NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 267

TOXICOLOGY AND CARCINOGENESIS STUDIES OF PROPYLENE OXIDE

(CAS NO. 75-56-9)

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, 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 OXIDE IN F344/N RATS AND B6C3F$_1$ MICE (INHALATION STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

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

NOTE TO THE READER

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 Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program. The study described in this Technical Report has been conducted under NTP health and safety requirements and/or guidelines for toxicity studies. Individual toxicology testing contractors are required to demonstrate corporate health and safety programs in compliance with NTP chemical health and safety requirements and to meet or exceed all applicable Federal, state, and local health and safety regulations.

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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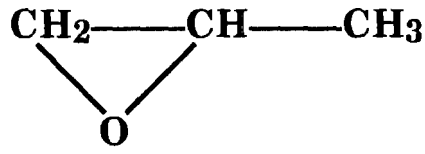

PROPYLENE OXIDE

CAS NO. 75-56-9
Mol. Wt. 58.08

ABSTRACT

The 2-year carcinogenesis studies of propylene oxide (greater than 99.9% pure) were conducted by exposing groups of 50 F344/N rats and 50 $B6C3F_1$ mice of each sex to air containing propylene oxide at concentrations of 0 (chamber control), 200, or 400 ppm for 6 hours per day, 5 days per week, for 103 weeks.

The survival of rats exposed to propylene oxide was comparable with that of the controls; terminal body weights were lower than those of the controls for high dose males (8%) and high dose females (6%). Survival of exposed male and female mice decreased relative to that of the controls (male: control, 42/50; low dose, 34/50; high dose, 29/50; female: 38/50; 29/50; 10/50), but the difference was significant only for animals in the high dose groups. High dose female mice had a mean terminal body weight 10% below that of the controls; high dose male mice had a terminal body weight 22% below that of the controls.

The respiratory epithelium of the nasal turbinates was one of the primary tissues affected in male and female rats; exposure-related increases occurred in the incidences of suppurative inflammation, epithelial hyperplasia, and squamous metaplasia. Papillary adenomas, involving the respiratory epithelium and underlying submucosal glands of the nasal turbinates, were observed in three female rats and two male rats exposed to propylene oxide at 400 ppm. The incidence of adenomas in females was significant by the trend tests.

The proportions of high dose female rats with C-cell adenomas and with C-cell carcinomas of the thyroid gland were increased, but only the combined incidence of these tumors was significant (2/45; 2/35; 7/37). These tumors were not considered to be related to exposure to propylene oxide because there was no other evidence for C-cells' being a target tissue and because there was no increase in C-cell hyperplasia.

The combined incidences of female rats with endometrial stromal polyps and endometrial stromal sarcomas of the uterus were significantly increased in the dosed groups (3/49; 12/50; 10/47). However, the occurrence of these lesions in the dosed groups was similar to the average (306/1,502, 20%) seen in untreated controls in NTP carcinogenesis studies, and hence this increase was not regarded as being related to exposure to propylene oxide.

The respiratory epithelium of the nasal turbinates was also one of the primary tissues affected in male and female mice; exposure-related increases occurred in the incidences of inflammation, and squamous metaplasia was observed in one low dose male and two high dose female mice. One squamous cell carcinoma and one papilloma occurred in the nasal cavity of different high dose male mice, and two high dose female mice had adenocarcinomas of the nasal cavity. The endothelial cells of the submucosal vascular plexus in the nasal turbinates also appeared to be a major site affected in high dose male mice. Three high dose male and three high dose female mice had a saccular dilation (classified as angiectasis) of submucosal turbinate vessels. Further, hemangiomas were seen in the nasal cavity of 5/50 high dose male mice and 3/50 high dose female mice, and hemangiosarcomas were found in the nasal cavity of 5/50 high dose male mice and 2/50 high dose female mice. The increased

incidences of hemangiomas in males and females and of hemangiosarcomas in males were statistically significant. Vascular tumors were not present in the nasal turbinates of any low dose or control mice.

Under the conditions of these studies, there was *some evidence of carcinogenicity** for F344/N rats, as indicated by increased incidences of papillary adenomas of the nasal turbinates in male and female rats exposed to propylene oxide at 400 ppm. For male and female $B6C3F_1$ mice, there was *clear evidence of carcinogenicity*, as indicated by increased incidences of hemangiomas or hemangiosarcomas of the nasal turbinates at 400 ppm. In the respiratory epithelium of the nasal turbinates, propylene oxide also caused suppurative inflammation, hyperplasia, and squamous metaplasia in rats and inflammation in mice.

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

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Propylene Oxide is based on the 13-week studies that began in March 1977 and ended in June 1977 at Industrial Biotest Laboratories and the 2-year studies that began in August 1979 and ended in December 1981 at Battelle Pacific Northwest Laboratories.

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The members of the Peer Review Panel who evaluated this Technical Report 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 OXIDE

On June 29, 1983, the Technical Report on propylene oxide 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. Holland, a principal reviewer for the Technical Report on the toxicology and carcinogenesis inhalation studies of propylene oxide, agreed in essence with the conclusions. He questioned whether propylene oxide "caused" hemangiomas and hemangiosarcomas in mice and suggested "associated with" the increased incidences as a preferable wording. Given the strong irritant properties of the chemical, tumor formation could be through indirect mechanisms. Dr. Friess agreed that the induction of nasal hemangiomas and hemangiosarcomas should be considered associated with, rather than caused by, the chemical. He suggested also that the tumors may have arisen from an action secondary to irritation, an action expressed only above a threshold level. Dr. Swenberg stated that these types of vascular tumors are so rare that the designation of clear evidence of carcinogenicity was appropriate. Dr. G. Boorman, NTP, noted that the mechanisms of action for most chemical carcinogens are unknown. Further, other evidence indicates that propylene oxide is a site-specific carcinogen.

Dr. Holland recommended that P values for assessing significance of survival between control and exposed groups should be summarized in the Technical Report. Dr. Haseman, NTP, indicated this would be done [see pages 34 and 43].

As a second principal reviewer, Dr. Slaga agreed with the conclusions but requested more discussion about why the increased incidence of adenomas and carcinomas of the thyroid in female rats was not considered chemically related. Dr. Boorman noted that the thyroid C-cell lesions were statistically significant only when combined, but were discounted because no increase in hyperplasias was observed and because no compelling evidence or rationale was apparent for C-cells' being a target tissue.

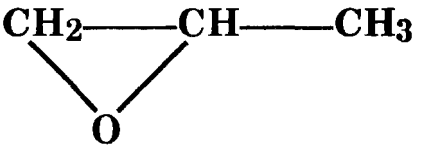
As a third principal reviewer, Dr. Harper agreed with the conclusions and also stated that the significance of differences in survival should be added routinely to the Technical Reports.

Dr. Davis noted that propylene oxide is an alkylating agent and is mutagenic and requested that nontumor data be given more prominent treatment. Dr. Boorman said this would be done where applicable. Dr. Scala noted the temperature fluctuations that occurred in the inhalation chambers and the variations in the concentrations of propylene oxide in the chamber, which reflected both overexposure and underexposure and which could temper the conclusions attributing a carcinogenic effect to a particular dose concentration. Dr. Boorman replied that there were only three instances of overexposure, the longest being 38 minutes, and he did not think they would influence the interpretations of the studies. Dr. Scala agreed.

Dr. Holland moved that the Technical Report on the toxicology and carcinogenesis studies of propylene oxide be accepted with the revisions discussed. Dr. Harper seconded the motion, and the Technical Report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION



PROPYLENE OXIDE
CAS NO. 75-56-9
Mol. Wt. 58.08

Propylene oxide is a volatile, colorless liquid used as an intermediate in the production of polyether polyols, polyurethane foams, and unsaturated polyester resins and also as a fumigant for sterilizing a variety of materials ranging from plastic medical instruments to foodstuffs (IARC, 1976). In the United States, propylene oxide is registered as a fumigant for packaged dried prunes and glacé fruits such as candied cherries and as an insecticidal and fungicidal fumigant for bulk quantities of cocoa, gums, and processed spices.

The concentration of propylene oxide residues in food is not to exceed 300 ppm (USCFR, 1979). In Japan, residues of propylene oxide at concentrations ranging from 10 ppm to several thousand parts per million have been measured in various foods fumigated with propylene oxide (Oguma et al., 1968, 1969). Plastic and cellulose products used as food wrappings also were shown to contain up to 6,000 ppm propylene oxide after being fumigated (Hirashima et al., 1970). Total production in the United States in 1980 was 1,767 million kilograms (USITC, 1981). Propylene oxide is also produced in Canada, Japan, and several European countries (IARC, 1976).

Propylene oxide is an irritant, a mild protoplastic poison, and a mild central nervous system depressant (Hine et al., 1981). Human exposure to propylene oxide vapors has caused corneal burns (McLaughlin, 1946) and contact dermatitis (Jensen, 1981; van Ketel, 1979). The current operating American Conference of Governmental Industrial Hygienists (ACGIH) and Occupational Safety and Health Administration (OSHA) limit for occupational exposure is 100 ppm (ACGIH, 1980). The recommended change is to 50 ppm.

In acute toxicity studies, LD_{50} values of 1.14 g/kg for rats and 0.69 g/kg for guinea pigs were obtained when propylene oxide was administered by gavage as a 5% aqueous solution (Jacobsen et al., 1956).

In inhalation studies, propylene oxide vapors appear to be about one-third as toxic as ethylene oxide (Hine et al., 1981). Groups of rats exposed to propylene oxide once for 30 minutes had 100% mortality at the 14,400-ppm concentration and 50% mortality at 7,200 ppm; a 2-hour exposure at 3,600 ppm killed 4/10 animals (Rowe et al., 1956; Jacobsen et al., 1956). Direct irritation of bronchi, bronchioles, and alveoli was found in animals that died after exposure at high concentrations. Effects included lacrimation, salivation, nasal discharge, and dyspnea; the injuries predisposed the animals to pulmonary infection (Hine et al., 1981).

Propylene oxide has been demonstrated to alkylate DNA in vitro. It reacts preferentially with guanine and adenine to produce hydroxypropyl adducts (Lawley and Jarman, 1972) and strand breaks (Walles, 1974). The strand breaks are presumably caused by alkylation of the phosphodiester backbone (Walles, 1974). Its alkylating ability has also been demonstrated with 4-(p-nitrobenzyl)pyridine (Hemminki and Falck, 1979; Hemminki et al., 1980). Consistent with this alkylating ability is propylene oxide's induction of mutations in bacteriophage and *Bacillus subtilis* single-stranded DNA in two different bacterial transformation assays (Phillips et al., 1980; Garro and Phillips, 1980). Con flicting results were obtained with respect to strand-breaking ability in both assays. Incubation of *Escherichia coli* bacteriophage T2 with propylene oxide did not produce mutation (Cookson et al., 1971).

Propylene oxide was found to be a direct-acting mutagen in Salmonella assays (Ames et al., 1975) performed in a number of laboratories using spot test, plate assay, and suspension test

protocols (Bootman et al.,1979; Hemminki and Falck, 1979; McMahon et al., 1979; Pfeiffer and Dunkelberg, 1980; Wade et al., 1978). It preferentially mutated strains TA1535 and TA100, indicating that only base-pair substitution mutations were induced. Propylene oxide was also a direct-acting mutagen in *Klebsiella pneumoniae* (Voogd et al., 1981) and *E. coli* (Bootman et al., 1979; Hemminki and Falck, 1979; Hemminki et al., 1980). Mutations were also induced in the yeast, *Schizosaccharomyces pombe* (Heslot, 1962), and in *Neurospora crassa* (Kolmark and Giles, 1955). In Drosophila, propylene oxide produced sex-linked recessive lethal mutations (Schalet, 1954; Hardin et al., 1983).

Propylene oxide produced a high frequency of chromatid aberrations (primarily gaps, but some exchanges and deletions) in an "epithelial-like" rat liver cell line that did not undergo exogenous metabolic activation (Dean and Hodson-Walker, 1979). In addition, human lymphocytes exhibited a high frequency of chromatid breaks and gaps following in vitro incubation with propylene oxide (Bootman et al.,1979).

A micronucleus test (i.e., measurement of the production of micronucleated, polychromatic erythrocytes) was negative in male CD-1 mice administered propylene oxide by gavage in two 100, 250, or 500 mg/kg doses (Bootman et al., 1979). A low-level, dose-related response was obtained, however, when two doses of 75 or 300 mg/kg propylene oxide in water were administered intraperitoneally; only the response to the 300 mg/kg dose was significantly elevated. A dominant lethal test in male CD-1 mice produced no decreases in total implants or increases in implant deaths when propylene oxide in 0.5% gum tragacanth was administered by gavage for 14 consecutive days at doses of 50 or 250 mg/kg (Bootman et al., 1979).

No significant increases occurred in the incidences of chromosomal aberrations or sister chromatid exchanges in peripheral lymphocytes from Cynomologus monkeys (*Macaca fascicularis*) exposed to propylene oxide by inhalation. Ethylene oxide produced weakly positive results in the same study (NIOSH, 1983).

Tumors of the forestomach, mainly squamous cell carcinomas, occurred in 4% and 40% of female Sprague-Dawley rats administered propylene oxide in salad oil by gavage at doses of 15 and 60 mg/kg body weight (Dunkelberg, 1982). Doses were administered twice per week for 150 days. These tumors were seen in 16% and 62% of the animals administered ethylene oxide at doses of 7.5 and 30 mg/kg, respectively, on the same schedule. There was no evidence that either compound induced tumors at sites other than the forestomach.

When administered subcutaneously, propylene oxide has been associated with tumors at the injection site in rats (Walpole, 1958) and mice (Dunkelberg, 1979, 1981). The National Institute for Occupational Safety and Health (NIOSH) concluded that inhalation exposure of male F344 rats to ethylene oxide (50 or 100 ppm) for 2 years was associated with an increased incidence of mesotheliomas (apparently from the tunica vaginalis) and a low incidence of central nervous system gliomas (NIOSH, 1983). Administration of propylene oxide (100 or 300 ppm) to male F344 rats under the same exposure conditions did not produce evidence of exposure-related tumors other than two adenomas of the nasal cavity in the high dose group. These findings were confirmed by an NTP Pathology Working Group.

A joint industry committee on propylene oxide sponsored a 28-month inhalation toxicity/carcinogenicity study of propylene oxide in rats (Reuzel and Kuper, 1983). Groups of 70 male and female rats (Cpb:Wu, Wistar Random) were exposed to propylene oxide at concentrations of 0, 30, 100, or 300 ppm, 6 hours per day, 5 days per week for 124 weeks (males) or 123 weeks (females). Additional groups of 10 animals were exposed and examined at 12, 18, and 24 months. At 300 ppm, there was a slight weight reduction and increased mortality in both males and females as compared with controls. Nonneoplastic compound-related changes were found only in the nasal cavity, where four levels were examined. These changes included degeneration of the olfactory epithelium and hyperplasia of the respiratory epithelium. Squamous metaplasia was not found. Compound-related tumors were restricted to the female rat; both the number of rats bearing mammary tumors and the number of mammary tumors per rat were significantly increased (Table 1).

I. INTRODUCTION

Propylene oxide was tested because of its extensive production, the potential for human exposure in the workplace or in food, the positive results of short-term genetic assays, and the inadequacy of available animal carcinogenesis data.

TABLE 1. INCIDENCES OF MAMMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE (a)

	Concentration Propylene Oxide (ppm)			
	0	30	100	300
No. with benign mammary tumors	32	30	39	47
Av. no. tumors/tumor-bearing animal	1.3	2.1	2.2	2.4
No. with carcinomas	3	6	5	8

(a) Reuzel and Kuper, 1983

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF PROPYLENE OXIDE

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

SINGLE-EXPOSURE STUDIES

REPEATED-EXPOSURE STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

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

PROCUREMENT AND CHARACTERIZATION OF PROPYLENE OXIDE

Propylene oxide was obtained from Leidy Chemical Corporation (Baltimore, MD) in two lots. Lot no. UC 5/10/76 was used for the single-exposure, repeated-exposure, and 13-week studies; and lot no. 6477-22 was used for the 2-year studies. Purity and identity analyses were conducted at Midwest Research Institute (Kansas City, MO). The identities of both lots of the chemical were confirmed by elemental and spectroscopic analyses (Appendix G). Elemental analyses for carbon and hydrogen agreed with theoretical values. Two gas chromatographic systems indicated only a major peak. Data obtained from these studies indicate that the propylene oxide used in these studies was greater than 99.9% pure.

After the test chemical was received from the analytical contractor, the testing laboratory performing the 2-year studies stored the chemical at room temperature and periodically reanalyzed it by infrared analysis and gas chromatography. These analyses indicated that no degradation of the stored chemical occurred during the course of the 2-year studies (Appendix G).

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

Propylene oxide was vaporized at room temperature, diluted with air, and introduced into the chambers (Appendix H). Concentrations in the exposure chambers were monitored 8-12 times per exposure period by a Hewlett-Packard 5840A Gas Chromatograph. Weekly mean exposure concentrations are presented in Appendix H. The vapor concentrations were within 10% of the mean values of the concentrations at all positions sampled within the chamber. On three occasions, high dose mice were exposed to propylene oxide at concentrations greater than 1,000 ppm. These incidents together with a summary of chamber concentrations for the 2-year studies are presented in Table 2.

SINGLE-EXPOSURE STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Center and observed before being placed on study. The study was conducted at Industrial Biotest Laboratories.

TABLE 2. SUMMARY OF CHAMBER CONCENTRATIONS OF PROPYLENE OXIDE DURING THE TWO-YEAR STUDIES

Target Concentration (ppm)	Average Chamber Concentation (a) (ppm)	Total No. of Readings
MICE		
200	198 ± 17	5,419
(b) 400	396 ± 36	5,438
RATS		
200	200 ± 15	5,419
(b) 400	397 ± 30	5,406

(a) ± Standard deviation
(b) The following overexposure incidents occurred during the studies: week 14, 17 min overexposure, ≤4,100 ppm; week 30, 12 min, ≤6,448 ppm; week 82, 38 min, ≤1,091 ppm.

Groups of five rats of each sex were exposed for 4 hours to air containing 1,277, 2,970, 3,794, or 3,900 ppm propylene oxide. Groups of five mice of each sex were exposed to air containing 387, 859, 1,102, 1,277, or 2,970 ppm propylene oxide on the same schedule.

Animals were observed daily for moribundity and mortality and were weighed on days 0 and 15. Gross necropsies were performed on all animals. Details of animal maintenance are presented in Table 3.

REPEATED-EXPOSURE STUDIES

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Center and observed for 11 days before being placed on study. The animals were approximately 6-8 weeks old when the studies began. The studies were conducted at Industrial Biotest Laboratories.

Groups of five rats of each sex were exposed to air containing propylene oxide at time-weighted average concentrations of 0, 47.2, 98.5, 196, 487, or 1,433 ppm 6 hours per day, 5 days per week for 2 weeks (10 exposures). Groups of five mice of each sex were similarly exposed to air containing propylene oxide at time-weighted average concentrations of 0, 20.1, 47.2, 98.5, 196, or 487 ppm.

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF PROPYLENE OXIDE

Single-Exposure Studies	Repeated-Exposure Studies	Thirteen-Week Studies	Two-Year Studies
EXPERIMENTAL DESIGN			
Size of Test Groups			
5 males and 5 females of each species	5 males and 5 females of each species	10 males and 10 females of each species	50 males and 50 females of each species
Doses			
Rats--1,277, 2,970, 3,794, or 3,900 ppm propylene oxide by inhalation; mice--387, 859, 1,102, 1,277,or 2,970 ppm by inhalation	Rats--0, 47.2, 98.5, 196, 487, or 1,433 ppm propylene oxide by inhalation; mice--0, 20.1, 47.2, 98.5, 196, or 487 ppm by inhalation	0, 31, 63, 125, 250, or 500 ppm propylene oxide by inhalation	0, 200, or 400 ppm propylene oxide by inhalation
Date of First Exposure			
10/25, 10/26, 10/27, 10/28, and 11/1/76	11/30/76	3/3/77	Rats--8/29/79; mice--8/29/79; low dose restart--12/31/79
Date of Last Exposure			
NA	12/10/76	Rats--6/1/77 Mice--6/2/77	Rats--8/14/81; mice--8/14/81; low dose restart--12/18/81
Duration of Exposure			
4 h	6 h/d, 10 exposures (excluding 12/5/76)	6 h/d, 5 d/wk for 13 wk Rats--62 exposures Mice--63 exposures	6 h/d, 5 d/wk;.rats and high dose mice--491 exposure days; low dose mice--495 exposure days
Type and Frequency of Observation			
Observed throughout exposure and 14 d observation period for moribundity and mortality; weighed on d 0 and 15	Observed 1 × d for moribundity and mortality; weighed on d 0, 4, 8, and 12	Observed 1 × d for moribundity and mortality; weighed on d 0 and 1 × wk thereafter	Observed 2 × d for signs of moribundity and mortality; examined 1 × mo for clinical signs of toxicity; all animals weighed 1 × wk for 13 wk, then 1 × mo, finally 2 × mo for remaining 3 mo or 6 mo (restart mice); palpation for tumor masses on 11/5/80 and at each weighing thereafter
Necropsy and Histologic Examination			
Necropsy performed on all animals (gross only)	Necropsy performed on all animals (gross only)	Necropsy performed on all animals; histopathologic exam performed on all control and high dose animals and those that died before final kill; tissues examined are similar to those in the 2-y studies except only one section of nasal turbinate was examined	Necropsy performed on all animals; the following tissues were examined: gross lesions, skin, mandibular lymph nodes, tissue masses and regional lymph nodes, thigh muscle, sciatic nerve, sternebrae, including marrow, costochondral junction (rib), thymus, larynx, pharynx, trachea, lungs and bronchi, heart, thyroid gland, parathyroids, esophagus, stomach, duodenum, jejunum, salivary gland, ileum, colon, cecum, rectum, liver, eyes, pancreas, spleen, kidneys, adrenal glands, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity and nasal turbinates (3 sections), brain, pituitary gland, spinal cord, and gallbladder (mice only); histopathologic exam(including blood smear) performed on all above tissues except: thigh muscle, sciatic nerve, costochondral junction (rib), duodenum,jejunum, salivary gland,

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF PROPYLENE OXIDE (Continued)

Single-Exposure Studies	Repeated-Exposure Studies	Thirteen-Week Studies	Two-Year Studies
Necropsy and Histologic Examination (Continued)			
			ileum, cecum, rectum, seminal vesicles, and eyes and pharynx unless grossly abnormal
ANIMALS AND ANIMAL MAINTENANCE			
Species			
F344/N rats; B6C3F$_1$ mice	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)	Frederick Cancer Research Center (Frederick, MD)	Charles River Breeding Labs, Inc. (Portage, MI)
Time Held Before Start of Test			
Data not available	11 d	14 d	21 d; 18 d (restart mice)
Age When Placed on Study			
Data not available	6-8 wk	Data not available	Rats--7-8 wk; mice--7-9 wk
Age When Killed			
Data not available	8-10 wk	Data not available	Rats--111-112 wk; mice--111-113 wk
Necropsy Dates			
Rats--11/9/76-11/16/76; mice--11/9/76-11/13/76	12/11/76	Rats--6/2/77; mice--6/3/77	Rats--8/24-8/26/81; mice--8/27-8/28/81; restart: 12/28/81
Method of Distribution			
Assigned to groups so that average weights were approximately equal	Same as single-exposure studies	Assigned to groups according to a table of random numbers	Stratified by weight; assigned to groups according to a table of random numbers
Feed			
Data not available	Wayne Lab-Blox® (Allied Mills, Inc., Chicago, IL); available ad libitum except during exposure	Same as repeated-exposure studies	Same as repeated-exposure studies
Bedding			
None	None	None	None
Water			
Automatic watering system; available freely	Automatic watering system; available freely	Automatic watering system; available freely	Automatic watering system (Edstrom Industries, Inc., Waterford, WI); filtered, softened tap water; available freely
Cages			
Stainless steel mesh Chamber--stainless steel and glass	Stainless steel mesh Chamber--stainless steel and glass; nominal volume--8 m^3	Stainless steel mesh (Unifab Corp., Kalamazoo, MI) Chamber--stainless steel and glass, nominal vol--8 m^3 (King-Lar Co., Decatur, IL)	Stainless steel wire cages (Lab Products, Inc., Rochelle Park, NJ); BNW-designed chambers (Hazelton Systems, Inc., Aberdeen, MD)
Animals per Cage			
1	1	1	1

TABLE 3. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF PROPYLENE OXIDE (Continued)

Single-Exposure Studies	Repeated-Exposure Studies	Thirteen-Week Studies	Two-Year Studies
Other Chemicals on Test in Same Room			
Acrylonitrile Methyl methacrylate	Acrylonitrile Methyl methacrylate	Methyl methacrylate	Propylene
Animal Room Environment			
Data not available	Data not available	12 h fluorescent light/d	20 changes room air/h (during nonexposure, chamber door left open); fluorescent light 12 h/d; chamber temp--18.3°-27.8° C (mice); 20.6°-29.4° C (rats); chamber hum--37%-81% (rats); 32%-84% (mice); room temp--21.1° C during exposure; 23.9° C during nonexposure
CHEMISTRY			
Lot Numbers Used			
UC 5/10/76	UC 5/10/76	UC 5/10/76	6477-22
Supplier			
Leidy Chemical Corp. (a division of Union Carbide) (Baltimore, MD)	Same as single-exposure studies	Same as single-exposure studies	Same as single-exposure studies
CHEMICAL/VEHICLE			
Preparation			
Clean dry air (−40° C dew-point) introduced through all-glass impingers containing chemical; desired concentrations were achieved by varying the amount of air which passed through the test material	Same as single-exposure studies	Same as single-exposure studies	Propylene oxide was vaporized at room temp, diluted with air, and introduced into the chamber (Appendix H)

Rats and mice were observed daily for moribundity and mortality and were weighed on days 0, 4, 8, and 12. Necropsies were performed on all animals on day 12. Details of animal maintenance are presented in Table 3.

THIRTEEN-WEEK STUDIES

Thirteen-week studies were conducted to evaluate the cumulative toxicity of propylene oxide and to determine the concentrations to be used in the 2-year studies. The 13-week studies were conducted at Industrial Biotest Laboratories.

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Center, observed for 2 weeks, and then assigned to test groups according to a table of random numbers. (The animals were presumed to be 5-6 weeks old when received. Data on actual ages are not available.) Feed was available freely during nonexposure periods, and water was available freely at all times.

Groups of 10 rats and 10 mice of each sex were exposed to air containing propylene oxide at concentrations of 0, 31, 63, 125, 250, or 500 ppm, 6 hours per day, 5 days per week, for 13 weeks. Animals were checked daily for signs of moribundity and mortality; moribund animals were killed, and necropsies were performed. Clinical examinations were performed weekly. Body weight data were collected weekly.

At the end of the 13-week studies, survivors were killed. Necropsies were performed on all animals, except for those excessively autolyzed or cannibalized. Tissues examined are listed in Table 3.

TWO-YEAR STUDIES

Study Design

These studies were conducted at Battelle Northwest Laboratories. Groups of 50 rats and 50 mice of each sex were exposed to air containing propylene oxide at concentrations of 0 (chamber controls), 200, or 400 ppm, 6 hours per day, 5 days per week for 103 weeks. Groups of low dose mice of each sex were restarted 19 weeks after the initial start date because a technical error produced excessive chamber concentrations of propylene oxide, which killed all low dose animals.

Source and Specifications of Test Animals

Four- to five-week-old male and female F344/N rats and B6C3F$_1$ mice (C57BL/6N x C3H/HeN MTV$^-$) were received from Charles River Breeding Laboratories and held for 21 days before the test began. The rats and mice were assigned to groups according to a table of random numbers.

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 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. The sentinel animal program is described in Appendix I.

Animal Maintenance

Rats and mice were housed individually. Food and water were available freely except during exposure periods; during the exposure periods, water but not food was available. Details of animal maintenance are presented in Table 3.

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 13 weeks, then once per month, and finally twice per month for the remaining 3 months or 6 months (restart mice). Mean body weights were calculated for each group. 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 3. 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. (1984). 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) extensions of Cox's method for testing 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 has been given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators 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 in each group examined during the time period. 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: 0-52 weeks, 53-78 weeks, 79-92 weeks, week 93 to the week before the terminal-kill period, and the terminal-kill period. The denominators of these proportions were the number of animals 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 Peto et al., 1980, 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's exact test for pairwise comparisons and the Cochran-Armitage linear trend test (Armitage, 1971; Gart et al.,1979) are given. These two tests are based on the overall proportion of tumor-bearing animals and do not adjust for survival differences.

III. RESULTS

RATS

SINGLE-EXPOSURE STUDIES

REPEATED-EXPOSURE STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

MICE

SINGLE-EXPOSURE STUDIES

REPEATED-EXPOSURE STUDIES

THIRTEEN-WEEK STUDIES

TWO-YEAR STUDIES

Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

SINGLE-EXPOSURE STUDIES

Deaths occurred in all exposure groups except those exposed at 1,277 ppm (Table 4). Dyspnea and a red nasal discharge were observed in animals in the three highest exposure groups. No compound-related gross pathologic effects were recorded.

REPEATED-EXPOSURE (TWELVE-DAY) STUDIES

One of five male rats exposed at 1,433 ppm died (Table 5). No other deaths occurred.

Dyspnea, hypoactivity, gasping, ataxia, and diarrhea were observed in rats in the highest dose group.

TABLE 4. SURVIVAL OF RATS IN THE SINGLE FOUR-HOUR-EXPOSURE INHALATION STUDIES OF PROPYLENE OXIDE

Concentration (a) (ppm)	Survival (b) (day of death)	
	Male	Female
1,277	5/5	5/5
2,970	4/5 (3)	3/5 (1,2)
3,794	1/5 (1,3,4,5)	1/5 (1,1,3,5)
3,900	2/5 (1,2,2)	2/5 (1,1,2)

(a) Time-averaged mean
(b) Number surviving/number per group

TABLE 5. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE TWO-WEEK REPEATED-EXPOSURE INHALATION STUDIES OF PROPYLENE OXIDE

Concentration (a) (ppm)	Survival (b)	Mean Body Weight (grams)			Final Weight Relative to Controls (d) (percent)
		Initial (c)	Final	Change	
MALE					
0	5/5	106.4 ± 3.2	161.8 ± 4.4	+ 55.4 ± 2.8	--
47.2	5/5	109.6 ± 3.0	163.6 ± 5.0	+ 54.0 ± 3.6	101.1
98.5	5/5	109.2 ± 3.5	165.4 ± 5.0	+ 56.2 ± 2.7	102.2
196	5/5	106.2 ± 2.5	159.8 ± 5.1	+ 53.6 ± 4.0	98.8
487	5/5	104.4 ± 6.6	156.0 ± 7.0	+ 51.6 ± 2.6	96.4
1,433	4/5	106.4 ± 3.2	91.8 ± 1.3	− 13.5 ± 3.2	56.7
FEMALE					
0	5/5	91.2 ± 3.1	121.4 ± 2.0	+ 30.2 ± 1.7	--
47.2	5/5	93.6 ± 2.9	122.8 ± 4.2	+ 29.2 ± 2.1	101.2
98.5	5/5	89.4 ± 2.3	114.4 ± 3.4	+ 25.0 ± 2.6	94.2
196	5/5	91.0 ± 3.6	122.2 ± 4.2	+ 31.2 ± 0.7	100.7
487	5/5	90.6 ± 3.4	117.4 ± 4.3	+ 26.8 ± 1.9	96.7
1,433	5/5	90.2 ± 3.3	91.0 ± 2.6	+ 0.8 ± 1.4	75.0

(a) Time-averaged mean
(b) Number surviving/number initially in the group
(c) Initial mean weight of all animals in the group ± standard error of the mean. Subsequent calculations are based on those animals surviving to the end of the studies.
(d) Final body weight of the dosed group relative to controls = $\frac{\text{Final Body Weight (Dosed)}}{\text{Final Body Weight (Control Group)}} \times 100$

THIRTEEN-WEEK STUDIES

No rats died. Final mean body weights relative to those of controls were 7.4% lower in males and 5.3% lower in females exposed to air containing 500 ppm propylene oxide (Table 6). No compound-related gross or microscopic pathologic effects were observed. One section of nasal turbinate per animal was prepared and examined. Chronic murine pneumonia was found in all groups of rats examined histologically.

Because of the weight gain depressions in males exposed at 500 ppm, exposure concentrations of 200 and 400 ppm were selected for rats in the 2-year studies.

TABLE 6. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE THIRTEEN-WEEK INHALATION STUDIES OF PROPYLENE OXIDE

Concentration (ppm)	Survival (a)	Mean Body Weight (grams) Initial	Final	Change (b)	Final Weight Relative to Controls (c) (percent)
MALE					
0	10/10	120.9 ± 3.6	299.3 ± 2.8	+178.4 ± 4.4	--
31	10/10	122.5 ± 2.5	295.7 ± 4.4	+173.2 ± 4.5	98.8
63	10/10	122.4 ± 2.6	305.4 ± 4.8	+183.0 ± 4.7	102.0
125	10/10	121.9 ± 2.7	296.9 ± 5.0	+175.0 ± 5.9	99.2
250	10/10	122.2 ± 2.3	299.2 ± 2.6	+177.0 ± 1.7	100.0
500	10/10	125.2 ± 2.5	277.1 ± 5.0	+151.9 ± 4.5	92.6
FEMALE					
0	10/10	98.7 ± 1.9	177.5 ± 3.5	+ 78.8 ± 2.4	--
31	10/10	98.1 ± 2.1	173.9 ± 1.2	+ 75.8 ± 2.0	98.0
63	10/10	98.6 ± 1.9	176.7 ± 3.0	+ 78.1 ± 2.1	99.5
125	10/10	98.5 ± 1.9	172.4 ± 3.1	+ 73.9 ± 2.6	97.1
250	10/10	99.1 ± 1.8	176.6 ± 2.6	+ 77.5 ± 2.7	99.5
500	10/10	100.7 ± 1.7	168.1 ± 1.1	+ 67.4 ± 1.5	94.7

(a) Number surviving/number initially in the group
(b) Mean weight change of the group ± standard error of the mean
(c) Final body weight of the dosed group relative to controls = $\frac{\text{Final Body Weight (Dosed)}}{\text{Final Body Weight (Control Group)}} \times 100$

TWO-YEAR STUDIES

Body Weights and Clinical Signs

After week 20 for males and week 40 for females, mean body weights of high dose rats were lower than those of the controls (Table 7 and Figure 1) No compound-related clinical signs were observed.

TABLE 7. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE OXIDE

Weeks on Study	Control		200 ppm			400 ppm		
	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	147	50	146	99 3	50	143	97 3	50
2	169	50	179	105 9	50	178	105 3	50
3	195	50	198	101 5	50	193	99 0	50
4	221	50	225	101 8	50	219	99 1	50
5	241	50	242	100 4	50	231	95 9	50
6	260	50	260	100 0	50	251	96 5	50
7	274	50	272	99 3	50	261	95 3	50
8	296	50	295	99 7	50	283	95 6	50
9	305	50	303	99 3	50	286	93 8	50
10	319	50	310	97 2	50	300	94 0	50
11	321	50	327	101 9	50	305	95 0	50
12	330	50	327	99 1	50	313	94 8	50
13	341	50	342	100 3	50	320	93 8	50
17	366	50	367	100 3	50	343	93 7	50
22	375	50	364	97 1	50	356	94 9	50
26	405	50	385	95 1	50	378	92 8	50
29	397	50	390	98 2	50	382	96 2	50
33	411	50	402	97 8	50	395	96 1	50
38	411	50	403	98 1	50	394	95 9	50
42	412	50	402	97 6	50	390	94 7	50
47	411	50	403	98 1	49	395	96 1	50
51	433	50	428	98 8	49	413	95 4	50
55	437	50	435	99 5	49	419	95 9	50
60	451	50	448	99 3	49	431	95 6	50
64	449	50	448	99 8	49	433	96 4	50
68	461	49	455	98 7	49	438	95 0	50
73	460	48	457	99 3	49	443	96 3	50
77	457	46	455	99 6	49	437	95 6	50
81	454	44	444	97 8	49	425	93 6	49
86	436	42	435	99 8	47	417	95 6	49
90	442	38	435	98 4	44	409	92 5	46
92	437	38	436	99 8	43	409	93 6	44
94	431	37	428	99 3	42	401	93 0	41
96	439	35	439	100 0	39	405	92 3	39
98	439	34	449	102 3	39	408	92 9	34
100	438	31	433	98 9	35	408	93 2	32
102	432	30	429	99 3	33	396	91 7	31
FEMALE								
1	116	50	117	100 9	50	114	98 3	50
2	129	50	134	103 9	50	133	103 1	50
3	140	50	143	102 1	50	136	97 1	50
4	153	50	156	102 0	50	151	98 7	50
5	162	50	161	99 4	50	158	97 5	50
6	171	50	170	99 4	50	164	95 9	50
7	176	50	174	98 9	50	167	94 9	50
8	183	50	181	98 9	50	178	97 3	50
9	185	50	184	99 5	50	179	96 8	50
10	190	50	189	99 5	50	184	96 8	50
11	192	50	195	101 6	50	186	96 9	50
12	198	50	199	100 5	50	191	96 5	50
13	200	50	201	100 5	50	195	97 5	50
17	209	50	208	99 5	50	204	97 6	50
22	213	50	215	100 9	50	211	99 1	50
26	223	50	229	102 7	50	221	99 1	50
29	226	50	228	100 9	50	222	98 2	50
33	235	50	235	100 0	50	228	97 0	50
38	234	50	239	102 1	50	232	99 1	50
42	244	50	244	100 0	50	234	95 9	50
47	248	50	244	98 4	50	238	96 0	50
51	254	49	255	100 4	50	247	97 2	50
55	262	49	262	100 0	50	251	95 8	50
60	282	49	273	96 8	49	264	93 6	49
64	288	49	279	96 9	48	272	94 4	49
68	291	49	288	99 0	48	279	95 9	49
73	302	48	298	98 7	48	286	94 7	49
77	301	48	296	98 3	47	282	93 7	49
81	299	48	298	99 7	47	283	94 6	48
86	308	43	295	95 8	46	282	91 6	47
90	309	39	291	94 2	43	284	91 9	45
92	307	38	289	94 1	43	285	92 8	44
94	310	38	290	93 5	41	289	93 2	44
96	313	38	300	95 8	36	290	92 7	39
98	311	37	301	96 8	35	299	96 1	35
100	314	37	303	96 5	34	291	92 7	34
102	312	35	304	97 4	32	293	93 9	32

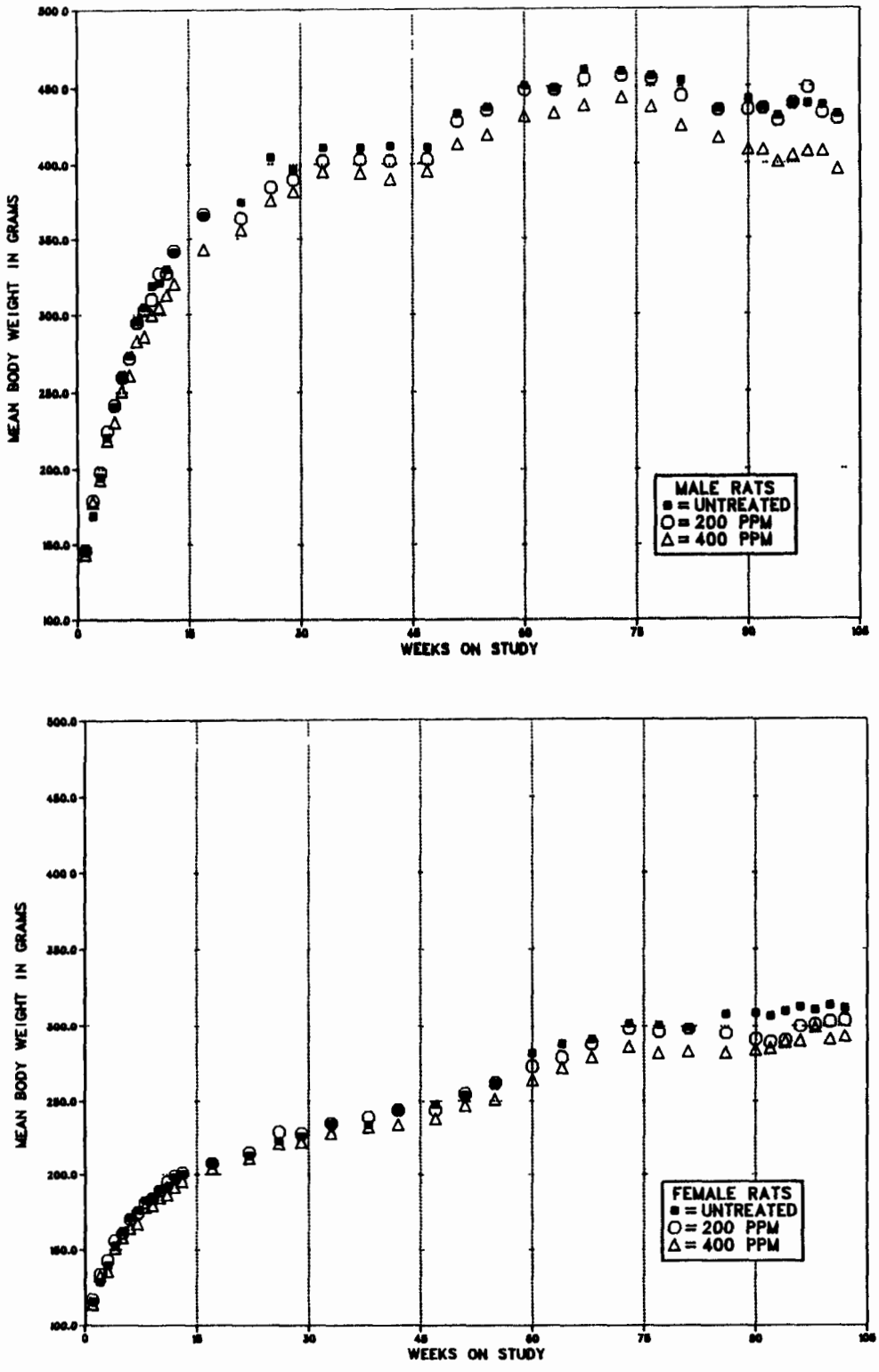


FIGURE 1. GROWTH CURVES FOR RATS EXPOSED TO PROPYLENE OXIDE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of the survival of male and female rats exposed to propylene oxide 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 8).

TABLE 8. SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE OXIDE

	Control	200 ppm	400 ppm
MALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	21	19	21
Killed at termination	29	30	29
Died during termination period	0	1	0
Survival P values (c)	0.834	0.717	0.881
FEMALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	15	18	19
Killed at termination	35	31	31
Died during termination period	0	1	0
Survival P values (c)	0.628	0.624	0.682

(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 those of the life table exact pairwise comparisons with the controls are in the dosed columns.

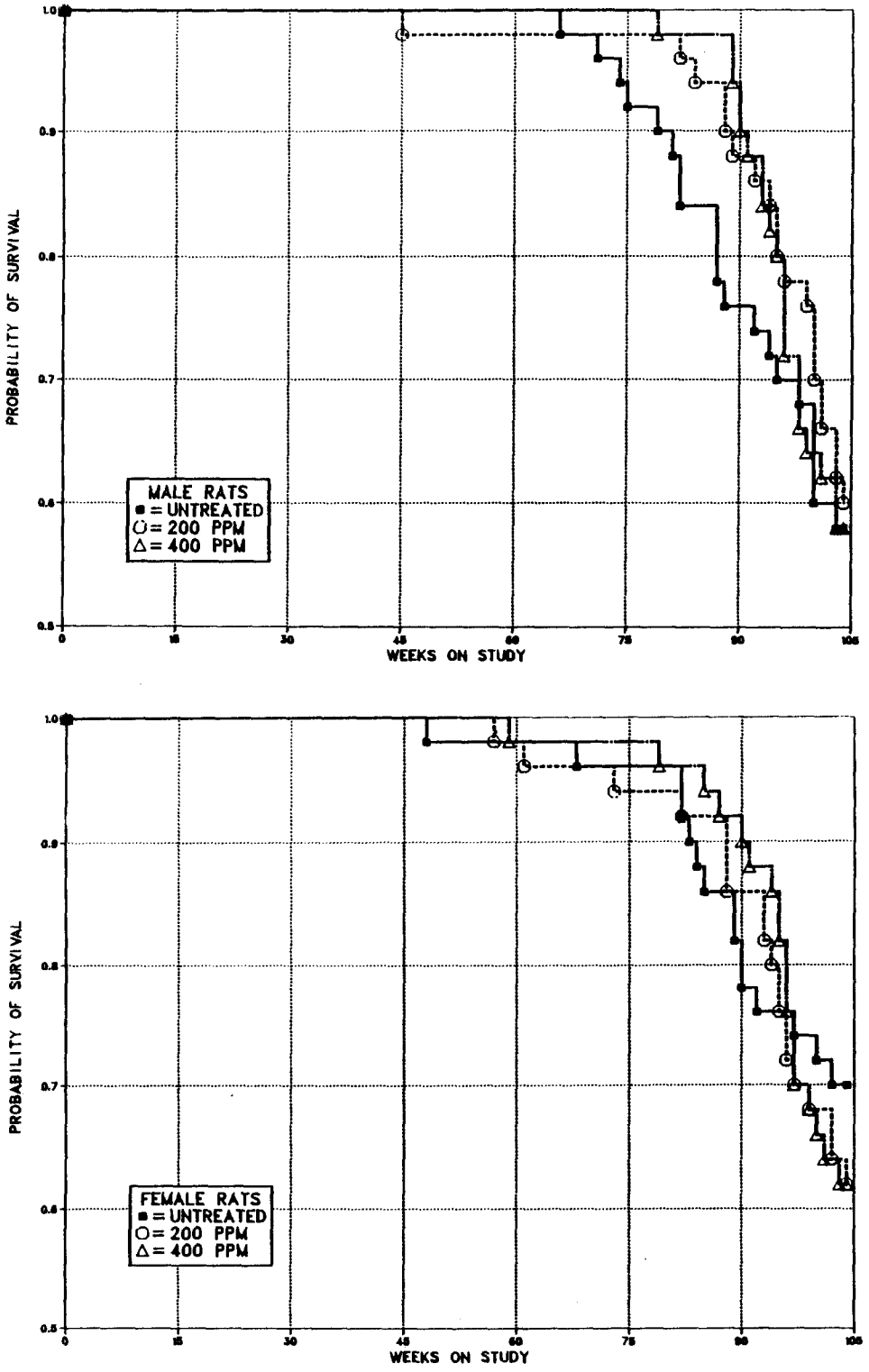


FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR RATS EXPOSED TO PROPYLENE OXIDE BY INHALATION FOR TWO YEARS

Pathology and Statistical Analyses of Results

This section describes the significant or noteworthy changes in the incidence of rats with neoplastic or nonneoplastic lesions. 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.

Nasal Cavity: A dose-related increase occurred in the incidences of suppurative inflammation of the mucosa and submucosa and of squamous metaplasia of the respiratory epithelium (Table 9). These lesions were evident in the most anterior section of the nasal cavity (at the level of the incisor teeth). The squamous metaplasia was usually observed on the greater curvatures of the nasal and maxillary turbinates and on the lateral wall of the nasal cavity between the nasal and maxillary turbinates. A small increase in the incidence of squamous metaplasia was observed in the nasolacrimal ducts of exposed rats (male: control, 4/50, 8%; low dose, 8/50, 16%; high dose, 9/50, 18%; female: control, 3/50, 6%; low dose, 9/50, 18%; high dose, 0/50). This lesion was also observed in the anterior section of the nasal cavity. Lesions of the nasolacrimal duct (squamous metaplasia or inflammation) were diagnosed only when the adjacent epithelium of the nasal mucosa was not similarly involved. A diagnosis of squamous metaplasia of the nasal cavity may include lesions of the nasolacrimal duct, but a lesion of the nasolacrimal duct per se was not diagnosed as squamous metaplasia.

Proliferation of the nasal cavity epithelial cells was seen mainly in animals exposed to propylene oxide at the highest concentration (Table 10). Papillary adenomas involving the

TABLE 9. INCIDENCES OF NASAL CAVITY LESIONS IN RATS IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE OXIDE (a)

Lesion	Male			Female		
	Control	200 ppm	400 ppm	Control	200 ppm	400 ppm
Suppurative inflammation	(b) 9	(b) 21	(b) 38	3	5	(b) 23
Epithelial hyperplasia	0	1	(b) 11	1	0	(b) 5
Squamous metaplasia	1	3	21	1	2	11
Papillary adenoma	0	0	2	0	0	3

(a) Fifty animals were examined histologically in each group.
(b) Because these incidence figures represent both the specific nonneoplastic effect and those recorded under multiple organs, the numbers do not correspond fully with those listed in Appendix C.

TABLE 10. ANALYSIS OF NASAL CAVITY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE (a)

	Control	200 ppm	400 ppm
Papillary Adenoma			
Overall Rates	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted Rates	0.0%	0.0%	9.7%
Terminal Rates	0/35 (0%)	0/32 (0%)	3/31 (10%)
Life Table Tests	P=0.031	(b)	P=0.100
Incidental Tumor Tests	P=0.031	(b)	P=0.100
Cochran-Armitage Trend Test	P=0.037		
Fisher Exact Tests		(b)	P=0.121

(a) The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).
(b) No P value is presented because no tumors were observed in the control and 200-ppm groups.

respiratory epithelium and the underlying submucosal glands were observed in three female rats and two male rats exposed at 400 ppm; the incidences in the females were significant by the trend tests. Most of these proliferative lesions appeared to originate in the mucosa of the lateral wall of the nasal cavity on or near the nasal turbinates.

Thyroid Gland: C-cell adenomas or carcinomas (combined) occurred in female rats with a significant positive trend, and the incidence in the high dose group was significantly greater than that in the controls (Table 11). Neither lesion occurred alone at an incidence that was significantly greater than that in the controls. All the C-cell adenomas and all but one of the C-cell carcinomas were observed after the terminal kill at week 104. The incidence of C-cell hyperplasia showed a slight, but not significant, decrease in dosed female rats. The incidence of C-cell adenomas or carcinomas in dosed male rats was greater than that in the controls, but the results of the statistical tests were not significant (Appendix E, Table E1). A dose-related decrease in C-cell hyperplasia also occurred in male rats.

C-cell lesions were classified as hyperplasia when the proliferating C-cells were interspersed among follicles and when there was no compression or distortion of the normal follicular architecture. The diagnosis of C-cell adenoma was based on the presence of a discrete nodule of C-cells which distorted the normal follicular architecture. Metastases or invasion of adjacent tissue, the thyroid capsule, or vessels were considered indicators of C-cell carcinoma.

Pancreas: Increased incidences of acinar cell atrophy occurred in dosed male rats (control, 1/47, 2%; low dose, 12/49, 24%; high dose, 17/47, 36%).

Adrenal Gland: Cytomegaly in the adrenal cortex was observed at increased incidences in dosed females (control, 1/48, 2%; low dose, 6/49, 12%; high dose, 11/48, 23%).

Testis: Testicular atrophy was observed at increased incidences in dosed male rats (controls, 18/49, 37%; low dose, 40/50, 80%; high dose, 24/50, 48%).

TABLE 11. ANALYSIS OF THYROID GLAND LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE

	Control	200 ppm	400 ppm
C-Cell Hyperplasia	7/45 (16%)	6/35 (17%)	5/37 (14%)
C-Cell Adenoma			
Overall Rates	1/45 (2%)	1/35 (3%)	4/37 (11%)
Adjusted Rates	3.0%	4.8%	16.7%
Terminal Rates	1/33 (3%)	1/21 (5%)	4/24 (17%)
Life Table Tests	P=0.056	P=0.658	P=0.095
Incidental Tumor Tests	P=0.056	P=0.658	P=0.095
Cochran-Armitage Trend Test	P=0.072		
Fisher Exact Tests		P=0.687	P=0.125
C-Cell Carcinoma			
Overall Rates	1/45 (2%)	1/35 (3%)	3/37 (8%)
Adjusted Rates	3.0%	4.8%	10.3%
Terminal Rates	1/33 (3%)	1/21 (5%)	2/24 (8%)
Life Table Tests	P=0.149	P=0.658	P=0.234
Incidental Tumor Tests	P=0.103	P=0.658	P=0.155
Cochran-Armitage Trend Test	P=0.156		
Fisher Exact Tests		P=0.687	P=0.238
C-Cell Adenoma or Carcinoma			
Overall Rates	2/45 (4%)	2/35 (6%)	7/37 (19%)
Adjusted Rates	6.1%	9.5%	26.6%
Terminal Rates	2/33 (6%)	2/21 (10%)	6/24 (25%)
Life Table Tests	P=0.017	P=0.523	P=0.031
Incidental Tumor Tests	P=0.011	P=0.523	P=0.019
Cochran-Armitage Trend Test	P=0.023		
Fisher Exact Tests		P=0.592	P=0.041

Uterus: Endometrial stromal polyps or sarcomas (combined) occurred with a significant positive trend, and the incidences in the dosed groups were significantly greater than that in the controls (Table 12).

The incidences of cystic endometrial hyperplasia were increased in dosed females (control, 0/49; low dose, 9/50, 18%; high dose, 6/47, 13%).

Skin: Keratoacanthomas occurred in male rats with a significant positive trend (control, 1/50, 2%; low dose, 1/50, 2%; high dose, 5/50, 10%).

Pituitary: Adenomas occurred in female rats with a significant negative trend, and the incidence in the high dose group was significantly lower than that in the controls (Table 13).

TABLE 12. ANALYSIS OF UTERINE TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE

	Control	200 ppm	400 ppm
Endometrial Stromal Polyp			
Overall Rates	3/49 (6%)	8/50 (16%)	8/47 (17%)
Adjusted Rates	8.1%	24.1%	21.5%
Terminal Rates	2/35 (6%)	7/32 (22%)	4/31 (13%)
Life Table Tests	P=0.073	P=0.082	P=0.095
Incidental Tumor Tests	P=0.131	P=0.085	P=0.209
Cochran-Armitage Trend Test	P=0.074		
Fisher Exact Tests		P=0.106	P=0.087
Endometrial Stromal Sarcoma			
Overall Rates	0/49 (0%)	4/50 (8%)	2/47 (4%)
Adjusted Rates	0.0%	11.5%	6.5%
Terminal Rates	0/35 (0%)	2/32 (6%)	2/31 (6%)
Life Table Tests	P=0.196	P=0.057	P=0.212
Incidental Tumor Tests	P=0.301	P=0.139	P=0.212
Cochran-Armitage Trend Test	P=0.208		
Fisher Exact Tests		P=0.061	P=0.237
Endometrial Stromal Polyp or Sarcoma			
Overall Rates	3/49 (6%)	12/50 (24%)	10/47 (21%)
Adjusted Rates	8.1%	34.1%	27.4%
Terminal Rates	2/35 (6%)	9/32 (28%)	6/31 (19%)
Life Table Tests	P=0.031	P=0.010	P=0.034
Incidental Tumor Tests	P=0.077	P=0.019	P=0.079
Cochran-Armitage Trend Test	P=0.032		
Fisher Exact Tests		P=0.013	P=0.029

TABLE 13. ANALYSIS OF PITUITARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE

	Control	200 ppm	400 ppm
Adenoma			
Overall Rates	25/48 (52%)	18/47 (38%)	14/46 (30%)
Adjusted Rates	60.5%	48.9%	43.6%
Terminal Rates	18/34 (53%)	13/31 (42%)	12/30 (40%)
Life Table Tests	P=0.041N	P=0.193N	P=0.052N
Incidental Tumor Tests	P=0.023N	P=0.123N	P=0.036N
Cochran-Armitage Trend Test	P=0.021N		
Fisher Exact Tests		P=0.126N	P=0.027N

SINGLE-EXPOSURE STUDIES

Dyspnea was observed in all exposed groups; sedation occurred in the two highest dose groups; and lacrimation occurred in the highest dose groups. All mice exposed at 2,970 ppm, 2/5 males and 5/5 females exposed at 1,277 ppm, and 2/5 males and 4/5 females exposed at 1,102 ppm died (Table 14). No compound-related effects were recorded at necropsy.

REPEATED-EXPOSURE STUDIES

No mice died (Table 15). Dyspnea occurred in the two highest exposure groups (196 and 487 ppm). Animals in the highest exposure groups were hypoactive.

TABLE 14. SURVIVAL OF MICE IN THE SINGLE FOUR-HOUR-EXPOSURE INHALATION STUDIES OF PROPYLENE OXIDE

Concentration (a) (ppm)	Survival (b) (Day of Death)	
	Male	Female
387	5/5	4/5 (6)
859	5/5	5/5
1,102	3/5 (1,1)	1/5 (1,1,1,2)
1,277	3/5 (1,1)	0/5 (1,1,1,1,1)
2,970	0/5 (1,1,1,1,1)	0/5 (1,1,1,1,1)

(a) Time-averaged mean
(b) Number surviving/number per group

TABLE 15. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE TWO-WEEK REPEATED-EXPOSURE INHALATION STUDIES OF PROPYLENE OXIDE

Concentration (a) (ppm)	Survival (b)	Mean Body Weight (grams)			Final Weight Relative to Controls (d) (percent)
		Initial (c)	Final	Change	
MALE					
0	5/5	23.8 ± 1.2	25.6 ± 0.6	+1.8 ± 0.7	--
20.1	5/5	23.4 ± 0.9	27.2 ± 0.9	+3.8 ± 0.6	106.2
47.2	5/5	22.6 ± 0.9	24.0 ± 1.5	+1.4 ± 1.7	93.8
98.5	5/5	23.6 ± 0.5	25.6 ± 1.0	+2.0 ± 0.9	100.0
196	5/5	21.8 ± 0.6	25.0 ± 0.3	+3.2 ± 0.5	97.7
487	5/5	22.2 ± 0.5	23.4 ± 0.5	+1.2 ± 0.2	91.4
FEMALE					
0	5/5	17.6 ± 0.7	22.4 ± 0.5	+4.8 ± 0.4	--
20.1	5/5	19.2 ± 0.7	23.4 ± 1.3	+4.2 ± 1.6	104.5
47.2	5/5	18.2 ± 0.4	20.8 ± 0.6	+2.6 ± 0.4	92.9
98.5	5/5	18.8 ± 0.7	21.0 ± 0.8	+2.2 ± 0.6	93.8
196	5/5	17.6 ± 0.2	20.0 ± 0.9	+2.4 ± 1.1	89.3
487	5/5	18.4 ± 0.5	20.4 ± 0.5	+2.0 ± 0.5	91.1

(a) Time-averaged mean
(b) Number surviving/number initially in the group
(c) Initial mean weight of all animals in the group ± standard error of the mean
(d) Final body weight of the dosed group relative to controls = $\frac{\text{Final Body Weight (Dosed)}}{\text{Final Body Weight (Control Group)}} \times 100$

THIRTEEN-WEEK STUDIES

One male mouse in the 125-ppm group died (Table 16). Final mean body weights relative to those of the controls were depressed 12.9% in male mice exposed at 500 ppm and 14.6% in female mice exposed at 500 ppm. No compound-related gross or microscopic pathologic effects were observed. One section of nasal turbinate was prepared and examined.

Because of the depressions in weight gain observed in mice exposed at 500 ppm, exposure concentrations of 200 and 400 ppm propylene oxide were selected for mice in the 2-year studies.

TABLE 16. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE THIRTEEN-WEEK INHALATION STUDIES OF PROPYLENE OXIDE

Concentration (ppm)	Survival (a)	Mean Body Weight (grams)			Final Weight Relative to Controls (c) (percent)
		Initial	Final	Change (b)	
MALE					
0	10/10	22.8 ± 0.4	31.1 ± 0.5	+8.3 ± 0.7	--
31	10/10	22.9 ± 0.4	32.3 ± 0.5	+9.4 ± 0.6	103.9
63	10/10	23.0 ± 0.4	31.0 ± 0.5	+8.0 ± 0.7	99.7
125	(d) 9/10	22.8 ± 0.5	31.1 ± 0.5	+8.3 ± 0.7	100.0
250	10/10	22.9 ± 0.3	30.3 ± 0.4	+7.4 ± 0.5	97.4
500	10/10	23.3 ± 0.4	27.1 ± 0.3	+3.8 ± 0.5	87.1
FEMALE					
0	10/10	17.8 ± 0.3	26.1 ± 0.5	+8.3 ± 0.4	--
31	10/10	17.9 ± 0.3	24.4 ± 0.5	+6.5 ± 0.3	93.5
63	10/10	17.9 ± 0.3	25.1 ± 0.4	+7.2 ± 0.4	96.2
125	10/10	17.8 ± 0.3	24.7 ± 0.3	+6.9 ± 0.3	94.6
250	10/10	17.8 ± 0.3	25.4 ± 0.3	+7.6 ± 0.2	97.3
500	10/10	18.1 ± 0.2	22.3 ± 0.3	+4.2 ± 0.2	85.4

(a) Number surviving/number initially in the group
(b) Mean weight change of the survivors of the group ± standard error of the mean
(c) Final body weight of the dosed group relative to controls = $\frac{\text{Final Body Weight (Dosed)}}{\text{Final Body Weight (Control Group)}} \times 100$
(d) Death occurred on day 14 of the study.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of high dose male and female mice were lower than those of the controls after week 29 (Table 17 and Figure 3). Mean body weights of low dose male mice were greater than those of the controls, except for the last 3 months of the study. Mean body weights of low dose female mice were lower than those of the controls after week 68. No compound-related clinical signs were recorded.

TABLE 17. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE OXIDE

Weeks on Study	Control		200 ppm			400 ppm		
	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	27	50	29	107.4	50	27	100.0	50
2	28	50	30	107.1	50	29	103.6	50
3	30	50	31	103.3	50	26	86.7	50
4	29	50	31	106.9	50	28	96.6	50
5	30	50	31	103.3	50	29	96.7	50
6	30	50	32	106.7	50	28	93.3	50
7	31	50	32	103.2	50	29	93.5	50
8	29	50	32	110.3	50	31	106.9	50
9	31	50	34	109.7	50	32	103.2	50
10	31	50	33	106.5	50	30	96.8	50
11	31	50	33	106.5	50	31	100.0	50
12	31	50	33	106.5	50	31	100.0	50
13	32	50	-	-	-	33	103.1	50
17	32	50	-	-	-	31	96.9	50
26	32	50	-	--	--	33	103.1	50
29	35	50	37	105.7	50	33	94.3	50
33	36	50	38	105.6	50	34	94.4	49
38	36	50	--	--	--	35	97.2	49
42	36	50	39	108.3	50	34	94.4	49
47	35	50	--	--	--	35	100.0	49
51	36	50	--	--	--	33	91.7	49
55	37	50	40	108.1	50	34	91.9	49
60	38	59	--	--	--	31	81.8	49
64	38	49	--	--	--	32	84.2	49
68	38	49	40	105.3	48	31	81.6	47
73	38	48	--	--	--	30	78.9	47
77	38	48	--	--	--	31	81.6	44
81	38	48	--	--	--	32	84.2	44
86	38	46	36	94.7	45	30	78.9	43
90	38	43	37	97.4	40	30	78.9	43
92	37	43	37	100.0	39	29	78.4	41
94	37	43	37	100.0	39	29	78.4	39
96	36	43	36	100.0	37	31	86.1	37
98	37	43	34	91.9	36	29	76.4	34
100	36	43	36	100.0	34	30	83.3	32
102	37	43	35	94.6	34	29	78.4	30
FEMALE								
1	21	50	23	109.5	50	21	100.0	50
2	23	50	23	100.0	50	23	100.0	49
3	24	50	23	95.8	50	21	87.5	48
4	23	49	24	104.3	50	22	95.7	48
5	25	49	24	96.0	50	24	96.0	48
6	25	49	25	100.0	50	24	96.0	47
7	26	49	26	100.0	50	24	92.3	47
8	25	48	25	100.0	50	25	100.0	47
9	26	48	25	96.2	50	26	100.0	46
10	25	48	25	100.0	50	25	100.0	46
11	26	48	26	100.0	50	26	100.0	46
12	26	48	27	103.8	50	26	100.0	46
13	27	48	--	--	--	27	100.0	46
17	28	48	-	--	--	26	92.9	46
22	29	48	--	--	--	28	96.6	46
29	28	47	28	100.0	49	28	100.0	45
33	30	47	29	96.7	49	28	93.3	45
38	31	46	--	--	--	28	90.3	45
42	29	46	30	103.4	49	28	96.6	45
47	29	46	--	--	--	28	96.6	45
51	30	46	--	--	-	29	96.7	45
55	31	46	30	96.8	48	30	96.8	44
60	33	46	--	--	--	28	84.8	44
64	31	46	--	--	-	29	93.5	43
68	31	46	31	100.0	48	27	87.1	40
73	33	46	--	--	--	26	78.8	38
77	32	46	-	--	--	25	78.1	38
81	31	46	-	--	--	27	87.1	34
86	31	45	29	93.5	43	27	87.1	28
90	32	43	30	93.8	38	27	84.4	23
92	32	43	29	90.6	38	22	68.8	21
94	30	40	29	96.7	38	22	73.3	19
96	31	40	29	93.5	35	25	80.6	18
98	31	39	27	87.1	33	23	74.2	14
100	31	39	27	87.1	32	21	67.7	13
102	30	39	28	93.3	30	27	90.0	10

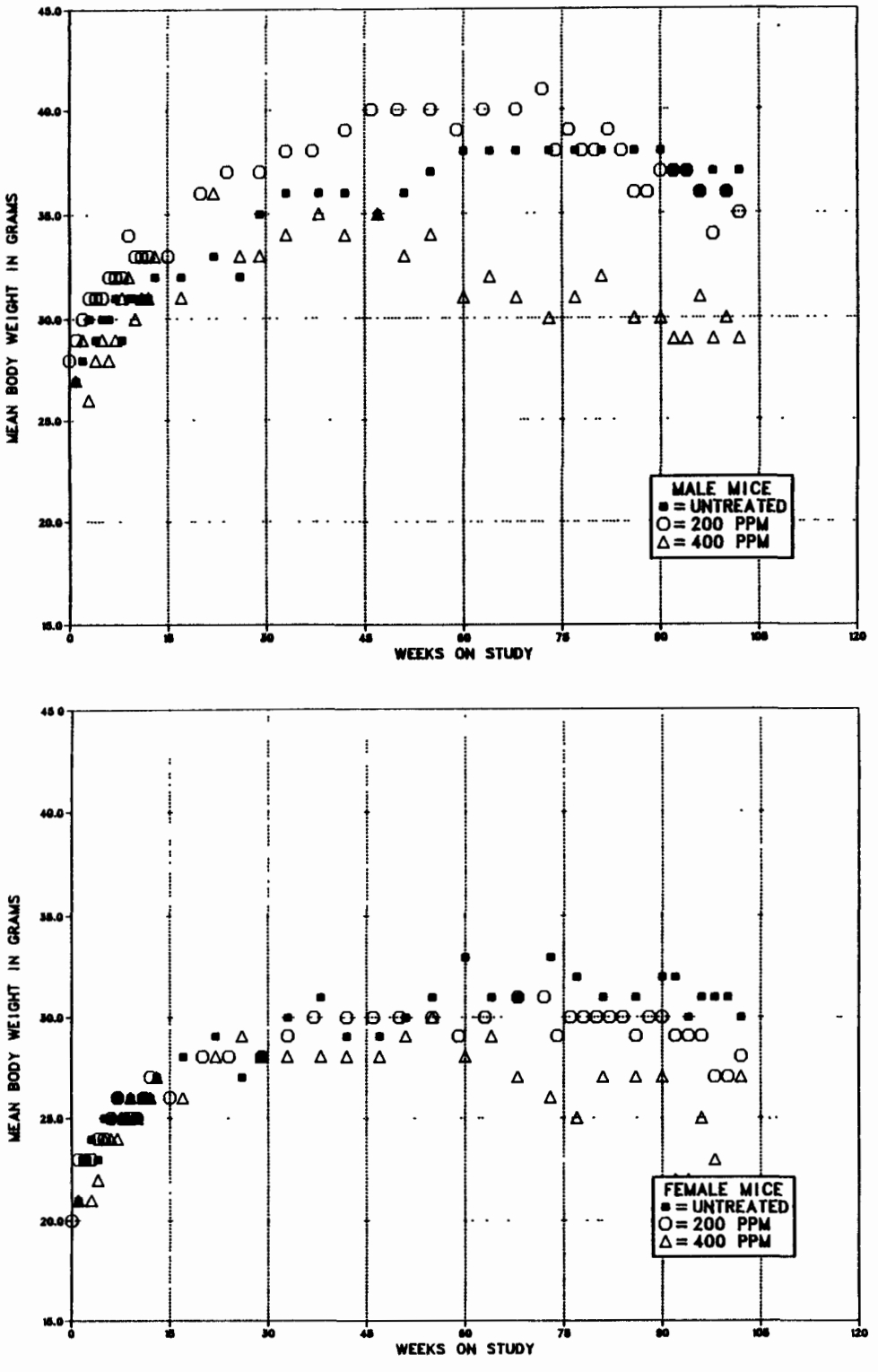


FIGURE 3. GROWTH CURVES FOR MICE EXPOSED TO PROPYLENE OXIDE BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival of male and female mice exposed to air containing propylene oxide at the concentrations in these studies and those of the controls are shown in the Kaplan and Meier curves in Figure 4. The survival of high dose male mice was significantly lower than that of the controls ($P = 0.006$). Survival of high dose female mice was significantly lower than that in the low dose and control groups ($P < 0.001$). (Table 18)

TABLE 18. SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE OXIDE

	Control	200 ppm	400 ppm
MALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	8	16	20
Accidentally killed	0	0	1
Killed at termination	42	34	27
Died during termination period	0	0	2
Survival P values (c)	0.006	0.105	0.006
FEMALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	12	20	39
Accidentally killed	0	1	1
Killed at termination	37	29	10
Died during termination period	1	0	0
Survival P values (c)	<0.001	0.207	<0.001

(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 those of the life table exact pairwise comparisons with the controls are in the dosed columns.

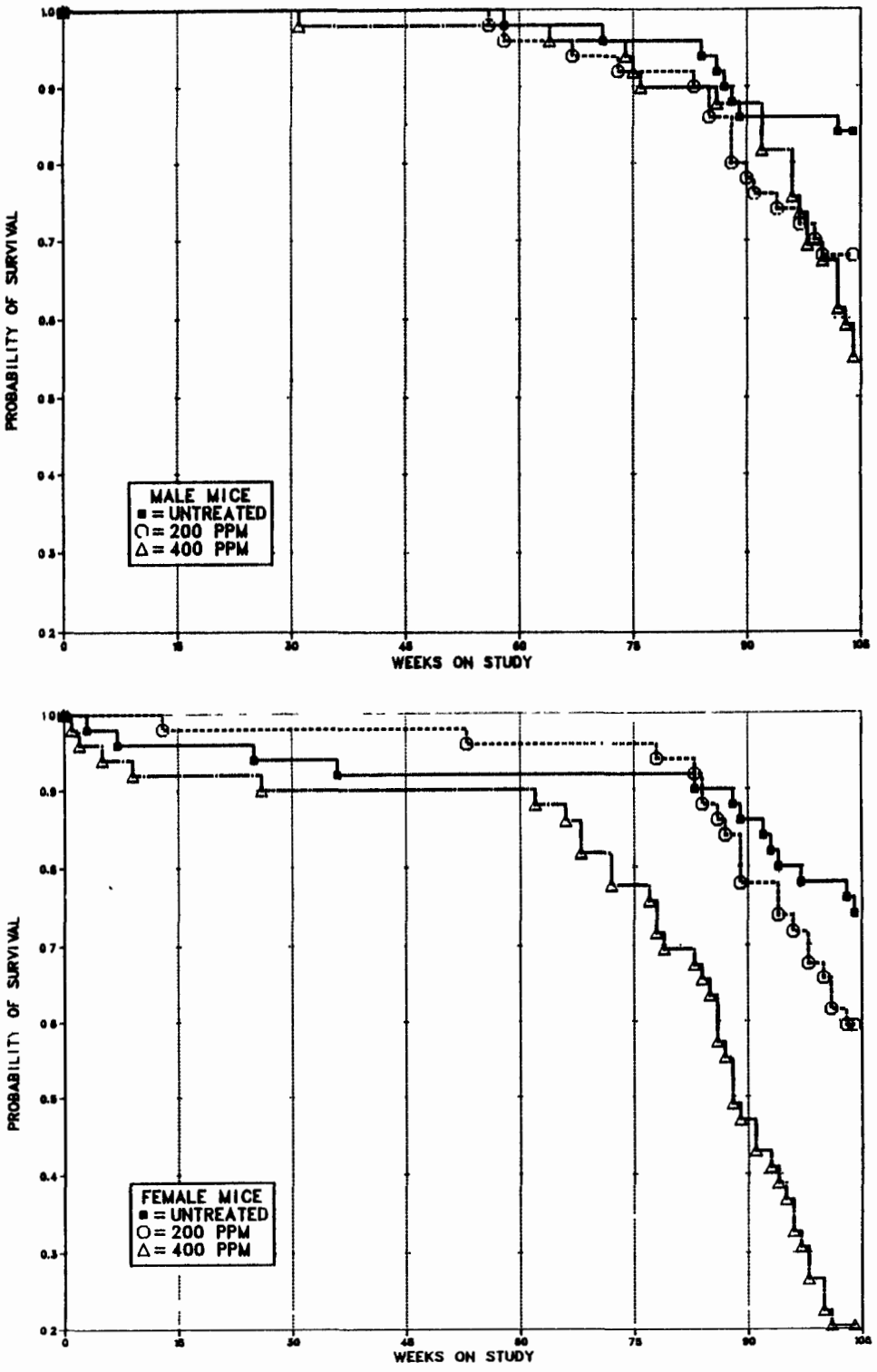


FIGURE 4. KAPLAN-MEIER SURVIVAL CURVES FOR MICE EXPOSED TO PROPYLENE OXIDE BY INHALATION FOR TWO YEARS

Pathology and Statistical Analyses of Results

This section describes the significant or noteworthy changes in the incidences of mice with neoplastic and nonneoplastic lesions. 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.

Nasal Cavity: The incidences of lesions affecting the respiratory epithelium of the nasal mucosa are shown in Table 19. The mildest recognized change was the accumulation of protein-rich fluid in the nasal cavity surrounding the turbinates. The fluid was usually acellular; however, the lesion was diagnosed as a serous inflammation because granulocytes were occasionally present in the respiratory mucosa, suggesting that a mild inflammatory change had occurred. Lesions that were almost entirely granulocytic occurred with a dose-related increase; these were diagnosed as suppurative inflammation. Lesions that also contained lymphocytes and macrophages were classified as acute/chronic inflammation. A papilloma and a squamous cell carcinoma were found in two separate high dose male mice. Two high dose female mice had adenocarcinomas of the nasal turbinates. The carcinoma and the adenocarcinomas appeared to arise from the submucosal glands; they were not exophytic, and they spread deeply along the nerve sheaths.

TABLE 19. INCIDENCES OF NASAL CAVITY EPITHELIAL LESIONS IN MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE OXIDE (a)

Lesion	Male			Female		
	Control	200 ppm	400 ppm	Control	200 ppm	400 ppm
Serous inflammation	0	13	2	2	(b) 6	(b) 2
Suppurative inflammation	0	8	4	0	(b) 16	(b) 23
Acute/chronic inflammation	1	(b) 14	38	(b) 0	(b) 14	(b) 18
Squamous metaplasia	0	1	0	0	0	2
Papilloma	0	0	1	0	0	0
Squamous cell carcinoma	0	0	1	0	0	0
Adenocarcinoma	0	0	0	0	0	2

(a) Fifty animals were examined histologically in each group.
(b) Because these incidence figures represent both the specific nonneoplastic effect and those recorded under multiple organs, the numbers do not correspond fully with those listed in Appendix D.

The endothelium of the vascular plexus beneath the respiratory epithelium also appeared to be affected. Angiectasis characterized by saccular dilation of submucosal vessels was found in three high dose males and three high dose females. In addition, hemangiomas in males and females plus hemangiosarcomas in males occurred with significant positive trends; the incidences in the high dose groups were significantly greater than those in the controls (Table 20).

TABLE 20. ANALYSIS OF VASCULAR TUMORS OF THE NASAL CAVITY IN MICE IN THE TWO-YEAR INHALATION STUDIES OF PROPYLENE OXIDE (a)

	Control	200 ppm	400 ppm
MALE			
Hemangioma			
Overall Rates	0/50 (0%)	0/50 (0%)	5/50 (10%)
Adjusted Rates	0.0%	0.0%	17.2%
Terminal Rates	0/42 (0%)	0/34 (0%)	5/29 (17%)
Life Table Tests	P=0.002	(a)	P=0.011
Incidental Tumor Tests	P=0.002	(b)	P=0.011
Cochran-Armitage Trend Test	P=0.006		
Fisher Exact Tests		(b)	P=0.028
Hemangiosarcoma			
Overall Rates (b)	0/50 (0%)	0/50 (0%)	5/50 (10%)
Adjusted Rates (b)	0.0%	0.0%	15.6%
Terminal Rates (c)	0/42 (0%)	0/34 (0%)	4/29 (14%)
Life Table Tests (d)	P=0.003	(b)	P=0.015
Incidental Tumor Tests (d)	P=0.004	(b)	P=0.021
Cochran-Armitage Trend Test (d)	P=0.006		
Fisher Exact Tests		(b)	P=0.028
Hemangioma or Hemangiosarcoma			
Overall Rates	0/50 (0%)	0/50 (0%)	10/50 (20%)
Adjusted Rates	0.0%	0.0%	32.4%
Terminal Rates	0/42 (0%)	0/34 (0%)	9/29 (31%)
Life Table Tests	P<0.001	(b)	P<0.001
Incidental Tumor Tests	P<0.001	(b)	P<0.001
Cochran-Armitage Trend Test	P<0.001		
Fisher Exact Tests		(b)	P=0.001
FEMALE			
Hemangioma			
Overall Rates	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted Rates	0.0%	0.0%	20.7%
Terminal Rates	0/38 (0%)	0/29 (0%)	0/10 (0%)
Life Table Tests	P=0.004	(b)	P=0.012
Incidental Tumor Tests	P=0.091	(b)	P=0.336
Cochran-Armitage Trend Test	P=0.037		
Fisher Exact Tests		(b)	P=0.121
Hemangiosarcoma			
Overall Rates	0/50 (0%)	0/50 (0%)	2/50 (4%)
Hemangioma or Hemangiosarcoma			
Overall Rates	0/50 (0%)	0/50 (0%)	5/50 (10%)
Adjusted Rates	0.0%	0.0%	32.2%
Terminal Rates	0/38 (0%)	0/29 (0%)	1/10 (10%)
Life Table Tests	P<0.001	(b)	P<0.001
Incidental Tumor Tests	P=0.008	(b)	P=0.062
Cochran-Armitage Trend Test	P=0.006		
Fisher Exact Tests		(a)	P=0.028

(a) The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).
(b) No P value is presented because no tumors were observed in the control and 200-ppm groups.

The differentiation between hemangioma and hemangiosarcoma was based primarily on the degree of anaplasia in the neoplastic cells. Cytologic details of neoplasms with obvious features of malignancy (e.g., invasion of the maxillary sinus, bone marrow of the maxilla, or bone marrow and subcutis) were used as the standard by which malignancy was determined. Hemangiosarcomas were composed of endothelial cells with large vesicular nuclei and a high mitotic index. They formed smaller vascular channels and sinusoids. Hemangiomas were usually composed of more well-differentiated endothelial cells; these cells were flattened, had smaller nuclei, had fewer or no mitotic figures, and formed larger vascular channels.

Circulatory System (all sites except nasal cavity): No evidence of exposure-related vascular tumors was found outside the nasal cavity. Hemangiosarcomas were found in the livers of two control male mice and at multiple sites in two low dose male mice. Vascular tumors outside the nasal cavity were not found in high dose males. One control and one high dose female mouse had an hemangioma of the uterus; a low dose female had an hemangiosarcoma of the liver, and a high dose female had an hemangiosarcoma of the urinary bladder.

Ovary: The incidences of ovarian atrophy were increased in dosed mice: control, 6/48 (13%); low dose, 8/46 (17%); high dose, 20/37 (54%).

Uterus: Suppurative inflammation of the uterus, peritoneum, or multiple organs or ovarian abscesses were observed in 2 control, 8 low dose, and 15 high dose female mice. Uterine endometrial hyperplasia occurred at a decreased incidence in dosed female mice: control, 24/48 (50%); low dose, 13/50 (26%); high dose, 1/48 (2%).

Mammary Gland: Adenocarcinomas (all types) occurred in females with a statistically significant positive trend, and the incidence in the high dose group was significantly greater than that in the controls (only by the life table test) (Table 21).

TABLE 21. ANALYSIS OF MAMMARY GLAND TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE

	Control	200 ppm	400 ppm
Adenocarcinoma			
Overall Rates	0/50 (0%)	3/50 (6%)	3/50 (6%)
Adjusted Rates	0.0%	8.1%	14.5%
Terminal Rates	0/38 (0%)	1/29 (3%)	1/10 (10%)
Life Table Tests	P=0.025	P=0.105	P=0.047
Incidental Tumor Tests	P=0.362	P=0.290	P=0.236
Cochran-Armitage Trend Test	P=0.101		
Fisher Exact Tests		P=0.121	P=0.121

IV. DISCUSSION AND CONCLUSIONS

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F344/N rats and B6C3F$_1$ mice were exposed to propylene oxide vapors in air for 103 weeks. Inhalation was chosen as the route of exposure, since the most common potential human exposure would be to propylene oxide vapors. The concentrations of 200 and 400 ppm were chosen because in short-term studies the compound at higher concentrations produced weight loss. Rats appeared to tolerate exposure well, for mortality was not increased in exposed animals and final weights were within 10% of control values. The excessive mortality and weight loss in high dose mice suggest that toxic levels were reached: 29/50 (58%) of the males and 10/50 (20%) of the females survived to the end of the study; mean body weights of males and females were 21% and 10% below those of the controls.

On three occasions, high dose mice were exposed for 12-38 minutes at concentrations exceeding 1,000 ppm; concentrations in one exposure period exceeded 6,000 ppm. Only one male (at week 31) and one female (at week 83) died during the 2-week periods following these incidents. Thus, these increases were not considered to increase mortality or to influence the findings in these studies.

Toxic effects in rats and mice were restricted to the nasal cavity, which was the primary site exposed in these inhalation studies. This finding is consistent with results of other studies in which propylene oxide was observed to act as an irritant and a carcinogen only at the site of administration. Propylene oxide produced squamous cell carcinomas, papillomas, and hyperplasia of the forestomach when administered for up to 150 weeks by gavage to fasted Sprague-Dawley rats (Dunkelberg, 1982). All reported effects in that study were restricted to the forestomach. Similarly, propylene oxide administered subcutaneously produced sarcomas at the injection site in rats (strain unknown) (Walpole, 1958) and in NMRI mice (Dunkelberg, 1979, 1981).

In the present studies, the irritant effects of propylene oxide on the respiratory epithelium of the nasal mucosa were shown by marked suppurative inflammation, epithelial hyperplasia, and squamous metaplasia. The lesions were most evident in the anterior portion of the nasal cavity and on the greater curvatures of the nasal and maxillary turbinates.

Papillary adenomas of the nasal cavity were found in two male and three female F344/N rats exposed to propylene oxide at concentrations of 400 ppm. The incidence of papillary adenomas in female rats was significant by the trend tests. The lesions appeared to arise from the respiratory epithelium of the submucosal glands and were generally in the lateral wall of the nasal turbinates. The glandular tumors were well differentiated, often projecting into the lumen of the nasal cavity. Exposed rats also had epithelial hyperplasia. These lesions were less focal and smaller than the papillary adenomas but were morphologically similar.

The significance of finding adenomas in the turbinates of only high dose (400 ppm) rats and the relationship of these lesions to administration of propylene oxide are not clear. In an inhalation study undertaken by the National Institute for Occupational Safety and Health, two nasal adenomas were found in a group of 80 male F344 rats exposed to propylene oxide at a concentration of 300 ppm (NIOSH, 1983). The chances of detecting microscopic tumors in that study were increased because three sections of turbinate were examined from each control and exposed rat, as is done for the NTP studies, including these on propylene oxide. Much of the NTP historical data on nasal tumors is based on a single section of turbinate.

High dose animals in the current study also had irritation of the respiratory mucosa. Irritation per se may affect the incidence of adenomas. Research on nasal tumors induced in rats by 1,4-dinitrosopiperazine suggests that nodular hyperplasia may be more important than papillomas of the nasal turbinate as a precursor of carcinoma development (Takano et al., 1982). For these reasons, the evidence for carcinogenicity of propylene oxide for the nasal turbinate of rats is not clear.

Mice had similar inflammatory changes of the respiratory epithelium of the nasal cavity. Mice dying early in the study had rhinitis characterized primarily by an accumulation of neutrophils in the lumen of the nasal cavity. Lymphocytes, histiocytes, plasma cells, and mild squamous metaplasia were found in mice surviving to at least week 72 of the studies. Incidences of inflammation in males and females were comparable.

Rhinitis was found in 4/100 control mice (both sexes), 69/100 low dose mice, and 88/100 high dose mice. One squamous cell carcinoma and one papilloma were found in the nasal cavity of high dose male mice, and two adenocarcinomas were seen in the nasal cavities of high dose female mice. The lesions were not exophytic; they appeared to arise from the submucosal glands, spread into the adjacent musculature, and grow along nerve sheaths. No lesions were observed in low dose and control mice. Squamous cell papillomas, carcinomas, and adenocarcinomas in the nasal cavity are rare in untreated mice and have not been observed in 1,615 male untreated control $B6C3F_1$ mice or in 1,668 female untreated control $B6C3F_1$ mice in the NTP carcinogenesis program. Therefore, the lesions observed in mice in the current study are considered to be related to exposure to propylene oxide.

Three levels of turbinates were examined in mice for this study. Although nasal tumors have not been found in historical control mice, an examination of turbinates is not required for all studies, and they are usually not examined unless a lesion is noted grossly. In inhalation studies, where examination of turbinates is required, recent studies include three sections and older studies, only one. Since turbinates have not been consistently examined in previous studies, historical data should be used with caution.

In the CIVO study of 28-month inhalation exposure of rats to propylene oxide (Reuzel and Kuper, 1983), 47 high dose (300 ppm) animals had slight-to-marked hyperplasia of the respiratory epithelium whereas only four controls were noted to have slight hyperplasia. Adenomas of the nasal cavity were not diagnosed in that study, but one high dose animal was found to have a squamous cell carcinoma of the nose, one of the trachea, and one of the larynx/pharynx with one animal having an adenocarcinoma of the larynx/ pharynx. Tumors at these sites were not found in controls. Because these tumors occurred in one animal at each site, they were not statistically significant, but taken together they may have some biologic significance, since squamous cell carcinomas of the upper respiratory tract are uncommon in the rat.

Hemangiomas or hemangiosarcomas (combined) of the nasal cavity occurred at significantly increased incidences in high dose (400 ppm) mice (male: control, 0/50; low dose, 0/50; high dose, 10/50; female: control, 0/50; low dose, 0/50; high dose, 5/50). Reduced survival among high dose female mice may explain the lower incidence of these neoplasms compared with male mice. The earliest recognizable lesion was classified as angiectasis and was found in three high dose males and in three high dose females. The lesion consisted of saccular dilatation of submucosal vessels in the nasal turbinates. Hemangiomas consisted of numerous small vascular channels lined by flattened endothelial cells. In the hemangiosarcomas, endothelial cells were prominent and had a higher mitotic rate. Obvious malignant properties were demonstrated by invasion of bones of the skull. A few vascular tumors were found at other sites (e.g., spleen or subcutis) in both exposed and control mice; they were considered to be unrelated to propylene oxide exposure. The only effect that was clearly carcinogenic occurred in high dose mice at the site of exposure.

Since propylene oxide is a direct-acting alkylating agent, a direct-acting mutagen in microorganisms, and a clastogen in cultured mammalian cells, it is not surprising that propylene oxide is tumorigenic at the site of exposure. Thus, the relatively weak response produced in exposed rats is unexpected. The tumorigenicity at the site of exposure has its parallel in the finding that propylene oxide did not induce micronuclei in mouse erythrocytes following gavage but did so following intraperitoneal injection (Bootman et al., 1979).

Propylene oxide was found to be the weakest alkylating agent and mutagen when compared with other epoxides, including epichlorohydrin, styrene oxide, and ethylene glycol. Comparisons were based on the rate and extent of the chemicals' reaction with 4-(*p*-nitrobenzyl)pyridine and their mutagenicity in *Escherichia coli* and *Salmonella typhimurium* strains. Compared with epichlorohydrin, the alkylating ability of propylene oxide was 17.2%-20% and the mutagenicity was 3.2% in Salmonella and 2%-10% in *E. coli* (Hemminki and Falck, 1979; Hemminki et al., 1980). Propylene oxide was also less mutagenic than epichlorohydrin in Klebsiella (Voogd et al., 1981) and Neurospora (Kolmark and Giles, 1955); however, propylene oxide did induce higher levels of chromatid

breaks and exchanges than did epichlorohydrin in cultures of rat liver cells (Dean and Hodson-Walker, 1979).

The mutagenicity of propylene oxide and ethylene oxide differed, depending on the systems tested. Both epoxides failed to mutate *E. coli* T2 bacteriophage (Cookson et al., 1971), but they were equally mutagenic in a preincubation modification of the Ames Salmonella test (Pfeiffer and Dunkelberg, 1980). Ethylene oxide induced low levels of chromatid aberrations in peripheral lymphocytes of monkeys exposed by inhalation, whereas propylene oxide did not (NIOSH, 1983).

Other tumors found in rats in the present study were considered to be unrelated to propylene oxide exposure. The incidence of female rats with C-cell adenomas or carcinomas (combined) of the thyroid gland occurred with a statistically significant trend, and the incidence in the high dose group was significantly greater than that of the controls (Table 11); however, the incidences of C-cell hyperplasia in the dosed groups were comparable to that in the controls. Proliferation of C-cells in the thyroid gland of aging rats is not uncommon and appears to begin as mild, diffuse, or small focal collections of C-cells adjacent to the follicular epithelium. As the proliferation continues, the follicular epithelium is compressed and contiguous follicles become involved. Lesions smaller than three follicles are arbitrarily classified as hyperplasia. Lesions that are larger and restricted to one lobe are adenomas; and lesions involving the thyroid capsule, invading adjacent tissue, or having obvious malignant characteristics (such as metastases) are classified as C-cell carcinomas. Since these lesions are relatively common in female F344/N rats (122/1,472, 8%) (Appendix F, Table F5) and the distinction between hyperplasia and adenoma is one of degree, the combined incidence of C-cell adenomas and carcinomas in this study is considered to be unrelated to administration of propylene oxide.

Incidences of cystic endometrial stromal polyps, endometrial stromal polyps, and endometrial stromal sarcomas of the uterus were increased in dosed female rats. The increase in the number of animals with sarcomas was not significant, but the incidence was significant when combined with polyps (Table 12). Historically, the incidences of endometrial stromal sarcomas are low and the incidences of endometrial stromal polyps are great in untreated female F344/N rats (Appendix F, Table F6). Since the progression from endometrial stromal polyps to sarcomas has not been established and the incidences of the tumors were low, these lesions cannot be clearly attributed to propylene oxide exposure.

Pituitary adenomas or adenomas and carcinomas (combined) occurred in female rats with significant negative trends. The incidences in the high dose groups were significantly lower than those in the controls. Lower tumor incidence and delay in the onset of tumors were reported for rats when feed consumption had been restricted (Ross and Bras, 1973; Tucker, 1979). Although the decreased weight gain in high dose female rats in the present study suggests that their feed consumption may have been reduced, this parameter was not measured. The lower incidence of pituitary tumors in the high dose female rats is consistent with decreased feed consumption.

Mammary gland adenocarcinomas occurred at significantly increased incidences in dosed female mice by the life table test, but these incidences are within the range found in untreated controls (Appendix F, Table F7). Thus, the incidence of this tumor is not considered to be related to exposure to propylene oxide.

Ovarian abscesses and suppurative inflammation of the uterus or peritoneum were observed in 2 control, 8 low dose, and 15 high dose female mice. *Klebsiella pneumonia* and *K. oxytoca* have been isolated from these mice and from mice in other NTP carcinogenesis studies at several laboratories. The presence of various serotypes of Klebsiella and the presence of other organisms such as *E. coli* suggest that the Klebsiella may be a secondary infection. The infection is definitely not related to propylene oxide exposure.

Conclusions: Under the conditions of these studies, there was *some evidence of carcinogenicity** for F344/N rats, as indicated by increased incidences of papillary adenomas of the nasal turbinates in male and female rats exposed to propylene oxide at 400 ppm. For male and female $B6C3F_1$ mice, there was *clear evidence of carcinogenicity*, as indicated by increased incidences of hemangiomas or hemangiosarcomas of the nasal turbinates at 400 ppm. In the respiratory epithelium of the nasal turbinates, propylene oxide also caused suppurative inflammation, hyperplasia, and squamous metaplasia in rats and inflammation in mice.

* 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 OXIDE

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

	CONTROL (CHAMBER)	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)
PAPILLOMA, NOS		1 (2%)	1 (2%)
KERATOACANTHOMA	1 (2%)	1 (2%)	5 (10%)
FIBROMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
FIBROMA	3 (6%)	2 (4%)	3 (6%)
LIPOMA			1 (2%)
OSTEOSARCOMA	1 (2%)		
NEURILEMOMA		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
PAPILLARY ADENOMA			2 (4%)
#LUNG	(50)	(47)	(49)
ALVEOLAR/BRONCHIOLAR CARCINOMA	2 (4%)		2 (4%)
FOLLICULAR-CELL CARCINOMA, METAS		1 (2%)	
C-CELL CARCINOMA, METASTATIC			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	2 (4%)		
LEUKEMIA,NOS	1 (2%)	3 (6%)	1 (2%)
LEUKEMIA,MONONUCLEAR CELL	19 (38%)	23 (46%)	22 (44%)
#THYMUS	(31)	(26)	(37)
SQUAMOUS CELL CARCINOMA	1 (3%)		
CIRCULATORY SYSTEM			
*DIAPHRAGM	(50)	(50)	(50)
HEMANGIOMA			1 (2%)
#SPLEEN	(50)	(47)	(48)
HEMANGIOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(49)
NEOPLASTIC NODULE		2 (4%)	2 (4%)
HEPATOCELLULAR CARCINOMA	1 (2%)		1 (2%)
#DUODENUM	(46)	(48)	(48)
MUCINOUS ADENOCARCINOMA		1 (2%)	
#ILEUM	(46)	(48)	(48)
MUCINOUS ADENOCARCINOMA		1 (2%)	
URINARY SYSTEM			
#KIDNEY/MEDULLA	(50)	(50)	(50)
SARCOMA, NOS			1 (2%)
#URINARY BLADDER	(48)	(48)	(45)
TRANSITIONAL-CELL CARCINOMA	1 (2%)		
SARCOMA, NOS		1 (2%)	
MESOTHELIOMA, NOS	1 (2%)		

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(47)	(48)
ADENOMA, NOS	19 (40%)	13 (28%)	12 (25%)
ADENOCARCINOMA, NOS			1 (2%)
#ANTERIOR PITUITARY	(47)	(47)	(48)
ADENOMA, NOS	2 (4%)	2 (4%)	3 (6%)
#ADRENAL	(48)	(49)	(49)
CORTICAL ADENOMA			1 (2%)
PHEOCHROMOCYTOMA	3 (6%)	3 (6%)	2 (4%)
#ADRENAL MEDULLA	(48)	(49)	(49)
PHEOCHROMOCYTOMA		2 (4%)	2 (4%)
#THYROID	(44)	(41)	(49)
CARCINOMA,NOS	1 (2%)		
FOLLICULAR-CELL ADENOMA	1 (2%)		2 (4%)
FOLLICULAR-CELL CARCINOMA		1 (2%)	
C-CELL ADENOMA	1 (2%)	1 (2%)	2 (4%)
C-CELL CARCINOMA		1 (2%)	2 (4%)
#PANCREATIC ISLETS	(47)	(49)	(47)
ISLET-CELL ADENOMA	1 (2%)	3 (6%)	1 (2%)
ISLET-CELL CARCINOMA	1 (2%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROMA			1 (2%)
FIBROADENOMA		2 (4%)	1 (2%)
#TESTIS	(49)	(50)	(50)
INTERSTITIAL-CELL TUMOR	29 (59%)	36 (72%)	35 (70%)
MESOTHELIOMA, NOS	1 (2%)	1 (2%)	1 (2%)
*VAS DEFERENS	(50)	(50)	(50)
CARCINOMA,NOS			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(47)	(50)	(49)
GLIOMA, NOS	1 (2%)	2 (4%)	
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
PAPILLOMA, NOS			1 (2%)
SQUAMOUS CELL CARCINOMA			1 (2%)
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
OSTEOMA	1 (2%)		
BODY CAVITIES			
*PERITONEAL CAVITY	(50)	(50)	(50)
LIPOMA			1 (2%)
*MESENTERY	(50)	(50)	(50)
FIBROSARCOMA		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
MESOTHELIOMA, NOS		1 (2%)	
MESOTHELIOMA, MALIGNANT			2 (4%)

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

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	14	16	13
MORIBUND SACRIFICE	7	4	8
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	29	30	29
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	47	49	48
TOTAL PRIMARY TUMORS	94	107	115
TOTAL ANIMALS WITH BENIGN TUMORS	41	46	45
TOTAL BENIGN TUMORS	61	68	78
TOTAL ANIMALS WITH MALIGNANT TUMORS	29	30	30
TOTAL MALIGNANT TUMORS	31	35	34
TOTAL ANIMALS WITH SECONDARY TUMORS##		1	1
TOTAL SECONDARY TUMORS		1	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	4	3
TOTAL UNCERTAIN TUMORS	2	4	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

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

	CONTROL (CHAMBER)	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)
PAPILLOMA, NOS		1 (2%)	
BASAL-CELL CARCINOMA			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS		1 (2%)	1 (2%)
FIBROMA	1 (2%)		1 (2%)
LIPOMA	1 (2%)		
RHABDOMYOSARCOMA	1 (2%)		
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
PAPILLARY ADENOMA			3 (6%)
#LUNG	(48)	(48)	(50)
TUBULAR-CELL ADENOCARCINOMA, MET	1 (2%)		
C-CELL CARCINOMA, METASTATIC			2 (4%)
GRANULOSA-CELL CARCINOMA, METAST	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
LEUKEMIA,NOS	3 (6%)	3 (6%)	6 (12%)
LEUKEMIA,MONONUCLEAR CELL	11 (22%)	20 (40%)	15 (30%)
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
*TONGUE	(50)	(50)	(50)
PAPILLOMA, NOS	1 (2%)		
#LIVER	(50)	(49)	(49)
NEOPLASTIC NODULE	1 (2%)		
#FORESTOMACH	(49)	(48)	(47)
SQUAMOUS CELL PAPILLOMA			1 (2%)
*RECTUM	(50)	(50)	(50)
SARCOMA, NOS, INVASIVE			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
TUBULAR-CELL ADENOMA		1 (2%)	
TUBULAR-CELL ADENOCARCINOMA	1 (2%)		
#URINARY BLADDER	(44)	(46)	(40)
SARCOMA, NOS, INVASIVE			1 (3%)
ENDOMETRIAL STROMAL SARCOMA, INV		1 (2%)	

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(47)	(46)
ADENOMA, NOS	17 (35%)	13 (28%)	13 (28%)
#ANTERIOR PITUITARY	(48)	(47)	(46)
CARCINOMA,NOS		2 (4%)	
ADENOMA, NOS	8 (17%)	5 (11%)	1 (2%)
#ADRENAL	(48)	(49)	(48)
CORTICAL ADENOMA	1 (2%)	1 (2%)	
CORTICAL CARCINOMA		1 (2%)	
PHEOCHROMOCYTOMA			1 (2%)
#ADRENAL MEDULLA	(48)	(49)	(48)
PHEOCHROMOCYTOMA	1 (2%)	1 (2%)	
#THYROID	(45)	(35)	(37)
ADENOMA, NOS			1 (3%)
FOLLICULAR-CELL ADENOMA		1 (3%)	
FOLLICULAR-CELL CARCINOMA		1 (3%)	1 (3%)
C-CELL ADENOMA	1 (2%)	1 (3%)	4 (11%)
C-CELL CARCINOMA	1 (2%)	1 (3%)	3 (8%)
#PANCREATIC ISLETS	(47)	(48)	(46)
ISLET-CELL ADENOMA		1 (2%)	1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)	1 (2%)	1 (2%)
FIBROADENOMA	7 (14%)	13 (26%)	13 (26%)
*CLITORAL GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA			1 (2%)
PAPILLARY ADENOMA			1 (2%)
#UTERUS	(49)	(50)	(47)
ADENOCARCINOMA, NOS			1 (2%)
SARCOMA, NOS			1 (2%)
ENDOMETRIAL STROMAL POLYP	3 (6%)	8 (16%)	7 (15%)
ENDOMETRIAL STROMAL SARCOMA		4 (8%)	2 (4%)
#CERVIX UTERI	(49)	(50)	(47)
ENDOMETRIAL STROMAL POLYP			1 (2%)
#OVARY	(48)	(50)	(46)
TUBULAR-CELL ADENOCARCINOMA, MET	1 (2%)		
GRANULOSA-CELL CARCINOMA	1 (2%)		
NERVOUS SYSTEM			
#CEREBRUM	(49)	(50)	(49)
CARCINOMA, NOS, INVASIVE		1 (2%)	
#BRAIN	(49)	(50)	(49)
GLIOMA, NOS			2 (4%)
OLIGODENDROGLIOMA		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS			1 (2%)
*ZYMBAL'S GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)		
SQUAMOUS CELL CARCINOMA		1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			

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

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	10	10	13
MORIBUND SACRIFICE	5	9	6
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	35	31	31
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	38	46	44
TOTAL PRIMARY TUMORS	63	83	84
TOTAL ANIMALS WITH BENIGN TUMORS	30	34	33
TOTAL BENIGN TUMORS	41	46	48
TOTAL ANIMALS WITH MALIGNANT TUMORS	19	28	30
TOTAL MALIGNANT TUMORS	21	37	36
TOTAL ANIMALS WITH SECONDARY TUMORS##	2	2	3
TOTAL SECONDARY TUMORS	3	2	4
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1		
TOTAL UNCERTAIN TUMORS	1		
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

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

ANIMAL NUMBER	0 0 1 1	0 0 2 1	0 0 3 1	0 0 4 1	0 0 5 1	0 0 6 1	0 0 7 1	0 0 8 1	0 0 9 1	0 1 0 1	0 1 1 1	0 1 2 1	0 1 3 1	0 1 4 1	0 1 5 1	0 1 6 1	0 1 7 1	0 1 8 1	0 1 9 1	0 2 0 1	0 2 1 1	0 2 2 1	0 2 3 1	0 2 4 1	0 2 5 1
WEEKS ON STUDY	1 0 4	1 0 4	1 0 4	1 0 3	1 0 4	1 0 0	0 7 5	0 8 7	0 8 7	0 9 4	0 9 0	0 9 8	1 0 4	1 0 8	1 0 4	1 0 6	0 8 7	1 0 4	1 0 4	1 0 4	1 0 0	1 0 4	1 0 4	1 0 4	1 0 4
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	N	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+
KERATOACANTHOMA																									
SUBCUTANEOUS TISSUE	+	+	+	N	+	+	+	+	N	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+
FIBROMA					X																				
OSTEOSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+
THYMUS	+	-	+	+	-	+	+	-	-	+	+	-	+	-	+	+	+	+	+	+	+	-	+	+	+
SQUAMOUS CELL CARCINOMA																									
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	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	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL CARCINOMA																									
MESOTHELIOMA, NOS													X												
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
ADENOMA, NOS			X	X	X			X		-	X	X	X				X	X	X	X					
ADRENAL	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA									X																
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-
CARCINOMA,NOS													X												
FOLLICULAR-CELL ADENOMA																									
C-CELL ADENOMA																									
PARATHYROID	-	-	-	+	+	-	+	-	+	-	+	-	-	+	+	+	-	+	+	-	+	-	-	-	-
PANCREATIC ISLETS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	+	N	N	N	N	N	N	N	N	N	+	N	N	N	N	+	N	N	N	N	N	+	N
TESTIS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X		X	X								X	X	X			X			X	X	X	X	X
MESOTHELIOMA, NOS													X												
PROSTATE	-	-	+	-	-	+	-	+	-	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+
GLIOMA, 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																									
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
MALIGNANT LYMPHOMA, NOS										X															
LEUKEMIA,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 MIS-SEXED
: 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	0030	0031	0032	0033	0034	0035	0036	0037	0038	0039	0040	0041	0042	0043	0044	0045	0046	0047	0048	0049	0050	TOTAL
WEEKS ON STUDY	104	041	021	031	041	079	104	092	104	104	104	104	082	041	088	094	041	071	010	046	074	044	044	044	044	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
KERATOACANTHOMA							X																			1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA														X	X											3
OSTEOSARCOMA													X													1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR CARCINOMA	X											X														2
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	-	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	44
THYMUS	+	-	-	-	-	-	+	+	+	+	-	+	-	+	+	-	-	+	+	-	-	+	+	+	-	31
SQUAMOUS CELL CARCINOMA																						X				1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	46
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA																										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	50N
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	-	+	+	+	+	-	-	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	41
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
TRANSITIONAL-CELL CARCINOMA															X											1
MESOTHELIOMA, NOS																										1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ADENOMA, NOS		X		X			X		X		X				X					X		X		X	X	21
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
PHEOCHROMOCYTOMA									X								X									3
THYROID	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	44
CARCINOMA,NOS																										1
FOLLICULAR-CELL ADENOMA																	X									1
C-CELL ADENOMA										X																1
PARATHYROID	-	-	+	-	-	-	+	-	-	-	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	26
PANCREATIC ISLETS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	47
ISLET-CELL ADENOMA																	X									1
ISLET-CELL CARCINOMA							X																			1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	+	M	+	N	+	M	N	N	+	38N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR	X				X	X	X	X		X	X			X	X	X	X	X		X			X	X	X	29
MESOTHELIOMA, NOS																										1
PROSTATE	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	38
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	47
GLIOMA, 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	N	50N
OSTEOMA		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	50N
MALIGNANT LYMPHOMA, NOS			X													X										2
LEUKEMIA,NOS																										1
LEUKEMIA,MONONUCLEAR CELL					X	X		X						X			X		X	X	X			X	X	19

N ANIMALS NECROPSIED

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

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	084	080	094	092	094	094	084	089	095	088	088	084	092	094	091	088	094	093	094	094	096	094	094	095
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+
PAPILLOMA, NOS										X															
KERATOACANTHOMA								X																	
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+
FIBROMA																X									
NEURILEMOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+
FOLLICULAR-CELL CARCINOMA, METAST				X																					
TRACHEA	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+
HEMANGIOMA																									
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
MUCINOUS ADENOCARCINOMA																			X		X				
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS			X								X					X	X		X			X		X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA				X						X															
THYROID	+	+	+	+	+	+	-	+	-	+	-	+	+	+	-	-	+	+	+	-	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA				X																					
C-CELL ADENOMA						X																			
C-CELL CARCINOMA																									
PARATHYROID	+	+	+	-	+	-	-	+	+	-	-	+	+	-	-	-	-	-	+	-	+	+	-	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA		X														X									
ISLET-CELL CARCINOMA			X																						
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	+	N	N	N	N	N	N	+	+	+	N	N	N	N	N	N	·	N	N	N	+	+
FIBROADENOMA																									X
TESTIS	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X		X	X	X	X	X		X	X	X	X	X			X	X		X	X		X		X
MESOTHELIOMA, NOS											X														
PROSTATE	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	-	+	+	-	+	+	+	-
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GLIOMA, NOS																									
BODY CAVITIES																									
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROSARCOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS									X																
LEUKEMIA,NOS									X													X			
LEUKEMIA,MONONUCLEAR CELL		X	X		X					X	X	X		X	X	X					X			X	

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: LOW-DOSE (Continued)

ANIMAL NUMBER	0262	0272	0282	0292	0301	0311	0321	0331	0341	0351	0361	0371	0381	0391	0401	0411	0421	0431	0441	0451	0461	0471	0481	0491	0501	TOTAL
WEEKS ON STUDY	1104	1108	0941	0882	0884	0804	0804	0804	0804	0905	0804	0453	0804	0804	0804	1104	1104	1104	1104	1104	0904	1008	1104	1303	0709	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	50N
PAPILLOMA, NOS																										1
KERATOACANTHOMA																										1
SUBCUTANEOUS TISSUE	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	50N
FIBROMA												X												X		2
NEURILEMOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
FOLLICULAR-CELL CARCINOMA, METAST																										1
TRACHEA	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMANGIOMA	X																									1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	-	-	-	+	+	+	+	+	-	-	+	-	+	+	+	+	+	+	-	-	-	+	-	-		26
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																							X			2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50N
PANCREAS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	-	37
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
MUCINOUS ADENOCARCINOMA																										2
LARGE INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SARCOMA, NOS		X																								1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	47
ADENOMA, NOS	X							X				X		X							X	X	X		X	15
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PHEOCHROMOCYTOMA	X						X											X								5
THYROID	-	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	41
FOLLICULAR-CELL CARCINOMA																										1
C-CELL ADENOMA						X																				1
C-CELL CARCINOMA																										1
PARATHYROID	-	+	-	-	+	+	-	+	+	+	-	-	+	+	+	-	+	+	+	-	-	-	+	+	+	28
PANCREATIC ISLETS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ISLET-CELL ADENOMA																		X								3
ISLET-CELL CARCINOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	N	N	+	+	+	N	N	N	N	+	N	N	+	+	+	+	+	+	N	+	N	N	N	50N
FIBROADENOMA							X																			2
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X			X	X		X	X		X			X	X	X	X	X	X	X		X	X	X	X	36
MESOTHELIOMA, NOS																										1
PROSTATE	+	+	-	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	-	+	+	+	-	39
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GLIOMA, NOS										X							X									2
BODY CAVITIES																										
MESENTERY	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	50N
FIBROSARCOMA															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	50N
MESOTHELIOMA, NOS																										1
LEUKEMIA,NOS												X														3
LEUKEMIA,MONONUCLEAR CELL	X	X	X				X		X	X			X			X				X		X	X		X	23

N = ANIMALS NECROPSIED

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

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025	0026	0027	0028	0029	0030	0031	0032	0033	0034	0035
WEEKS ON STUDY	1 0 4	0 9 8	1 0 4	1 0 4	0 9 6	0 9 6	1 0 4	1 0 4	1 0 4	1 0 4	0 9 8	1 0 3	0 9 3	0 8 9	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 3	1 0 4	0 9 0	1 0 4	1 0 4	0 9 4
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																					X				
KERATOACANTHOMA						X											X								
FIBROMA																	X								
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																									
LIPOMA						X																		X	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA							X																		
C-CELL CARCINOMA, METASTATIC																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
NASAL CAVITY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLARY ADENOMA											X														
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	–	+	+	+	+	–	+	+	+	+	+	–	+	–	+	+	+	–	–	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																									
HEPATOCELLULAR CARCINOMA										X															
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS		X																							
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS		X							X			X	X		X	X					X		X		
ADENOCARCINOMA, NOS																								X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA							X										X							X	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA	X																								
C-CELL ADENOMA															X								X		
C-CELL CARCINOMA																									
PARATHYROID	+	+	+	+	+	+	–	+	+	+	–	+	+	–	+	–	–	+	+	–	+	–	+	–	–
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+
ISLET-CELL ADENOMA															X										
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	N	N	N	N	+	N	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	N	N
FIBROMA																			X						
FIBROADENOMA																									
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X			X	X	X	X	X	X	X	X			X		X		X	X	X			X		X
MESOTHELIOMA, NOS																									
PROSTATE	+	+	+	+	–	–	+	–	+	+	–	+	+	+	–	–	+	–	–	+	+	+	–	+	+
VAS DEFERNES, SPERMATIC CORD	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA, NOS					X																				
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N
PAPILLOMA, NOS																									
SQUAMOUS CELL CARCINOMA			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
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
MESOTHELIOMA, MALIGNANT																						X			
LEUKEMIA, NOS	X						X	X		X	X	X	X			X		X	X	X				X	
LEUKEMIA, MONONUCLEAR CELL																									
DIAPHRAGM NOS																									
HEMANGIOMA																									

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: HIGH-DOSE (Continued)

ANIMAL NUMBER	0246	0247	0248	0249	0250	0251	0252	0253	0254	0255	0256	0257	0258	0259	0260	0261	0262	0263	0264	0265	0266	0267	0268	0269	0270	TOTAL TISSUES TUMORS
WEEKS ON STUDY	096	104	090	104	096	104	104	095	091	104	104	091	089	104	104	104	091	093	104	104	098	091	091	104	097	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
PAPILLOMA, NOS																X					X		X			1
KERATOACANTHOMA																										5
FIBROMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA		X					X																			3
LIPOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR CARCINOMA				X																						2
C-CELL CARCINOMA, METASTATIC																			X							1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NASAL CAVITY	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	50M
PAPILLARY ADENOMA																X										2
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LYMPH NODES	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	46
THYMUS	+	+	-	+	-	+	+	-	+	+	-	-	-	+	+	+	+	+	+	+	+	+	+	+	-	37
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASTIC NODULE	X															X										2
HEPATOCELLULAR CARCINOMA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	46
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SARCOMA, NOS																										1
URINARY BLADDER	+	+	+	+	+	+	-	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+		45
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-		48
ADENOMA, NOS						X		X		X				X	X				X				X			15
ADENOCARCINOMA, NOS																										1
ADRENAL	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CORTICAL ADENOMA					X							X														1
PHEOCHROMOCYTOMA																										4
THYROID	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
FOLLICULAR-CELL ADENOMA							X																			2
C-CELL ADENOMA																										2
C-CELL CARCINOMA																		X		X						2
PARATHYROID	+	-	+	-	+	+	+	+	+	-	+	-	+	+	+	+	+	-	-	-	+	-	-	+	-	31
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	47
ISLET-CELL ADENOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	M	+	M	M	+	+	+	M	+	M	M	M	+	+	M	M	M	M	M	M	M	M	+	+		50M
FIBROMA																							X			1
FIBROADENOMA																										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		35
MESOTHELIOMA, NOS																		X								1
PROSTATE	-	+	-	+	-	-	-	+	-	-	-	-	+	-	+	+	+	+	+	+	-	+	-	-	+	28
VAS DEFERNES, SPERMATIC CORD	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
CARCINOMA, NOS																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																										
ZYMBAL'S GLAND	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
PAPILLOMA, NOS												X														1
SQUAMOUS CELL CARCINOMA																										1
BODY CAVITIES																										
PERITONEUM	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
LIPOMA																								X		1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
MESOTHELIOMA, MALIGNANT									X																	2
LEUKEMIA,NOS											X															1
LEUKEMIA,MONONUCLEAR CELL	X		X						X	X				X		X	X	X				X	X			22
DIAPHRAGM NOS															X											1
HEMANGIOMA																										

M ANIMALS NECROPSIED

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE: 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	101	101	101	104	085	104	104	083	082	104	088	095	096	096	096	093	096	048	046	084	104	082	090	104	089
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	M	+	+
FIBROMA												X													
LIPOMA																									
RHABDOMYOSARCOMA								X																	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA, META																									
GRANULOSA-CELL CARCINOMA, METASTA																									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
PAPILLOMA, NOS																							X		
SALIVARY GLAND	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																							X		
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	
ESOPHAGUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	
LARGE INTESTINE	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOCARCINOMA																									
URINARY BLADDER	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS	X	X		X		X	X	X				X			X	X	X				X	X	X		
ADRENAL	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	-
C-CELL ADENOMA																									
C-CELL CARCINOMA																									
PARATHYROID	+	+	+	+	-	+	+	-	+	-	+	-	+	+	-	+	-	-	-	+	+	-	+	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	+	N	+	+	+	N	+	+	+	N	+	+	+	N	N	+	N	N	N	+	N	N
ADENOCARCINOMA, NOS																							X		
FIBROADENOMA		X		X																					
UTERUS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP				X															X						
OVARY	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
TUBULAR-CELL ADENOCARCINOMA, META																									
GRANULOSA-CELL CARCINOMA																									X
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N
CARCINOMA,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					X																				
LEUKEMIA,NOS									X		X												X		
LEUKEMIA,MONONUCLEAR CELL			X									X				X	X								

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

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CHAMBER CONTROL (Continued)

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES TUMORS
INTEGUMENTARY SYSTEM	
SUBCUTANEOUS TISSUE	50M
FIBROMA	1
LIPOMA	1
RHABDOMYOSARCOMA	1
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	48
TUBULAR-CELL ADENOCARCINOMA, META	1
GRANULOSA-CELL CARCINOMA, METASTA	1
TRACHEA	50
HEMATOPOIETIC SYSTEM	
BONE MARROW	49
SPLEEN	49
LYMPH NODES	46
THYMUS	24
CIRCULATORY SYSTEM	
HEART	49
DIGESTIVE SYSTEM	
ORAL CAVITY	50M
PAPILLOMA, NOS	1
SALIVARY GLAND	48
LIVER	50
NEOPLASTIC NODULE	1
BILE DUCT	50
GALLBLADDER & COMMON BILE DUCT	50M
PANCREAS	47
ESOPHAGUS	47
STOMACH	49
SMALL INTESTINE	47
LARGE INTESTINE	45
URINARY SYSTEM	
KIDNEY	50
TUBULAR-CELL ADENOCARCINOMA	1
URINARY BLADDER	44
ENDOCRINE SYSTEM	
PITUITARY	48
ADENOMA, NOS	25
ADRENAL	48
CORTICAL ADENOMA	1
PHEOCHROMOCYTOMA	1
THYROID	49
C-CELL ADENOMA	1
C-CELL CARCINOMA	1
PARATHYROID	32
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50M
ADENOCARCINOMA, NOS	1
FIBROADENOMA	7
UTERUS	49
ENDOMETRIAL STROMAL POLYP	3
OVARY	48
TUBULAR-CELL ADENOCARCINOMA, META	1
GRANULOSA-CELL CARCINOMA	1
NERVOUS SYSTEM	
BRAIN	49
SPECIAL SENSE ORGANS	
ZYMBAL'S GLAND	50M
CARCINOMA,NOS	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50M
MALIGNANT LYMPHOMA, NOS	1
LEUKEMIA,NOS	3
LEUKEMIA,MONONUCLEAR CELL	11

M ANIMALS NECROPSIED

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

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025	0026	0027	0028	0029	0030	0031	0032	0033	0034	0035
WEEKS ON STUDY	104	104	104	104	104	104	099	104	104	104	104	088	095	104	104	091	091	104	088	061	093	102	104	082	104
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA																									
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	−	+	+	+	+
ENDOMETRIAL STROMAL SARCOMA, INVA																									
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
CARCINOMA,NOS																					X				
ADENOMA, NOS	X	X	X		X	X		X				X		X			X						X	X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+
CORTICAL ADENOMA													X												
CORTICAL CARCINOMA																									
PHEOCHROMOCYTOMA																									
THYROID	+	+	−	−	+	+	+	+	+	+	+	+	−	+	+	+	+	−	−	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
FOLLICULAR-CELL CARCINOMA																									
C-CELL ADENOMA																									
C-CELL CARCINOMA																									X
PARATHYROID	+	−	−	−	+	+	+	−	+	−	+	−	−	−	+	−	+	−	−	−	−	+	−	−	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	−	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	N	+	N	+	N	+	+	+	N	+	+	N	+	+	+	N	+	+	+	+	+
ADENOCARCINOMA, NOS																									
FIBROADENOMA			X			X				X							X	X				X		
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP		X	X			X	X	_	X																
ENDOMETRIAL STROMAL SARCOMA																								X	
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, INVASIVE																									
OLIGODENDROGLIOMA	X																								
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																				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, HISTIOCYTIC TYPE											X														
LEUKEMIA,NOS																									
LEUKEMIA,MONONUCLEAR CELL	X					X	X		X		X	X		X	X	X		X				X	X	X

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: LOW-DOSE (Continued)

ANIMAL NUMBER	0226	0227	0228	0229	0330	0331	0332	0333	0334	0335	0336	0337	0338	0339	0340	0341	0342	0343	0344	0345	0346	0347	0348	0349	0350	TOTAL TISSUES / TUMORS
WEEKS ON STUDY	088	104	104	104	096	082	571	041	041	041	093	086	096	041	041	097	044	044	073	041	041	041	041	041	046	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	N	N	+	+	+	+	+	N	N	+	+	+	+	+	+	+	N	+	+	+	+	+	50M
PAPILLOMA, NOS														X												1
SUBCUTANEOUS TISSUE	+	+	+	N	N	+	+	+	+	+	N	N	+	+	+	+	+	+	+	N	+	+	+	+	+	50M
SARCOMA, NOS																X										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
TRACHEA	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	49
LYMPH NODES	-	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
THYMUS	-	+	+	-	-	-	-	+	+	-	-	+	+	-	+	-	+	+	-	-	+	+	-	+	-	26
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
BILE DUCT	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	-	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	+	-	-	34
STOMACH	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOMA																						X				1
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	46
ENDOMETRIAL STROMAL SARCOMA, INVA																X										1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	47
CARCINOMA,NOS												X														2
ADENOMA, NOS		X		X		X				X			X		X								X			18
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CORTICAL ADENOMA																										1
CORTICAL CARCINOMA														X												1
PHEOCHROMOCYTOMA																X										1
THYROID	+	-	-	+	-	+	+	-	+	-	+	-	+	-	+	-	+	-	+	+	-	+	+	+	+	35
FOLLICULAR-CELL ADENOMA																				X						1
FOLLICULAR-CELL CARCINOMA									X																	1
C-CELL ADENOMA									X																	1
C-CELL CARCINOMA																										1
PARATHYROID	+	-	-	+	+	+	+	+	-	-	+	-	-	-	+	-	-	-	-	-	-	+	-	-		19
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ISLET-CELL ADENOMA						X																				1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	H	+	+	H	+	H	+	+	+	H	+	+	+	+	N	50M
ADENOCARCINOMA, NOS							X																			1
FIBROADENOMA	X	X			X			X													X	X	X			13
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP		X								X															X	8
ENDOMETRIAL STROMAL SARCOMA									X							X					X					4
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA, NOS, INVASIVE												X														1
GLIOBLASTOMA																										1
SPECIAL SENSE ORGANS																										
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL CARCINOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
LEUKEMIA,NOS				X		X			X		X							X			X					3
LEUKEMIA,MONONUCLEAR CELL														X										X	X	20

M ANIMALS NECROPSIED

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

ANIMAL NUMBER	0 0 1 4	0 0 2 6	0 0 3 0	0 0 4 9	0 0 5 4	0 0 6 4	0 0 7 4	0 0 8 4	0 0 9 4	0 1 0 4	0 1 1 4	0 1 2 4	0 1 3 4	0 1 4 4	0 1 5 4	0 1 6 4	0 1 7 6	0 1 8 5	0 1 9 3	0 2 0 7	0 2 1 4	0 2 2 8	0 2 3 1	0 2 4 9	0 2 5 4
WEEKS ON STUDY	1 0 4	0 9 6	0 9 0	0 9 9	1 1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	0 9 6	0 9 6	0 9 5	1 3	0 9 7	1 0 4	0 8 7	1 0 1	0 9 7	1 0 4
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	+	+	+
BASAL-CELL CARCINOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	+	+	+
SARCOMA, NOS																									
FIBROMA				X																					
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL CARCINOMA, METASTATIC			X											X											
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-
NASAL CAVITY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+
PAPILLARY ADENOMA														X											X
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
SQUAMOUS CELL PAPILLOMA																									
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
SARCOMA, NOS, INVASIVE																		X							
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	-	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	-	-	-	-	+	+
SARCOMA, NOS, INVASIVE																		X							
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	+	+	
ADENOMA, NOS						X					X		X		X				X		X				
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+
ADENOMA, NOS																				X					
FOLLICULAR-CELL CARCINOMA																									
C-CELL ADENOMA	X							X	X		X														
C-CELL CARCINOMA			X											X											
PARATHYROID	-	+	-	-	-	+	-	-	-	+	+	+	+	+	+	-	-	-	-	+	-	-	+	+	-
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	-	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	+	N	+	+	+	+	+	N	+	+	+	+	N	N	+	N	+	+	N	N	+	+
ADENOCARCINOMA, NOS				X																					
FIBROADENOMA			X			X	X		X			X													
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																									
PAPILLARY ADENOMA																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS				X																					
SARCOMA, NOS																		X							
ENDOMETRIAL STROMAL POLYP		X		X						X	X			X						X					
ENDOMETRIAL STROMAL SARCOMA	X							X																	
OVARY	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GLIOMA, NOS																X									
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS																	X	X		X		X	X		
LEUKEMIA,MONONUCLEAR CELL	X	X		X		X							X												

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE 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 TISSUES TUMORS
WEEKS ON STUDY	085	104	104	104	104	104	059	104	104	095	104	097	104	100	104	104	104	104	104	091	079	104	094	104	104	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	50M
BASAL-CELL CARCINOMA																		X								1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS							X																			1
FIBROMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL CARCINOMA, METASTATIC																										2
TRACHEA	-	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
NASAL CAVITY	M	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	50M
PAPILLARY ADENOMA		X																								3
HEMATOPOIETIC SYSTEM																										
BONE MARROW	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
THYMUS	-	+	-	-	-	-	-	+	+	+	+	-	+	+	-	+	+	+	+	-	-	+	-	+	-	29
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
BILE DUCT	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ESOPHAGUS	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	44
STOMACH	-	+	+	+	+	+	+	+	+	+	+	+	X	-	+	+	+	+	+	+	+	+	+	+	+	47
SQUAMOUS CELL PAPILLOMA																										1
SMALL INTESTINE	-	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	43
LARGE INTESTINE	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	42
RECTUM	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
SARCOMA, NOS, INVASIVE																										1
URINARY SYSTEM																										
KIDNEY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SARCOMA, NOS, INVASIVE																										1
ENDOCRINE SYSTEM																										
PITUITARY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ADENOMA, NOS					X				X		X			X				X		X			X		X	14
ADRENAL	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
PHEOCHROMOCYTOMA					X																					1
THYROID	-	+	+	+	+	+	-	+	+	+	+	+	+	+	-	-	-	-	+	-	+	+	+	-	-	37
ADENOMA, NOS																										1
FOLLICULAR-CELL CARCINOMA				X																						1
C-CELL ADENOMA																			X							4
C-CELL CARCINOMA																										3
PARATHYROID	-	-	+	+	-	+	-	+	+	-	+	+	+	-	-	-	-	-	-	-	-	-	-	+	-	28
PANCREATIC ISLETS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ISLET-CELL ADENOMA						X																				1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	M	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	N	N	+	N	N	+	50M
ADENOCARCINOMA, NOS																										1
FIBROADENOMA		X			X	X		X						X	X	X						X				13
PREPUTIAL/CLITORAL GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	N	M	M	M	M	M	M	N	M	M	M	50M
SQUAMOUS CELL CARCINOMA																						X				1
PAPILLARY ADENOMA															X											1
UTERUS	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ADENOCARCINOMA, NOS																										1
SARCOMA, NOS																										1
ENDOMETRIAL STROMAL POLYP					X					X																8
ENDOMETRIAL STROMAL SARCOMA																										2
OVARY	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GLIOMA, NOS																				X						2
SPECIAL SENSE ORGANS																										
LACRIMAL GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
CARCINOMA, NOS					X																					1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
LEUKEMIA, NOS														X												6
LEUKEMIA, MONONUCLEAR CELL			X						X	X		X			X	X			X			X	X		X	15

M ANIMALS NECROPSIED

APPENDIX B

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

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

	CONTROL (CHAMBER)	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)
ADNEXAL ADENOMA		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
PAPILLOMA, NOS			1 (2%)
SQUAMOUS CELL CARCINOMA			1 (2%)
#LUNG	(50)	(50)	(50)
HEPATOCELLULAR CARCINOMA, METAST		2 (4%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	14 (28%)	12 (24%)	8 (16%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	2 (4%)	2 (4%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	4 (8%)	2 (4%)	4 (8%)
MALIGNANT LYMPHOMA, MIXED TYPE		3 (6%)	
LEUKEMIA,NOS	1 (2%)		
#LYMPH NODE	(44)	(48)	(42)
MALIGNANT LYMPHOMA, MIXED TYPE	1 (2%)		
CIRCULATORY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
HEMANGIOSARCOMA		1 (2%)	
#SPLEEN	(48)	(50)	(47)
HEMANGIOMA			1 (2%)
HEMANGIOSARCOMA		1 (2%)	
*NASAL CAVITY	(50)	(50)	(50)
HEMANGIOMA			5 (10%)
HEMANGIOSARCOMA			5 (10%)
#HEART	(50)	(50)	(50)
HEMANGIOSARCOMA		1 (2%)	
#LIVER	(50)	(50)	(50)
HEMANGIOSARCOMA	2 (4%)	1 (2%)	
DIGESTIVE SYSTEM			
*TOOTH	(50)	(50)	(50)
ODONTOMA	1 (2%)	1 (2%)	1 (2%)
#LIVER	(50)	(50)	(50)
HEPATOCELLULAR ADENOMA	8 (16%)	6 (12%)	5 (10%)
HEPATOCELLULAR CARCINOMA	6 (12%)	10 (20%)	5 (10%)
URINARY SYSTEM			
#KIDNEY/TUBULE	(50)	(50)	(50)
CYSTADENOMA, NOS			1 (2%)
ENDOCRINE SYSTEM			
#ADRENAL	(50)	(43)	(49)
CORTICAL ADENOMA		2 (5%)	
CORTICAL CARCINOMA	1 (2%)		
#THYROID	(43)	(48)	(46)
FOLLICULAR-CELL ADENOMA		1 (2%)	

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
#TESTIS	(48)	(49)	(49)
INTERSTITIAL-CELL TUMOR		1 (2%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE/LACRIMAL GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS		1 (2%)	
PAPILLARY CYSTADENOMA, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY			
* NUMBER OF ANIMALS NECROPSIED			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	7	14	17
MORIBUND SACRIFICE	1	2	5
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	42	34	27
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			1
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	29	31	27
TOTAL PRIMARY TUMORS	42	46	37
TOTAL ANIMALS WITH BENIGN TUMORS	20	21	17
TOTAL BENIGN TUMORS	23	24	21
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	17	14
TOTAL MALIGNANT TUMORS	18	21	15
TOTAL ANIMALS WITH SECONDARY TUMORS##		2	
TOTAL SECONDARY TUMORS		2	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	1	1
TOTAL UNCERTAIN TUMORS	1	1	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

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

	CONTROL (CHAMBER)	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)	
FIBROMA			1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
ADENOCARCINOMA, NOS			2 (4%)
OSTEOMA	1 (2%)		
#LUNG	(50)	(50)	(50)
ADENOCARCINOMA, NOS, METASTATIC		1 (2%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	4 (8%)	7 (14%)	6 (12%)
ADENOSQUAMOUS CARCINOMA, METASTA			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	7 (14%)	3 (6%)	5 (10%)
MALIG.LYMPHOMA, UNDIFFER-TYPE			1 (2%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)	3 (6%)	
MALIGNANT LYMPHOMA, MIXED TYPE	3 (6%)	4 (8%)	1 (2%)
#SPLEEN	(48)	(49)	(44)
ADENOCARCINOMA, NOS, METASTATIC		1 (2%)	
MALIGNANT LYMPHOMA, MIXED TYPE	1 (2%)		
CIRCULATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
HEMANGIOMA			3 (6%)
HEMANGIOSARCOMA			2 (4%)
#HEART	(50)	(50)	(48)
ADENOCARCINOMA, NOS, METASTATIC		1 (2%)	
#LIVER	(50)	(50)	(49)
HEMANGIOSARCOMA		1 (2%)	
#URINARY BLADDER	(44)	(47)	(42)
HEMANGIOSARCOMA			1 (2%)
#UTERUS	(48)	(50)	(48)
HEMANGIOMA	1 (2%)		1 (2%)
DIGESTIVE SYSTEM			
*TOOTH	(50)	(50)	(50)
ODONTOMA	1 (2%)		
#LIVER	(50)	(50)	(49)
HEPATOCELLULAR ADENOMA	1 (2%)	3 (6%)	2 (4%)
HEPATOCELLULAR CARCINOMA	2 (4%)	4 (8%)	1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
ADENOCARCINOMA, NOS, METASTATIC		1 (2%)	
SARCOMA, NOS			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(48)	(38)
CARCINOMA,NOS	1 (2%)		
ADENOMA, NOS	8 (17%)	6 (13%)	1 (3%)
#ADRENAL	(48)	(48)	(48)
PHEOCHROMOCYTOMA	1 (2%)		
SARCOMA, NOS			1 (2%)
#THYROID	(45)	(50)	(43)
FOLLICULAR-CELL ADENOMA	1 (2%)	1 (2%)	

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS		3 (6%)	
ADENOSQUAMOUS CARCINOMA			3 (6%)
#UTERUS	(48)	(50)	(48)
ADENOCARCINOMA, NOS		1 (2%)	
LEIOMYOMA		1 (2%)	
LEIOMYOSARCOMA		1 (2%)	
ENDOMETRIAL STROMAL POLYP	2 (4%)	1 (2%)	
#UTERUS/ENDOMETRIUM	(48)	(50)	(48)
ADENOMA, NOS		1 (2%)	
#OVARY	(48)	(46)	(37)
ADENOMA, NOS	1 (2%)		
GRANULOSA-CELL TUMOR		1 (2%)	
TERATOMA, NOS	1 (2%)		
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
SARCOMA, NOS, METASTATIC			1 (2%)
OSTEOSARCOMA, METASTATIC		1 (2%)	
LEG			
OSTEOSARCOMA		1	

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

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	12	14	36
MORIBUND SACRIFICE	1	6	3
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	37	29	10
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			1
ACCIDENTALLY KILLED, NOS		1	
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	28	35	23
TOTAL PRIMARY TUMORS	37	44	32
TOTAL ANIMALS WITH BENIGN TUMORS	16	18	12
TOTAL BENIGN TUMORS	20	21	14
TOTAL ANIMALS WITH MALIGNANT TUMORS	13	20	16
TOTAL MALIGNANT TUMORS	15	22	18
TOTAL ANIMALS WITH SECONDARY TUMORS##		3	2
TOTAL SECONDARY TUMORS		5	2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	1	
TOTAL UNCERTAIN TUMORS	2	1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE: 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	85	104	104	104	104	104	104	104	104	85	104	104	104	87	104	104	53	104	104	104	104	104	104	86
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA				X		X				X		X					X								X
ALVEOLAR/BRONCHIOLAR CARCINOMA					X																				
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
MALIGNANT LYMPHOMA, MIXED TYPE				X																					
THYMUS	-	-	+	+	+	-	-	-	+	+	-	+	+	-	-	-	-	-	-	+	-	-	+	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
ORAL CAVITY	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
ODONTOMA																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA										X							X			X					
HEPATOCELLULAR CARCINOMA														X	X							X			X
HEMANGIOSARCOMA																								X	
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	M	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+
LARGE INTESTINE	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL CARCINOMA																									
THYROID	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+
PARATHYROID	-	-	-	-	-	-	-	+	-	-	+	+	-	+	-	+	-	-	-	+	-	-	-	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
TESTIS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+
PROSTATE	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
ADENOCARCINOMA, NOS															X										
HARDERIAN GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
PAPILLARY CYSTADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
MALIGNANT LYMPHOMA, NOS		X						X																	
LEUKEMIA, NOS																									

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

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: CHAMBER CONTROL (Continued)

ANIMAL NUMBER	0221	0227	0229	0230	0231	0232	0233	0234	0235	0236	0237	0238	0239	0240	0241	0242	0243	0244	0245	0246	0247	0248	0249	0250	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	104	104	104	104	104	071	104	102	104	104	083	104	104	104	104	104	104	104	104	104	104	104	104	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA		X	X				X				X								X	X	X		X		14
ALVEOLAR/BRONCHIOLAR CARCINOMA																							X		2
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	47
SPLEEN	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LYMPH NODES	-	+	+	+	+	+	-	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	44
MALIGNANT LYMPHOMA, MIXED TYPE																									1
THYMUS	+	-	+	+	-	-	+	+	-	+	-	+	-	-	+	-	+	-	-	-	-	+	+	+	22
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																									
ORAL CAVITY	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
ODONTOMA						X																			1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA		X				X			X	X						X				X					8
HEPATOCELLULAR CARCINOMA																								X	6
HEMANGIOSARCOMA																							X		2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	M	+	+	M	+	+	M	+	M	+	+	+	M	+	+	+	+	+	50M
PANCREAS	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	45
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	44
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL CARCINOMA							X																		1
THYROID	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	43
PARATHYROID	-	+	+	-	-	-	-	+	+	+	+	+	-	+	-	-	+	+	+	-	-	-	-	+	28
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PROSTATE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	47
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																									
LACRIMAL GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
ADENOCARCINOMA, NOS																									1
HARDERIAN GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
PAPILLARY CYSTADENOMA, NOS																							X		1
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	X	M	M	M	M	M	M	M	M	X	M	M	M	M	M	50M
MALIGNANT LYMPHOMA, NOS									X																4
LEUKEMIA, NOS													X												1

M ANIMALS NECROPSIED

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

ANIMAL NUMBER	3 0 1	3 0 2	3 0 3	3 0 4	3 0 5	3 0 6	3 0 7	3 0 8	3 0 9	3 1 0	3 1 1	3 1 2	3 1 3	3 1 4	3 1 5	3 1 6	3 1 7	3 1 8	3 1 9	3 2 0	3 2 1	3 2 2	3 2 3	3 2 4	3 2 5
WEEKS ON STUDY	0 8 8	1 0 4	1 0 4	1 0 4	0 9 7	1 0 4	1 0 4	0 9 1	0 8 3	1 0 4	0 9 6	1 0 4	1 0 4	0 8 8	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	1 0 4	0 8 4	0 8 5	1 0 4
INTEGUMENTARY SYSTEM																									
SKIN	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADNEXAL ADENOMA														X											
SUBCUTANEOUS TISSUE	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA											X														
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA					X		X																		
ALVEOLAR/BRONCHIOLAR ADENOMA							X				X						X				X				
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA											X														
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	-	+	-	-	-	-	-	-	+	-	-	-	-	+	+	+	+	-	-	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA															X										
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
ODONTOMA																	X								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA														X	X	X									X
HEPATOCELLULAR CARCINOMA					X		X														X	X			
HEMANGIOSARCOMA																X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	N	N	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
ADRENAL	+	+	+	+	-	+	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																							X		X
THYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA							X																		
PARATHYROID	-	-	-	+	-	+	+	+	-	+	-	+	+	-	-	+	-	-	-	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	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
ADENOMA, NOS																						X			
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS					X																		X		
MALIGNANT LYMPHOMA, MIXED TYPE																									

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: LOW-DOSE (Continued)

ANIMAL NUMBER	5 2 6	5 2 7	5 2 8	5 2 9	5 3 0	5 3 1	5 3 2	5 3 3	5 3 4	5 3 5	5 3 6	5 3 7	5 3 8	5 3 9	5 4 0	5 4 1	5 4 2	5 4 3	5 4 4	5 4 5	5 4 6	5 4 7	5 4 8	5 4 9	5 5 0	TOTAL TISSUES TUMORS
WEEKS ON STUDY	0 5 8	1 0 4	1 0 4	1 0 4	1 0 4	0 5 6	1 0 4	1 0 4	1 0 4	0 9 1	1 0 4	1 0 4	1 0 4	0 8 8	0 7 3	1 0 4	1 0 4	1 0 4	1 0 4	0 8 3	0 6 7	1 0 4	1 0 4	0 9 9	1 0 4	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADNEXAL ADENOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																										2
ALVEOLAR/BRONCHIOLAR ADENOMA		X	X		X	X			X		X					X								X		12
ALVEOLAR/BRONCHIOLAR CARCINOMA							X	X																		2
TRACHEA	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	46
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA																										1
LYMPH NODES	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	48
THYMUS	-	+	-	-	-	-	+	-	+	-	-	+	+	-	-	-	-	-	+	-	+	-	+	-	+	19
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA																										1
DIGESTIVE SYSTEM																										
ORAL CAVITY	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
ODONTOMA																										1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA													X									X				6
HEPATOCELLULAR CARCINOMA				X		X								X			X		X		X					18
HEMANGIOSARCOMA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	M	+	+	+	+	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	48
SMALL INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	46
ENDOCRINE SYSTEM																										
PITUITARY	-	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
ADRENAL	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	43
CORTICAL ADENOMA																										2
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	-	-	+	+	+	+	+	-	+	+	+	-	-	+	-	+	-	+	+	+	-	+	+	+	-	30
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
TESTIS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR																										1
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
ADENOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	X	M	M	M	M	X	M	M	M	M	M	M	M	M	M	50M
MALIGNANT LYMPHOMA, NOS																										2
MALIGNANT LYMPHOMA, MIXED TYPE				X																						1

* ANIMALS NECROPSIED

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE: 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	102	075	104	104	086	104	104	031	104	104	053	104	104	104	096	104	098	104	104	104	102	104	104	092
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA	X			X											X								X	X	
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
NASAL CAVITY	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																									
SQUAMOUS CELL CARCINOMA																									
HEMANGIOMA				X						X			X		X					X				
HEMANGIOSARCOMA																									
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
HEMANGIOMA																				X					
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
ODONTOMA																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA														X			X			X					
HEPATOCELLULAR CARCINOMA			X								X						X			X					
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CYSTADENOMA, NOS											X														
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	+	-	-	-	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	N
MALIGNANT LYMPHOMA, NOS												X													

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: HIGH-DOSE (Continued)

ANIMAL NUMBER	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	TOTAL TISSUES TUMORS
WEEKS ON STUDY	0 9 6	1 0 5	0 7 6	0 9 2	0 9 8	0 8 4	1 0 8	0 9 6	0 8 6	0 9 2	0 8 4	0 9 7	0 6 6	0 6 4	0 8 0	0 8 4	0 8 4	0 8 4	0 9 2	0 8 4	0 8 4	0 7 4	0 8 4	0 8 4	0 8 4	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																		X					X	X		8
TRACHEA	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NASAL CAVITY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
PAPILLOMA, NOS				X																						1
SQUAMOUS CELL CARCINOMA																						X				1
HEMANGIOMA																										3
HEMANGIOSARCOMA							X	X						X										X	X	5
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	47
HEMANGIOMA																										1
LYMPH NODES	+	+	+	-	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	-	+	42
THYMUS	-	-	-	-	-	+	+	-	+	-	+	-	-	-	-	-	+	+	-	-	+	-	+	-	+	15
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
ORAL CAVITY	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
ODONTOMA															X											1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA	X																								X	5
HEPATOCELLULAR CARCINOMA							X	X																		5
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	M	+	M	+	+	M	+	M	M	M	M	M	+	M	+	+	+	+	M	M	+	+	+	38M
PANCREAS	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	46
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
STOMACH	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	-	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	45
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CYSTADENOMA, NOS																										1
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	43
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYROID	+	+	+	-	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	46
PARATHYROID	+	+	-	-	-	-	+	-	-	-	-	-	+	-	+	-	-	-	+	-	-	-	-	-	-	14
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PROSTATE	+	+	-	+	-	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	-	+	+	+	43
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	M	M	N	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	N	M	M	M	M	M	M	50M
MALIGNANT LYMPHOMA, NOS			X	X															X							4

+ ANIMALS NECROPSIED

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

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0110	0111	0112	0113	0114	0115	0116	0117	0118	0119	0120	0121	0122	0123	0124	0125
WEEKS ON STUDY	104	104	104	104	104	104	104	104	104	104	089	104	104	088	104	097	104	104	091	025	104	104	104	094	097
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	X	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																				X		X			
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
NASAL CAVITY	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
OSTEOMA																									
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
MALIGNANT LYMPHOMA, MIXED TYPE																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	-
THYMUS	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	A	+	+	+	-	+	+	+	-	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ODONTOMA																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA					X																				
HEPATOCELLULAR CARCINOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	A	+	+	+	-	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ENDOCRINE SYSTEM																									
PITUITARY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS																									
ADENOMA, NOS						X												X				X		X	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																X									
THYROID	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	A	+	+	+	+	+	+	+	+	-
FOLLICULAR-CELL ADENOMA																									
PARATHYROID	-	-	-	+	+	+	+	-	+	+	-	+	-	-	+	A	+	+	-	-	-	-	-	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	+	+	+	+	+	+	N	N	+	+	N	+	N	+	+	+	N	+	+	+	+	N
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ENDOMETRIAL STROMAL POLYP							X																		
HEMANGIOMA																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ADENOMA, NOS																									
TERATOMA, NOS																									
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	N
MALIGNANT LYMPHOMA, NOS											X		X	X											X
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																			X						
MALIGNANT LYMPHOMA, MIXED TYPE																									

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

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

ANIMAL NUMBER	0226	0227	0228	0229	0230	0231	0232	0233	0234	0235	0236	0237	0238	0239	0240	0241	0242	0243	0244	0245	0246	0247	0248	0249	0250	TOTAL
WEEKS ON STUDY	1046	1046	1031	1046	1046	1036	1046	1046	1046	1046	1046	1046	1043	1046	1046	1092	1046	1046	1046	1031	1046	1046	1046	1046	1046	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA										X						X										4
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	48
NASAL CAVITY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
OSTEOMA										X																1
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
MALIGNANT LYMPHOMA, MIXED TYPE																					X					1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	46
THYMUS	+	+	+	+	+	-	+	-	+	+	+	-	-	-	-	-	+	+	+	-	+	-	+	+	+	34
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
ORAL CAVITY	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
ODONTOMA																		X								1
SALIVARY GLAND	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA																										1
HEPATOCELLULAR CARCINOMA										X									X							2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	M	+	+	+	M	+	M	+	+	M	50M
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	44
ENDOCRINE SYSTEM																										
PITUITARY	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
CARCINOMA,NOS													X													1
ADENOMA, NOS				X							X				X							X				8
ADRENAL	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	45
FOLLICULAR-CELL ADENOMA															X											1
PARATHYROID	-	-	+	+	+	-	-	-	-	+	+	-	-	-	-	-	-	-	+	-	-	+	+	+	+	28
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	M	+	+	+	M	+	+	+	+	+	M	+	+	+	M	+	+	M	M	+	M	+	+	M	50M
UTERUS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOMETRIAL STROMAL POLYP				X																						2
HEMANGIOMA										X																1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS		X																								1
TERATOMA, NOS			X																							1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	50M
MALIGNANT LYMPHOMA, NOS							X							X		X										7
MALIG.LYMPHOMA, HISTIOCYTIC TYPE								X																		1
MALIGNANT LYMPHOMA, MIXED TYPE													X							X						3

M ANIMALS NECROPSIED

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

ANIMAL NUMBER	50112	50123	50134	50145	50156	50167	50178	50189	50191	50201	50212	50223	50234	50245	50256	50267	50278	50289	50291	50302	50313	50324	50335
WEEKS ON STUDY	10 4	10 4	10 4	08 8	10 1	10 3	08 9	08 4	10 4	10 4	10 4	08 9	09 4	10 4	10 1	10 4	07 8	08 1	10 4	10 3	10 4	10 4	08 9	10 4
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																	X							
ALVEOLAR/BRONCHIOLAR ADENOMA			X	X			X								X							X		
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
ADENOCARCINOMA, NOS, METASTATIC																				X				
LYMPH NODES	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
THYMUS	-	+	-	-	-	-	-	-	+	+	-	-	-	+	+	+	-	-	+	-	-	-	-	+
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																	X							
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA	X																							
HEPATOCELLULAR CARCINOMA								X																
HEMANGIOSARCOMA																								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	M	+	M	+	M	+	+	M	+	M	+	+	M	+	+	M	+	M	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																				X				
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
ADENOMA, NOS										X			X											
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																								
PARATHYROID	-	-	-	-	-	-	-	+	+	+	+	-	-	+	-	-	-	+	+	+	+	-	+	+
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	+	M	+	+	+	+	+	M	+	+	+	N	N	N	M	+	+	+	N	M	M	+	+	+
ADENOCARCINOMA, NOS																	X							
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																				X				
ADENOCARCINOMA, NOS																								
LEIOMYOMA																						X		
LEIOMYOSARCOMA																								
ENDOMETRIAL STROMAL POLYP																								
OVARY	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR																								
NERVOUS SYSTEM																								
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																								
HARDERIAN GLAND	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
ADENOMA, NOS																								
MUSCULOSKELETAL SYSTEM																								
BONE	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
OSTEOSARCOMA				X																				
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
OSTEOSARCOMA, METASTATIC					X										X									
MALIGNANT LYMPHOMA, NOS						X						X												
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																		X						
MALIGNANT LYMPHOMA, MIXED TYPE																								
LEG NOS																								
OSTEOSARCOMA																								

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: LOW-DOSE (Continued)

ANIMAL NUMBER	52267	52279	52281	52283	52285	52287	52289	52291	52293	52295	52297	52299	52301	52303	52305	52307	52309	52311	52313	52315	52317	52319	52321	52323	52325	TOTAL TISSUES TUMORS
WEEKS ON STUDY	08047	08049	08051	08041	08045	08045	08046	08046	08046	08046	08049	08048	08046	08046	08046	08049	08046	08045	08045	08045	08045	08047	08046	08046	08046	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC																										1
ALVEOLAR/BRONCHIOLAR ADENOMA						X												X								7
TRACHEA	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOCARCINOMA, NOS, METASTATIC																										1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYMUS	-	-	+	+	-	+	+	+	+	+	-	-	+	+	-	-	+	-	+	-	-	+	+	-	+	22
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC																										1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	X	+	50
HEPATOCELLULAR ADENOMA																										3
HEPATOCELLULAR CARCINOMA																					X				X	4
HEMANGIOSARCOMA																								X		1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	N	+	+	+	+	+	+	+	+	50N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC																										1
URINARY BLADDER	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ADENOMA, NOS				X					X					X											X	6
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FOLLICULAR-CELL ADENOMA													X													1
PARATHYROID	+	+	+	+	+	-	-	+	-	+	-	-	+	-	+	-	+	-	+	+	-	-	+	+	-	25
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	50N
ADENOCARCINOMA, NOS				X												X										3
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																										X	1
ADENOCARCINOMA, NOS																											1
LEIOMYOMA																											1
LEIOMYOSARCOMA																		X									1
ENDOMETRIAL STROMAL POLYP																						X					1
OVARY	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
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	N	50N
ADENOMA, 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	N	N	50N
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	N	50N
OSTEOSARCOMA, METASTATIC	X																										1
MALIGNANT LYMPHOMA, NOS					X																						5
MALIG.LYMPHOMA, HISTIOCYTIC TYPE											X																3
MALIGNANT LYMPHOMA, MIXED TYPE		X																			X		X				4
LEG NOS																											
OSTEOSARCOMA	X																										1

N ANIMALS NECROPSIED

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF PROPYLENE OXIDE: 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	104	086	083	084	084	095	089	062	085	084	066	077	093	088	104	104	100	096	078	091	024	104	092	095
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE FIBROMA	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA ADENOSQUAMOUS CARCINOMA, METASTAT	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+ X	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NASAL CAVITY ADENOCARCINOMA, NOS HEMANGIOMA HEMANGIOSARCOMA	+	+	+	+	+	+	+ X	+	+	N	+	+	+	+	+	+ X	+	+	+	N	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+
SPLEEN	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-
LYMPH NODES	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	-	-
THYMUS	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	+	+	+	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	N	N	+	N	N	N	N	+	N	+	N	+	+	+	N	+	N	N	N	+	N
PANCREAS	+	+	-	+	+	+	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	-
ESOPHAGUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	-	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
SMALL INTESTINE	+	+	-	+	-	+	+	-	-	-	+	-	-	+	-	+	+	-	+	-	-	+	+	+	-
LARGE INTESTINE	+	+	-	-	-	+	+	+	-	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	-
URINARY SYSTEM																									
KIDNEY SARCOMA, NOS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER HEMANGIOSARCOMA	+	+	-	-	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS	+	+	+	+	+	+	+	+	+	-	-	+	-	+ X	+	+	+	+	+	+	+	-	+	-	-
ADRENAL SARCOMA, NOS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
THYROID	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
PARATHYROID	+	-	-	-	-	+	+	+	-	+	-	-	-	+	+	+	+	+	-	-	+	-	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND ADENOSQUAMOUS CARCINOMA	+	+	N	N	N	N	N	N	N	+	+	+ X	N	+	N	+	+	+	N	+	N	N	N	N	N
UTERUS HEMANGIOMA	+	+	+	+	+	+	+	+ X	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+
OVARY	+	+	+	+	+	+	+	+	+	-	+	-	-	+	+	+	+	+	-	+	+	-	-	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS SARCOMA, NOS, METASTATIC MALIGNANT LYMPHOMA, NOS MALIG.LYMPHOMA, UNDIFFER-TYPE MALIGNANT LYMPHOMA, MIXED TYPE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 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 TISSUES TUMORS
WEEKS ON STUDY	088	011	014	096	094	098	084	097	104	104	100	091	072	104	087	088	080	068	098	072	068	091	078	091	052	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	50N
FIBROMA																		X								1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA								X	X	X	X								X							6
ADENOSQUAMOUS CARCINOMA, METASTAT																										1
TRACHEA	+	+	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
NASAL CAVITY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	50N
ADENOCARCINOMA, NOS																										2
HEMANGIOMA		X		X							X															3
HEMANGIOSARCOMA					X				X																	2
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	45
SPLEEN	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	44
LYMPH NODES	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	A	+	+	-	-	-	+	+	-	37
THYMUS	-	-	+	-	-	-	+	-	+	+	-	-	+	-	-	-	A	+	-	-	-	-	-	A	+	13
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	-	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA									X								X									2
HEPATOCELLULAR CARCINOMA							X																			1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	N	+	+	+	+	+	N	+	+	+	+	N	+	+	N	+	+	N	N	N	N	38N
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	42
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	46
SMALL INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	-	A	+	33
LARGE INTESTINE	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SARCOMA, NOS																		X								1
URINARY BLADDER	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	42
HEMANGIOSARCOMA													X													1
ENDOCRINE SYSTEM																										
PITUITARY	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	-	A	+	38
ADENOMA, NOS																										1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SARCOMA, NOS																		X								1
THYROID	-	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	A	+	+	+	+	+	+	+	+	43
PARATHYROID	-	-	-	+	-	-	+	-	-	-	-	-	+	+	-	+	A	-	-	-	-	+	-	A	-	19
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	N	+	N	+	+	+	+	+	+	X	N	N	+	+	+	N	N	N	+	N	N	N	+	N	N	38N
ADENOSQUAMOUS CARCINOMA																								X		1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMANGIOMA																										1
OVARY	-	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	-	-	+	-	37
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	50N
SARCOMA, NOS, METASTATIC																		X								1
MALIGNANT LYMPHOMA, NOS	X			X	X	X													X							5
MALIG.LYMPHOMA, UNDIFFER-TYPE																										1
MALIGNANT LYMPHOMA, MIXED TYPE															X											1

N ANIMALS NECROPSIED

APPENDIX C

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

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST			2 (4%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
INFLAMMATION, PYOGRANULOMATOUS		1 (2%)	
ACANTHOSIS	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	
GRANULOMA, FOREIGN BODY			1 (2%)
NECROSIS, FAT		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
FOREIGN BODY, NOS	1 (2%)	4 (8%)	3 (6%)
CONGESTION, NOS		1 (2%)	1 (2%)
CONGESTION, ACUTE			1 (2%)
HEMORRHAGE	1 (2%)		
INFLAMMATION, SUPPURATIVE	7 (14%)	19 (38%)	33 (66%)
INFLAMMATION, ACUTE			1 (2%)
INFLAMMATION, ACUTE FOCAL			1 (2%)
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
DEGENERATION, NOS		3 (6%)	
HYPERPLASIA, EPITHELIAL		1 (2%)	9 (18%)
HYPERPLASIA, FOCAL			2 (4%)
HYPERKERATOSIS			1 (2%)
METAPLASIA, SQUAMOUS	1 (2%)	3 (6%)	21 (42%)
*LARYNX	(50)	(50)	(50)
FOREIGN BODY, NOS	1 (2%)		
VEGETABLE FOREIGN BODY	1 (2%)		
ULCER, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE	2 (4%)	8 (16%)	7 (14%)
INFLAMMATION, NECROTIZING			1 (2%)
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC FOCAL	1 (2%)		2 (4%)
HYPERPLASIA, EPITHELIAL		1 (2%)	2 (4%)
HYPERPLASIA, FOCAL		1 (2%)	
*SUBMUCOSA OF LARYNX	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	2 (4%)
#TRACHEA	(49)	(46)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
HYPERPLASIA, EPITHELIAL			2 (4%)
#TRACHEAL SUBMUCOSA	(49)	(46)	(49)
INFLAMMATION, SUPPURATIVE		3 (7%)	1 (2%)
#LUNG/BRONCHUS	(50)	(47)	(49)
BRONCHIECTASIS			1 (2%)
#LUNG/BRONCHIOLE	(50)	(47)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
HYPERPLASIA, EPITHELIAL			2 (4%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
#LUNG	(50)	(47)	(49)
FOREIGN BODY, NOS	1 (2%)		
CONGESTION, NOS	5 (10%)	3 (6%)	3 (6%)
HEMORRHAGE	1 (2%)	4 (9%)	6 (12%)
INFLAMMATION, INTERSTITIAL	1 (2%)	2 (4%)	1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)	5 (11%)	4 (8%)
INFLAMMATION, ACUTE SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC FOCAL	6 (12%)	3 (6%)	7 (14%)
GRANULOMA, NOS	1 (2%)		
FIBROSIS, FOCAL	1 (2%)		2 (4%)
FIBROSIS, MULTIFOCAL			1 (2%)
NECROSIS, FOCAL	1 (2%)		1 (2%)
CALCIFICATION, FOCAL			4 (8%)
ALVEOLAR MACROPHAGES	4 (8%)	3 (6%)	4 (8%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	7 (14%)	4 (9%)	10 (20%)
#LUNG/ALVEOLI	(50)	(47)	(49)
HEMORRHAGE	1 (2%)		
INFLAMMATION, CHRONIC FOCAL			1 (2%)
FIBROSIS, FOCAL	2 (4%)	1 (2%)	2 (4%)
FIBROSIS, MULTIFOCAL	1 (2%)		5 (10%)
HISTIOCYTOSIS	1 (2%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(49)	(48)
FIBROSIS			1 (2%)
HYPOPLASIA, NOS	2 (4%)		
ATROPHY, NOS	1 (2%)		2 (4%)
HYPERPLASIA, NOS	2 (4%)		
#SPLEEN	(50)	(47)	(48)
HEMORRHAGE	3 (6%)		
FIBROSIS	1 (2%)	1 (2%)	
FIBROSIS, FOCAL	3 (6%)	7 (15%)	4 (8%)
FIBROSIS, MULTIFOCAL			1 (2%)
FIBROSIS, DIFFUSE			2 (4%)
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL	1 (2%)	3 (6%)	2 (4%)
INFARCT, NOS			1 (2%)
PIGMENTATION, NOS	1 (2%)	1 (2%)	1 (2%)
HEMOSIDEROSIS		1 (2%)	
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	3 (6%)
HEMATOPOIESIS	1 (2%)		
#SPLENIC FOLLICLES	(50)	(47)	(48)
NECROSIS, NOS	1 (2%)		
#LYMPH NODE	(44)	(49)	(46)
INFLAMMATION, ACUTE/CHRONIC	2 (5%)	4 (8%)	1 (2%)
PLASMACYTOSIS		1 (2%)	
#MANDIBULAR L. NODE	(44)	(49)	(46)
FIBROSIS			1 (2%)
#BRONCHIAL LYMPH NODE	(44)	(49)	(46)
HEMORRHAGE	2 (5%)		2 (4%)
INFLAMMATION, ACUTE			2 (4%)
ANGIECTASIS			7 (15%)
#AXILLARY LYMPH NODE	(44)	(49)	(46)
HEMORRHAGE		1 (2%)	
#LIVER	(50)	(50)	(49)
HEMATOPOIESIS			1 (2%)
#THYMUS	(31)	(26)	(37)
ATROPHY, NOS	1 (3%)	2 (8%)	1 (3%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#BRAIN/MENINGES	(47)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		
*NASAL CAVITY	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		
#LUNG	(50)	(47)	(49)
THROMBOSIS, NOS	1 (2%)		
#HEART	(50)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL		2 (4%)	
FIBROSIS	1 (2%)	1 (2%)	1 (2%)
FIBROSIS, MULTIFOCAL	1 (2%)		
HEMOSIDEROSIS	1 (2%)		
METAPLASIA, CARTILAGINOUS	1 (2%)		
#HEART/ATRIUM	(50)	(50)	(49)
THROMBOSIS, NOS		3 (6%)	
#HEART/VENTRICLE	(50)	(50)	(49)
DILATATION, NOS			1 (2%)
#MYOCARDIUM	(50)	(50)	(49)
INFLAMMATION, INTERSTITIAL	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC FOCAL	3 (6%)		2 (4%)
FIBROSIS	11 (22%)	19 (38%)	13 (27%)
FIBROSIS, FOCAL	6 (12%)	1 (2%)	
FIBROSIS, MULTIFOCAL	4 (8%)	1 (2%)	
FIBROSIS, DIFFUSE	1 (2%)		
DEGENERATION, NOS	1 (2%)		
NECROSIS, FOCAL	1 (2%)		
#ENDOCARDIUM	(50)	(50)	(49)
HYPERPLASIA, FOCAL			1 (2%)
#CARDIAC VALVE	(50)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		
METAPLASIA, CARTILAGINOUS	3 (6%)	4 (8%)	7 (14%)
#AORTIC VALVE	(50)	(50)	(49)
METAPLASIA, CARTILAGINOUS	2 (4%)		
*AORTA	(50)	(50)	(50)
CALCIFICATION, FOCAL		1 (2%)	
*CORONARY ARTERY	(50)	(50)	(50)
METAPLASIA, CARTILAGINOUS			1 (2%)
*PULMONARY ARTERY	(50)	(50)	(50)
THROMBOSIS, NOS			1 (2%)
CALCIFICATION, NOS		2 (4%)	4 (8%)
CALCIFICATION, FOCAL	7 (14%)	7 (14%)	8 (16%)
*ARTERY OF HEAD NECK	(50)	(50)	(50)
THROMBOSIS, NOS			1 (2%)
*PANCREATIC ARTERY	(50)	(50)	(50)
CALCIFICATION, NOS			1 (2%)
#PANCREAS	(47)	(49)	(47)
PERIARTERITIS	1 (2%)		
#COLON	(48)	(48)	(48)
PERIARTERITIS			1 (2%)
#TESTIS	(49)	(50)	(50)
PERIARTERITIS			1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(46)	(49)	(47)
METAMORPHOSIS FATTY		1 (2%)	
ATROPHY, FOCAL		1 (2%)	
#LIVER	(50)	(50)	(49)
CONGESTION, NOS	1 (2%)		
INFLAMMATION, FOCAL			1 (2%)
INFLAMMATION, SUPPURATIVE	2 (4%)		

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#LIVER (Continued)	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	2 (4%)		
FIBROSIS	1 (2%)		
DEGENERATION, NOS	1 (2%)	1 (2%)	
DEGENERATION, LIPOID	2 (4%)	1 (2%)	
NECROSIS, FOCAL	5 (10%)	3 (6%)	6 (12%)
NECROSIS, CENTRAL	2 (4%)	3 (6%)	
PIGMENTATION, NOS		1 (2%)	
CYTOPLASMIC VACUOLIZATION	8 (16%)	7 (14%)	5 (10%)
BASOPHILIC CYTO CHANGE		9 (18%)	2 (4%)
EOSINOPHILIC CYTO CHANGE		2 (4%)	5 (10%)
CLEAR-CELL CHANGE		1 (2%)	
HEPATOCYTOMEGALY	4 (8%)	1 (2%)	3 (6%)
HYPERPLASIA, NODULAR	1 (2%)		
ANGIECTASIS	1 (2%)		1 (2%)
#PORTAL TRACT	(50)	(50)	(49)
FIBROSIS	5 (10%)	19 (38%)	9 (18%)
FIBROSIS, FOCAL			4 (8%)
FIBROSIS, MULTIFOCAL	2 (4%)		1 (2%)
#LIVER/CENTRILOBULAR	(50)	(50)	(49)
DEGENERATION, NOS	2 (4%)	1 (2%)	1 (2%)
#LIVER/HEPATOCYTES	(50)	(50)	(49)
CYTOPLASMIC VACUOLIZATION	1 (2%)	2 (4%)	
BASOPHILIC CYTO CHANGE	3 (6%)		1 (2%)
EOSINOPHILIC CYTO CHANGE		1 (2%)	4 (8%)
CLEAR-CELL CHANGE	1 (2%)		
HYPERPLASIA, NODULAR			1 (2%)
#BILE DUCT	(50)	(50)	(49)
INFLAMMATION, MULTIFOCAL	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
HYPERPLASIA, NOS	30 (60%)	46 (92%)	41 (84%)
HYPERPLASIA, FOCAL	6 (12%)	1 (2%)	1 (2%)
HYPERPLASIA, DIFFUSE	2 (4%)		
#PANCREAS	(47)	(49)	(47)
HEMORRHAGE	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOUS			1 (2%)
GRANULOMA, FOREIGN BODY			1 (2%)
FIBROSIS			1 (2%)
FIBROSIS, FOCAL	4 (9%)		2 (4%)
FIBROSIS, MULTIFOCAL	1 (2%)		1 (2%)
FIBROSIS, DIFFUSE	3 (6%)		2 (4%)
NECROSIS, NOS	1 (2%)		
ATROPHY, NOS	3 (6%)		
ATROPHY, FOCAL	7 (15%)	1 (2%)	
#PANCREATIC ACINUS	(47)	(49)	(47)
ATROPHY, NOS	1 (2%)	11 (22%)	12 (26%)
ATROPHY, FOCAL		1 (2%)	5 (11%)
#STOMACH	(49)	(49)	(50)
ULCER, NOS	1 (2%)	1 (2%)	
INFLAMMATION, FOCAL		2 (4%)	
INFLAMMATION, SUPPURATIVE	1 (2%)		
ULCER, ACUTE	1 (2%)		
INFLAMMATION, ACUTE NECROTIZING			1 (2%)
NECROSIS, NOS	1 (2%)		
NECROSIS, FOCAL			2 (4%)
HYPERPLASIA, EPITHELIAL			1 (2%)
ACANTHOSIS		1 (2%)	2 (4%)
#GASTRIC MUCOSA	(49)	(49)	(50)
ULCER, NOS		2 (4%)	
HYPERKERATOSIS		1 (2%)	
ACANTHOSIS		1 (2%)	

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#GASTRIC SUBMUCOSA	(49)	(49)	(50)
HEMORRHAGE	1 (2%)		
#COLON	(48)	(48)	(48)
PARASITISM	4 (8%)	3 (6%)	3 (6%)
#CECUM	(48)	(48)	(48)
NECROSIS, FOCAL	1 (2%)		
INFARCT, FOCAL	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
PYELONEPHRITIS, ACUTE	2 (4%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
FIBROSIS, FOCAL			1 (2%)
NEPHROPATHY	45 (90%)	48 (96%)	48 (96%)
NEPHROSIS, NOS	1 (2%)	1 (2%)	
PIGMENTATION, NOS	1 (2%)		
#KIDNEY/CORTEX	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	1 (2%)
FIBROSIS, DIFFUSE	1 (2%)		
NECROSIS, DIFFUSE			2 (4%)
METAMORPHOSIS FATTY		1 (2%)	
#KIDNEY/MEDULLA	(50)	(50)	(50)
METAMORPHOSIS FATTY		1 (2%)	
URINARY SYSTEM (Continued)			
#KIDNEY/TUBULE	(50)	(50)	(50)
DILATATION, NOS	1 (2%)		
DEGENERATION, NOS	1 (2%)		2 (4%)
NECROSIS, NOS	1 (2%)		
NECROSIS, DIFFUSE		1 (2%)	
PIGMENTATION, NOS	6 (12%)	2 (4%)	2 (4%)
REGENERATION, NOS	3 (6%)		
#KIDNEY/PELVIS	(50)	(50)	(50)
DILATATION, NOS			1 (2%)
CALCIFICATION, FOCAL			1 (2%)
HYPERPLASIA, EPITHELIAL			2 (4%)
HYPERPLASIA, FOCAL			1 (2%)
#URINARY BLADDER	(48)	(48)	(45)
CALCULUS,UNKN GROSS OR MICRO	1 (2%)		
INFLAMMATION, SUPPURATIVE	1 (2%)		
HYPERPLASIA, EPITHELIAL	3 (6%)	3 (6%)	
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(47)	(48)
CYST, NOS	6 (13%)	2 (4%)	3 (6%)
CALCIFICATION, FOCAL			1 (2%)
HYPERPLASIA, NOS	2 (4%)	3 (6%)	1 (2%)
HYPERPLASIA, FOCAL		1 (2%)	
ANGIECTASIS			1 (2%)
#ANTERIOR PITUITARY	(47)	(47)	(48)
HYPERPLASIA, NOS			2 (4%)
#ADRENAL	(48)	(49)	(49)
DEGENERATION, LIPOID	3 (6%)		
NECROSIS, FOCAL	1 (2%)		
#ADRENAL CORTEX	(48)	(49)	(49)
DEGENERATION, LIPOID		3 (6%)	
NECROSIS, FOCAL		1 (2%)	
CYTOPLASMIC VACUOLIZATION	3 (6%)	5 (10%)	7 (14%)
CYTOMEGALY	2 (4%)	6 (12%)	6 (12%)
HYPERPLASIA, FOCAL	2 (4%)		2 (4%)
ANGIECTASIS			1 (2%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM (Continued)			
#ADRENAL MEDULLA	(48)	(49)	(49)
HYPERPLASIA, FOCAL	2 (4%)	2 (4%)	10 (20%)
ANGIECTASIS			1 (2%)
#THYROID	(44)	(41)	(49)
THYROGLOSSAL DUCT CYST	1 (2%)		
CYSTIC FOLLICLES			1 (2%)
HYPERPLASIA, C-CELL	8 (18%)	5 (12%)	4 (8%)
HYPERPLASIA, FOLLICULAR-CELL		1 (2%)	3 (6%)
#PARATHYROID	(26)	(28)	(31)
CYTOMEGALY			1 (3%)
HYPERPLASIA, NOS			1 (3%)
#PANCREATIC ISLETS	(47)	(49)	(47)
HYPERPLASIA, FOCAL		1 (2%)	2 (4%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE			1 (2%)
HYPERPLASIA, NOS		1 (2%)	1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		
HYPERPLASIA, CYSTIC			1 (2%)
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
ABSCESS, NOS			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIVE			1 (2%)
HYPERKERATOSIS		1 (2%)	
METAPLASIA, SQUAMOUS			1 (2%)
#PROSTATE	(38)	(39)	(28)
INFLAMMATION, SUPPURATIVE	7 (18%)	5 (13%)	1 (4%)
INFLAMMATION, CHRONIC			1 (4%)
INFLAMMATION, CHRONIC FOCAL		1 (3%)	
INFLAMMATION, CHRONIC SUPPURATIVE	2 (5%)		
CALCIFICATION, FOCAL		1 (3%)	
HYPERPLASIA, NOS	2 (5%)		
HYPERPLASIA, EPITHELIAL		1 (3%)	1 (4%)
*SEMINAL VESICLE	(50)	(50)	(50)
CYST, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE	12 (24%)	13 (26%)	16 (32%)
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)	1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC SUPPURATIVE	3 (6%)		
CALCIFICATION, FOCAL	1 (2%)		
HYPERPLASIA, EPITHELIAL	1 (2%)		1 (2%)
HYPERPLASIA, FOCAL			1 (2%)
#TESTIS	(49)	(50)	(50)
HEMORRHAGE		1 (2%)	
NECROSIS, FOCAL		1 (2%)	
CALCIFICATION, NOS		9 (18%)	4 (8%)
CALCIFICATION, FOCAL	10 (20%)	11 (22%)	15 (30%)
ATROPHY, NOS	18 (37%)	40 (80%)	23 (46%)
ATROPHY, FOCAL			1 (2%)
HYPERPLASIA, INTERSTITIAL CELL	8 (16%)	1 (2%)	3 (6%)
*VAS DEFERENS	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		
NECROSIS, FAT	1 (2%)		
*SCROTUM	(50)	(50)	(50)
NECROSIS, FAT			1 (2%)
NERVOUS SYSTEM			
#CEREBRUM	(47)	(50)	(49)
HEMORRHAGE	1 (2%)		

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM (Continued)			
#BRAIN	(47)	(50)	(49)
HEMORRHAGE	2 (4%)	3 (6%)	4 (8%)
GLIOSIS	1 (2%)		1 (2%)
NECROSIS, FOCAL	1 (2%)		2 (4%)
PIGMENTATION, NOS	1 (2%)		
CYTOPLASMIC VACUOLIZATION			1 (2%)
#CEREBRAL WHITE MATTE	(47)	(50)	(49)
CYTOPLASMIC VACUOLIZATION	2 (4%)	4 (8%)	4 (8%)
#CEREBELLUM	(47)	(50)	(49)
HEMORRHAGE	1 (2%)		
#CEREBELLAR WHITE MAT	(47)	(50)	(49)
CYTOPLASMIC VACUOLIZATION			1 (2%)
*OLFACTORY SENSORY EP	(50)	(50)	(50)
DEGENERATION, NOS		1 (2%)	3 (6%)
SPECIAL SENSE ORGANS			
*EYE/CRYSTALLINE LENS	(50)	(50)	(50)
CALCIFICATION, FOCAL		1 (2%)	
*NASOLACRIMAL DUCT	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	4 (8%)	3 (6%)	
METAPLASIA, SQUAMOUS	4 (8%)	8 (16%)	9 (18%)
*EAR CANAL	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	2 (4%)		1 (2%)
MUSCULOSKELETAL SYSTEM			
*STERNUM	(50)	(50)	(50)
HYPERPLASIA, NOS			1 (2%)
*SKELETAL MUSCLE	(50)	(50)	(50)
DEGENERATION, NOS		1 (2%)	
*MUSCLE OF HEAD	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
HEMORRHAGE			1 (2%)
INFLAMMATION, NECROTIZING		1 (2%)	
*PERITONEUM	(50)	(50)	(50)
NECROSIS, FAT		3 (6%)	
*PERITONEAL CAVITY	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		
NECROSIS, FAT	1 (2%)	1 (2%)	
*PLEURA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
FIBROSIS, FOCAL	1 (2%)		1 (2%)
*SUBPLEURAL TISSUE	(50)	(50)	(50)
INFLAMMATION, FOCAL	1 (2%)		
INFLAMMATION, CHRONIC FOCAL		1 (2%)	1 (2%)
FIBROSIS			1 (2%)
FIBROSIS, FOCAL	2 (4%)		3 (6%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)	2 (4%)	4 (8%)
FIBROSIS			1 (2%)
CALCIFICATION, FOCAL			1 (2%)
LEG			
CONGENITAL MALFORMATION, NOS			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 OXIDE

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
HYPERKERATOSIS			1 (2%)
ACANTHOSIS	1 (2%)	3 (6%)	1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
FOREIGN BODY, NOS	1 (2%)	1 (2%)	7 (14%)
HEMORRHAGE		1 (2%)	
INFLAMMATION, SUPPURATIVE	3 (6%)	5 (10%)	20 (40%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
DEGENERATION, NOS			1 (2%)
HYPERPLASIA, EPITHELIAL	1 (2%)		4 (8%)
HYPERPLASIA, FOCAL			1 (2%)
ACANTHOSIS			1 (2%)
METAPLASIA, SQUAMOUS	1 (2%)	2 (4%)	11 (22%)
*MAXILLARY SINUS	(50)	(50)	(50)
ATROPHY, FOCAL			1 (2%)
*LARYNX	(50)	(50)	(50)
FOREIGN BODY, NOS			2 (4%)
INFLAMMATION, SUPPURATIVE	8 (16%)	9 (18%)	12 (24%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL			2 (4%)
HYPERPLASIA, EPITHELIAL	4 (8%)	2 (4%)	
HYPERPLASIA, FOCAL			1 (2%)
ACANTHOSIS	1 (2%)	1 (2%)	5 (10%)
METAPLASIA, SQUAMOUS		2 (4%)	
*SUBMUCOSA OF LARYNX	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
#TRACHEA	(50)	(48)	(44)
INFLAMMATION, SUPPURATIVE		3 (6%)	2 (5%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	1 (2%)	
HYPERPLASIA, EPITHELIAL			1 (2%)
METAPLASIA, SQUAMOUS			1 (2%)
#TRACHEAL SUBMUCOSA	(50)	(48)	(44)
INFLAMMATION, SUPPURATIVE	1 (2%)		
#LUNG/BRONCHUS	(48)	(48)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
#LUNG/BRONCHIOLE	(48)	(48)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
HYPERPLASIA, EPITHELIAL			1 (2%)
HYPERPLASIA, FOCAL		1 (2%)	
#LUNG (Continued)	(48)	(48)	(50)
FOREIGN BODY, NOS		1 (2%)	
CONGESTION, NOS		2 (4%)	2 (4%)
HEMORRHAGE	8 (17%)	12 (25%)	7 (14%)
BRONCHOPNEUMONIA, FOCAL	1 (2%)		
PNEUMONIA, ASPIRATION	1 (2%)		
INFLAMMATION, SUPPURATIVE	4 (8%)	1 (2%)	1 (2%)
PNEUMONIA INTERSTITIAL CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	2 (4%)	5 (10%)	2 (4%)
INFLAMMATION, FOCAL GRANULOMATOUS		1 (2%)	1 (2%)
GRANULOMA, FOREIGN BODY			6 (12%)
FIBROSIS, DIFFUSE	1 (2%)		
CALCIFICATION, FOCAL	1 (2%)		

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
RESPIRATORY SYSTEM (Continued)			
#LUNG (Continued)	(48)	(48)	(50)
FOREIGN MATERIAL, NOS	1 (2%)		
PIGMENTATION, NOS	1 (2%)	1 (2%)	
CYTOPLASMIC VACUOLIZATION	1 (2%)		
BASOPHILIC CYTO CHANGE			1 (2%)
ALVEOLAR MACROPHAGES	5 (10%)	16 (33%)	10 (20%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	4 (8%)	5 (10%)	6 (12%)
METAPLASIA, SQUAMOUS			1 (2%)
HISTIOCYTOSIS			1 (2%)
#LUNG/ALVEOLI	(48)	(48)	(50)
FIBROSIS			1 (2%)
FIBROSIS, FOCAL	3 (6%)	2 (4%)	3 (6%)
FIBROSIS, MULTIFOCAL	1 (2%)	1 (2%)	2 (4%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49) (48)	(48)	
HYPOPLASIA, NOS	1 (2%)		1 (2%)
ATROPHY, NOS	1 (2%)	1 (2%)	
HYPERPLASIA, NOS	1 (2%)	1 (2%)	
#SPLEEN	(49) (49)	(47)	
FIBROSIS		2 (4%)	3 (6%)
FIBROSIS, FOCAL		6 (12%)	3 (6%)
NECROSIS, FOCAL		1 (2%)	
CALCIFICATION, FOCAL			1 (2%)
PIGMENTATION, NOS	3 (6%)	3 (6%)	1 (2%)
HEMOSIDEROSIS		1 (2%)	
ATROPHY, NOS			1 (2%)
HYPERPLASIA, LYMPHOID	6 (12%)		5 (11%)
HEMATOPOIESIS	1 (2%)		
#SPLENIC CAPSULE	(49) (49)	(47)	
FIBROSIS, FOCAL		1 (2%)	
#LYMPH NODE	(46) (46)	(47)	
CONGESTION, NOS	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	2 (4%)	1 (2%)	1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		
PLASMACYTOSIS	1 (2%)		
#MANDIBULAR L. NODE	(46) (46)	(47)	
HEMORRHAGE	1 (2%)		
INFLAMMATION, SUPPURATIVE		1 (2%)	
HYPERPLASIA, LYMPHOID	1 (2%)	1 (2%)	1 (2%)
#BRONCHIAL LYMPH NODE	(46) (46)	(47)	
HEMORRHAGE	1 (2%)	1 (2%)	
#LIVER	(50) (49)	(49)	
HYPERPLASIA, RETICULUM CELL		1 (2%)	
HEMATOPOIESIS	1 (2%)		
#ADRENAL	(48) (49)	(48)	
HEMATOPOIESIS	1 (2%)		
#THYMUS	(24) (26)	(29)	
ATROPHY, NOS	3 (13%)		1 (3%)
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50) (50)	(50)	
PERIVASCULITIS	1 (2%)		
*NASAL CAVITY	(50) (50)	(50)	
THROMBOSIS, NOS	1 (2%)		
#HEART	(49) (49)	(48)	
INFLAMMATION, CHRONIC FOCAL			1 (2%)
PERIVASCULITIS	1 (2%)		
METAPLASIA, CARTILAGINOUS			1 (2%)
#HEART/ATRIUM	(49)	(49)	(48)
THROMBOSIS, NOS			2 (4%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM (Continued)			
#MYOCARDIUM	(49)	(49)	(48)
INFLAMMATION, INTERSTITIAL	1 (2%)		
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC		1 (2%)	2 (4%)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	1 (2%)
FIBROSIS	10 (20%)	9 (18%)	11 (23%)
FIBROSIS, FOCAL	4 (8%)		2 (4%)
FIBROSIS, MULTIFOCAL			1 (2%)
FIBROSIS, DIFFUSE		1 (2%)	
#ENDOCARDIUM	(49) (49)	(48)	
FIBROSIS, FOCAL	1 (2%)		
#CARDIAC VALVE	(49) (49)	(48)	
METAPLASIA, CARTILAGINOUS	1 (2%)	6 (12%)	1 (2%)
*CORONARY ARTERY	(50) (50)	(50)	
INFLAMMATION, FOCAL			1 (2%)
METAPLASIA, CARTILAGINOUS	1 (2%)		
*PULMONARY ARTERY	(50) (50)	(50)	
CALCIFICATION, NOS	6 (12%)	3 (6%)	2 (4%)
CALCIFICATION, FOCAL	4 (8%)	4 (8%)	2 (4%)
#PANCREAS	(47) (48)	(46)	
PERIARTERITIS	1 (2%)	2 (4%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(48)	(47)	(48)
ATROPHY, NOS		1 (2%)	
#LIVER	(50)	(49)	(49)
HEMORRHAGE		1 (2%)	
INFLAMMATION, SUPPURATIVE			1 (2%)
FIBROSIS	1 (2%)		
INFECTION, BACTERIAL		1 (2%)	
DEGENERATION, LIPOID			1 (2%)
NECROSIS, FOCAL		4 (8%)	2 (4%)
NECROSIS, CENTRAL	2 (4%)		1 (2%)
CYTOPLASMIC CHANGE, NOS	3 (6%)		
CYTOPLASMIC VACUOLIZATION	7 (14%)	6 (12%)	9 (18%)
BASOPHILIC CYTO CHANGE	23 (46%)	16 (33%)	15 (31%)
EOSINOPHILIC CYTO CHANGE	5 (10%)	1 (2%)	
CLEAR-CELL CHANGE	1 (2%)	1 (2%)	
HEPATOCYTOMEGALY	2 (4%)	2 (4%)	1 (2%)
ANGIECTASIS		1 (2%)	
#HEPATIC CAPSULE	(50)	(49)	(49)
FIBROSIS, FOCAL		1 (2%)	
#PORTAL TRACT	(50)	(49)	(49)
FIBROSIS	2 (4%)	3 (6%)	8 (16%)
FIBROSIS, FOCAL	1 (2%)		
FIBROSIS, DIFFUSE	1 (2%)		
#LIVER/CENTRILOBULAR	(50)	(49)	(49)
DEGENERATION, NOS	2 (4%)		
#LIVER/HEPATOCYTES	(50)	(49)	(49)
CYTOPLASMIC VACUOLIZATION		1 (2%)	1 (2%)
HYPERPLASIA, NODULAR	1 (2%)		
#BILE DUCT	(50)	(49)	(49)
HYPERPLASIA, NOS	21 (42%)	26 (53%)	33 (67%)
HYPERPLASIA, FOCAL	1 (2%)		
#PANCREAS	(47)	(48)	(46)
FIBROSIS, MULTIFOCAL		1 (2%)	
NECROSIS, FAT	1 (2%)		
ATROPHY, NOS	1 (2%)		
#PANCREATIC ACINUS	(47)	(48)	(46)
ATROPHY, NOS	3 (6%)	7 (15%)	6 (13%)
ATROPHY, FOCAL	4 (9%)	1 (2%)	1 (2%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#ESOPHAGUS	(45)	(34)	(44)
HYPERPLASIA, EPITHELIAL		1 (3%)	
#STOMACH	(49)	(48)	(47)
ULCER, NOS		1 (2%)	
INFLAMMATION, SUPPURATIVE	2 (4%)		
NECROSIS, FOCAL		1 (2%)	
HYPERPLASIA, EPITHELIAL	1 (2%)		
ACANTHOSIS	2 (4%)		1 (2%)
#GASTRIC SUBMUCOSA	(49)	(48)	(47)
CALCIFICATION, FOCAL	1 (2%)		
#COLON	(45)	(45)	(42)
PARASITISM	2 (4%)	3 (7%)	3 (7%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	1 (2%)	1 (2%)	
FIBROSIS, DIFFUSE		1 (2%)	
NEPHROPATHY	40 (80%)	42 (84%)	34 (69%)
NEPHROSIS, NOS	2 (4%)		
NECROSIS, FOCAL		1 (2%)	
#KIDNEY/CORTEX	(50)	(50)	(49)
CALCIFICATION, FOCAL	2 (4%)		
#KIDNEY/MEDULLA	(50)	(50)	(49)
CALCIFICATION, NOS		1 (2%)	
CALCIFICATION, FOCAL		2 (4%)	
#RENAL PAPILLA	(50)	(50)	(49)
CALCIFICATION, NOS		1 (2%)	
#KIDNEY/TUBULE	(50)	(50)	(49)
DEGENERATION, NOS	1 (2%)	1 (2%)	1 (2%)
NECROSIS, NOS		1 (2%)	
NECROSIS, DIFFUSE		1 (2%)	
CALCIFICATION, NOS		1 (2%)	
CALCIFICATION, FOCAL		1 (2%)	
PIGMENTATION, NOS	5 (10%)	1 (2%)	2 (4%)
#KIDNEY/PELVIS	(50)	(50)	(49)
DILATATION, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)		
CALCIFICATION, NOS	1 (2%)	9 (18%)	5 (10%)
CALCIFICATION, FOCAL	5 (10%)	6 (12%)	11 (22%)
HYPERPLASIA, EPITHELIAL		2 (4%)	
HYPERPLASIA, FOCAL	1 (2%)	1 (2%)	
#URINARY BLADDER	(44)	(46)	(40)
INFLAMMATION, SUPPURATIVE		1 (2%)	
HYPERPLASIA, EPITHELIAL	2 (5%)	1 (2%)	
#U. BLADDER/MUCOSA	(44)	(46)	(40)
ULCER, NOS		1 (2%)	
CALCIFICATION, FOCAL		1 (2%)	
#U.BLADDER/SUBMUCOSA	(44)	(46)	(40)
EDEMA, NOS		2 (4%)	
#U.BLADDER/SEROSA	(44)	(46)	(40)
CALCIFICATION, FOCAL	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(47)	(46)
CYST, NOS	6 (13%)	10 (21%)	6 (13%)
CYTOMEGALY	1 (2%)		
HYPERPLASIA, NOS	3 (6%)	2 (4%)	3 (7%)
HYPERPLASIA, FOCAL		1 (2%)	2 (4%)
ANGIECTASIS	1 (2%)		
#ANTERIOR PITUITARY	(48)	(47)	(46)
HYPERPLASIA, NOS	1 (2%)		

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM (Continued)			
#ADRENAL	(48)	(49)	(48)
DEGENERATION, LIPOID	2 (4%)		
ATROPHY, NOS		1 (2%)	
ANGIECTASIS	1 (2%)		1 (2%)
#ADRENAL CORTEX	(48)	(49)	(48)
HEMORRHAGE	1 (2%)	1 (2%)	
CYTOPLASMIC VACUOLIZATION	4 (8%)	1 (2%)	3 (6%)
CYTOMEGALY	1 (2%)	6 (12%)	11 (23%)
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, FOCAL		1 (2%)	1 (2%)
#ADRENAL MEDULLA	(48)	(49)	(48)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL	2 (4%)	2 (4%)	3 (6%)
#THYROID	(45)	(35)	(37)
CYST, NOS			1 (3%)
HYPERPLASIA, C-CELL	7 (16%)	6 (17%)	5 (14%)
ANGIECTASIS			1 (3%)
#PARATHYROID	(32)	(19)	(20)
HYPERPLASIA, NOS		1 (5%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	1 (2%)		
HYPERPLASIA, NOS	2 (4%)	1 (2%)	
HYPERPLASIA, FOCAL			1 (2%)
*LACTIFEROUS DUCT	(50)	(50)	(50)
HYPERKERATOSIS	1 (2%)		
*CLITORAL GLAND	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
METAPLASIA, SQUAMOUS	1 (2%)		1 (2%)
#UTERUS	(49)	(50)	(47)
HEMORRHAGE		2 (4%)	
INFLAMMATION, SUPPURATIVE	3 (6%)	1 (2%)	2 (4%)
METAPLASIA, SQUAMOUS		1 (2%)	
#UTERUS/ENDOMETRIUM	(49)	(50)	(47)
PIGMENTATION, NOS			1 (2%)
HYPERPLASIA, CYSTIC		9 (18%)	6 (13%)
HYPERPLASIA, STROMAL		1 (2%)	
#OVARY	(48)	(50)	(46)
CYST, NOS	1 (2%)	4 (8%)	2 (4%)
CALCIFICATION, FOCAL		1 (2%)	
ATROPHY, NOS	4 (8%)		
NERVOUS SYSTEM			
#CEREBRUM	(49)	(50)	(49)
HEMORRHAGE		1 (2%)	
CYTOPLASMIC VACUOLIZATION		1 (2%)	
#BRAIN	(49)	(50)	(49)
HYDROCEPHALUS, NOS	1 (2%)		
HEMORRHAGE		3 (6%)	1 (2%)
INFLAMMATION, MULTIFOCAL			1 (2%)
GLIOSIS		1 (2%)	
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL			1 (2%)
MALACIA			1 (2%)
CALCIFICATION, FOCAL		1 (2%)	
CYTOPLASMIC VACUOLIZATION		1 (2%)	
#CEREBRAL CORTEX	(49)	(50)	(49)
GLIOSIS	1 (2%)		
#CEREBRAL WHITE MATTE	(49)	(50)	(49)
CYTOPLASMIC VACUOLIZATION	15 (31%)	5 (10%)	15 (31%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM (Continued)			
#CEREBELLUM	(49)	(50)	(49)
HEMORRHAGE			1 (2%)
#MEDULLA OBLONGATA	(49)	(50)	(49)
HEMORRHAGE	1 (2%)	1 (2%)	
*OLFACTORY SENSORY EP	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)	2 (4%)	3 (6%)
SPECIAL SENSE ORGANS			
*EYE/CRYSTALLINE LENS	(50)	(50)	(50)
CALCIFICATION, NOS		1 (2%)	
*NASOLACRIMAL DUCT	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	8 (16%)	8 (16%)	1 (2%)
METAPLASIA, SQUAMOUS	3 (6%)	9 (18%)	
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)		
BODY CAVITIES			
*PERITONEAL CAVITY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		
*PLEURA	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		
FIBROSIS, FOCAL			1 (2%)
*SUBPLEURAL TISSUE	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC FOCAL		2 (4%)	1 (2%)
FIBROSIS		1 (2%)	
FIBROSIS, FOCAL		3 (6%)	
FIBROSIS, MULTIFOCAL		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			2 (4%)
OMENTUM			
INFLAMMATION, NECROTIZING	1		
SPECIAL MORPHOLOGY SUMMARY			
NONE			

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 OXIDE

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
ABSCESS, NOS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
INFLAMMATION, GRANULOMATOUS		1 (2%)	
HYPERKERATOSIS	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
ABSCESS, NOS		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
INFLAMMATION, SEROUS		13 (26%)	2 (4%)
INFLAMMATION, SUPPURATIVE		8 (16%)	4 (8%)
INFLAMMATION, ACUTE	1 (2%)		4 (8%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	13 (26%)	38 (76%)
ANGIECTASIS			3 (6%)
METAPLASIA, SQUAMOUS		1 (2%)	
*NASAL TURBINATE	(50)	(50)	(50)
HEMORRHAGE			1 (2%)
*LARYNX	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			6 (12%)
#TRACHEA	(48)	(46)	(48)
INFLAMMATION, SUPPURATIVE			3 (6%)
INFLAMMATION, ACUTE SUPPURATIVE			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
#LUNG	(50)	(50)	(50)
CONGESTION, NOS	2 (4%)	1 (2%)	2 (4%)
CONGESTION, ACUTE		1 (2%)	
HEMORRHAGE		1 (2%)	
LOBAR PNEUMONIA, NOS		1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR		2 (4%)	
INFLAMMATION, INTERSTITIAL	1 (2%)	2 (4%)	
INFLAMMATION, SUPPURATIVE			3 (6%)
BRONCHOPNEUMONIA SUPPURATIVE			1 (2%)
INFLAMMATION, NECROTIZING			4 (8%)
INFLAMMATION, ACUTE SUPPURATIVE			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	3 (6%)	1 (2%)	8 (16%)
PNEUMONIA INTERSTITIAL CHRONIC	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOUS	1 (2%)		
INFLAMMATION PROLIFERATIVE		2 (4%)	
HISTIOCYTOSIS	1 (2%)		
#LUNG/ALVEOLI	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(47)	(49)	(48)
HYPERPLASIA, GRANULOCYTIC		4 (8%)	5 (10%)
#SPLEEN	(48)	(50)	(47)
CONGESTION, NOS		1 (2%)	
INFARCT, NOS	1 (2%)		
HYPERPLASIA, LYMPHOID		1 (2%)	
HEMATOPOIESIS	1 (2%)	3 (6%)	
#SPLENIC FOLLICLES	(48)	(50)	(47)
ATROPHY, NOS		1 (2%)	
#LYMPH NODE	(44)	(48)	(42)
MULTIPLE CYSTS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, PLASMA CELL		1 (2%)	
#MANDIBULAR L. NODE	(44)	(48)	(42)
CYST, NOS			1 (2%)
ANGIECTASIS			1 (2%)
HYPERPLASIA, LYMPHOID		3 (6%)	2 (5%)
#BRONCHIAL LYMPH NODE	(44)	(48)	(42)
INFLAMMATION, FOCAL GRANULOMATOUS			1 (2%)
HYPERPLASIA, LYMPHOID	2 (5%)	1 (2%)	1 (2%)
#MESENTERIC L. NODE	(44)	(48)	(42)
CONGESTION, NOS	1 (2%)	1 (2%)	2 (5%)
HYPERPLASIA, PLASMA CELL	1 (2%)		
HYPERPLASIA, LYMPHOID	1 (2%)		
#COLON	(49)	(48)	(45)
HYPERPLASIA, LYMPHOID	1 (2%)		1 (2%)
#CECUM	(49)	(48)	(45)
HYPERPLASIA, LYMPHOID		1 (2%)	
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	2 (4%)
PERIVASCULITIS	2 (4%)		2 (4%)
CALCIFICATION, FOCAL			1 (2%)
#CARDIAC VALVE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
PIGMENTATION, NOS	3 (6%)		2 (4%)
#KIDNEY	(50)	(50)	(50)
EMBOLUS, SEPTIC		1 (2%)	
DIGESTIVE SYSTEM			
*TOOTH	(50)	(50)	(50)
CONGENITAL MALFORMATION, NOS	2 (4%)	1 (2%)	3 (6%)
*PULP OF TOOTH	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
ABSCESS, NOS	3 (6%)	2 (4%)	3 (6%)
#SALIVARY GLAND	(50)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC	14 (28%)	23 (46%)	6 (12%)
#LIVER	(50)	(50)	(50)
CYST, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, NECROTIZING	1 (2%)	1 (2%)	
INFLAMMATION, ACUTE NECROTIZING	2 (4%)		
INFLAMMATION, ACUTE/CHRONIC	9 (18%)	6 (12%)	8 (16%)
INFLAMMATION PROLIFERATIVE		1 (2%)	
NECROSIS, FOCAL	1 (2%)	3 (6%)	2 (4%)
METAMORPHOSIS FATTY		2 (4%)	
CYTOLOGIC DEGENERATION	1 (2%)		
ANGIECTASIS		1 (2%)	

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#PANCREAS	(48)	(49)	(46)
AGENESIS		1 (2%)	
ATROPHY, FOCAL			1 (2%)
#STOMACH	(49)	(48)	(48)
INFLAMMATION, ACUTE/CHRONIC	2 (4%)		
HYPERKERATOSIS	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
HYDRONEPHROSIS		1 (2%)	
GLOMERULONEPHRITIS, NOS		1 (2%)	
INFLAMMATION, SUPPURATIVE		1 (2%)	
PYELONEPHRITIS, ACUTE		4 (8%)	
INFLAMMATION, ACUTE/CHRONIC	15 (30%)	13 (26%)	4 (8%)
FIBROSIS, FOCAL	1 (2%)		
NEPHROSIS, NOS	1 (2%)		
CALCINOSIS, NOS	1 (2%)		
ATROPHY, NOS		1 (2%)	
#KIDNEY/CAPSULE	(50)	(50)	(50)
CYST, NOS	1 (2%)		
#KIDNEY/CORTEX	(50)	(50)	(50)
CYST, NOS		1 (2%)	
#KIDNEY/TUBULE	(50)	(50)	(50)
CAST, NOS	1 (2%)		
CALCIFICATION, FOCAL			1 (2%)
#URINARY BLADDER	(47)	(46)	(48)
INFLAMMATION, SUPPURATIVE		5 (11%)	
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
*URETHRA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
ENDOCRINE SYSTEM			
#ADRENAL	(50)	(43)	(49)
CYST, NOS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
HYPERPLASIA, NOS	2 (4%)		
#ADRENAL/CAPSULE	(50)	(43)	(49)
HYPERPLASIA, NOS	3 (6%)		
#ADRENAL CORTEX	(50)	(43)	(49)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL		1 (2%)	
#THYROID	(43)	(48)	(46)
HYPOPLASIA, NOS			1 (2%)
HYPERPLASIA, FOCAL		3 (6%)	
HYPERPLASIA, CYSTIC	1 (2%)		
REPRODUCTIVE SYSTEM			
*PREPUCE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
#PROSTATE	(47)	(49)	(43)
INFLAMMATION, SUPPURATIVE		3 (6%)	
*SEMINAL VESICLE	(50)	(50)	(50)
DISTENTION	2 (4%)		
#TESTIS	(48)	(49)	(49)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN/MENINGES	(49)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
#BRAIN	(49)	(50)	(50)
MINERALIZATION	3 (6%)	4 (8%)	1 (2%)
INFLAMMATION, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, ACUTE FOCAL			1 (2%)
CORPORA AMYLACEA	23 (47%)	21 (42%)	25 (50%)
SPECIAL SENSE ORGANS			
*NASOLACRIMAL DUCT	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
*EAR	(50)	(50)	(50)
ULCER, NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(50)
FIBROUS OSTEODYSTROPHY	2 (4%)		
*COCCYX	(50)	(50)	(50)
HEALED FRACTURE	1 (2%)		
*STERNUM	(50)	(50)	(50)
NECROSIS, FOCAL		1 (2%)	
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
BACTERIAL SEPTICEMIA		1 (2%)	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	1		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 OXIDE

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
ABSCESS, NOS			1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
DILATATION, NOS			1 (2%)
INFLAMMATION, SEROUS	2 (4%)	6 (12%)	2 (4%)
INFLAMMATION, SUPPURATIVE		16 (32%)	19 (38%)
INFLAMMATION, ACUTE			1 (2%)
INFLAMMATION, ACUTE/CHRONIC		13 (26%)	17 (34%)
HYPERPLASIA, EPITHELIAL			1 (2%)
ANGIECTASIS			3 (6%)
METAPLASIA, SQUAMOUS			2 (4%)
*NASAL TURBINATE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
*LARYNX	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			2 (4%)
#TRACHEA	(48)	(49)	(47)
INFLAMMATION, SUPPURATIVE			2 (4%)
#TRACHEAL SUBMUCOSA	(48)	(49)	(47)
INFLAMMATION, ACUTE			1 (2%)
#LUNG	(50)	(50)	(50)
CONGESTION, NOS	1 (2%)	2 (4%)	3 (6%)
HEMORRHAGE	1 (2%)	1 (2%)	1 (2%)
BRONCHOPNEUMONIA, NOS			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR		3 (6%)	
INFLAMMATION, INTERSTITIAL			1 (2%)
INFLAMMATION, SUPPURATIVE			4 (8%)
INFLAMMATION, NECROTIZING			2 (4%)
BRONCHOPNEUMONIA, ACUTE			1 (2%)
INFLAMMATION, ACUTE SUPPURATIVE			2 (4%)
INFLAMMATION, ACUTE/CHRONIC	3 (6%)	1 (2%)	
INFLAMMATION PROLIFERATIVE		1 (2%)	
PIGMENTATION, NOS	1 (2%)		
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(47)	(49)	(45)
HYPERPLASIA, GRANULOCYTIC		3 (6%)	11 (24%)
#SPLEEN	(48)	(49)	(44)
INFLAMMATION, SUPPURATIVE		1 (2%)	
PIGMENTATION, NOS			4 (9%)
HEMOSIDEROSIS			1 (2%)
HYPERPLASIA, PLASMA CELL		1 (2%)	
HYPERPLASIA, LYMPHOID	3 (6%)	4 (8%)	
HEMATOPOIESIS		2 (4%)	4 (9%)
#SPLENIC FOLLICLES	(48)	(49)	(44)
ATROPHY, NOS			1 (2%)
#LYMPH NODE	(46)	(48)	(37)
INFLAMMATION, ACUTE/CHRONIC			4 (11%)
HISTIOCYTOSIS			1 (3%)
PLASMACYTOSIS			2 (5%)
HYPERPLASIA, LYMPHOID	1 (2%)		

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#MANDIBULAR L. NODE	(46)	(48)	(37)
CYST, NOS			1 (3%)
PIGMENTATION, NOS			1 (3%)
ANGIECTASIS			1 (3%)
HYPERPLASIA, RETICULUM CELL			1 (3%)
HYPERPLASIA, LYMPHOID	2 (4%)	3 (6%)	2 (5%)
#CERVICAL LYMPH NODE	(46)	(48)	(37)
HYPERPLASIA, LYMPHOID		1 (2%)	
#BRONCHIAL LYMPH NODE	(46)	(48)	(37)
INFLAMMATION, SUPPURATIVE		2 (4%)	
ABSCESS, NOS		1 (2%)	
ANGIECTASIS			1 (3%)
HYPERPLASIA, PLASMA CELL		2 (4%)	
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	
#MESENTERIC L. NODE	(46)	(48)	(37)
ANGIECTASIS		1 (2%)	
HYPERPLASIA, LYMPHOID	2 (4%)		
#RENAL LYMPH NODE	(46)	(48)	(37)
HYPERPLASIA, LYMPHOID	1 (2%)		
#LIVER	(50)	(50)	(49)
LEUKEMOID REACTION		1 (2%)	1 (2%)
HEMATOPOIESIS	1 (2%)	1 (2%)	2 (4%)
#PANCREAS	(48)	(49)	(42)
HYPERPLASIA, LYMPHOID	1 (2%)		
#PITUITARY	(46)	(48)	(38)
HEMATOPOIESIS		1 (2%)	
#ADRENAL	(48)	(48)	(48)
HEMATOPOIESIS			3 (6%)
CIRCULATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
THROMBOSIS, NOS			1 (2%)
#HEART	(50)	(50)	(48)
FIBROSIS, FOCAL			1 (2%)
PERIVASCULITIS	1 (2%)	2 (4%)	5 (10%)
CALCIFICATION, NOS		2 (4%)	
#CARDIAC VALVE	(50)	(50)	(48)
PIGMENTATION, NOS	3 (6%)		1 (2%)
#PANCREAS	(48)	(49)	(42)
PERIVASCULITIS			1 (2%)
#ADRENAL	(48)	(48)	(48)
THROMBOSIS, NOS			1 (2%)
DIGESTIVE SYSTEM			
*TOOTH	(50)	(50)	(50)
CONGENITAL MALFORMATION, NOS		1 (2%)	2 (4%)
*PULP OF TOOTH	(50)	(50)	(50)
ABSCESS, NOS	1 (2%)	1 (2%)	1 (2%)
#SALIVARY GLAND	(49)	(48)	(47)
INFLAMMATION, ACUTE/CHRONIC	15 (31%)	18 (38%)	6 (13%)
#LIVER	(50)	(50)	(49)
CYSTIC DUCTS		1 (2%)	
INFLAMMATION, SUPPURATIVE		1 (2%)	2 (4%)
INFLAMMATION, NECROTIZING		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	11 (22%)	18 (36%)	9 (18%)
NECROSIS, FOCAL			3 (6%)
CALCIFICATION, NOS		1 (2%)	1 (2%)
#PANCREAS	(48)	(49)	(42)
DILATATION/DUCTS		1 (2%)	
INFLAMMATION, SUPPURATIVE		1 (2%)	
ABSCESS, NOS	1 (2%)		

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
*PHARYNX	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			3 (6%)
#STOMACH	(49)	(50)	(44)
ULCER, NOS		4 (8%)	
HYPERPLASIA, EPITHELIAL		4 (8%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
PYELONEPHRITIS, ACUTE		1 (2%)	4 (8%)
INFLAMMATION, ACUTE/CHRONIC	12 (24%)	19 (38%)	4 (8%)
FIBROSIS			1 (2%)
CALCINOSIS, NOS	1 (2%)		
ATROPHY, NOS			1 (2%)
#KIDNEY/TUBULE	(50)	(50)	(49)
DEGENERATION, NOS	1 (2%)		
#KIDNEY/PELVIS	(50)	(50)	(49)
DILATATION, NOS		1 (2%)	
#URINARY BLADDER	(44)	(47)	(42)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	3 (7%)		
HYPERPLASIA, EPITHELIAL	1 (2%)		
METAPLASIA, SQUAMOUS			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(48)	(38)
CONGESTION, NOS	2 (4%)	5 (10%)	
HYPERPLASIA, FOCAL		3 (6%)	
#ADRENAL	(48)	(48)	(48)
ANGIECTASIS	1 (2%)		1 (2%)
#ADRENAL/CAPSULE	(48)	(48)	(48)
HYPERPLASIA, NOS			1 (2%)
#ADRENAL CORTEX	(48)	(48)	(48)
CYST, NOS		1 (2%)	
#THYROID	(45)	(50)	(43)
FOLLICULAR CYST, NOS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
CRYSTALS, NOS	1 (2%)		
HYPERTROPHY, FOCAL	1 (2%)		1 (2%)
HYPERPLASIA, FOCAL		2 (4%)	
HYPERPLASIA, C-CELL	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
DILATATION/DUCTS		1 (2%)	
*VAGINA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
#UTERUS	(48)	(50)	(48)
INFLAMMATION, SUPPURATIVE	1 (2%)	3 (6%)	8 (17%)
ABSCESS, NOS		2 (4%)	1 (2%)
#UTERUS/ENDOMETRIUM	(48)	(50)	(48)
CYST, NOS		1 (2%)	
INFLAMMATION, SUPPURATIVE	1 (2%)		2 (4%)
HYPERPLASIA, NOS	24 (50%)	13 (26%)	1 (2%)
HYPERPLASIA, CYSTIC	1 (2%)		1 (2%)
METAPLASIA, SQUAMOUS			1 (2%)
#FALLOPIAN TUBE	(48)	(50)	(48)
INFLAMMATION, CHRONIC SUPPURATIVE			1 (2%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM (Continued)			
#OVARY	(48)	(46)	(37)
CYST, NOS	3 (6%)	6 (13%)	6 (16%)
MULTIPLE CYSTS	1 (2%)	1 (2%)	
HEMORRHAGIC CYST	3 (6%)	3 (7%)	1 (3%)
INFLAMMATION, NOS			1 (3%)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
INFLAMMATION, SUPPURATIVE			1 (3%)
ABSCESS, NOS	1 (2%)	3 (7%)	
#OVARY (Continued)			
INFLAMMATION, CHRONIC	1 (2%)		
CALCIFICATION, NOS			2 (5%)
ATROPHY, NOS	6 (13%)	8 (17%)	20 (54%)
HYPERPLASIA, EPITHELIAL		1 (2%)	
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(48)
INFLAMMATION, SUPPURATIVE			1 (2%)
#BRAIN	(50)	(50)	(48)
MINERALIZATION	4 (8%)	2 (4%)	3 (6%)
CONGESTION, NOS	1 (2%)		1 (2%)
HEMATOMA, NOS	1 (2%)		
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, NOS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
CORPORA AMYLACEA	29 (58%)	20 (40%)	14 (29%)
SPECIAL SENSE ORGANS			
*NASOLACRIMAL DUCT	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(50)
FIBROUS OSTEODYSTROPHY	1 (2%)		1 (2%)
*STERNUM	(50)	(50)	(50)
FIBROUS OSTEODYSTROPHY	38 (76%)	33 (66%)	7 (14%)
BODY CAVITIES			
*THORACIC CAVITY	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		2 (4%)	
*PERITONEAL CAVITY	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			2 (4%)
INFLAMMATION, CHRONIC SUPPURATIVE			1 (2%)
ADHESION, NOS			1 (2%)
*PLEURA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
*EPICARDIUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL			1 (2%)

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

	CONTROL (CHAMBER)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	4 (8%)
INFLAMMATION, ACUTE/CHRONIC	4 (8%)	1 (2%)	1 (2%)
BACTERIAL SEPTICEMIA		3 (6%)	
TOE			
DEFORMITY, NOS	1		
SITE UNKNOWN			
MULTILOCULAR CYST			1
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED		1	
AUTO/NECROPSY/HISTO PERF	1		2

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 OXIDE

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

	Chamber Control	200 ppm	400 ppm
Skin: Keratoacanthoma			
Overall Rates (a)	1/50 (2%)	1/50 (2%)	5/50 (10%)
Adjusted Rates (b)	3.5%	3.2%	15.3%
Terminal Rates (c)	1/29 (3%)	1/31 (3%)	3/29 (10%)
Life Table Tests (d)	P=0.051	P=0.747N	P=0.114
Incidental Tumor Tests (d)	P=0.068	P=0.747N	P=0.154
Cochran-Armitage Trend Test (d)	P=0.049		
Fisher Exact Tests		P=0.753N	P=0.102
Subcutaneous Tissue: Fibroma			
Overall Rates (a)	3/50 (6%)	2/50 (4%)	3/50 (6%)
Adjusted Rates (b)	10.3%	5.8%	10.3%
Terminal Rates (c)	3/29 (10%)	0/31 (0%)	3/29 (10%)
Life Table Tests (d)	P=0.583N	P=0.460N	P=0.665
Incidental Tumor Tests (d)	P=0.518N	P=0.409N	P=0.665
Cochran-Armitage Trend Test (d)	P=0.588		
Fisher Exact Tests		P=0.500N	P=0.661
Skin or Subcutaneous Tissue: Fibroma			
Overall Rates (a)	3/50 (6%)	2/50 (4%)	4/50 (8%)
Adjusted Rates (b)	10.3%	5.8%	13.8%
Terminal Rates (c)	3/29 (10%)	0/31 (0%)	4/29 (14%)
Life Table Tests (d)	P=0.421	P=0.460N	P=0.500
Incidental Tumor Tests (d)	P=0.483	P=0.409N	P=0.500
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)	19/50 (38%)	23/50 (46%)	22/50 (44%)
Adjusted Rates (b)	48.8%	53.9%	54.1%
Terminal Rates (c)	10/29 (34%)	12/31 (39%)	11/29 (38%)
Life Table Tests (d)	P=0.376	P=0.429	P=0.411
Incidental Tumor Tests (d)	P=0.508	P=0.377	P=0.522
Cochran-Armitage Trend Test (d)	P=0.307		
Fisher Exact Tests		P=0.272	P=0.342
Hematopoietic System: Leukemia			
Overall Rates (a)	20/50 (40%)	26/50 (52%)	23/50 (46%)
Adjusted Rates (b)	50.1%	56.9%	55.1%
Terminal Rates (c)	10/29 (34%)	12/31 (39%)	11/29 (38%)
Life Table Tests (d)	P=0.399	P=0.324	P=0.428
Incidental Tumor Tests (d)	P=0.489	P=0.284	P=0.488
Cochran-Armitage Trend Test (d)	P=0.308		
Fisher Exact Tests		P=0.158	P=0.343
Liver: Neoplastic Nodule or Carcinoma			
Overall Rates (a)	1/50 (2%)	2/50 (4%)	3/49 (6%)
Adjusted Rates (b)	2.9%	6.5%	9.5%
Terminal Rates (c)	0/29 (0%)	2/31 (6%)	2/28 (7%)
Life Table Tests (d)	P=0.217	P=0.528	P=0.308
Incidental Tumor Tests (d)	P=0.276	P=0.562	P=0.412
Cochran-Armitage Trend Test (d)	P=0.216		
Fisher Exact Tests		P=0.500	P=0.301
Pituitary: Adenoma			
Overall Rates (a)	21/47 (45%)	15/47 (32%)	15/48 (31%)
Adjusted Rates (b)	59.9%	38.9%	44.3%
Terminal Rates (c)	13/26 (50%)	7/29 (24%)	11/29 (38%)
Life Table Tests (d)	P=0.083N	P=0.094N	P=0.093N
Incidental Tumor Tests (d)	P=0.041N	P=0.070N	P=0.056N
Cochran-Armitage Trend Test (d)	P=0.105N		
Fisher Exact Tests		P=0.144N	P=0.128N

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

	Chamber Control	200 ppm	400 ppm
Pituitary: Adenoma or Adenocarcinoma			
Overall Rates (a)	21/47 (45%)	15/47 (32%)	16/48 (33%)
Adjusted Rates (b)	59.9%	38.9%	47.4%
Terminal Rates (c)	13/26 (50%)	7/29 (24%)	12/29 (41%)
Life Table Tests (d)	P=0.117N	P=0.094N	P=0.128N
Incidental Tumor Tests (d)	P=0.065N	P=0.070N	P=0.085N
Cochran-Armitage Trend Test (d)	P=0.150N		
Fisher Exact Tests		P=0.144N	P=0.178N
Adrenal: Pheochromocytoma			
Overall Rates (a)	3/48 (6%)	5/49 (10%)	4/49 (8%)
Adjusted Rates (b)	8.4%	16.7%	11.4%
Terminal Rates (c)	1/28 (4%)	5/30 (17%)	2/29 (7%)
Life Table Tests (d)	P=0.466	P=0.404	P=0.549
Incidental Tumor Tests (d)	P=0.503	P=0.393	P=0.613
Cochran-Armitage Trend Test (d)	P=0.439		
Fisher Exact Tests		P=0.369	P=0.512
Thyroid: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	1/44 (2%)	2/41 (5%)	4/49 (8%)
Adjusted Rates (b)	3.7%	8.0%	14.3%
Terminal Rates (c)	1/27 (4%)	2/25 (8%)	4/28 (14%)
Life Table Tests (d)	P=0.126	P=0.473	P=0.187
Incidental Tumor Tests (d)	P=0.126	P=0.473	P=0.187
Cochran-Armitage Trend Test (d)	P=0.148		
Fisher Exact Tests		P=0.473	P=0.216
Pancreatic Islets: Islet Cell Adenoma			
Overall Rates (a)	1/47 (2%)	3/49 (6%)	1/47 (2%)
Adjusted Rates (b)	2.7%	8.9%	3.7%
Terminal Rates (c)	0/29 (0%)	2/31 (6%)	1/27 (4%)
Life Table Tests (d)	P=0.600	P=0.343	P=0.754N
Incidental Tumor Tests (d)	P=0.549N	P=0.392	P=0.709N
Cochran-Armitage Trend Test (d)	P=0.611		
Fisher Exact Tests		P=0.324	P=0.753
Pancreatic Islets: Islet Cell Adenoma or Carcinoma			
Overall Rates (a)	2/47 (4%)	4/49 (8%)	1/47 (2%)
Adjusted Rates (b)	6.1%	12.1%	3.7%
Terminal Rates (c)	1/29 (3%)	3/31 (10%)	1/27 (4%)
Life Table Tests (d)	P=0.423N	P=0.380	P=0.502N
Incidental Tumor Tests (d)	P=0.360N	P=0.422	P=0.453N
Cochran-Armitage Trend Test (d)	P=0.406N		
Fisher Exact Tests		P=0.359	P=0.500N
Testis: Interstitial Cell Tumor			
Overall Rates (a)	29/49 (59%)	36/50 (72%)	35/50 (70%)
Adjusted Rates (b)	77.8%	89.7%	80.8%
Terminal Rates (c)	21/29 (72%)	27/31 (87%)	21/29 (72%)
Life Table Tests (d)	P=0.205	P=0.260	P=0.253
Incidental Tumor Tests (d)	P=0.277	P=0.191	P=0.375
Cochran-Armitage Trend Test (d)	P=0.151		
Fisher Exact Tests		P=0.129	P=0.180
All Sites: Mesotheliomas			
Overall Rates (a)	1/50 (2%)	2/50 (4%)	3/50 (6%)
Adjusted Rates (b)	3.4%	5.4%	7.7%
Terminal Rates (c)	1/29 (3%)	1/31 (3%)	1/29 (3%)
Life Table Tests (d)	P=0.253	P=0.535	P=0.338
Incidental Tumor Tests (d)	P=0.209	P=0.469	P=0.324
Cochran-Armitage Trend Test (d)	P=0.222		
Fisher Exact Tests		P=0.500	P=0.309

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

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences 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's 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 OXIDE

	Chamber Control	200 ppm	400 ppm
Nasal Cavity: Papillary Adenoma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	0.0%	9.7%
Terminal Rates (c)	0/35 (0%)	0/32 (0%)	3/31 (10%)
Life Table Tests (d)	P=0.031	(e)	P=0.100
Incidental Tumor Tests (d)	P=0.031	(e)	P=0.100
Cochran-Armitage Trend Test (d)	P=0.037		
Fisher Exact Tests		(e)	P=0.121
Hematopoietic System: Mononuclear Cell Leukemia			
Overall Rates (a)	11/50 (22%)	20/50 (40%)	15/50 (30%)
Adjusted Rates (b)	27.9%	52.3%	40.3%
Terminal Rates (c)	7/35 (20%)	14/32 (44%)	10/31 (32%)
Life Table Tests (d)	P=0.173	P=0.035	P=0.202
Incidental Tumor Tests (d)	P=0.456	P=0.113	P=0.469
Cochran-Armitage Trend Test (d)	P=0.224		
Fisher Exact Tests		P=0.041	P=0.247
Hematopoietic System: Leukemia			
Overall Rates (a)	14/50 (28%)	23/50 (46%)	21/50 (42%)
Adjusted Rates (b)	32.6%	55.6%	49.1%
Terminal Rates (c)	7/35 (20%)	14/32 (44%)	10/31 (32%)
Life Table Tests (d)	P=0.094	P=0.053	P=0.110
Incidental Tumor Tests (d)	P=0.355	P=0.190	P=0.392
Cochran-Armitage Trend Test (d)	P=0.091		
Fisher Exact Tests		P=0.048	P=0.104
Pituitary: Adenoma			
Overall Rates (a)	25/48 (52%)	18/47 (38%)	14/46 (30%)
Adjusted Rates (b)	60.5%	48.9%	43.6%
Terminal Rates (c)	18/34 (53%)	13/31 (42%)	12/30 (40%)
Life Table Tests (d)	P=0.041N	P=0.193N	P=0.052N
Incidental Tumor Tests (d)	P=0.023N	P=0.123N	P=0.036N
Cochran-Armitage Trend Test (d)	P=0.021N		
Fisher Exact Tests		P=0.126N	P=0.027N
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	25/48 (52%)	20/47 (43%)	14/46 (30%)
Adjusted Rates (b)	60.5%	52.9%	43.6%
Terminal Rates (c)	18/34 (53%)	14/31 (45%)	12/30 (40%)
Life Table Tests (d)	P=0.043N	P=0.314N	P=0.052N
Incidental Tumor Tests (d)	P=0.020N	P=0.200N	P=0.036N
Cochran-Armitage Trend Test (d)	P=0.022N		
Fisher Exact Tests		P=0.234N	P=0.027N
Thyroid: C-Cell Adenoma			
Overall Rates (a)	1/45 (2%)	1/35 (3%)	4/37 (11%)
Adjusted Rates (b)	3.0%	4.8%	16.7%
Terminal Rates (c)	1/33 (3%)	1/21 (5%)	4/24 (17%)
Life Table Tests (d)	P=0.056	P=0.658	P=0.095
Incidental Tumor Tests (d)	P=0.056	P=0.658	P=0.095
Cochran-Armitage Trend Test (d)	P=0.072		
Fisher Exact Tests		P=0.687	P=0.125
Thyroid: C-Cell Carcinoma			
Overall Rates (a)	1/45 (2%)	1/35 (3%)	3/37 (8%)
Adjusted Rates (b)	3.0%	4.8%	10.3%
Terminal Rates (c)	1/33 (3%)	1/21 (5%)	2/24 (8%)
Life Table Tests (d)	P=0.149	P=0.658	P=0.234
Incidental Tumor Tests (d)	P=0.103	P=0.658	P=0.155
Cochran-Armitage Trend Test (d)	P=0.156		
Fisher Exact Tests		P=0.687	P=0.238

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

	Chamber Control	200 ppm	400 ppm
Thyroid: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	2/45 (4%)	2/35 (6%)	7/37 (19%)
Adjusted Rates (b)	6.1%	9.5%	26.6%
Terminal Rates (c)	2/33 (6%)	2/21 (10%)	6/24 (25%)
Life Table Tests (d)	P=0.017	P=0.523	P=0.031
Incidental Tumor Tests (d)	P=0.011	P=0.523	P=0.019
Cochran-Armitage Trend Test (d)	P=0.023		
Fisher Exact Tests		P=0.592	P=0.041
Mammary Gland: Fibroadenoma			
Overall Rates (a)	7/50 (14%)	13/50 (26%)	13/50 (26%)
Adjusted Rates (b)	19.2%	36.4%	38.7%
Terminal Rates (c)	6/35 (17%)	10/32 (31%)	11/31 (35%)
Life Table Tests (d)	P=0.058	P=0.080	P=0.067
Incidental Tumor Tests (d)	P=0.061	P=0.081	P=0.059
Cochran-Armitage Trend Test (d)	P=0.092		
Fisher Exact Tests		P=0.105	P=0.105
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	3/49 (6%)	8/50 (16%)	8/47 (17%)
Adjusted Rates (b)	8.1%	24.1%	21.5%
Terminal Rates (c)	2/35 (6%)	7/32 (22%)	4/31 (13%)
Life Table Tests (d)	P=0.073	P=0.082	P=0.095
Incidental Tumor Tests (d)	P=0.131	P=0.085	P=0.209
Cochran-Armitage Trend Test (d)	P=0.074		
Fisher Exact Tests		P=0.106	P=0.087
Uterus: Endometrial Stromal Sarcoma			
Overall Rates (a)	0/49 (0%)	4/50 (8%)	2/47 (4%)
Adjusted Rates (b)	0.0%	11.5%	6.5%
Terminal Rates (c)	0/35 (0%)	2/32 (6%)	2/31 (6%)
Life Table Tests (d)	P=0.196	P=0.057	P=0.212
Incidental Tumor Tests (d)	P=0.301	P=0.139	P=0.212
Cochran-Armitage Trend Test (d)	P=0.208		
Fisher Exact Tests		P=0.061	P=0.237
Uterus: Endometrial Stromal Polyp or Sarcoma			
Overall Rates (a)	3/49 (6%)	12/50 (24%)	10/47 (21%)
Adjusted Rates (b)	8.1%	34.1%	27.4%
Terminal Rates (c)	2/35 (6%)	9/32 (28%)	6/31 (19%)
Life Table Tests (d)	P=0.031	P=0.010	P=0.034
Incidental Tumor Tests (d)	P=0.077	P=0.019	P=0.079
Cochran-Armitage Trend Test (d)	P=0.032		
Fisher Exact Tests		P=0.013	P=0.029

(a) Number of tumor bearing-animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences 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's 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 200-ppm and control groups.

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

	Chamber Control	200 ppm	400 ppm
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	14/50 (28%)	12/50 (24%)	8/50 (16%)
Adjusted Rates (b)	31.6%	31.8%	27.6%
Terminal Rates (c)	12/42 (29%)	9/34 (26%)	8/29 (28%)
Life Table Tests (d)	P=0.336N	P=0.553	P=0.373N
Incidental Tumor Tests (d)	P=0.183N	P=0.418N	P=0.339N
Cochran-Armitage Trend Test (d)	P=0.095N		
Fisher Exact Tests		P=0.410N	P=0.114N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	15/50 (30%)	14/50 (28%)	8/50 (16%)
Adjusted Rates (b)	33.9%	37.2%	27.6%
Terminal Rates (c)	13/42 (31%)	11/34 (32%)	8/29 (28%)
Life Table Tests (d)	P=0.287N	P=0.438	P=0.302N
Incidental Tumor Tests (d)	P=0.150N	P=0.538N	P=0.270N
Cochran-Armitage Trend Test (d)	P=0.066N		
Fisher Exact Tests		P=0.500N	P=0.077N
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	2.4%	8.4%	0.0%
Terminal Rates (c)	1/42 (2%)	2/34 (6%)	0/29 (0%)
Life Table Tests (d)	P=0.481N	P=0.240	P=0.574N
Incidental Tumor Tests (d)	P=0.310N	P=0.352	P=0.574N
Cochran-Armitage Trend Test (d)	P=0.378N		
Fisher Exact Tests		P=0.309	P=0.500N
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	5/50 (10%)	5/50 (10%)	4/50 (8%)
Adjusted Rates (b)	11.2%	12.7%	9.9%
Terminal Rates (c)	3/42 (7%)	2/34 (6%)	0/29 (0%)
Life Table Tests (d)	P=0.556N	P=0.523	P=0.621N
Incidental Tumor Tests (d)	P=0.215N	P=0.435N	P=0.316N
Cochran-Armitage Trend Test (d)	P=0.432N		
Fisher Exact Tests		P=0.630	P=0.500N
Hematopoietic System: Lymphoma or Leukemia			
Overall Rates (a)	6/50 (12%)	5/50 (10%)	4/50 (8%)
Adjusted Rates (b)	13.2%	12.7%	9.9%
Terminal Rates (c)	3/42 (7%)	2/34 (6%)	0/29 (0%)
Life Table Tests (d)	P=0.429N	P=0.605N	P=0.490N
Incidental Tumor Tests (d)	P=0.129N	P=0.284N	P=0.208N
Cochran-Armitage Trend Test (d)	P=0.309N		
Fisher Exact Tests		P=0.500N	P=0.370N
Nasal Cavity: Hemangioma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	5/50 (10%)
Adjusted Rates (b)	0.0%	0.0%	17.2%
Terminal Rates (c)	0/42 (0%)	0/34 (0%)	5/29 (17%)
Life Table Tests (d)	P=0.002	(e)	P=0.011
Incidental Tumor Tests (d)	P=0.002	(e)	P=0.011
Cochran-Armitage Trend Test (d)	P=0.006		
Fisher Exact Tests		(e)	P=0.028
Nasal Cavity: Hemangiosarcoma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	5/50 (10%)
Adjusted Rates (b)	0.0%	0.0%	15.6%
Terminal Rates (c)	0/42 (0%)	0/34 (0%)	4/29 (14%)
Life Table Tests (d)	P=0.003	(e)	P=0.015
Incidental Tumor Tests (d)	P=0.004	(e)	P=0.021
Cochran-Armitage Trend Test (d)	P=0.006		
Fisher Exact Tests		(e)	P=0.028

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

	Chamber Control	200 ppm	400 ppm
Nasal Cavity: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	10/50 (20%)
Adjusted Rates (b)	0.0%	0 0%	32.4%
Terminal Rates (c)	0/42 (0%)	0/34 (0%)	9/29 (31%)
Life Table Tests (d)	P<0.001	(e)	P<0.001
Incidental Tumor Tests (d)	P<0.001	(e)	P<0.001
Cochran-Armitage Trend Test (d)	P<0.001		
Fisher Exact Tests		(e)	P=0.001
Circulatory System: Hemangiosarcoma			
Overall Rates (a)	2/50 (4%)	2/50 (4%)	5/50 (10%)
Adjusted Rates (b)	4.8%	5.5%	15.6%
Terminal Rates (c)	2/42 (5%)	1/34 (3%)	4/29 (14%)
Life Table Tests (d)	P=0.078	P=0.624	P=0.110
Incidental Tumor Tests (d)	P=0.141	P=0.648N	P=0.142
Cochran-Armitage Trend Test (d)	P=0.146		
Fisher Exact Tests		P=0.691	P=0.218
Circulatory System: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	2/50 (4%)	2/50 (4%)	10/50 (20%)
Adjusted Rates (b)	4.8%	5 5%	32.4%
Terminal Rates (c)	2/42 (5%)	1/34 (3%)	9/29 (31%)
Life Table Tests (d)	P<0.001	P=0.624	P=0 002
Incidental Tumor Tests (d)	P=0.002	P=0.648N	P=0.003
Cochran-Armitage Trend Test (d)	P=0.005		
Fisher Exact Tests		P=0.691	P=0.014
Liver: Adenoma			
Overall Rates (a)	8/50 (16%)	6/50 (12%)	5/50 (10%)
Adjusted Rates (b)	18.6%	16.7%	15.9%
Terminal Rates (c)	7/42 (17%)	5/34 (15%)	4/29 (14%)
Life Table Tests (d)	P=0 454N	P=0.546N	P=0.522N
Incidental Tumor Tests (d)	P=0.297N	P=0.434N	P=0.298N
Cochran-Armitage Trend Test (d)	P=0 226N		
Fisher Exact Tests		P=0.387N	P=0.277N
Liver: Carcinoma			
Overall Rates (a)	6/50 (12%)	10/50 (20%)	5/50 (10%)
Adjusted Rates (b)	13.5%	24.4%	14 5%
Terminal Rates (c)	4/42 (10%)	5/34 (15%)	3/29 (10%)
Life Table Tests (d)	P=0.475	P=0.138	P=0.575
Incidental Tumor Tests (d)	P=0 320N	P=0 348	P=0.532N
Cochran-Armitage Trend Test (d)	P=0.443N		
Fisher Exact Tests		P=0.207	P=0.500N
Liver: Adenoma or Carcinoma			
Overall Rates (a)	14/50 (28%)	16/50 (32%)	9/50 (18%)
Adjusted Rates (b)	31 0%	39.0%	26.3%
Terminal Rates (c)	11/42 (26%)	10/34 (29%)	6/29 (21%)
Life Table Tests (d)	P=0.433N	P=0.231	P=0.444N
Incidental Tumor Tests (d)	P=0.124N	P=0.516	P=0.184N
Cochran-Armitage Trend Test (d)	P=0.153N		
Fisher Exact Tests		P=0.414	P=0.171N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences 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's 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 200-ppm and control groups.

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

	Chamber Control	200 ppm	400 ppm
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (a)	4/50 (8%)	7/50 (14%)	6/50 (12%)
Adjusted Rates (b)	10.1%	20.9%	43.5%
Terminal Rates (c)	3/38 (8%)	4/29 (14%)	3/10 (30%)
Life Table Tests (d)	P=0.007	P=0.160	P=0.009
Incidental Tumor Tests (d)	P=0.134	P=0.322	P=0.141
Cochran-Armitage Trend Test (d)	P=0.318		
Fisher Exact Tests		P=0.262	P=0.370
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	2.6%	8.2%	0.0%
Terminal Rates (c)	1/38 (3%)	0/29 (0%)	0/10 (0%)
Life Table Tests (d)	P=0.601	P=0.251	P=0.764N
Incidental Tumor Tests (d)	P=0.223N	P=0.504	P=0.764N
Cochran-Armitage Trend Test (d)	P=0.378N		
Fisher Exact Tests		P=0.309	P=0.500N
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Overall Rates (a)	4/50 (8%)	4/50 (8%)	1/50 (2%)
Adjusted Rates (b)	9.9%	9.9%	3.6%
Terminal Rates (c)	2/38 (5%)	1/29 (3%)	0/10 (0%)
Life Table Tests (d)	P=0.448N	P=0.554	P=0.566N
Incidental Tumor Tests (d)	P=0.048N	P=0.420N	P=0.105N
Cochran-Armitage Trend Test (d)	P=0.146N		
Fisher Exact Tests		P=0.643N	P=0.181N
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	12/50 (24%)	10/50 (20%)	7/50 (14%)
Adjusted Rates (b)	26.5%	25.2%	29.4%
Terminal Rates (c)	5/38 (13%)	2/29 (7%)	0/10 (0%)
Life Table Tests (d)	P=0.336	P=0.566N	P=0.359
Incidental Tumor Tests (d)	P=0.003N	P=0.047N	P=0.006N
Cochran-Armitage Trend Test (d)	P=0.127N		
Fisher Exact Tests		P=0.405N	P=0.154N
Nasal Cavity: Hemangioma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	0.0%	20.7%
Terminal Rates (c)	0/38 (0%)	0/29 (0%)	0/10 (0%)
Life Table Tests (d)	P=0.004	(e)	P=0.012
Incidental Tumor Tests (d)	P=0.091	(e)	P=0.336
Cochran-Armitage Trend Test (d)	P=0.037		
Fisher Exact Tests		(e)	P=0.121
Nasal Cavity: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	5/50 (10%)
Adjusted Rates (b)	0.0%	0.0%	32.2%
Terminal Rates (c)	0/38 (0%)	0/29 (0%)	1/10 (10%)
Life Table Tests (d)	P<0.001	(e)	P<0.001
Incidental Tumor Tests (d)	P=0.008	(e)	P=0.062
Cochran-Armitage Trend Test (d)	P=0.006		
Fisher Exact Tests		(e)	P=0.028
Circulatory System: Hemangioma			
Overall Rates (a)	1/50 (2%)	0/50 (0%)	4/50 (8%)
Adjusted Rates (b)	2.6%	0.0%	24.0%
Terminal Rates (c)	1/38 (3%)	0/29 (0%)	0/10 (0%)
Life Table Tests (d)	P=0.008	P=0.554N	P=0.014
Incidental Tumor Tests (d)	P=0.153	P=0.554N	P=0.366
Cochran-Armitage Trend Test (d)	P=0.082		
Fisher Exact Tests		P=0.500N	P=0.181

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

	Chamber Control	200 ppm	400 ppm
Circulatory System: Hemangiosarcoma			
Overall Rates (a)	0/50 (0%)	1/50 (2%)	3/50 (6%)
Adjusted Rates (b)	0.0%	3.4%	16.6%
Terminal Rates (c)	0/38 (0%)	1/29 (3%)	1/10 (10%)
Life Table Tests (d)	P=0.009	P=0.446	P=0.030
Incidental Tumor Tests (d)	P=0.050	P=0.446	P=0.176
Cochran-Armitage Trend Test (d)	P=0.060		
Fisher Exact Tests		P=0.500	P=0.121
Circulatory System: Hemangioma or Hemangiosarcoma			
Overall Rates (a)	1/50 (2%)	1/50 (2%)	7/50 (14%)
Adjusted Rates (b)	2.6%	3.4%	36.7%
Terminal Rates (c)	1/38 (3%)	1/29 (3%)	1/10 (10%)
Life Table Tests (d)	P<0.001	P=0.701	P<0.001
Incidental Tumor Tests (d)	P=0.017	P=0.701	P=0.096
Cochran-Armitage Trend Test (d)	P=0.010		
Fisher Exact Tests		P=0.753	P=0.030
Liver: Adenoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	2/49 (4%)
Adjusted Rates (b)	2.6%	10.3%	13.3%
Terminal Rates (c)	1/38 (3%)	3/29 (10%)	1/10 (10%)
Life Table Tests (d)	P=0.074	P=0.214	P=0.171
Incidental Tumor Tests (d)	P=0.125	P=0.214	P=0.332
Cochran-Armitage Trend Test (d)	P=0.391		
Fisher Exact Tests		P=0.309	P=0.492
Liver: Carcinoma			
Overall Rates (a)	2/50 (4%)	4/50 (8%)	1/49 (2%)
Adjusted Rates (b)	5.1%	9.8%	10.0%
Terminal Rates (c)	1/38 (3%)	1/29 (3%)	1/10 (10%)
Life Table Tests (d)	P=0.439	P=0.282	P=0.569
Incidental Tumor Tests (d)	P=0.331N	P=0.548	P=0.687N
Cochran-Armitage Trend Test (d)	P=0.415N		
Fisher Exact Tests		P=0.339	P=0.508N
Liver: Adenoma or Carcinoma			
Overall Rates (a)	3/50 (6%)	7/50 (14%)	3/49 (6%)
Adjusted Rates (b)	7.7%	19.5%	23.0%
Terminal Rates (c)	2/38 (5%)	4/29 (14%)	2/10 (20%)
Life Table Tests (d)	P=0.099	P=0.100	P=0.140
Incidental Tumor Tests (d)	P=0.397	P=0.217	P=0.438
Cochran-Armitage Trend Test (d)	P=0.558		
Fisher Exact Tests		P=0.159	P=0.651
Pituitary: Adenoma			
Overall Rates (a)	8/46 (17%)	6/48 (13%)	1/38 (3%)
Adjusted Rates (b)	20.9%	19.4%	4.8%
Terminal Rates (c)	7/37 (19%)	5/29 (17%)	0/10 (0%)
Life Table Tests (d)	P=0.271N	P=0.561N	P=0.298N
Incidental Tumor Tests (d)	P=0.125N	P=0.475N	P=0.124N
Cochran-Armitage Trend Test (d)	P=0.027N		
Fisher Exact Tests		P=0.354N	P=0.030N
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	9/46 (20%)	6/48 (13%)	1/38 (3%)
Adjusted Rates (b)	23.5%	19.4%	4.8%
Terminal Rates (c)	8/37 (22%)	5/29 (17%)	0/10 (0%)
Life Table Tests (d)	P=0.201N	P=0.461N	P=0.249N
Incidental Tumor Tests (d)	P=0.085N	P=0.377N	P=0.100N
Cochran-Armitage Trend Test (d)	P=0.014N		
Fisher Exact Tests		P=0.257N	P=0.017N

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

	Chamber Control	200 ppm	400 ppm
Mammary Gland: Adenosquamous Carcinoma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	0.0%	14.5%
Terminal Rates (c)	0/38 (0%)	0/29 (0%)	1/10 (10%)
Life Table Tests (d)	P=0 013	(e)	P=0.047
Incidental Tumor Tests (d)	P=0.079	(e)	P=0.236
Cochran-Armitage Trend Test (d)	P=0 037		
Fisher Exact Tests		(e)	P=0.121
Mammary Gland: All Adenocarcinoma			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	0.0%	8.1%	14.5%
Terminal Rates (c)	0/38 (0%)	1/29 (3%)	1/10 (10%)
Life Table Tests (d)	P=0.025	P=0.105	P=0.047
Incidental Tumor Tests (d)	P=0 362	P=0.290	P=0.236
Cochran-Armitage Trend Test (d)	P=0.101		
Fisher Exact Tests		P=0.121	P=0.121

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidences 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's 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 200-ppm and control groups.

APPENDIX F

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

TABLE F1. HISTORICAL INCIDENCE OF INTEGUMENTARY TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

Laboratory	Keratoacanthoma (Skin)	Keratoacanthoma (Subcutaneous)
Battelle Columbus	0/240 (0%)	1/240 (<1%)
Hazleton	2/99 (2%)	0/99 (0%)
Litton	0/200 (0%)	1/200 (1%)
Mason	1/549 (<1%)	0/549 (0%)
Southern	1/389 (<1%)	1/389 (<1%)
TOTAL	4/1,477 (0.3%)	3/1,477 (0.2%)
SD (b)	0.90%	0.62%
Overall historical range (c)		
High	2/49	1/50
Low	0/90	0/90

(a) Data as of June 28, 1982, 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 NASAL CAVITY TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

Laboratory	At Risk	Number	Diagnosis
Battelle Columbus	240	0	
Hazleton	99	0	
Litton	200	0	
Mason	549	1	Nose, NOS: squamous cell papilloma
Southern	389	0	
TOTAL	1,477	1	

(a) Data as of June 28, 1982, for studies of at least 104 weeks

TABLE F3. HISTORICAL INCIDENCE OF NASAL CAVITY TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

Laboratory	At Risk	Number	Diagnosis
Battelle Columbus	238	0	
Hazleton	100	1	Squamous cell carcinoma
Litton	199	1	Nose, NOS: papilloma, NOS
Mason	597	1	Nose, NOS: squamous cell papilloma
Southern	389	0	
TOTAL	1,523	3	

(a) Data as of June 28, 1982, for studies of at least 104 weeks

TABLE F4. HISTORICAL INCIDENCE OF CIRCULATORY SYSTEM TUMORS IN MALE F344/N RATS RECEIVING NO TREATMENT (a)

Laboratory	Hemangioma	Hemangiosarcoma
Battelle Columbus	0/240 (0%)	0/240 (0%)
Hazleton	0/99 (0%)	1/99 (1%)
Litton	0/200 (0%)	(b) 0/200 (0%)
Mason	2/549 (<1%)	(b) 4/549 (1%)
Southern	0/388(0%)	1/388 (<1%)
TOTAL	2/1,476 (0.1%)	6/1,476(0.4%)
SD (c)	0.52%	0.98%
Overall historical range (d)		
High	1/50	2/50
Low	0/90	0/90

(a) Data as of June 28, 1982, for studies of at least 104 weeks
(b) In addition, one angiosarcoma was present.
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.

TABLE F5. HISTORICAL INCIDENCE OF THYROID GLAND TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

Laboratory	C-Cell Adenoma	C-Cell Carcinoma	C-Cell Adenoma or Carcinoma
Battelle Columbus	2/232 (1%)	9/232 (4%)	11/232 (5%)
Hazleton	4/98 (4%)	1/98 (1%)	5/98 (5%)
Litton	9/176 (5%)	5/176 (3%)	14/176 (8%)
Mason	18/580 (3%)	22/580 (4%)	40/580 (7%)
Southern	37/386 (10%)	17/386 (4%)	52/386 (13%)
TOTAL	70/1,472 (4.8%)	54/1,472 (3.7%)	122/1,472 (8.3%)
SD (b)	3.85%	2.98%	4.34%
Overall historical range (c)			
High	6/50	5/50	9/50
Low	0/86	0/50	1/49

(a) Data as of June 28, 1982, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F6. HISTORICAL INCIDENCE OF UTERINE TUMORS IN FEMALE F344/N RATS RECEIVING NO TREATMENT (a)

Laboratory	Endometrial Stromal Polyp	Endometrial Stromal Sarcoma
Battelle Columbus	52/236 (22%)	0/236 (0%)
Hazleton	11/98 (11%)	1/98 (1%)
Litton	52/194 (27%)	0/194 (0%)
Mason	123/586 (21%)	3/586 (1%)
Southern	61/388 (16%)	3/388 (1%)
TOTAL	299/1,502 (19.9%)	7/1502 (0.5%)
SD (b)	8.47%	0.88%
Overall historical range (c)		
High	18/49	1/48
Low	2/47	0/87

(a) Data as of June 28, 1982, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F7. HISTORICAL INCIDENCE OF MAMMARY GLAND TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

Laboratory	Adenocarcinoma (NOS)	Papillary Adenocarcinoma	Adenosquamous Carcinoma
Battelle Columbus	1/300 (1%)	0/300 (0%)	0/300 (0%)
Hazleton	3/100 (3%)	0/100 (0%)	0/100 (0%)
IIT Research	0/74 (0%)	0/74 (0%)	0/74 (0%)
Litton	7/200 (4%)	0/200 (0%)	0/200 (0%)
Mason	7/598 (1%)	1/598 (1%)	0/598 (0%)
Southern	5/396 (1%)	0/396 (0%)	1/396 (1%)
TOTAL	23/1,668(1.4%)	1/1,668 (0.1%)	1/1,668 (0.1%)
SD (b)	2.40%	0.35%	0.37%
Overall historical range (c)			
High	6/50	1/50	1/48
Low	0/50	0/50	0/50

(a) Data as of June 28, 1982, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE F8. HISTORICAL INCIDENCE OF CIRCULATORY SYSTEM TUMORS IN MALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

	Hemangioma	Hemangiosaroma	Hemangioma or Hemangiosarcoma
Historical Incidence at Battelle Northwest			
Propylene oxide	0/50	2/50	2/50
Propylene	0/50	0/50	0/50
TOTAL	0/100 (0.0%)	2/100 (2.0%)	2/100 (2.0%)
Overall Historical Incidence			
TOTAL	34/2,343 (1.5%)	64/2,343 (2.7%)	97/2,343 (4.1%)
SD (b)	2.45%	2.57%	3.92%
Range (c)			
High	7/50	5/49	10/50
Low	0/50	0/50	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 F9. HISTORICAL INCIDENCE OF CIRCULATORY SYSTEM TUMORS IN FEMALE B6C3F$_1$ MICE RECEIVING NO TREATMENT (a)

	Hemangioma	Hemangiosaroma	Hemangioma or Hemangiosarcoma
Historical Incidence at Battelle Northwest			
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	39/2,486 (1.6%)	48/2,486 (1.9%)	87/2,486 (3.5%)
SD (b)	1.88%	2.33%	2.61%
Range (c)			
High	3/47	4/50	5/49
Low	0/50	0/50	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.

APPENDIX G

CHEMICAL CHARACTERIZATION

OF PROPYLENE OXIDE

APPENDIX G. CHEMICAL CHARACTERIZATION

I. Identity and Purity Determinations Performed by the Analytical Chemistry Laboratory

A. Lot No. UC 5/10/76

1. Boiling Point:

Determined	Literature Values
34.7°-36.5° C at 758 mm Hg (Dupont 900 DTA)	35° C (Henry, 1903)

2. Water Analysis (Karl Fischer):

0.13% ± 0.02 (δ)%

3. Elemental Analysis:

Element	C	H
Theory	62.04	10.41
Determined	61.96 62.04	10.20 10.34

4. Index of Refraction:

Determined	Literature Values
n_D^{10}: 1.3695	n_D^{20}: 1.3667 (Zimakov & Sokolova, 1953)

5. Spectral Data

a. Infrared

	Determined	Literature Values
Instrument:	Beckman IR-12	
Cell:	0.015 mm liquid cell, sodium chloride windows	
Results:	See Figure 5	Consistent with literature spectrum (Sadtler Standard Spectra)

b. Ultraviolet/Visible

	Determined	Literature Values
Instrument:	Cary 118	
Solvent:	Methanol	
Concentration:	10 mg/ml	
Results:	No absorbance between 215 and 350 nm or between 350 and 800 nm	No literature reference found

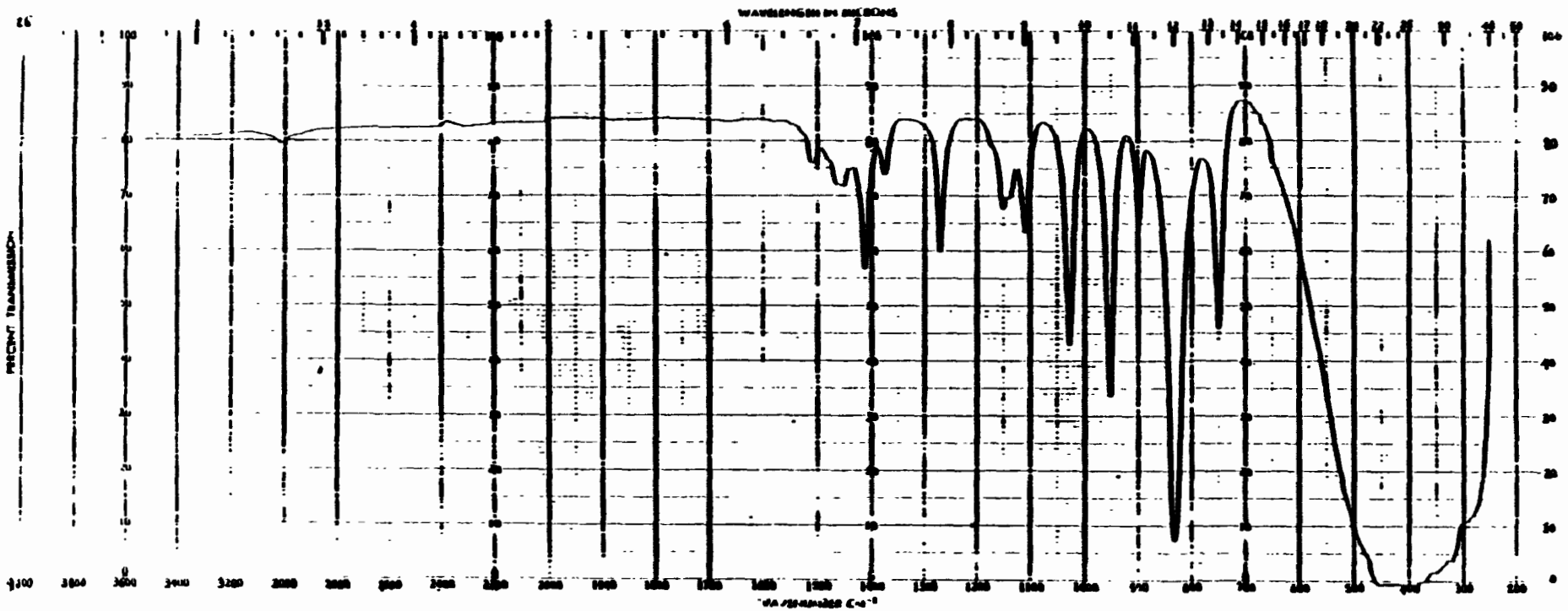

FIGURE 5. INFRARED ABSORPTION SPECTRUM OF PROPYLENE OXIDE (LOT NO. UC 5/10/76)

c. Nuclear Magnetic Resonance

	Determined	Literature Values
Instrument:	Varian HA-100	
Solvent:	Neat, tetramethyl-silane added	
Assignments:	See Figure 6	Consistent with literature spectra (Elleman et al., 1965; Sadtler Standard Spectra)

Chemical Shift (δ): **Coupling Constant:**

a -- d, 1.20 ppm — $J_{a-d} = 5$ Hz
b -- dd, 2.26 ppm — $J_{b-c} = 5.5$ Hz, $J_{b-d} = 2.6$ Hz
c -- m, 2.58 ppm — $J_{d-c} \sim 4$ Hz
d -- m, 2.72-2.98 ppm

Integration Ratios:

a -- 2.61
b -- 1.16
c -- 1.13
d -- 1.10

6. Gas Chromatography

Instrument: Tracor MT 220
Detector: Flame ionization
Inlet temperature: 200° C
Detector temperature: 270° C

a. System 1

Column: Chromosorb 102 on 100/120, 1.8 m x 4 mm ID, glass
Oven temperature program: 5 min at 50° C, then 50°-200° C at 10° C/min
Results: Single homogeneous peak, retention time: 15.1 min

b. System 2

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m × 4 mm ID, glass
Oven temperature program: 5 min at 50° C, then 50°-150° C at 10° C/min
Results: Single homogeneous peak, retention time: 1.8 min

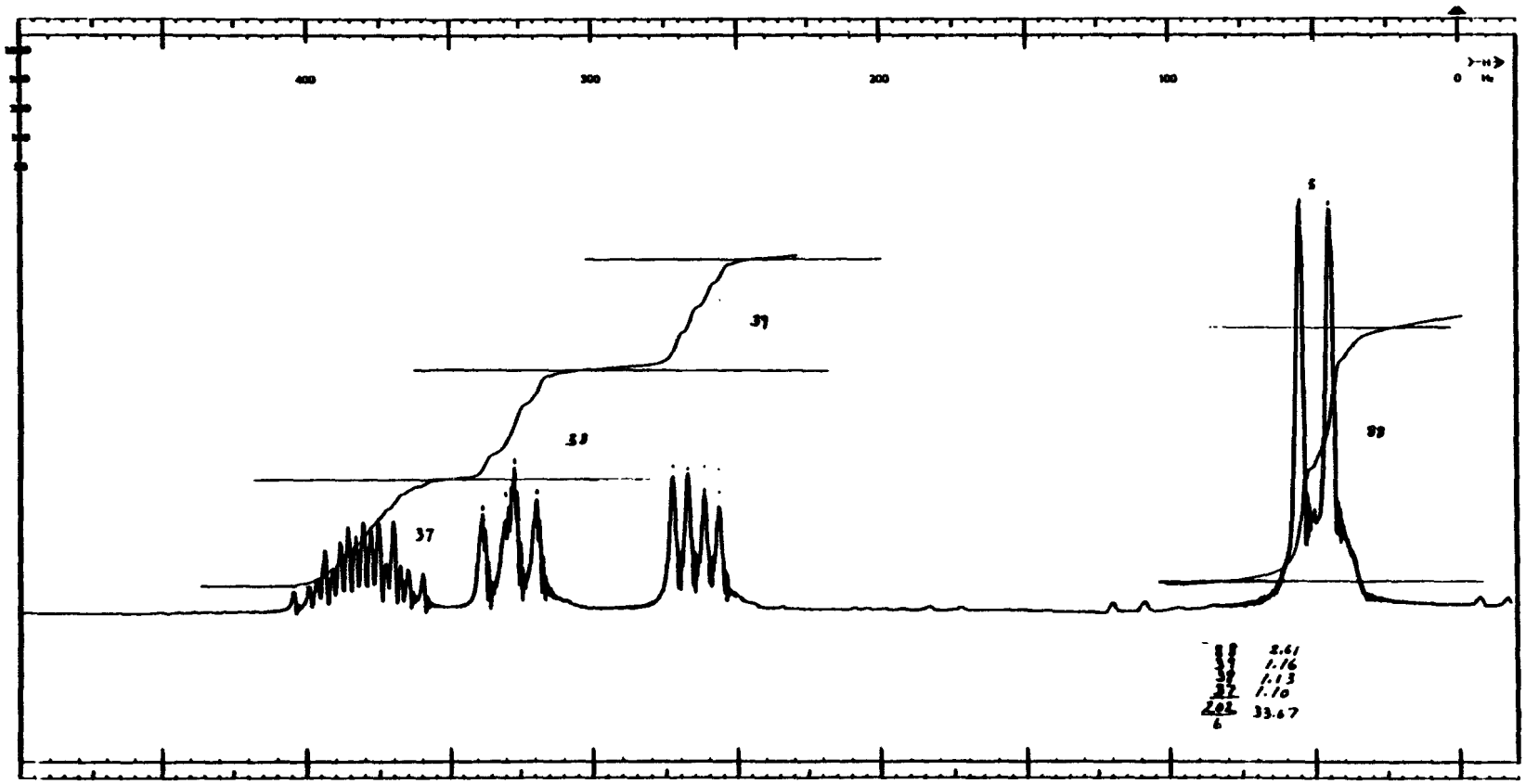

FIGURE 6. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF PROPYLENE OXIDE (LOT NO. UC 5/10/76)

B. Lot No. 6477-22

1. Water Analysis (Karl Fischer):

0.15% ± 0.002 (δ)%

2. Elemental Analysis:

Element	C	H
Theory	62.04	10.41
Determined	62.06 62.25	10.55 10.40

3. Spectral Data

a. Infrared	**Determined**	**Literature Values**
Instrument:	Beckman IR-12	
Cell:	Silver chloride 0.025 mm pathlength	
Results:	See Figure 7	Consistent with literature spectrum

b. Ultraviolet/Visible	**Determined**	**Literature Values**
Instrument:	Cary 118	
Results:	A 10% (v/v) solution in hexane had no absorbance in either the visible (350-800 nm) or ultraviolet (210-350 nm) range	No literature reference found

c. Nuclear Magnetic Resonance

	Determined	**Literature Values**
Instrument:	Varian EM360-A	
Solvent:	Neat, tetramethyl-silane internal standard	
Assignments:	See Figure 8	Consistent with literature spectrum (Aldrich Library)

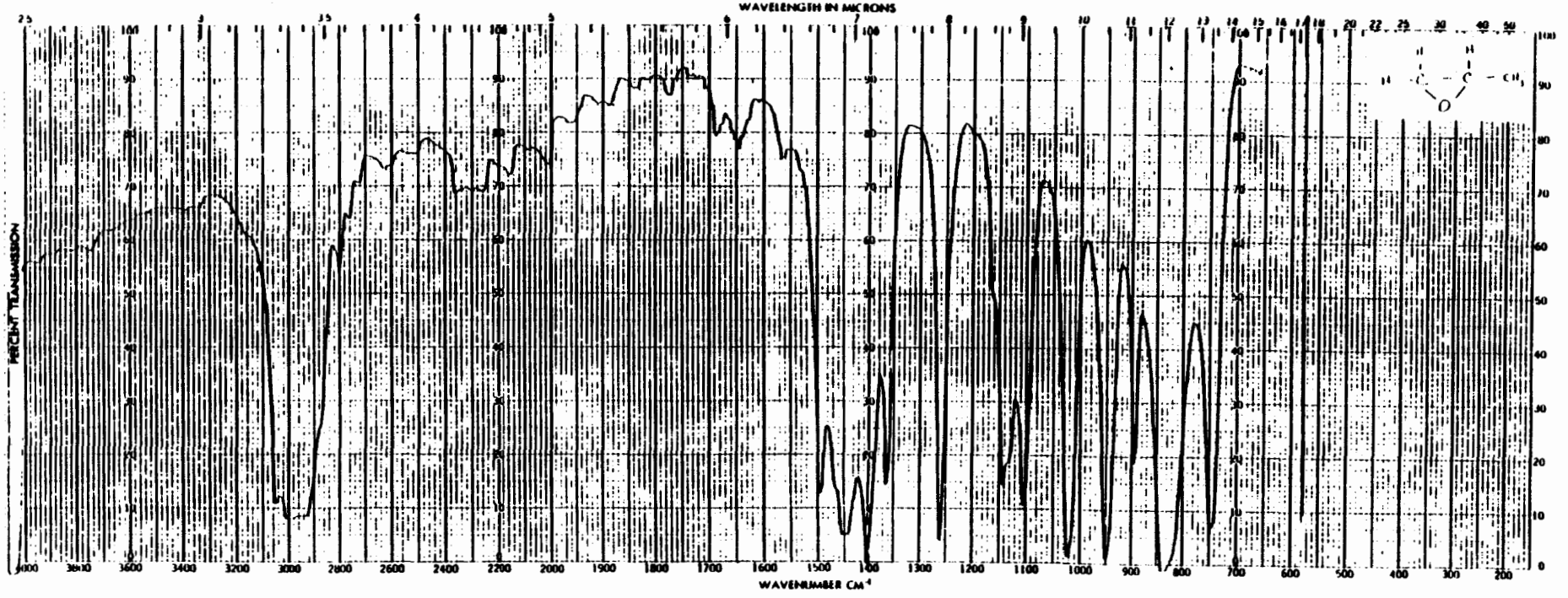

FIGURE 7. INFRARED ABSORPTION SPECTRUM OF PROPYLENE OXIDE (LOT NO. 6477-22)

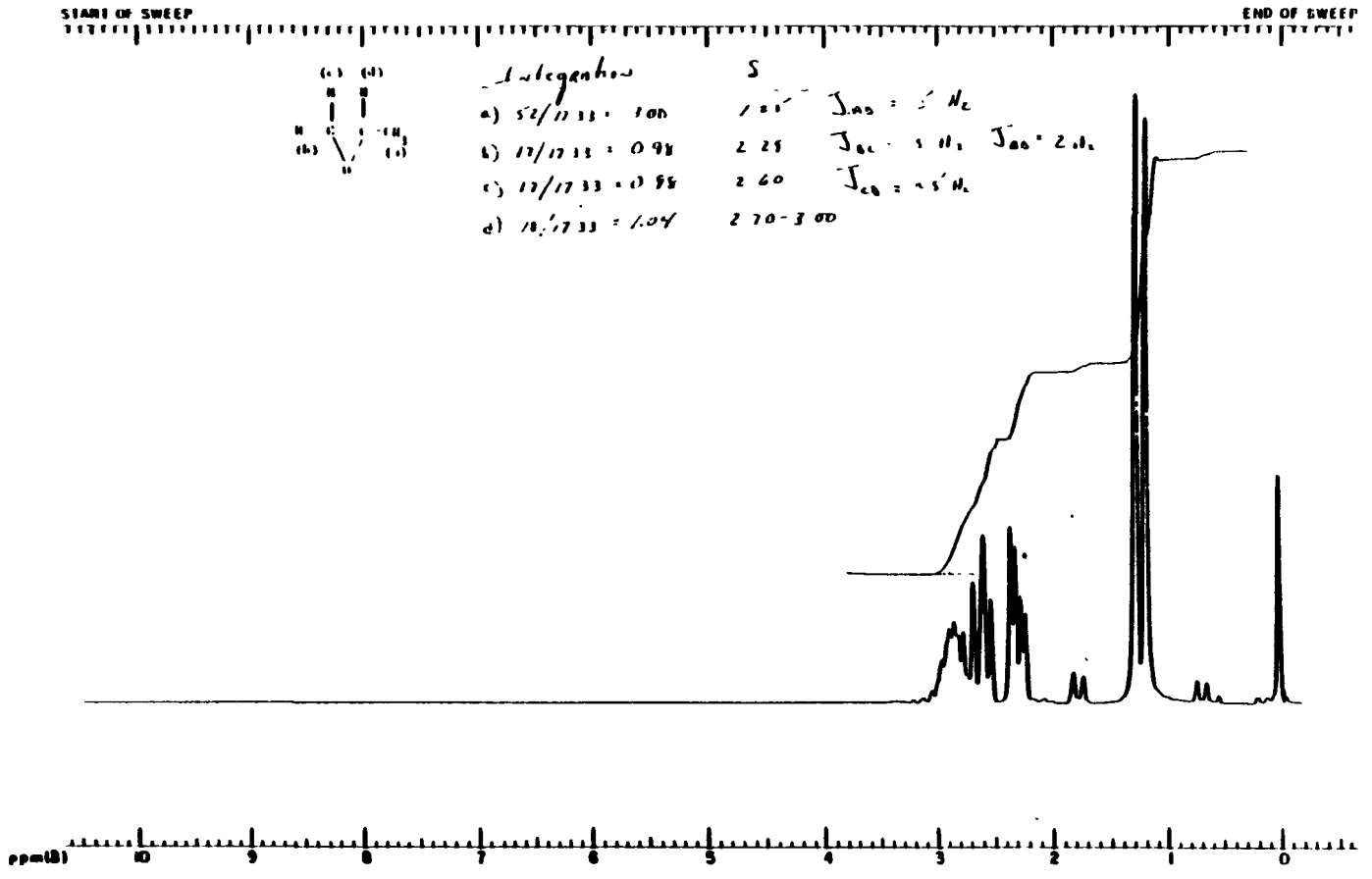

FIGURE 8. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF PROPYLENE OXIDE (LOT NO. 6477-22

Chemical Shift (δ):	Coupling Constant:
a -- d, 1.25 ppm	J_{a-d} = 5 Hz
b -- dd, 2.29 ppm	J_{b-c} = 5.3 Hz,
c -- dd, 2.60 ppm	J_{b-d} = 2.4 Hz
d -- m, 2.70-3.00 ppm	J_{c-d} = 4 Hz

Integration Ratios:

a -- 52/17.33 = 3.00
b -- 17/17.33 = 0.98
b -- 17/17.33 = 0.98
b -- 18/17.33 = 1.04

4. Gas Chromatography

Instrument: Perkin Elmer 3920
Detector: Flame ionization
Inlet temperature: 120° C
Detector temperature: 270° C
Carrier gas: Nitrogen

a. System 1

Column: 20% SP 2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m × 4 mm ID, glass
Carrier flow rate: 25 ml/min
Oven temperature program: 4 min at 30° C, then 30°-150° C at 8° C/min
Samples injected: 0.6 µl of propylene oxide (neat) to detect impurities; 1.5 µl of a 1.0% and 0.5% (v/v) solution in isooctane to establish detector response linearity
Results: A major peak, retention time: 2.7 min; no impurities >0.01%

b. System 2

Column: Results: Carbopack C on 80/100/0.1% SP 2100, 1.8 m × 4 mm ID, glass
Carrier flow rate: 50 ml/min
Oven temperature program: 4 min at 30° C, then 30°-200° C at 32° C/min
Samples injected: 0.6 µl of propylene oxide (neat) to detect impurities; 3 and 1.5 µl of a 1% (w/v) solution in isooctane to establish detector response linearity
Results: A major peak, retention time: 2.0 min; no impurities >0.01%

II. Test Chemical Stability Studies Performed at the Testing Laboratory

Analytical Methods

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

Column: Porapak QS 80/100 mesh, 2.35 m × 2 mm ID, glass
Column oven temperature: 125° C, isothermal
Injector temperature: 200° C
Detector: Flame ionization
Detector temperature: 275° C
Carrier: Helium
Carrier flow rate: 20 ml/min

The percent purity (percentage of total peak area contributed by propylene oxide) for each analysis is summarized in Table G1:

TABLE G1. ANALYSIS OF PROPYLENE OXIDE (Lot No. 6477-22)

Sample	Date Analyzed	Percent Purity (a)
Exposure	7/18/79	99.99
Reference	12/10/79	99.99
Exposure	12/10/79	99.99
Reference	5/02/80	99.99
Exposure	5/02/80	100.00
Reference	9/02/80	100.00
Exposure	9/02/80	100.00
Reference	12/31/80	99.99
Exposure	12/31/80	100.00
Reference	5/05/81	100.00
Exposure	5/05/81	99.99
Reference	7/29/81	99.99
Exposure	7/29/81	100.00
Reference	1/13/82	99.99
Exposure	1/13/82	99.99

(a) The purity value is derived from the percentage of the total peak area contributed by propylene oxide.

2. Identity Determination: The infrared absorption spectra were obtained on the neat material between NaCl plates using a Beckman Acculab 6. All spectra were consistent with those of Midwest Research Institute.

3. Conclusion: No notable degradation occurred throughout the 2-year studies.

APPENDIX H

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

I. Generation System in the 2-year Studies: The liquid to be vaporized was contained in a 1.6-liter stainless steel reservoir that was housed in a vapor hood within the exposure room. The liquid was pumped from this reservoir to a vaporizer by a stable micrometering pump with adjustable drift-free pump rates ranging from 0.03 to 20 ml/min. Four pump/vaporizer systems were fed from the single reservoir by incorporating a manifold liquid distribution system. Clear Teflon® tubes of measured volume, preceded by a three-way valve, were attached just upstream of each pump to facilitate measurements of liquid flow rate to each vapor generator. This was accomplished by momentarily switching the three-way valve from the run to the test position. A small bubble of air was pulled by the pump from the room through the valve and into the clear tube. The progress of this bubble from one end of the tube to the other (calibrated volume) was timed with a stopwatch. Flow rate was calculated by dividing the volume by the time. The volume of the tubes was chosen so that the error due to start and stop time ambiguity (introduced by the pulsatile nature of the pumps) was less than 5%. Measurement of this flow, along with measurement of chamber dilution air flow, was used to calculate expected concentration of vapor in the chamber. This provided a method, secondary to that of the gas chromatograph, of monitoring concentration. Three-way valves and lines returning from the vaporizer to a beaker in the vapor hood facilitated filling the distribution system (Figure 9).

The vaporizer (Figure 10) comprises a stainless steel cylinder covered with a glass fiber wick from which the liquid was vaporized. This wick could be inexpensively and quickly replaced if necessitated by residue buildup. No residue was detectable on the wicks used for propylene oxide; nonetheless, wicks were replaced at least every 2 months. The vapor pressure of propylene oxide was sufficient at room temperature to generate the desired concentrations. Each cylindrical vaporizer was positioned in the fresh air duct leading directly into the exposure chamber to minimize material loss due to condensation on duct walls.

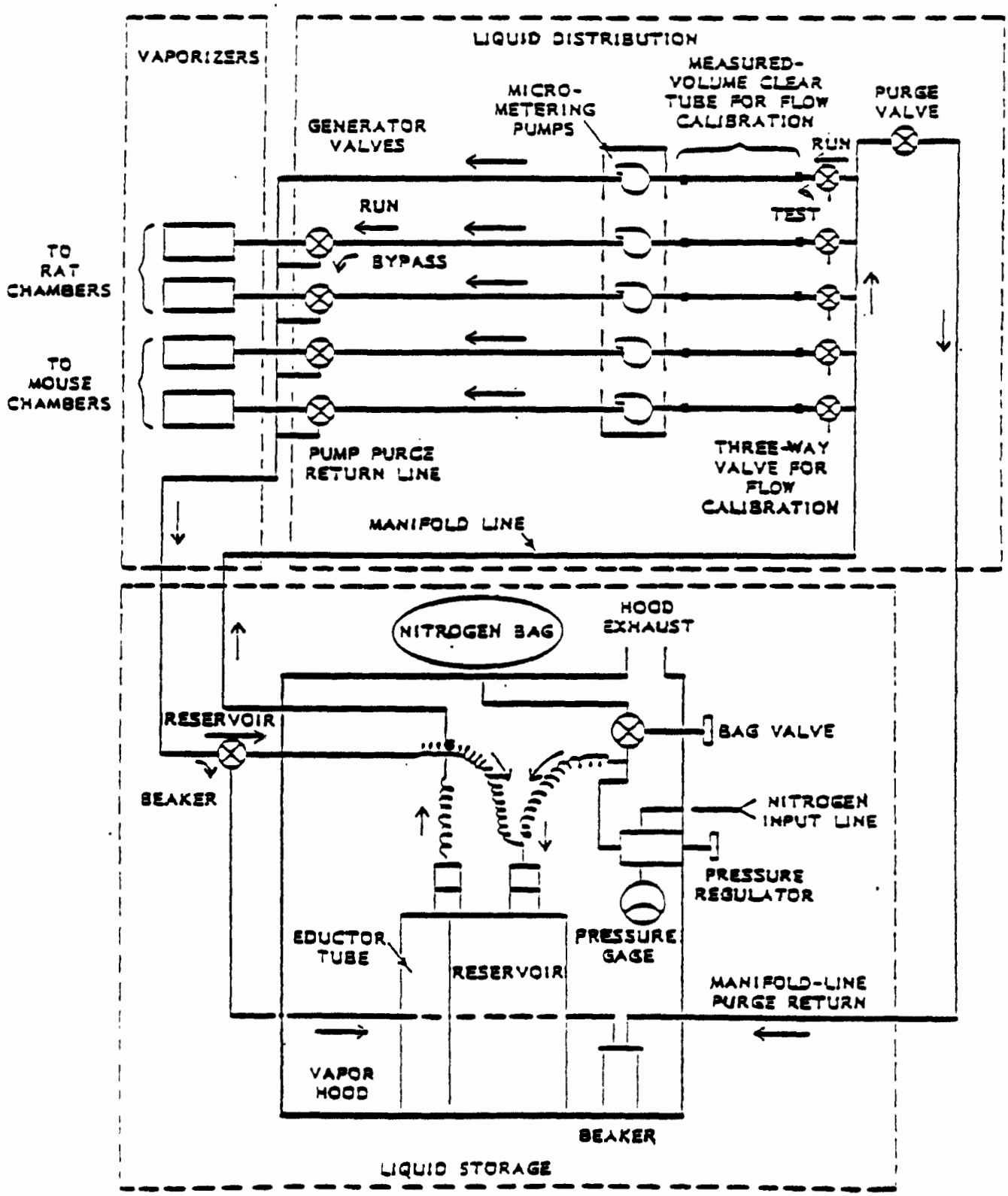

FIGURE 9. PROPYLENE OXIDE VAPOR GENERATION SYSTEM

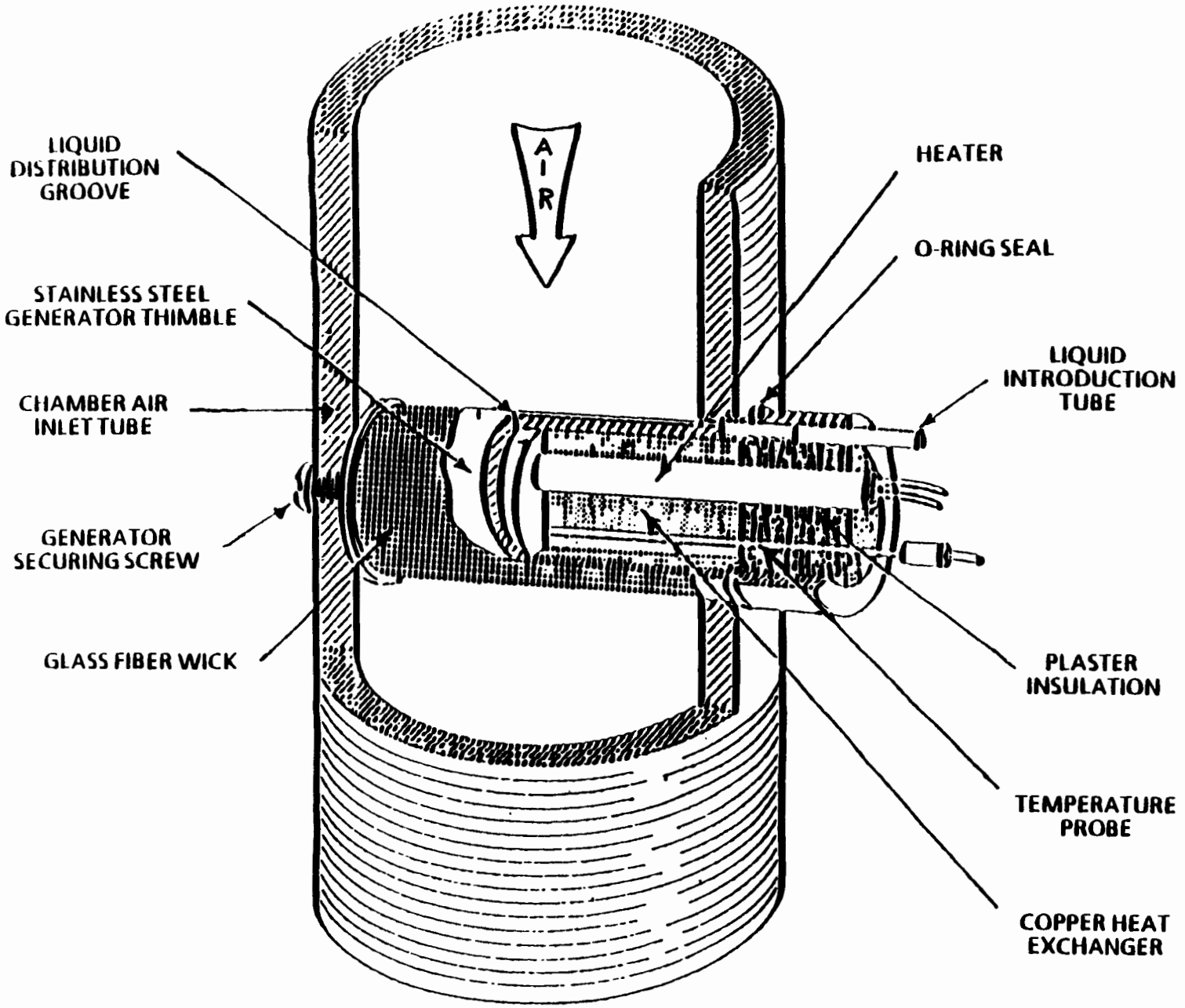

FIGURE 10. CUTAWAY DRAWING OF THE LIQUID VAPOR GENERATOR

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 using a portable photoionization detector (PID) at 12 positions (2 positions, 1 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 11). The data, normalized to the average concentration at all 12 sample positions for each chamber, are presented in Table H1. In no case was a sample position in a chamber found to be out of balance by more than ± 10% of the mean values of concentration of all sample positions within the chamber.

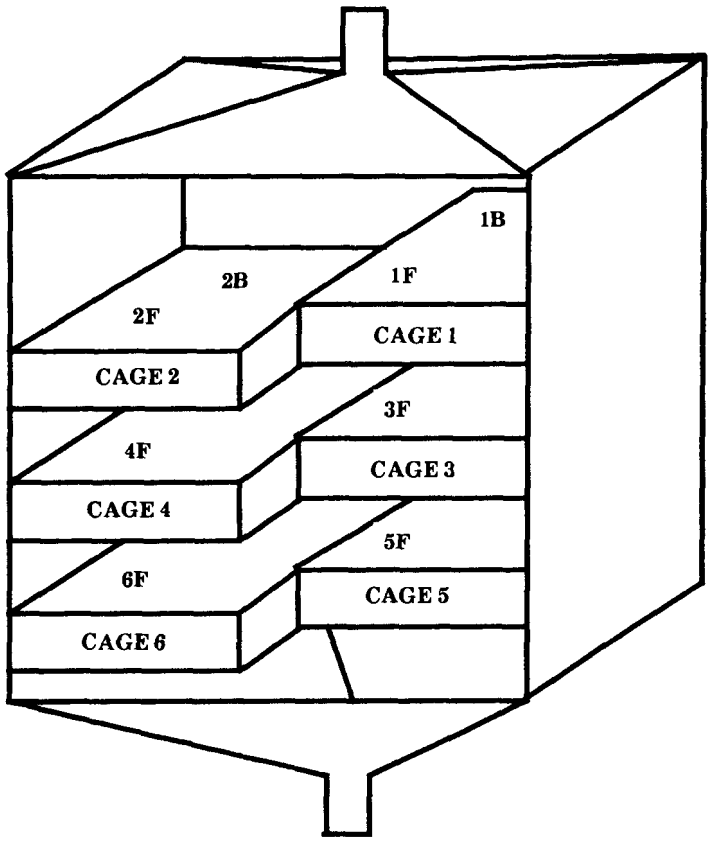

FIGURE 11. SCHEMATIC FRONT VIEW OF CHAMBER SHOWING APPROXIMATE SAMPLE SITES
(1F, 1B, 2F, 2B, ETC.)

TABLE H1. PROPYLENE OXIDE VAPOR CONCENTRATION UNIFORMITY TEST RESULTS

Sample Location	Test Results (a)			
RATS				
	400 ppm (b)	**400 ppm(c)**	**200 ppm (d)**	**400 ppm (d)**
1F	99	99	105	92
1B	(e)	98	102	101
2F	99	103	100	103
2B	(e)	103	96	106
3F	100	98	96	106
3B	(e)	97	96	110
4F	100	109	105	99
4B	(e)	103	105	109
5F	99	93	102	92
5B	(e)	95	95	92
6F	102	108	104	92
6B	(e)	95	96	95
Mean ± standard deviation	100 ± 1	100 ± 5	100 ± 4	100 ± 7
	200 ppm (f)	**400 ppm (f)**	**200 ppm (g)**	**400 ppm (g)**
1F	106	99	102	98
1B	96	99	110	102
2F	101	108	96	98
2B	96	110	101	99
3F	106	94	96	96
3B	96	96	102	98
4F	101	99	92	100
4B	96	99	98	101
5F	106	96	104	96
5B	96	94	103	98
6F	101	103	94	108
6B	96	101	100	107
Mean ± standard deviation	100 ± 4	100 ± 6	100 ± 5	100 ± 4

MICE						
	200 ppm (d)	**400 ppm (d)**	**200 ppm (f)**	**400 ppm (f)**	**200 ppm (g)**	**400 ppm (g)**
1F	100	96	109	96	100	94
1B	100	97	105	98	99	98
2F	98	96	101	96	100	98
2B	100	96	101	107	101	106
3F	100	103	97	96	98	97
3B	100	99	97	105	99	102
4F	100	101	97	93	97	96
4B	103	106	97	105	100	102
5F	100	104	101	100	100	103
5B	100	104	101	103	100	102
6F	100	99	97	98	99	98
6B	100	103	97	105	104	104
Mean ± standard deviation	100 ± 1	100 ± 4	100 ± 5	100 ± 2	100 ± 2	100 ± 4

(a) Mean as percent of target concentration. Data normalized to the average concentration at all positions in each chamber.
(b) August 1979
(c) January 1980
(d) September 1980
(e) Data not taken
(f) January 1981
(g) March 1981

III. Chamber Concentration Monitoring System: Propylene oxide concentrations in the exposure chambers, control chambers, and exposure room were automatically monitored approximately 8-12 times during each exposure period with a Hewlett-Packard® 5840A gas chromatograph equipped with a flame ionization detector. An 18-inch × 2-mm ID Porapak Q 80/100 mesh column held at 100° C was used. The calibration of the gas chromatograph was checked approximately once per month using a "bag" standard prepared by the testing facility and sampled at the end of the chamber sampling line.

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 eight-port sample valve. The constant flow assured fresh samples at the eight-port valve.

Weekly concentrations are graphically presented in Figures 12-15.

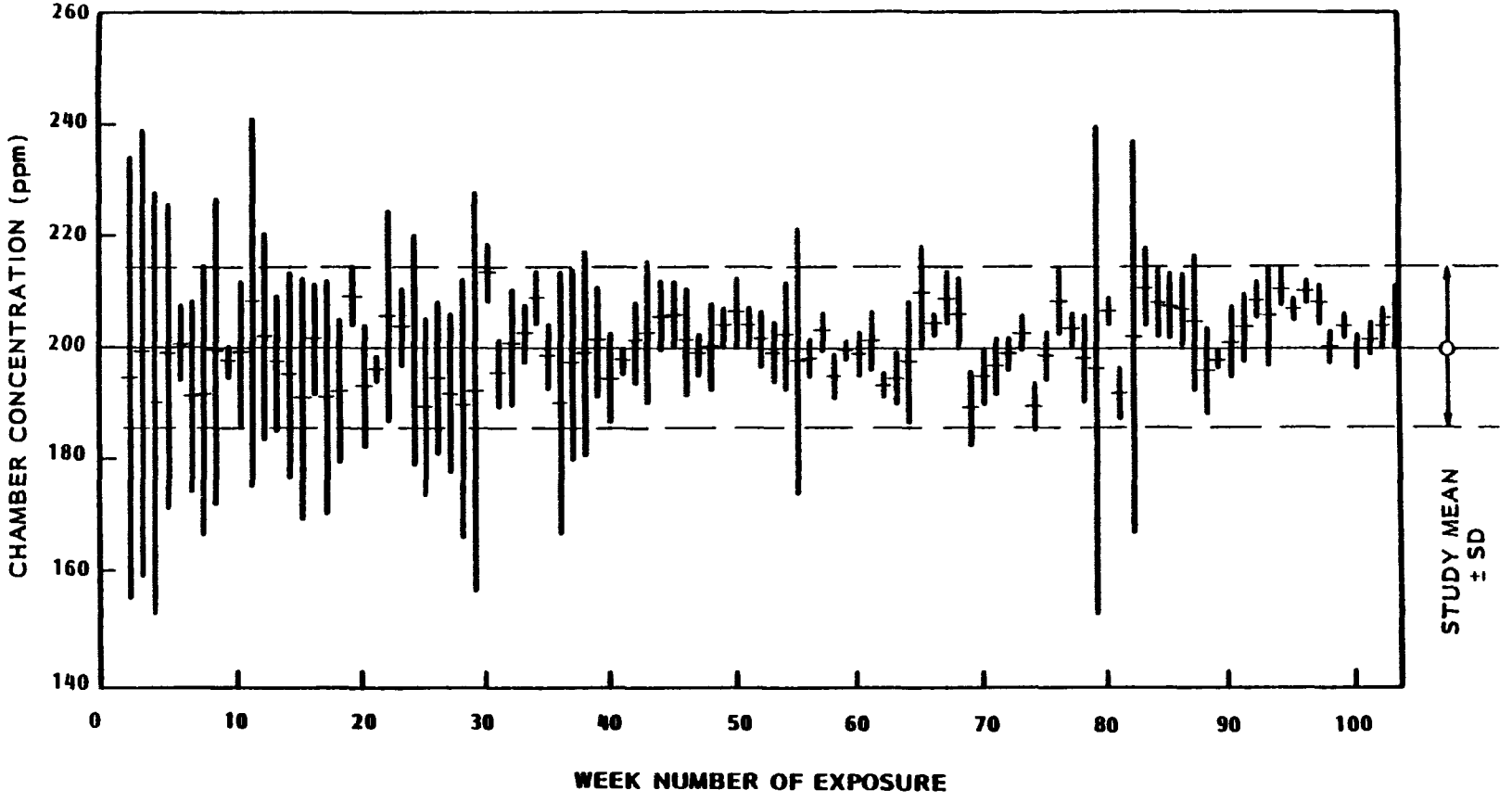

FIGURE 12. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN 200-PPM RAT EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDY

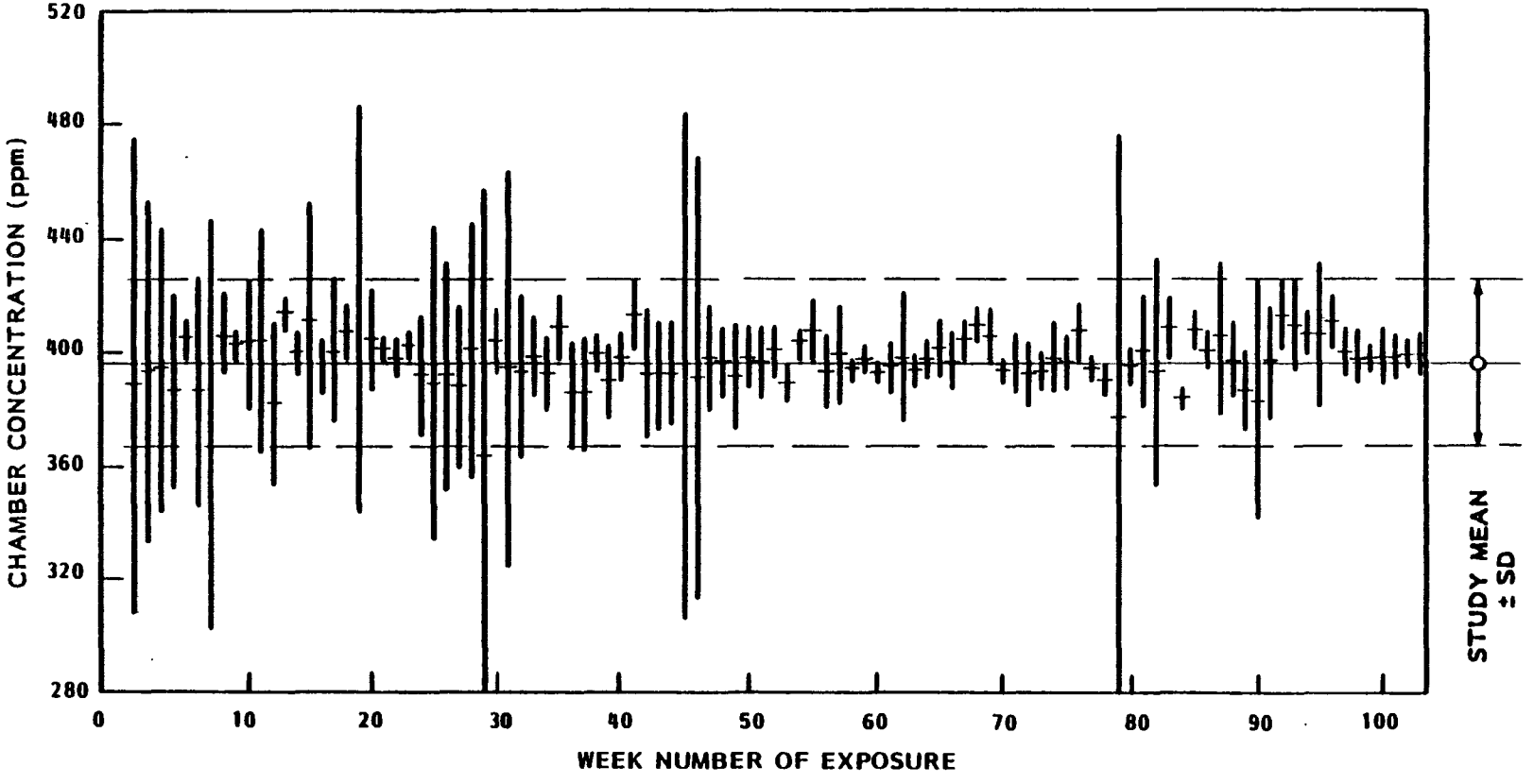

FIGURE 13. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN 400-PPM RAT EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDY

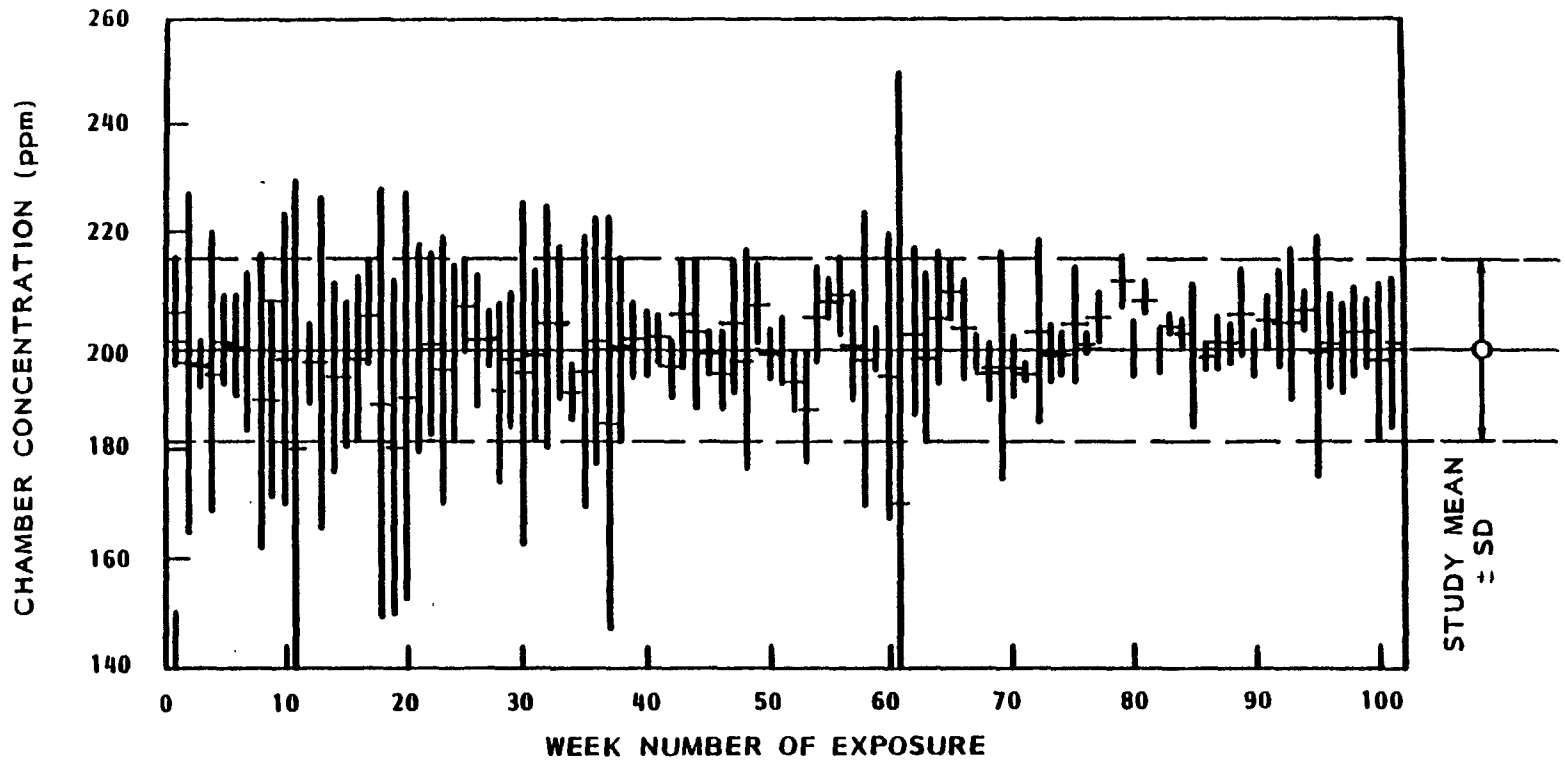

FIGURE 14. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN 200-PPM MICE EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDY

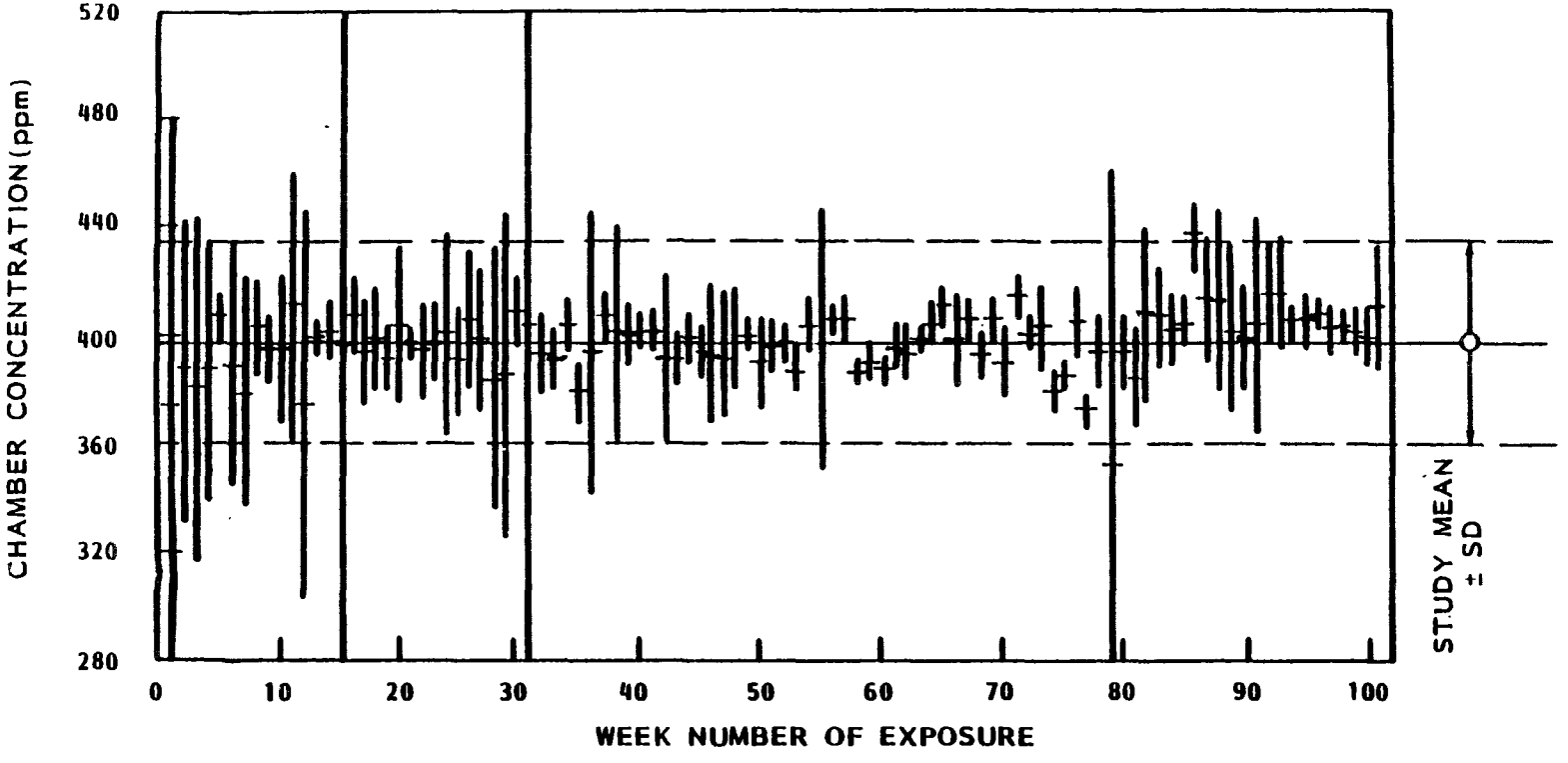

FIGURE 15. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION (bars) IN 400-PPM MICE EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDY

APPENDIX I

SENTINEL ANIMAL PROGRAM

APPENDIX I. SENTINEL ANIMAL PROGRAM

A. 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 and 15 F344/N rats of each sex are selected at the time of randomization and allocation of the animals to the various study groups. Animals of each designated sentinel group were killed at 6, 12, and 18 months on study. A total of 39 rats were examined (10 per time period except 18 months when only 9 rats were available). Nine mice were examined at 6 months, 10 at 12 months, 8 at 18 months, and 10 at 24 months. Data from animals surviving 24 months were collected from 5/50 randomly selected control animals of each sex and species. The blood from each animal was collected and clotted and the serum was separated. The serum was cooled on ice and shipped to Microbiological Associates' Comprehensive Animal Diagnostic Service for deter-mination of the viral antibody titers. The following tests were performed:

	Hemagglutination Inhibition	Complement Fixation
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 (ectromelia virus)	M.Ad. (mouse adenovirus) MHV (mouse hepatitis virus) Sendai LCM (lymphocytic choriomeningitis virus)
Rats	PVM KRV (Kilham rat virus) H-1 (Toolan's H-1 virus)	RCV (rat coronavirus) Sendai

B. RESULTS

Viral titers were not found in rats. In mice, no viral titers were found with the exception of one mouse that was positive for Reo 3 at a 1:20 dilution at 6 months. This result is considered to be spurious. Thus, there was no evidence for the presence of murine viruses during the conduct of this study.

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 Oxide 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 August 1979, prior to NTP's requirement for full compliance with Good Laboratory Practices regulations initiated in October 1981, and completed in December 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., Clement Associates, and NTP staff in October 1983. The audit team included Chris Dippel, M.S., Curt Lunchick, M.S., Debra McCall, James Plautz, M.S., Ronald Schueler, D.V.M., Gary Boorman, D.V.M., Ph.D., and Miriam Anver, D.V.M., Ph.D. The full report of the audit is on file at the National Toxicology Program, NIEHS, and is available upon 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 at least 10% were reviewed for animal identification and untrimmed lesions. A complete slide/block match was performed for high dose and control groups of each sex and species.

Study animals were identified by ear tags, but records contain frequent notations of animals with missing tags (83 of 300 rats and 38 of 300 mice). Discrepancies were found in clinical observation, body weight, and mortality records relating to animal identification; these discrepancies may have been due to missing ear tags and failure to identify definitively the animals concerned. Daily observation records occasionally note that mice were observed free within the exposure chamber or "missing" without 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 in-life experimental data. The chemistry data were considered adequate and support the stated conclusions in the Technical Report.

Animal identification in wet tissue bags could not be confirmed for 24 of 81 rats and 21 of 90 mice because of missing ear tags. The wet tissue bag labeled low dose female mouse #545 contained the ear tag for low dose female mouse #546, and the ear tag was missing from the bag labeled low dose female mouse #546. It seems probable that these two mice were interchanged. The slide/block match was good with a single questionable match in rats and mice each. There was good correlation of gross observations at necropsy with histologic diagnoses. Only two discrepancies in rats and a single discrepancy in mice involved target organs (lung).

The most important problem occurring in the 2-year inhalation studies of Propylene Oxide 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 mixups between dose groups. Therefore, these discrepancies are not believed to influence the final interpretation of these studies in rats and mice. The data examined in this audit are adequate to support the conclusion of the Technical Report.