
Liver: Adenoma or Carcinoma			
Overall Rates (a)	14/50 (28%)	11/49 (22%)	14/49 (29%)
Adjusted Rates (b)	31.0%	24.8%	32.9%
Terminal Rates (c)	13/44 (30%)	9/42 (21%)	11/39 (28%)
Life Table Tests (d)	P=0.417	P=0.370N	P=0.453
Incidental Tumor Tests (d)	P=0.512N	P=0.339N	P=0.567N
Cochran-Armitage Trend Test (d)	P=0.522		
Fisher Exact Tests		P=0.343N	P=0.563

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

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE

	Chamber Control	5,000 ppm	10,000 ppm
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	6/50 (12%)	4/49 (8%)	6/50 (12%)
Adjusted Rates (b)	17.1%	12.1%	16.4%
Terminal Rates (c)	5/33 (15%)	4/33 (12%)	5/35 (14%)
Life Table Tests (d)	P=0.526N	P=0.367N	P=0.581N
Incidental Tumor Tests (d)	P=0.516N	P=0.343N	P=0.570N
Cochran-Armitage Trend Test (d)	P=0.564		
Fisher Exact Tests		P=0.383N	P=0.620
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	6/50 (12%)	4/49 (8%)	7/50 (14%)
Adjusted Rates (b)	17.1%	12.1%	18.6%
Terminal Rates (c)	5/33 (15%)	4/33 (12%)	5/35 (14%)
Life Table Tests (d)	P=0.481	P=0.367N	P=0.547
Incidental Tumor Tests (d)	P=0.498	P=0.343N	P=0.567
Cochran-Armitage Trend Test (d)	P=0.438		
Fisher Exact Tests		P=0.383N	P=0.500
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Overall Rates (a)	4/50 (8%)	3/49 (6%)	6/50 (12%)
Adjusted Rates (b)	12.1%	6.8%	14.4%
Terminal Rates (c)	4/33 (12%)	0/33 (0%)	2/35 (6%)
Life Table Tests (d)	P=0.330	P=0.496N	P=0.406
Incidental Tumor Tests (d)	P=0.297	P=0.483N	P=0.386
Cochran-Armitage Trend Test (d)	P=0.298		
Fisher Exact Tests		P=0.512N	P=0.370
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Overall Rates (a)	11/50 (22%)	10/49 (20%)	15/50 (30%)
Adjusted Rates (b)	29.2%	28.0%	37.6%
Terminal Rates (c)	7/33 (21%)	8/33 (24%)	11/35 (31%)
Life Table Tests (d)	P=0.259	P=0.507N	P=0.309
Incidental Tumor Tests (d)	P=0.235	P=0.520N	P=0.298
Cochran-Armitage Trend Test (d)	P=0.207		
Fisher Exact Tests		P=0.521N	P=0.247
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	16/50 (32%)	14/49 (29%)	23/50 (46%)
Adjusted Rates (b)	42.8%	34.6%	51.6%
Terminal Rates (c)	12/33 (36%)	8/33 (24%)	14/35 (40%)
Life Table Tests (d)	P=0.145	P=0.424N	P=0.178
Incidental Tumor Tests (d)	P=0.104	P=0.404N	P=0.134
Cochran-Armitage Trend Test (d)	P=0.087		
Fisher Exact Tests		P=0.440N	P=0.109
Circulatory System: Hemangiosarcoma			
Overall Rates (a)	0/50 (0%)	0/49 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	0.0%	8.6%
Terminal Rates (c)	0/33 (0%)	0/33 (0%)	3/35 (9%)
Life Table Tests (d)	P=0.041	(e)	P=0.131
Incidental Tumor Tests (d)	P=0.041	(e)	P=0.131
Cochran-Armitage Trend Test (d)	P=0.038		
Fisher Exact Tests		(e)	P=0.121
Circulatory System: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	0/50 (0%)	1/49 (2%)	4/50 (8%)
Adjusted Rates (b)	0.0%	2.7%	11.4%
Terminal Rates (c)	0/33 (0%)	0/33 (0%)	4/35 (11%)
Life Table Tests (d)	P=0.030	P=0.500	P=0.070
Incidental Tumor Tests (d)	P=0.024	P=0.500	P=0.070
Cochran-Armitage Trend Test (d)	P=0.026		
Fisher Exact Tests		P=0.495	P=0.059

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	Chamber Control	5,000 ppm	10,000 ppm
Liver: Carcinoma			
Overall Rates (a)	2/50 (4%)	3/49 (6%)	5/49 (10%)
Adjusted Rates (b)	5.3%	9.1%	14.3%
Terminal Rates (c)	1/33 (3%)	3/33 (9%)	5/35 (14%)
Life Table Tests (d)	P=0.178	P=0.502	P=0.241
Incidental Tumor Tests (d)	P=0.199	P=0.536	P=0.278
Cochran-Armitage Trend Test (d)	P=0.152		
Fisher Exact Tests		P=0.490	P=0.210
Pituitary: Chromophobe Adenoma			
Overall Rates (a)	11/41 (27%)	9/44 (20%)	9/44 (20%)
Adjusted Rates (b)	33.3%	27.0%	26.8%
Terminal Rates (c)	10/32 (31%)	8/32 (25%)	8/32 (25%)
Life Table Tests (d)	P=0.342N	P=0.400N	P=0.392N
Incidental Tumor Tests (d)	P=0.347N	P=0.399N	P=0.385N
Cochran-Armitage Trend Test (d)	P=0.286N		
Fisher Exact Tests		P=0.331N	P=0.331N
Pituitary: Adenoma			
Overall Rates (a)	13/41 (32%)	11/44 (25%)	10/44 (23%)
Adjusted Rates (b)	39.3%	33.1%	29.9%
Terminal Rates (c)	12/32 (38%)	10/32 (31%)	9/32 (28%)
Life Table Tests (d)	P=0.262N	P=0.405N	P=0.304N
Incidental Tumor Tests (d)	P=0.266N	P=0.403N	P=0.298N
Cochran-Armitage Trend Test (d)	P=0.209N		
Fisher Exact Tests		P=0.328N	P=0.246N
Pituitary: Chromophobe Carcinoma			
Overall Rates (a)	0/41 (0%)	4/44 (9%)	3/44 (7%)
Adjusted Rates (b)	0.0%	11.8%	8.4%
Terminal Rates (c)	0/32 (0%)	3/32 (9%)	2/32 (6%)
Life Table Tests (d)	P=0.123	P=0.064	P=0.124
Incidental Tumor Tests (d)	P=0.093	P=0.064	P=0.099
Cochran-Armitage Trend Test (d)	P=0.131		
Fisher Exact Tests		P=0.067	P=0.134
Pituitary: Chromophobe Adenoma or Carcinoma			
Overall Rates (a)	11/41 (27%)	13/44 (30%)	12/44 (27%)
Adjusted Rates (b)	33.3%	37.9%	34.5%
Terminal Rates (c)	10/32 (31%)	11/32 (34%)	10/32 (31%)
Life Table Tests (d)	P=0.461	P=0.404	P=0.508
Incidental Tumor Tests (d)	P=0.427	P=0.405	P=0.493
Cochran-Armitage Trend Test (d)	P=0.533		
Fisher Exact Tests		P=0.486	P=0.579
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	13/41 (32%)	15/44 (34%)	13/44 (30%)
Adjusted Rates (b)	39.3%	43.8%	37.5%
Terminal Rates (c)	12/32 (38%)	13/32 (41%)	11/32 (34%)
Life Table Tests (d)	P=0.538N	P=0.407	P=0.586N
Incidental Tumor Tests (d)	P=0.524	P=0.408	P=0.588
Cochran-Armitage Trend Test (d)	P=0.458N		
Fisher Exact Tests		P=0.499	P=0.507N
Thyroid: Follicular Cell Adenoma			
Overall Rates (a)	4/45 (9%)	2/48 (4%)	5/47 (11%)
Adjusted Rates (b)	12.9%	6.1%	14.7%
Terminal Rates (c)	4/31 (13%)	2/33 (6%)	5/34 (15%)
Life Table Tests (d)	P=0.475	P=0.307N	P=0.559
Incidental Tumor Tests (d)	P=0.475	P=0.307N	P=0.559
Cochran-Armitage Trend Test (d)	P=0.447		
Fisher Exact Tests		P=0.308N	P=0.528

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE (Continued)

	Chamber Control	5,000 ppm	10,000 ppm
Thyroid: Follicular Cell Adenoma or Carcinoma			
Overall Rates (a)	4/45 (9%)	3/48 (6%)	5/47 (11%)
Adjusted Rates (b)	12.9%	9.1%	14.7%
Terminal Rates (c)	4/31 (13%)	3/33 (9%)	5/34 (15%)
Life Table Tests (d)	P=0.480	P=0.465N	P=0.559
Incidental Tumor Tests (d)	P=0.480	P=0.465N	P=0.559
Cochran-Armitage Trend Test (d)	P=0.451		
Fisher Exact Tests		P=0.464N	P=0.528
Mammary Gland: Adenocarcinoma			
Overall Rates (a)	2/50 (4%)	3/49 (6%)	0/50 (0%)
Adjusted Rates (b)	5.8%	8.7%	0.0%
Terminal Rates (c)	1/33 (3%)	2/33 (6%)	0/35 (0%)
Life Table Tests (d)	P=0.190N	P=0.495	P=0.224N
Incidental Tumor Tests (d)	P=0.164N	P=0.424	P=0.202N
Cochran-Armitage Trend Test (d)	P=0.202N		
Fisher Exact Tests		P=0.490	P=0.247N
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	0/47 (0%)	0/47 (0%)	3/48 (6%)
Adjusted Rates (b)	0.0%	0.0%	8.6%
Terminal Rates (c)	0/31 (0%)	0/33 (0%)	3/35 (9%)
Life Table Tests (d)	P=0.044	(e)	P=0.143
Incidental Tumor Tests (d)	P=0.044	(e)	P=0.143
Cochran-Armitage Trend Test (d)	P=0.038		
Fisher Exact Tests		(e)	P=0.125

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No P value is presented because no tumors were observed in the 5,000 ppm and control groups.

APPENDIX F

HISTORICAL INCIDENCE OF TUMORS IN F344/N RATS AND B6C3F$_1$ MICE RECEIVING NO TREATMENT

TABLE F1. HISTORICAL INCIDENCE OF THYROID GLAND C-CELL TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Battelle Northwest Laboratories			
Propylene Oxide	1/45	1/45	2/45
Propylene	5/39	1/39	6/39
TOTAL	6/84 (7.1%)	2/84 (2.4%)	8/84 (9.5%)
Overall Historical Incidence			
TOTAL	119/2,317 (5.1%)	81/2,317 (3.5%)	197/2,317 (8.5%)
SD (b)	4.34%	2.99%	4.74%
Range (c)			
High	8/52	6/48	9/50
Low	0/86	0/52	0/50

(a) Data as of March 16, 1983, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F2. HISTORICAL INCIDENCE OF CIRCULATORY SYSTEM TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Hemangioma	Hemangiosarcoma	Hemangioma or Hemangiosarcoma
Historical Incidence at Battelle Northwest Laboratories			
Propylene Oxide	1/50	0/50	1/50
Propylene	0/50	0/50	0/50
TOTAL	1/100 (1.0%)	0/100 (0.0%)	1/100 (1.0%)
Overall Historical Incidence			
TOTAL	(b) 39/2,537 (1.5%)	(b) 51/2,537 (2.0%)	(b) 90/2,537 (3.5%)
SD (c)	1.87%	2.37%	2.61%
Range (d)			
High	3/47	4/50	5/49
Low	0/51	0/50	0/50

(a) Data as of March 16, 1983, for studies of at least 104 weeks
(b) Total includes three angiomas and eight angiosarcomas.
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.

TABLE F3. HISTORICAL INCIDENCE OF UTERINE ENDOMETRIAL STROMAL TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Polyp	Sarcoma	Polyp or Sarcoma
Historical Incidence at Battelle Northwest Laboratories			
Propylene Oxide	2/48	0/48	2/48
Propylene	0/47	0/47	0/47
TOTAL	2/95 (2.1%)	0/95 (0.0%)	2/95 (2.1%)
Overall Historical Incidence			
TOTAL	22/2,411 (0.9%)	8/2,411 (0.3%)	29/2,411 (1.2%)
SD (b)	1.47%	0.98%	1.84%
Range (c)			
High	3/50	2/47	3/47
Low	0/51	0/51	0/51

(a) Data as of March 16, 1983, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F4. HISTORICAL INCIDENCE OF LUNG ALVEOLAR/BRONCHIOLAR TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Battelle Northwest Laboratories			
Propylene Oxide	14/50	2/50	15/50
Propylene	7/50	9/50	16/50
TOTAL	21/100 (21.0%)	11/100 (11.0%)	31/100 (31.0%)
Overall Historical Incidence			
TOTAL	286/2,380 (12.0%)	119/2,380 (5.0%)	397/2,380 (16.7%)
SD (b)	6.69%	4.42%	8.34%
Range (c)			
High	14/50	(d) 9/50	17/50
Low	0/47	0/52	1/49

(a) Data as of March 16, 1983, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.
(d) Second highest incidence: 8/48 (16.6%)

APPENDIX G

CHEMICAL CHARACTERIZATION OF PROPYLENE

I. Identity and Purity Determinations of Lot No. Y-458 Performed by the Analytical Chemistry Laboratory

A. Gas Chromatography

1. Batch 02:

Instrument: Varian Aerograph, Series 1400
Detector: Thermal conductivity
Detector temperature: 150° C
Inlet temperature: 30° C (heater off)

a. System 1:

Column: Chromosorb 102, 100/120, 1.83 m × 3.2 mm, stainless steel
Sample injected: 1 ml using a gas syringe

(1) Run 1

Column temperature: 30° C, isothermal

Results: A major peak preceded by three impurities, the combined area of which is less than 0.11% that of the major peak

Peak	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	0.5	0.08	0.007
2	1.5	0.25	0.009
3	2.0	0.34	0.091
4	5.9	1.00	100

(2) Run 2

Column temperature: 75° C, isothermal

Results: A major peak and two impurities with a combined area of less than 0.11% that of the major peak

Peak	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	1.00	0.433	0.009
2	1.25	0.541	0.100
3	2.31	1.000	100

(3) Run 3

Column temperature program: 30°-120° C, at 15° C/min

Results: A major peak and four impurities whose combined area is less than 0.31% that of the major peak

Peak	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	0.5	0.14	0.004
2	1.5	0.41	0.008
3	2.5	0.69	0.086
4	3.6	1.00	100
5	10.3	2.86	0.21

b. System 2:

Column: Carbosieve B, 60/80, 3.05 m × 3.2 mm, stainless steel
Column temperature: 150° C, isothermal

Results: A major peak preceded by three impurities, the combined area of which is less than 0.11% that of the major peak

Peak	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	0.6	0.03	0.005
2	3.0	0.14	0.008
3	4.6	0.21	0.093
4	21.6	1.00	100

2. Batches 03 and 04:

Instrument: Varian Aerograph, Series 1400
Detector: Thermal conductivity
Detector temperature: 170° C
Inlet temperature: 84° C
Column: Chromosorb 102, 100/120, 1.83 m × 3.2 mm, stainless steel
Sample injected: 1 ml using a gas syringe
Column temperature: 50° C, isothermal

Results: A major peak preceded by two impurities for both batches, the combined area of which is less than 0.12% of the major peak for both

Batch 03

Peak	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	1.2	0.23	0.011
2	1.6	0.30	0.11
3	5.3	1.00	100

Batch 04

Peak	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	1.2	0.29	0.007
2	1.6	0.39	0.091
3	4.1	1.00	100

3. Batch 05:

Instrument: Varian 2400
Detector: Flame ionization
Detector temperature: 150° C
Inlet temperature: 30° C
Column: Chromosorb 102, 100/120, 1.83 m × 3.2 mm, stainless steel
Column temperature: 50° C, isothermal
Carrier gas: Nitrogen
Carrier flow rate: 20 ml/min
Sample injected: 1 ml using a gas syringe

Results: A major peak preceded by three impurities, the combined area of which is 0.1% that of the major peak. The data presented are for one of the five cylinders analyzed and are typical of the other four.

Peak	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	0.6	0.11	0.01
2	1.6	0.30	0.01
3	2.1	0.39	0.08
4	5.4	1.00	100

B. Infrared Spectroscopy: The infrared spectra of batches 02, 03, 04, and 05 of lot no. Y-458 were all determined under the following conditions:

Instrument: Beckman IR-12
Cell: 10 cm gas cell with sodium chloride windows

Results: The spectra of each batch of Y-458 were identical with a literature spectrum (Sadtler Standard Spectra; Pierson et al., 1956). See Figure 5.

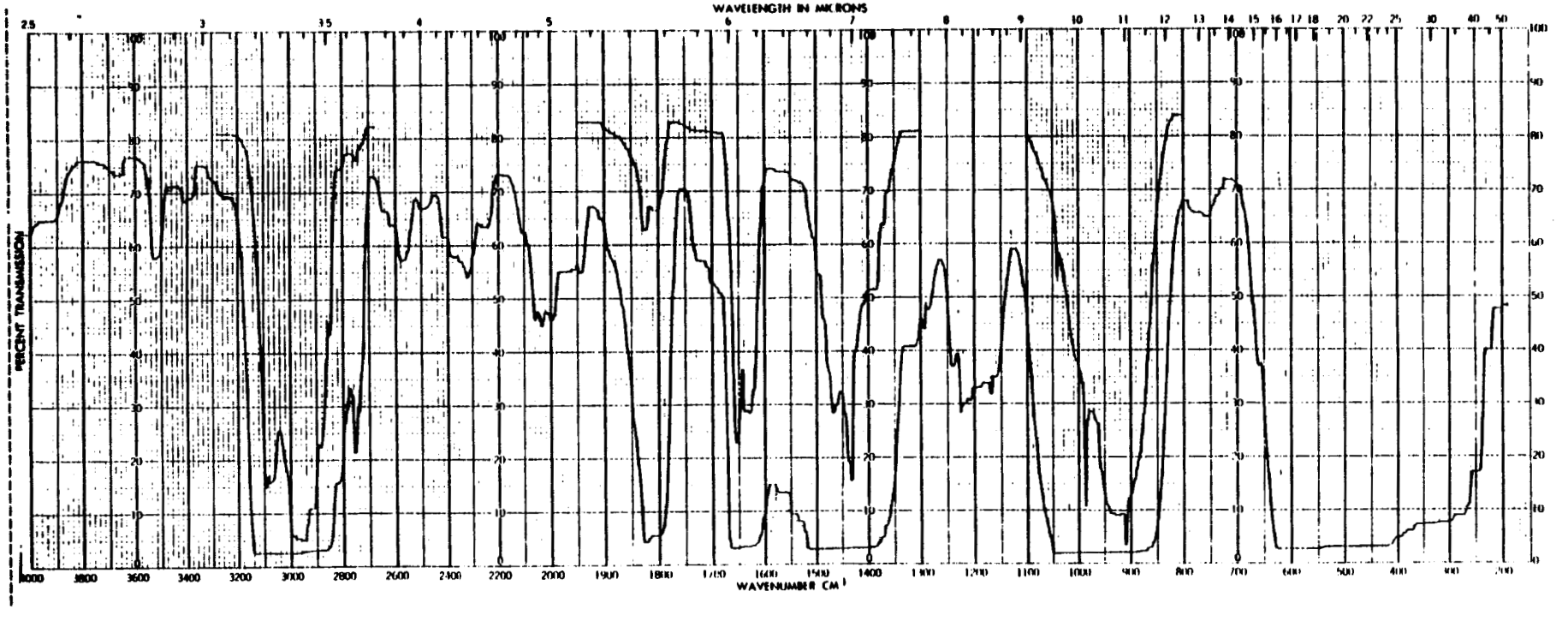

FIGURE 5. INFRARED ABSORPTION SPECTRUM OF PROPYLENE (LOT NO. Y-458)

II. Test Chemical Purity Determinations at the Testing Laboratory

A. Purity determination: Gas chromatographic analysis of the chemical was performed on a HP 5830A or HP 5840A using the following conditions:

Column: Porapak QS 80/100, 2.35 m × 2 mm ID, glass
Column temperature: 50° C, isothermal
Injector temperature: 100° C
Detector: Flame ionization
Detector temperature: 250° C

The percent purity (percentage of total peak area contributed by propylene) for each analysis is summarized below:

Lot	Date Analyzed	Percent Purity
Y-458	10/18/79	98.97
	6/13/80	98.95
B644	6/13/80	99.20
	9/23/80	99.47
	11/21/80	99.16
B887	2/27/81	99.65
	5/20/81	99.38
	7/14/81	99.58
	10/23/81	99.69

B. Identity Determination: The infrared absorption spectra were obtained on the gas in a 10-cm-path gas cell with sodium chloride windows by a Beckman Acculab 8. All spectra were consistent with those provided by the analytical chemistry laboratory.

C. Conclusion: These studies showed that the purity of the propylene ranged from 98.6% to 99.7%.

APPENDIX H

GENERATION AND MONITORING OF CHAMBER CONCENTRATIONS

I. Atmospheric Generation System: The generation system used to deliver propylene gas to each exposure chamber is depicted in Figure 6. Propylene was supplied in a 28-gallon gas cylinder located in the animal exposure room. The natural bottle pressure (about 147 psi at room temperature) was reduced to an operating pressure of 54 psi by a Union Carbide single-stage regulator. A nitrogen purge tee and check valve preceded this regulator to allow clearing of the entire gas distribution system for system maintenance or exchange of gas bottles.

The propylene was piped to a polyethylene vapor hood containing safety devices, comprising a flow-limiting valve, two emergency shut-off valves, a pop-off valve, and a pressure gauge. Since the exposure chambers were being operated with concentrations of propylene close to the lower explosive limit (LEL) of the gas (25% and 50% of the LEL), these safety devices were incorporated in the hood (vented to the room exhaust) to minimize the hazard to animals and personnel in the event of a leak. The gas was then piped to a second hood containing four double-pattern metering valves. Since the upstream pressure to these valves was well regulated, these valves provided stable control of the gas flow rate and ultimately of the concentration in the chambers. To provide the proper chamber concentration, the valves were set and periodically checked, by matching the calculated with the actual flow measured by a bubble meter. From the double-pattern metering valves, the gas was piped to each exposure chamber. A shut-off valve at the entrance to the chamber permitted easy, rapid termination of gas flow. All materials in the gas distribution system were stainless steel, Teflon®, viton, or brass.

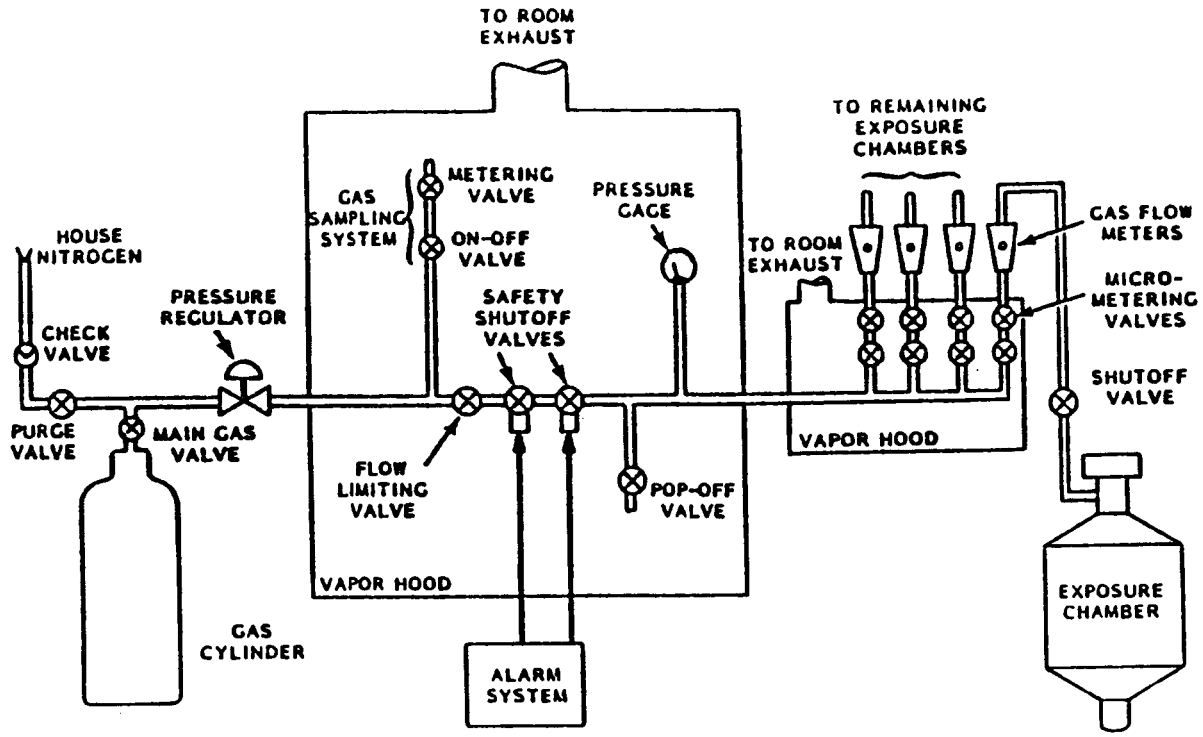

FIGURE 6. BLOCK DIAGRAM OF THE PROPYLENE GAS DISTRIBUTION SYSTEM

II. Vapor Concentration Uniformity in the Chamber: Uniformity of vapor concentration in the exposure chambers was measured periodically throughout the study. The vapor concentration was measured with a portable photoionization detector at 12 positions (2 positions, one at the front (F) and 1 at the back (B), for each of the six animal cage units per chamber). The sample point was just above and about 10 cm in from the front or back center of each cage unit (Figure 7). The data, normalized to the average concentration at all 12 sample positions for each chamber, are presented in Table H1.

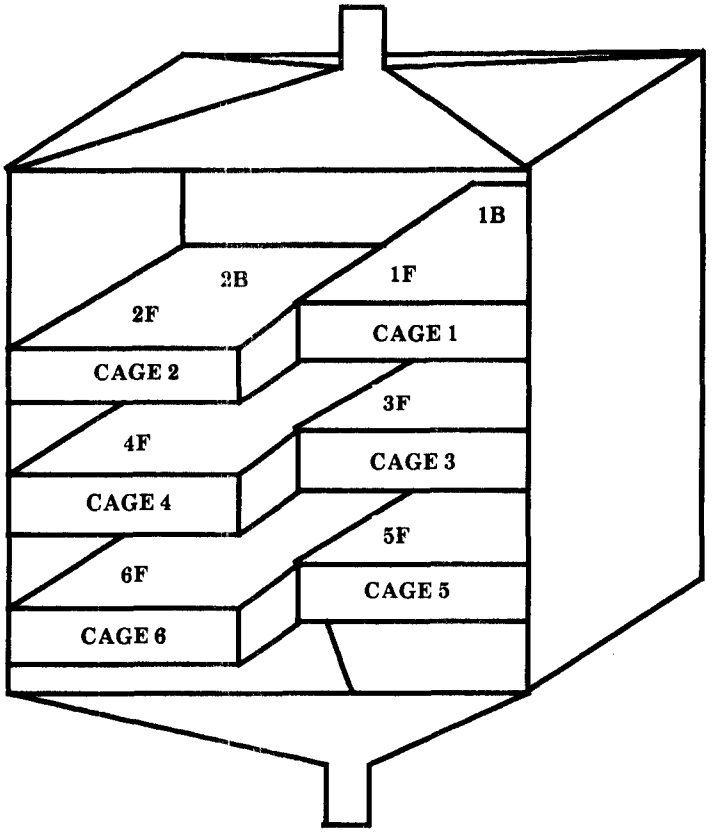

FIGURE 7. SCHEMATIC FRONT VIEW OF CHAMBER SHOWING APPROXIMATE SAMPLE SITES

TABLE H1. PROPYLENE VAPOR CONCENTRATION UNIFORMITY TEST (a)

Sample Location	10,000 ppm Rats	5,000 ppm Rats	10,000 ppm Mice	5,000 ppm Mice
Sample Date: 10/29/79				
1F	107	102	103	103
1B	(b)	(b)	(b)	97
2F	108	110	106	109
2B	(b)	100	(b)	97
3F	90	102	105	100
3B	103	77	94	100
4F	95	105	103	106
4B	102	102	94	91
5F	95	95	103	106
5B	107	90	96	88
6F	93	105	106	109
6B	100	112	89	91
Mean ± Standard Deviation	100 ± 6	100 ± 10	100 ± 6	100 ± 7
Sample Date: 3/06/80				
1F	94	100	97	97
1B	105	108	98	95
2F	96	100	98	98
2B	111	106	98	106
3F	92	94	99	97
3B	98	99	99	103
4F	93	98	100	93
4B	100	98	101	105
5F	93	97	104	100
5B	100	97	98	100
6F	111	101	103	100
6B	107	101	104	106
Mean ± Standard Deviation	100 ± 7	100 ± 4	100 ± 3	100 ± 4
Sample Date: 9/23/80				
1F	100	103	100	97
1B	97	100	100	103
2F	101	99	102	99
2B	103	102	100	103
3F	100	100	101	100
3B	100	99	97	100
4F	100	97	101	99
4B	100	102	100	100
5F	100	98	101	98
5B	99	100	97	100
6F	100	96	100	101
6B	100	103	100	99
Mean ± Standard Deviation	100 ± 6	100 ± 10	100 ± 6	100 ± 7

TABLE H1. PROPYLENE VAPOR CONCENTRATION UNIFORMITY TEST (Continued)

Sample Location	10,000 ppm Rats	5,000 ppm Rats	10,000 ppm Mice	5,000 ppm Mice
Sample Date: 1/29/81				
1F	94	96	98	96
1B	103	100	100	93
2F	91	100	103	103
2B	100	100	105	100
3F	94	96	103	100
3B	105	100	100	100
4F	97	100	98	100
4B	105	107	100	100
5F	100	96	98	100
5B	105	103	98	106
6F	97	103	98	100
6B	108	100	100	103
Mean ± Standard Deviation	100 ± 5	100 ± 3	100 ± 3	100 ± 3

(a) Percent of target concentration. Data normalized to the average concentration at all positions in each chamber.
(b) Data not taken

III. Chamber Concentration Monitoring System: Propylene concentrations in the exposure chambers, control chambers, and exposure room were automatically monitored approximately 10 times during each exposure day with a Hewlett-Packard 5840A gas chromatograph equipped with a flame ionization detector. A 50-cm × 4-mm ID glass column packed with Porapak QS 80/100 mesh held at 80° C was used. The calibration of the gas chromatograph was checked every 2 weeks using a "bag" standard prepared by the testing facility (10/79-3/81) or daily with an online standard (3/81-10/81).

During exposures, samples from each sampling location were continuously drawn by vacuum through stainless steel sample lines to near the input of an automatic multiplexed 8-port sample valve. The constant flow assured fresh samples at the 8-port valve.

Weekly mean concentrations are graphically presented in Figures 8-11, and monthly average chamber concentrations, in Table H2.

TABLE H2. ANALYSIS OF CHAMBER AIR FOR CONCENTRATIONS OF PROPYLENE IN THE TWO-YEAR INHALATION STUDIES

Date	Rats		Mice	
	5,000 ppm	10,000 ppm	5,000 ppm	10,000 ppm
11/79	5,010	9,790	5,024	9,817
12/79	5,007	10,037	5,150	10,001
1/80	4,982	10,001	5,127	9,983
2/80	4,701	9,964	4,842	9,863
3/80	4,951	9,962	4,894	9,917
4/80	5,012	9,721	4,881	9,732
5/80	4,871	9,656	4,901	9,935
6/80	4,953	9,832	4,993	9,822
7/80	4,967	9,879	4,996	10,087
8/80	4,963	9,853	4,893	9,828
9/80	5,010	10,099	5,131	10,152
10/80	4,867	9,830	5,075	9,888
11/80	5,064	9,845	5,055	9,930
12/80	5,153	10,126	5,131	9,826
1/81	4,963	9,918	5,039	9,738
2/81	4,973	9,939	5,043	10,041
3/81	5,080	10,009	4,998	10,048
4/81	4,972	9,708	4,964	9,955
5/81	4,965	9,792	4,953	9,860
6/81	5,088	10,085	5,089	10,174
7/81	5,056	10,048	5,083	10,083
8/81	5,052	9,955	5,043	9,993
9/81	5,012	9,940	4,913	10,092
10/81	5,070	9,931	4,915	9,953
Mean (ppm)	4,989	9,913	5,006	9,947
Standard deviation	89.8	126.2	91.2	123.1
Coefficient of variation (percent)	1.83	2.58	1.86	2.51
Range (ppm)	4,701 - 5,153	9,656 - 10,126	4,842 - 5,150	9,732 - 10,174

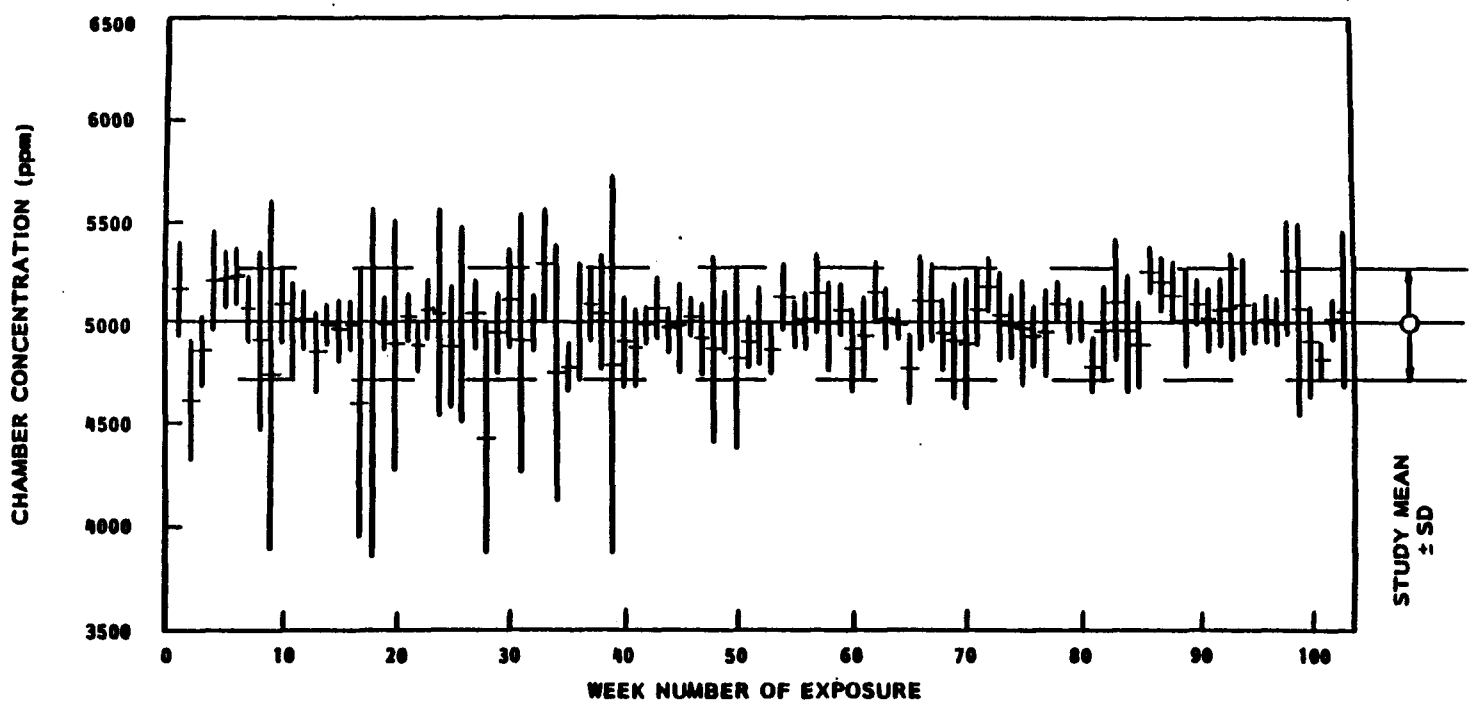

FIGURE 8. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN THE 5,000-ppm RAT EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

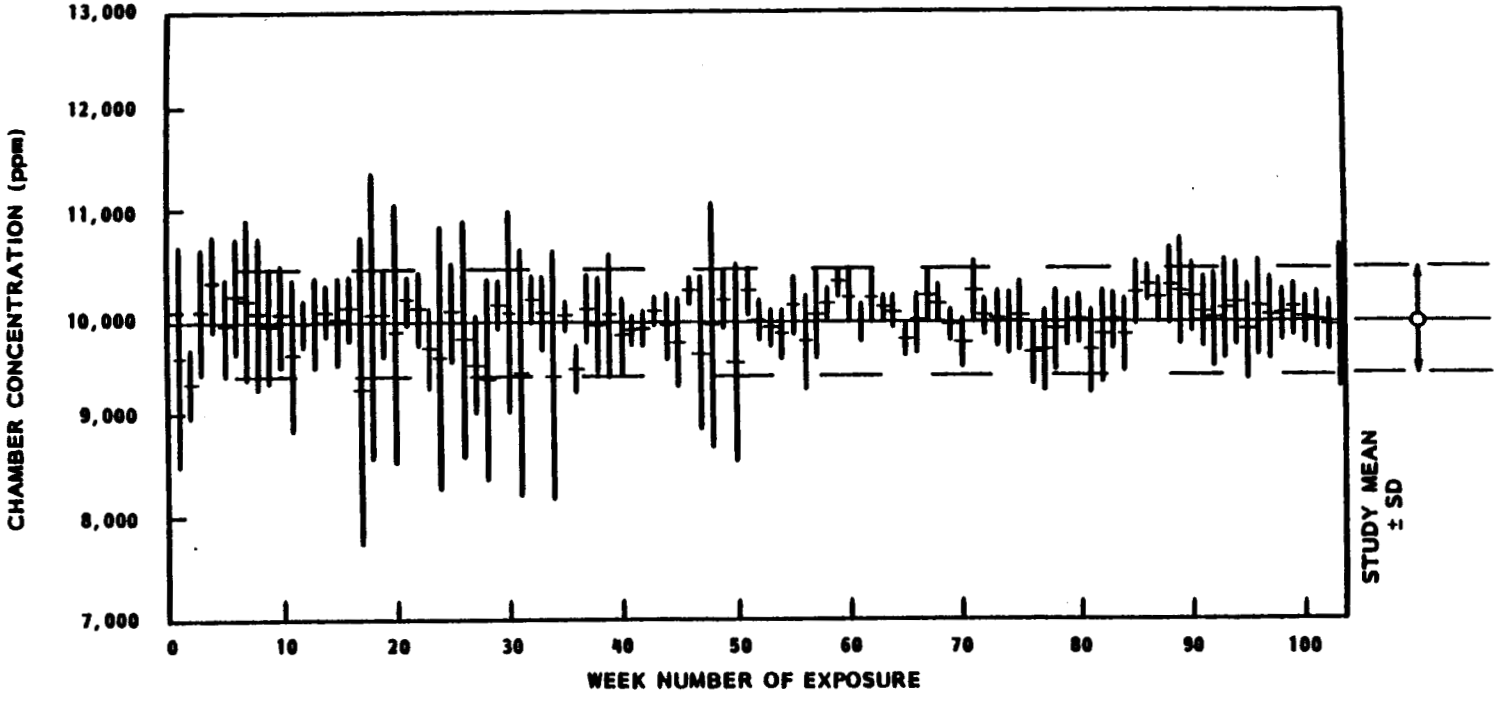

FIGURE 9. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN THE 10,000-ppm RAT EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

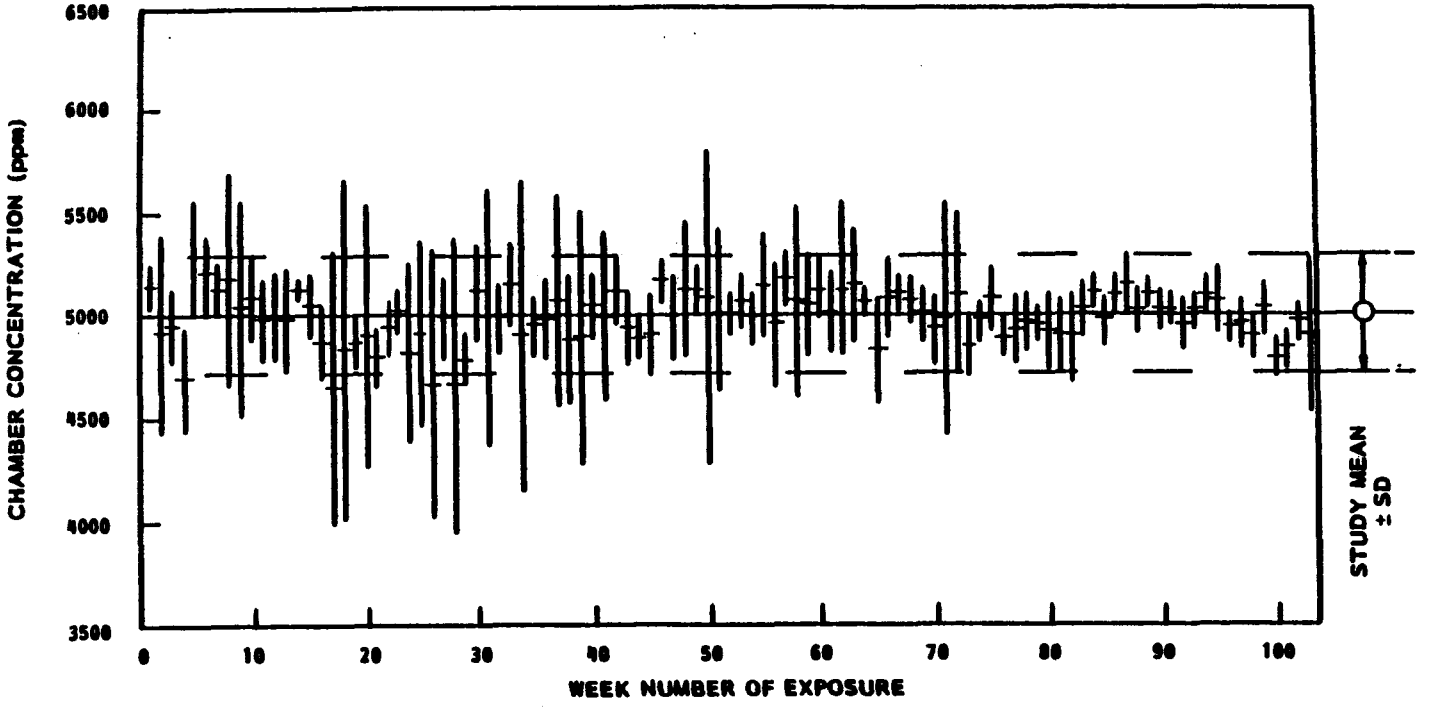

FIGURE 10. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN THE 5,000-ppm MOUSE EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

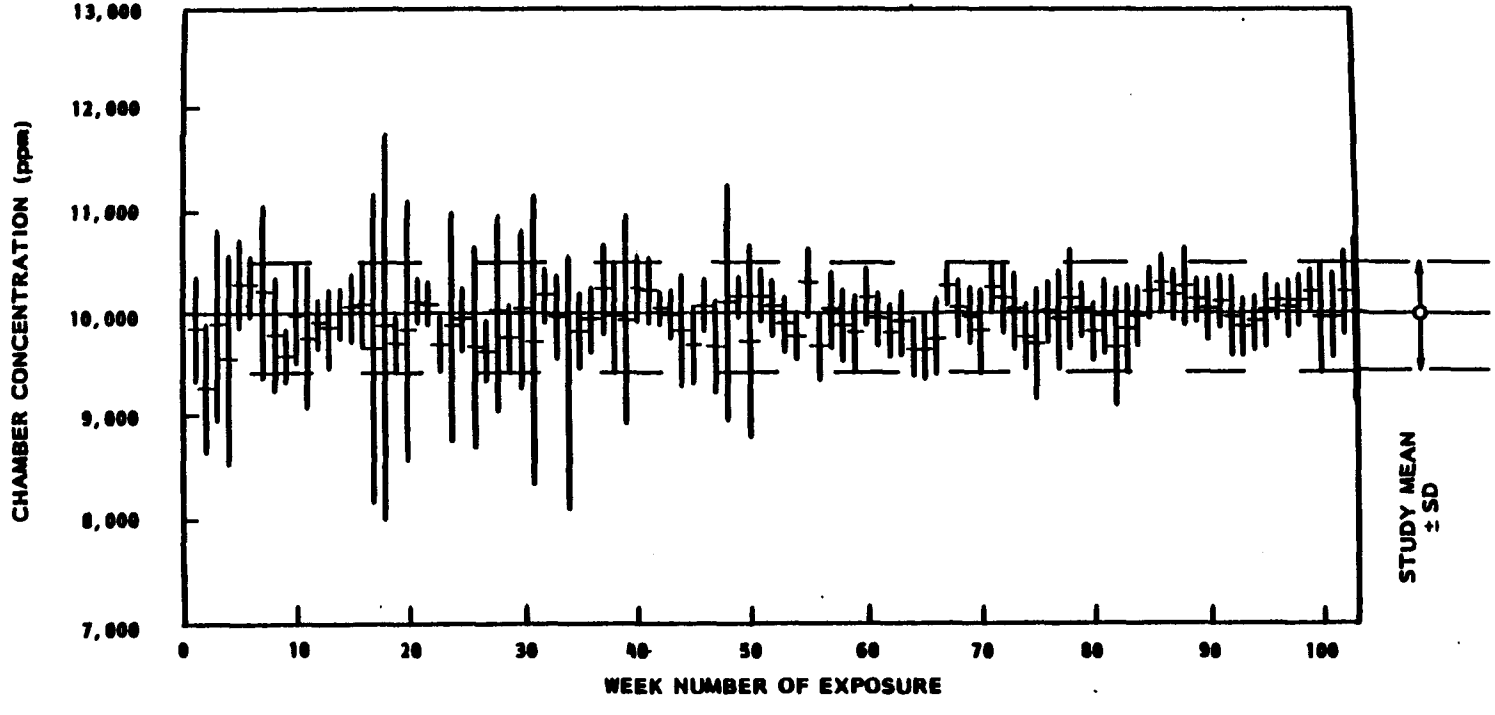

FIGURE 11. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN THE 10,000-ppm MOUSE EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

APPENDIX I

SENTINEL ANIMAL PROGRAM

APPENDIX I. SENTINEL ANIMAL PROGRAM

I. Methods

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

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

	Hemagglutination Inhibition	Complement Fixation	ELISA
Mice	PVM (pneumonia virus of mice) Reo 3 (reovirus type 3) GDVII (Theiler's encephalomyelitis virus) Poly (polyoma virus) MVM (minute virus of mice) Ectro (infectious ectromelia)	M.Ad. (mouse adenovirus) LCM (lymphocytic choriomeningitis virus) Sendai	MHV (mouse hepatitis virus)
Rats	PVM KRV (Kilham rat virus) H-1 (Toolan's H-1 virus)	RCV (rat coronavirus) Sendai	

II. Results

Results are presented in Table I1.

TABLE I1. MURINE VIRUS ANTIBODY DETERMINATIONS FOR RATS AND MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE (a)

Interval (months)	No. of Animals	Positive Serologic Reaction for
RATS		
6	--	None positive
12	--	None positive
18	--	None positive
24	7/10	Sendai
MICE		
6	--	None positive
12	--	None positive
18	1/10	PVM
24	8/10	MHV

(a) Blood samples were taken from sentinel animals at 6, 12, and 18 months after the start of dosing and from the control animals just before they were killed; samples were sent to Microbiological Associates, Inc. (Bethesda, MD) for the Animal Disease Screening Program.

APPENDIX J

DATA AUDIT SUMMARY

APPENDIX J. DATA AUDIT SUMMARY

The experimental data and draft NTP Technical Report on the 2-year inhalation studies of propylene in F344/N rats and B6C3F$_1$ mice were examined for completeness, consistency, and accuracy and for procedures consistent with Good Laboratory Practices. The 2-year studies were initiated by the National Cancer Institute in October 1979 and were completed in October 1981, prior to NTP's requirement for full compliance with Good Laboratory Practices regulations that were instituted in October 1981,. The studies were conducted by Battelle Pacific Northwest Laboratories, Richland, Washington, under subcontract with Tracor Jitco, Inc.

The audit of these studies was performed by Argus Research Laboratories, Inc., and Clement Associates in November 1983. The audit team included James H. Hills, Peter D. Ference, Alan M. Hoberman, Ph.D., Ronald L. Schueler, D.V.M., Ph.D., Cindy Sunier, Carol L. Vergle (H.T.), Erika Eckstut, and Dawn Goodman, D.V.M., Ph.D. The full report of the audit is on file at the National Toxicology Program, NIEHS, and is available on request. The audit included, but was not limited to, a review of the records of the in-life portion of the studies for 10% of the animals; records of room, chamber, and cage environment; 100% of available chemistry data except for daily exposure summaries; and 10% of the daily exposure summaries and corresponding chromatograms. All individual animal data records (IADR's) were examined for correspondence between necropsy observations and histopathologic findings. All wet tissue bags were counted, and 100% were reviewed for animal identification. Ten percent of the wet tissues were examined for untrimmed lesions. A complete slide/block match for each sex of both species in the high dose and control groups was performed. Records not available for audit included study animal receipt records, quarantine/acclimation records, and randomization methodology records.

Study animals were identified by ear tags, but records contain frequent notations of animals with missing tags (104/300 rats and 44/300 mice). Discrepancies relating to animal identification were found in clinical observation, body weight, and mortality records; these discrepancies may have been caused by missing ear tags. Daily observation records occasionally note that mice were observed free within the exposure chamber but were identified and returned to the appropriate cages. In one instance, mice were reported "missing" without later reference to location found. Although missing ear tags provided the potential for animal mixups within dose groups, the raw data that were audited gave no evidence of mixups between exposure groups. The audit did not identify other major problems with the conduct of the study or with collection and documentation of the experimental data. The chemistry data were adequate and support the stated conclusions in the Technical Report.

Animal identification in wet tissue bags could not be confirmed for 131/300 rats and 45/300 mice because of missing ear tags. In one instance, the wet tissue bag was mislabeled. Bag labeled LF (low dose female) 08 1175 should have been UF (untreated female) 08 1175. The ear tag belonged to UF 08, and 1175 is the histology number for UF 08. The slide/block match was good, with only two mismatches for rats and one for mice (2/1,884 and 1/1,695 matches, respectively). In general, there was good correlation of gross observations at necropsy with histologic diagnoses. In rats, only one discrepancy involved a target organ (lung); in mice, there were no discrepancies involving target organs. Untrimmed lesions were found in the wet tissue of three rats and five mice, but these did not involve target organs.

The only potentially significant problem occurring in the 2-year inhalation studies of propylene in rats and mice was the loss of ear tags, which caused discrepancies relating to animal identification when clinical observations, body weights, and mortality dates were recorded. Although the missing ear tags provided the potential for animal mixups within dose groups at necropsy, there was no evidence of animal mixups between exposure groups. Therefore, these are not believed to influence the final interpretation of these studies. The data examined in the audit are considered adequate to support the conclusions of the Technical Report.

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