NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 376

TOXICOLOGY AND CARCINOGENESIS STUDIES OF ALLYL GLYCIDYL ETHER

(CAS NO. 106-92-3)

IN OSBORNE-MENDEL RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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

FOREWORD

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

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

The studies described in this Technical Report were performed under the direction of the NIEHS and were conducted in compliance with NTP chemical health and safety requirements and must meet or exceed all applicable Federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals. All NTP toxicology and carcinogenesis studies are subjected to a comprehensive audit before being presented for public review. This Technical Report has been reviewed and approved by the NTP Board of Scientific Counselors' Peer Review Panel in public session; the interpretations described herein represent the official scientific position of the NTP.

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

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NTP TECHNICAL REPORT

ON THE

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IN OSBORNE-MENDEL RATS AND B6C3F$_1$ MICE

(INHALATION STUDIES)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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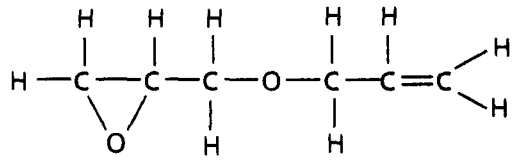

ALLYL GLYCIDYL ETHER

CAS No. 106-92-3

$C_6H_{10}O_2$ Molecular weight 114.1

Synonyms: allyl 2,3-epoxypropyl ether; 1-allyloxy-2,3-epoxypropane; 1,2-epoxy-3-allyloxypropane; glycidyl allyl ether; ((2-propenyloxy)methyl)oxirane; 1-(allyloxy)-2,3-epoxypropane

ABSTRACT

Allyl glycidyl ether is used as a resin intermediate and as a stabilizer of chlorinated compounds, vinyl resins, and rubber. Toxicology and carcinogenesis studies were conducted by exposing groups of Osborne-Mendel rats and B6C3F$_1$ mice of each sex to allyl glycidyl ether (greater than 97% pure) by inhalation for 6 hours per day, 5 days per week for 2 weeks, 13 weeks, or 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, Chinese hamster ovary (CHO) cells, and *Drosophila melanogaster*. Studies of reproductive effects were conducted in rats and mice exposed to allyl glycidyl ether for 8 weeks.

Two-Week Studies: Exposure concentrations ranged up to 500 ppm in rats and 100 ppm in mice. All rats that were exposed to 500 ppm died; no deaths occurred at the next lower (200 ppm) exposure concentration. All male mice and 3/5 female mice exposed to 100 ppm and 2/5 male mice and 1/5 female mice exposed to 50 ppm died. Compound-related lesions in rats and mice included acute inflammation of the nasal passage and major airways.

Eight-Week Studies of Reproductive Effects: Rats were exposed to 0-200 ppm allyl glycidyl ether, and mice were exposed to 0-30 ppm, 6 hours per day, 5 days per week for 8 weeks. The mating performance of exposed male rats was markedly reduced; however, sperm motility and number were not affected. No deficiencies were seen in the reproductive performance of exposed female rats or male or female mice.

Thirteen-Week Studies: Exposure concentrations ranged up to 200 ppm for rats and 30 ppm for mice. All rats lived to the end of the studies. The final mean body weights of male rats exposed to 10-200 ppm were 7%-24% lower than that of controls. Final mean body weights of female rats exposed to 30-200 ppm were 7%-13% lower than that of controls. Clinical signs attributable to irritation of the upper respiratory tract and eyes were seen in exposed animals. Histologic lesions included squamous metaplasia of the nasal passage in all exposure groups (4 ppm, lowest concentration) and involved both the respiratory epithelium and the olfactory epithelium. The lesions were more severe anteriorly and dorsally and with increasing concentration. At 30 ppm and higher, erosion was seen in the nasal passage and squamous metaplasia was seen in the upper airways.

There were no compound-related deaths in mice. The final mean body weights of mice exposed to 30 ppm were 12% lower than those of controls for both males and females. Mice exposed to 10 or 30 ppm allyl glycidyl ether had squamous metaplasia of the nasal passage, involving both the respiratory

epithelium and the olfactory epithelium, which tended to be more severe in the anterior and dorsal portions of the nasal passage. In mice exposed to 30 ppm, epithelial erosions were also found.

Body Weights and Survival in the Two-Year Studies: Two-year studies were conducted by exposing groups of 50 Osborne-Mendel rats and B6C3F$_1$ mice of each sex to 0, 5, or 10 ppm allyl glycidyl ether by inhalation for 6 hours per day, 5 days per week for 102 or 103 weeks. Mean body weights of the exposed rats were within 8% of those of the controls throughout the studies. Mean body weights of mice exposed to 5 or 10 ppm were 5%-20% lower than those of controls. Deaths were seen in all groups of male rats beginning at 1 year of age (final survival--control, 12/50; 5 ppm, 11/50; 10 ppm, 8/50). Survival of female rats was not exposure related (24/50; 30/50; 25/50). Exposed mice had slightly increased survival (male mice: 38/50; 39/50; 46/50; female mice: 33/50; 42/50; 41/50).

Nonneoplastic and Neoplastic Effects in the Two-Year Studies: In male rats exposed to 10 ppm allyl glycidyl ether, three apparently unrelated neoplasms of the nasal passage were found. Two neoplasms, a papillary adenoma and a squamous cell carcinoma, appeared to arise from different cell types in the respiratory epithelium. One poorly differentiated adenocarcinoma in the olfactory region was also found. One papillary adenoma of respiratory epithelial origin was found in a female rat exposed to 5 ppm. Exposure-related nonneoplastic lesions of the nasal passages in rats included inflammation, squamous metaplasia, respiratory metaplasia (replacement of olfactory epithelium by ciliated epithelium), hyperplasia of the respiratory epithelium, and degeneration of the olfactory epithelium. In male mice exposed to 10 ppm allyl glycidyl ether, a hemangioma and three papillary adenomas were present in the nasal passage. In female mice exposed to 10 ppm, a hemangioma and an adenoma were found in the nasal passage. Nonneoplastic lesions of the nasal passages in mice included inflammation, squamous metaplasia, hyperplasia, basal cell hyperplasia, dysplasia of the respiratory epithelium, and metaplasia of the olfactory epithelium. In male mice, there was an exposure-related decrease in the incidences of hepatocellular neoplasms; in female mice, there was a decrease in the incidences of pituitary gland adenomas.

Genetic Toxicology: Allyl glycidyl ether was mutagenic in *S. typhimurium* strains TA100 and TA1535 with and without exogenous metabolic activation; no mutagenic activity was observed in strains TA98 or TA1537. Allyl glycidyl ether induced sister chromatid exchanges and chromosomal aberrations in CHO cells both in the presence and the absence of metabolic activation. A significant increase in sex-linked recessive lethal mutations was recorded in the germ cells of male *D. melanogaster* fed a sucrose solution containing allyl glycidyl ether, but no increase in reciprocal translocations occurred in these cells.

Conclusions: Under the conditions of these 2-year inhalation studies, there was *equivocal evidence of carcinogenic activity** of allyl glycidyl ether for male Osborne-Mendel rats, based on the presence of one papillary adenoma of respiratory epithelial origin, one squamous cell carcinoma of respiratory epithelial origin, and one poorly differentiated adenocarcinoma of olfactory epithelial origin, all occurring in the nasal passage of males exposed to 10 ppm. There was *no evidence of carcinogenic activity* of allyl glycidyl ether for female rats. One papillary adenoma of the respiratory epithelium was present in a female rat exposed to 5 ppm. There was *some evidence of carcinogenic activity* of allyl glycidyl ether for male $B6C3F_1$ mice, based on the presence of three adenomas of the respiratory epithelium, dysplasia in four males, and focal basal cell hyperplasia of the respiratory epithelium in seven males in the nasal passage of mice exposed to 10 ppm. There was *equivocal evidence of carcinogenic activity* of allyl glycidyl ether for female mice, based on the presence of one adenoma of the respiratory epithelium and focal basal cell hyperplasia of the respiratory epithelium in seven females exposed to 10 ppm. The sensitivity of the assay to detect potential carcinogenicity may have been reduced in male rats because of poor survival in all groups.

In exposed mice, body weights were decreased 10% or more, mortality was decreased, and there were lower incidences of liver neoplasms (males) and pituitary gland adenomas (females) compared with controls.

Significant exposure-related nonneoplastic lesions were restricted to the nasal passage in both rats and mice and included inflammation, metaplasia, respiratory epithelial hyperplasia, and olfactory epithelial degeneration. Basal cell hyperplasia and dysplasia of the respiratory epithelium of the nasal passage were found only in the mice.

*Explanation of Levels of Evidence of Carcinogenic Activity is on page 7.
A summary of the Peer Review comments and the public discussion on this Technical Report appears on page 10.

SUMMARY OF THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Male Osborne-Mendel Rats	Female Osborne-Mendel Rats	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Exposure concentrations			
0, 5, or 10 ppm allyl glycidyl ether, 6 h/d, 5 d/wk	0, 5, or 10 ppm allyl glycidyl ether, 6 h/d, 5 d/wk	0, 5, or 10 ppm allyl glycidyl ether, 6 h/d, 5 d/wk	0, 5, or 10 ppm allyl glycidyl ether, 6 h/d, 5 d/wk
Body weights in the 2-year study			
Exposed and controls similar	Exposed slightly lower than controls	Exposed lower than controls	Exposed lower than controls
Survival in the 2-year study			
12/50; 11/50; 8/50	24/50; 30/50; 25/50	38/50; 39/50; 46/50	33/50; 42/50; 41/50
Nonneoplastic effects			
Nasal passage: inflammation, metaplasia, respiratory epithelial hyperplasia, and olfactory epithelial degeneration	Nasal passage: inflammation, metaplasia, respiratory epithelial hyperplasia, and olfactory epithelial degeneration	Nasal passage: inflammation, metaplasia, respiratory epithelial dysplasia and hyperplasia, and olfactory epithelial metaplasia	Nasal passage: inflammation, metaplasia, respiratory epithelial dysplasia and hyperplasia, and olfactory epithelial metaplasia
Neoplastic effects			
Nasal passage (respiratory or olfactory epithelium): 1 papillary adenoma, 1 squamous cell carcinoma, 1 poorly differentiated adenocarcinoma at 10 ppm	Nasal passage: 1 papillary adenoma of the respiratory epithelium at 5 ppm	Nasal passage: 3 adenomas of the respiratory epithelium	Nasal passage: 1 adenoma of the respiratory epithelium
Level of evidence of carcinogenic activity			
Equivocal evidence	No evidence	Some evidence	Equivocal evidence
Other considerations			
Poor survival in all groups		Lower incidences of hepatocellular neoplasms	Lower incidences of pituitary gland neoplasms

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

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

Five categories of evidence of carcinogenic activity are used in the Technical Report series to summarize the strength of the evidence observed in each experiment: two categories for positive results ("Clear Evidence" and "Some Evidence"); one category for uncertain findings ("Equivocal Evidence"); one category for no observable effects ("No Evidence"); and one category for experiments that because of major flaws cannot be evaluated ("Inadequate Study"). These categories of interpretative conclusions were first adopted in June 1983 and then revised in March 1986 for use in the Technical Reports series to incorporate more specifically the concept of actual weight of evidence of carcinogenic activity. For each separate experiment (male rats, female rats, male mice, female mice), one of the following quintet is 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 Carcinogenic Activity** is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.

- **Some Evidence of Carcinogenic Activity** is demonstrated by studies that are interpreted as showing a chemically related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.

- **Equivocal Evidence of Carcinogenic Activity** is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemically related.

- **No Evidence of Carcinogenic Activity** is demonstrated by studies that are interpreted as showing no chemically related increases in malignant or benign neoplasms.

- **Inadequate Study of Carcinogenic Activity** is demonstrated by studies that because of major qualitative or quantitative limitations cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

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

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

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of Allyl Glycidyl Ether is based on 13-week studies that began in September 1981 and ended in December 1981 and on 2-year studies that began in June 1982 and ended in June 1984 at Battelle Pacific Northwest Laboratories (Richland, WA).

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PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the draft Technical Report on allyl glycidyl ether on June 27, 1989, 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 TOXICOLOGY AND CARCINOGENESIS STUDIES OF ALLYL GLYCIDYL ETHER

On June 27, 1989, the draft Technical Report on the toxicology and carcinogenesis studies of allyl glycidyl ether received public review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. G. Boorman, NIEHS, began the discussion by reviewing the experimental design, results, and proposed conclusions (equivocal evidence of carcinogenic activity for male rats, no evidence of carcinogenic activity for female rats, some evidence of carcinogenic activity for male mice, equivocal evidence of carcinogenic activity for female mice).

Dr. Ashby, a principal reviewer, agreed with the conclusions. He expressed surprise that the chemical was not a more potent carcinogen, as suggested by its chemical structure, structural similarity to glycidol, and genotoxicity, and wondered if there may have been a more marked expression of carcinogenic potential by a different route of exposure. He asked that a cross-reference to the potential carcinogenicity of glycidol and a comparative discussion of the genetic toxicity be included in the Discussion. Dr. Boorman said that this would be done.

Dr. Mirer, the second principal reviewer, agreed with the conclusions. He thought that the sensitivity of the study in male rats was reduced by excessive mortality, which was unrelated to compound administration. Dr. Mirer commented on the reproductive studies, noting that exposure at 30 ppm appeared to have produced adverse effects in male rats. This was the lowest dose used in the study; therefore, a no-effect level was not established. Dr. Boorman said that reproductive studies would be given more emphasis and that the reproductive toxicology group at NIEHS planned to study other chemicals in the glycidyl ether series, including glycidol.

Dr. Lijinsky, the third principal reviewer, did not agree with the conclusions. He opined that these studies were not designed to produce carcinogenic effects, mainly because the inhalation route limits the dose that may be administered for a high boiling-point compound; he felt that the reproductive studies suffered from the same limitation. Dr. Lijinsky considered the numbers of neoplasms observed to be too few to justify the levels of evidence chosen in male rats and mice. Dr. Boorman responded that the large numbers of preneoplastic lesions, particularily in mice, made the difference. Drs. Popp and Garman supported the level of evidence in male mice; however, Dr. Popp was unsure as to whether he could support equivocal evidence in male rats and female mice. Dr. Lijinsky supported Dr. Ashby's suggestion favoring gavage studies of allyl glycidyl ether, especially since higher concentrations could be given and would allow comparison with the glycidol studies (NTP TR 374).

Dr. Gold said that, based on poor survival (particularly in the high dose group), she considered the studies in male rats to be inadequate. Dr. Boorman noted that the low survival was due primarily to renal disease. Dr. J. Haartz, NIOSH, said that the current NIOSH estimate for the number of workers exposed to allyl gylcidyl ether is about 400.

Dr. Ashby moved (a) that the Technical Report on allyl glycidyl ether be accepted with the conclusions as written for male rats and female mice, equivocal evidence of carcinogenic activity; for female rats, no evidence of carcinogenic activity; and for male mice, some evidence of carcinogenic activity, and (b) that a statement be added to the conclusion for male rats to indicate that the sensitivity for detecting a carcinogenic effect was reduced by excessive mortality. Dr. Garman seconded the motion, for which the vote resulted in a tie, with four affirmative votes (Drs. Ashby, Garman, McKnight, and Mirer) and four negative votes (Drs. Gold, Klaassen, Lijinsky, and Popp). Dr. Scala, the Chair, then cast the tie-breaking vote in favor of acceptance.

I. INTRODUCTION

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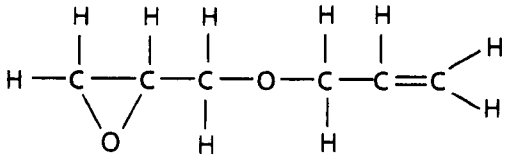

ALLYL GLYCIDYL ETHER

CAS No. 106-92-3

$C_6H_{10}O_2$ Molecular weight 114.1

Synonyms: allyl 2,3-epoxypropyl ether; 1-allyloxy-2,3-epoxypropane; 1,2-epoxy-3-allyloxypropane; glycidyl allyl ether; ((2-propenyloxy)methyl)oxirane; 1-(allyloxy)-2,3-epoxypropane

Physical Properties, Production, and Use

Allyl glycidyl ether is manufactured by the condensation of allyl alcohol and epichlorohydrin, with subsequent dehydrochlorination with caustic to form the epoxy ring (Clayton and Clayton, 1981). It is a clear, combustible, volatile liquid with a boiling point of 153.9° C. Allyl glycidyl ether is used as a resin intermediate and as a stabilizer of chlorinated compounds, vinyl resins, and rubber (Verschueren, 1977; NIOSH, 1978). Precise production data were not found; over 4.5 million kg of glycidyl compounds, the majority of which are glycidyl ethers and glycidyl esters, is produced in or imported by the United States annually (Fed. Regist., 1982).

The allyl group of allyl glycidyl ether can be incorporated into polymer chains, leaving the glycidyl group free for subsequent cross-linking reactions; by varying the amount of allyl glycidyl ether, the degree of cross-linking and the hardness of the final product can be controlled. Cross-linking by bifunctional monomers, including allyl glycidyl ether, is widely used to alter the properties of plastics, vinyl resins, and synthetic rubber.

Human Exposure and Health Effects

Few data on human exposure to allyl glycidyl ether were found in the literature. The National Institute for Occupational Safety and Health (NIOSH) occupational hazard survey estimated that 2,000 workers are potentially exposed to allyl glycidyl ether (Stein et al., 1979). According to a more recent survey, which used National Occupational Exposure Survey data, an estimated 413 people were exposed to allyl glycidyl ether, but this survey was without trade name resolution, suggesting that the exposure numbers are underestimated (NIOSH, 1983). In 1979, the Occupational Safety and Health Administration (OSHA) exposure standard and the NIOSH-recommended exposure ceiling were set at 10 ppm. For 1988/1989, the American Conference of Governmental Industrial Hygienists recommended an exposure limit of 5 ppm for skin, with a short-term exposure limit (STEL) of 10 ppm. In humans, irritation and occasional sensitization may occur from exposure to this compound. The chemical has a pronounced aldehydelike odor at low levels, so that voluntary exposure to serious lung-irritating concentrations is unlikely (Clayton and Clayton, 1981).

Short-Term Toxicity Studies

Oral administration of allyl glycidyl ether to rats and mice produced moderate depression and dyspnea within 20 minutes; death occurred within 4 hours to 5 days after dosing (Hine et al., 1956, 1961). The oral LD_{50} for mice is 0.39 g/kg and for rats is 1.6 g/kg (Hine et al., 1956). Extensive adhesions of the stomach to adjacent tissues were found in rats and mice given lethal doses. The LD_{50} for rabbits by percutaneous absorption is 2.55 g/kg. The inhalation-exposure LC_{50} is 270 ppm for mice (4-hour exposure) and 670 ppm for rats (8-hour exposure). Clinical

signs for inhalation exposure included lacrimation, salivation, and dyspnea. Corneal opacities were also seen in rats (Hine et al., 1961). In rats given four intraperitoneal injections of 400 mg/kg over 9 days and killed 3 days later, focal necrosis of the testis was found in one of three surviving animals and lymphoid atrophy was found in two of three (Kodama et al., 1961).

Reproductive and Developmental Toxicity

A search of the literature did not reveal any studies on reproductive or developmental toxicity of allyl glycidyl ether in animals or humans.

Distribution and Metabolism

A search of the literature did not reveal any studies on distribution and metabolism of this compound.

Genetic Toxicity

Allyl glycidyl ether is clearly genotoxic in in vitro tests, where it has induced gene mutations in bacteria (Wade et al., 1979; Hemminki et al., 1980; Voogd et al., 1981; Canter et al., 1986) and sister chromatid exchanges and chromosomal aberrations in Chinese hamster ovary cells both in the presence and the absence of metabolic activation (Tables K2 and K3). It also induced gene mutations in *Drosophila melanogaster* (Yoon et al., 1985). Because it contains an epoxide group, allyl glycidyl ether may also be clastogenic in vivo, but the limited data available are not sufficient to determine this. Yoon et al. (1985) did not detect an increase in reciprocal translocations after exposing male *D. melanogaster* to 5,500 ppm allyl glycidyl ether, but in a procedure stated to be more sensitive to detection of germ cell clastogens than the reciprocal translocation test, Zimmering (1983) reported induction of chromosomal loss and breakage in a repair-deficient strain of *D. melanogaster* (*mei-9*^{a} test). Results of mouse bone marrow micronucleus tests with a closely related structural analog, *n*-butyl glycidyl ether, indicate that the clastogenic in vivo activity of glycidyl ethers may depend on the route of administration. *n*-Butyl glycidyl ether, which is also mutagenic in bacterial assays (Wade et al., 1979; Conner et al., 1980; Thompson et al., 1981; Canter et al., 1986), did not increase the incidence of micronucleated polychromatic erythrocytes (PCEs) in mice when administered by gavage on 5 consecutive days at doses of 200 mg/kg per day, whereas one or two intraperitoneal injections of 675 or 900 mg/kg produced a significant ($P<0.05$) increase in micronucleated PCEs in mice (Conner et al., 1980). Multiple topical applications (1,500 mg/kg three times per week for 8 weeks) of *n*-butyl glycidyl ether did not induce a significant increase in dominant lethal mutations in the germ cells of male mice (Whorton et al., 1983).

Additional data related to the genotoxic activity of allyl glycidyl ether derive from studies of other compounds in the glycidyl ether series. Two of these related compounds, glycidol (NTP, 1990) and diglycidyl resorcinol ether (NTP, 1986) have activity in a wide variety of bacterial and eukaryotic in vitro and in vivo test systems.

Carcinogenicity

No reports of carcinogenicity studies of allyl glycidyl ether in animals were found in the literature. The epoxide group in this chemical has the potential to form macromolecular adducts, possibly leading to cancer in animals.

Study Rationale

Allyl glycidyl ether was nominated for testing by NIOSH and OSHA because of relatively extensive worker exposure, because its chemical structure (containing an epoxy group and an allyl group) suggests that it may be carcinogenic, and because there was little or no information on the possible toxicity and carcinogenicity of this chemical. Inhalation was chosen as the route of exposure because this chemical is volatile and most worker exposure is by inhalation. At the time the study was designed, several rat strains were being evaluated as potential models to detect chemical toxicity and carcinogenicity; the Osborne-Mendel rat was selected for these studies. The F344/N rat has since become the strain of choice for the National Toxicology Program because of its size, generally lower neoplasm incidence, less severe renal disease, and a more extensive historical data base.

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF ALLYL GLYCIDYL ETHER

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

- Vapor Generation System
- Vapor Concentration Monitoring
- Degradation Study of Allyl Glycidyl Ether in Chamber
- Chamber Characterization

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK TOXICOLOGIC STUDIES AND EIGHT-WEEK STUDIES OF REPRODUCTIVE EFFECTS

TWO-YEAR STUDIES

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

PROCUREMENT AND CHARACTERIZATION OF ALLYL GLYCIDYL ETHER

Allyl glycidyl ether was obtained as a clear, colorless liquid from Alcolac, Inc. (Baltimore, MD) in four lots. Purity and identity analyses for each lot were conducted at Midwest Research Institute, Kansas City, MO (Appendix G). The identity of all lots was confirmed by infrared, nuclear magnetic resonance, and ultraviolet/visible spectroscopic analyses.

The purity of each lot was found to be approximately 99%, as determined by elemental analysis, Karl Fischer water analysis, titration of the epoxide group with 0.1 N perchloric acid, and gas chromatography.

The identity of each lot of the study chemical at the study laboratory was confirmed by infrared spectrometry. The stability of the study material was monitored during the animal studies by gas chromatography and nonaqueous titration of the epoxide group. No deterioration of the study material was seen over the course of the studies.

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

Vapor Generation System

No additional preparation of the liquid allyl glycidyl ether was necessary before introduction into the vapor generation system. The liquid was pumped from a stainless steel reservoir to a vaporizer by a stable micrometering pump with adjustable pump rates.

Vapor Concentration Monitoring

Concentrations of allyl glycidyl ether in the chambers and the exposure room were measured by gas chromatography with a flame ionization detector. During the 14-day and 13-week studies, exposure concentrations of allyl glycidyl ether were within ±10% of the target concentrations. Weekly mean exposure concentrations for the 2-year studies are presented in Appendix G. A summary of the chamber concentrations is presented in Table G2; Table G3 summarizes the distribution of mean daily concentrations.

Degradation Study of Allyl Glycidyl Ether in Chamber

Samples of allyl glycidyl ether exposure atmospheres were analyzed for the presence of potential degradation products by gas chromatography with flame ionization detection. No impurities were observed by gas chromatographic analysis to indicate significant decomposition of allyl glycidyl ether under study conditions.

Chamber Characterization

Uniformity of vapor concentration in each exposure chamber was measured before the start of the studies and was checked by gas chromatography at intervals of approximately 3 months throughout the studies. In most instances, the vapor concentrations were within 10% of the mean target concentration values at all 12 positions sampled within the chamber, indicating good, homogeneous distribution of the study vapor.

FOURTEEN-DAY STUDIES

Groups of five Osborne-Mendel rats of each sex were exposed to air containing allyl glycidyl ether at target concentrations of 0, 25, 50, 100, 200, or 500 ppm, 6 hours per day for 10 days of exposure over 14 days.

Groups of five $B6C3F_1$ mice of each sex were exposed to air containing allyl glycidyl ether at target concentrations of 0, 25, 50, or 100 ppm on the same schedule.

Rats and mice were observed two or three times per day and were weighed before exposure, at week 1, and at necropsy. A necropsy was performed on all animals. Histopathologic examinations were performed on selected animals dying before the end of the studies or exhibiting gross lesions. Further details are presented in Table 1.

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Fourteen-Day Studies	Eight-Week and Thirteen-Week Studies	Two-Year Studies
EXPERIMENTAL DESIGN		
Size of Study Groups		
5 males and 5 females of each species	13 wk--10 males and 10 females of each species; 8-wk reproductive effects studies--20 males and 20 females of each species	50 males and 50 females of each species
Doses		
Rats--0, 25, 50, 100, 200, or 500 ppm allyl glycidyl ether by inhalation; mice--0, 25, 50, or 100 ppm	13 wk--rats: 0, 4, 10, 30, 100, or 200 ppm allyl glycidyl ether by inhalation; mice: 0, 1, 4, 10, or 30 ppm; 8-wk reproductive effects studies--rats: 0, 30, 100, or 200 ppm; mice: 0, 4, 10, or 30 ppm	0, 5, or 10 ppm allyl glycidyl ether by inhalation
Date of First Exposure		
9/3/80	13 wk--9/2/81	6/21/82
Date of Last Exposure		
9/16/80	13 wk--12/1/81	Rats--6/15/84; mice--6/8/84
Duration of Exposure		
6 h/d for 10 exposures over 14 d	6 h/d, 5 d/wk for 8 (reproductive effects studies) or 13 wk	Rats--6 h/d, 5 d/wk for 103 wk; mice--6 h/d, 5 d/wk for 102 wk
Type and Frequency of Observation		
Weighed initially and 1 × wk thereafter; observed 2 or 3 × d	Observed continuously during exposure and 2 × d during nonexposure periods; weighed initially and 1 × wk thereafter	Observed 2 × d; weighed initially, 1 × wk for 12 (rats) or 11 (mice) wk, and then 1 × mo
Necropsy and Histologic Examinations		
Necropsy performed on all animals; histologic exams performed on 1 or 2 animals from the 50-, 100-, 200-, and 500-ppm rat groups and the 25-, 50-, and 100-ppm mouse groups	13 wk--necropsy and histologic exams performed on all animals; the following tissues were examined for the control and high dose groups: adrenal glands, bone marrow, brain, colon, duodenum, esophagus, gallbladder (mice), heart, kidneys, larynx, liver, lungs and bronchi, mammary gland, mandibular lymph nodes, nasal cavity, pancreas, parathyroid glands, pitutitary gland, salivary glands, seminal vesicles/prostate/testes or ovaries/uterus, skin, spleen, stomach, thymus, thyroid gland, trachea, and urinary bladder. Tissues examined for lower dose groups include esophagus, larynx, lungs and bronchi, nasal cavity, thyroid gland, and trachea for rats and larynx, nasal cavity, and trachea for mice	Necropsy performed on all animals; histologic exams performed on all rats and on all control and high dose mice and on mice dying before the end of the studies. Tissues examined include adrenal glands, brain, cecum, colon, duodenum, epididymis/prostate/testes or ovaries/uterus, esophagus, gallbladder (mice), gross lesions and tissue masses with regional lymph nodes, heart, ileum, jejunum, kidneys, larynx, liver, lungs and mainstem bronchi, mammary gland, mandibular lymph nodes, nasal cavity and turbinates, pancreas, parathyroid glands, pituitary gland, preputial or clitoral gland (rats), rectum, salivary glands, skin, spleen, sternebrae including marrow, stomach, thymus, thyroid gland, trachea, tracheobronchial lymph nodes, and urinary bladder. Nasal cavity and gross lesions examined for low dose mice
ANIMALS AND ANIMAL MAINTENANCE		
Strain and Species		
Osborne-Mendel rats; B6C3F$_1$ mice	Osborne-Mendel rats; B6C3F$_1$ mice	Osborne-Mendel rats; B6C3F$_1$ mice
Animal Source		
Rats--CAMM Research Institute (Wayne, NJ); mice--Charles River Breeding Laboratories (Portage, MI)	Rats--CAMM Research Institute (Wayne, NJ); mice--Charles River Breeding Laboratories (Kingston, NY)	Rats--CAMM Research Institute (Wayne, NJ); mice--Charles River Breeding Laboratories (Kingston, NY)

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (Continued)

Fourteen-Day Studies	Eight-Week and Thirteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE (Continued)		
Study Laboratory Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories	Battelle Pacific Northwest Laboratories
Method of Animal Identification Ear tags and cage numbers	Ear tags and cage numbers	Ear tags
Time Held Before Study 21 d	21 d	Rats--24 d; mice--26 d
Age When Placed on Study Rats--8 wk; mice--8-9 wk	Rats--8 wk; mice--8-9 wk	Rats--8 wk; mice--9-10 wk
Age When Killed Rats--10 wk; mice--10-11 wk	13 wk--21 wk	Rats--114 wk; mice--114-115 wk
Necropsy Dates 9/17/80	13 wk--12/2/81-12/4/81	Rats--6/26/84-6/28/84; mice--6/18/84-6/22/84
Method of Animal Distribution Assigned to groups according to tables of random numbers	Animals distributed to weight classes and then assigned to cages by one table of random numbers and to groups by another table of random numbers	Same as 13-wk studies
Diet NIH 07 Rat and Mouse Ration (Zeigler Bros., Inc., Gardners, PA); available ad libitum except during exposure periods	Same as 14-d studies	Same as 14-d studies
Water Automatic watering system (Edstrom Industries, Waterford, WI); available ad libitum	Same as 14-d studies	Same as 14-d studies
Cages Stainless steel wire (Hazleton Systems, Aberdeen, MD)	Same as 14-d studies	Same as 14-d studies
Animals per Cage 1	1	1
Other Chemicals on Study in the Same Room None	None	Bromoethane--12/30/81-12/30/83
Chamber Environment Temp--73°-76° F; hum--44%-70%; fluorescent light 12 h/d; 10 (exposure) or 20 (nonexposure) room air changes/h	Temp--69°-80° F; hum--32%-75%; fluorescent light 12 h/d	Temp--67°-82° F; hum--36%-89%; fluorescent light 12 h/d; approximately 20 room air changes/h

THIRTEEN-WEEK TOXICOLOGIC STUDIES AND EIGHT-WEEK STUDIES OF REPRODUCTIVE EFFECTS

Thirteen-week studies were conducted to evaluate the cumulative toxic effects of repeated exposure to allyl glycidyl ether and to determine the concentrations to be used in the 2-year studies.

Male and female Osborne-Mendel rats were obtained from CAMM Research Laboratory; male and female B6C3F$_1$ mice were obtained from Charles River Breeding Laboratories. Animals were observed for 21 days, distributed to weight classes, and assigned to groups according to tables of random numbers. Feed was available ad libitum during nonexposure periods; water was available at all times.

Groups of 10 rats of each sex were exposed to air containing allyl glycidyl ether at target concentrations of 0, 4, 10, 30, 100, or 200 ppm for 6 hours per day, 5 days per week for 13 weeks. Groups of 10 mice of each sex were exposed to air containing allyl glycidyl ether at target concentrations of 0, 1, 4, 10, or 30 ppm on the same schedule. For studies of reproductive effects, groups of 20 rats of each sex were exposed to air containing allyl glycidyl ether at target concentrations of 0, 30, 100, or 200 ppm for 6 hours per day, 5 days per week for 8 weeks. Groups of 20 mice of each sex were exposed to air containing allyl glycidyl ether at target concentrations of 0, 4, 10, or 30 ppm on the same schedule. Further experimental details are summarized in Table 1.

Animals were observed continuously during exposure and were observed before and after exposure; moribund animals were humanely killed. Animal weights were recorded before the studies, once per week, and at necropsy. At the end of the 13-week studies, survivors were killed. A necropsy was performed on all animals except one male rat in the 100-ppm group. Histopathologic examinations were performed on tissues of all control and the highest dose groups and on selected tissues of lower dose groups. Further experimental details are summarized in Table 1.

Mating was begun 2 days after the end of the 8-week exposure period for the reproductive effects studies--controls with controls, exposed males with control females, and control males with exposed females. Animals cohabitated up to 7 days or until sperm were detected in the vaginal lavage of female rats or a vaginal plug was detected in female mice. Males were then separated from females. Three control mice and one mouse exposed to 10 ppm were removed from the study after becoming pregnant during the exposure period; three controls from the 13-week studies were substituted for the pregnant controls.

All male animals were killed 13-14 days after the last allyl glycidyl ether exposure. Both cauda epididymides were removed from eight males of each species. Sperm were counted and examined for motility and for abnormalities.

Females in which copulation was detected were separated into two groups. One group of mice was killed on day 17 of pregnancy, and one group of rats was killed on day 19 of pregnancy; rats in the second group, together with mated females for which copulation was not detected, were killed along with their pups on day 21 post partum. Animals killed during pregnancy were weighed, necropsies were performed, and uteri and ovaries were removed and weighed. Corpora lutea were counted, and implantation sites were located. The number of live and dead fetuses and resorption sites were counted in each uterine horn. Fetuses were killed, weighed, and examined for sex and malformations.

Pregnant animals were observed twice per day. On days 1 and 4 after birth, the gender of pups was determined and pups were weighed and examined for external abnormalities. Dams were weighed on day 13 post partum. At necropsy, ovaries and uteri of dams were removed, and corpora lutea and implantation sites were counted. A necropsy was performed on all animals. Further details are given in Appendix H.

TWO-YEAR STUDIES

Study Design

Groups of 50 rats and 50 mice of each sex were exposed to air containing allyl glycidyl ether at concentrations of 0 (chamber controls), 5, or 10 ppm for 6 hours per day, 5 days per week for 103

weeks for rats or 102 weeks for mice. Actual concentrations are summarized in Tables G2 and G3 and Figures G7 through G10. On December 7, 1983, rats and mice in the 5-ppm chamber were inadvertently exposed to *N,N*-dimethylformamide (maximum concentration, 13 ppm; mean concentration, 6 ppm) for 71 minutes.

Source and Specifications of Animals

The male and female Osborne-Mendel rats were obtained from CAMM Research Institute. The male and female B6C3F$_1$ (C57BL/6N, female × C3H/HeN MTV$^-$, male) mice used in these studies were produced under strict barrier conditions at Charles River Breeding Laboratories. Breeding stock for the foundation colony of mice at the production facility originated at the National Institutes of Health Repository. Animals shipped for study were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. Rats were shipped to the study laboratory at 5 weeks of age, and mice were shipped at 5-6 weeks of age. The animals were quarantined at the study laboratory for 3-4 weeks. Thereafter, a complete necropsy was performed on five animals of each sex and species to assess their health status. Rats were placed on study at 8 weeks of age and mice at 9-10 weeks of age.

Animal Maintenance

Rats and mice were housed individually. Feed (Appendix F) was available ad libitum during nonexposure periods; water was available at all times. Serologic analyses were performed as described in Appendix E. Further details of animal maintenance are summarized in Table 1.

Clinical Examinations and Pathology

All animals were observed two times per day. Body weights were recorded once per week for the first 12 weeks of the study (rats) or 11 weeks (mice) and once per month thereafter. Mean body weights were calculated for each group. Animals found moribund and those surviving to the end of the studies were humanely killed. A necropsy was performed, but certain tissues and organs were not examined for some animals because of loss or extensive autolysis. 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.

During necropsy, all organs and tissues were examined for grossly visible lesions. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. For mice, histopathologic examination of tissues was performed according to an "inverse pyramid" design (McConnell, 1983a,b). That is, complete histopathologic examinations (Table 1) were performed on all high dose and control animals and on low dose animals dying before the end of the study. In addition, histopathologic examinations were performed on all grossly visible lesions in all dose groups. Potential target organs for chemically related neoplastic and nonneoplastic effects were identified from the short-term studies or the literature and were determined by examination of the pathology data; these target organs/tissues in the lower dose group were examined histopathologically.

When the pathology evaluation was completed by the laboratory pathologist and the pathology data entered into the Toxicology Data Management System, the slides, paraffin blocks, and residual formalin-fixed tissues were sent to the National Toxicology Program (NTP) Archives. The slides, blocks, and residual wet tissues were audited for accuracy of labeling and animal identification and for thoroughness of tissue trimming. The slides, individual animal necropsy records, and pathology tables were sent to an independent pathology quality assessment laboratory. The individual animal records and pathology tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tissues with a tumor diagnosis, all potential target tissues (male rats: nasal passage, lung, thyroid gland; female rats: nasal passage, lung; male mice: nasal passage, kidney; female mice: nasal passage, kidney, bone marrow), and all tissues from a randomly selected 10% of the animals were reevaluated microscopically by a quality assessment pathologist. Nonneoplastic lesions were evaluated for accuracy and consistency of diagnosis only in the potential target organs, in the

randomly selected 10% of animals, and in tissues with unusual incidence patterns or trends. Tissues are generally not evaluated in a "blind" fashion (i.e., without knowledge of dose group) unless the lesions in question are subtle.

The quality assessment report and slides were submitted to a Pathology Working Group (PWG) Chairperson, who reviewed microscopically the nasal passage and lung in rats and the nasal passage and kidney in mice as potential target tissues and any other tissues for which there was a disagreement in diagnosis between the laboratory and quality assessment pathologists. The pituitary gland and liver neoplasms in mice were also reviewed because of negative trends. Representative examples of potential chemical-related nonneoplastic lesions and neoplasms, especially those of the nasal passage, and examples of disagreements in diagnosis between the laboratory and quality assessment pathologists were evaluated by the PWG. The PWG included the laboratory pathologist (for rats but not mice), the quality assessment pathologist, and other pathologists experienced in rodent toxicology (especially nasal lesions) who examined the tissues without knowledge of dose group or previously rendered diagnoses. When the consensus diagnosis of the PWG differed from that of the laboratory pathologist, the diagnosis was changed to reflect the opinion of the PWG. This procedure has been described, in part, by Maronpot and Boorman (1982) and Boorman et al. (1985). The final pathology data represent a consensus of contractor pathologists and the NTP Pathology Working Group. For subsequent analysis of pathology data, the diagnosed lesions for each tissue type are combined according to the guidelines of McConnell et al. (1986).

Statistical Methods

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

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

Analysis of Tumor Incidence: The majority of tumors in this study were considered to be incidental to the cause of death or not rapidly lethal. Thus, the primary statistical method used was a logistic regression analysis, which assumed that the diagnosed tumors were discovered as the result of death from an unrelated cause and thus did not affect the risk of death. In this approach, tumor prevalence was modeled as a logistic function of chemical exposure and time. Both linear and quadratic terms in time were incorporated initially, and the quadratic term was eliminated if it did not significantly enhance the fit of the model. The dosed and control groups were compared on the basis of the likelihood score test for the regression coefficient of dose. This method of adjusting for intercurrent mortality is the prevalence analysis of Dinse and Lagakos (1983), further described and illustrated by Dinse and Haseman (1986). When tumors are incidental, this comparison of the time-specific tumor prevalences also provides a comparison of the time-specific tumor incidences (McKnight and Crowley, 1984).

In addition to logistic regression, alternative methods of statistical analysis were used, and the results of these tests are summarized in the appendixes. These include the life table test

(Cox, 1972; Tarone, 1975), appropriate for rapidly lethal tumors, and the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart et al., 1979), procedures based on the overall proportion of tumor-bearing animals.

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

Historical Control Data: Although the concurrent control group is always the first and most appropriate control group used for evaluation, there are certain instances in which historical control data can be helpful in the overall assessment of tumor incidence. Consequently, control tumor incidences for $B6C3F_1$ mice from the NTP historical control data base (Haseman et al., 1984, 1985) are included for those tumors appearing to show compound-related effects. Only one study using untreated control Osborne-Mendel rats is included in the NTP data base (NTP, 1988). The incidences of tumors observed in that study are included for appropriate sites.

III. RESULTS

RATS

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK TOXOCOLOGIC STUDIES AND EIGHT-WEEK STUDIES OF REPRODUCTIVE EFFECTS

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

FOURTEEN-DAY STUDIES

THIRTEEN-WEEK TOXOCOLOGIC STUDIES AND EIGHT-WEEK STUDIES OF REPRODUCTIVE EFFECTS

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

GENETIC TOXICOLOGY

FOURTEEN-DAY STUDIES

All rats exposed to 500 ppm and one male rat exposed to 100 ppm died before the end of the studies (Table 2). The final mean body weights of male rats exposed to 25, 50, 100, or 200 ppm were 8%-12% lower than that of the controls. Mean body weights of exposed rats at necropsy were 55%-77% those of controls for males and 66%-83% for females. Rats exposed to 200 or 500 ppm had signs of respiratory distress, and initially, all exposed rats had excessive lacrimation and rhinorrhea. Two male rats and one female rat in the 50-ppm groups, two rats in the 100-ppm groups, one rat in the 200-ppm group, and two male rats and one female rat in the 500-ppm groups were examined histologically. Rhinitis was seen in all examined rats; the severity increased with increasing exposure concentration from slight rhinitis to marked fibrinopurulent rhinitis at 500 ppm. Moderate-to-marked laryngitis and tracheitis, marked destruction of the entire upper respiratory tract epithelium, and evidence of widespread lymphoid depletion/necrosis were seen in rats exposed to 500 ppm. Mild squamous metaplasia of the nasal turbinate epithelium was seen in all three nasal passage sections examined in animals exposed to 200 ppm.

TABLE 2. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-DAY INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Necropsy	Change (c)	Necropsy Weight Relative to Controls (percent)
MALE					
0	5/5	235 ± 4	316 ±11	+81 ± 8	
25	5/5	230 ± 3	292 ± 5	+63 ± 3	92
50	5/5	232 ± 4	291 ± 3	+58 ± 2	92
100	(d) 4/5	233 ± 5	282 ± 8	+50 ± 7	89
200	5/5	234 ± 6	279 ± 8	+45 ± 2	88
500	(e) 0/5	235 ± 8	(f)	(f)	(f)
FEMALE					
0	5/5	168 ± 3	214 ± 3	+47 ± 4	
25	5/5	169 ± 4	202 ± 5	+33 ± 3	94
50	5/5	167 ± 3	198 ± 3	+31 ± 2	93
100	5/5	171 ± 2	207 ± 3	+36 ± 3	97
200	5/5	171 ± 5	209 ± 5	+39 ± 4	98
500	(g) 0/5	168 ± 3	(f)	(f)	(f)

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean, based on prerandomization weights. Subsequent calculations are based on animals surviving to the end of the study.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Day of death: 11
(e) Day of death: 2,3,3,4,5
(f) No data are reported due to 100% mortality in this group.
(g) Day of death: 2,3,4,4,5

THIRTEEN-WEEK TOXICOLOGIC STUDIES AND EIGHT-WEEK STUDIES OF REPRODUCTIVE EFFECTS

All rats lived to the end of the 13-week studies (Table 3). The final mean body weights of male rats exposed to 10, 30, 100, or 200 ppm were 7%, 13%, 19%, or 24% lower than that of controls. The final mean body weights of female rats exposed to 30, 100, or 200 ppm were 7%, 8%, or 13% lower than that of controls. Primarily because of lower body weights, the liver weight to body weight ratios for exposed rats were greater than those for controls; liver weight to body weight ratios were concentration related for females but not for males (Table 4). Nasal lesions, including inflammation, epithelial hyperplasia, and squamous metaplasia, were seen in all exposed groups of rats, and hyperostosis of the nasal turbinate bone was seen in rats exposed to 30, 100, or 200 ppm (Table 5). The lesion diagnosed as hyperostosis was very minimal, consisting of mucosal fibrosis with slight bone remodeling and sclerosis associated with overlying inflammatory lesions. The lesion was not diffuse and was not typical of the hyperostosis that is commonly seen in F344/N rats. Metaplasia of the larynx, trachea, and bronchi was seen in rats exposed to 10, 30, 100, or 200 ppm. Focal fibrosis of the anterior dorsal part of the nasal passage was seen at 200 ppm in males and at 100 or 200 ppm in females. A chronic inflammatory change characteristic of viral pneumonia was seen in the lung of control animals. All control males had a focal inflammatory change of the lung with a mean severity of 2.6 (1 = minimal, 4 = marked), whereas exposed animals had lower incidences and less severe lesions than did the controls (mean severity less than 1). The lesions were multifocal infiltrates of alveolar macrophages, perivascular lymphoid infiltrates, and type II cell hyperplasia. A similar pattern of a higher incidence and more severe inflammatory lesions in controls was also found for the female rats. In contrast, inflammatory lesions of the nasal passage were exposure related, with a higher incidence and greater severity in exposed than in control animals. Positive titers to pneumonia virus of mice were seen in 9/10 rats tested at the beginning and at the end of the studies. Positive titers to Sendai virus were seen in 4/10 rats tested at the beginning of the studies and in 10/10 rats tested at the end of the studies.

Two of 20 male rats exposed to 200 ppm died before the end of the 8-week studies of reproductive effects. The reproductive performance of males, but not of females, was found to be impaired, but only at overtly toxic concentrations (Table I2). Although copulation plugs were detected, few females bred to males exposed to allyl glycidyl ether produced litters (Table I3). No increase in malformed fetuses was observed. The glycidyls are being evaluated by the National Toxicology Program to determine if further reproductive studies are warranted.

Dose Selection Rationale: Because of lower weight gain at higher concentrations, exposure concentrations of allyl glycidyl ether selected for rats for the 2-year studies were 5 and 10 ppm, 6 hours per day, 5 days per week. The doses selected were expected to induce lesions of the nasal passage, but they were not considered life threatening.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of male rats exposed to 10 ppm were within 7% of those of controls throughout most of the studies (Table 6 and Figure 1). Mean body weights of female rats exposed to 10 ppm were 6%-8% lower than those of controls after week 35. No compound-related clinical signs were observed.

TABLE 3. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE THIRTEEN-WEEK INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	263 ± 3	448 ± 8	+185 ± 5	
4	10/10	261 ± 4	432 ± 10	+171 ± 7	96
10	10/10	269 ± 3	415 ± 5	+146 ± 3	93
30	10/10	271 ± 4	390 ± 5	+119 ± 4	87
100	10/10	266 ± 5	363 ± 8	+97 ± 6	81
200	10/10	264 ± 4	339 ± 8	+75 ± 5	76
FEMALE					
0	10/10	178 ± 3	262 ± 4	+84 ± 2	
4	10/10	180 ± 4	255 ± 7	+75 ± 4	97
10	10/10	188 ± 3	261 ± 8	+73 ± 5	100
30	10/10	184 ± 4	243 ± 8	+59 ± 10	93
100	10/10	181 ± 3	242 ± 5	+61 ± 2	92
200	10/10	179 ± 4	228 ± 6	+49 ± 4	87

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

TABLE 4. LIVER WEIGHTS OF RATS IN THE THIRTEEN-WEEK INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

Concentration (ppm)	Number Weighed	Necropsy Body Weight (grams)	Liver Weight (grams)	Liver Weight/ Necropsy Body Weight (mg/g)
MALE				
0	9	423 ± 6.9	12.4 ± 0.5	29.3 ± 1.13
4	9	*396 ± 9.3	14.1 ± 0.9	*35.6 ± 2.21
10	10	*395 ± 4.4	13.5 ± 0.8	34.2 ± 1.71
30	9	**375 ± 5.0	13.4 ± 0.4	*35.7 ± 1.17
100	10	**343 ± 8.5	10.7 ± 0.3	31.2 ± 1.21
200	10	**317 ± 7.3	10.7 ± 0.5	33.8 ± 0.96
FEMALE				
0	10	250 ± 13.3	6.4 ± 0.4	25.6 ± 0.97
4	9	237 ± 6.3	6.8 ± 0.4	28.7 ± 1.43
10	10	240 ± 4.6	7.4 ± 0.5	*30.8 ± 1.77
30	10	231 ± 5.8	7.1 ± 0.3	*30.7 ± 1.84
100	9	222 ± 6.1	7.4 ± 0.4	**33.3 ± 1.26
200	10	**210 ± 5.5	7.1 ± 0.3	**33.8 ± 0.86

(a) Mean ± standard error; P values vs. the controls by Dunnett's test (Dunnett, 1955).
*P<0.05
**P<0.01

TABLE 5. NUMBERS OF RATS WITH SELECTED LESIONS IN THE THIRTEEN-WEEK INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

Site/Lesion	Control	4 ppm	10 ppm	30 ppm	100 ppm	200 ppm
MALE						
Nasal passage (b)						
Inflammation	0	5 (0.8)	5 (1.0)	10 (1.4)	8 (1.9)	10 (2.8)
Epithelial hyperplasia	0	10 (2.0)	10 (2.4)	10 (3.0)	9 (3.7)	10 (3.4)
Squamous metaplasia	0	10 (2.0)	10 (2.2)	10 (3.0)	9 (3.2)	10 (3.9)
Hyperostosis	0	0	0	(c) 2	8 (1.1)	9 (2.4)
Focal fibrosis (c)	0	0	0	1	1	7
Larynx, metaplasia	0	--	1 (1.0)	5 (0.7)	9 (1.5)	10 (3.0)
Trachea, metaplasia	0	--	0	0	3 (1.0)	10 (2.5)
Bronchi, metaplasia	0	--	0	0	0	10 (2.4)
FEMALE						
Nasal passage						
Inflammation	0	8 (1.0)	9 (1.2)	7 (1.1)	10 (2.0)	10 (2.9)
Epithelial hyperplasia	0	10 (1.2)	10 (2.9)	10 (2.5)	10 (2.3)	10 (3.0)
Squamous metaplasia	0	10 (1.3)	10 (2.0)	10 (2.6)	10 (3.0)	10 (3.9)
Hyperostosis	0	0	0	1 (1.0)	6 (1.0)	10 (2.4)
Focal fibrosis (c)	0	0	0	0	3	6
Larynx, metaplasia	0	--	0	4 (0.5)	4 (0.6)	7 (1.9)
Trachea, metaplasia	0	--	0	0	1 (1.0)	6 (1.5)
Bronchi, metaplasia	0	--	0	0	0	4 (1.0)

(a) Ten animals were examined for each group unless otherwise specified. Mean severity is indicated in parentheses; (0) = no lesion; (1) = minimal; (2) = mild; (3) = moderate; (4) = marked.
(b) Nine animals were examined in the 100-ppm group.
(c) No severity was reported.

TABLE 6. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

Weeks on Study	Chamber Control		5 ppm			10 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors
MALE								
1	177	50	187	106	50	182	103	50
2	256	50	257	100	50	254	99	50
3	293	50	290	99	50	291	99	50
4	324	50	320	99	50	315	97	50
5	342	50	340	99	50	335	98	50
6	363	50	357	98	50	352	97	50
7	379	50	369	97	50	367	97	50
8	390	50	383	98	50	381	98	50
9	405	50	396	98	50	391	97	50
10	412	50	402	98	50	400	97	50
11	424	50	413	97	50	408	96	50
12	431	50	417	97	50	414	96	50
13	441	50	430	98	50	420	95	50
17	453	50	439	97	50	437	96	49
21	466	50	462	99	50	457	98	49
26	486	50	473	97	50	468	96	49
30	505	50	492	97	50	487	96	49
35	516	50	510	99	49	500	97	49
39	522	50	511	98	49	508	97	49
43	512	50	521	102	49	515	101	47
47	547	50	519	95	49	518	95	45
51	531	49	514	97	49	511	96	45
56	537	48	523	97	49	516	96	45
60	544	47	531	98	49	523	96	45
66	549	45	536	98	46	531	97	44
70	560	44	548	98	44	544	97	44
74	563	42	532	94	42	538	96	43
79	559	41	542	97	38	541	97	39
84	555	37	535	96	34	524	94	35
88	551	31	535	97	30	534	97	25
91	553	29	536	97	27	524	95	21
95	554	25	538	97	21	514	93	16
99	553	21	524	95	15	508	92	11
103	540	18	524	97	12	518	96	9
Mean for weeks								
1-13	356.7		350.8	98		346.9	97	
17-51	504.2		493.4	98		489.0	97	
56-103	551.5		533.7	97		526.3	95	

TABLE 6. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (Continued)

Weeks on Study	Chamber Control		5 ppm			10 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors
FEMALE								
1	157	50	154	98	50	150	96	50
2	187	50	187	100	50	181	97	50
3	201	50	203	101	50	197	98	50
4	218	50	220	101	50	209	96	50
5	227	50	229	101	50	216	95	50
6	234	50	235	100	50	226	97	49
7	243	50	242	100	50	232	95	49
8	249	50	250	100	50	237	95	49
9	254	50	255	100	50	242	95	49
10	258	50	259	100	50	245	95	49
11	261	50	263	101	50	249	95	49
12	267	50	266	100	50	253	95	49
13	271	50	272	100	50	256	94	49
17	276	50	279	101	50	263	95	49
21	282	50	285	101	50	270	96	49
26	291	50	287	99	49	276	95	49
30	292	50	293	100	49	283	97	49
35	296	49	298	101	49	285	96	48
39	302	49	299	99	49	285	94	48
43	308	48	305	99	49	290	94	46
47	311	48	304	98	48	292	94	46
51	310	48	305	98	47	292	94	44
56	315	48	310	98	47	292	93	43
60	318	48	314	99	46	299	94	43
66	325	48	325	100	45	300	92	42
70	331	46	331	100	44	306	92	42
74	336	46	333	99	44	308	92	42
79	338	43	341	101	44	318	94	42
84	336	42	347	103	41	313	93	39
88	345	39	344	100	39	317	92	38
91	343	38	343	100	38	315	92	36
95	350	36	343	98	35	321	92	33
99	358	33	344	96	33	336	94	32
103	365	29	344	94	33	338	93	29
Mean for weeks								
1-13	232.8		233.5	100		222.5	96	
17-51	296.4		295.0	100		281.8	95	
56-103	338.3		334.9	99		313.6	93	

(a) Weeks on study calculated from 6/11/82

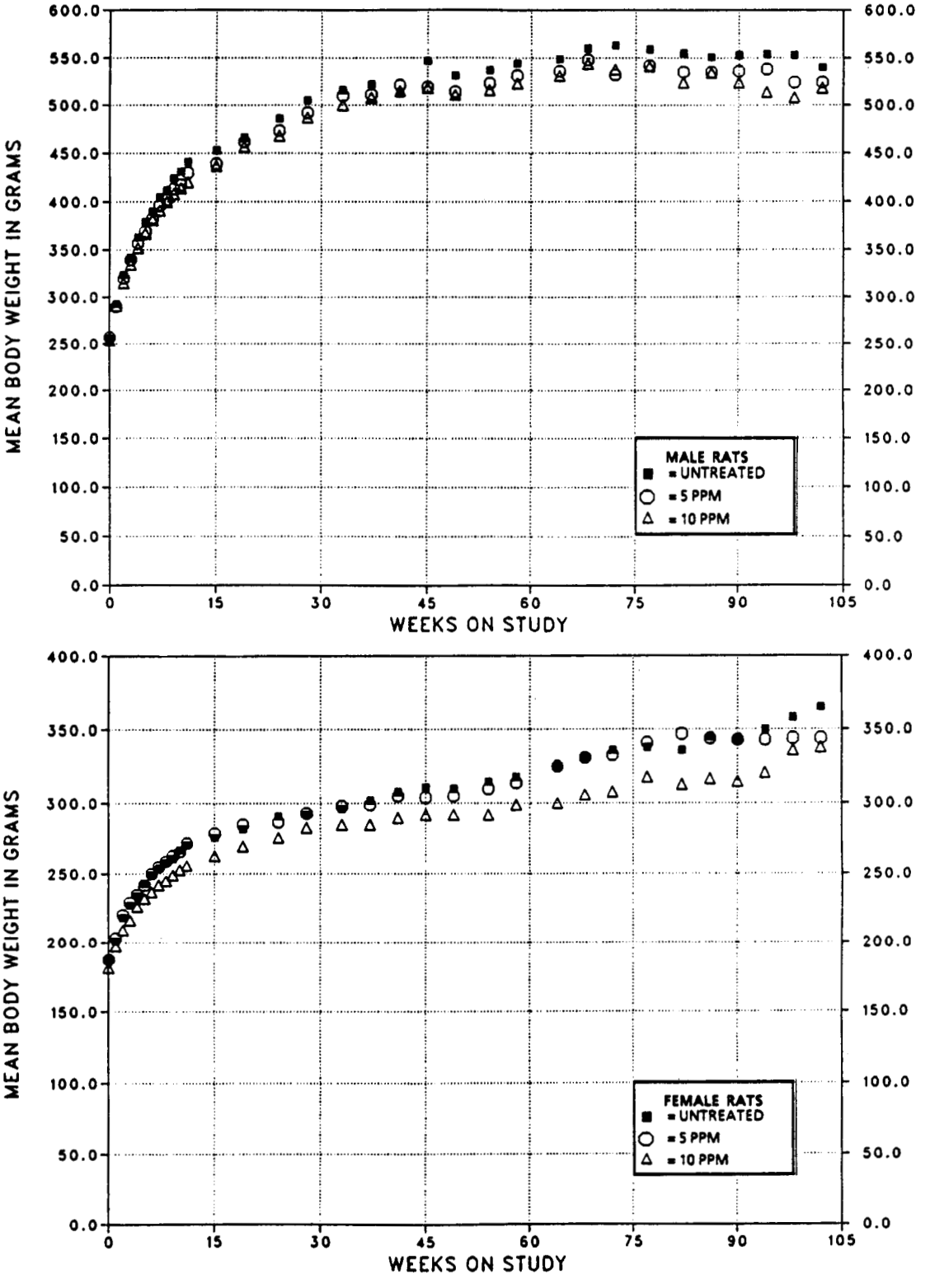

FIGURE 1. GROWTH CURVES FOR OSBORNE-MENDEL RATS EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female rats exposed to allyl glycidyl ether at the concentrations used in these studies and for controls are shown in Table 7 and in the Kaplan and Meier curves in Figure 2. No significant differences in survival were seen between any groups of either sex. The survival of all groups of male rats was low. Since there were no contemporary inhalation studies using Osborne-Mendel rats fed NIH 07 Rat and Mouse Ration, it cannot be determined if the survival in the current studies was usual. Most male rats had advanced renal disease.

Pathology and Statistical Analyses of Results

This section describes the statistically significant or biologically noteworthy changes in the incidences of rats with neoplastic or nonneoplastic lesions of the nasal passage and lung.

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one animal group are presented in Appendixes A and B for male and female rats, respectively.

TABLE 7. SURVIVAL OF RATS IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
MALE (a)			
Animals initially in study	50	50	50
Natural deaths	27	27	29
Moribund kills	11	13	13
Animals surviving until study termination	12	(b) 11	8
Mean survival (days)	631	618	590
Survival P values (c)	0.124	0.592	0.138
FEMALE (a)			
Animals initially in study	50	50	50
Natural deaths	9	8	5
Moribund kills	17	12	20
Animals surviving until study termination	24	30	25
Mean survival (days)	668	663	637
Survival P values (c)	0.942	0.428	1.000

(a) First day of termination period: 737
(b) One animal died or was killed in a moribund condition during the termination period and was combined, for statistical purposes, with those killed at termination.
(c) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

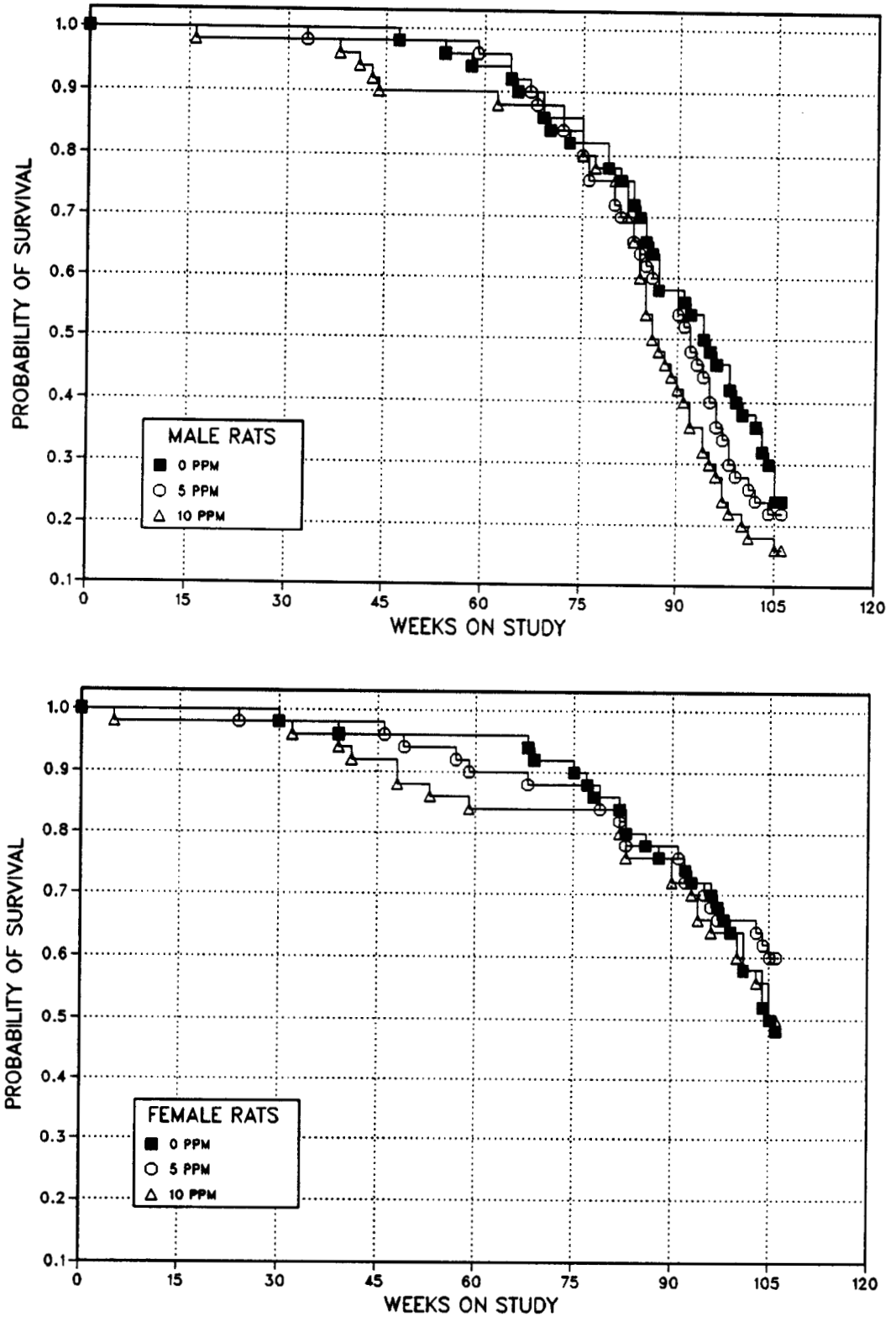

FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR OSBORNE-MENDEL RATS EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR TWO YEARS

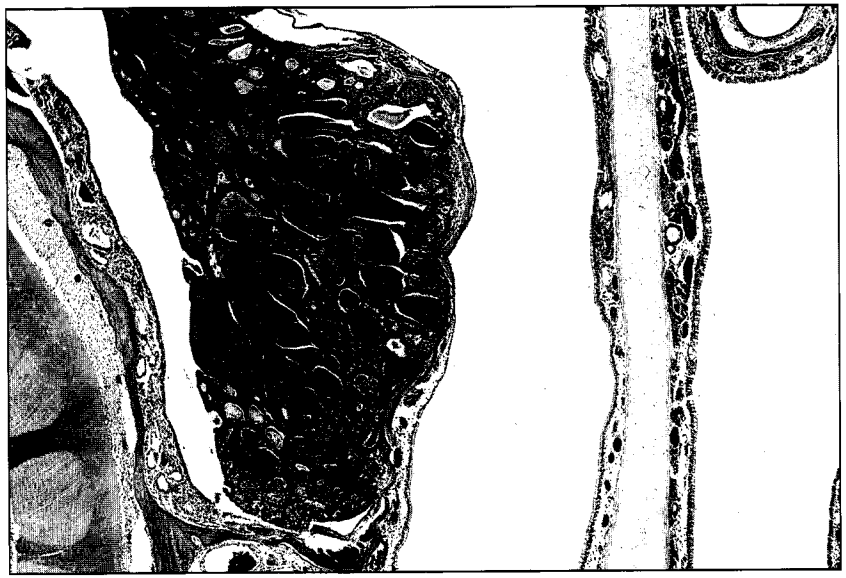

Figure 3. Papillary adenoma arising from the maxilloturbinate in the nasal passage of high concentration (10 ppm) male rat CID no. 2071.

Figure 4. Squamous cell carcinoma from the nasal passage of high concentration (10 ppm) male rat CID no. 2121. Areas of keratin production (arrows) can be seen.

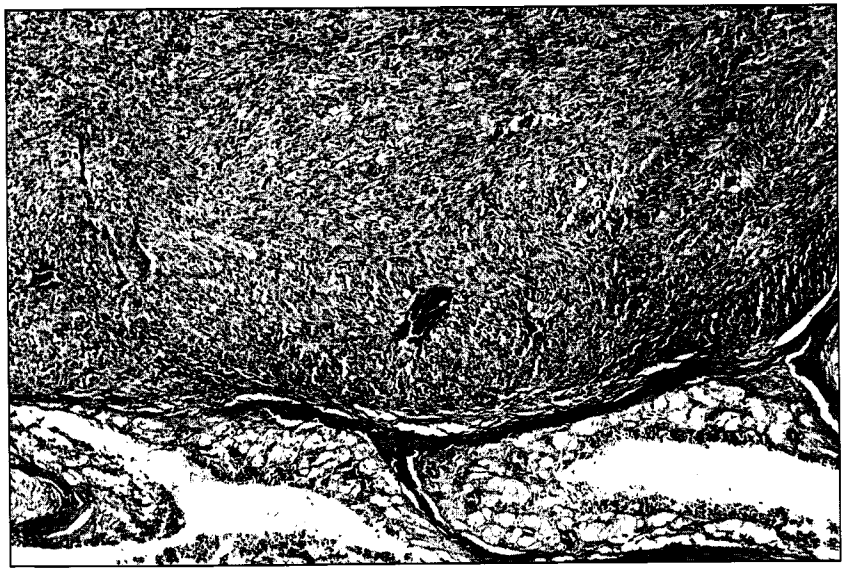

Figure 5. Nasal passage of high concentration (10 ppm) male rat CID no. 2391 with a poorly differentiated adenocarcinoma considered to be of olfactory origin. In this area, the tumor cells have a spindle appearance.

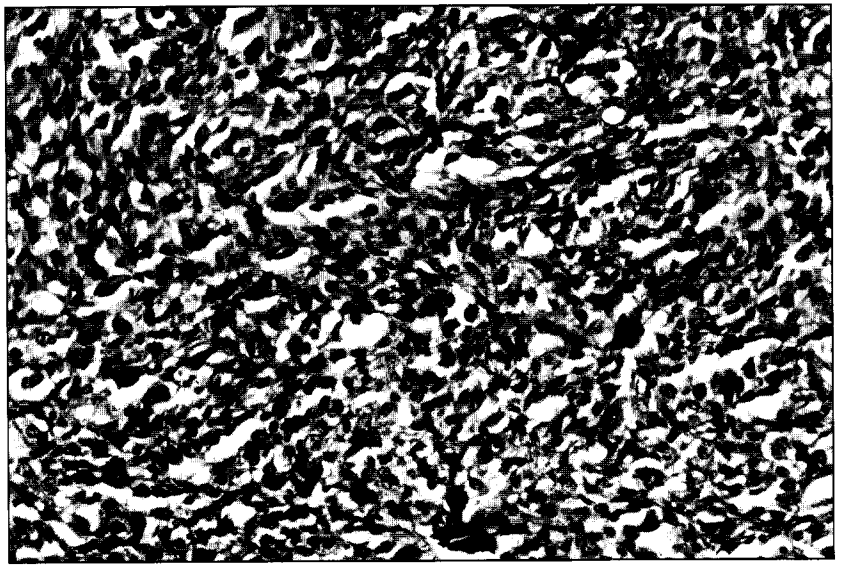

Figure 6. Higher magnification of the neoplasm in high concentration (10 ppm) male rat CID no. 2391 showing the poorly differentiated pattern.

Nasal Passage: Suppurative inflammation, dilatation of the nasal gland, degeneration and metaplasia of the olfactory epithelium, and hyperplasia and metaplasia of the respiratory epithelium were observed at increased incidences in exposed rats (Table 8). Three male rats exposed at 10 ppm had neoplasms of the nasal passage, including an adenocarcinoma of the olfactory epithelium and a papillary adenoma and a squamous cell carcinoma of the respiratory epithelium (Figures 3 through 6). The adenoma was a sessile projection on a narrow base; the neoplasm was composed of cuboidal-to-columnar cells forming small acini and growing in solid sheets. Mitotic figures were uncommon. The squamous cell carcinoma appeared to arise in the dorsal meatus at level I (the most anterior histologic section of the nasal passage taken for examination) and obliterated most of the nasal passage on that side. The neoplasm invaded the bone, numerous mitotic figures were seen, and the tumor cells produced abundant keratin. There is no evidence of other preneoplastic lesions that would be expected to lead to either the papillary adenoma or the squamous cell carcinoma. The adenocarcinoma of the olfactory epithelium contained both areas of spindle cells and areas of epithelial cells containing rosettes, suggestive of neuroblast origin.

Lung: Hyperplasia of the alveolar epithelium was observed at increased incidences in exposed female rats (Table 8). Aggregates of alveolar macrohages (histiocytes) were observed at higher incidences in rats exposed to allyl glycidyl ether than in controls, but the lesion appeared similar to naturally occurring lesions of aging rats. The lesions were often associated with type II cell hyperplasia, but the lesions were minimal and were not of a greater severity in exposed than in control animals.

TABLE 8. NUMBERS OF RATS WITH SELECTED LESIONS OF THE RESPIRATORY TRACT IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Site/Lesion	Male			Female		
	Chamber Control	5 ppm	10 ppm	Chamber Control	5 ppm	10 ppm
Nasal passage (number examined)	44	46	43	49	48	47
Suppurative inflammation	9	**27	*18	5	7	11
Nasal glands						
Dilatation	8	*20	**21	9	**29	**39
Olfactory epithelium						
Degeneration	0	**45	**43	0	**46	**47
Metaplasia	0	*6	**9	0	**9	**31
Squamous metaplasia	0	**19	**35	0	4	*6
Adenocarcinoma	0	0	1	0	0	0
Respiratory epithelium						
Hyperplasia	4	**33	**30	1	**18	**22
Metaplasia	4	**40	**38	0	**37	**38
Papillary adenoma	0	0	1	0	1	0
Squamous cell carcinoma	0	0	1	0	0	0
Lung (number examined)	42	48	45	49	50	49
Alveolar epithelium hyperplasia	2	6	5	4	**14	**14
Alveolar histiocytic cellular infiltration	7	*17	**19	21	**41	*31
Adenosquamous carcinoma	0	0	0	0	1	0

* $P<0.05$ vs. controls by logistic regression analysis
** $P<0.01$ vs. controls by logistic regression analysis

FOURTEEN-DAY STUDIES

All male mice and 3/5 female mice exposed to 100 ppm and 2/5 male and 1/5 female mice exposed to 50 ppm died before the end of the studies (Table 9). Male mice exposed to 50 ppm and female mice exposed to 25 or 100 ppm lost weight. The final mean body weight of male mice exposed to 25 ppm was 15% lower than that of controls; the final mean body weight of female mice exposed to 50 ppm was 10% lower than that of controls. One male and two female mice in the 100-ppm groups were examined histologically. All had slight-to-mild suppurative rhinitis, and two had slight squamous metaplasia of the nasal turbinate epithelium.

THIRTEEN-WEEK TOXICOLOGIC STUDIES AND EIGHT-WEEK STUDIES OF REPRODUCTIVE EFFECTS

Three of 10 male mice and 2/10 female mice exposed to 1 ppm died before the end of the 13-week studies (Table 10). No deaths occurred at 4, 10, or 30 ppm. Final mean body weights at 4, 10, or 30 ppm were 6%, 12%, or 13% lower than that of controls for males and 11%, 18%, or 12% lower for females. Liver weights were not affected by exposure to allyl glycidyl ether (Table 11). Nasal passage lesions, including squamous metaplasia of the respiratory epithelium and the olfactory epithelium, and chronic inflammation of the mucosa were seen in male and female mice at all exposure concentrations (Table 12). Squamous metaplasia was more severe in the anterior nasal passage and most prominent in the dorsal portion of the dorsal meatus. Epithelial erosion was seen at 30 ppm only. Positive titers to Sendai virus were seen in 8/10 mice tested at the end of the studies.

The reproductive performance of exposed males and females was unaffected by exposure to allyl glycidyl ether (Appendix J).

Dose Selection Rationale: Because of lower weight gain at higher concentrations (males), exposure concentrations of allyl glycidyl ether selected for mice for the 2-year studies were 5 and 10 ppm, 6 hours per day, 5 days per week. Because nasal passage lesions were seen at all exposure concentrations, much lower exposure

TABLE 9. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	5/5	23.2 ± 0.4	27.0 ± 0.6	+3.8 ± 0.4	
25	5/5	21.8 ± 1.0	23.0 ± 0.9	+1.2 ± 0.4	85.2
50	(d) 3/5	22.8 ± 0.8	21.3 ± 0.9	−2.0 ± 0.6	78.9
100	(e) 0/5	21.6 ± 0.4	(f)	(f)	(f)
FEMALE					
0	5/5	18.2 ± 0.4	22.6 ± 0.4	+4.4 ± 0.2	
25	5/5	20.8 ± 0.4	20.2 ± 0.2	−0.6 ± 0.2	89.4
50	(g) 4/5	19.2 ± 0.2	20.3 ± 0.8	+1.0 ± 0.7	89.8
100	(d) 2/5	20.0 ± 0.4	19.5 ± 0.5	−1.5 ± 0.5	86.3

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean. Subsequent calculations are based on animals surviving to the end of the study.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Day of death: all 3
(e) Day of death: 3,3,3,3,4
(f) No data are reported due to 100% mortality in this group.
(g) Day of death: 4

TABLE 10. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE THIRTEEN-WEEK INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Concentration (ppm)	Survival (a)	Mean Body Weights (grams) Initial (b)	Final	Change (c)	Final Weight Relative to Controls (percent)
MALE					
0	10/10	25.0 ± 0.7	30.6 ± 0.8	+5.6 ± 0.6	
1	(d) 7/10	25.7 ± 0.5	32.1 ± 1.0	+6.1 ± 1.0	104.9
4	10/10	25.4 ± 0.5	28.9 ± 0.8	+3.5 ± 0.6	94.4
10	10/10	25.6 ± 0.7	26.8 ± 0.5	+1.2 ± 0.3	87.6
30	10/10	26.1 ± 0.6	26.6 ± 0.8	+0.5 ± 0.7	86.9
FEMALE					
0	(e) 7/7	21.4 ± 0.4	27.4 ± 0.7	+6.0 ± 0.8	
1	(f) 8/10	20.1 ± 0.2	26.5 ± 0.5	+6.3 ± 0.6	96.7
4	10/10	19.5 ± 0.4	24.5 ± 0.7	+5.0 ± 0.5	89.4
10	10/10	20.0 ± 0.4	22.4 ± 0.4	+2.4 ± 0.3	81.8
30	10/10	19.7 ± 0.4	24.0 ± 0.5	+4.3 ± 0.5	87.6

(a) Number surviving/number initially in group
(b) Initial group mean body weight ± standard error of the mean. Subsequent calculations based on animals surviving to the end of the study.
(c) Mean body weight change of the survivors ± standard error of the mean
(d) Week of death: all 3
(e) Three of the 10 original animals were used as replacements in the studies of reproductive effects.
(f) Week of death: 4,8

TABLE 11. LIVER WEIGHTS OF MICE IN THE THIRTEEN-WEEK INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

Concentration (ppm)	Number Weighed	Necropsy Body Weight (grams)	Liver Weight (mg)	Liver Weight/ Necropsy Body Weight (mg/g)
MALE				
0	10	25.0 ± 0.76	1,093 ± 58	43.7 ± 1.66
1	7	*(b) 29.3 ± 0.72	*(b) 1,393 ± 79	(b) 47.4 ± 1.68
4	10	24.9 ± 0.43	1,148 ± 27	46.1 ± 0.64
10	10	23.9 ± 0.29	1,009 ± 22	42.3 ± 0.78
30	(c) 9	23.1 ± 0.57	992 ± 39	43.0 ± 1.23
FEMALE				
0	7	22.4 ± 0.70	954 ± 71	42.4 ± 2.26
1	8	(b) 23.8 ± 0.50	*(b) 1,150 ± 25	**(b) 48.6 ± 1.61
4	10	21.7 ± 0.27	1,011 ± 18	46.6 ± 1.10
10	(c) 9	*19.9 ± 0.37	891 ± 14	44.9 ± 0.65
30	10	*20.2 ± 0.39	929 ± 28	45.9 ± 0.91

(a) Mean ± standard error; P values vs. the controls by Dunnett's test (Dunnett, 1955).
(b) The 1-ppm animals were inadvertently fed before being killed.
(c) One liver weight was not recorded at necropsy.
*P<0.05
**P<0.01

TABLE 12. NUMBERS OF MICE WITH SELECTED NASAL PASSAGE LESIONS IN THE THIRTEEN-WEEK INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

Lesion	Control	1 ppm	4 ppm	10 ppm	30 ppm
MALE					
Inflammation	0	0	4 (1.0)	(b) 8 (1.0)	10 (2.7)
Metaplasia	0	1 (1.0)	9 (1.0)	(b) 8 (2.0)	10 (2.0)
Erosion	0	0	0	(b) 0	(c) 10
FEMALE					
Inflammation	(b) 0	2 (1.0)	4 (1.0)	10 (1.3)	10 (2.0)
Metaplasia	(b) 0	1 (1.0)	8 (1.0)	10 (1.9)	10 (2.0)
Erosion	(b) 0	0	0	0	(c) 8

(a) Number of mice with lesions; 10 animals were examined unless otherwise specified. Mean severity in animals with the lesion is indicated in parentheses; (1) = minimal; (2) = mild; (3) = moderate; (4) = marked.
(b) Eight animals were examined.
(c) Severity was not reported.

concentrations were considered. However, it was decided that the nasal lesions were not life threatening and that the mice could tolerate the higher concentrations, which would maximize the sensitivity of the studies for determining the carcinogenic potential of the chemical.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Exposure to allyl glycidyl ether caused a prominent decrease in body weight gain in all exposed mice. Mean body weights of male mice exposed to 10 ppm were 9%-22% lower than those of controls after week 3; mean body weights of male mice exposed to 5 ppm were 6%-16% lower than those of controls after week 15 (Table 13 and Figure 7). Mean body weights of female mice exposed to 10 ppm were 8%-12% lower than those of controls from week 5 to week 24 and 12%-21% lower thereafter; mean body weights of female mice exposed to 5 ppm were 8%-14% lower than those of controls from week 37 to the end of the study. No compound-related clinical signs were observed, and more exposed mice survived until the termination period than did controls.

TABLE 13. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Weeks on Study	Chamber Control		5 ppm			10 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors
MALE								
0	26.1	50	23.9	92	50	24.2	93	50
1	27.0	50	26.5	98	50	24.6	91	50
2	27.2	50	26.4	97	50	25.6	94	50
3	29.6	50	27.3	92	50	25.7	87	50
4	29.5	50	27.6	94	50	25.9	88	50
5	29.8	50	28.4	95	50	26.5	89	50
6	30.7	50	28.2	92	50	27.4	89	50
7	30.4	50	28.6	94	50	27.2	89	50
8	30.6	50	28.8	94	49	27.4	90	50
9	31.9	50	29.7	93	49	27.8	87	50
10	31.5	50	30.5	97	49	27.7	88	50
11	31.7	50	31.7	100	49	28.2	89	50
15	32.7	50	30.8	94	49	28.5	87	49
19	33.4	49	30.8	92	49	28.7	86	49
24	34.6	49	32.1	93	49	31.0	90	49
28	38.1	49	33.2	87	49	31.4	82	49
33	35.4	49	32.5	92	49	30.2	85	49
37	37.8	49	32.0	85	49	30.2	80	49
41	37.7	49	33.6	89	49	31.6	84	48
45	39.1	49	33.4	85	49	30.5	78	48
49	38.2	49	33.9	89	49	32.1	84	48
54	38.4	49	34.6	90	49	31.7	83	48
58	38.2	49	34.1	89	49	34.7	91	48
64	38.1	49	33.7	88	49	31.6	83	48
68	39.1	48	35.3	90	49	32.4	83	48
72	37.7	48	34.1	90	49	31.0	82	48
77	39.3	47	34.9	89	49	31.6	80	48
82	40.4	47	35.5	88	48	32.4	80	48
86	41.9	47	35.4	84	47	32.7	78	48
90	41.1	45	35.0	85	45	32.8	80	48
94	39.7	43	35.6	90	44	33.2	84	48
98	40.5	41	34.4	85	41	32.4	80	48
102	40.2	39	35.2	88	41	32.1	80	46
Mean for weeks								
1-11	30.0		28.5	95		26.7	89	
15-49	36.3		32.5	90		30.8	84	
54-102	39.6		34.8	88		32.4	82	

TABLE 13. MEAN BODY WEIGHTS AND SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (Continued)

Weeks on Study	Chamber Control		5 ppm			10 ppm		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of ch. controls)	No. of Survivors
FEMALE								
0	21.5	50	20.0	93	50	18.1	84	49
1	22.9	50	22.7	99	50	21.1	92	49
2	24.3	50	23.1	95	50	21.7	89	49
3	24.6	50	24.0	98	50	22.4	91	49
4	25.1	50	23.7	94	50	24.3	97	49
5	25.2	50	23.8	94	50	23.0	91	49
6	26.5	50	24.7	93	50	24.0	91	49
7	26.8	50	25.1	94	50	24.7	92	49
8	27.2	50	25.5	94	50	24.1	89	49
9	27.5	50	25.8	94	50	24.3	88	49
10	27.5	49	27.1	99	50	24.5	89	49
11	27.8	49	26.1	94	50	24.5	88	49
15	28.7	49	27.5	96	50	25.9	90	49
19	28.8	49	27.6	96	50	26.3	91	49
24	30.0	49	29.2	97	50	27.3	91	49
28	32.2	49	30.6	95	50	28.2	88	49
33	32.6	48	30.6	94	50	28.1	86	49
37	33.1	48	29.7	90	50	27.7	84	49
41	33.0	48	30.3	92	50	28.1	85	49
45	34.3	48	31.2	91	50	29.2	85	49
49	34.1	48	30.9	91	49	29.2	86	48
54	34.9	47	32.0	92	48	28.8	83	48
58	35.0	47	31.5	90	48	29.0	83	48
64	34.8	47	31.4	90	48	29.1	84	48
68	34.9	47	31.9	91	48	28.9	83	48
72	36.9	46	32.7	89	48	29.4	80	48
77	35.6	45	32.0	90	48	29.2	82	48
82	37.7	45	32.6	86	47	29.8	79	48
86	38.3	43	32.9	86	47	30.5	80	46
90	38.0	43	33.7	89	46	30.9	81	44
94	37.2	39	33.0	89	45	30.5	82	44
98	36.4	39	32.0	88	43	30.1	83	44
102	37.1	35	33.1	89	43	30.3	82	42
Mean for weeks91								
1-11	25.9		24.7	95		23.5	91	
15-49	31.9		29.7	93		27.8	87	
54-102	36.4		32.4	89		29.7	82	

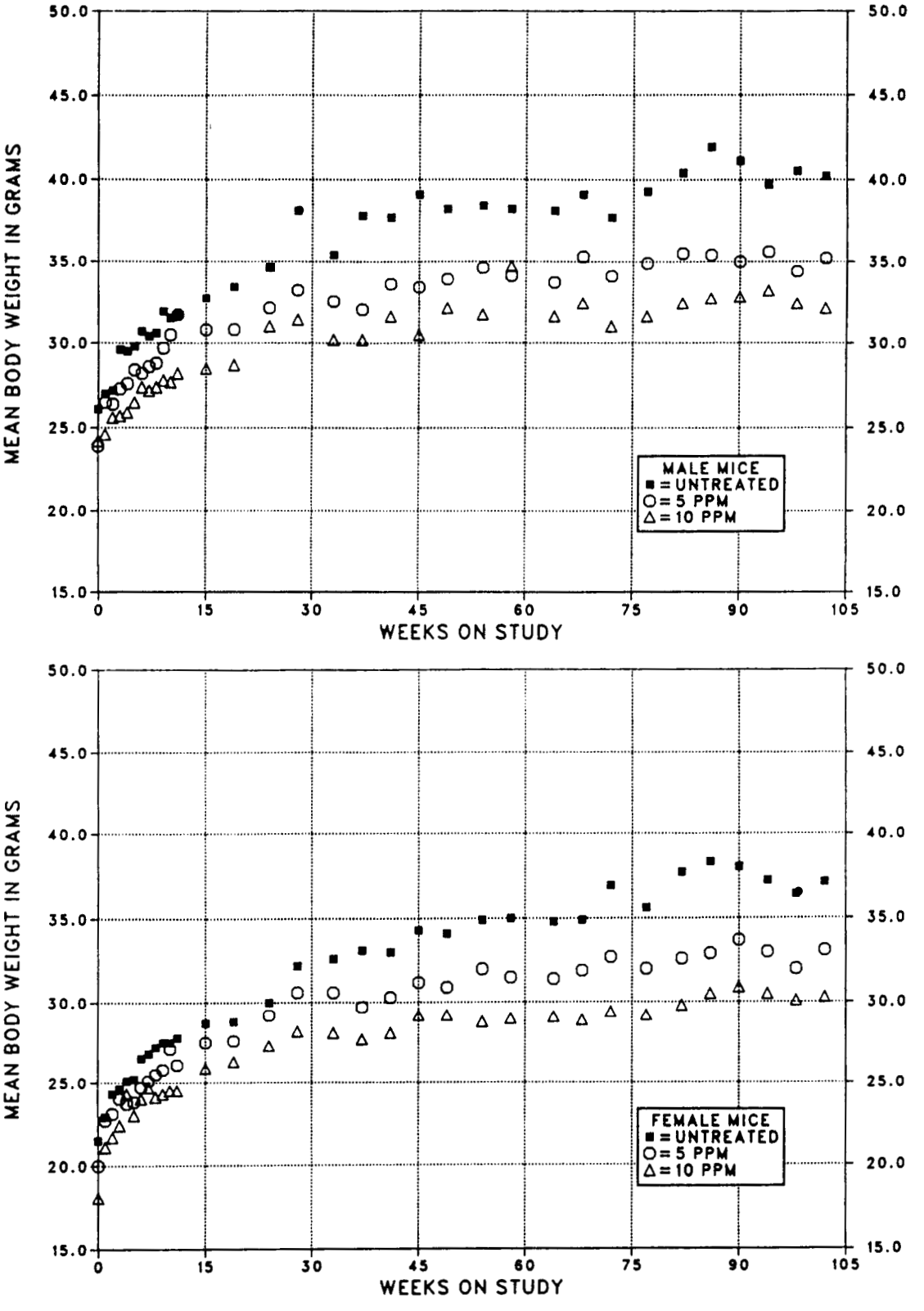

FIGURE 7. GROWTH CURVES FOR MICE EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival for male and female mice exposed to allyl glycidyl ether at the concentrations used in these studies and for controls are shown in Table 14 and in the Kaplan and Meier curves in Figure 8. Four mice (one control male, two exposed males, and one exposed female) died during the first 4 months of the study; the cause of death was not established. Overall survival was excellent, and no significant differences in survival were observed between any groups of either sex.

Pathology and Statistical Analyses of Results

This section describes the statistically significant or biologically noteworthy changes in the incidences of mice with neoplastic or nonneoplastic lesions of the nasal passage, Harderian gland, liver, and anterior pituitary gland.

Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary tumors that occurred with an incidence of at least 5% in at least one animal group, and historical control incidences for the neoplasms mentioned in this section are presented in Appendixes C and D for male and female mice, respectively.

Nasal Passage: A variety of inflammatory, degenerative, and proliferative lesions were observed in the nasal passage of mice exposed to vapors of allyl glycicyl ether for up to 2 years (Table 15). Suppurative inflammation, regeneration, and hyperplasia of the respiratory epithelium, hyperplasia of the septal and Bowman's glands, and respiratory metaplasia of the olfactory epithelium occurred in nearly all exposed male and female mice. There were small numbers of neutrophils diffusely scattered in the lamina propria, with accumulations in the lumina of the septal glands and Bowman's glands.

TABLE 14. SURVIVAL OF MICE IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
MALE (a)			
Animals initially in study	50	50	50
Natural deaths	7	2	1
Moribund kills	6	9	3
Animals surviving until study termination	(b) 38	39	46
Mean survival (days)	696	699	706
Survival P values (c)	0.054	0.968	0.058
FEMALE (a)			
Animals initially in study	50	50	50
Natural deaths	10	4	6
Moribund kills	7	5	3
Animals surviving until study termination	33	(b) 42	41
Mean survival (days)	675	704	698
Survival P values (c)	0.068	0.068	0.101

(a) First day of termination period: male--729; female--730
(b) One animal died or was killed in a moribund condition during the termination period and was combined, for statistical purposes, with those killed at termination.
(c) The result of the life table trend test is in the control column, and the results of the life table pairwise comparisons with the controls are in the dosed columns.

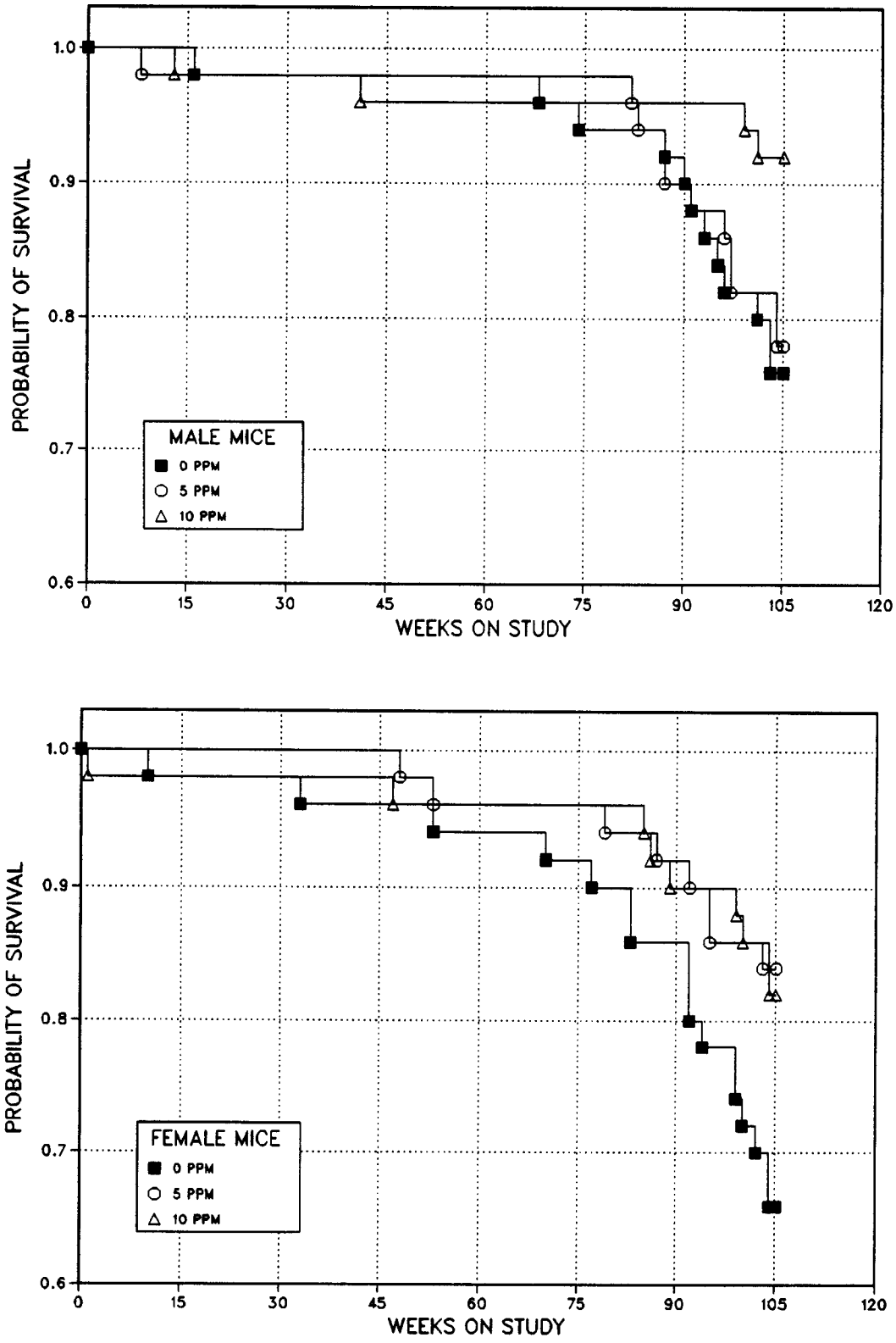

FIGURE 8. KAPLAN-MEIER SURVIVAL CURVES FOR MICE EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR TWO YEARS

TABLE 15. NUMBERS OF MICE WITH LESIONS OF THE NASAL PASSAGE IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Site/Lesion	Male			Female		
	Chamber Control	5 ppm	10 ppm	Chamber Control	5 ppm	10 ppm
Number examined	50	50	50	49	49	50
Nasal glands						
Hyperplasia	8	**47	**48	32	**46	**49
Mucosa						
Suppurative inflammation	2	**48	**47	8	**48	**49
Submucosal angiectasis	1	2	5	0	0	2
Submucosal hemangioma	0	0	(a) 1	0	0	(a) 1
Olfactory epithelium						
Metaplasia, respiratory	4	**49	**50	7	**48	**49
Respiratory epithelium						
Dysplasia	0	1	4	0	0	3
Hyperplasia	0	**25	**40	0	**39	**48
Basal cell hyperplasia	0	1	**7	0	2	**7
Squamous metaplasia	0	4	**8	0	**9	**12
Regeneration	0	**46	**46	5	**47	**46
Adenoma	0	0	3	0	0	1

(a) Hemangioma of the nasal passage
**P<0.01 vs. controls by logistic regression analysis

In some areas, the respiratory epithelium lacked ciliated columnar cells and consisted of small, less differentiated cells (regeneration) or the pseudostratified epithelium was slightly thickened with prominent goblet cells (hyperplasia). Part of the olfactory epithelium, particularly in the posterior, dorsal aspect of the septum and dorsal meatus, was replaced by ciliated columnar epithelium (respiratory metaplasia) (Figures 9, 10, and 13). The underlying Bowman's glands were dilated and lined with tall columnar cells, some of which were ciliated (hyperplasia).

Squamous metaplasia, basal cell hyperplasia, and dysplasia occurred in the respiratory epithelium of some male and female mice, and the incidences were concentration dependent. These lesions occurred primarily on the nasal or maxillary turbinates and less frequently on the dorsal or lateral walls (Figures 11 and 12). Squamous metaplasia was characterized by focal replacement of the pseudostratified ciliated columnar epithelium by three to five layers of cells with moderately abundant eosinophilic cytoplasm. Basal cell hyperplasia consisted of 3-10 layers of basal cells with scant to modest amounts of cytoplasm and uniform round to oval nuclei. At the margins of some of these lesions, a layer of differentiated ciliated columnar epithelium overlay the basal cells. When cellular atypia and pleomorphism occurred in foci of basal cell hyperplasia, the term dysplasia was applied; thus, dysplasia was not a separate and distinct lesion from basal cell hyperplasia.

Adenomas of the respiratory epithelium were seen in three male mice and one female mouse exposed to 10 ppm allyl glycidyl ether (Figures 14 to 16). These adenomas were exophytic, polypoid nodules that protruded into the lumen of the nasal passage; no invasion occurred at the site of attachment. The largest adenoma in the male mice was attached to the septum and nasal turbinate, occluding the dorsal meatus. It consisted of irregular tubular or glandlike structures separated by a scant fibrovascular stroma. The epithelium was usually single-layered and the cells were cuboidal to columnar with round to oval nuclei and moderate amphophilic or eosinophilic cytoplasm. In some areas, the cells were stratifiedand showed slight atypia and pleomorphism. The sites of attachment or stalks of the other two adenomas in high dose male mice were not in the plane of section. One of these was similar to the largest adenoma, but the other was a very small lesion that lacked complexity. It consisted only of a layer of epithelium overlying an edematous stroma protruding into

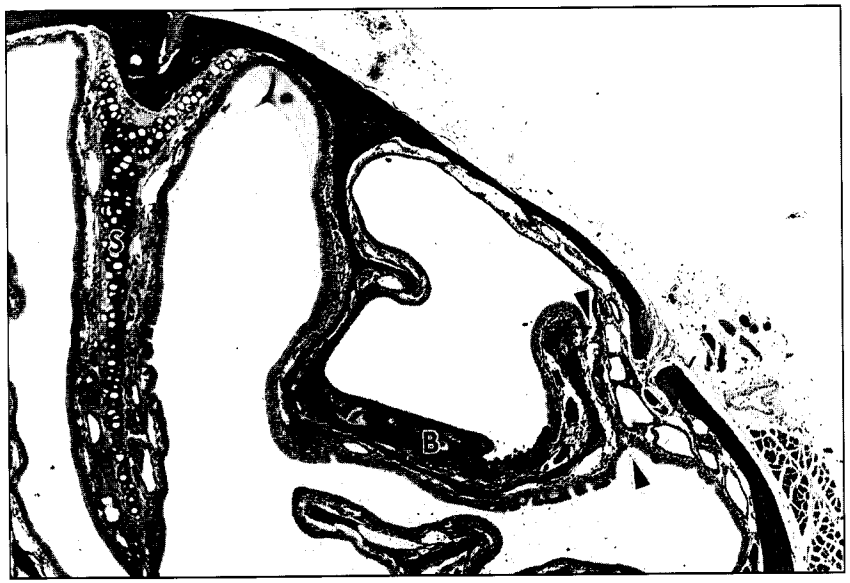

Figure 9. Nasal passage of high concentration (10 ppm) male mouse CID no. 2111 showing synechia of nasoturbinate (arrows) to the lateral wall with basal cell hyperplasia (B) on the nasoturbinate. Nasal septum (S).

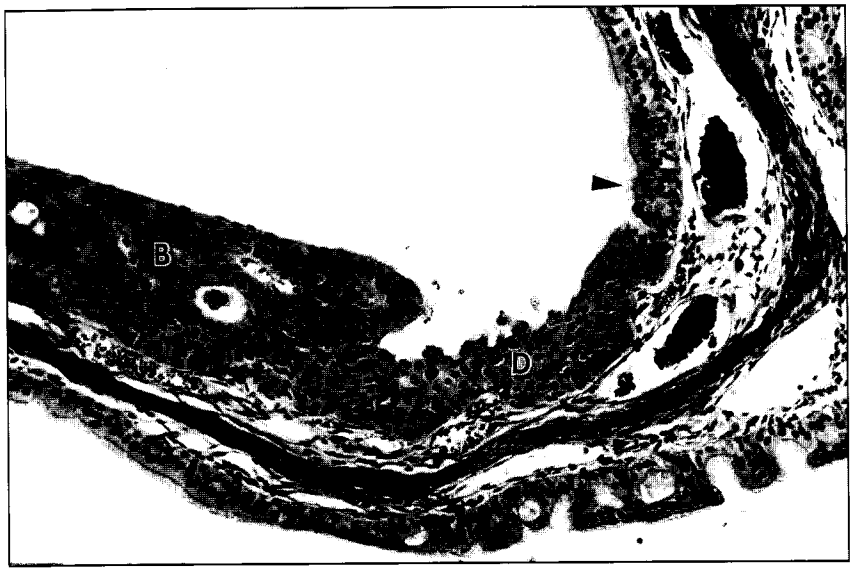

Figure 10. Higher magnification of Figure 9 showing hyperplastic basal cells (B) with a lighter area of dysplastic cells (D). Ciliated respiratory epithelium is present at the margin of the lesion (arrow).

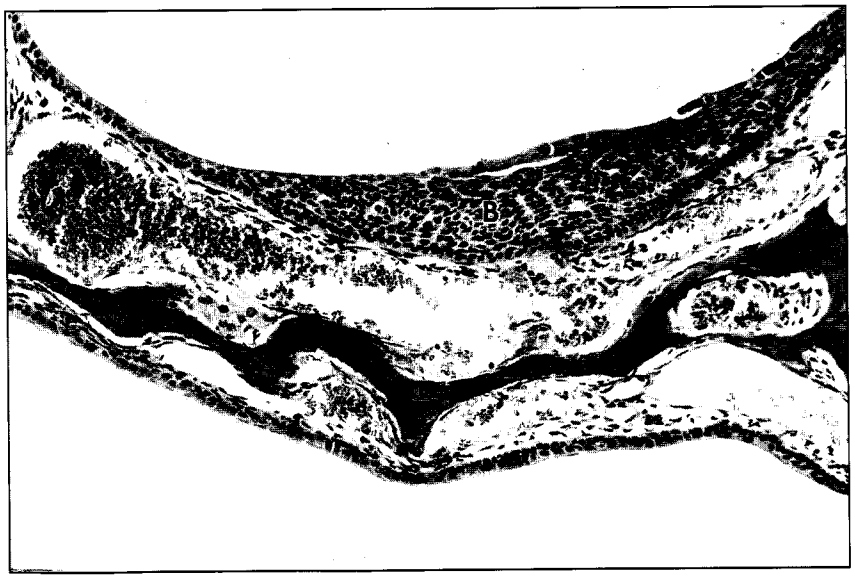

Figure 11. Nasal passage of high concentration (10 ppm) female mouse CID no. 2911 showing hyperplastic basal cells (B) extending beneath the overlying cuboidal transitional epithelium on the maxilloturbinate.

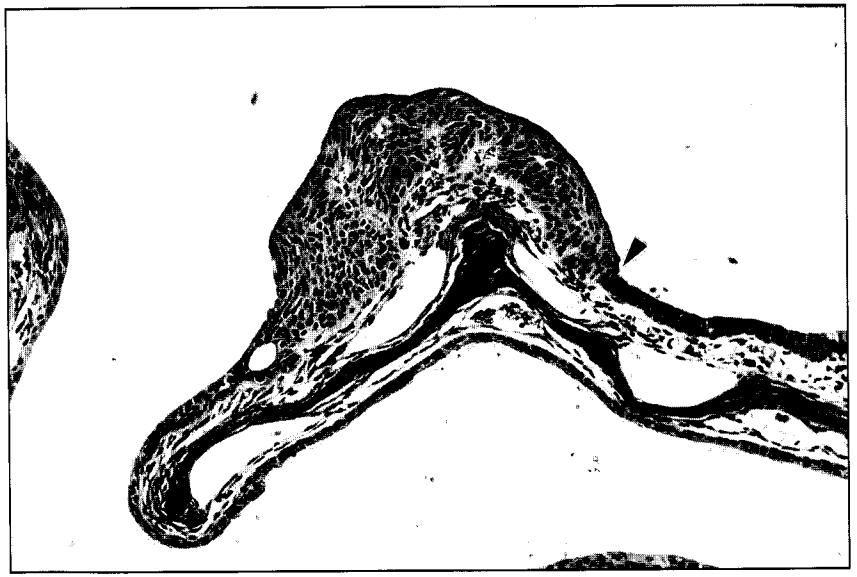

Figure 12. Nasal passage showing focal basal cell hyperplasia on the tip of the maxilloturbinate of a high concentration (10 ppm) female mouse (CID no. 2681). There is a sharp demarcation between the lesions and the normal transitional epithelium (arrow) covering the turbinate.

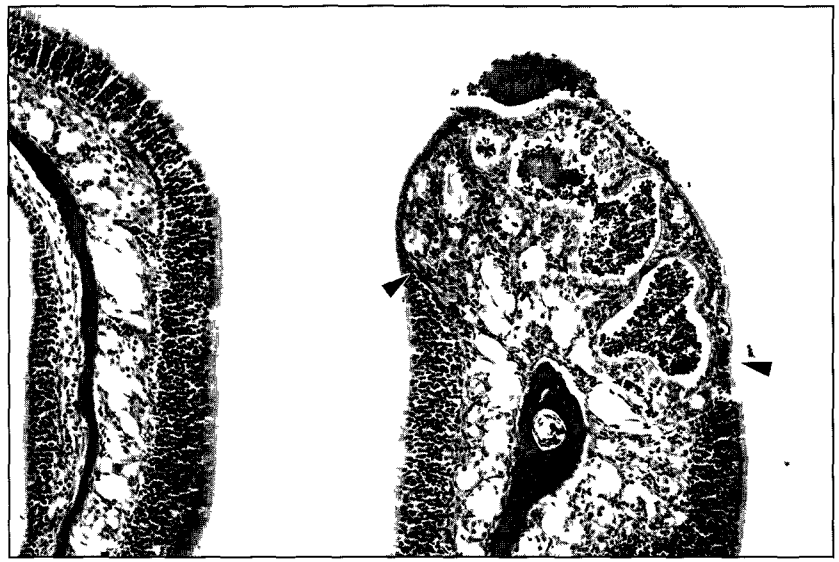

Figure 13 Nasal passage of high concentration (10 ppm male mouse CID no 2021 showing the tip of an ethmoid turbinate where the olfactory epithelium has been replaced by an area of hyperplastic ciliated cells (arrows)

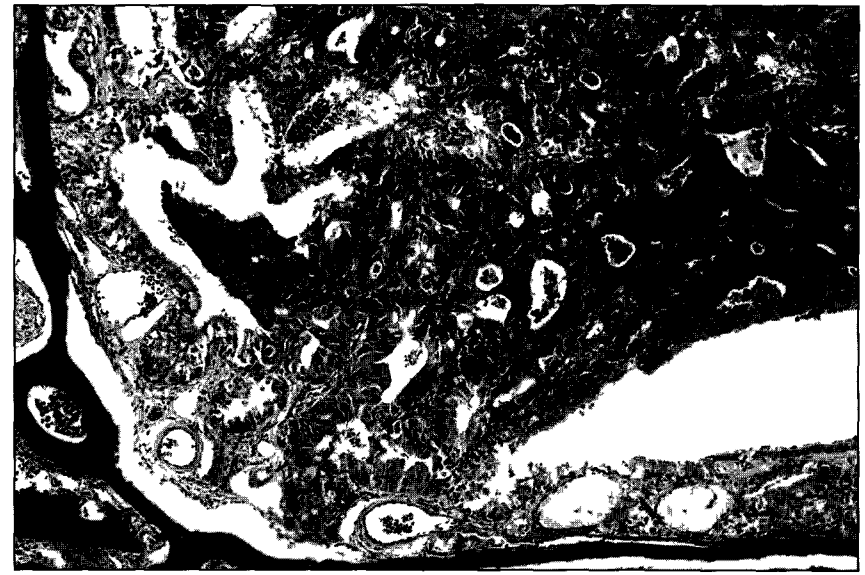

Figure 14 Nasal passage of high concentration (10 ppm) male mouse CID no 2011 showing an adenoma of the respiratory epithelium

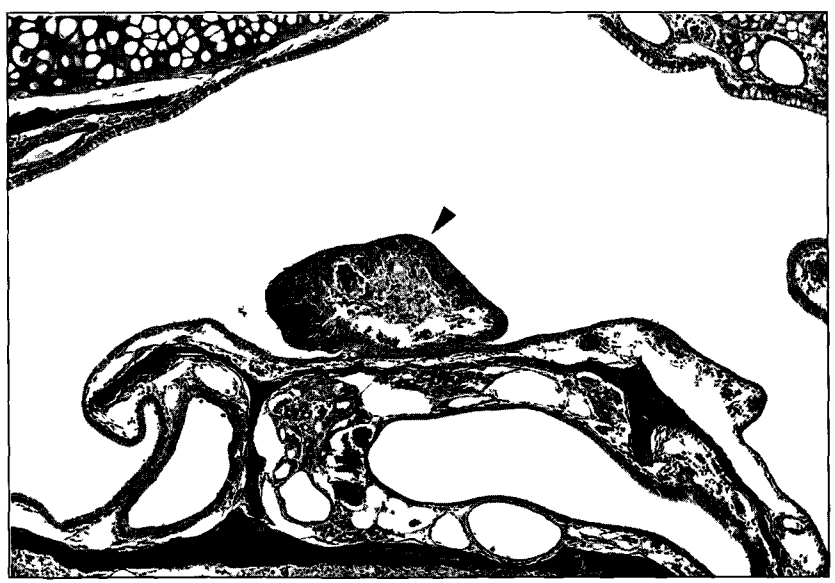

Figure 15 Nasal passage of high concentration (10 ppm) female mouse showing a small adenoma (arrow) on the maxilloturbinate

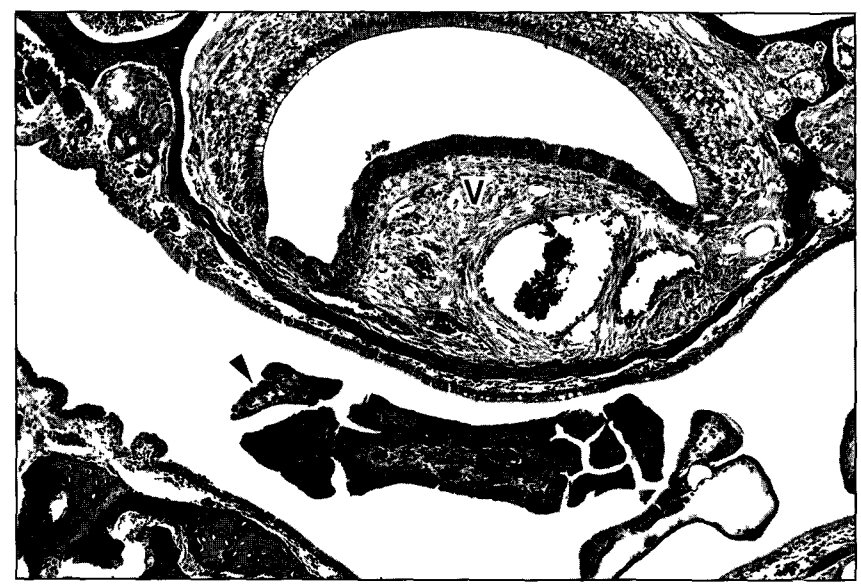

Figure 16 Nasal passage of high concentration (10 ppm) male mouse showing a small adenoma (arrow) within the ventral meatus adjacent to the vomeronasal organ (V)

the nasal passage. The Pathology Working Group was uncertain of the biologic potential of this lesion and recommended recuts of the block to demonstrate more of the lesion. The recuts, however, did not demonstrate any different features. The adenoma in the high dose female was attached to the dorsal wall lateral to the nasal turbinate. It was similar to the largest of the adenomas in the males.

Angiectasis, characterized by markedly dilated capillaries and/or venules, occurred in the submucosa of the turbinates or wall of the nasal passage in several male and female mice exposed to allyl glycidyl ether and in one control male. Hemangiomas occurred in one high dose male mouse and one high dose female mouse. These were space-occupying lesions that distorted the submucosa and protruded into the lumen of the nasal passage. They consisted of widely dilated, irregular vascular channels lined by a single layer of well-differentiated endothelium. The biologic nature of these lesions is uncertain.

Harderian Gland: Adenomas occurred with a significant positive trend in female mice; the incidence in the group exposed to 10 ppm was not significantly greater than that in the controls by the logistic regression test (Table 16) and was within the historical control range of incidences in untreated control female B6C3F$_1$ mice (highest observed incidence, 6/50) but was greater than the highest observed incidence in chamber controls (2/50) (Table D4b). Interpretation of the incidences of adenomas is complicated because all the neoplasms were observed fortuitously when the nasal passage was sectioned. Harderian gland adenomas in male mice occurred with a significant negative trend (Table 16).

Liver: The incidences of hepatocellular adenomas in males exposed to 10 ppm, hepatocellular carcinomas in males and females exposed to 10 ppm, and hepatocellular adenomas or carcinomas (combined) in males exposed to 10 ppm were significantly lower than those in controls (Table 17). The lowest previously observed incidences of hepatocellular adenomas or carcinomas (combined) in historical controls were 7/48 for males and 2/50 for females.

Anterior Pituitary Gland: The incidences of adenomas of the pars distalis in females exposed to 10 ppm were significantly lower than those in controls (Table 18).

TABLE 16. HARDERIAN GLAND TUMORS IN MICE IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

	Chamber Control	5 ppm	10 ppm
MALE			
Adenoma (b)			
Overall Rates	4/50 (8%)	2/50 (4%)	0/50 (0%)
Terminal Rates	4/38 (11%)	2/39 (5%)	0/46 (0%)
Day of First Observation	729	729	
Logistic Regression Tests	P=0.025N	P=0.324N	P=0.042N
FEMALE			
Adenoma (c)			
Overall Rates	0/50 (0%)	0/50 (0%)	5/50 (10%)
Terminal Rates	0/33 (0%)	0/42 (0%)	4/41 (10%)
Day of First Observation			727
Logistic Regression Tests	P=0.009	(d)	P=0.052

(a) For a complete explanation of the entries in this table, see Table C3 (footnotes); the statistical analyses used are discussed in Section II (Statistical Methods).
(b) Historical incidence of adenomas or carcinomas (combined) in chamber controls at study laboratory (mean ± SD): 19/398 (5% ± 4%); historical incidence in untreated controls in NTP studies: 67/1,692 (4% ± 4%)
(c) Historical incidence of adenomas or carcinomas (combined) in chamber controls at study laboratory (mean ± SD): 7/398 (2% ± 2%); historical incidence in untreated controls in NTP studies: 51/1,689 (3% ± 3%)
(d) No P value is reported because no tumors were observed in the 5-ppm and control groups.

TABLE 17. HEPATOCELLULAR TUMORS IN MICE IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

	Chamber Control	5 ppm	10 ppm
MALE			
Adenoma			
Overall Rates	15/49 (31%)	(b) 7/19 (37%)	5/49 (10%)
Terminal Rates	11/38 (29%)		4/46 (9%)
Day of First Observation	474		690
Logistic Regression Test			P=0.012N
Carcinoma			
Overall Rates	10/49 (20%)	(b) 4/19 (21%)	1/49 (2%)
Terminal Rates	5/38 (13%)		1/46 (2%)
Day of First Observation	608		729
Logistic Regression Test			P=0.005N
Adenoma or Carcinoma (c)			
Overall Rates	23/49 (47%)	(b) 11/19 (58%)	6/49 (12%)
Terminal Rates	14/38 (37%)		5/46 (11%)
Day of First Observation	474		690
Logistic Regression Test			P<0.001N
FEMALE			
Adenoma			
Overall Rates	1/50 (2%)	(b) 2/15 (13%)	2/50 (4%)
Carcinoma			
Overall Rates	5/50 (10%)	(b) 3/15 (20%)	0/50 (0%)
Terminal Rates	4/33 (12%)		0/41 (0%)
Day of First Observation	642		
Logistic Regression Test			P=0.028N
Adenoma or Carcinoma (d)			
Overall Rates	6/50 (12%)	(b) 5/15 (33%)	2/50 (4%)
Terminal Rates	5/33 (15%)		1/41 (2%)
Day of First Observation	642		727
Logistic Regression Test			P=0.107N

(a) For a complete explanation of the entries in this table, see Table C3 (footnotes); the statistical analyses used are discussed in Section II (Statistical Methods).
(b) Incomplete sampling of tissues
(c) Historical incidence in chamber controls at study laboratory (mean ± SD): 133/397 (34% ± 6%); historical incidence in untreated controls in NTP studies: 494/1,678 (29% ± 8%)
(d) Historical incidence in chamber controls at study laboratory (mean ± SD): 34/397 (9% ± 3%); historical incidence in untreated controls in NTP studies: 163/1,683 (10% ±4%)

TABLE 18. ANTERIOR PITUITARY GLAND LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (a)

	Chamber Control	5 ppm	10 ppm
Hyperplasia			
Overall Rates	15/44 (34%)	(b) 6/17 (35%)	9/45 (20%)
Adenoma			
Overall Rates	12/44 (27%)	(b) 8/17 (47%)	2/45 (4%)
Terminal Rates	11/32 (34%)		2/37 (5%)
Day of First Observation	696		730
Logistic Regression Test			P=0.002N
Adenoma or Carcinoma (c)			
Overall Rates	13/44 (30%)	(b) 8/17 (47%)	2/45 (4%)
Terminal Rates	12/32 (38%)		2/37 (5%)
Day of First Observation	696		730
Logistic Regression Test			P<0.001N

(a) For a complete explanation of the entries in this table, see Table D3 (footnotes); the statistical analyses used are discussed in Section II (Statistical Methods).
(b) Incomplete sampling of tissues
(c) Historical incidence in chamber controls at study laboratory (mean ± SD): 74/370 (20% ± 14%); historical incidence in untreated controls in NTP studies: 256/1,528 (17% ± 11%)

Allyl glycidyl ether (concentration range of 100-10,000 µg/plate) was mutagenic in *Salmonella typhimurium* base-substitution strains TA100 and TA1535 when tested in a preincubation protocol in the presence and absence of Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver S9; no mutagenic activity was observed in the frame-shift strains TA98 or TA1537 with or without S9 (Canter et al., 1986; Table K1). In cytogenetic tests with Chinese hamster ovary cells, allyl glycidyl ether induced highly significant increases in sister chromatid exchanges (SCEs) and chromosomal aberrations both with and without Aroclor 1254-induced male Sprague Dawley rat liver S9 (Table K2). In the SCE test, cultures treated with the highest concentrations tested, with and without S9, required delayed harvest to offset chemical-induced cell cycle delay; however, positive responses in the assay were obtained at concentrations that allowed normal harvest times as well as in the cultures that exhibited delay. The protocol for the chromosomal aberration test was also modifed to allow for later harvest times. Allyl glycidyl ether induced a significant increase in sex-linked recessive lethal mutations in the germ cells of male Canton-S *Drosophila melanogaster* fed a sucrose solution containing 5,500 ppm of the chemical (Table K4); however, this same treatment with allyl glycidyl ether did not induce reciprocal translocations in the germ cells of these flies (Yoon et al., 1985; Table K5). The methodology and full results are presented in Appendix K.

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

Allyl glycidyl ether was evaluated for toxicity and carcinogenicity in 2-week, 13-week, and 2-year studies and in 8-week studies of reproductive effects. Groups of Osborne-Mendel rats and B6C3F$_1$ mice of each sex were exposed to the chemical by inhalation. Allyl glycidyl ether was studied because of worker exposure to this volatile chemical during the manufacture of epoxy resins, because chemicals that contain epoxy and allyl groups may cause cancer, and because allyl glycidyl ether was reported to cause testicular atrophy and hemopoietic abnormalities in laboratory animals (Kodama et al., 1961). Glycidol, a related chemical, was recently evaluated by the National Toxicology Program (NTP) for possible toxicity and carcinogenicity by oral gavage in 2-year studies (NTP, 1990).

In the 8-week studies to evaluate the possible reproductive effects of allyl glycidyl ether, rats were exposed at concentrations up to 200 ppm and mice up to 30 ppm; the exposed animals of each sex were then mated with controls. The mating performance of exposed male rats was markedly reduced, especially during the first few days of the mating trials; at the high concentrations, these animals showed significantly decreased weight gain and marked histologic evidence of olfactory epithelial degeneration, which may have contributed to the lack of mating. Normal sperm numbers, motility, and morphology and the lack of reproductive effects in female rats and mice suggest that the toxic effect on male rats was nonspecific. One of the studies cited by the National Institute for Occupational Safety and Health (Stein et al., 1979) reported testicular necrosis in one of three rats given a total intramuscular dose of 1,600 mg/kg allyl glycidyl ether over 9 days and surviving to day 12, but the necrosis may have been a nonspecific effect. The inhalation of allyl glycidyl ether apparently has little potential for direct effect on reproduction in rats and mice.

In 13-week studies of allyl glycidyl ether, exposure concentrations ranged up to 200 ppm for rats and 30 ppm for mice. There were no compound-related deaths, and decreased body weight gain was the most prominent clinical sign. Signs of conjunctivitis (ocular discharge, redness) were common in male rats and occurred less frequently in female rats. Since there were no apparent differences between control and exposed rats, these signs were attributed to a sialodacryoadenitis virus infection that occurred during the exposure period. An opthalmologic examination during week 86 of the 2-year studies revealed bilateral superficial keratitis and chronic dacryoadenitis in approximately half of the control and exposed rats. Chronic uveitis and secondary cataracts were occasional findings.

Exposure-related lesions were limited to the airways, suggesting that allyl glycidyl ether is very reactive, with most of its effects being seen in the anterior part of the nasal passage and upper airways. In all exposure groups, histologic lesions included squamous metaplasia of the nasal passage and involved both the respiratory epithelium and the olfactory epithelium. The lesions were more severe in the anterior and dorsal portions of the nasal passage and with increasing concentration. Squamous metaplasia apparently is an adaptive response to chronic irritation.

Focally, the olfactory epithelium was also replaced by ciliated epithelium, especially in the dorsal meatus; this also appears to be an adaptive response to chronic irritation. A similar type of response was seen in rats and mice exposed to methyl isocyanate (Boorman et al., 1987; Uraih et al., 1987) and in rats exposed to formaldehyde at high levels (Kerns et al., 1983). Although the metaplastic olfactory epithelium is ciliated, it is not known whether this represents a transition to a true respiratory epithelium or whether it is a modification of the remaining olfactory epithelium. Degenerative changes were also found in the remaining olfactory epithelium. These severe morphologic changes suggest that the sense of olfaction in the rats must have been severely impaired.

In the 2-year studies, the mean body weights of exposed rats were lower than those of controls. The differences were not marked, however, and the body weights of exposed animals were within 8% of controls throughout the studies. Large numbers of deaths were seen in all groups of male rats beginning at 1 year of age; the lowest survival at the end of the study was in the highest concentration group (control, 12/50; 5 ppm,

11/50; 10 ppm, 8/50). Forty-nine control, 49 low concentration, and 45 high concentration male rats were alive at week 51; at week 79, 41 control, 38 low concentration, and 39 high concentration males were still alive; thus, survival of male rats, although far from optimal, was sufficient to consider the study adequate for the detection of carcinogenic activity. Survival in the 10-ppm group decreased most sharply between months 19 and 20, when survival dropped from 70% to 50%. At month 24, survival was poor in all groups; this appears to have been related to the presence of severe renal disease in the Osborne-Mendel rats. More than half the animals died with severe nephropathy, accounting for the reduced survival near the end of the study. Survival of female rats was not exposure related (control, 24/50; 5 ppm, 30/50; 10 ppm, 25/50). The females, with better survival, had nephropathy that ranged from minimal to mild. Essentially no recent historical data exist to judge whether the survival observed in these studies is typical for Osborne-Mendel rats.

In the 2-year studies in mice, mean body weights of animals exposed to 10 ppm were 10%-20% lower than those of controls throughout most of the studies; mean body weights of mice exposed to 5 ppm averaged 5%-15% lower than those of controls. However, exposed mice had slightly greater survival (male: control, 38/50; 5 ppm, 39/50; 10 ppm, 46/50; female: 33/50; 42/50; 41/50). Since allyl glycidyl ether had a severe effect on the olfactory epithelium, the lower body weight may be related in part to reduced feed consumption (not measured), making lower body weight secondary to the loss of olfaction rather than simply a function of the toxic effect of the compound. Decreased feed intake is associated with increased survival and lower incidences of certain neoplasms (Rao et al., 1987).

Exposure of rats and mice of each sex to vapors of allyl glycidyl ether for up to 2 years resulted in a variety of inflammatory, degenerative, and proliferative lesions of the nasal mucosa. The irritant or toxic effects of the chemical are clearly demonstrated by the inflammation, hyperplasia of the septum and Bowman's glands, respiratory metaplasia of the olfactory epithelium, and squamous metaplasia of the respiratory epithelium. The nature of the lesions did not appear different between sexes or species and was indicative of a response to cell necrosis and cellular degeneration caused by a toxic chemical.

Low incidences of a variety of neoplasms were found in the nasal passage of exposed rats and mice. However, the number and type of neoplasms and the pattern of potentially preneoplastic lesions varied with sex and species, resulting in different levels of evidence for carcinogenic activity. In rats exposed to allyl glycidyl ether, no lesions considered to be preneoplastic were found.

Three neoplasms were found in the nasal passage of male rats exposed to 10 ppm allyl glycidyl ether. One appeared to be composed of undifferentiated epithelial cells but contained areas of spindle cells and structures resembling rosettes, suggestive of neuroblast origin. This neoplasm was diagnosed as a poorly differentiated adenocarcinoma arising in the olfactory region. The neoplasm occurred early in the study (after 62 weeks of exposure) and was not accompanied by other changes in the olfactory epithelium. It would seem likely that a chemical causing a malignant neoplasm this early in the study would also induce preneoplastic lesions or benign neoplasms of the olfactory epithelium; thus, this lesion appeared to be an incidental finding unrelated to allyl glycidyl ether exposure. The other two neoplasms of the nasal passage, a papillary adenoma and a squamous cell carcinoma, appeared to arise from the respiratory epithelium. Mitotic figures were uncommon. The squamous cell carcinoma appeared to arise in the dorsal meatus at level I (the most anterior histologic section of the nasal passage taken for examination) and obliterated most of the nasal passage on that side. There is no evidence of other preneoplastic lesions that would be expected to lead to either the papillary adenoma or the squamous cell carcinoma. In a formaldehyde study (Kerns et al., 1983), squamous cell carcinomas were accompanied by a variety of preneoplastic lesions and progression to malignant neoplasms was found.

The current historical data base for Osborne-Mendel rats includes only one (noninhalation) study; one malignant neoplasm of the nasal passage was found in 1/50 control males in that

study. Three apparently unrelated neoplasms occurred without any evidence of preneoplastic lesions in male rats exposed to 10 ppm allyl glycidyl ether. The fact that there are three different types of neoplasms arising from at least two different cell types makes it difficult to attribute the neoplasms with any certainty to the allyl glycidyl ether exposure. However, these three neoplasms in the high concentration group cannot be entirely dismissed, and thus, the level of evidence for male rats is equivocal. The severe metaplastic changes in the nasal passage and the lower body weight gain suggest that allyl glycidyl ether was studied at the highest possible concentration. A papillary adenoma was found in one female rat exposed to 5 ppm. The occurrence of a solitary benign neoplasm in the low concentration group without any evidence of preneoplastic lesions is not considered to be exposure related.

The mice differed from the rats in that, in addition to low incidences of neoplasms, lesions were found in the nasal passage which were considered to be preneoplastic. Basal cell hyperplasia was found in one 5-ppm and seven 10-ppm males. The lesion consisted of focal increased layers of basal cells, usually on the tips of the nasoturbinates but occasionally on the maxilloturbinate and lateral walls. These were the locations of the papillomas that were diagnosed. In four exposed mice, basal cell hyperplasia contained cells with abundant eosinophilic cytoplasm and moderate cellular atypia, and the lesion was diagnosed as dysplasia. Three 10-ppm male mice were diagnosed as having adenomas of the respiratory epithelium. Neoplasms of the nasal mucosa are extremely rare in $B6C3F_1$ mice; none has been observed in 398 male chamber control $B6C3F_1$ mice at the study laboratory or in 1,692 male untreated controls in NTP studies. Although the incidence of nasal adenomas in high concentration male mice is not statistically significant when compared with that in concurrent controls, the rarity of these neoplasms suggests that they were caused by exposure to allyl glycidyl ether. The presence of preneoplastic lesions at the same location in the nasal passage supports this conclusion. A single papilloma was found in the nasal passage of a female mouse exposed to 10 ppm allyl glycidyl ether. Although no neoplasms have been observed in the 398 female chamber controls at the study laboratory, a single papilloma was observed in 1,698 untreated controls in NTP studies. The incidences of preneoplastic lesions in the female mice were similar to those in males, with two low concentration and seven high concentration females having basal cell hyperplasia; dysplasia was found in three of these animals. Since only one adenoma of the nasal passage occurred in exposed female mice, it cannot be concluded with certainty that the neoplasm was caused by exposure to allyl glycidyl ether. It was therefore concluded that there was equivocal evidence of carcinogenic activity for female mice.

In spite of the evidence of marked irritation found in the nasal passage of both rats and mice, there was no evidence of irritation of the integumentary system. Since rats and mice groom extensively, it might have been predicted that irritant effects would also have been seen in the oral cavity or stomach, but there was no evidence of such toxic effects in either mice or rats.

One hemangioma was found in a male mouse and one in a female mouse exposed to 10 ppm. The neoplasms appeared to be arising in the submucosal vascular plexus. Angiectasis of the submucosal vessels in the nasal passage was seen in one control male, two 5-ppm male, and five 10-ppm male mice. Angiectasis of submucosal vessels of the nasal passage was also seen in two 10-ppm female mice. The relationship between angiectasis and the formation of benign vascular neoplasms is not known. In mice exposed to propylene oxide by inhalation, angiectasis, hemangiomas, and hemangiosarcomas were found in the nasal passage (NTP, 1985).

The choice of exposure concentrations for the mouse studies appears appropriate. The mean body weights in the the low concentration groups were 5%-16% lower than those in controls, and even greater weight differences were seen in the 10-ppm exposure groups. Thus, these concentrations likely represent the maxima for 2-year studies in $B6C3F_1$ mice.

The pronounced lower weight gain of exposed mice was accompanied by increased survival and decreased total incidences of neoplasms in males

and females (see pages 109 and 137). More specifically, the incidences of hepatocellular neoplasms were decreased in exposed mice of each sex. Exposed female mice also had lower incidences of pituitary gland neoplasms.

Five Harderian gland neoplasms were found in the 10-ppm female mice, whereas none was found in the controls or in the 5-ppm group. Six Harderian gland neoplasms have been found in an untreated control group of female $B6C3F_1$ mice (NTP, 1982), and five have been seen in a corn oil gavage control group (NTP, 1989). Because the number of Harderian gland neoplasms in female mice was within the historical range for controls and because a negative trend was observed for male mice (control, 4/50; 5 ppm, 2/50; 10 ppm, 0/50), these neoplasms were not considered compound related.

In retrospect, the choice of Osborne-Mendel rats for these studies was unfortunate. It would have been easier to judge the significance of low incidences of nasal neoplasms in a species for which a larger set of historical data and experience exist. It might have been predicted that survival would have been better in F344 males because the incidence of renal disease is lower than in Osborne-Mendel rats. The Osborne-Mendel rat was chosen because it was considered to be the strain of choice for studies of reproductive effects and because, at the time these studies were designed, several rat strains were being evaluated as experimental models.

Glycidol was tested by the NTP for potential toxicity and carcinogenicity in $B6C3F_1$ mice and F344/N rats by administering the material in corn oil by gavage at 25 or 50 mg/kg body weight in mice and at 37.5 or 75 mg/kg in rats (NTP, 1990). Under the conditions of those studies, the chemical was considered to be clearly carcinogenic in each sex of rats and mice, causing a variety of neoplasms at numerous tissue sites. The remarkable difference in study results between allyl glycidyl ether, which contains a glycidol moiety, and glycidol may be due to the route of administration and amount of chemical available to the tissues. Alternately, the ether bond in allyl glycidyl ether is not subject to easy breakage, and little free glycidol would be expected to be available to the tissues. These two studies indicate that structure alone cannot always be used to predict potential carcinogenicity. Further studies on metabolism and tissue distribution of metabolites of these two chemicals by various routes of administration may offer some clues to the different results in carcinogenicity studies.

The experimental and tabulated data for the NTP Technical Report on allyl glycidyl ether were examined for accuracy, consistency, completeness, and compliance with Good Laboratory Practice regulations. As summarized in Appendix L, the audit revealed no major problems with the conduct of the studies or with collection and documentation of the experimental data. No discrepancies were found that influenced the final interpretation of the results of these studies.

IV. DISCUSSION AND CONCLUSIONS

Under the conditions of these 2-year inhalation studies, there was *equivocal evidence of carcinogenic activity** of allyl glycidyl ether for male Osborne-Mendel rats, based on the presence of one papillary adenoma of respiratory epithelial origin, one squamous cell carcinoma of respiratory epithelial origin, and one poorly differentiated adenocarcinoma of olfactory epithelial origin, all occurring in the nasal passage of males exposed to 10 ppm. There was *no evidence of carcinogenic activity* of allyl glycidyl ether for female rats. One papillary adenoma of the respiratory epithelium was present in a female rat exposed to 5 ppm. There was *some evidence of carcinogenic activity* of allyl glycidyl ether for male $B6C3F_1$ mice, based on the presence of three adenomas of the respiratory epithelium, dysplasia in four males, and focal basal cell hyperplasia of the respiratory epithelium in seven males in the nasal passage of mice exposed to 10 ppm. There was *equivocal evidence of carcinogenic activity* of allyl glycidyl ether for female mice, based on the presence of one adenoma of the respiratory epithelium and focal basal cell hyperplasia of the respiratory epithelium in seven females exposed to 10 ppm. The sensitivity of the assay to detect potential carcinogenicity may have been reduced in male rats because of poor survival in all groups.

In exposed mice, body weights were decreased 10% or more, mortality was decreased, and there were lower incidences of liver neoplasms (males) and pituitary gland adenomas (females) compared with controls.

Significant exposure-related nonneoplastic lesions were restricted to the nasal passage in both rats and mice and included inflammation, metaplasia, respiratory epithelial hyperplasia, and olfactory epithelial degeneration. Basal cell hyperplasia and dysplasia of the respiratory epithelium of the nasal passage were found only in the mice.

*Explanation of Levels of Evidence of Carcinogenic Activity is on page 7.
A summary of the Peer Review comments and the public discussion on this Technical Report appears on page 10.

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APPENDIX A

SUMMARY OF LESIONS IN MALE OSBORNE-MENDEL RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

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

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine large, cecum	(23)	(21)	(15)
Lymphoma malignant undifferentiated cell type			1 (7%)
Intestine large, colon	(39)	(38)	(34)
Lymphoma malignant undifferentiated cell type			1 (3%)
Intestine large, rectum	(40)	(42)	(38)
Lymphoma malignant undifferentiated cell type			1 (3%)
Intestine small, duodenum	(33)	(37)	(33)
Lymphoma malignant histiocytic			1 (3%)
Lymphoma malignant undifferentiated cell type			1 (3%)
Intestine small, ileum	(24)	(27)	(23)
Lymphoma malignant undifferentiated cell type			1 (4%)
Intestine small, jejunum	(24)	(27)	(25)
Adenocarcinoma, mucinous	1 (4%)		
Lymphoma malignant histiocytic			1 (4%)
Lymphoma malignant undifferentiated cell type			1 (4%)
Liver	(49)	(49)	(47)
Adenoma		1 (2%)	
Hepatocellular carcinoma		1 (2%)	
Lymphoma malignant histiocytic	1 (2%)	1 (2%)	1 (2%)
Lymphoma malignant	1 (2%)	1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	2 (4%)
Pancreas	(48)	(48)	(44)
Lymphoma malignant histiocytic		1 (2%)	1 (2%)
Lymphoma malignant		1 (2%)	
Salivary glands	(50)	(46)	(47)
Carcinoma, metastatic, harderian gland		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
Stomach, forestomach	(45)	(43)	(44)
Papilloma squamous	1 (2%)		
Squamous cell carcinoma	1 (2%)	2 (5%)	1 (2%)
Stomach, glandular	(48)	(48)	(45)
Lymphoma malignant		1 (2%)	
CARDIOVASCULAR SYSTEM			
Heart	(50)	(50)	(50)
Lymphoma malignant histiocytic		1 (2%)	
Lymphoma malignant		1 (2%)	
Lymphoma malignant undifferentiated cell type		1 (2%)	1 (2%)
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(48)	(48)	(48)
Adenoma	1 (2%)	1 (2%)	2 (4%)
Carcinoma	1 (2%)		
Lymphoma malignant histiocytic		1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)		2 (4%)
Adrenal gland, medulla	(47)	(47)	(47)
Lymphoma malignant histiocytic		1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)		2 (4%)
Pheochromocytoma malignant	5 (11%)		3 (6%)
Pheochromocytoma malignant, multiple	2 (4%)		1 (2%)
Pheochromocytoma benign	9 (19%)	7 (15%)	12 (26%)
Pheochromocytoma benign, multiple	1 (2%)	7 (15%)	2 (4%)
Bilateral, pheochromocytoma benign	1 (2%)		
Islets, pancreatic	(48)	(48)	(45)
Adenoma		2 (4%)	1 (2%)

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

	Chamber Control	5 ppm	10 ppm
ENDOCRINE SYSTEM (Continued)			
Parathyroid gland	(36)	(30)	(38)
Adenoma	1 (3%)		2 (5%)
Pituitary gland	(47)	(46)	(44)
Lymphoma malignant histiocytic		1 (2%)	1 (2%)
Lymphoma malignant		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
Pars distalis, adenoma	11 (23%)	12 (26%)	13 (30%)
Pars distalis, carcinoma	2 (4%)		
Pars intermedia, adenoma		2 (4%)	2 (5%)
Thyroid gland	*(50)	(46)	(46)
C-cell, adenoma	8 (16%)	9 (20%)	10 (22%)
C-cell, adenoma, multiple		1 (2%)	2 (4%)
C-cell, carcinoma	5 (10%)	1 (2%)	3 (7%)
Follicular cell, adenoma		1 (2%)	1 (2%)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Preputial gland	(49)	(48)	(46)
Lymphoma malignant		1 (2%)	
Prostate	(49)	(49)	(46)
Lymphoma malignant		1 (2%)	
Sarcoma, metastatic, seminal vesicle		1 (2%)	
Seminal vesicle	(49)	(49)	(45)
Lymphoma malignant histiocytic		1 (2%)	
Lymphoma malignant		1 (2%)	
Sarcoma		1 (2%)	
Testes	(49)	(49)	(49)
Lymphoma malignant		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(46)	(48)	(44)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
Lymph node	(48)	(44)	(45)
Inguinal, lymphoma malignant histiocytic			1 (2%)
Mesenteric, lymphoma malignant undifferentiated cell type	1 (2%)		
Pancreatic, lymphoma malignant histiocytic			1 (2%)
Renal, lymphoma malignant histiocytic		1 (2%)	
Lymph node, bronchial	(40)	(29)	(38)
Carcinoma, metastatic, thyroid gland	1 (3%)		
Lymphoma malignant histiocytic	1 (3%)	1 (3%)	1 (3%)
Lymphoma malignant	1 (3%)	1 (3%)	
Lymphoma malignant undifferentiated cell type	1 (3%)		2 (5%)
Lymph node, mandibular	(44)	(40)	(42)
Carcinoma, metastatic, harderian gland		1 (3%)	
Lymphoma malignant histiocytic		1 (3%)	1 (2%)
Lymphoma malignant	1 (2%)	1 (3%)	
Lymphoma malignant undifferentiated cell type	1 (2%)		2 (5%)
Spleen	(50)	(49)	(46)
Lymphoma malignant histiocytic	1 (2%)	1 (2%)	1 (2%)
Lymphoma malignant	1 (2%)	1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	2 (4%)

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

	Chamber Control	5 ppm	10 ppm
HEMATOPOIETIC SYSTEM (Continued)			
Thymus	(46)	(46)	(44)
Carcinoma, metastatic, uncertain primary site			1 (2%)
Lymphoma malignant histiocytic		1 (2%)	1 (2%)
Lymphoma malignant		1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)		1 (2%)
Thymoma malignant	1 (2%)		
INTEGUMENTARY SYSTEM			
Mammary gland	(27)	(40)	(32)
Fibroadenoma			2 (6%)
Skin	(49)	(49)	(49)
Carcinoma, metastatic, thyroid gland	1 (2%)		
Fibroma	2 (4%)		1 (2%)
Hemangioma		1 (2%)	
Keratoacanthoma		1 (2%)	
Sarcoma		2 (4%)	
Lip, squamous cell carcinoma			1 (2%)
MUSCULOSKELETAL SYSTEM			
Bone	(50)	(50)	(49)
Cranium, schwannoma malignant, metastatic, brain		1 (2%)	
Cranium, squamous cell carcinoma, metastatic, nose			1 (2%)
Skeletal muscle	*(50)	*(50)	*(50)
Sarcoma, metastatic, skin		1 (2%)	
NERVOUS SYSTEM			
Brain	(50)	(50)	(50)
Lymphoma malignant histiocytic			1 (2%)
Oligodendroglioma malignant			1 (2%)
Schwannoma malignant		1 (2%)	
Meninges, granular cell tumor benign	1 (2%)		
RESPIRATORY SYSTEM			
Larynx	(39)	(45)	(43)
Carcinoma, metastatic, thyroid gland	1 (3%)		
Lung	(42)	(48)	(45)
Carcinoma, metastatic, harderian gland		1 (2%)	
Carcinoma, metastatic, thyroid gland	1 (2%)		
Lymphoma malignant histiocytic	1 (2%)	1 (2%)	1 (2%)
Lymphoma malignant	1 (2%)	1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	2 (4%)
Pheochromocytoma malignant, metastatic	1 (2%)		
Sarcoma, metastatic, skin		1 (2%)	
Schwannoma malignant, metastatic, brain		1 (2%)	
Nose	(44)	(46)	(43)
Carcinoma, metastatic, harderian gland		1 (2%)	
Lymphoma malignant histiocytic		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
Olfactory epithelium, adenocarcinoma, poorly differentiated			1 (2%)
Respiratory epithelium, adenoma, papillary			1 (2%)
Respiratory epithelium, squamous cell carcinoma			1 (2%)
Trachea	(40)	(45)	(42)
Carcinoma, metastatic, thyroid gland	1 (3%)		

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

	Chamber Control	5 ppm	10 ppm
SPECIAL SENSES SYSTEM			
Eye	*(50)	*(50)	*(50)
Lymphoma malignant undifferentiated cell type			1 (2%)
Harderian gland	*(50)	*(50)	*(50)
Carcinoma		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
URINARY SYSTEM			
Kidney	(50)	(49)	(48)
Adenoma	1 (2%)		
Adenoma, multiple	1 (2%)		
Carcinoma, metastatic, thyroid gland	1 (2%)		
Lymphoma malignant histiocytic		1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)		2 (4%)
Urinary bladder	(46)	(49)	(44)
Lymphoma malignant histiocytic			1 (2%)
Lymphoma malignant		1 (2%)	
Sarcoma, metastatic, seminal vesicle		1 (2%)	
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Lymphoma malignant undifferentiated cell	1 (2%)	1 (2%)	2 (4%)
Lymphoma malignant histiocytic	1 (2%)	1 (2%)	1 (2%)
Lymphoma malignant	1 (2%)	1 (2%)	1 (2%)
Hemangioma		1 (2%)	
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Dead	27	27	29
Moribund	11	13	13
Terminal sacrifice	12	10	8
TUMOR SUMMARY			
Total animals with primary neoplasms **	30	37	38
Total primary neoplasms	59	57	67
Total animals with benign neoplasms	25	31	32
Total benign neoplasms	38	45	51
Total animals with malignant neoplasms	18	12	14
Total malignant neoplasms	21	12	16
Total animals with secondary neoplasms ***	2	4	2
Total secondary neoplasms	7	10	2
Total animals with malignant neoplasms--uncertain primary site			1

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: CHAMBER CONTROL

WEEKS ON STUDY	047	054	058	064	065	069	069	070	073	079	079	081	083	083	084	085	085	086	087	087	087	091	092	094	094
CARCASS ID	4011	0111	2411	0911	3811	0711	4311	4911	2811	3911	5011	1611	1911	1711	1311	1211	3711	1811	4611	0811	4811	4511	1011	2211	1511
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	A	+	+	+	+	A	A	A	+	+	+	+	+	A	A	A	+	+	+
Intestine large, cecum	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	A	+	+	A
Intestine large, colon	+	+	+	+	+	+	A	A	+	+	+	A	M	A	+	+	+	+	+	A	A	A	+	+	+
Intestine large, rectum	+	+	+	+	+	+	A	+	+	+	+	A	A	A	+	+	+	I	+	A	A	+	+	+	A
Intestine small	+	+	+	+	+	+	A	A	+	+	+	A	A	A	+	A	A	A	+	A	A	A	+	+	A
Intestine small, duodenum	+	+	+	+	+	+	A	A	+	+	+	A	M	A	+	A	A	A	+	A	A	A	+	+	A
Intestine small, ileum	+	A	+	A	A	A	A	A	+	A	A	A	A	A	+	A	A	A	A	A	A	A	+	+	A
Intestine small, jejunum	+	A	+	A	A	A	A	A	+	A	A	A	A	A	+	A	A	A	A	A	A	A	+	+	A
Adenocarcinoma, mucinous																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant					X																				
Lymphoma malignant undifferentiated cell type															X										
Mesentery																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																									
Squamous cell carcinoma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Tongue												+													
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									
Lymphoma malignant undifferentiated cell type															X										
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	M	+	+
Lymphoma malignant undifferentiated cell type															X										
Pheochromocytoma malignant																			X					X	
Pheochromocytoma malignant, multiple																									
Pheochromocytoma benign															X						X				
Pheochromocytoma benign, multiple																									
Bilateral, pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	M	M	+	+	+	M	M	M	+	M	+	+	M	+	+	+	M	+	+	+	+	+	+
Adenoma																					X				
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	A
Pars distalis, adenoma													X				X								
Pars distalis, carcinoma																									
Thyroid gland	+	+	+	+	A	+	A	+	+	+	+	A	A	A	+	+	+	+	+	+	+	A	+	+	+
C-cell, adenoma															X										
C-cell, carcinoma																									
GENERAL BODY SYSTEM																									
Tissue, NOS																+									
GENITAL SYSTEM																									
Epididymis	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+
Preputial gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+

+: Tissue examined microscopically
: Not examined
−: Present but not examined microscopically
I: Insufficient tissue
M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	095	096	098	098	099	100	102	103	103	104	105	105	105	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	231	291	411	211	351	031	321	331	471	301	021	141	421	041	051	061	111	201	251	261	271	311	341	361	441	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	41
Intestine large, cecum	+	A	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	23
Intestine large, colon	+	A	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	39
Intestine large, rectum	+	+	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	40
Intestine small	+	A	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	35
Intestine small, duodenum	+	A	A	A	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	33
Intestine small, ileum	A	A	A	+	A	+	A	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	24
Intestine small, jejunum	A	A	A	+	A	+	A	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	24
Adenocarcinoma, mucinous																	X									1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Mesentery				+																						1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, forestomach	+	A	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	45
Papilloma squamous				X																						1
Squamous cell carcinoma															X											1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Tongue																	+									2
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma											X															1
Carcinoma						X																				1
Lymphoma malignant undifferentiated cell type																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant undifferentiated cell type																										1
Pheochromocytoma malignant						X													X			X				5
Pheochromocytoma malignant, multiple				X																	X					2
Pheochromocytoma benign			X							X	X								X	X			X	X		9
Pheochromocytoma benign, multiple																X										1
Bilateral, pheochromocytoma benign																									X	1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	M	+	M	+	+	+	+	+	M	+	M	+	+	+	+	36
Adenoma																										1
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma		X					X				X	X	X						X	X	X		X			11
Pars distalis, carcinoma								X																X		2
Thyroid gland	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
C cell, adenoma		X				X	X		X						X	X			X							8
C cell, carcinoma									X			X	X			X									X	5
GENERAL BODY SYSTEM																										
Tissue, NOS														+												2
GENITAL SYSTEM																										
Epididymis	+	+	M	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	43
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	047	054	058	064	065	069	069	070	073	079	079	081	083	083	084	085	085	086	087	087	087	091	092	094	094
CARCASS ID	401	011	241	091	381	071	431	491	281	391	501	161	191	171	131	121	371	181	461	081	481	451	101	221	151
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	A
Lymph node	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenteric, lymphoma malignant undifferentiated cell type															X										
Lymph node, bronchial	+	M	M	M	+	+	+	+	+	+	+	M	A	M	+	+	+	+	M	+	+	+	M	+	+
Carcinoma, metastatic, thyroid gland																									
Lymphoma malignant histiocytic																									
Lymphoma malignant					X																				
Lymphoma malignant undifferentiated cell type															X										
Lymph node, mandibular	+	M	M	+	+	M	+	M	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Lymphoma malignant					X																				
Lymphoma malignant undifferentiated cell type															X										
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																									
Lymphoma malignant					X																				
Lymphoma malignant undifferentiated cell type															X										
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+
Lymphoma malignant undifferentiated cell type															X										
Thymoma malignant																									
INTEGUMENTARY SYSTEM																									
Mammary gland	M	M	+	+	M	+	+	+	M	+	M	+	M	M	+	+	M	M	+	+	+	M	M	M	A
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A
Carcinoma, metastatic, thyroid gland																									
Fibroma	X																								
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Meninges, granular cell tumor benign																			X						
RESPIRATORY SYSTEM																									
Larynx	+	A	+	+	+	+	A	+	+	+	+	A	A	A	+	A	+	+	+	A	A	+	+	+	A
Carcinoma, metastatic, thyroid gland																									
Lung	+	+	+	+	+	+	A	+	+	+	+	A	A	A	+	+	+	+	+	+	+	+	+	+	A
Carcinoma, metastatic, thyroid gland																									
Lymphoma malignant histiocytic																									
Lymphoma malignant					X																				
Lymphoma malignant undifferentiated cell type															X										
Pheochromocytoma malignant, metastatic																								X	
Nose	+	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	A
Trachea	+	A	+	+	+	+	+	+	+	+	+	A	A	A	+	A	+	+	+	A	A	+	+	+	A
Carcinoma, metastatic, thyroid gland																									
SPECIAL SENSES SYSTEM																									
Eye																									
Harderian gland				+	+		A																		
Lacrimal gland																		+				+		+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Adenoma, multiple																									
Carcinoma, metastatic, thyroid gland																									
Lymphoma malignant undifferentiated cell type															X										
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	A

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	095	096	098	098	099	100	102	103	103	104	105	105	105	106	106	106	106	106	106	106	106	106	106	106	TOTAL
CARCASS ID	2311	2911	4111	2111	3511	0311	3211	3311	4711	3011	0211	1411	4211	0411	0511	0611	1111	2011	2511	2611	2711	3111	3411	3611	4411	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Mesenteric, lymphoma malignant undifferentiated cell type																										1
Lymph node, bronchial	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	40
Carcinoma, metastatic, thyroid gland																									X	1
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Thymus	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant undifferentiated cell type																										1
Thymoma malignant									X																	1
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	M	+	+	+	M	+	M	+	+	+	+	M	M	+	+	M	M	+	+	+	+	+	M	27
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, thyroid gland																									X	1
Fibroma												X														2
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle						+																				1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Meninges, granular cell tumor benign																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	I	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Carcinoma, metastatic, thyroid gland																									X	1
Lung	+	A	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Carcinoma, metastatic, thyroid gland																									X	1
Lymphoma malignant histiocytic																						X				1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Pheochromocytoma malignant meta																										1
Nose	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Trachea	A	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	40
Carcinoma, metastatic, thyroid gland																									X	1
SPECIAL SENSES SYSTEM																										
Eye										+									+							2
Harderian gland			+																							3
Lacrimal gland	+			+		+	+				+	+		+	+	+	+		+	+	+			+	+	19
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma									X																	1
Adenoma, multiple																		X								1
Carcinoma, metastatic, thyroid gland																									X	1
Lymphoma malignant undifferentiated cell type																										1
Urinary bladder	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 5 ppm

WEEKS ON STUDY	033	059	064	064	067	068	072	072	075	075	076	076	080	080	081	081	083	083	084	085	086	087	090	090	091	092
CARCASS ID	12601	15001	13001	12401	12231	12271	10091	14491	13991	10101	11211	14211	10201	12281	11411	11311	13211	14011	11181	13331	14711	11011	14411	14311	10411
ALIMENTARY SYSTEM																										
Esophagus	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	A	+	+	+	+	+	+	A	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	A	+	+
Intestine large, colon	+	+	A	+	+	M	+	+	+	A	A	+	+	A	A	+	A	+	+	+	+	A	A	+	+	+
Intestine large, rectum	+	+	A	+	+	+	+	+	+	A	A	I	+	A	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	A	+	+	A	A	+	+	A	A	+	A	A	A	A	A	+	+	A	A	+	A	+	+	+
Intestine small, duodenum	+	+	A	+	+	A	+	+	+	A	+	+	A	A	A	A	A	+	+	A	A	+	A	+	+	+
Intestine small, ileum	+	+	A	+	A	A	A	+	+	A	A	A	A	A	A	A	A	+	+	A	A	M	A	+	+	+
Intestine small, jejunum	A	A	A	+	A	A	A	+	+	A	A	A	A	A	A	A	A	+	+	A	A	M	A	+	+	+
Liver	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Hepatocellular carcinoma																										
Lymphoma malignant histiocytic																								X		
Lymphoma malignant																										
Lymphoma malignant undifferentiated cell type																										
Pancreas	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																								X		
Lymphoma malignant																										
Salivary glands	+	M	A	+	+	+	+	+	+	+	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland																										
Stomach	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	A	+	M	A	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Squamous cell carcinoma											X			X												
Stomach, glandular	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant																										
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																								X		
Lymphoma malignant																										
Lymphoma malignant undifferentiated cell type																										
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Lymphoma malignant histiocytic																								X		
Adrenal gland, medulla	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	M	+	+	+	+	+	+
Lymphoma malignant histiocytic																								X		
Pheochromocytoma benign								X																		
Pheochromocytoma benign, multiple																		X	X							
Islets, pancreatic	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+
Adenoma																										
Parathyroid gland	M	+	M	M	M	+	+	M	M	M	+	M	+	M	M	+	M	+	+	I	+	+	+	+	+	M
Pituitary gland	+	+	A	+	+	+	+	+	+	+	+	+	+	M	+	I	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																								X		
Lymphoma malignant																										
Pars distalis, adenoma																			X	X	X		X			
Pars intermedia, adenoma																										
Thyroid gland	+	+	A	+	+	A	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+
C-cell, adenoma												X											X			
C-cell, adenoma, multiple																										
C-cell, carcinoma																										
Follicular cell, adenoma												X														
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis	+	+	A	+	M	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	
Preputial gland	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant																										
Prostate	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant																										
Sarcoma, metastatic, seminal vesicle																										
Seminal vesicle	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																								X		
Lymphoma malignant																										
Sarcoma																										
Testes	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant																										

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 5 ppm (Continued)

WEEKS ON STUDY	092	093	094	095	095	096	096	097	098	098	099	101	102	104	106	106	106	106	106	106	106	106	106	106	TOTAL: TISSUES TUMORS
CARCASS ID	14601	13701	10501	14801	12201	11601	13501	12101	10301	12501	11301	14401	12001	10801	10601	10701	11101	11501	11701	11901	12901	13401	13601	13801	14501	
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine large, cecum	+	A	A	A	+	+	+	+	+	A	+	M	A	+	+	+	+	+	+	+	+	+	+	+	+	21
Intestine large, colon	+	A	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Intestine large, rectum	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Intestine small	+	+	A	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	34
Intestine small, duodenum	+	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	37
Intestine small, ileum	+	A	A	A	+	+	M	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	27
Intestine small, jejunum	+	A	A	A	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	27
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma																							X			1
Hepatocellular carcinoma				X																						1
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Lymphoma malignant undifferentiated cell type											X															1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Carcinoma, metastatic, harderian gland							X																			1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	43
Squamous cell carcinoma																										2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant												X														1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Lymphoma malignant undifferentiated cell type											X															1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma											X															1
Lymphoma malignant histiocytic																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant histiocytic																										1
Pheochromocytoma benign		X				X		X					X		X										X	7
Pheochromocytoma benign, multiple							X			X				X		X								X		7
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma																	X				X					2
Parathyroid gland	+	M	M	M	M	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	M	+	30
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	46
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Pars distalis, adenoma				X			X			X			X	X					X	X					X	12
Pars intermedia, adenoma																X			X							2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
C-cell, adenoma					X		X			X		X			X		X					X				9
C-cell, adenoma, multiple																		X								1
C-cell, carcinoma																								X		1
Follicular cell, adenoma																										1
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	I	+	+	+	M	+	+	+	+	+	42
Preputial gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant												X														1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant												X														1
Sarcoma, metastatic, seminal vesicle	X																									1
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Sarcoma	X																									1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant												X														1

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 5 ppm (Continued)

WEEKS ON STUDY	033	059	064	064	067	068	072	072	075	075	076	076	080	080	081	083	083	084	085	086	087	090	090	091	092
CARCASS ID	12601	15001	13001	12401	12301	12701	10901	14901	13901	10101	11201	14201	10201	12801	11401	13101	13201	14001	11801	13301	14701	11001	14101	14331	10401
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant																									
Lymph node	+	M	A	M	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	M	+	+
Renal, lymphoma malignant histiocytic																								X	
Lymph node, bronchial	+	M	A	M	+	+	M	+	+	+	+	+	+	M	+	M	+	+	+	+	+	M	M	+	+
Lymphoma malignant histiocytic																								X	
Lymphoma malignant																									
Lymph node, mandibular	+	M	M	M	M	M	+	+	+	+	+	+	+	A	+	+	+	M	+	+	+	+	M	+	+
Carcinoma, metastatic, harderian gland																									
Lymphoma malignant histiocytic																								X	
Lymphoma malignant																									
Spleen	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																								X	
Lymphoma malignant																									
Lymphoma malignant undifferentiated cell type																									
Thymus	+	+	A	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																								X	
Lymphoma malignant																									
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	M	+	+	+	+	+	+	M	+	+	M	M	+	+	+	+	+	+	M	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma															X										
Keratoacanthoma																									
Sarcoma				X					X																
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cranium, schwannoma malignant, metastatic, brain																									
Skeletal muscle				+																					
Sarcoma, metastatic, skin				X																					
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Schwannoma malignant																									
RESPIRATORY SYSTEM																									
Larynx	+	+	A	+	+	A	+	+	+	+	+	A	+	A	+	+	+	+	+	A	+	+	+	+	+
Lung	+	+	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, harderian gland																									
Lymphoma malignant histiocytic																								X	
Lymphoma malignant																									
Lymphoma malignant undifferentiated cell type																									
Sarcoma, metastatic, skin				X																					
Schwannoma malignant, metastatic, brain																									
Nose	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+
Carcinoma, metastatic, harderian gland																									
Lymphoma malignant histiocytic																								X	
Trachea	+	+	A	+	+	A	+	+	+	+	+	A	+	A	A	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye																									
Harderian gland																									
Carcinoma																									
Lacrimal gland																			+				+		+
Zymbal gland																									
URINARY SYSTEM																									
Kidney	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																								X	
Urinary bladder	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant																									
Sarcoma, metastatic, seminal vesicle																									

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 5 ppm (Continued)

WEEKS ON STUDY	092	093	094	095	095	096	096	097	098	098	099	101	102	104	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	14611	13711	10511	14811	12211	11611	13511	12111	10311	12511	11311	14411	12011	10811	10611	10711	11111	11511	11711	11911	12911	13411	13611	13811	14511	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant												X														1
Lymph node	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Renal, lymphoma malignant histiocytic																										1
Lymph node, bronchial	+	+	M	M	+	M	M	M	+	+	M	+	+	M	+	M	M	+	M	M	+	+	+	M	M	29
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	40
Carcinoma, metastatic, harderian gland								X																		1
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Lymphoma malignant undifferentiated cell type											X															1
Thymus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
INTEGUMENTARY SYSTEM																										
Mammary gland	M	+	+	+	+	M	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	40
Skin	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangioma																										1
Keratoacanthoma										X																1
Sarcoma																										2
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cranium, schwannoma malignant, metastatic, brain					X																					1
Skeletal muscle																										1
Sarcoma, metastatic, skin																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Schwannoma malignant					X																					1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, harderian gland								X																		1
Lymphoma malignant histiocytic																										1
Lymphoma malignant												X														1
Lymphoma malignant undifferentiated cell type											X															1
Sarcoma, metastatic, skin																										1
Schwannoma malignant, meta., brain					X																					1
Nose	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Carcinoma, metastatic, harderian gland								X																		1
Lymphoma malignant histiocytic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
SPECIAL SENSES SYSTEM																										
Eye															+											1
Harderian gland								+					+													2
Carcinoma								X																		1
Lacrimal gland	+	+	+	+	+						+		+	+	+		+	+	+	+	+	+	+	+	+	21
Zymbal gland													+													1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant												X														1
Sarcoma, metastatic, seminal vesicle	X																									1

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 10 ppm

WEEKS ON STUDY	0 1 6	0 3 8	0 4 1	0 4 3	0 4 4	0 6 2	0 6 9	0 7 5	0 7 5	0 7 5	0 7 7	0 8 0	0 8 2	0 8 2	0 8 2	0 8 3	0 8 3	0 8 4	0 8 4	0 8 4	0 8 5	0 8 5	0 8 5	0 8 6	0 8 6
CARCASS ID	20411	22411	22611	20911	24511	23911	20511	25011	23111	21811	20811	24811	22311	20211	22511	24911	23511	24211	22911	23311	21911	21211	22711	20611	20111
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	A	+	+	+	A	+	+	+	A	A	+	A	A	+	+	+	+	A	+	+	+	+	A	+	A
Intestine large, cecum	M	M	M	M	M	M	M	M	A	A	M	A	M	M	M	M	M	M	M	M	M	M	M	M	A
Lymphoma malignant undifferentiated cell type																									
Intestine large, colon	A	+	A	+	A	+	+	+	A	A	+	A	A	+	A	+	+	A	+	A	+	+	A	+	A
Lymphoma malignant undifferentiated cell type																									
Intestine large, rectum	A	+	+	+	A	+	+	+	A	A	+	A	A	+	+	+	+	A	+	+	+	+	A	+	A
Lymphoma malignant undifferentiated cell type																									
Intestine small	A	+	+	+	A	+	A	+	A	A	+	A	A	A	+	+	+	A	+	+	+	+	A	+	A
Intestine small, duodenum	A	+	+	A	A	+	A	+	A	A	+	A	A	A	+	+	+	A	+	+	+	+	A	+	A
Lymphoma malignant histiocytic																					X				
Lymphoma malignant undifferentiated cell type																									
Intestine small, ileum	A	+	A	+	A	+	A	+	A	A	A	A	A	A	A	+	A	A	+	A	M	+	A	A	A
Lymphoma malignant undifferentiated cell type																									
Intestine small, jejunum	A	+	A	+	A	+	A	+	A	A	A	A	A	A	A	+	A	A	+	A	+	+	A	A	A
Lymphoma malignant histiocytic																					X				
Lymphoma malignant undifferentiated cell type																									
Liver	+	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																					X				
Lymphoma malignant undifferentiated cell type																			X						
Mesentery											+														
Pancreas	A	+	+	+	A	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																					X				
Salivary glands	A	+	+	+	+	+	+	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																									
Stomach	A	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Stomach, forestomach	A	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	M	+	+
Squamous cell carcinoma																									
Stomach, glandular	A	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																			X						
ENDOCRINE SYSTEM																									
Adrenal gland	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma														X											
Lymphoma malignant undifferentiated cell type																			X						
Adrenal gland, medulla	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Lymphoma malignant undifferentiated cell type																			X						
Pheochromocytoma malignant																							X		
Pheochromocytoma malignant, multiple																									
Pheochromocytoma benign					X								X			X		X		X				X	
Pheochromocytoma benign, multiple														X											
Islets, pancreatic	A	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Adenoma																									
Parathyroid gland	M	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	M	+
Adenoma					X												X								
Pituitary gland	M	+	+	+	A	I	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																					X				
Lymphoma malignant undifferentiated cell type																									
Pars distalis, adenoma													X	X		X	X						X		
Pars intermedia, adenoma								X																	
Thyroid gland	M	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																							X		
C-cell, adenoma, multiple																									X
C-cell, carcinoma																									
Follicular cell, adenoma																									
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Epididymis	M	+	+	+	+	+	+	+	M	+	+	+	I	+	M	+	+	A	+	+	+	+	+	+	+
Preputial gland	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	A	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Seminal vesicle	A	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																			X						

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 10 ppm
(*Continued*)

WEEKS ON STUDY	087	088	089	090	091	092	092	094	094	095	096	097	097	098	100	101	105	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	24111	23011	20311	23411	22211	23811	24411	21311	23611	24311	21611	21111	21411	22111	21011	24711	23711	20711	21511	21711	22011	22281	23211	24011	24611	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	A	A	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	37
Intestine large, cecum	M	M	M	M	+	+	+	+	A	+	A	+	A	A	+	M	A	+	+	+	+	+	+	+	+	15
Lymphoma malignant undifferentiated cell type						X																				1
Intestine large, colon	A	A	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	34
Lymphoma malignant undifferentiated cell type						X																				1
Intestine large, rectum	M	+	+	+	+	+	+	+	+	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	38
Lymphoma malignant undifferentiated cell type						X																				1
Intestine small	A	A	+	+	+	+	+	+	A	+	+	+	A	+	+	A	+	+	+	+	+	+	+	+	+	34
Intestine small, duodenum	A	A	+	+	+	+	+	+	A	+	+	+	M	+	+	A	+	+	+	+	+	+	+	+	+	33
Lymphoma malignant histiocytic																										1
Lymphoma malignant undifferentiated cell type						X																				1
Intestine small, ileum	A	M	+	+	+	+	+	+	A	+	A	A	A	A	+	A	A	+	+	+	+	+	+	+	+	23
Lymphoma malignant undifferentiated cell type						X																				1
Intestine small, jejunum	A	A	+	+	+	+	+	+	A	A	+	A	A	A	+	A	+	+	+	+	+	+	+	+	+	25
Lymphoma malignant histiocytic																										1
Lymphoma malignant undifferentiated cell type						X																				1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant histiocytic																										1
Lymphoma malignant undifferentiated cell type						X																				2
Mesentery																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	44
Lymphoma malignant histiocytic																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant undifferentiated cell type						X																				1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Stomach, forestomach	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Squamous cell carcinoma																			X							1
Stomach, glandular	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant undifferentiated cell type																										1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma														X												2
Lymphoma malignant undifferentiated cell type						X																				2
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant undifferentiated cell type						X																				2
Pheochromocytoma malignant										X									X							3
Pheochromocytoma malignant, multiple																									X	1
Pheochromocytoma benign					X	X			X		X		X								X					12
Pheochromocytoma benign, multiple								X																		2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	45
Adenoma																						X				1
Parathyroid gland	+	+	+	+	+	M	M	+	+	+	+	+	+	M	+	+	M	+	+	+	M	+	M	+	+	38
Adenoma																										2
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	M	44
Lymphoma malignant histiocytic																										1
Lymphoma malignant undifferentiated cell type						X																				1
Pars distalis, adenoma	X						X				X			X	X		X	X						X		13
Pars intermedia, adenoma																					X					2
Thyroid gland	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
C-cell, adenoma	X	X			X		X			X						X		X				X				10
C-cell, adenoma, multiple						X													X							2
C-cell, carcinoma														X			X				X					3
Follicular cell, adenoma													X													1
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis	+	I	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Preputial gland	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Seminal vesicle	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 10 ppm (Continued)

WEEKS ON STUDY	016	038	041	043	044	062	069	075	075	075	077	080	082	082	082	083	083	084	084	084	084	085	085	085	086	086
CARCASS ID	20411	22411	22611	20911	24511	23911	20511	25011	23111	21811	20811	24811	22311	20211	22511	24911	23511	24211	22911	23311	21911	21211	22711	20611	20111
HEMATOPOIETIC SYSTEM																										
Blood																										
Bone marrow	A	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																					X					
Lymphoma malignant undifferentiated cell type																										
Lymph node	A	+	+	+	+	+	M	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	
Inguinal, lymphoma malignant histiocytic																					X					
Pancreatic, lymphoma malignant histiocytic																					X					
Lymph node, bronchial	A	+	+	+	+	M	M	+	+	+	+	M	M	+	M	M	M	+	+	+	+	M	+	+	M	
Lymphoma malignant histiocytic																					X					
Lymphoma malignant undifferentiated cell type																			X							
Lymph node, mandibular	A	+	+	M	+	+	M	M	+	M	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																					X					
Lymphoma malignant undifferentiated cell type																			X							
Spleen	+	+	+	+	+	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																					X					
Lymphoma malignant undifferentiated cell type																			X							
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+	
Carcinoma, metastatic, uncertain primary site															X											
Lymphoma malignant histiocytic																					X					
Lymphoma malignant																	X									
Lymphoma malignant undifferentiated cell type																										
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	+	+	+	+	+	+	+	M	M	M	M	+	M	M	+	M	+	+	+	+	+	+	+	
Fibroadenoma								X																		
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Fibroma																										
Lip, squamous cell carcinoma																										
MUSCULOSKELETAL SYSTEM																										
Bone	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Cranium, squamous cell carcinoma, metastatic, nose																						X				
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																					X					
Oligodendroglioma malignant				X																						
RESPIRATORY SYSTEM																										
Larynx	A	+	+	+	A	+	+	+	A	+	+	+	A	A	+	+	+	A	+	+	+	+	+	+	+	
Lung	A	+	+	+	A	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																					X					
Lymphoma malignant undifferentiated cell type																			X							
Nose	A	+	+	+	A	+	+	+	A	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	
Lymphoma malignant undifferentiated cell type																										
Olfactory epithelium, adenocarcinoma, poorly differentiated						X																				
Respiratory epithelium, adenoma, papillary																										
Respiratory epithelium, squamous cell carcinoma																						X				
Trachea	A	+	+	+	A	+	A	+	A	+	+	+	A	A	+	+	+	A	+	+	+	+	+	+	+	
SPECIAL SENSES SYSTEM																										
Eye						+																				
Lymphoma malignant undifferentiated cell type																										
Harderian gland																					+					
Lymphoma malignant undifferentiated cell type																										
Lacrimal gland																										
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	A	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																					X					
Lymphoma malignant undifferentiated cell type																			X							
Urinary bladder	A	+	+	+	+	+	+	+	A	+	+	+	A	A	+	+	+	A	+	+	+	+	+	+	+	
Lymphoma malignant histiocytic																					X					

TABLE A2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: 10 ppm (Continued)

WEEKS ON STUDY	087	088	089	090	091	092	092	094	094	095	096	097	097	098	100	101	105	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	24111	23011	20311	23411	22211	23811	24411	21311	23611	24311	21611	21111	21411	22111	21011	24711	23711	20711	21511	21711	22011	22281	23211	24011	24461	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																									
Blood															+										1
Bone marrow	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	44
Lymphoma malignant histiocytic																									1
Lymphoma malignant undifferentiated cell type						X																			1
Lymph node	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Inguinal, lymphoma malignant histiocytic																									1
Pancreatic, lymphoma malignant histiocytic																									1
Lymph node, bronchial	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Lymphoma malignant histiocytic																									1
Lymphoma malignant undifferentiated cell type						X																			2
Lymph node, mandibular	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Lymphoma malignant histiocytic																									1
Lymphoma malignant undifferentiated cell type						X																			2
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	46
Lymphoma malignant histiocytic																									1
Lymphoma malignant undifferentiated cell type						X																			2
Thymus	+	+	+	M	+	+	+	M	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	44
Carcinoma, metastatic, uncertain primary site																									1
Lymphoma malignant histiocytic																									1
Lymphoma malignant																									1
Lymphoma malignant undifferentiated cell type						X																			1
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	M	M	M	+	+	+	+	+	+	M	M	M	M	+	+	+	M	+	+	M	+	32
Fibroadenoma				X																					2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	49
Fibroma								X																	1
Lip, squamous cell carcinoma										X															1
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cranium, squamous cell carcinoma, metastatic, nose																									1
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																									1
Oligodendroglioma malignant																									1
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	43
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymphoma malignant histiocytic																									1
Lymphoma malignant undifferentiated cell type						X																			2
Nose	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	43
Lymphoma malignant undifferentiated cell type						X																			1
Olfactory epithelium, adenocarcinoma, poorly differentiated																									1
Respiratory epithelium, adenoma, papillary																		X							1
Respiratory epithelium, squamous cell carcinoma																									1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	42
SPECIAL SENSES SYSTEM																									
Eye						+																			2
Lymphoma malignant undifferentiated cell type						X																			1
Harderian gland		+		+		+			+					+							+		+		8
Lymphoma malignant undifferentiated cell type						X																			1
Lacrimal gland			M		+			+		+				+			+		+	+					7
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant histiocytic																									1
Lymphoma malignant undifferentiated cell type						X																			2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	44
Lymphoma malignant histiocytic																									1

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Adrenal Medulla: Pheochromocytoma			
Overall Rates (a)	11/47 (23%)	14/47 (30%)	14/47 (30%)
Adjusted Rates (b)	60.7%	62.1%	50.7%
Terminal Rates (c)	6/12 (50%)	4/11 (36%)	1/8 (13%)
Day of First Observation	586	500	303
Life Table Tests (d)	P=0.069	P=0.197	P=0.099
Logistic Regression Tests (d)	P=0.184	P=0.227	P=0.241
Cochran-Armitage Trend Test (d)	P=0.282		
Fisher Exact Test (d)		P=0.321	P=0.321
Adrenal Medulla: Malignant Pheochromocytoma			
Overall Rates (a)	7/47 (15%)	0/47 (0%)	4/47 (9%)
Adjusted Rates (b)	36.6%	0.0%	32.2%
Terminal Rates (c)	3/12 (25%)	0/11 (0%)	2/8 (25%)
Day of First Observation	604		593
Life Table Tests (d)	P=0.355N	P=0.019N	P=0.544N
Logistic Regression Tests (d)	P=0.264N	P=0.012N	P=0.414N
Cochran-Armitage Trend Test (d)	P=0.168N		
Fisher Exact Test (d)		P=0.006N	P=0.261N
Adrenal Medulla: Pheochromocytoma or Malignant Pheochromocytoma			
Overall Rates (a)	17/47 (36%)	14/47 (30%)	18/47 (38%)
Adjusted Rates (b)	77.8%	62.1%	68.2%
Terminal Rates (c)	8/12 (67%)	4/11 (36%)	3/8 (38%)
Day of First Observation	586	500	303
Life Table Tests (d)	P=0.106	P=0.537N	P=0.122
Logistic Regression Tests (d)	P=0.297	P=0.425N	P=0.347
Cochran-Armitage Trend Test (d)	P=0.457		
Fisher Exact Test (d)		P=0.331N	P=0.500
Pituitary Gland/Pars Distalis: Adenoma			
Overall Rates (a)	11/47 (23%)	12/46 (26%)	13/44 (30%)
Adjusted Rates (b)	56.3%	55.9%	61.2%
Terminal Rates (c)	4/11 (36%)	3/10 (30%)	2/7 (29%)
Day of First Observation	578	591	568
Life Table Tests (d)	P=0.093	P=0.343	P=0.120
Logistic Regression Tests (d)	P=0.167	P=0.397	P=0.202
Cochran-Armitage Trend Test (d)	P=0.293		
Fisher Exact Test (d)		P=0.476	P=0.335
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma			
Overall Rates (a)	13/47 (28%)	12/46 (26%)	13/44 (30%)
Adjusted Rates (b)	64.6%	55.9%	61.2%
Terminal Rates (c)	5/11 (45%)	3/10 (30%)	2/7 (29%)
Day of First Observation	578	591	568
Life Table Tests (d)	P=0.171	P=0.492	P=0.201
Logistic Regression Tests (d)	P=0.299	P=0.581	P=0.335
Cochran-Armitage Trend Test (d)	P=0.469		
Fisher Exact Test (d)		P=0.525N	P=0.513
Thyroid Gland: C-Cell Adenoma			
Overall Rates (a)	8/43 (19%)	10/46 (22%)	12/46 (26%)
Adjusted Rates (b)	40.6%	52.8%	61.4%
Terminal Rates (c)	3/12 (25%)	4/11 (36%)	3/8 (38%)
Day of First Observation	586	531	593
Life Table Tests (d)	P=0.036	P=0.263	P=0.049
Logistic Regression Tests (d)	P=0.092	P=0.346	P=0.126
Cochran-Armitage Trend Test (d)	P=0.235		
Fisher Exact Test (d)		P=0.459	P=0.278

TABLE A3. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR INHALATION STUDYOF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
Thyroid Gland: C-Cell Carcinoma			
Overall Rates (a)	5/43 (12%)	1/46 (2%)	3/46 (7%)
Adjusted Rates (b)	32.5%	9.1%	28.7%
Terminal Rates (c)	2/12 (17%)	1/11 (9%)	1/8 (13%)
Day of First Observation	719	737	681
Life Table Tests (d)	P=0.495N	P=0.150N	P=0.644
Logistic Regression Tests (d)	P=0.525N	P=0.166N	P=0.646
Cochran-Armitage Trend Test (d)	P=0.235N		
Fisher Exact Test (d)		P=0.087N	P=0.319N
Thyroid Gland: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	11/43 (26%)	11/46 (24%)	15/46 (33%)
Adjusted Rates (b)	54.7%	59.5%	74.9%
Terminal Rates (c)	4/12 (33%)	5/11 (45%)	4/8 (50%)
Day of First Observation	586	531	593
Life Table Tests (d)	P=0.028	P=0.424	P=0.036
Logistic Regression Tests (d)	P=0.061	P=0.515	P=0.079
Cochran-Armitage Trend Test (d)	P=0.262		
Fisher Exact Test (d)		P=0.525N	P=0.311
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (e)	3/50 (6%)	3/50 (6%)	4/50 (8%)
Adjusted Rates (b)	12.8%	16.5%	13.7%
Terminal Rates (c)	1/12 (8%)	0/11 (0%)	0/8 (0%)
Day of First Observation	449	635	580
Life Table Tests (d)	P=0.282	P=0.591	P=0.408
Logistic Regression Tests (d)	P=0.409	P=0.659	P=0.521
Cochran-Armitage Trend Test (d)	P=0.421		
Fisher Exact Test (d)		P=0.661N	P=0.500

(a) Number of tumor-bearing animals/number of animals examined microscopically at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals killed at the end of the study
(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 logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) Number of tumor-bearing animals/number of animals examined grossly at the site

TABLE A4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine large, cecum	(23)	(21)	(15)
Parasite metazoan	2 (9%)	1 (5%)	2 (13%)
Artery, inflammation			1 (7%)
Intestine large, colon	(39)	(38)	(34)
Parasite metazoan	4 (10%)	3 (8%)	4 (12%)
Intestine large, rectum	(40)	(42)	(38)
Parasite metazoan	4 (10%)	2 (5%)	
Artery, inflammation		2 (5%)	
Intestine small, ileum	(24)	(27)	(23)
Artery, inflammation			1 (4%)
Liver	(49)	(49)	(47)
Angiectasis	1 (2%)	1 (2%)	2 (4%)
Basophilic focus	1 (2%)	1 (2%)	
Clear cell focus	1 (2%)	4 (8%)	3 (6%)
Developmental malformation	1 (2%)		
Hematopoietic cell proliferation	1 (2%)	2 (4%)	1 (2%)
Inflammation, granulomatous	3 (6%)		
Inflammation, suppurative		1 (2%)	
Necrosis		3 (6%)	2 (4%)
Bile duct, cyst			1 (2%)
Bile duct, fibrosis	1 (2%)	2 (4%)	6 (13%)
Bile duct, hyperplasia		1 (2%)	2 (4%)
Mesentery	(1)		(1)
Inflammation	1 (100%)		
Artery, inflammation			1 (100%)
Pancreas	(48)	(48)	(44)
Atrophy	2 (4%)	6 (13%)	2 (5%)
Fibrosis			1 (2%)
Hemorrhage			1 (2%)
Infarct			1 (2%)
Inflammation, chronic		1 (2%)	
Inflammation, suppurative		1 (2%)	
Acinus, hyperplasia	1 (2%)	1 (2%)	2 (5%)
Artery, inflammation	6 (13%)	7 (15%)	9 (20%)
Artery, thrombus			1 (2%)
Salivary glands	(50)	(46)	(47)
Cyst		1 (2%)	
Inflammation, chronic	12 (24%)	6 (13%)	5 (11%)
Inflammation, granulomatous		1 (2%)	
Inflammation, suppurative	2 (4%)		
Karyomegaly	21 (42%)	23 (50%)	20 (43%)
Stomach	(48)	(49)	(46)
Cyst			1 (2%)
Necrosis			1 (2%)
Artery, inflammation	1 (2%)	1 (2%)	
Stomach, forestomach	(45)	(43)	(44)
Acanthosis		2 (5%)	
Hyperkeratosis			1 (2%)
Inflammation, suppurative	1 (2%)		1 (2%)
Stomach, glandular	(48)	(48)	(45)
Developmental malformation		1 (2%)	
Hemorrhage			1 (2%)
Hyperplasia			1 (2%)
Inflammation, necrotizing			1 (2%)
Mineralization	4 (8%)	1 (2%)	1 (2%)
Necrosis		1 (2%)	
Artery, inflammation	2 (4%)		1 (2%)

TABLE A4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
ALIMENTARY SYSTEM (Continued)			
Tongue	(2)		
Hyperplasia, squamous	1 (50%)		
CARDIOVASCULAR SYSTEM			
Heart	(50)	(50)	(50)
Cardiomyopathy	12 (24%)	12 (24%)	19 (38%)
Inflammation, suppurative			2 (4%)
Aortic valve, mineralization	2 (4%)		
Artery, inflammation	2 (4%)	1 (2%)	1 (2%)
Artery, mineralization	7 (14%)	2 (4%)	2 (4%)
Atrium, mineralization	1 (2%)		
Atrium, thrombus	8 (16%)	3 (6%)	8 (16%)
Endocardium, fibrosis		1 (2%)	1 (2%)
Myocardium, hemorrhage			1 (2%)
Ventricle, mineralization	1 (2%)		
Ventricle, thrombus			1 (2%)
Ventricle right, dilatation			1 (2%)
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(48)	(48)	(48)
Angiectasis		1 (2%)	
Hemorrhage	1 (2%)		
Hyperplasia	8 (17%)	15 (31%)	13 (27%)
Hypertrophy			1 (2%)
Infarct			1 (2%)
Inflammation, chronic		1 (2%)	
Mineralization		1 (2%)	
Necrosis		1 (2%)	1 (2%)
Vacuolization cytoplasmic	10 (21%)	14 (29%)	17 (35%)
Adrenal gland, medulla	(47)	(47)	(47)
Hemorrhage			1 (2%)
Hyperplasia	10 (21%)	11 (23%)	10 (21%)
Hyperplasia, multiple	1 (2%)		
Mineralization	1 (2%)		
Islets, pancreatic	(48)	(48)	(45)
Hyperplasia		1 (2%)	1 (2%)
Parathyroid gland	(36)	(30)	(38)
Hyperplasia	2 (6%)	1 (3%)	1 (3%)
Hyperplasia, multiple		1 (3%)	
Pituitary gland	(47)	(46)	(44)
Pars distalis, cyst	2 (4%)	3 (7%)	3 (7%)
Pars distalis, hyperplasia	2 (4%)	2 (4%)	4 (9%)
Pars intermedia, hyperplasia			1 (2%)
Thyroid gland	(43)	(46)	(46)
Inflammation, chronic	1 (2%)		
Ultimobranchial cyst	4 (9%)	2 (4%)	3 (7%)
C-cell, hyperplasia	10 (23%)	7 (15%)	7 (15%)
Follicular cell, hyperplasia		1 (2%)	
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Epididymis	(43)	(42)	(42)
Artery, inflammation	1 (2%)		

TABLE A4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
GENITAL SYSTEM (Continued)			
Preputial gland	(49)	(48)	(46)
Cyst	7 (14%)	2 (4%)	2 (4%)
Hyperplasia			1 (2%)
Inflammation, suppurative	22 (45%)	23 (48%)	15 (33%)
Prostate	(49)	(49)	(46)
Cyst		1 (2%)	
Inflammation, suppurative	3 (6%)	4 (8%)	4 (9%)
Mineralization			1 (2%)
Artery, inflammation			1 (2%)
Epithelium, hyperplasia			1 (2%)
Seminal vesicle	(49)	(49)	(45)
Inflammation, suppurative	3 (6%)	2 (4%)	4 (9%)
Artery, inflammation	1 (2%)		1 (2%)
Testes	(49)	(49)	(49)
Infarct			1 (2%)
Mineralization	1 (2%)	6 (12%)	7 (14%)
Artery, inflammation	10 (20%)	10 (20%)	11 (22%)
Seminiferous tubule, atrophy	7 (14%)	6 (12%)	3 (6%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(46)	(48)	(44)
Fibrosis			1 (2%)
Lymph node	(48)	(44)	(45)
Fibrosis		1 (2%)	
Hyperplasia, lymphoid	1 (2%)		
Mediastinal, hemorrhage		1 (2%)	
Renal, hemorrhage	3 (6%)		
Lymph node, bronchial	(40)	(29)	(38)
Hemorrhage	5 (13%)		6 (16%)
Inflammation, granulomatous		1 (3%)	
Lymph node, mandibular	(44)	(40)	(42)
Hemorrhage	2 (5%)		3 (7%)
Hyperplasia, lymphoid	1 (2%)	1 (3%)	2 (5%)
Infiltration cellular, histiocytic	1 (2%)		
Inflammation, chronic	1 (2%)		
Inflammation, suppurative	1 (2%)		2 (5%)
Spleen	(50)	(49)	(46)
Hematopoietic cell proliferation		4 (8%)	1 (2%)
Hemorrhage		2 (4%)	
Infarct		1 (2%)	1 (2%)
Thymus	(46)	(46)	(44)
Hemorrhage			2 (5%)
Thrombus			1 (2%)
Artery, inflammation	1 (2%)		2 (5%)
INTEGUMENTARY SYSTEM			
Skin	(49)	(49)	(49)
Giant cell	1 (2%)		
Granuloma	1 (2%)		
Inflammation, suppurative		1 (2%)	
MUSCULOSKELETAL SYSTEM			
Bone	(50)	(50)	(49)
Osteoporosis			1 (2%)
Skeletal muscle	(1)	(1)	
Laryngeal, degeneration	1 (100%)		

TABLE A4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
NERVOUS SYSTEM			
Brain	(50)	(50)	(50)
Compression	1 (2%)	1 (2%)	
Demyelination	1 (2%)		
Gliosis		1 (2%)	
Hemorrhage	4 (8%)	2 (4%)	3 (6%)
Necrosis			1 (2%)
Thrombus	1 (2%)		
Ventricle, dilatation	1 (2%)		
RESPIRATORY SYSTEM			
Larynx	(39)	(45)	(43)
Inflammation, chronic	2 (5%)		2 (5%)
Inflammation, suppurative		1 (2%)	2 (5%)
Artery, inflammation			1 (2%)
Epithelium, hyperplasia			2 (5%)
Lung	(42)	(48)	(45)
Foreign body	1 (2%)	1 (2%)	
Hemorrhage	7 (17%)	7 (15%)	8 (18%)
Inflammation, granulomatous	5 (12%)	3 (6%)	2 (4%)
Leukocytosis		1 (2%)	
Alveolar epithelium, hyperplasia	2 (5%)	6 (13%)	5 (11%)
Alveolus, edema	1 (2%)	2 (4%)	2 (4%)
Alveolus, fibrosis	2 (5%)	4 (8%)	2 (4%)
Alveolus, infiltration cellular, histiocytic	7 (17%)	17 (35%)	19 (42%)
Alveolus, inflammation, suppurative	6 (14%)	5 (10%)	7 (16%)
Alveolus, mineralization			1 (2%)
Artery, inflammation	7 (17%)	12 (25%)	6 (13%)
Artery, mineralization	18 (43%)	22 (46%)	16 (36%)
Bronchiole, infiltration cellular, histiocytic		1 (2%)	
Bronchiole, inflammation, suppurative	1 (2%)	1 (2%)	1 (2%)
Nose	(44)	(46)	(43)
Foreign body	1 (2%)	3 (7%)	1 (2%)
Inflammation, suppurative	9 (20%)	27 (59%)	18 (42%)
Inflammation, membranous	3 (7%)	4 (9%)	7 (16%)
Glands, dilatation	8 (18%)	20 (43%)	21 (49%)
Nasolacrimal duct, inflammation, suppurative	7 (16%)	3 (7%)	9 (21%)
Olfactory epithelium, degeneration		45 (98%)	43 (100%)
Olfactory epithelium, metaplasia		6 (13%)	9 (21%)
Olfactory epithelium, metaplasia, squamous		19 (41%)	35 (81%)
Respiratory epithelium, hyperplasia	4 (9%)	33 (72%)	30 (70%)
Respiratory epithelium, metaplasia, squamous	4 (9%)	40 (87%)	38 (88%)
Trachea	(40)	(45)	(42)
Inflammation, chronic			2 (5%)
Inflammation, suppurative	1 (3%)		
Artery, inflammation			1 (2%)
SPECIAL SENSES SYSTEM			
Eye	(2)	(1)	(2)
Cataract			1 (50%)
Harderian gland	(3)	(2)	(8)
Hyperplasia	2 (67%)		
Inflammation, chronic	1 (33%)		8 (100%)
Karyomegaly			7 (88%)
Lacrimal gland	(19)	(21)	(7)
Hyperplasia			1 (14%)
Inflammation, chronic	19 (100%)	21 (100%)	7 (100%)
Inflammation, suppurative		1 (5%)	
Karyomegaly	19 (100%)	21 (100%)	7 (100%)

TABLE A4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
URINARY SYSTEM			
Kidney	(50)	(49)	(48)
Cyst	1 (2%)	1 (2%)	2 (4%)
Hemorrhage	1 (2%)		
Inflammation, suppurative	1 (2%)		
Nephropathy, chronic	49 (98%)	49 (100%)	47 (98%)
Artery, mineralization	1 (2%)		
Glomerulus, mineralization			1 (2%)
Pelvis, hemorrhage		1 (2%)	
Pelvis, hyperplasia	2 (4%)	2 (4%)	2 (4%)
Pelvis, inflammation, suppurative		2 (4%)	3 (6%)
Pelvis, mineralization	3 (6%)	3 (6%)	2 (4%)
Renal tubule, mineralization	2 (4%)		1 (2%)
Urinary bladder	(46)	(49)	(44)
Calculus gross observation	2 (4%)		
Calculus micro observation only	3 (7%)		
Hemorrhage			1 (2%)
Hyperplasia	2 (4%)	1 (2%)	3 (7%)
Inflammation, chronic	1 (2%)		
Inflammation, suppurative	1 (2%)	2 (4%)	4 (9%)
Artery, inflammation		1 (2%)	

APPENDIX B

SUMMARY OF LESIONS IN FEMALE OSBORNE-MENDEL RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine small, ileum	(40)	(43)	(45)
Lymphoma malignant undifferentiated cell type			1 (2%)
Liver	(50)	(48)	(49)
Adenocarcinoma, metastatic, uterus			1 (2%)
Adenoma	2 (4%)	3 (6%)	1 (2%)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant		1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type		1 (2%)	1 (2%)
Neoplastic nodule	1 (2%)		
Mesentery	*(50)	*(50)	*(50)
Adenocarcinoma, metastatic, uterus			2 (4%)
Pancreas	(50)	(48)	(49)
Adenocarcinoma, metastatic, uterus			2 (4%)
Lymphoma malignant histiocytic	1 (2%)		
Salivary glands	(48)	(47)	(48)
Lymphoma malignant undifferentiated cell type		1 (2%)	
Stomach, forestomach	(50)	(47)	(46)
Papilloma squamous			1 (2%)
Squamous cell carcinoma		1 (2%)	
Glandular, adenocarcinoma, metastatic, uterus			1 (2%)
CARDIOVASCULAR SYSTEM			
Heart	(50)	(49)	(50)
Adenocarcinoma, metastatic, uterus			1 (2%)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant undifferentiated cell type		1 (2%)	
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(50)	(49)	(49)
Adenocarcinoma, metastatic, uterus			1 (2%)
Adenoma	3 (6%)	5 (10%)	2 (4%)
Adenoma, multiple		1 (2%)	
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant		1 (2%)	
Lymphoma malignant undifferentiated cell type		1 (2%)	1 (2%)
Adrenal gland, medulla	(49)	(48)	(47)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant		1 (2%)	
Lymphoma malignant undifferentiated cell type			1 (2%)
Pheochromocytoma benign	6 (12%)	2 (4%)	3 (6%)
Pheochromocytoma benign, multiple			3 (6%)
Islets, pancreatic	(50)	(48)	(48)
Adenoma	4 (8%)		
Carcinoma		1 (2%)	
Pituitary gland	(50)	(45)	(48)
Lymphoma malignant histiocytic	1 (2%)		
Pars distalis, adenoma	26 (52%)	26 (58%)	20 (42%)
Pars distalis, carcinoma	1 (2%)		1 (2%)
Thyroid gland	(49)	(47)	(47)
Lymphoma malignant histiocytic	1 (2%)		
C-cell, adenoma	10 (20%)	14 (30%)	10 (21%)
C-cell, adenoma, multiple	1 (2%)	5 (11%)	2 (4%)
C-cell, carcinoma	4 (8%)	2 (4%)	4 (9%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Clitoral gland	(43)	(45)	(43)
Lymphoma malignant histiocytic	1 (2%)		
Ovary	(49)	(48)	(49)
Adenocarcinoma, metastatic, uterus			2 (4%)
Embryonal carcinoma			1 (2%)
Granulosa cell tumor malignant			1 (2%)
Granulosa cell tumor benign	1 (2%)		
Granulosa theca tumor benign	1 (2%)		
Hamartoma	1 (2%)		
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant		1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type		1 (2%)	1 (2%)
Sarcoma stromal, metastatic, uterus		1 (2%)	
Squamous cell carcinoma, metastatic, uterus			1 (2%)
Uterus	(50)	(50)	(50)
Adenocarcinoma	2 (4%)		3 (6%)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant undifferentiated cell type			1 (2%)
Polyp stromal	10 (20%)	11 (22%)	9 (18%)
Sarcoma		1 (2%)	
Sarcoma stromal	1 (2%)	2 (4%)	1 (2%)
Squamous cell carcinoma			1 (2%)
Endometrium, adenoma, papillary			1 (2%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(49)	(45)	(48)
Lymphoma malignant			1 (2%)
Lymph node	(48)	(50)	(49)
Mesenteric, lymphoma malignant undifferentiated cell type		1 (2%)	
Pancreatic, lymphoma malignant histiocytic	1 (2%)		
Lymph node, bronchial	(34)	(39)	(43)
Adenocarcinoma, metastatic, uterus			2 (5%)
Basosquamous tumor malignant, metastatic, thymus	1 (3%)		
Lymphoma malignant histiocytic	1 (3%)		
Lymphoma malignant			1 (2%)
Lymphoma malignant undifferentiated cell type		1 (3%)	
Lymph node, mandibular	(43)	(45)	(44)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant			1 (2%)
Lymphoma malignant undifferentiated cell type		1 (2%)	
Spleen	(50)	(48)	(49)
Adenocarcinoma, metastatic, uterus			2 (4%)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant		1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type		1 (2%)	1 (2%)
Thymus	(41)	(47)	(43)
Adenocarcinoma, metastatic, uterus			1 (2%)
Basosquamous tumor malignant	1 (2%)		
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant undifferentiated cell type		1 (2%)	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
INTEGUMENTARY SYSTEM			
Mammary gland	(50)	(50)	(50)
Adenocarcinoma	2 (4%)	5 (10%)	4 (8%)
Adenocarcinoma, multiple		1 (2%)	
Fibroadenoma	23 (46%)	17 (34%)	20 (40%)
Fibroadenoma, multiple		2 (4%)	2 (4%)
Fibrosarcoma			1 (2%)
Skin	(48)	(49)	(49)
Fibroma		1 (2%)	
Lymphoma malignant			1 (2%)
Sarcoma		2 (4%)	
MUSCULOSKELETAL SYSTEM			
Skeletal muscle	*(50)	*(50)	*(50)
Diaphragm, adenocarcinoma, metastatic, uterus			2 (4%)
NERVOUS SYSTEM			
Brain	(49)	(50)	(50)
Carcinoma, metastatic, pituitary gland	1 (2%)		
Granular cell tumor benign	2 (4%)		
RESPIRATORY SYSTEM			
Lung	(49)	(50)	(49)
Adenocarcinoma, metastatic, mammary gland		1 (2%)	
Adenocarcinoma, metastatic, uterus			2 (4%)
Basosquamous tumor malignant, metastatic, thymus	1 (2%)		
Carcinoma adenosquamous		1 (2%)	
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant			1 (2%)
Lymphoma malignant undifferentiated cell type		1 (2%)	1 (2%)
Sarcoma, metastatic, uterus		1 (2%)	
Nose	(49)	(48)	(47)
Lymphoma malignant histiocytic	1 (2%)		
Respiratory epithelium, adenoma, papillary		1 (2%)	
SPECIAL SENSES SYSTEM			
None			
URINARY SYSTEM			
Kidney	(50)	(48)	(49)
Adenocarcinoma, metastatic, uterus			1 (2%)
Liposarcoma		1 (2%)	
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant			1 (2%)
Lymphoma malignant undifferentiated cell type			1 (2%)
Nephroblastoma			1 (2%)
Urinary bladder	(49)	(47)	(47)
Adenocarcinoma, metastatic, uterus			1 (2%)
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Lymphoma malignant histiocytic	1 (2%)		
Lymphoma malignant undifferentiated cell		1 (2%)	1 (2%)
Lymphoma malignant		1 (2%)	1 (2%)

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Terminal sacrifice	24	30	25
Dead	9	8	5
Moribund	17	12	20
TUMOR SUMMARY			
Total animals with primary neoplasms **	43	47	44
Total primary neoplasms	103	107	94
Total animals with benign neoplasms	40	44	37
Total benign neoplasms	91	88	74
Total animals with malignant neoplasms	12	19	17
Total malignant neoplasms	12	19	20
Total animals with secondary neoplasms ***	2	3	3
Total secondary neoplasms	3	3	22

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: CHAMBER CONTROL

WEEKS ON STUDY	030	039	068	069	075	077	078	082	083	083	086	088	092	093	096	097	098	099	101	101	101	104	104	104	105
CARCASS ID	98 1	85 1	99 1	96 1	78 1	63 1	68 1	64 1	52 1	76 1	59 1	81 1	74 1	71 1	82 1	58 1	62 1	89 1	60 1	72 1	77 1	55 1	57 1	00 1	95 1
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	M	M	M	M	M	M	M	M	+	M	M	+	A	+	A	M	+	+	+	+	+	+	+	A
Intestine large, colon	+	+	+	+	+	+	+	+	A	+	+	A	+	A	+	+	+	+	+	+	+	A	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	A	+	A	+	+	+	+	+	+	+	M	+	+	+
Intestine small	+	+	+	+	+	+	+	+	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	M	+	+	A	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	A	M	+	A	+	A	+	A	M	+	+	+	+	A	+	+	A
Intestine small, jejunum	+	+	+	+	+	+	+	+	A	+	+	A	+	A	+	A	M	+	+	+	+	A	+	A	A
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Lymphoma malignant histiocytic																		X							
Neoplastic nodule																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
Pharynx	+																								
Salivary glands	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth	+																								
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma					X																				
Lymphoma malignant histiocytic																		X							
Adrenal gland, medulla	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
Pheochromocytoma benign															X							X			
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																			X						
Parathyroid gland	+	+	M	M	+	+	+	+	+	+	+	M	+	+	M	+	M	M	M	+	+	+	M	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
Pars distalis, adenoma				X				X		X	X		X		X			X	X	X	X	X	X	X	
Pars distalis, carcinoma																	X								
Thyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
C-cell, adenoma																		X		X	X		X	X	
C-cell, adenoma, multiple																									
C-cell, carcinoma																									
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	M	M	+	M	M	+	+
Lymphoma malignant histiocytic																		X							
Ovary	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor benign																							X		
Granulosa theca tumor benign																							X		
Hamartoma																									
Lymphoma malignant histiocytic																		X							
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																								X	X
Lymphoma malignant histiocytic																		X							
Polyp stromal																		X			X			X	X
Sarcoma stromal									X																

+: Tissue examined microscopically
: Not examined
−: Present but not examined microscopically
I: Insufficient tissue

M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	731	511	531	541	561	611	651	661	671	691	701	751	791	801	831	841	861	871	881	901	911	921	931	941	971	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	34
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	45
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	46
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	46
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	A	+	+	+	+	+	40
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	41
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma														X									X			2
Lymphoma malignant histiocytic																										1
Neoplastic nodule													X													1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Pharynx								+																		2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma					X							X														3
Lymphoma malignant histiocytic																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																										1
Pheochromocytoma benign	X							X				X													X	6
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma						X				X			X													4
Parathyroid gland	+	+	+	+	+	M	M	M	M	M	M	M	+	M	M	+	I	M	M	+	M	+	M	M	M	26
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Pars distalis, adenoma	X		X					X	X	X	X	X	X	X	X			X				X			X	26
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																										1
C-cell, adenoma			X							X				X				X					X			10
C-cell, adenoma, multiple																					X					1
C-cell, carcinoma				X												X							X	X		4
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	43
Lymphoma malignant histiocytic																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Granulosa cell tumor benign				X																						1
Granulosa theca tumor benign																										1
Hamartoma																										1
Lymphoma malignant histiocytic																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																										2
Lymphoma malignant histiocytic																										1
Polyp stromal						X			X			X							X			X			X	10
Sarcoma stromal																										1

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	0 3 0	0 3 9	0 6 8	0 6 9	0 7 5	0 7 7	0 7 8	0 8 2	0 8 3	0 8 3	0 8 6	0 8 8	0 9 2	0 9 3	0 9 6	0 9 7	0 9 8	0 9 9	1 0 1	1 0 1	1 0 1	1 0 4	1 0 4	1 0 4	1 0 5
CARCASS ID	9 8 1	8 5 1	9 9 1	9 6 1	7 8 1	6 3 1	6 8 1	6 4 1	5 2 1	7 6 1	5 9 1	8 1 1	7 4 1	7 1 1	8 2 1	5 8 1	6 2 1	8 9 1	6 0 1	7 2 1	7 7 1	5 5 1	5 7 1	0 0 1	9 5 1
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pancreatic, lymphoma malignant histiocytic																		X							
Lymph node, bronchial	+	+	+	+	+	+	M	M	+	M	M	M	M	M	+	+	M	+	M	+	+	M	M	+	+
Basosquamous tumor malignant, metastatic, thymus		X																							
Lymphoma malignant histiocytic																		X							
Lymph node, mandibular	M	M	+	+	+	M	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
Thymus	+	+	+	+	+	+	+	+	+	M	M	+	A	+	+	+	+	+	M	+	+	+	+	+	+
Basosquamous tumor malignant		X																							
Lymphoma malignant histiocytic																		X							
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma								X													X				
Fibroadenoma			X	X		X				X		X	X		X		X		X	X			X	X	X
Skin	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland																	X								
Granular cell tumor benign										X															
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Basosquamous tumor malignant, metastatic, thymus		X																							
Lymphoma malignant histiocytic																		X							
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
Trachea	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Lacrimal gland																							+		
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic																		X							
Urinary bladder	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	731	511	531	541	561	611	651	661	671	691	701	751	791	801	831	841	861	871	881	901	911	921	931	941	971	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pancreatic, lymphoma malignant histiocytic																										1
Lymph node, bronchial	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M	M	+	34
Basosquamous tumor malignant, metastatic, thymus																										1
Lymphoma malignant histiocytic																										1
Lymph node, mandibular	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	43
Lymphoma malignant histiocytic																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Thymus	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M	+	M	41
Basosquamous tumor malignant																										1
Lymphoma malignant histiocytic																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																										2
Fibroadenoma		X	X		X						X		X	X					X		X	X	X			23
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, pituitary gland																										1
Granular cell tumor benign																								X		2
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Basosquamous tumor malignant, metastatic, thymus																										1
Lymphoma malignant histiocytic																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant histiocytic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSES SYSTEM																										
Lacrimal gland	+	+				+									+											5
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 5 ppm

WEEKS ON STUDY	024	046	049	057	059	068	079	079	082	083	083	091	092	092	095	096	097	103	104	105	106	106	106	106	106	106
CARCASS ID	16211	16511	18211	18411	16811	19311	18611	16311	19111	16411	19511	16911	16711	17811	19911	16011	15811	17411	17711	16111	15111	15211	15311	15411	15511
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	A	A	+	+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine large, cecum	M	M	M	M	M	M	M	M	M	+	M	M	+	+	M	+	+	M	+	A	+	+	+	+	+
Intestine large, colon	+	+	A	A	+	+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine large, rectum	+	+	A	A	+	+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine small	+	+	A	A	+	+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	A	A	+	+	+	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine small, ileum	M	+	A	A	+	+	+	A	+	M	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	A	A	+	+	A	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+
Liver	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																						X			
Lymphoma malignant																		X							
Lymphoma malignant undifferentiated cell type																	X								
Mesentery	+																								
Pancreas	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	A	+	+	M	M	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																	X								
Stomach	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	M	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma				X																					
Stomach, glandular	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth										+															
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	−	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																	X								
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																X	X								
Adenoma, multiple											X														
Lymphoma malignant																		X							
Lymphoma malignant undifferentiated cell type																	X								
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+
Lymphoma malignant																		X							
Pheochromocytoma benign																						X			X
Islets, pancreatic	+	+	M	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Parathyroid gland	+	+	M	+	+	+	+	M	+	+	+	M	+	M	M	M	+	+	+	+	M	+	M	+	+
Pituitary gland	+	+	A	+	+	+	M	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma									X				X	X	X	X		X	X	X	X	X	X	X	X
Thyroid gland	+	+	I	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma														X	X					X					X
C-cell, adenoma, multiple							X														X				
C-cell, carcinoma													X												
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Clitoral gland	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant																		X							
Lymphoma malignant undifferentiated cell type																	X								
Sarcoma stromal, metastatic, uterus																								X	
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal		X	X															X		X			X		X
Sarcoma												X													
Sarcoma stromal					X																			X	

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 5 ppm (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	15611	15711	15911	16611	17011	17111	17211	17311	17511	17611	17911	18011	18111	18311	18511	18711	18811	18911	19011	19211	19411	19611	19711	19811	20101	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, cecum	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	35
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma									X											X						3
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Mesentery																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant undifferentiated cell type																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Squamous cell carcinoma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Tooth																										1
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant undifferentiated cell type																										1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma						X	X														X					5
Adenoma, multiple																										1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant																										1
Pheochromocytoma benign																										2
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma																				X						1
Parathyroid gland	M	M	+	M	+	+	+	+	M	+	M	+	+	+	M	+	M	+	M	+	+	+	+	M	M	32
Pituitary gland	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	45
Pars distalis, adenoma		X	X	X	X	X	X	X				X	X	X					X			X			X	26
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
C-cell, adenoma	X			X		X	X		X				X	X			X			X			X			14
C-cell, adenoma, multiple								X								X					X					5
C-cell, carcinoma										X																2
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Clitoral gland	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	45
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Sarcoma stromal, metastatic, uterus																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal						X	X						X					X	X							11
Sarcoma																										1
Sarcoma stromal																										2

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 5 ppm (Continued)

WEEKS ON STUDY	024	046	049	057	059	068	079	079	082	083	083	091	092	092	095	096	097	103	104	105	106	106	106	106	106
CARCASS ID	16211	16511	18211	18411	16811	19311	18611	16311	19111	16411	19511	16911	16711	17811	19911	16011	15811	17411	17711	16111	15111	15211	15311	15411	15511
HEMATOPOIETIC SYSTEM																									
Blood																					+				
Bone marrow	+	+	A	+	+	+	+	+	+	M	+	A	+	+	+	+	M	A	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesenteric, lymphoma malignant undifferentiated cell type																	X								
Lymph node, bronchial	+	+	M	+	+	M	+	M	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																	X								
Lymph node, mandibular	+	+	+	+	M	M	+	+	+	+	+	A	+	+	M	M	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																	X								
Spleen	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant																		X							
Lymphoma malignant undifferentiated cell type																	X								
Thymus	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	M	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																	X								
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma															X				X	X			X		
Adenocarcinoma, multiple		X																							
Fibroadenoma						X			X	X	X	X	X			X						X	X	X	X
Fibroadenoma, multiple														X											
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+
Fibroma																									
Sarcoma							X																		
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
Larynx	A	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland		X																							
Carcinoma adenosquamous																									
Lymphoma malignant undifferentiated cell type																	X								
Sarcoma, metastatic, uterus												X													
Nose	+	+	+	A	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory epithelium, adenoma, papillary																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye																									
Lacrimal gland																									
URINARY SYSTEM																									
Kidney	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+
Liposarcoma																									
Urinary bladder	+	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	M	+

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 5 ppm (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	15611	15711	15911	16611	17011	17111	17211	17311	17511	17611	17911	18011	18111	18311	18511	18711	18811	18911	19011	19211	19411	19611	19711	19811	20011	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood																										1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesenteric, lymphoma malignant undifferentiated cell type																										1
Lymph node, bronchial	+	+	+	M	M	+	+	+	+	+	M	+	M	+	+	M	+	+	+	+	+	+	+	M	+	39
Lymphoma malignant undifferentiated cell type																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymphoma malignant undifferentiated cell type																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Thymus	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant undifferentiated cell type																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma					X																					5
Adenocarcinoma, multiple																										1
Fibroadenoma	X								X		X		X							X			X			17
Fibroadenoma, multiple																					X					2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibroma																							X			1
Sarcoma								X																		2
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, mammary gland																										1
Carcinoma adenosquamous														X												1
Lymphoma malignant undifferentiated cell type																										1
Sarcoma, metastatic, uterus																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Respiratory epithelium, adenoma, papillary												X														1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPECIAL SENSES SYSTEM																										
Eye				+				+								+										3
Lacrimal gland															+											1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liposarcoma							X																			1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 10 ppm

WEEKS ON STUDY	005	032	039	041	048	048	053	059	082	082	083	083	090	090	093	094	094	096	100	100	101	103	105	105	105
CARCASS ID	25911	26911	27911	25111	29881	29911	28311	26511	25511	29411	26001	28811	27111	27211	29311	25811	28711	26611	29001	29511	25611	26811	28111	29711	28001
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	A	A	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	M	M	M	M	M	M	M	M	M	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	A	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	A	A	+	A	A	+	M	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	A	+	A	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	A	+	A	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	A	+	A	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type															X										
Intestine small, jejunum	A	A	+	A	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X														
Adenoma																									
Lymphoma malignant				X																					
Lymphoma malignant undifferentiated cell type															X										
Mesentery											+					+									
Adenocarcinoma, metastatic, uterus											X					X									
Pancreas	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X					X									
Salivary glands	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																X									
Glandular, adenocarcinoma, metastatic, uterus											X														
Stomach, glandular	A	A	+	A	A	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARDIOVASCULAR SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus																X									
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X														
Adenoma														X											
Lymphoma malignant undifferentiated cell type															X										
Adrenal gland, medulla	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type															X										
Pheochromocytoma benign														X											
Pheochromocytoma benign, multiple																									
Islets, pancreatic	+	+	+	+	A	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	M	+	+	M	M	+	+	+	+	M	M	+	+	+	+	M	M	M	M	+	M	+	M	M	M
Pituitary gland	M	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																	X			X					X
Pars distalis, carcinoma								X																	
Thyroid gland	+	+	+	M	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma													X												X
C-cell, adenoma, multiple																	X		X						
C-cell, carcinoma													X									X			X
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Clitoral gland	M	M	+		A	M	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Ovary	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X					X									
Embryonal carcinoma												X													
Granulosa cell tumor malignant																									
Lymphoma malignant				X																					
Lymphoma malignant undifferentiated cell type															X										
Squamous cell carcinoma, metastatic, uterus																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma											X					X									
Lymphoma malignant undifferentiated cell type															X										
Polyp stromal														X											
Sarcoma stromal																							X		
Squamous cell carcinoma																									
Endometrium, adenoma, papillary															X										

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 10 ppm (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL:
CARCASS ID	25211	25311	25411	25711	26111	26211	26311	26411	26711	27011	27311	27411	27511	27611	27711	27811	28211	28411	28511	28611	28911	29111	29211	29611	30011	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymphoma malignant undifferentiated cell type																										1
Intestine small, jejunum	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, uterus																										1
Adenoma											X															1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Mesentery												+														3
Adenocarcinoma, metastatic, uterus																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, uterus																										2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	49
Stomach, forestomach	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	M	46
Papilloma squamous																										1
Glandular, adenocarcinoma, metastatic, uterus																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	44
CARDIOVASCULAR SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, uterus																										1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, uterus																										1
Adenoma				X																						2
Lymphoma malignant undifferentiated cell type																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Lymphoma malignant undifferentiated cell type																										1
Pheochromocytoma benign						X		X																		3
Pheochromocytoma benign, multiple			X									X	X													3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid gland	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	M	M	+	+	+	33
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma	X		X	X	X	X		X		X				X	X	X	X		X	X		X	X	X	X	20
Pars distalis, carcinoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
C-cell, adenoma	X				X	X				X	X			X	X	X										10
C-cell, adenoma, multiple																										2
C-cell, carcinoma																						X				4
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, uterus																										2
Embryonal carcinoma																										1
Granulosa cell tumor malignant							X																			1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Squamous cell carcinoma, metastatic, uterus			X																							1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																						X				3
Lymphoma malignant undifferentiated cell type																										1
Polyp stromal										X				X		X	X		X	X		X		X		9
Sarcoma stromal																										1
Squamous cell carcinoma			X																							1
Endometrium, adenoma, papillary																										1

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 10 ppm (Continued)

WEEKS ON STUDY	005	032	039	041	048	048	053	059	082	082	083	083	090	090	093	094	094	096	100	100	101	103	105	105	105
CARCASS ID	25911	26911	27911	25111	29881	29911	28831	26511	25511	29411	26011	28811	27111	27211	29331	25881	28711	26611	29001	29511	25611	26811	28111	29711	28001
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant				X																					
Lymph node	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, bronchial	+	+	+	+	M	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X					X									
Lymphoma malignant				X																					
Lymph node, mandibular	+	M	+	+	A	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant				X																					
Spleen	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X					X									
Lymphoma malignant				X																					
Lymphoma malignant undifferentiated cell type															X										
Thymus	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+
Adenocarcinoma, metastatic, uterus																X									
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma			X						X																
Fibroadenoma						X	X	X					X						X	X			X	X	X
Fibroadenoma, multiple										X												X			
Fibrosarcoma																								X	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant				X																					
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle											+					+									
Diaphragm, adenocarcinoma, metastatic, uterus											X					X									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spinal cord																		+							
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X					X									
Lymphoma malignant				X																					
Lymphoma malignant undifferentiated cell type															X										
Nose	A	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Lacrimal gland																					+				
URINARY SYSTEM																									
Kidney	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X														
Lymphoma malignant				X																					
Lymphoma malignant undifferentiated cell type															X										
Nephroblastoma		X																							
Urinary bladder	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, uterus											X														

TABLE B2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: 10 ppm (Continued)

WEEKS ON STUDY	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	106	TOTAL: TISSUES TUMORS
CARCASS ID	25211	25311	25411	25711	26111	26211	26311	26411	26711	27011	27311	27411	27511	27611	27711	27811	28211	28411	28511	28611	28911	29111	29211	29611	30011	
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, bronchial	+	+	M	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	43
Adenocarcinoma, metastatic, uterus																										2
Lymphoma malignant																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	M	+	+	+	+	+	+	+	44
Lymphoma malignant																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, uterus																										2
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Thymus	+	M	+	+	+	+	+	+	+	+	+	+	M	M	M	+	+	+	+	+	+	+	+	+	+	43
Adenocarcinoma, metastatic, uterus																										1
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma			X																X							4
Fibroadenoma	X	X									X			X	X	X	X	X		X				X	X	20
Fibroadenoma, multiple																										2
Fibrosarcoma																										1
Skin	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										2
Diaphragm, adenocarcinoma, meta., uterus																										2
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spinal cord																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, uterus																										2
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPECIAL SENSES SYSTEM																										
Lacrimal gland														+												2
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, metastatic, uterus																										1
Lymphoma malignant																										1
Lymphoma malignant undifferentiated cell type																										1
Nephroblastoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenocarcinoma, metastatic, uterus																										1

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Adrenal Cortex: Adenoma			
Overall Rates (a)	3/50 (6%)	6/49 (12%)	2/49 (4%)
Adjusted Rates (b)	10.3%	17.2%	6.5%
Terminal Rates (c)	2/24 (8%)	3/30 (10%)	1/25 (4%)
Day of First Observation	521	579	624
Life Table Tests (d)	P=0.430N	P=0.305	P=0.497N
Logistic Regression Tests (d)	P=0.449N	P=0.231	P=0.517N
Cochran-Armitage Trend Test (d)	P=0.435N		
Fisher Exact Test (d)		P=0.233	P=0.510N
Adrenal Medulla: Pheochromocytoma			
Overall Rates (a)	6/49 (12%)	2/48 (4%)	6/47 (13%)
Adjusted Rates (b)	21.1%	6.7%	22.9%
Terminal Rates (c)	3/24 (13%)	2/30 (7%)	5/24 (21%)
Day of First Observation	667	737	624
Life Table Tests (d)	P=0.564	P=0.090N	P=0.612
Logistic Regression Tests (d)	P=0.512	P=0.126N	P=0.557
Cochran-Armitage Trend Test (d)	P=0.542		
Fisher Exact Test (d)		P=0.141N	P=0.590
Pancreatic Islets: Adenoma			
Overall Rates (a)	4/50 (8%)	0/48 (0%)	0/48 (0%)
Adjusted Rates (b)	15.2%	0.0%	0.0%
Terminal Rates (c)	3/24 (13%)	0/30 (0%)	0/25 (0%)
Day of First Observation	705		
Life Table Tests (d)	P=0.013N	P=0.044N	P=0.062N
Logistic Regression Tests (d)	P=0.015N	P=0.056N	P=0.065N
Cochran-Armitage Trend Test (d)	P=0.016N		
Fisher Exact Test (d)		P=0.064N	P=0.064N
Pancreatic Islets: Adenoma or Carcinoma			
Overall Rates (a)	4/50 (8%)	1/48 (2%)	0/48 (0%)
Adjusted Rates (b)	15.2%	3.3%	0.0%
Terminal Rates (c)	3/24 (13%)	1/30 (3%)	0/25 (0%)
Day of First Observation	705	737	
Life Table Tests (d)	P=0.021N	P=0.129N	P=0.062N
Logistic Regression Tests (d)	P=0.025N	P=0.160N	P=0.065N
Cochran-Armitage Trend Test (d)	P=0.028N		
Fisher Exact Test (d)		P=0.194N	P=0.064N
Liver: Adenoma or Neoplastic Nodule			
Overall Rates (a)	3/50 (6%)	3/48 (6%)	1/49 (2%)
Adjusted Rates (b)	12.5%	10.0%	4.0%
Terminal Rates (c)	3/24 (13%)	3/30 (10%)	1/25 (4%)
Day of First Observation	737	737	737
Life Table Tests (d)	P=0.214N	P=0.557N	P=0.288N
Logistic Regression Tests (d)	P=0.214N	P=0.557N	P=0.288N
Cochran-Armitage Trend Test (d)	P=0.247N		
Fisher Exact Test (d)		P=0.641	P=0.316N
Mammary Gland: Adenocarcinoma			
Overall Rates (e)	2/50 (4%)	6/50 (12%)	4/50 (8%)
Adjusted Rates (b)	5.4%	16.7%	12.1%
Terminal Rates (c)	0/24 (0%)	2/30 (7%)	2/25 (8%)
Day of First Observation	569	318	269
Life Table Tests (d)	P=0.290	P=0.179	P=0.339
Logistic Regression Tests (d)	P=0.317	P=0.137	P=0.378
Cochran-Armitage Trend Test (d)	P=0.290		
Fisher Exact Test (d)		P=0.134	P=0.339

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
Mammary Gland: Fibroadenoma			
Overall Rates (e)	23/50 (46%)	19/50 (38%)	22/50 (44%)
Adjusted Rates (b)	60.0%	48.4%	59.8%
Terminal Rates (c)	10/24 (42%)	11/30 (37%)	11/25 (44%)
Day of First Observation	474	471	332
Life Table Tests (d)	P=0.469N	P=0.175N	P=0.501N
Logistic Regression Tests (d)	P=0.510N	P=0.277N	P=0.556N
Cochran-Armitage Trend Test (d)	P=0.460N		
Fisher Exact Test (d)		P=0.272N	P=0.500N
Mammary Gland: Fibroadenoma or Adenocarcinoma			
Overall Rates (e)	25/50 (50%)	24/50 (48%)	26/50 (52%)
Adjusted Rates (b)	62.2%	56.4%	67.1%
Terminal Rates (c)	10/24 (42%)	12/30 (40%)	13/25 (52%)
Day of First Observation	474	318	269
Life Table Tests (d)	P=0.461	P=0.333N	P=0.498
Logistic Regression Tests (d)	P=0.427	P=0.505N	P=0.462
Cochran-Armitage Trend Test (d)	P=0.460		
Fisher Exact Test (d)		P=0.500N	P=0.500
Pituitary Gland/Pars Distalis: Adenoma			
Overall Rates (a)	26/50 (52%)	26/45 (58%)	20/48 (42%)
Adjusted Rates (b)	67.4%	71.6%	71.1%
Terminal Rates (c)	12/24 (50%)	18/28 (64%)	17/25 (68%)
Day of First Observation	478	569	658
Life Table Tests (d)	P=0.137N	P=0.380N	P=0.165N
Logistic Regression Tests (d)	P=0.185N	P=0.376	P=0.212N
Cochran-Armitage Trend Test (d)	P=0.182N		
Fisher Exact Test (d)		P=0.360	P=0.206N
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma			
Overall Rates (a)	27/50 (54%)	26/45 (58%)	21/48 (44%)
Adjusted Rates (b)	68.4%	71.6%	71.8%
Terminal Rates (c)	12/24 (50%)	18/28 (64%)	17/25 (68%)
Day of First Observation	478	569	570
Life Table Tests (d)	P=0.144N	P=0.320N	P=0.175N
Logistic Regression Tests (d)	P=0.192N	P=0.456	P=0.222N
Cochran-Armitage Trend Test (d)	P=0.183N		
Fisher Exact Test (d)		P=0.435	P=0.208N
Skin: Fibroma or Sarcoma			
Overall Rates (e)	0/50 (0%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	8.8%	0.0%
Terminal Rates (c)	0/24 (0%)	2/30 (7%)	0/25 (0%)
Day of First Observation		547	
Life Table Tests (d)	P=0.637N	P=0.151	(f)
Logistic Regression Tests (d)	P=0.633	P=0.120	(f)
Cochran-Armitage Trend Test (d)	P=0.640		
Fisher Exact Test (d)		P=0.121	(f)
Thyroid Gland: C-Cell Adenoma			
Overall Rates (a)	11/49 (22%)	19/47 (40%)	12/47 (26%)
Adjusted Rates (b)	36.7%	55.2%	40.1%
Terminal Rates (c)	6/24 (25%)	15/30 (50%)	8/25 (32%)
Day of First Observation	690	547	624
Life Table Tests (d)	P=0.478	P=0.175	P=0.516
Logistic Regression Tests (d)	P=0.379	P=0.053	P=0.440
Cochran-Armitage Trend Test (d)	P=0.404		
Fisher Exact Test (d)		P=0.046	P=0.454

TABLE B3. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
Thyroid Gland: C-Cell Carcinoma			
Overall Rates (a)	4/49 (8%)	2/47 (4%)	4/47 (9%)
Adjusted Rates (b)	16.7%	5.9%	13.2%
Terminal Rates (c)	4/24 (17%)	1/30 (3%)	1/25 (4%)
Day of First Observation	737	642	624
Life Table Tests (d)	P=0.570N	P=0.253N	P=0.628N
Logistic Regression Tests (d)	P=0.546	P=0.332N	P=0.615
Cochran-Armitage Trend Test (d)	P=0.557		
Fisher Exact Test (d)		P=0.359N	P=0.619
Thyroid Gland: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	14/49 (29%)	21/47 (45%)	14/47 (30%)
Adjusted Rates (b)	47.2%	59.3%	45.6%
Terminal Rates (c)	9/24 (38%)	16/30 (53%)	9/25 (36%)
Day of First Observation	690	547	624
Life Table Tests (d)	P=0.517N	P=0.274	P=0.563N
Logistic Regression Tests (d)	P=0.460	P=0.087	P=0.531
Cochran-Armitage Trend Test (d)	P=0.484		
Fisher Exact Test (d)		P=0.077	P=0.537
Uterus: Adenocarcinoma			
Overall Rates (e)	2/50 (4%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	7.3%	0.0%	9.1%
Terminal Rates (c)	0/24 (0%)	0/30 (0%)	1/25 (4%)
Day of First Observation	723		578
Life Table Tests (d)	P=0.385	P=0.206N	P=0.493
Logistic Regression Tests (d)	P=0.376	P=0.226N	P=0.482
Cochran-Armitage Trend Test (d)	P=0.390		
Fisher Exact Test (d)		P=0.247N	P=0.500
Uterus: Stromal Polyp			
Overall Rates (e)	10/50 (20%)	11/50 (22%)	9/50 (18%)
Adjusted Rates (b)	34.7%	31.0%	33.8%
Terminal Rates (c)	6/24 (25%)	7/30 (23%)	8/25 (32%)
Day of First Observation	690	318	624
Life Table Tests (d)	P=0.433N	P=0.519N	P=0.478N
Logistic Regression Tests (d)	P=0.502N	P=0.494	P=0.537N
Cochran-Armitage Trend Test (d)	P=0.450N		
Fisher Exact Test (d)		P=0.500	P=0.500N

(a) Number of tumor-bearing animals/number of animals examined microscopically at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals killed at the end of the study
(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 logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) Number of tumor-bearing animals/number of animals examined grossly at the site
(f) No P value is reported because no tumors were observed in the 10-ppm and control groups.

TABLE B4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Esophagus	(47)	(50)	(49)
Acanthosis	1 (2%)		
Hyperkeratosis	1 (2%)		
Inflammation, chronic	1 (2%)		
Intestine large, cecum	(34)	(35)	(38)
Granuloma			1 (3%)
Hemorrhage		1 (3%)	
Inflammation			1 (3%)
Parasite metazoan	3 (9%)	2 (6%)	3 (8%)
Intestine large, colon	(45)	(45)	(46)
Inflammation, suppurative	1 (2%)	1 (2%)	
Necrosis		1 (2%)	
Parasite metazoan	4 (9%)	2 (4%)	5 (11%)
Ulcer		1 (2%)	
Intestine large, rectum	(46)	(45)	(43)
Hyperplasia, lymphoid		1 (2%)	
Parasite metazoan	2 (4%)	3 (7%)	
Intestine small, jejunum	(41)	(43)	(44)
Inflammation, suppurative	1 (2%)		
Muscularis, hyperplasia	1 (2%)		
Liver	(50)	(48)	(49)
Angiectasis	1 (2%)	3 (6%)	3 (6%)
Basophilic focus		2 (4%)	
Basophilic focus, multiple		1 (2%)	
Clear cell focus	1 (2%)	1 (2%)	2 (4%)
Developmental malformation		1 (2%)	1 (2%)
Eosinophilic focus	3 (6%)	1 (2%)	
Hematopoietic cell proliferation	7 (14%)	4 (8%)	3 (6%)
Inflammation, suppurative			1 (2%)
Leukocytosis	1 (2%)		1 (2%)
Necrosis	2 (4%)	3 (6%)	3 (6%)
Vacuolization cytoplasmic	2 (4%)		
Bile duct, cyst	1 (2%)		1 (2%)
Bile duct, hyperplasia	1 (2%)	3 (6%)	2 (4%)
Hepatocyte, cytomegaly		1 (2%)	
Mesentery		(1)	(3)
Artery, inflammation		1 (100%)	1 (33%)
Pancreas	(50)	(48)	(49)
Atrophy	1 (2%)	3 (6%)	2 (4%)
Inflammation, chronic			1 (2%)
Acinus, hyperplasia		2 (4%)	
Artery, inflammation		1 (2%)	5 (10%)
Pharynx	(2)		
Necrosis	1 (50%)		
Ulcer	1 (50%)		
Epithelium, hyperplasia	1 (50%)		
Palate, ulcer	1 (50%)		
Salivary glands	(48)	(47)	(48)
Inflammation, chronic	1 (2%)		1 (2%)
Inflammation, suppurative	1 (2%)		
Karyomegaly	4 (8%)	1 (2%)	2 (4%)
Stomach, forestomach	(50)	(47)	(46)
Acanthosis	1 (2%)	3 (6%)	2 (4%)
Hyperkeratosis			1 (2%)
Perforation		1 (2%)	

TABLE B4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
ALIMENTARY SYSTEM (Continued)			
Stomach, glandular	(50)	(48)	(44)
Erosion			1 (2%)
Hyperplasia		1 (2%)	
Inflammation, suppurative			1 (2%)
Mineralization	1 (2%)	2 (4%)	2 (5%)
Tooth	(1)	(1)	
Inflammation, suppurative		1 (100%)	
Incisor, developmental malformation	1 (100%)		
CARDIOVASCULAR SYSTEM			
Heart	(50)	(49)	(50)
Cardiomyopathy	7 (14%)	4 (8%)	5 (10%)
Embolus bacterial	1 (2%)		
Inflammation, suppurative	1 (2%)	1 (2%)	1 (2%)
Artery, mineralization		1 (2%)	1 (2%)
Atrium, thrombus	2 (4%)		
Myocardium, mineralization			1 (2%)
Myocardium, necrosis			1 (2%)
ENDOCRINE SYSTEM			
Adrenal gland, cortex	(50)	(49)	(49)
Angiectasis	30 (60%)	36 (73%)	22 (45%)
Angiectasis, multiple	1 (2%)		
Atrophy			1 (2%)
Cyst	1 (2%)		
Hemorrhage	1 (2%)		1 (2%)
Hyperplasia	16 (32%)	11 (22%)	12 (24%)
Necrosis		1 (2%)	
Vacuolization cytoplasmic	13 (26%)	11 (22%)	9 (18%)
Adrenal gland, medulla	(49)	(48)	(47)
Hematopoietic cell proliferation	1 (2%)		
Hyperplasia	8 (16%)	10 (21%)	4 (9%)
Hyperplasia, multiple		2 (4%)	
Parathyroid gland	(26)	(32)	(33)
Hyperplasia	1 (4%)		
Pituitary gland	(50)	(45)	(48)
Hemorrhage			1 (2%)
Pars distalis, cyst	1 (2%)	2 (4%)	
Pars distalis, hyperplasia	4 (8%)		5 (10%)
Thyroid gland	(49)	(47)	(47)
Ultimobranchial cyst	4 (8%)	9 (19%)	4 (9%)
C-cell, hyperplasia	10 (20%)	12 (26%)	10 (21%)
Follicular cell, cyst	1 (2%)	1 (2%)	
Follicular cell, hyperplasia	2 (4%)		1 (2%)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Clitoral gland	(43)	(45)	(43)
Cyst	6 (14%)	12 (27%)	14 (33%)
Cyst, multiple		1 (2%)	
Inflammation, suppurative	15 (35%)	13 (29%)	15 (35%)
Ovary	(49)	(48)	(49)
Cyst	4 (8%)	10 (21%)	8 (16%)
Inflammation, suppurative	1 (2%)	1 (2%)	
Capsule, hyperplasia			1 (2%)

TABLE B4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
GENITAL SYSTEM (Continued)			
Uterus	(50)	(50)	(50)
Inflammation, suppurative	7 (14%)	1 (2%)	3 (6%)
Thrombus			1 (2%)
Artery, inflammation			1 (2%)
Endometrium, hyperplasia	14 (28%)	22 (44%)	12 (24%)
Endometrium, metaplasia, squamous	2 (4%)	5 (10%)	6 (12%)
Lumen, dilatation	2 (4%)	4 (8%)	3 (6%)
Lumen, hemorrhage		2 (4%)	1 (2%)
Wall, necrosis		1 (2%)	
HEMATOPOIETIC SYSTEM			
Bone marrow	(49)	(45)	(48)
Atrophy	4 (8%)		
Lymph node	(48)	(50)	(49)
Mesenteric, hemorrhage		1 (2%)	
Renal, hyperplasia, lymphoid		1 (2%)	
Lymph node, bronchial	(34)	(39)	(43)
Fibrosis			1 (2%)
Hemorrhage	1 (3%)	1 (3%)	1 (2%)
Lymph node, mandibular	(43)	(45)	(44)
Hemorrhage		2 (4%)	
Hyperplasia, lymphoid		1 (2%)	1 (2%)
Spleen	(50)	(48)	(49)
Cyst			1 (2%)
Hematopoietic cell proliferation	6 (12%)	5 (10%)	8 (16%)
Artery, inflammation			1 (2%)
Thymus	(41)	(47)	(43)
Cyst		4 (9%)	
Inflammation, suppurative		1 (2%)	
INTEGUMENTARY SYSTEM			
Mammary gland	(50)	(50)	(50)
Cyst	1 (2%)		
Galactocele	2 (4%)	1 (2%)	1 (2%)
Inflammation, suppurative	2 (4%)	1 (2%)	
Skin	(48)	(49)	(49)
Acanthosis			2 (4%)
Cyst epithelial inclusion			1 (2%)
Hyperkeratosis			1 (2%)
Inflammation, suppurative	1 (2%)	1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM			
Bone	(49)	(49)	(50)
Fibrous osteodystrophy		1 (2%)	1 (2%)
Osteopetrosis			1 (2%)
Cranium, necrosis	1 (2%)		
NERVOUS SYSTEM			
Brain	(49)	(50)	(50)
Compression	3 (6%)	5 (10%)	2 (4%)
Gliosis			1 (2%)
Hemorrhage	2 (4%)	2 (4%)	
Ventricle, dilatation		1 (2%)	
Spinal cord			(1)
White matter, degeneration			1 (100%)

TABLE B4. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
RESPIRATORY SYSTEM			
Larynx	(50)	(48)	(48)
Foreign body		1 (2%)	
Inflammation, suppurative	3 (6%)	5 (10%)	
Epithelium, hyperplasia		1 (2%)	
Lung	(49)	(50)	(49)
Foreign body	1 (2%)	1 (2%)	1 (2%)
Hemorrhage	2 (4%)		
Inflammation, granulomatous	3 (6%)	7 (14%)	3 (6%)
Leukocytosis	1 (2%)		
Thrombus	2 (4%)		
Alveolar epithelium, hyperplasia	4 (8%)	14 (28%)	14 (29%)
Alveolus, fibrosis	1 (2%)	2 (4%)	2 (4%)
Alveolus, infiltration cellular, histiocytic	21 (43%)	41 (82%)	31 (63%)
Alveolus, inflammation, suppurative	13 (27%)	5 (10%)	4 (8%)
Artery, inflammation			1 (2%)
Artery, *mineralization*	20 (41%)	16 (32%)	15 (31%)
Bronchiole, hyperplasia			1 (2%)
Pleura, inflammation, chronic			1 (2%)
Nose	(49)	(48)	(47)
Inflammation, suppurative	5 (10%)	7 (15%)	11 (23%)
Glands, dilatation	9 (18%)	29 (60%)	39 (83%)
Nasolacrimal duct, inflammation, suppurative	4 (8%)	1 (2%)	
Olfactory epithelium, degeneration		46 (96%)	47 (100%)
Olfactory epithelium, metaplasia		4 (8%)	6 (13%)
Olfactory epithelium, metaplasia, squamous		9 (19%)	31 (66%)
Respiratory epithelium, dysplasia			1 (2%)
Respiratory epithelium, hyperplasia	1 (2%)	18 (38%)	22 (47%)
Respiratory epithelium, metaplasia, squamous		37 (77%)	38 (81%)
Trachea	(49)	(49)	(48)
Inflammation, suppurative	2 (4%)	1 (2%)	
Mineralization		1 (2%)	
Glands, dilatation	1 (2%)		
SPECIAL SENSES SYSTEM			
Eye		(3)	
Cataract, multiple		1 (33%)	
Lacrimal gland	(5)	(1)	(2)
Hyperplasia		1 (100%)	
Inflammation, chronic	3 (60%)	1 (100%)	2 (100%)
Inflammation, suppurative	1 (20%)		
Karyomegaly	4 (80%)	1 (100%)	2 (100%)
Necrosis	1 (20%)		
URINARY SYSTEM			
Kidney	(50)	(48)	(49)
Cyst		1 (2%)	3 (6%)
Nephropathy, chronic	48 (96%)	42 (88%)	46 (94%)
Pelvis, dilatation	1 (2%)		
Pelvis, hyperplasia	3 (6%)	3 (6%)	2 (4%)
Pelvis, mineralization	15 (30%)	15 (31%)	15 (31%)
Renal tubule, degeneration		1 (2%)	
Renal tubule, mineralization	14 (28%)	18 (38%)	11 (22%)
Urinary bladder	(49)	(47)	(47)
Hemorrhage			1 (2%)
Hyperplasia	1 (2%)	1 (2%)	
Inflammation, suppurative		1 (2%)	

APPENDIX C

SUMMARY OF LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Gallbladder	(41)	*(50)	(46)
Lymphoma malignant lymphocytic			1 (2%)
Intestine small, duodenum	(43)	*(50)	(49)
Lymphoma malignant lymphocytic			1 (2%)
Intestine small, ileum	(45)	*(50)	(49)
Lymphoma malignant mixed		1 (2%)	
Lymphoma malignant undifferentiated cell type	1 (2%)		
Intestine small, jejunum	(44)	*(50)	(48)
Lymphoma malignant undifferentiated cell type		2 (4%)	
Liver	(49)	*(50)	(49)
Carcinosarcoma, metastatic, uncertain primary site	1 (2%)		
Hemangiosarcoma, multiple			1 (2%)
Hepatocellular carcinoma	10 (20%)	4 (8%)	1 (2%)
Hepatocellular adenoma	12 (24%)	7 (14%)	5 (10%)
Hepatocellular adenoma, multiple	3 (6%)		
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)	1 (2%)	
Mesentery	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic			1 (2%)
Pancreas	(49)	*(50)	(49)
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed		1 (2%)	
Salivary glands	(49)	*(50)	(49)
Lymphoma malignant undifferentiated cell type		1 (2%)	
Stomach, forestomach	(50)	*(50)	(49)
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed		1 (2%)	
Papilloma squamous	1 (2%)		
Stomach, glandular	(50)	*(50)	(49)
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed		1 (2%)	
CARDIOVASCULAR SYSTEM			
Blood vessel	*(50)	*(50)	*(50)
Aorta, lymphoma malignant lymphocytic			1 (2%)
Heart	(50)	*(50)	(50)
Hemangiosarcoma, metastatic, liver			1 (2%)
Lymphoma malignant lymphocytic			1 (2%)
ENDOCRINE SYSTEM			
Adrenal gland	(49)	*(50)	(50)
Capsule, carcinosarcoma, metastatic, uncertain primary site	1 (2%)		
Capsule, lymphoma malignant undifferentiated cell type		1 (2%)	
Adrenal gland, cortex	(49)	*(50)	(49)
Lymphoma malignant mixed		1 (2%)	
Medulla, lymphoma malignant lymphocytic			1 (2%)
Adrenal gland, medulla	(48)	*(50)	(48)
Lymphoma malignant mixed		1 (2%)	
Pheochromocytoma, NOS	1 (2%)		
Islets, pancreatic	(46)	*(50)	(46)
Lymphoma malignant mixed		1 (2%)	

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
ENDOCRINE SYSTEM (Continued)			
Pituitary gland	(44)	*(50)	(49)
Pars intermedia, adenoma	1 (2%)		1 (2%)
Thyroid gland	(50)	*(50)	(49)
Follicular cell, adenoma	1 (2%)		3 (6%)
GENERAL BODY SYSTEM			
Tissue, NOS	*(50)	*(50)	*(50)
Carcinosarcoma, metastatic, uncertain primary site	1 (2%)		
GENITAL SYSTEM			
Epididymis	(48)	*(50)	(49)
Lymphoma malignant mixed		1 (2%)	
Prostate	(45)	*(50)	(44)
Lymphoma malignant mixed		1 (2%)	
Seminal vesicle	*(50)	*(50)	*(50)
Lymphoma malignant mixed		1 (2%)	
HEMATOPOIETIC SYSTEM			
Blood	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic			1 (2%)
Lymph node	(43)	*(50)	(45)
Axillary, lymphoma malignant lymphocytic			1 (2%)
Inguinal, lymphoma malignant lymphocytic			1 (2%)
Mediastinal, lymphoma malignant lymphocytic			1 (2%)
Mediastinal, lymphoma malignant mixed	2 (5%)	1 (2%)	1 (2%)
Mediastinal, mesenteric, carcinosarcoma, metastatic, uncertain primary site	1 (2%)		
Mesenteric, lymphoma malignant lymphocytic			1 (2%)
Mesenteric, lymphoma malignant mixed	2 (5%)	4 (8%)	1 (2%)
Mesenteric, lymphoma malignant undifferentiated cell type		1 (2%)	
Renal, lymphoma malignant lymphocytic			1 (2%)
Renal, lymphoma malignant mixed	1 (2%)	1 (2%)	
Lymph node, bronchial	(29)	*(50)	(29)
Alveolar/bronchiolar carcinoma, metastatic, lung		1 (2%)	
Lymphoma malignant lymphocytic			1 (3%)
Lymphoma malignant mixed	1 (3%)	2 (4%)	
Lymphoma malignant undifferentiated cell type		1 (2%)	
Lymph node, mandibular	(34)	*(50)	(33)
Lymphoma malignant lymphocytic			2 (6%)
Lymphoma malignant mixed	2 (6%)	2 (4%)	
Lymphoma malignant undifferentiated cell type		1 (2%)	
Spleen	(49)	*(50)	(49)
Hemangioma		1 (2%)	
Lymphoma malignant lymphocytic			3 (6%)
Lymphoma malignant mixed	2 (4%)	3 (6%)	
Lymphoma malignant undifferentiated cell type		1 (2%)	
Capsule, carcinosarcoma, metastatic, uncertain primary site	1 (2%)		
Thymus	(30)	*(50)	(31)
Lymphoma malignant lymphocytic			2 (6%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
INTEGUMENTARY SYSTEM			
Skin	(50)	*(50)	(50)
Fibroma	1 (2%)		
Sebaceous gland, adenoma			1 (2%)
MUSCULOSKELETAL SYSTEM			
None			
NERVOUS SYSTEM			
Brain	(50)	*(50)	(50)
Lymphoma malignant lymphocytic			1 (2%)
RESPIRATORY SYSTEM			
Lung	(50)	*(50)	(50)
Alveolar/bronchiolar adenoma	5 (10%)	2 (4%)	5 (10%)
Alveolar/bronchiolar adenoma, multiple	2 (4%)		1 (2%)
Alveolar/bronchiolar carcinoma		5 (10%)	2 (4%)
Alveolar/bronchiolar carcinoma, multiple		2 (4%)	1 (2%)
Carcinosarcoma, metastatic, uncertain primary site	1 (2%)		
Hepatocellular carcinoma, metastatic, multiple, liver	1 (2%)	1 (2%)	
Leiomyosarcoma			1 (2%)
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed		2 (4%)	
Nose	(50)	(50)	(50)
Respiratory epithelium, adenoma			3 (6%)
Submucosa, hemangioma			1 (2%)
SPECIAL SENSES SYSTEM			
Eye	*(50)	*(50)	*(50)
Sarcoma	1 (2%)		
Harderian gland	*(50)	*(50)	*(50)
Adenoma	4 (8%)	2 (4%)	
Sarcoma, metastatic, eye	1 (2%)		
URINARY SYSTEM			
Kidney	(49)	*(50)	(49)
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed	1 (2%)	2 (4%)	
Lymphoma malignant undifferentiated cell type	1 (2%)		
Capsule, carcinosarcoma, metastatic, uncertain primary site	1 (2%)		
Urinary bladder	(49)	*(50)	(49)
Hemangiosarcoma	1 (2%)		
Lymphoma malignant lymphocytic			1 (2%)
Lymphoma malignant mixed		1 (2%)	
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Hemangiosarcoma	1 (2%)		1 (2%)
Lymphoma malignant mixed	2 (4%)	5 (10%)	1 (2%)
Lymphoma malignant undifferentiated cell	1 (2%)	3 (6%)	
Hemangioma		1 (2%)	1 (2%)
Lymphoma malignant lymphocytic			3 (6%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Terminal sacrifice	37	39	46
Dead	7	2	1
Moribund	6	9	3
TUMOR SUMMARY			
Total animals with primary neoplasms **	32	26	21
Total primary neoplasms	46	31	30
Total animals with benign neoplasms	25	10	18
Total benign neoplasms	30	12	20
Total animals with malignant neoplasms	13	18	10
Total malignant neoplasms	15	19	10
Total animals with secondary neoplasms ***	3	2	1
Total secondary neoplasms	9	2	1
Total animals with malignant neoplasms--uncertain primary site	1		
Total animals with neoplasms--uncertain benign or malignant	1		
Total uncertain neoplasms	1		

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: CHAMBER CONTROL

WEEKS ON STUDY	016	068	074	087	090	091	093	095	096	101	103	103	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	0911	2711	2611	4911	2511	2011	4711	1311	1011	0811	4411	1411	4311	3811	0111	0211	0311	0411	0511	0611	0711	1111	1211	1511	1611
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	+	+	M	A	+	M	+	+	A	+	+	+	+	+	+	+	+	+	+	A	A	+	+	+
Intestine large	+	+	+	+	A	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	+	M	+	A	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	A	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	A	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	A	A	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	A	A	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	A	A	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant undifferentiated cell type																									
Intestine small, jejunum	M	+	+	+	A	A	A	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinosarcoma, metastatic, uncertain primary site												X													
Hepatocellular carcinoma				X	X			X		X		X										X			
Hepatocellular adenoma		X				X			X		X										X		X		
Hepatocellular adenoma, multiple																									
Lymphoma malignant mixed																									
Mesentery																	+								
Pancreas	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth				+																					
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, carcinosarcoma, metastatic, uncertain primary site												X													
Adrenal gland, cortex	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Pheochromocytoma, NOS														X											
Islets, pancreatic	+	+	+	I	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	M	M	M	+	+	M	+	M	+	+	M	M	+	+	+	+	+	M	M	+	+	M	+	I
Pituitary gland	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+
Pars intermedia, adenoma														X											
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell, adenoma																					X				
GENERAL BODY SYSTEM																									
Tissue, NOS												+													
Carcinosarcoma, metastatic, uncertain primary site												X													
GENITAL SYSTEM																									
Epididymis	+	+	+	+	+	+	A	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis											+														
Preputial gland		–	+						–		+				+							+			
Prostate	+	+	+	+	+		A	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	M	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+
Testes	+	+	+	+	+	+	A	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

+: Tissue examined microscopically
: Not examined
–: Present but not examined microscopically
I: Insufficient tissue

M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	17 1	18 1	19 1	21 1	22 1	23 1	24 1	28 1	29 1	30 1	31 1	32 1	33 1	34 1	35 1	36 1	37 1	39 1	40 1	41 1	42 1	45 1	46 1	48 1	50 1	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+		48
Gallbladder	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+		41
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	I	+	+	+	M	+	+	+	+	+	+	+	+	+		43
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Lymphoma malignant undifferentiated cell type			X																							1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		44
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Carcinosarcoma, metastatic, uncertain primary site																										1
Hepatocellular carcinoma		X											X					X					X			10
Hepatocellular adenoma			X						X				X		X							X			X	12
Hepatocellular adenoma, multiple														X				X		X						3
Lymphoma malignant mixed							X																			1
Mesentery														+												2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Papilloma squamous					X																					1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Tooth	+						+																			3
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Capsule, carcinosarcoma, metastatic, uncertain primary site																										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Pheochromocytoma, NOS																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	I	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+		46
Parathyroid gland	+	+	+	M	+	M	M	+	M	+	M	M	+	M	+	M	M	+	M	M	M	+	M	+	M	25
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	44
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Follicular cell, adenoma																										1
GENERAL BODY SYSTEM																										
Tissue, NOS																										1
Carcinosarcoma, metastatic, uncertain primary site																										1
GENITAL SYSTEM																										
Epididymis	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+		48
Penis																										1
Preputial gland															+						+					8
Prostate	+			+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		45
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+		47
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	016	068	074	087	090	091	093	095	096	101	103	103	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	091	271	261	491	251	201	471	131	101	081	441	141	431	381	011	021	031	041	051	061	071	111	121	151	161
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	A	+	+	+	+	+	+	+	M	+	+	+	+	I	+	+	+	+	+
Mediastinal, lymphoma malignant mixed																						X			
Mediastinal, mesenteric, carcinosarcoma, metastatic, uncertain primary site												X													
Mesenteric, lymphoma malignant mixed																						X			
Renal, lymphoma malignant mixed																						X			
Lymph node, bronchial	+	+	M	M	M	+	M	M	I	+	+	M	+	M	M	+	M	M	+	I	+	+	+	M	+
Lymphoma malignant mixed																									
Lymph node, mandibular	M	+	+	+	+	M	A	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	M	+	+
Lymphoma malignant mixed																						X			
Spleen	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																						X			
Capsule, carcinosarcoma, metastatic, uncertain primary site												X													
Thymus	+	M	M	+	I	M	M	M	M	M	M	M	+	M	+	+	M	+	M	M	I	+	I	+	+
INTEGUMENTARY SYSTEM																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma									X								X					X			
Alveolar/bronchiolar adenoma, multiple																X									
Carcinosarcoma, metastatic, uncertain primary site												X													
Hepatocellular carcinoma, metastatic, multiple, liver																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSES SYSTEM																									
Eye						+																			
Sarcoma						X																			
Harderian gland						+																		+	
Adenoma																								X	
Sarcoma, metastatic, eye						X																			
URINARY SYSTEM																									
Kidney	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type																									
Capsule, carcinosarcoma, metastatic, uncertain primary site												X													
Urinary bladder	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																						X			

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	171	181	191	211	221	231	241	281	291	301	311	321	331	341	351	361	371	391	401	411	421	451	461	481	501	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	43
Mediastinal, lymphoma malig. mixed							X																			2
Mediastinal, mesenteric, carcinosarcoma, metastatic, uncertain primary site																										1
Mesenteric, lymphoma malignant mixed							X																			2
Renal, lymphoma malignant mixed																										1
Lymph node, bronchial	+	M	+	+	M	+	+	+	M	+	+	+	+	+	M	M	M	+	+	+	M	M	+	+	+	29
Lymphoma malignant mixed							X																			1
Lymph node, mandibular		+	+	+	M	+	+	+	M	M	+	+	M	M	+	M	+	+	+	+	+	M	M	M	+	34
Lymphoma malignant mixed							X																			2
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant mixed							X																			2
Capsule, carcinosarcoma, metastatic, uncertain primary site																										1
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	M	30
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma															X											1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma								X			X															5
Alveolar/bronchiolar adenoma, multiple		X																								2
Carcinosarcoma, metastatic, uncertain primary site																										1
Hepatocellular carcinoma, metastatic, multiple, liver													X													1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSES SYSTEM																										
Eye																										1
Sarcoma																										1
Harderian gland				+										+				+								5
Adenoma				X										X				X								4
Sarcoma, metastatic, eye																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant mixed							X																			1
Lymphoma malignant undifferentiated cell type			X																							1
Capsule, carcinosarcoma, metastatic, uncertain primary site																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																										1

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 5 ppm

WEEKS ON STUDY	008	082	083	087	087	091	096	097	097	104	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	12601	10301	15001	13501	14901	10601	13001	12501	11401	11101	12801	10101	10201	10401	10501	10701	10801	10901	11001	11201	11301	11501	11601	11701	11801
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+														
Gallbladder	M	A	M	M	+	+	M	A	M	+	+														
Intestine large	+	+	+	+	+	+	+	A	+	+	+														
Intestine large, cecum	M	M	M	M	M	+	+	A	+	+	+														
Intestine large, colon	+	+	+	+	+	+	+	A	+	+	+														
Intestine large, rectum	+	+	+	+	+	+	+	A	+	+	+														
Intestine small	+	+	+	+	+	+	+	A	+	+	+		+												
Intestine small, duodenum	+	+	+	+	+	+	+	A	+	+	+														
Intestine small, ileum	+	+	+	+	+	+	+	A	+	+	+														
Lymphoma malignant mixed																									
Intestine small, jejunum	+	+	+	+	+	+	+	A	+	+	+		+												
Lymphoma malignant undifferentiated cell type													X												
Liver	+	+	+	+	+	+	+	+	+	+	+							+				+			+
Hepatocellular carcinoma			X		X																				
Hepatocellular adenoma									X	X								X				X			X
Lymphoma malignant mixed		X																							
Pancreas	+	+	+	+	+	+	+	+	+	+	+														
Lymphoma malignant mixed		X																							
Salivary glands	+	M	+	+	+	+	+	+	+	+	+														
Lymphoma malignant undifferentiated cell type						X																			
Stomach	+	+	+	+	+	+	+	+	+	+	+								+		+				
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+										+				
Lymphoma malignant mixed		X																							
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+								+		+				
Lymphoma malignant mixed		X																							
Tooth																					+				
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+														
Heart	+	+	+	+	+	+	+	+	+	+	+														
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+														
Capsule, lymphoma malignant undifferentiated cell type						X																			
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+														
Lymphoma malignant mixed		X																							
Adrenal gland, medulla	+	+	+	+	I	+	+	+	+	+	+														
Lymphoma malignant mixed		X																							
Islets, pancreatic	+	+	+	+	+	+	+	+	I	+	+														
Lymphoma malignant mixed		X																							
Parathyroid gland	M	M	M	M	M	+	M	M	M	M	M														
Pituitary gland	M	+	+	+	+	+	M	+	+	+	+														
Thyroid gland	+	+	+	+	+	+	+	M	+	+	+														
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Epididymis	M	+	+	+	+	+	+	+	+	+	+														
Lymphoma malignant mixed		X																							
Penis								+			+														
Preputial gland						+					+						+			+	+				
Prostate	+	+	+	+	+	+	+	+	+	+	+														
Lymphoma malignant mixed		X																							
Seminal vesicle	+	+	+	+		+	+	+	+		+														
Lymphoma malignant mixed		X																							
Testes	+	+	+	+	+	+	+	+	+	+	+														

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 5 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	11901	12001	12111	12221	12231	12241	12271	12291	13111	13231	13331	13441	13661	13771	13881	13991	14001	14111	14211	14431	14441	14551	14661	14771	14881	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus																										11
Gallbladder																										4
Intestine large																										10
Intestine large, cecum																										5
Intestine large, colon																										10
Intestine large, rectum																										10
Intestine small											+									+						13
Intestine small, duodenum																										10
Intestine small, ileum																				+						11
Lymphoma malignant mixed																				X						1
Intestine small, jejunum											+									+						13
Lymphoma malignant undifferentiated cell type											X															2
Liver	+			+				+	+						+											19
Hepatocellular carcinoma	X								X																	4
Hepatocellular adenoma								X							X											7
Lymphoma malignant mixed																										1
Pancreas	+																									12
Lymphoma malignant mixed								•																		1
Salivary glands																										10
Lymphoma malignant undifferentiated cell type																										1
Stomach				+													+							+		16
Stomach, forestomach				+													+							+		15
Lymphoma malignant mixed																										1
Stomach, glandular				+													+									15
Lymphoma malignant mixed																										1
Tooth																						+		+		3
CARDIOVASCULAR SYSTEM																										
Blood vessel																										11
Heart																										11
ENDOCRINE SYSTEM																										
Adrenal gland																										11
Capsule, lymphoma malignant undifferentiated cell type																										1
Adrenal gland, cortex																										11
Lymphoma malignant mixed																										1
Adrenal gland, medulla																										10
Lymphoma malignant mixed																										1
Islets, pancreatic																										10
Lymphoma malignant mixed																										1
Parathyroid gland																										1
Pituitary gland																										9
Thyroid gland																										10
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis																										10
Lymphoma malignant mixed																										1
Penis																										2
Preputial gland				+								+					+								+	9
Prostate																										11
Lymphoma malignant mixed																										1
Seminal vesicle				+																						10
Lymphoma malignant mixed																										1
Testes																										11

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 5 ppm (Continued)

WEEKS ON STUDY	008	082	083	087	087	091	096	097	097	104	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	1261	1031	1501	1351	1491	1061	1301	1251	1411	1111	1281	1011	1021	1041	1051	1071	1081	1091	1101	1121	1131	1151	1161	1171	1181	
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+															
Bone marrow	+	+	+	+	+	+	+	+	+	+	+															
Lymph node	+	+	+	+	+	+	+	+	M	+	+															
Mediastinal, lymphoma malignant mixed																										
Mesenteric, lymphoma malignant mixed		X																								
Mesenteric, lymphoma malignant undifferentiated cell type																										
Renal, lymphoma malignant mixed																										
Lymph node, bronchial	M	+	M	M	+	+	+	M	M	+	+															
Alveolar/bronchiolar carcinoma, metastatic, lung							X																			
Lymphoma malignant mixed		X																								
Lymphoma malignant undifferentiated cell type						X																				
Lymph node, mandibular	+	+	+	+	M	+	+	+	M	I	M															
Lymphoma malignant mixed		X																								
Lymphoma malignant undifferentiated cell type						X																				
Spleen	+	+	+	+	+	+	M	A	+	+	+								+		+					
Hemangioma																										
Lymphoma malignant mixed		X																								
Lymphoma malignant undifferentiated cell type						X																				
Thymus	M	M	M	+	+	M	M	M	+	M	+															
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M															
Skin	+	+	+	+	+	+	+	+	+	+	+			+						+						
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+															
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+															
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+															
Lung	+	+	+	+	+	+	+	+	+	+	+		+			+	+			+	+					
Alveolar/bronchiolar adenoma										X																
Alveolar/bronchiolar carcinoma													X							X	X					
Alveolar/bronchiolar carcinoma, multiple							X										X									
Hepatocellular carcinoma, metastatic, multiple, liver					X																					
Lymphoma malignant mixed		X																								
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	M	+	+	+															
SPECIAL SENSES SYSTEM																										
Eye																										
Harderian gland																										+
Adenoma																										X
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+															
Lymphoma malignant mixed		X																								
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+															
Lymphoma malignant mixed		X																								

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 5 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	11191	12011	12111	12221	12231	12241	12271	12291	13111	13211	13331	13411	13611	13711	13811	13911	14011	14111	14211	14311	14411	14511	14611	14711	14811		TISSUES TUMORS
HEMATOPOIETIC SYSTEM																											
Blood																											11
Bone marrow																											11
Lymph node		+			+						+										+		+				15
Mediastinal, lymphoma malig. mixed																					X						1
Mesenteric, lymphoma malignant mixed		X			X																X						4
Mesenteric, lymphoma malignant undifferentiated cell type											X																1
Renal, lymphoma malignant mixed																					X						1
Lymph node, bronchial																					+						7
Alveolar/bronchiolar carcinoma, metastatic, lung																											1
Lymphoma malignant mixed																					X						2
Lymphoma malignant undifferentiated cell type																											1
Lymph node, mandibular																					+		+				9
Lymphoma malignant mixed																					X						2
Lymphoma malignant undifferentiated cell type																											1
Spleen	+	+							+								+				+						16
Hemangioma																	X										1
Lymphoma malignant mixed		X																			X						3
Lymphoma malignant undifferentiated cell type																											1
Thymus																											4
INTEGUMENTARY SYSTEM																											
Mammary gland																											
Skin				+				+								+								+			17
MUSCULOSKELETAL SYSTEM																											
Bone																											11
NERVOUS SYSTEM																											
Brain																											11
RESPIRATORY SYSTEM																											
Larynx																											11
Lung				+													+				+						19
Alveolar/bronchiolar adenoma																					X						2
Alveolar/bronchiolar carcinoma				X													X										5
Alveolar/bronchiolar carcinoma, multiple																											2
Hepatocellular carcinoma, metastatic, multiple, liver																											1
Lymphoma malignant mixed																					X						2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Trachea																											10
SPECIAL SENSES SYSTEM																											
Eye																+											1
Harderian gland																+											2
Adenoma																X											2
URINARY SYSTEM																											
Kidney												+	+								+			+			15
Lymphoma malignant mixed																					X						2
Urinary bladder																											11
Lymphoma malignant mixed																											1

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 10 ppm

WEEKS ON STUDY	013	041	099	101	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	24111	20071	20111	23711	20021	20031	20411	20051	20061	20081	20091	21011	21111	21221	21331	21441	21551	21661	21771	21881	21991	22001	22111	22221	22331
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Gallbladder	M	+	+	A	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+
Lymphoma malignant lymphocytic							X																		
Intestine large	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	I	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		
Intestine small, ileum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	M	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma, multiple			X																						
Hepatocellular carcinoma																X									
Hepatocellular adenoma			X										X	X				X							
Lymphoma malignant lymphocytic							X																		
Mesentery							+																		
Lymphoma malignant lymphocytic							X																		
Pancreas	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		
Salivary glands	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		
Stomach, glandular	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		
Tooth																							+		
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Aorta, lymphoma malignant lymphocytic							X																		
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma, metastatic, liver			X																						
Lymphoma malignant lymphocytic							X																		
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Medulla, lymphoma malignant lymphocytic							X																		
Adrenal gland, medulla	+	+	+	A	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	A	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	M	M	+	M	M	+	M	+	+	M	+	+	+	+	+	+	+	M	M	+	M	+	M	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars intermedia, adenoma										X															
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Follicular cell, adenoma				X																					
GENERAL BODY SYSTEM																									
None																									
GENITAL SYSTEM																									
Epididymis	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+						+							+	+						+				
Prostate	+	+	+	A	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+
Seminal vesicle	+	+		A		+		+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 10 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	22441	22551	22661	22771	22881	22991	23001	23111	23221	23331	23441	23551	23661	23881	23991	24001	24212	24313	24414	24515	24661	24771	24881	24991	25001	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant lymphocytic																										1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma, multiple																										1
Hepatocellular carcinoma																										1
Hepatocellular adenoma																							X			5
Lymphoma malignant lymphocytic																										1
Mesentery																										1
Lymphoma malignant lymphocytic																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Tooth							+									+										3
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Aorta, lymphoma malig. lymphocytic																										1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma, metastatic, liver																										1
Lymphoma malignant lymphocytic																										1
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Medulla, lymphoma malignant lymphocytic																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Islets, pancreatic	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	46
Parathyroid gland	+	+	M	M	M	+	M	M	M	M	+	M	M	+	M	M	M	M	+	M	M	M	+	+	M	23
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	49
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell, adenoma	X											X														3
GENERAL BODY SYSTEM																										
None																										
GENITAL SYSTEM																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland													+			+				+						8
Prostate	+	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	44
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	44
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 10 ppm (Continued)

WEEKS ON STUDY	013	041	099	101	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	24111	20711	20111	23711	20211	20311	20411	20511	20611	20811	20911	21011	21111	21211	21311	21411	21511	21611	21711	21811	21911	22011	22111	22211	22311
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Axillary, lymphoma malignant lymphocytic							X																		
Inguinal, lymphoma malignant lymphocytic							X																		
Mediastinal, lymphoma malignant lymphocytic							X																		
Mediastinal, lymphoma malignant mixed																									
Mesenteric, lymphoma malignant lymphocytic							X																		
Mesenteric, lymphoma malignant mixed																									
Renal, lymphoma malignant lymphocytic							X																		
Lymph node, bronchial	M	M	M	M	+	M	+	+	+	+	+	+	+	M	+	M	+	+	M	+	+	+	+	M	M
Lymphoma malignant lymphocytic							X																		
Lymph node, mandibular	+	+	+	M	+	+	+	+	M	M	+	+	M	+	M	+	+	M	+	+	+	+	+	+	M
Lymphoma malignant lymphocytic							X												X						
Spleen	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X												X						
Thymus	+	M	M	M	+	+	+	+	+	+	+	I	+	M	M	M	+	+	+	+	+	+	+	M	M
Lymphoma malignant lymphocytic							X												X						
INTEGUMENTARY SYSTEM																									
Mammary gland	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sebaceous gland, adenoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		
RESPIRATORY SYSTEM																									
Larynx	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma						X										X									
Alveolar/bronchiolar adenoma, multiple																									
Alveolar/bronchiolar carcinoma					X								X												
Alveolar/bronchiolar carcinoma, multiple																									
Leiomyosarcoma				X																					
Lymphoma malignant lymphocytic							X																		
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory epithelium, adenoma			X																						
Submucosa, hemangioma					X																				
Trachea	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
SPECIAL SENSES SYSTEM																									
Ear																									
URINARY SYSTEM																									
Kidney	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		
Urinary bladder	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic							X																		

TABLE C2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: 10 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	22441	22551	22661	22771	22881	22991	23091	23111	23211	23311	23411	23511	23611	23811	23911	24011	24211	24311	24411	24511	24611	24711	24811	24911	25011	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	M	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	45
Axillary, lymphoma malignant lymphocytic																										1
Inguinal, lymphoma malignant lymphocytic																										1
Mediastinal, lymphoma malignant lymphocytic																										1
Mediastinal, lymphoma malig. mixed																							X			1
Mesenteric, lymphoma malignant lymphocytic																										1
Mesenteric, lymphoma malignant mixed																							X			1
Renal, lymphoma malig. lymphocytic																										1
Lymph node, bronchial	M	+	M	M	+	+	M	M	+	+	+	M	M	+	+	M	M	+	M	M	+	+	+	+	+	29
Lymphoma malignant lymphocytic																										1
Lymph node, mandibular	M	M	M	+	M	+	+	+	+	M	M	+	M	+	M	+	+	M	+	+	+	+	M	+	+	33
Lymphoma malignant lymphocytic																										2
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic				X																						3
Thymus	+	+	+	+	M	+	+	+	M	+	+	M	M	+	+	M	M	M	+	+	M	+	M	M	+	31
Lymphoma malignant lymphocytic																										2
INTEGUMENTARY SYSTEM																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M	M	3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sebaceous gland, adenoma									X																	1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma			X	X							X															5
Alveolar/bronchiolar adenoma, multiple																				X						1
Alveolar/bronchiolar carcinoma																										2
Alveolar/bronchiolar carcinoma, multiple																					X					1
Leiomyosarcoma																										1
Lymphoma malignant lymphocytic																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory epithelium, adenoma											X					X										3
Submucosa, hemangioma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPECIAL SENSES SYSTEM																										
Ear																		•								1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1

TABLE C3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Harderian Gland: Adenoma			
Overall Rates (a)	4/50 (8%)	2/50 (4%)	0/50 (0%)
Adjusted Rates (b)	10.5%	5.1%	0.0%
Terminal Rates (c)	4/38 (11%)	2/39 (5%)	0/46 (0%)
Day of First Observation	729	729	
Life Table Tests (d)	P=0.025N	P=0.324N	P=0.042N
Logistic Regression Tests (d)	P=0.025N	P=0.324N	P=0.042N
Cochran-Armitage Trend Test (d)	P=0.037N		
Fisher Exact Test (d)		P=0.339N	P=0.059N
Liver: Hepatocellular Adenoma			
Overall Rates (e)	15/49 (31%)	(f) 7/19 (37%)	5/49 (10%)
Adjusted Rates (b)	35.2%		10.6%
Terminal Rates (c)	11/38 (29%)		4/46 (9%)
Day of First Observation	474		690
Life Table Test (d)			P=0.005N
Logistic Regression Test (d)			P=0.012N
Fisher Exact Test (d)			P=0.011N
Liver: Hepatocellular Carcinoma			
Overall Rates (e)	10/49 (20%)	(f) 4/19 (21%)	1/49 (2%)
Adjusted Rates (b)	22.8%		2.2%
Terminal Rates (c)	5/38 (13%)		1/46 (2%)
Day of First Observation	608		729
Life Table Test (d)			P=0.003N
Logistic Regression Test (d)			P=0.005N
Fisher Exact Test (d)			P=0.004N
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (e)	23/49 (47%)	(f) 11/19 (58%)	6/49 (12%)
Adjusted Rates (b)	48.8%		12.7%
Terminal Rates (c)	14/38 (37%)		5/46 (11%)
Day of First Observation	474		690
Life Table Test (d)			P<0.001N
Logistic Regression Test (d)			P<0.001N
Fisher Exact Test (d)			P<0.001N
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (e)	7/50 (14%)	(f) 2/19 (11%)	6/50 (12%)
Adjusted Rates (b)	17.8%		13.0%
Terminal Rates (c)	6/38 (16%)		6/46 (13%)
Day of First Observation	667		729
Life Table Test (d)			P=0.360N
Logistic Regression Test (d)			P=0.439N
Fisher Exact Test (d)			P=0.500N
Lung: Alveolar/Bronchiolar Carcinoma			
Overall Rates (e)	0/50 (0%)	(f) 7/19 (37%)	3/50 (6%)
Adjusted Rates (b)	0.0%		6.5%
Terminal Rates (c)	0/38 (0%)		3/46 (7%)
Day of First Observation			729
Life Table Test (d)			P=0.157
Logistic Regression Test (d)			P=0.157
Fisher Exact Test (d)			P=0.121
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (e)	7/50 (14%)	(f) 9/19 (47%)	9/50 (18%)
Adjusted Rates (b)	17.8%		19.6%
Terminal Rates (c)	6/38 (16%)		9/46 (20%)
Day of First Observation	667		729
Life Table Test (d)			P=0.554
Logistic Regression Test (d)			P=0.469
Fisher Exact Test (d)			P=0.393

TABLE C3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
Nose (Respiratory Epithelium): Adenoma			
Overall Rates (e)	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted Rates (b)	0.0%	0.0%	6.3%
Terminal Rates (c)	0/38 (0%)	0/39 (0%)	2/46 (4%)
Day of First Observation			690
Life Table Tests (d)	P=0.052	(g)	P=0.157
Logistic Regression Tests (d)	P=0.038	(g)	P=0.124
Cochran-Armitage Trend Test (d)	P=0.037		
Fisher Exact Test (d)		(g)	P=0.121
Thyroid Gland: Follicular Cell Adenoma			
Overall Rates (e)	1/50 (2%)	(f) 0/10 (0%)	3/49 (6%)
Adjusted Rates (b)	2.6%		6.5%
Terminal Rates (c)	1/38 (3%)		2/45 (4%)
Day of First Observation	729		701
Life Table Test (d)			P=0.366
Logistic Regression Test (d)			P=0.316
Fisher Exact Test (d)			P=0.301
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	3/50 (6%)	(h) 8/50 (16%)	4/50 (8%)
Adjusted Rates (b)	7.9%	19.0%	8.7%
Terminal Rates (c)	3/38 (8%)	6/39 (15%)	4/46 (9%)
Day of First Observation	729	570	729
Life Table Tests (d)	P=0.549	P=0.112	P=0.604
Logistic Regression Tests (d)	P=0.445	P=0.102	P=0.604
Cochran-Armitage Trend Test (d)	P=0.434		
Fisher Exact Test (d)		P=0.100	P=0.500

(a) Number of tumor-bearing animals/number of animals examined grossly at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals killed at the end of the study
(d) Beneath the control incidence are the P values associated with the trend test. Beneath the dosedgroup 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 logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) Number of tumor-bearing animals/number of animals examined microscopically at the site
(f) Incomplete sampling of tissues
(g) No P value is reported because no tumors were observed in the 5-ppm and control groups.
(h) Fifteen lymph nodes and 16 spleens were examined microscopically.

TABLE C4a. HISTORICAL INCIDENCE OF NASAL CAVITY TUMORS IN MALE B6C3F$_1$ MICE (a)

	Number Examined	Number of Tumors
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories		
	398	0
Overall Historical Incidence for Untreated Controls in NTP Studies		
	1,692	0

(a) Data as of May 12, 1988, for studies of at least 104 weeks

TABLE C4b. HISTORICAL INCIDENCE OF HARDERIAN GLAND TUMORS IN MALE B6C3F$_1$ MICE (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	1/50	0/50	1/50
Methyl methacrylate	4/50	2/50	6/50
Propylene	2/50	0/50	2/50
1,2-Epoxybutane	3/49	0/49	3/49
Dichloromethane	0/50	0/50	0/50
Ethylene oxide	1/50	0/50	1/50
Bromoethane	3/50	2/50	5/50
Tetrachloroethylene	0/49	1/49	1/49
TOTAL	(b) 14/398 (3.5%)	(c) 5/398 (1.3%)	(b,c) 19/398 (4.8%)
SD (d)	2.99%	1.83%	4.27%
Range (e)			
High	4/50	2/50	6/50
Low	0/50	0/50	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	(f) 61/1,692 (3.6%)	(g) 6/1,692 (0.4%)	(f,g) 67/1,692 (4.0%)
SD (d)	3.23%	0.78%	3.90%
Range (e)			
High	6/50	1/49	6/50
Low	0/50	0/50	0/50

(a) Data as of May 12, 1988, for studies of at least 104 weeks
(b) Includes one papillary adenoma and four papillary cystadenomas
(c) Includes four adenocarcinomas, NOS, and one papillary cystadenocarcinoma, NOS
(d) Standard deviation
(e) Range and SD are presented for groups of 35 or more animals.
(f) Includes five papillary adenomas, five cystadenomas, and six papillary cystadenomas, NOS
(g) Includes two adenocarcinomas, NOS

TABLE C4c. HISTORICAL INCIDENCE OF HEPATOCELLULAR TUMORS IN MALE B6C3F$_1$ MICE (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	8/50	6/50	14/50
Methyl methacrylate	9/50	8/50	16/50
Propylene	5/50	9/50	14/50
1,2-Epoxybutane	4/49	11/49	14/49
Dichloromethane	10/50	13/50	22/50
Ethylene oxide	6/49	9/49	15/49
Bromoethane	10/50	11/50	21/50
Tetrachloroethylene	12/49	7/49	17/49
TOTAL	64/397 (16.1%)	74/397 (18.6%)	133/397 (33.5%)
SD (b)	5.60%	4.64%	6.32%
Range (c)			
High	12/49	13/50	22/50
Low	4/49	6/50	14/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	233/1,678 (13.9%)	285/1,678 (17.0%)	494/1,678 (29.4%)
SD (b)	7.50%	6.31%	8.04%
Range (c)			
High	22/50	15/50	29/50
Low	2/45	4/50	7/48

(a) Data as of May 12, 1988, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Intestine large, cecum	(45)	(5)	(48)
Inflammation, suppurative	1 (2%)		
Intestine large, colon	(47)	(10)	(49)
Inflammation, suppurative	1 (2%)		
Parasite metazoan	1 (2%)		
Intestine large, rectum	(47)	(10)	(47)
Inflammation, suppurative	2 (4%)		
Parasite metazoan	1 (2%)		
Intestine small	(45)	(13)	(49)
Lymphoid tissue, hyperplasia	1 (2%)		
Intestine small, ileum	(45)	(11)	(49)
Hyperplasia, lymphoid	1 (2%)		
Submucosa, amyloid deposition	1 (2%)		
Liver	(49)	(19)	(49)
Basophilic focus		1 (5%)	
Cyst, multiple		1 (5%)	
Developmental malformation	1 (2%)		
Focal cellular change	2 (4%)		2 (4%)
Inflammation, acute, focal			1 (2%)
Inflammation, chronic, multifocal		1 (5%)	2 (4%)
Necrosis, coagulative	1 (2%)		1 (2%)
Proliferation connective tissue		1 (5%)	
Bile duct, cyst			1 (2%)
Centrilobular, fatty change, multifocal	1 (2%)		
Serosa, fibrosis	1 (2%)		
Mesentery	(2)		(1)
Inflammation, chronic	1 (50%)		
Pancreas	(49)	(12)	(49)
Cyst		1 (8%)	
Fibrosis, diffuse	1 (2%)		
Salivary glands	(49)	(10)	(49)
Inflammation, chronic	2 (4%)		4 (8%)
Stomach, forestomach	(50)	(15)	(49)
Hyperkeratosis	3 (6%)	1 (7%)	1 (2%)
Hyperplasia, squamous		1 (7%)	
Mineralization, focal	1 (2%)		
Ulcer		2 (13%)	2 (4%)
Stomach, glandular	(50)	(15)	(49)
Atrophy	1 (2%)		
Atrophy, diffuse	1 (2%)		
Cyst	1 (2%)		
Dysplasia, focal	1 (2%)		
Necrosis, multifocal	1 (2%)		
Ulcer, multiple		1 (7%)	
Tooth	(3)	(3)	(3)
Abscess		3 (100%)	
Developmental malformation	2 (67%)		
Inflammation, chronic, focal	1 (33%)		
Peridontal tissue, inflammation, chronic			3 (100%)

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
CARDIOVASCULAR SYSTEM			
Heart	(50)	(11)	(50)
Atrium, thrombus	1 (2%)		
Coronary artery, inflammation, chronic, focal	1 (2%)		
Myocardium, inflammation, acute, focal			1 (2%)
Myocardium, inflammation, chronic			2 (4%)
Valve, inflammation, chronic, focal	1 (2%)		
Valve, pigmentation, focal	1 (2%)		
ENDOCRINE SYSTEM			
Adrenal gland	(49)	(11)	(50)
Accessory adrenal cortical nodule			1 (2%)
Hypertrophy, focal	1 (2%)		
Subcapsular, hyperplasia	46 (94%)	10 (91%)	49 (98%)
Adrenal gland, cortex	(49)	(11)	(49)
Degeneration, focal	2 (4%)		
Hyperplasia, focal			2 (4%)
Hypertrophy, focal			1 (2%)
Pituitary gland	(44)	(9)	(49)
Cyst			1 (2%)
Thyroid gland	(50)	(10)	(49)
Follicular cell, hyperplasia	4 (8%)		2 (4%)
GENERAL BODY SYSTEM			
None			
GENITAL SYSTEM			
Penis	(1)	(2)	
Inflammation, necrotizing	1 (100%)	1 (50%)	
Preputial gland	(8)	(9)	(8)
Cyst	2 (25%)	4 (44%)	5 (63%)
Cyst, multiple			1 (13%)
Inflammation, chronic	1 (13%)	1 (11%)	
Inflammation, suppurative	5 (63%)	3 (33%)	
Prostate	(45)	(11)	(44)
Inflammation, suppurative	2 (4%)		
Seminal vesicle	(47)	(10)	(44)
Dilatation	1 (2%)	1 (10%)	
Hemorrhage, diffuse	1 (2%)		
Inflammation, suppurative	2 (4%)		
Testes	(49)	(11)	(49)
Mineralization	2 (4%)		
Bilateral, atrophy	2 (4%)		
Interstitial cell, hyperplasia	2 (4%)		
HEMATOPOIETIC SYSTEM			
Lymph node	(43)	(15)	(45)
Mesenteric, hemorrhage, acute		1 (7%)	
Mesenteric, hyperplasia	1 (2%)		
Lymph node, bronchial	(29)	(7)	(29)
Edema	1 (3%)		
Hyperplasia, lymphoid	1 (3%)		1 (3%)
Lymph node, mandibular	(34)	(9)	(33)
Hyperplasia, lymphoid	1 (3%)	1 (11%)	1 (3%)
Infiltration cellular, histiocytic	7 (21%)		1 (3%)

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
HEMATOPOIETIC SYSTEM (Continued)			
Spleen	(49)	(16)	(49)
Atrophy		1 (6%)	2 (4%)
Hematopoietic cell proliferation	3 (6%)	2 (13%)	2 (4%)
Hyperplasia, lymphoid			3 (6%)
Capsule, fibrosis	1 (2%)		
Thymus	(30)	(4)	(31)
Cyst	3 (10%)		
Mediastinum, inflammation, chronic			1 (3%)
INTEGUMENTARY SYSTEM			
Skin	(50)	(17)	(50)
Inflammation, chronic, focal			1 (2%)
Dermis, abscess	1 (2%)		
Epidermis, necrosis, acute	1 (2%)		
Hair follicle, atrophy	3 (6%)	5 (29%)	
Prepuce, inflammation, suppurative	3 (6%)		
Prepuce, ulcer		3 (18%)	
Sebaceous gland, hyperplasia		1 (6%)	
Subcutaneous tissue, edema		1 (6%)	
Subcutaneous tissue, hemorrhage, acute	1 (2%)		
Subcutaneous tissue, inflammation, acute		1 (6%)	
Subcutaneous tissue, inflammation, chronic	1 (2%)	1 (6%)	
Subcutaneous tissue, inflammation, suppurative	3 (6%)		
MUSCULOSKELETAL SYSTEM			
None			
NERVOUS SYSTEM			
Brain	(50)	(11)	(50)
Cerebrum, mineralization			1 (2%)
Hypothalamus, atrophy			1 (2%)
Thalamus, atrophy	1 (2%)		
Thalamus, hemorrhage, acute, focal	1 (2%)		
Thalamus, mineralization	29 (58%)	3 (27%)	8 (16%)
RESPIRATORY SYSTEM			
Lung	(50)	(19)	(50)
Congestion, diffuse	1 (2%)		
Granuloma			1 (2%)
Infiltration cellular, histiocytic	2 (4%)	1 (5%)	2 (4%)
Inflammation, chronic, multifocal	17 (34%)	3 (16%)	21 (42%)
Inflammation, suppurative			1 (2%)
Alveolus, adenomatosis, focal	2 (4%)	1 (5%)	
Alveolus, hyperplasia, focal	2 (4%)		
Glands, ectasia	8 (16%)		
Glands, inflammation, suppurative	1 (2%)		
Interstitium, inflammation, acute	3 (6%)		

TABLE C5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
RESPIRATORY SYSTEM (Continued)			
Nose	(50)	(50)	(50)
Glands, dilatation	1 (2%)		
Glands, hyperplasia	8 (16%)	47 (94%)	48 (96%)
Mucosa, inflammation, suppurative	2 (4%)	48 (96%)	47 (94%)
Olfactory epithelium, metaplasia	4 (8%)	49 (98%)	50 (100%)
Respiratory epithelium, dysplasia		1 (2%)	3 (6%)
Respiratory epithelium, dysplasia, focal			1 (2%)
Respiratory epithelium, hyperplasia		25 (50%)	40 (80%)
Respiratory epithelium, hyperplasia, basal cell		1 (2%)	7 (14%)
Respiratory epithelium, metaplasia, squamous		4 (8%)	8 (16%)
Respiratory epithelium, regeneration		46 (92%)	46 (92%)
Submucosa, angiectasis	1 (2%)	2 (4%)	5 (10%)
Trachea	(50)	(10)	(48)
Epithelium, metaplasia, squamous			1 (2%)
Glands, dilatation	41 (82%)		27 (56%)
Mediastinum, hyperplasia, lymphoid	1 (2%)		
SPECIAL SENSES SYSTEM			
None			
URINARY SYSTEM			
Kidney	(49)	(15)	(49)
Inflammation, chronic	39 (80%)	4 (27%)	30 (61%)
Inflammation, suppurative	4 (8%)	1 (7%)	
Capsule, fibrosis		1 (7%)	
Cortex, cyst		2 (13%)	
Cortex, metaplasia, osseous	1 (2%)		
Medulla, cyst		1 (7%)	
Renal tubule, dilatation, diffuse	1 (2%)		
Renal tubule, regeneration	32 (65%)	3 (20%)	32 (65%)
Renal tubule, regeneration, multifocal			2 (4%)
Urinary bladder	(49)	(11)	(49)
Calculus micro observation only		1 (9%)	
Inflammation, chronic	2 (4%)		
Inflammation, chronic, multifocal			2 (4%)
Inflammation, suppurative	4 (8%)	1 (9%)	
Transitional epithelium, hyperplasia		1 (9%)	
Transitional epithelium, necrosis	1 (2%)		

APPENDIX D

SUMMARY OF LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Esophagus	(47)	*(50)	(48)
Lymphoma malignant lymphocytic			1 (2%)
Gallbladder	(45)	*(50)	(42)
Lymphoma malignant lymphocytic	1 (2%)		1 (2%)
Lymphoma malignant mixed			1 (2%)
Intestine large, colon	(49)	*(50)	(49)
Lymphoma malignant mixed			1 (2%)
Intestine large, rectum	(50)	*(50)	(49)
Lymphoma malignant lymphocytic	1 (2%)		
Intestine small, duodenum	(46)	*(50)	(46)
Lymphoma malignant lymphocytic	1 (2%)		
Intestine small, ileum	(47)	*(50)	(47)
Lymphoma malignant lymphocytic	1 (2%)		
Lymphoma malignant mixed		1 (2%)	3 (6%)
Liver	(50)	*(50)	(50)
Fibrosarcoma, metastatic, skin			1 (2%)
Hepatocellular carcinoma	4 (8%)	3 (6%)	
Hepatocellular carcinoma, multiple	1 (2%)		
Hepatocellular adenoma	1 (2%)	2 (4%)	1 (2%)
Hepatocellular adenoma, multiple			1 (2%)
Histiocytic sarcoma	2 (4%)		
Histiocytic sarcoma, metastatic, uterus	1 (2%)		
Lymphoma malignant lymphocytic	5 (10%)	1 (2%)	1 (2%)
Lymphoma malignant	1 (2%)		
Lymphoma malignant mixed	6 (12%)	1 (2%)	1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	1 (2%)
Mesentery	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic	3 (6%)	1 (2%)	4 (8%)
Lymphoma malignant	1 (2%)		
Lymphoma malignant mixed	2 (4%)		1 (2%)
Lymphoma malignant undifferentiated cell type		1 (2%)	
Pancreas	(49)	*(50)	(50)
Histiocytic sarcoma	2 (4%)		
Lymphoma malignant lymphocytic	3 (6%)		3 (6%)
Lymphoma malignant mixed	5 (10%)		3 (6%)
Salivary glands	(50)	*(50)	(50)
Histiocytic sarcoma	1 (2%)		
Lymphoma malignant lymphocytic	6 (12%)	1 (2%)	2 (4%)
Lymphoma malignant mixed	1 (2%)		4 (8%)
Lymphoma malignant undifferentiated cell type	1 (2%)		1 (2%)
Stomach, forestomach	(50)	*(50)	(49)
Lymphoma malignant lymphocytic	2 (4%)	1 (2%)	
Lymphoma malignant mixed	1 (2%)		
Papilloma squamous	1 (2%)	1 (2%)	1 (2%)
Stomach, glandular	(49)	*(50)	(48)
Lymphoma malignant lymphocytic	2 (4%)	1 (2%)	1 (2%)
Lymphoma malignant mixed	1 (2%)		
CARDIOVASCULAR SYSTEM			
Heart	(50)	*(50)	(50)
Fibrosarcoma, metastatic, skin			1 (2%)
Lymphoma malignant lymphocytic	3 (6%)		3 (6%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
ENDOCRINE SYSTEM			
Adrenal gland	(47)	*(50)	(48)
Histiocytic sarcoma, metastatic, uterus	1 (2%)		
Lymphoma malignant lymphocytic	3 (6%)	1 (2%)	
Lymphoma malignant mixed	1 (2%)		1 (2%)
Capsule, lymphoma malignant lymphocytic			1 (2%)
Subcapsular, adenoma			1 (2%)
Adrenal gland, cortex	(47)	*(50)	(48)
Lymphoma malignant lymphocytic	1 (2%)		1 (2%)
Lymphoma malignant mixed	1 (2%)		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	
Adrenal gland, medulla	(47)	*(50)	(47)
Lymphoma malignant lymphocytic	1 (2%)		1 (2%)
Lymphoma malignant mixed	1 (2%)		1 (2%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	
Pheochromocytoma malignant		1 (2%)	
Islets, pancreatic	(49)	*(50)	(48)
Lymphoma malignant lymphocytic	1 (2%)		1 (2%)
Pituitary gland	(44)	*(50)	(45)
Pars distalis, adenoma	12 (27%)	8 (16%)	2 (4%)
Pars distalis, carcinoma	1 (2%)		
Pars intermedia, adenoma	1 (2%)		2 (4%)
Thyroid gland	(50)	*(50)	(50)
Lymphoma malignant lymphocytic	1 (2%)		1 (2%)
Lymphoma malignant mixed	1 (2%)		
Bilateral, follicular cell, carcinoma		1 (2%)	
Follicular cell, adenoma	2 (4%)		3 (6%)
GENERAL BODY SYSTEM			
Tissue, NOS	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic	2 (4%)		
Lymphoma malignant	1 (2%)		
Lymphoma malignant mixed	1 (2%)		
GENITAL SYSTEM			
Clitoral gland	*(50)	*(50)	*(50)
Hemangiosarcoma	1 (2%)		
Ovary	(49)	*(50)	(50)
Cystadenocarcinoma			1 (2%)
Granulosa cell tumor, NOS	1 (2%)		1 (2%)
Histiocytic sarcoma	1 (2%)		
Histiocytic sarcoma, metastatic, uterus	1 (2%)		
Luteoma	1 (2%)		
Lymphoma malignant lymphocytic	7 (14%)		3 (6%)
Lymphoma malignant mixed	4 (8%)		3 (6%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	
Uterus	(50)	*(50)	(50)
Histiocytic sarcoma	2 (4%)		
Lymphoma malignant lymphocytic	3 (6%)	1 (2%)	1 (2%)
Lymphoma malignant mixed	2 (4%)		1 (2%)
Polyp stromal		1 (2%)	1 (2%)
Sarcoma stromal	1 (2%)		
Cervix, leiomyoma			1 (2%)
HEMATOPOIETIC SYSTEM			
Bone marrow	(50)	*(50)	(48)
Histiocytic sarcoma	1 (2%)		
Lymphoma malignant lymphocytic	2 (4%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
HEMATOPOIETIC SYSTEM (Continued)			
Lymph node	(48)	*(50)	(48)
Iliac, lymphoma malignant lymphocytic	1 (2%)		
Iliac, lymphoma malignant mixed	1 (2%)		
Iliac, lymphoma malignant undifferentiated cell type		1 (2%)	
Inguinal, lymphoma malignant undifferentiated cell type		1 (2%)	
Mediastinal, histiocytic sarcoma	1 (2%)		
Mediastinal, lymphoma malignant lymphocytic	4 (8%)		
Mediastinal, lymphoma malignant	1 (2%)		
Mediastinal, lymphoma malignant mixed	3 (6%)		4 (8%)
Mesenteric, lymphoma malignant lymphocytic		1 (2%)	2 (4%)
Mesenteric, lymphoma malignant mixed	3 (6%)		3 (6%)
Mesenteric, lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	
Renal, histiocytic sarcoma	1 (2%)		
Renal, lymphoma malignant lymphocytic		1 (2%)	1 (2%)
Renal, lymphoma malignant mixed	2 (4%)		1 (2%)
Renal, lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	
Lymph node, bronchial	(38)	*(50)	(37)
Adenocarcinoma, metastatic, mammary gland	1 (3%)		
Histiocytic sarcoma	2 (5%)		
Lymphoma malignant lymphocytic	7 (18%)	1 (2%)	3 (8%)
Lymphoma malignant	1 (3%)		
Lymphoma malignant mixed	6 (16%)		4 (11%)
Lymphoma malignant undifferentiated cell type	1 (3%)	1 (2%)	1 (3%)
Lymph node, mandibular	(42)	*(50)	(40)
Adenocarcinoma, metastatic, mammary gland	1 (2%)	1 (2%)	
Histiocytic sarcoma	2 (5%)		
Lymphoma malignant lymphocytic	7 (17%)	1 (2%)	3 (8%)
Lymphoma malignant	1 (2%)		
Lymphoma malignant mixed	7 (17%)		4 (10%)
Lymphoma malignant undifferentiated cell type		1 (2%)	1 (3%)
Spleen	(50)	*(50)	(50)
Histiocytic sarcoma	2 (4%)		
Lymphoma malignant lymphocytic	9 (18%)	1 (2%)	4 (8%)
Lymphoma malignant	1 (2%)	1 (2%)	
Lymphoma malignant mixed	10 (20%)	3 (6%)	11 (22%)
Lymphoma malignant undifferentiated cell type	2 (4%)	3 (6%)	1 (2%)
Thymus	(34)	*(50)	(42)
Lymphoma malignant lymphocytic	3 (9%)	1 (2%)	3 (7%)
Lymphoma malignant mixed	2 (6%)		5 (12%)
Lymphoma malignant undifferentiated cell type		1 (2%)	
Mediastinum, lymphoma malignant lymphocytic	3 (9%)		
INTEGUMENTARY SYSTEM			
Mammary gland	(35)	*(50)	(30)
Adenocarcinoma	4 (11%)	1 (2%)	1 (3%)
Carcinoma			1 (3%)
Lymphoma malignant lymphocytic	2 (6%)	1 (2%)	2 (7%)
Skin	(50)	*(50)	(50)
Fibrosarcoma			1 (2%)
Lymphoma malignant lymphocytic	1 (2%)	1 (2%)	2 (4%)
Squamous cell carcinoma			1 (2%)
Subcutaneous tissue, hemangiosarcoma	1 (2%)		
Subcutaneous tissue, lymphoma malignant lymphocytic	1 (2%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
MUSCULOSKELETAL SYSTEM			
Bone	(50)	*(50)	(50)
Sarcoma, metastatic, brain		1 (2%)	
Skeletal muscle	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic	1 (2%)		1 (2%)
Intercostal, lymphoma malignant mixed			1 (2%)
NERVOUS SYSTEM			
Brain	(50)	*(50)	(50)
Carcinoma, metastatic, pituitary gland	1 (2%)		
Lymphoma malignant mixed	1 (2%)		
Meninges, meningioma, NOS			1 (2%)
Meninges, sarcoma	1 (2%)	1 (2%)	
RESPIRATORY SYSTEM			
Larynx	(49)	*(50)	(50)
Lymphoma malignant lymphocytic	1 (2%)		1 (2%)
Lung	(50)	*(50)	(50)
Adenocarcinoma, metastatic, mammary gland	1 (2%)		
Adenocarcinoma, metastatic, multiple, mammary gland		1 (2%)	
Alveolar/bronchiolar adenoma		1 (2%)	3 (6%)
Alveolar/bronchiolar carcinoma			1 (2%)
Fibrosarcoma, metastatic, multiple, skin			1 (2%)
Hepatocellular carcinoma, metastatic, multiple, liver	1 (2%)	1 (2%)	
Histiocytic sarcoma	2 (4%)		
Histiocytic sarcoma, metastatic, uterus	1 (2%)		
Lymphoma malignant lymphocytic	8 (16%)	1 (2%)	4 (8%)
Lymphoma malignant	1 (2%)		
Lymphoma malignant mixed	8 (16%)		7 (14%)
Lymphoma malignant undifferentiated cell type	1 (2%)	1 (2%)	1 (2%)
Squamous cell carcinoma, metastatic, ear			1 (2%)
Nose	(49)	(49)	(50)
Hemangioma			1 (2%)
Lymphoma malignant lymphocytic	1 (2%)		
Respiratory epithelium, adenoma			1 (2%)
Trachea	(50)	*(50)	(49)
Lymphoma malignant lymphocytic	2 (4%)		2 (4%)
SPECIAL SENSES SYSTEM			
Ear	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic			1 (2%)
Squamous cell carcinoma			1 (2%)
Harderian gland	*(50)	*(50)	*(50)
Adenoma			5 (10%)
Lymphoma malignant lymphocytic			1 (2%)
Lacrimal gland	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic			1 (2%)
URINARY SYSTEM			
Kidney	(50)	*(50)	(49)
Histiocytic sarcoma	1 (2%)		
Histiocytic sarcoma, metastatic, uterus	1 (2%)		
Lymphoma malignant lymphocytic	9 (18%)	1 (2%)	3 (6%)
Lymphoma malignant mixed	6 (12%)		8 (16%)
Lymphoma malignant undifferentiated cell type		2 (4%)	1 (2%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
URINARY SYSTEM (Continued)			
Urinary bladder	(47)	*(50)	(47)
Histiocytic sarcoma	1 (2%)		
Lymphoma malignant lymphocytic	8 (17%)		4 (9%)
Lymphoma malignant mixed	6 (13%)		6 (13%)
Lymphoma malignant undifferentiated cell type		1 (2%)	
SYSTEMIC LESIONS			
Multiple organs	*(50)	*(50)	*(50)
Lymphoma malignant lymphocytic	9 (18%)	1 (2%)	4 (8%)
Lymphoma malignant	2 (4%)	1 (2%)	
Lymphoma malignant mixed	10 (20%)	4 (8%)	11 (22%)
Lymphoma malignant undifferentiated cell	2 (4%)	3 (6%)	1 (2%)
Hemangiosarcoma	2 (4%)		
Hemangioma			1 (2%)
ANIMAL DISPOSITION SUMMARY			
Animals initially in study	50	50	50
Terminal sacrifice	33	41	41
Dead	10	4	6
Moribund	7	5	3
TUMOR SUMMARY			
Total animals with primary neoplasms **	35	21	31
Total primary neoplasms	77	29	48
Total animals with benign neoplasms	14	12	15
Total benign neoplasms	18	13	23
Total animals with malignant neoplasms	30	15	21
Total malignant neoplasms	58	16	23
Total animals with secondary neoplasms ***	5	2	2
Total secondary neoplasms	10	4	4
Total animals with neoplasms-- uncertain benign or malignant	1		2
Total uncertain neoplasms	1		2

* Number of animals receiving complete necropsy examination; all gross lesions including masses examined microscopically.
** Primary tumors: all tumors except secondary tumors
*** Secondary tumors: metastatic tumors or tumors invasive into an adjacent organ

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: CHAMBER CONTROL

WEEKS ON STUDY	0 1 0	0 3 3	0 5 3	0 7 0	0 7 7	0 8 3	0 8 3	0 9 2	0 9 2	0 9 2	0 9 4	0 9 9	0 9 9	1 0 0	1 0 2	1 0 4	1 0 4	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5
CARCASS ID	9 4 1	9 2 1	5 3 1	8 5 1	6 1 1	8 6 1	7 6 1	6 5 1	6 9 1	9 7 1	8 1 1	9 9 1	7 9 1	5 4 1	5 7 1	6 6 1	7 7 1	5 1 1	5 2 1	5 5 1	5 6 1	5 8 1	5 9 1	6 0 1	6 2 1
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	A	+	+	+	A	+	A	+	+	+	A	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	M	+	+	M	+	M	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Intestine small	+	+	+	+	+	+	A	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	+	+	A	+	+	+	A	+	I	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Intestine small, ileum	+	+	+	+	+	+	M	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Intestine small, jejunum	+	A	+	+	+	+	A	+	+	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma									X															X	
Hepatocellular carcinoma, multiple																							X		
Hepatocellular adenoma																									
Histiocytic sarcoma																X				X					
Histiocytic sarcoma, metastatic, uterus								X																	
Lymphoma malignant lymphocytic														X	X										
Lymphoma malignant																							X		
Lymphoma malignant mixed										X	X						X								
Lymphoma malignant undifferentiated cell type									X																
Mesentery				+	+	+																			
Lymphoma malignant lymphocytic																									
Lymphoma malignant																									
Lymphoma malignant mixed																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X				X					
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed										X							X						X		
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Lymphoma malignant lymphocytic														X	X										X
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type									X																
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed																									
Papilloma squamous																									
Stomach, glandular	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed																									
Tooth	+	+																							
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
ENDOCRINE SYSTEM																									
Adrenal gland	M	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma, metastatic, uterus								X																	
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																									
Adrenal gland, cortex	M	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed										X															
Lymphoma malignant undifferentiated cell type									X																
Adrenal gland, medulla	M	+	+	+	+	+	A	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed										X															
Lymphoma malignant undifferentiated cell type									X																
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic															X										
Parathyroid gland	M	M	+	M	+	M	+	+	M	+	+	+	+	M	M	M	+	M	+	+	M	M	+	M	+
Pituitary gland	M	+	M	+	+	+	+	+	M	I	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma														X				X			X	X			X
Pars distalis, carcinoma																									
Pars intermedia, adenoma																		X							
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																									
Follicular cell, adenoma								X													X				

+: Tissue examined microscopically
: Not examined
−: Present but not examined microscopically
I: Insufficient tissue

M: Missing
A: Autolysis precludes examination
X: Incidence of listed morphology

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
CARCASS ID	631	841	671	681	701	711	721	731	741	751	781	801	821	831	841	871	881	891	901	911	931	951	961	981	001	TOTAL: TISSUES / TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	47
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	45
Lymphoma malignant lymphocytic																										1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymphoma malignant lymphocytic																										1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic										X																1
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma									X										X							4
Hepatocellular carcinoma, multiple																										1
Hepatocellular adenoma					X																					1
Histiocytic sarcoma																										2
Histiocytic sarcoma, metastatic, uterus																										1
Lymphoma malignant lymphocytic			X							X									X							5
Lymphoma malignant																										1
Lymphoma malignant mixed				X	X				X																	6
Lymphoma malignant undifferentiated cell type																										1
Mesentery						+		+			+	+					+		+	+	+	+			+	13
Lymphoma malignant lymphocytic												X							X	X						3
Lymphoma malignant																	X									1
Lymphoma malignant mixed																						X			X	2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Histiocytic sarcoma																										2
Lymphoma malignant lymphocytic										X									X							3
Lymphoma malignant mixed					X		X																			5
Salivary glands	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant lymphocytic		X																	X	X						6
Lymphoma malignant mixed							X																			1
Lymphoma malignant undifferentiated cell type																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic												X														2
Lymphoma malignant mixed				X																						1
Papilloma squamous							X																			1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic												X														2
Lymphoma malignant mixed				X																						1
Tooth												+														3
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																			X	X						3
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Histiocytic sarcoma, metastatic, uterus																										1
Lymphoma malignant lymphocytic										X		X								X						3
Lymphoma malignant mixed					X																					1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Lymphoma malignant undifferentiated cell type																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										1
Parathyroid gland	M	+	+	+	M	M	M	+	+	M	+	+	M	M	M	+	M	+	+	M	+	+	+	+	M	27
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	44
Pars distalis, adenoma		X			X		X						X		X		X					X				12
Pars distalis, carcinoma			X																							1
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																			X							1
Lymphoma malignant mixed					X																					1
Follicular cell, adenoma																										2

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	010	033	053	070	077	083	083	092	092	092	094	099	099	100	102	104	104	105	105	105	105	105	105	105	105
CARCASS ID	941	921	531	851	611	861	761	651	691	971	811	991	791	541	571	661	771	511	521	551	561	581	591	601	621
GENERAL BODY SYSTEM																									
Tissue, NOS																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant																									
Lymphoma malignant mixed																									
GENITAL SYSTEM																									
Clitoral gland																									
Hemangiosarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Granulosa cell tumor, NOS																									
Histiocytic sarcoma																X									
Histiocytic sarcoma, metastatic, uterus								X																	
Luteoma												X													
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed										X															
Lymphoma malignant undifferentiated cell type									X																
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma								X								X									
Lymphoma malignant lymphocytic															X										
Lymphoma malignant mixed										X															
Sarcoma stromal																							X		
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																				X					
Lymphoma malignant lymphocytic															X										
Lymph node	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Iliac, lymphoma malignant lymphocytic																									
Iliac, lymphoma malignant mixed																									
Mediastinal, histiocytic sarcoma																				X					
Mediastinal, lymphoma malignant lymphocytic														X											
Mediastinal, lymphoma malignant																									
Mediastinal, lymphoma malignant mixed																	X						X		
Mesenteric, lymphoma malignant mixed																	X						X		
Mesenteric, lymphoma malignant undifferentiated cell type																									
Renal, histiocytic sarcoma																				X					
Renal, lymphoma malignant mixed																							X		
Renal, lymphoma malignant undifferentiated cell type																									
Lymph node, bronchial	M	M	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	M	+	M	+
Adenocarcinoma, metastatic, mammary gland					X																				
Histiocytic sarcoma																X				X					
Lymphoma malignant lymphocytic															X										X
Lymphoma malignant																									
Lymphoma malignant mixed										X							X						X		
Lymphoma malignant undifferentiated cell type																									
Lymph node, mandibular	M	+	+	M	M	+	M	M	M	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Adenocarcinoma, metastatic, mammary gland																									
Histiocytic sarcoma																X				X					
Lymphoma malignant lymphocytic														X	X										X
Lymphoma malignant																									
Lymphoma malignant mixed										X													X		
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X				X					
Lymphoma malignant lymphocytic														X	X										X
Lymphoma malignant																									
Lymphoma malignant mixed										X	X						X								
Lymphoma malignant undifferentiated cell type									X																
Thymus	+	M	+	+	M	M	+	+	M	+	+	M	M	M	+	M	M	+	M	+	+	+	M	M	+
Lymphoma malignant lymphocytic																									X
Lymphoma malignant mixed																									
Mediastinum, lymphoma malignant lymphocytic															X										

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	631	641	671	681	701	711	721	731	741	751	781	801	821	831	841	871	881	891	901	911	931	951	961	981	001	TISSUES TUMORS
GENERAL BODY SYSTEM																										
Tissue, NOS				+								+					+			+		+			5
Lymphoma malignant lymphocytic												X								X					2
Lymphoma malignant																	X								1
Lymphoma malignant mixed																						X			1
GENITAL SYSTEM																										
Clitoral gland								+																		1
Hemangiosarcoma								X																		1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Granulosa cell tumor, NOS													X													1
Histiocytic sarcoma																										1
Histiocytic sarcoma, metastatic, uterus																										1
Luteoma																										1
Lymphoma malignant lymphocytic		X	X							X		X							X	X						7
Lymphoma malignant mixed				X	X		X																			4
Lymphoma malignant undifferentiated cell type																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										2
Lymphoma malignant lymphocytic												X							X							3
Lymphoma malignant mixed					X																					2
Sarcoma stromal																										1
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Lymphoma malignant lymphocytic		X																								2
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Iliac, lymphoma malignant lymphocytic												X														1
Iliac, lymphoma malignant mixed							X																			1
Mediastinal, histiocytic sarcoma																										1
Mediastinal, lymphoma malignant lymphocytic										X		X							X							4
Mediastinal, lymphoma malignant																	X									1
Mediastinal, lymphoma malig. mixed							X																			3
Mesenteric, lymphoma malignant mixed							X																			3
Mesenteric, lymphoma malignant undifferentiated cell type																								X		1
Renal, histiocytic sarcoma																										1
Renal, lymphoma malignant mixed							X																			2
Renal, lymphoma malignant undifferentiated cell type																								X		1
Lymph node, bronchial	M	+	M	+	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	38
Adenocarcinoma, metastatic, mammary gland																										1
Histiocytic sarcoma																										2
Lymphoma malignant lymphocytic		X								X		X							X	X						7
Lymphoma malignant																	X									1
Lymphoma malignant mixed				X			X															X				6
Lymphoma malignant undifferentiated cell type																								X		1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	42
Adenocarcinoma, metastatic, mammary gland																		X								1
Histiocytic sarcoma																										2
Lymphoma malignant lymphocytic		X								X		X							X							7
Lymphoma malignant																	X									1
Lymphoma malignant mixed				X	X		X		X													X				7
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										2
Lymphoma malignant lymphocytic		X	X							X		X							X	X						9
Lymphoma malignant																	X									1
Lymphoma malignant mixed				X	X		X		X													X			X	10
Lymphoma malignant undifferentiated cell type																								X		2
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	M	+	+	+	+	M	+	+	+	34
Lymphoma malignant lymphocytic												X							X							3
Lymphoma malignant mixed					X		X																			2
Mediastinum, lymphoma malignant lymphocytic		X								X																3

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	010	033	053	070	077	083	083	092	092	092	094	099	099	100	102	104	104	105	105	105	105	105	105	105	105
CARCASS ID	941	921	531	851	611	861	761	651	691	971	811	991	791	541	571	661	771	511	521	551	561	581	591	601	621
INTEGUMENTARY SYSTEM																									
Mammary gland	+	M	+	+	+	M	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	M	+	+
Adenocarcinoma					X										X	X									
Lymphoma malignant lymphocytic															X										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Subcutaneous tissue, hemangiosarcoma												X													
Subcutaneous tissue, lymphoma malignant lymphocytic															X										
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																									
Lymphoma malignant lymphocytic																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland																									
Lymphoma malignant mixed																									
Meninges, sarcoma														X											
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, metastatic, mammary gland					X																				
Hepatocellular carcinoma, metastatic, multiple, liver																									
Histiocytic sarcoma																X				X					
Histiocytic sarcoma, metastatic, uterus								X																	
Lymphoma malignant lymphocytic														X	X										X
Lymphoma malignant																									
Lymphoma malignant mixed										X							X						X		
Lymphoma malignant undifferentiated cell type																									
Nose	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
SPECIAL SENSES SYSTEM																									
Ear																M									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Histiocytic sarcoma, metastatic, uterus								X																	
Lymphoma malignant lymphocytic														X	X										X
Lymphoma malignant mixed										X							X								
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+
Histiocytic sarcoma																X									
Lymphoma malignant lymphocytic														X	X										X
Lymphoma malignant mixed										X													X		

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: CHAMBER CONTROL (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	631	641	671	681	701	711	721	731	741	751	781	801	821	831	841	871	881	891	901	911	931	951	961	981	001	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Mammary gland	+	+	+	+	M	+	+	+	+	M	+	M	+	M	+	M	+	+	+	M	+	M	M	M	M	35
Adenocarcinoma																		X								4
Lymphoma malignant lymphocytic																			X							2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																			X							1
Subcutaneous tissue, hemangiosarcoma																										1
Subcutaneous tissue, lymphoma malignant lymphocytic																										1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle												+														1
Lymphoma malignant lymphocytic												X														1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pituitary gland			X																							1
Lymphoma malignant mixed					X																					1
Meninges, sarcoma																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic		X																								1
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, metastatic, mammary gland																										1
Hepatocellular carcinoma, metastatic, multiple, liver																			X							1
Histiocytic sarcoma																										2
Histiocytic sarcoma, metastatic, uterus																										1
Lymphoma malignant lymphocytic		X	X							X		X								X						8
Lymphoma malignant																	X									1
Lymphoma malignant mixed				X	X		X		X																X	8
Lymphoma malignant undifferentiated cell type																								X		1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic			X																							1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																			X	X						2
SPECIAL SENSES SYSTEM																										
Ear							+																			1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Histiocytic sarcoma																										1
Histiocytic sarcoma, metastatic, uterus																										1
Lymphoma malignant lymphocytic		X	X							X		X							X	X						9
Lymphoma malignant mixed				X	X		X		X																	6
Urinary bladder	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	47
Histiocytic sarcoma																										1
Lymphoma malignant lymphocytic		X	X									X							X	X						8
Lymphoma malignant mixed				X	X		X															X				6

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 5 ppm

WEEKS ON STUDY	048	053	079	087	092	095	095	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	15881	19881	18861	15441	17111	18881	15331	19711	16551	15111	15212	15551	15561	15711	15991	16011	16111	16211	16331	16441	16661	16711	16881	16991	17001
ALIMENTARY SYSTEM																											
Esophagus	+	+	+	+	+	+	+	+	+																		
Gallbladder	+	A	+	+	A	+	A	+	+																		
Intestine large	+	+	+	+	+	+	+	+	+																		
Intestine large, cecum	M	M	M	M	+	+	+	+	+																		
Intestine large, colon	+	+	+	+	+	+	+	+	+																		
Intestine large, rectum	+	+	+	M	+	+	+	+	+																		
Intestine small	+	A	+	+	+	+	A	+	+					+													
Intestine small, duodenum	+	A	+	+	+	+	A	+	+																		
Intestine small, ileum	+	A	+	M	+	+	A	+	+					+													
Lymphoma malignant mixed														X													
Intestine small, jejunum	+	A	+	+	+	+	A	+	+																		
Liver	+	+	+	+	+	+	+	+	+					+				+	+					+			
Hepatocellular carcinoma			X																X					X			
Hepatocellular adenoma									X					X													
Lymphoma malignant lymphocytic				X																							
Lymphoma malignant mixed																											
Lymphoma malignant undifferentiated cell type								X																			
Mesentery				+				+																			
Lymphoma malignant lymphocytic				X																							
Lymphoma malignant undifferentiated cell type								X																			
Pancreas	+	+	+	M	+	+	+	+	+																		
Salivary glands	+	+	+	+	+	+	+	+	+																		
Lymphoma malignant lymphocytic				X																							
Stomach	+	+	+	+	+	+	+	+	+									+									
Stomach, forestomach	+	+	+	+	+	+	+	+	+									+									
Lymphoma malignant lymphocytic				X																							
Papilloma squamous																											
Stomach, glandular	+	A	+	+	+	+	+	+	+									+									
Lymphoma malignant lymphocytic				X																							
CARDIOVASCULAR SYSTEM																											
Blood vessel	+	+	+	+	+	+	+	+	+																		
Heart	+	+	+	+	+	+	+	+	+																		
ENDOCRINE SYSTEM																											
Adrenal gland	+	+	+	+	+	+	M	+	+						+												
Lymphoma malignant lymphocytic				X																							
Adrenal gland, cortex	+	A	+	+	+	+	M	+	+						+												
Lymphoma malignant undifferentiated cell type								X																			
Adrenal gland, medulla	+	A	+	I	+	+	M	+	+						+												
Lymphoma malignant undifferentiated cell type								X																			
Pheochromocytoma malignant															X												
Islets, pancreatic	+	+	+	M	+	+	+	+	+																		
Parathyroid gland	M	M	M	M	+	M	M	+	+																		
Pituitary gland	+	+	+	+	+	+	+	+	+			+	+	+				+									
Pars distalis, adenoma						X	X						X	X				X									
Thyroid gland	+	+	+	+	+	+	+	+	+					+													
Bilateral, follicular cell, carcinoma														X													
GENERAL BODY SYSTEM																											
None																											
GENITAL SYSTEM																											
Ovary	+	+	+	M	+	+	+	+	+					+					+	+							+
Lymphoma malignant undifferentiated cell type								X																			
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+		+		+		+				
Lymphoma malignant lymphocytic				X																							
Polyp stromal																											

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 5 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	1721	1731	1741	1751	1761	1771	1781	1791	1801	1811	1821	1831	1841	1851	1871	1891	1901	1911	1921	1931	1941	1951	1961	1991	2001		TISSUES TUMORS
ALIMENTARY SYSTEM																											
Esophagus																											9
Gallbladder																											6
Intestine large																											9
Intestine large, cecum																											5
Intestine large, colon																											9
Intestine large, rectum																											8
Intestine small																											8
Intestine small, duodenum																											7
Intestine small, ileum																											7
Lymphoma malignant mixed																											1
Intestine small, jejunum																											7
Liver				+									+														15
Hepatocellular carcinoma																											3
Hepatocellular adenoma																											2
Lymphoma malignant lymphocytic																											1
Lymphoma malignant mixed				X																							1
Lymphoma malignant undifferentiated cell type																											1
Mesentery							+								+												4
Lymphoma malignant lymphocytic																											1
Lymphoma malignant undifferentiated cell type																											1
Pancreas							+								+												10
Salivary glands																											9
Lymphoma malignant lymphocytic																											1
Stomach														+								+					12
Stomach, forestomach														+								+					12
Lymphoma malignant lymphocytic																											1
Papilloma squamous														X													1
Stomach, glandular																						+					10
Lymphoma malignant lymphocytic																											1
CARDIOVASCULAR SYSTEM																											
Blood vessel																											9
Heart																											9
ENDOCRINE SYSTEM																											
Adrenal gland																											9
Lymphoma malignant lymphocytic																											1
Adrenal gland, cortex																											8
Lymphoma malignant undifferentiated cell type																											1
Adrenal gland, medulla																											7
Lymphoma malignant undifferentiated cell type																											1
Pheochromocytoma malignant																											1
Islets, pancreatic																											8
Parathyroid gland																											3
Pituitary gland				+	+								+								+						17
Pars distalis, adenoma				X									X								X						8
Thyroid gland																											10
Bilateral, follicular cell, carcinoma																											1
GENERAL BODY SYSTEM																											
None																											
GENITAL SYSTEM																											
Ovary				+					+		+				+		+				+			+			19
Lymphoma malignant undifferentiated cell type																											1
Uterus	+							+						+	+								+				24
Lymphoma malignant lymphocytic																											1
Polyp stromal															X												1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 5 ppm (Continued)

WEEKS ON STUDY	048	053	079	087	092	095	095	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	15881	19881	18861	15541	17111	18881	15331	19711	16511	15111	15221	15551	15681	15771	15991	16011	16111	16211	16331	16441	16661	16671	16881	16991	17001
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+	+	+	+																
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+					+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+																
Iliac, lymphoma malignant undifferentiated cell type																									
Inguinal, lymphoma malignant undifferentiated cell type								X																	
Mesenteric, lymphoma malignant lymphocytic				X																					
Mesenteric, lymphoma malignant undifferentiated cell type																									
Renal, lymphoma malignant lymphocytic				X																					
Renal, lymphoma malignant undifferentiated cell type																									
Lymph node, bronchial	+	+	+	+	+	+	M	M	M																
Lymphoma malignant lymphocytic				X																					
Lymphoma malignant undifferentiated cell type																									
Lymph node, mandibular	M	M	+	+	M	M	+	+	+																
Adenocarcinoma, metastatic, mammary gland									X																
Lymphoma malignant lymphocytic				X																					
Lymphoma malignant undifferentiated cell type																									
Spleen	+	+	+	+	+	+	+	+	+		+								+					+	
Lymphoma malignant lymphocytic				X																					
Lymphoma malignant																									
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type								X																	
Thymus	+	+	+	+	+	M	+	+	+																
Lymphoma malignant lymphocytic				X																					
Lymphoma malignant undifferentiated cell type								X																	
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	+	+	+	+	M	+	+																
Adenocarcinoma									X																
Lymphoma malignant lymphocytic				X																					
Skin	+	+	+	+	+	+	+	+	+				+				+	+		+					
Lymphoma malignant lymphocytic				X																					
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+																
Sarcoma, metastatic, brain			X																						
Skeletal muscle							+																		
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+																
Meninges, sarcoma			X																						
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+																
Lung	+	+	+	+	+	+	+	+	+																
Adenocarcinoma, metastatic, multiple, mammary gland									X																
Alveolar/bronchiolar adenoma				X																					
Hepatocellular carcinoma, metastatic, multiple, liver			X																						
Lymphoma malignant lymphocytic				X																					
Lymphoma malignant undifferentiated cell type								X																	
Nose	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+																
SPECIAL SENSES SYSTEM																									
None																									
URINARY SYSTEM																									
Kidney	+	A	+	+	+	+	+	+	+																
Lymphoma malignant lymphocytic				X																					
Lymphoma malignant undifferentiated cell type								X																	
Urinary bladder	+	+	+	+	+	+	+	+	+																
Lymphoma malignant undifferentiated cell type								X																	

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 5 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	17211	17311	17411	17511	17611	17711	17811	17911	18011	18111	18211	18311	18411	18511	18711	18911	19011	19111	19211	19311	19411	19511	19611	19911	20011		TISSUES TUMORS
HEMATOPOIETIC SYSTEM																											
Blood																											9
Bone marrow	+	+	+			+	+	+	+	+	+					.+	+	+	+				+	+			35
Lymph node																					+				+		11
Iliac, lymphoma malignant undifferentiated cell type																									X		1
Inguinal, lymphoma malignant undifferentiated cell type																											1
Mesenteric, lymphoma malignant lymphocytic																											1
Mesenteric, lymphoma malignant undifferentiated cell type																					X						1
Renal, lymphoma malig. lymphocytic																											1
Renal, lymphoma malignant undifferentiated cell type																									X		1
Lymph node, bronchial																									+		7
Lymphoma malignant lymphocytic																											1
Lymphoma malignant undifferentiated cell type																									X		1
Lymph node, mandibular																									+		6
Adenocarcinoma, metastatic, mammary gland																											1
Lymphoma malignant lymphocytic																											1
Lymphoma malignant undifferentiated cell type																									X		1
Spleen	+			+		+			+												+				+		18
Lymphoma malignant lymphocytic																											1
Lymphoma malignant	X																										1
Lymphoma malignant mixed				X		X			X																		3
Lymphoma malignant undifferentiated cell type																					X				X		3
Thymus																											8
Lymphoma malignant lymphocytic																											1
Lymphoma malignant undifferentiated cell type																											1
INTEGUMENTARY SYSTEM																											
Mammary gland																											8
Adenocarcinoma																											1
Lymphoma malignant lymphocytic																											1
Skin				+						+		+						+							+		18
Lymphoma malignant lymphocytic																											1
MUSCULOSKELETAL SYSTEM																											
Bone																											9
Sarcoma, metastatic, brain																											1
Skeletal muscle																											1
NERVOUS SYSTEM																											
Brain																											9
Meninges, sarcoma																											1
RESPIRATORY SYSTEM																											
Larynx																											9
Lung																											9
Adenocarcinoma, metastatic, multiple, mammary gland																											1
Alveolar/bronchiolar adenoma																											1
Hepatocellular carcinoma, metastatic, multiple, liver																											1
Lymphoma malignant lymphocytic																											1
Lymphoma malignant undifferentiated cell type																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		49
Trachea																											9
SPECIAL SENSES SYSTEM																											
None																											
URINARY SYSTEM																											
Kidney										+															+		10
Lymphoma malignant lymphocytic																											1
Lymphoma malignant undifferentiated cell type																									X		2
Urinary bladder																											9
Lymphoma malignant undifferentiated cell type																											1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER: 10 ppm

WEEKS ON STUDY	001	047	085	086	089	099	100	104	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	28311	26411	28611	27811	26711	27311	26311	29011	29511	25111	25211	25311	25411	25511	25611	25711	25811	25911	26011	26111	26211	26511	26611	26811	26911
ALIMENTARY SYSTEM																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Gallbladder	A	+	+	A	+	A	+	A	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	M
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																									
Intestine large	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	M	+	M	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Intestine large, rectum	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	A	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	M	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed															X										
Intestine small, jejunum	M	+	+	A	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic, skin				X																					
Hepatocellular adenoma									X																
Hepatocellular adenoma, multiple																									
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type											X														
Mesentery									+									+		+					
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed													X		X										
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Lymphoma malignant mixed													X		X										
Lymphoma malignant undifferentiated cell type											X														
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																									
Stomach, glandular	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Tooth																									
CARDIOVASCULAR SYSTEM																									
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma, metastatic, skin				X																					
Lymphoma malignant lymphocytic									X											X					
ENDOCRINE SYSTEM																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed						X																			
Capsule, lymphoma malignant lymphocytic									X																
Subcapsular, adenoma																									
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed															X										
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic																									
Lymphoma malignant mixed															X										
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Parathyroid gland	+	M	+	+	M	+	M	+	M	+	+	+	+	+	+	+	+	M	+	+	M	M	M	+	M
Pituitary gland	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma																									
Pars intermedia, adenoma					X		X																		
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Follicular cell, adenoma																									
GENERAL BODY SYSTEM																									
Tissue, NOS					+																				
GENITAL SYSTEM																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenocarcinoma																									X
Granulosa cell tumor, NOS										X															
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed						X									X										
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Lymphoma malignant mixed						X																			
Polyp stromal																									
Cervix, leiomyoma																					X				

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 10 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	27011	27111	27211	27411	27511	27611	27711	27911	28011	28111	28211	28411	28511	28711	28811	28911	29111	29211	29311	29411	29611	29711	29811	29911	30011	TISSUES TUMORS
ALIMENTARY SYSTEM																										
Esophagus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
Lymphoma malignant lymphocytic																										1
Gallbladder	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	42
Lymphoma malignant lymphocytic					X																					1
Lymphoma malignant mixed						X																				1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant mixed												X														1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant mixed						X						X														3
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic, skin																										1
Hepatocellular adenoma																										1
Hepatocellular adenoma, multiple				X																						1
Lymphoma malignant lymphocytic					X																					1
Lymphoma malignant mixed						X																				1
Lymphoma malignant undifferentiated cell type																										1
Mesentery					+	+			+		+														+	8
Lymphoma malignant lymphocytic					X																				X	4
Lymphoma malignant mixed						X																				1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic					X																					3
Lymphoma malignant mixed						X																				3
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic					X																					2
Lymphoma malignant mixed							X									X										4
Lymphoma malignant undifferentiated cell type																										1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Papilloma squamous								X																		1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant lymphocytic																										1
Tooth					+																					1
CARDIOVASCULAR SYSTEM																										
Blood vessel	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma, metastatic, skin																										1
Lymphoma malignant lymphocytic					X																					3
ENDOCRINE SYSTEM																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	I	+	+	+	+	+	+	48
Lymphoma malignant mixed																										1
Capsule, lymphoma malignant lymphocytic																										1
Subcapsular, adenoma				X																						1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	I	+	+	+	+	+	+	48
Lymphoma malignant lymphocytic					X																					1
Lymphoma malignant mixed																										1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	I	+	+	I	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic					X																					1
Lymphoma malignant mixed																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+	+	+	+	+	48
Lymphoma malignant lymphocytic																										1
Parathyroid gland	M	M	M	+	+	M	M	+	M	+	+	+	+	+	M	+	M	M	+	M	M	+	+	M	+	29
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	I	+	I	+	+	M	+	+	I	+	+	+	+	+	45
Pars distalis, adenoma								X					X													2
Pars intermedia, adenoma																										2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Follicular cell, adenoma		X	X	X																						3
GENERAL BODY SYSTEM																										
Tissue, NOS																										1
GENITAL SYSTEM																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenocarcinoma																										1
Granulosa cell tumor, NOS																										1
Lymphoma malignant lymphocytic					X																					3
Lymphoma malignant mixed															X											3
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Lymphoma malignant mixed																										1
Polyp stromal													X													1
Cervix, leiomyoma																										1

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 10 ppm (Continued)

WEEKS ON STUDY	001	047	085	086	089	099	100	104	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
CARCASS ID	28311	26411	28611	27811	26711	27311	26311	29011	29511	25111	25211	25311	25411	25511	25611	25711	25811	25911	26011	26111	26211	26511	26611	26811	26911
HEMATOPOIETIC SYSTEM																									
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, lymphoma malignant mixed													X												
Mesenteric, lymphoma malignant lymphocytic																				X					
Mesenteric, lymphoma malignant mixed						X																			
Renal, lymphoma malignant lymphocytic																				X					
Renal, lymphoma malignant mixed						X																			
Lymph node, bronchial	M	+	M	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed						X							X								X				
Lymphoma malignant undifferentiated cell type											X														
Lymph node, mandibular	A	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	M	+	M	+	+
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed															X										
Lymphoma malignant undifferentiated cell type											X														
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed						X							X		X						X				
Lymphoma malignant undifferentiated cell type											X														
Thymus	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed						X																			
INTEGUMENTARY SYSTEM																									
Mammary gland	+	+	M	+	+	M	+	+	+	M	M	+	+	M	+	+	+	+	M	+	M	+	+	+	M
Adenocarcinoma															X										
Carcinoma																									
Lymphoma malignant lymphocytic									X																
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma				X																					
Lymphoma malignant lymphocytic									X											X					
Squamous cell carcinoma																									
MUSCULOSKELETAL SYSTEM																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle						+			+																
Lymphoma malignant lymphocytic									X																
Intercostal, lymphoma malignant mixed						X																			
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Meninges, meningioma, NOS																X									
RESPIRATORY SYSTEM																									
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma														X											
Alveolar/bronchiolar carcinoma																									
Fibrosarcoma, metastatic, multiple, skin				X																					
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed						X							X												
Lymphoma malignant undifferentiated cell type											X														
Squamous cell carcinoma, metastatic, ear																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma									X																
Respiratory epithelium, adenoma																									
Trachea	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X											X					
SPECIAL SENSES SYSTEM																									
Ear									+																
Lymphoma malignant lymphocytic									X																
Squamous cell carcinoma																									
Harderian gland									+			+								+					
Adenoma									X			X								X					
Lymphoma malignant lymphocytic									X																
Lacrimal gland									+																
Lymphoma malignant lymphocytic									X																
URINARY SYSTEM																									
Kidney	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X																
Lymphoma malignant mixed						X							X												
Lymphoma malignant undifferentiated cell type											X														
Urinary bladder	A	+	+	A	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic									X											X					
Lymphoma malignant mixed						X									X										

TABLE D2. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: 10 ppm (Continued)

WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TOTAL:
CARCASS ID	27011	27111	27211	27411	27511	27611	27711	27911	28011	28111	28211	28411	28511	28711	28811	28911	29111	29211	29311	29411	29611	29711	29811	29911	30011	TISSUES TUMORS
HEMATOPOIETIC SYSTEM																										
Blood	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	I	+	+	48
Lymph node	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Mediastinal, lymphoma malig. mixed						X	X									X										4
Mesenteric, lymphoma malignant lymphocytic					X																					2
Mesenteric, lymphoma malignant mixed				X								X														3
Renal, lymphoma malig. lymphocytic																										1
Renal, lymphoma malignant mixed																										1
Lymph node, bronchial	+	+	+	+	+	+	M	M	+	+	+	M	+	+	M	M	+	M	+	+	M	+	M	+	M	37
Lymphoma malignant lymphocytic					X																					3
Lymphoma malignant mixed						X																				4
Lymphoma malignant undifferentiated cell type																										1
Lymph node, mandibular	M	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	40
Lymphoma malignant lymphocytic					X																					3
Lymphoma malignant mixed				X		X										X										4
Lymphoma malignant undifferentiated cell type																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic					X																				X	4
Lymphoma malignant mixed				X		X	X	X				X			X	X										11
Lymphoma malignant undifferentiated cell type																										1
Thymus	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	M	+	+	M	+	M	+	+	42
Lymphoma malignant lymphocytic					X																					3
Lymphoma malignant mixed				X		X	X									X										5
INTEGUMENTARY SYSTEM																										
Mammary gland	+	M	M	M	+	M	M	+	+	M	M	+	+	+	+	+	+	M	M	+	M	M	+	+	M	30
Adenocarcinoma																										1
Carcinoma																								X		1
Lymphoma malignant lymphocytic					X																					2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrosarcoma																										1
Lymphoma malignant lymphocytic																										2
Squamous cell carcinoma										X																1
MUSCULOSKELETAL SYSTEM																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										2
Lymphoma malignant lymphocytic																										1
Intercostal, lymphoma malignant mixed																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Meninges, meningioma, NOS																										1
RESPIRATORY SYSTEM																										
Larynx	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										1
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X																					X			3
Alveolar/bronchiolar carcinoma												X														1
Fibrosarcoma, metastatic, multiple, skin																										1
Lymphoma malignant lymphocytic					X																				X	4
Lymphoma malignant mixed						X	X	X				X				X										7
Lymphoma malignant undifferentiated cell type																										1
Squamous cell carcinoma, metastatic, ear														X												1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma																										1
Respiratory epithelium, adenoma							X																			1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic																										2
SPECIAL SENSES SYSTEM																										
Ear														+												2
Lymphoma malignant lymphocytic																										1
Squamous cell carcinoma														X												1
Harderian gland		+												+												5
Adenoma		X												X												5
Lymphoma malignant lymphocytic																										1
Lacrimal gland																										1
Lymphoma malignant lymphocytic																										1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymphoma malignant lymphocytic					X																				X	3
Lymphoma malignant mixed				X		X	X	X							X	X										8
Lymphoma malignant undifferentiated cell type																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymphoma malignant lymphocytic					X																				X	4
Lymphoma malignant mixed				X		X	X									X										6

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Harderian Gland: Adenoma			
Overall Rates (a)	0/50 (0%)	0/50 (0%)	5/50 (10%)
Adjusted Rates (b)	0.0%	0.0%	11.9%
Terminal Rates (c)	0/33 (0%)	0/42 (0%)	4/41 (10%)
Day of First Observation			727
Life Table Tests (d)	P=0.009	(e)	P=0.058
Logistic Regression Tests (d)	P=0.009	(e)	P=0.052
Cochran-Armitage Trend Test (d)	P=0.006		
Fisher Exact Test (d)		(e)	P=0.028
Liver: Hepatocellular Carcinoma			
Overall Rates (f)	5/50 (10%)	(g) 3/15 (20%)	0/50 (0%)
Adjusted Rates (b)	14.2%		0.0%
Terminal Rates (c)	4/33 (12%)		0/41 (0%)
Day of First Observation	642		
Life Table Test (d)			P=0.021N
Logistic Regression Test (d)			P=0.028N
Fisher Exact Test (d)			P=0.028N
Liver: Hepatocellular Adenoma or Carcinoma			
Overall Rates (f)	6/50 (12%)	(g) 5/15 (33%)	2/50 (4%)
Adjusted Rates (b)	17.2%		4.7%
Terminal Rates (c)	5/33 (15%)		1/41 (2%)
Day of First Observation	642		727
Life Table Test (d)			P=0.082N
Logistic Regression Test (d)			P=0.107N
Fisher Exact Test (d)			P=0.134N
Lung: Alveolar/Bronchiolar Adenoma			
Overall Rates (f)	0/50 (0%)	(g) 1/9 (11%)	3/50 (6%)
Adjusted Rates (b)	0.0%		7.3%
Terminal Rates (c)	0/33 (0%)		3/41 (7%)
Day of First Observation			730
Life Table Test (d)			P=0.162
Logistic Regression Test (d)			P=0.162
Fisher Exact Test (d)			P=0.121
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (f)	0/50 (0%)	(g) 1/9 (11%)	4/50 (8%)
Adjusted Rates (b)	0.0%		9.8%
Terminal Rates (c)	0/33 (0%)		4/41 (10%)
Day of First Observation			730
Life Table Test (d)			P=0.094
Logistic Regression Test (d)			P=0.094
Fisher Exact Test (d)			P=0.059
Mammary Gland: Adenocarcinoma			
Overall Rates (a)	4/50 (8%)	1/50 (2%)	1/50 (2%)
Adjusted Rates (b)	10.4%	2.4%	2.4%
Terminal Rates (c)	1/33 (3%)	1/42 (2%)	1/41 (2%)
Day of First Observation	534	730	730
Life Table Tests (d)	P=0.073N	P=0.136N	P=0.137N
Logistic Regression Tests (d)	P=0.100N	P=0.180N	P=0.179N
Cochran-Armitage Trend Test (d)	P=0.101N		
Fisher Exact Test (d)		P=0.181N	P=0.181N

TABLE D3. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
Mammary Gland: Carcinoma or Adenocarcinoma			
Overall Rates (a)	4/50 (8%)	1/50 (2%)	2/50 (4%)
Adjusted Rates (b)	10.4%	2.4%	4.9%
Terminal Rates (c)	1/33 (3%)	1/42 (2%)	2/41 (5%)
Day of First Observation	534	730	730
Life Table Tests (d)	P=0.181N	P=0.136N	P=0.263N
Logistic Regression Tests (d)	P=0.234N	P=0.180N	P=0.332N
Cochran-Armitage Trend Test (d)	P=0.238N		
Fisher Exact Test (d)		P=0.181N	P=0.339N
Pituitary Gland/Pars Distalis: Adenoma			
Overall Rates (f)	12/44 (27%)	(g) 8/17 (47%)	2/45 (4%)
Adjusted Rates (b)	36.1%		5.4%
Terminal Rates (c)	11/32 (34%)		2/37 (5%)
Day of First Observation	696		730
Life Table Test (d)			P=0.002N
Logistic Regression Test (d)			P=0.002N
Fisher Exact Test (d)			P=0.003N
Pituitary Gland/Pars Distalis: Adenoma or Carcinoma			
Overall Rates (f)	13/44 (30%)	(g) 8/17 (47%)	2/45 (4%)
Adjusted Rates (b)	39.2%		5.4%
Terminal Rates (c)	12/32 (38%)		2/37 (5%)
Day of First Observation	696		730
Life Table Test (d)			P<0.001N
Logistic Regression Test (d)			P<0.001N
Fisher Exact Test (d)			P=0.001N
Thyroid Gland: Follicular Cell Adenoma			
Overall Rates (f)	2/50 (4%)	(g,h) 0/10 (0%)	3/50 (6%)
Adjusted Rates (b)	5.3%		7.3%
Terminal Rates (c)	1/33 (3%)		3/41 (7%)
Day of First Observation	638		730
Life Table Test (d)			P=0.582
Logistic Regression Test (d)			P=0.525
Fisher Exact Test (d)			P=0.500
Hematopoietic System: Lymphoma, All Malignant			
Overall Rates (a)	22/50 (44%)	(i) 9/50 (18%)	16/50 (32%)
Adjusted Rates (b)	56.0%	20.3%	37.1%
Terminal Rates (c)	16/33 (48%)	7/42 (17%)	14/41 (34%)
Day of First Observation	642	604	688
Life Table Tests (d)	P=0.036N	P<0.001N	P=0.041N
Logistic Regression Tests (d)	P=0.068N	P=0.002N	P=0.074N
Cochran-Armitage Trend Test (d)	P=0.118N		
Fisher Exact Test (d)		P=0.004N	P=0.151N

(a) Number of tumor-bearing animals/number of animals examined grossly at the site
(b) Kaplan-Meier estimated tumor incidences at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence in animals killed at the end of the study
(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 logistic regression test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group than in controls is indicated by (N).
(e) No P value is reported because no tumors were observed in the 5-ppm and control groups.
(f) Number of tumor-bearing animals/number of animals examined microscopically at the site
(g) Incomplete sampling of tissues
(h) A follicular cell carcinoma was observed in one animal receiving 5 ppm.
(i) Eleven lymph nodes and 18 spleens were examined microscopically.

TABLE D4a. HISTORICAL INCIDENCE OF NASAL CAVITY TUMORS IN FEMALE B6C3F$_1$ MICE (a)

	Number Examined	Number of Tumors	Diagnosis
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
	398	0	--
Overall Historical Incidence for Untreated Controls in NTP Studies			
	1,689	1	Papilloma, NOS

(a) Data as of May 12, 1988, for studies of at least 104 weeks

TABLE D4b. HISTORICAL INCIDENCE OF HARDERIAN GLAND TUMORS IN FEMALE B6C3F$_1$ MICE (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	0/50	0/50	0/50
Methyl methacrylate	0/50	0/50	0/50
Propylene	0/50	0/50	0/50
1,2-Epoxybutane	(b) 2/50	0/50	2/50
Dichloromethane	0/50	(c) 1/50	1/50
Ethylene oxide	(d) 1/49	0/49	1/49
Bromoethane	2/50	0/50	2/50
Tetrachloroethylene	1/49	0/49	1/49
TOTAL	6/398 (1.5%)	1/398 (0.3%)	7/398 (1.8%)
SD (e)	1.78%	0.71%	1.67%
Range (f)			
High	2/50	1/50	2/50
Low	0/50	0/50	0/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	(g) 43/1,689 (2.5%)	(h) 8/1,689 (0.5%)	(g,h) 51/1,689 (3.0%)
SD (e)	2.89%	0.99%	2.93%
Range (f)			
High	6/50	2/50	6/50
Low	0/50	0/50	0/50

(a) Data as of May 12, 1988, for studies of at least 104 weeks
(b) Includes one papillary adenoma
(c) Adenocarcinoma, NOS
(d) Papillary cystadenoma, NOS
(e) Standard deviation
(f) Range and SD are presented for groups of 35 or more animals.
(g) Includes three papillary adenomas and two papillary cystadenomas, NOS
(h) Includes two adenocarcinomas, NOS, two papillary adenocarcinomas, and one papillary cystadenocarcinoma, NOS

TABLE D4c. HISTORICAL INCIDENCE OF HEPATOCELLULAR TUMORS IN FEMALE B6C3F$_1$ MICE (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	1/50	2/50	3/50
Methyl methacrylate	7/50	0/50	7/50
Propylene	0/50	2/50	2/50
1,2-Epoxybutane	2/50	2/50	4/50
Dichloromethane	2/50	1/50	3/50
Ethylene oxide	1/49	5/49	6/49
Bromoethane	3/50	2/50	5/50
Tetrachloroethylene	3/48	1/48	4/48
TOTAL	19/397 (4.8%)	15/397 (3.8%)	34/397 (8.6%)
SD (b)	4.28%	2.97%	3.37%
Range (c)			
High	7/50	5/49	7/50
Low	0/50	0/50	2/50
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	100/1,683 (5.9%)	68/1,683 (4.0%)	163/1,683 (9.7%)
SD (b)	3.75%	2.30%	4.25%
Range (c)			
High	8/49	4/48	10/49
Low	0/50	0/49	2/50

(a) Data as of May 12, 1988, for studies of at least 104 weeks
(b) Standard deviation
(c) Range and SD are presented for groups of 35 or more animals.

TABLE D4d. HISTORICAL INCIDENCE OF ANTERIOR PITUITARY GLAND TUMORS IN FEMALE $B6C3F_1$ MICE (a)

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence for Chamber Controls at Battelle Pacific Northwest Laboratories			
Propylene oxide	8/46	1/46	9/46
Methyl methacrylate	12/49	0/49	12/49
Propylene	(b) 13/41	0/41	(b) 13/41
1,2-Epoxybutane	19/47	3/47	22/47
Dichloromethane	4/46	0/46	4/46
Ethylene oxide	4/48	1/48	5/48
Bromoethane	2/48	0/48	2/48
Tetrachloroethylene	2/45	5/45	7/45
TOTAL	64/370 (17.3%)	10/370 (2.7%)	74/370 (20.0%)
SD (c)	13.55%	4.04%	13.97%
Range (d)			
High	19/47	5/45	22/47
Low	2/48	0/49	2/48
Overall Historical Incidence for Untreated Controls in NTP Studies			
TOTAL	(e) 244/1,528 (16.0%)	(f) 12/1,528 (0.8%)	(e,f) 256/1,528 (16.8%)
SD (c)	10.80%	1.42%	11.09%
Range (d)			
High	18/49	3/50	19/49
Low	0/48	0/50	0/48

(a) Data as of May 12, 1988, for studies of at least 104 weeks
(b) Includes 11 chromophobe adenomas
(c) Standard deviation
(d) Range and SD are presented for groups of 35 or more animals.
(e) Includes four chromophobe adenomas
(f) Includes three adenocarcinomas, NOS

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER

	Chamber Control	5 ppm	10 ppm
Animals initially in study	50	50	50
Animals removed	50	50	50
Animals examined histopathologically	50	50	50
ALIMENTARY SYSTEM			
Gallbladder	(45)	(6)	(42)
Fibrosis	1 (2%)		
Inflammation, chronic	1 (2%)		1 (2%)
Intestine large, colon	(49)	(9)	(49)
Hyperplasia, lymphoid			2 (4%)
Intestine small, ileum	(47)	(7)	(47)
Hyperplasia, lymphoid	1 (2%)		3 (6%)
Liver	(50)	(15)	(50)
Basophilic focus		1 (7%)	
Cyst		2 (13%)	
Focal cellular change			1 (2%)
Hematopoietic cell proliferation	2 (4%)	1 (7%)	
Hyperplasia, lymphoid	1 (2%)		
Inflammation, chronic, focal	1 (2%)		
Inflammation, chronic, multifocal	4 (8%)		1 (2%)
Leukocytosis	1 (2%)		
Hepatocyte, cytomegaly	1 (2%)		
Mesentery	(13)	(4)	(8)
Hyperplasia, lymphoid	2 (15%)		2 (25%)
Inflammation, chronic		1 (25%)	
Inflammation, suppurative	2 (15%)		
Fat, necrosis	1 (8%)	1 (25%)	1 (13%)
Pancreas	(49)	(10)	(50)
Atrophy	3 (6%)	1 (10%)	1 (2%)
Cyst		1 (10%)	1 (2%)
Hyperplasia, lymphoid	2 (4%)	1 (10%)	
Inflammation, chronic		1 (10%)	
Duct, ectasia	1 (2%)		
Salivary glands	(50)	(9)	(50)
Hyperplasia, lymphoid	1 (2%)		2 (4%)
Inflammation, chronic, multifocal	2 (4%)	1 (11%)	1 (2%)
Stomach, forestomach	(50)	(12)	(49)
Granuloma	1 (2%)		
Hyperkeratosis	1 (2%)	1 (8%)	2 (4%)
Hyperplasia	1 (2%)	1 (8%)	2 (4%)
Hyperplasia, squamous	1 (2%)		
Ulcer			2 (4%)
Stomach, glandular	(49)	(10)	(48)
Atrophy	1 (2%)		2 (4%)
Atrophy, focal		1 (10%)	
Cyst	1 (2%)		
Tooth	(3)		(1)
Peridontal tissue, inflammation, chronic	1 (33%)		1 (100%)
Peridontal tissue, inflammation, suppurative	2 (67%)		
CARDIOVASCULAR SYSTEM			
Blood vessel	(49)	(9)	(50)
Inflammation, acute	1 (2%)		
Heart	(50)	(9)	(50)
Fibrosis, focal	1 (2%)		
Inflammation, chronic	1 (2%)		
Atrium, inflammation, suppurative, focal	1 (2%)		
Myocardium, inflammation, chronic		1 (11%)	

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
ENDOCRINE SYSTEM			
Adrenal gland	(47)	(9)	(48)
Accessory adrenal cortical nodule	2 (4%)		1 (2%)
Hematopoietic cell proliferation	1 (2%)		
Subcapsular, hyperplasia	42 (89%)	8 (89%)	46 (96%)
Adrenal gland, cortex	(47)	(8)	(48)
Cyst	1 (2%)		
Degeneration	37 (79%)	5 (63%)	40 (83%)
Fibrosis	36 (77%)	5 (63%)	40 (83%)
Adrenal gland, medulla	(47)	(7)	(47)
Cyst			1 (2%)
Pituitary gland	(44)	(17)	(45)
Pars distalis, cyst	1 (2%)		
Pars distalis, hyperplasia	15 (34%)	6 (35%)	9 (20%)
Thyroid gland	(50)	(10)	(50)
C-cell, hyperplasia	1 (2%)		1 (2%)
Follicle, degeneration	1 (2%)		
Follicular cell, hyperplasia	3 (6%)	1 (10%)	1 (2%)
GENERAL BODY SYSTEM			
Tissue, NOS	(5)		(1)
Abscess	1 (20%)		
GENITAL SYSTEM			
Ovary	(49)	(19)	(50)
Atrophy			1 (2%)
Cyst	14 (29%)	10 (53%)	18 (36%)
Inflammation, chronic			1 (2%)
Inflammation, suppurative	4 (8%)	3 (16%)	2 (4%)
Capsule, fibrosis			1 (2%)
Capsule, inflammation, chronic			1 (2%)
Capsule, mineralization			1 (2%)
Uterus	(50)	(24)	(50)
Endometrium, hyperplasia, cystic	36 (72%)	22 (92%)	29 (58%)
Endometrium, inflammation, acute	1 (2%)		
Endometrium, inflammation, suppurative	3 (6%)	2 (8%)	1 (2%)
Endometrium, necrosis	1 (2%)		
HEMATOPOIETIC SYSTEM			
Blood	(49)	(9)	(50)
Leukocytosis	1 (2%)		
Bone marrow	(50)	(35)	(48)
Hyperplasia	1 (2%)		
Myelofibrosis	36 (72%)	32 (91%)	45 (94%)
Lymph node	(48)	(11)	(48)
Mesenteric, hyperplasia, lymphoid	1 (2%)		
Renal, hyperplasia, lymphoid			1 (2%)
Renal, inflammation, suppurative	1 (2%)		
Lymph node, bronchial	(38)	(7)	(37)
Hyperplasia, lymphoid	1 (3%)		5 (14%)
Lymph node, mandibular	(42)	(6)	(40)
Cyst	1 (2%)		
Hyperplasia, lymphoid	8 (19%)		8 (20%)
Infiltration cellular, histiocytic		1 (17%)	
Inflammation, suppurative	1 (2%)		
Pigmentation, hemosiderin	1 (2%)		
Spleen	(50)	(18)	(50)
Atrophy	1 (2%)		
Hematopoietic cell proliferation	6 (12%)	3 (17%)	4 (8%)
Hyperplasia, lymphoid	8 (16%)	1 (6%)	10 (20%)

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
HEMATOPOIETIC SYSTEM (Continued)			
Thymus	(34)	(8)	(42)
Atrophy	1 (3%)		
Hyperplasia, lymphoid	1 (3%)		1 (2%)
Inflammation, necrotizing	1 (3%)		
Inflammation, suppurative			1 (2%)
Mediastinum, inflammation, suppurative	1 (3%)		
INTEGUMENTARY SYSTEM			
Skin	(50)	(18)	(50)
Inflammation, suppurative	1 (2%)		
Hair follicle, atrophy	5 (10%)	8 (44%)	2 (4%)
MUSCULOSKELETAL SYSTEM			
Bone	(50)	(9)	(50)
Cranium, fibrous osteodystrophy			1 (2%)
Skeletal muscle	(1)	(1)	(2)
Back, inflammation, chronic		1 (100%)	
NERVOUS SYSTEM			
Brain	(50)	(9)	(50)
Hypothalamus, atrophy	5 (10%)		1 (2%)
Lateral ventricle, dilatation	1 (2%)		
Thalamus, mineralization	5 (10%)	1 (11%)	4 (8%)
RESPIRATORY SYSTEM			
Larynx	(49)	(9)	(50)
Epithelium, hyperplasia, focal	1 (2%)		
Lung	(50)	(9)	(50)
Hyperplasia, lymphoid	3 (6%)		5 (10%)
Infiltration cellular, histiocytic, diffuse			1 (2%)
Inflammation, acute, focal	1 (2%)		
Inflammation, chronic, multifocal	17 (34%)	2 (22%)	24 (48%)
Leukocytosis	2 (4%)	1 (11%)	1 (2%)
Alveolus, granuloma			1 (2%)
Bronchiole, hyperplasia	1 (2%)		
Nose	(49)	(49)	(50)
Hemorrhage			1 (2%)
Thrombus			1 (2%)
Glands, hyperplasia	32 (65%)	46 (94%)	49 (98%)
Glands, inflammation		1 (2%)	
Glands, regeneration		1 (2%)	
Mucosa, inflammation	1 (2%)		
Mucosa, inflammation, acute	1 (2%)		
Mucosa, inflammation, suppurative	8 (16%)	48 (98%)	49 (98%)
Olfactory epithelium, metaplasia	7 (14%)	48 (98%)	49 (98%)
Respiratory epithelium, dysplasia			3 (6%)
Respiratory epithelium, hyperplasia		39 (80%)	48 (96%)
Respiratory epithelium, hyperplasia, basal cell		2 (4%)	7 (14%)
Respiratory epithelium, metaplasia, squamous		9 (18%)	12 (24%)
Respiratory epithelium, regeneration	5 (10%)	47 (96%)	46 (92%)
Submucosa, angiectasis, focal			2 (4%)
Trachea	(50)	(9)	(49)
Metaplasia, squamous, focal			1 (2%)
Glands, inflammation, suppurative	1 (2%)		
Mediastinum, inflammation, suppurative	1 (2%)		

TABLE D5. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR INHALATION STUDY OF ALLYL GLYCIDYL ETHER (Continued)

	Chamber Control	5 ppm	10 ppm
SPECIAL SENSES SYSTEM			
Ear	(1)		(2)
Inflammation, necrotizing	1 (100%)		
URINARY SYSTEM			
Kidney	(50)	(10)	(49)
Hyperplasia, lymphoid	4 (8%)		1 (2%)
Inflammation, chronic	10 (20%)	3 (30%)	18 (37%)
Inflammation, suppurative	2 (4%)	1 (10%)	
Metaplasia, osseous, focal			2 (4%)
Regeneration			1 (2%)
Cortex, cyst		1 (10%)	
Cortex, infarct	1 (2%)		
Renal tubule, necrosis		1 (10%)	
Renal tubule, regeneration	5 (10%)		5 (10%)
Renal tubule, regeneration, focal	1 (2%)		
Urinary bladder	(47)	(9)	(47)
Hyperplasia, lymphoid	3 (6%)		4 (9%)
Inflammation, chronic	10 (21%)	3 (33%)	6 (13%)

APPENDIX E

RESULTS OF SEROLOGIC ANALYSIS

APPENDIX E. RESULTS OF SEROLOGIC ANALYSIS

Methods

Rodents used in the Carcinogenesis Program of the National Toxicology Program are produced in optimally clean facilities to eliminate potential pathogens that may affect study results.

Sera were obtained from nine moribund Osborne-Mendel rats between months 7 and 17 and from eight moribund $B6C3F_1$ mice between months 18 and 24. Data from animals surviving 24 months were collected from 10/50 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 determination of the antibody titers. The following tests were performed:

	Hemagglutination Inhibition	Complement Fixation	ELISA
Mice	PVM (pneumonia virus of mice) Reo 3 (reovirus type 3) Poly (polyoma virus) MVM (minute virus of mice) Ectro (infectious ectromelia) Sendai	M. Ad. (mouse adenovirus) LCM (lymphocytic choriomeningitis virus)	MHV (mouse hepatitis virus) (a) GDVII (Theiler's encephalomyelitis virus) *M. pul. (Mycoplasma pulmonis)* (24 mo) (b)
Rats	PVM KRV (Kilham rat virus) H-1 (Toolan's H-1 virus) Sendai	LCM (13 mo) RCV (rat coronavirus) (7,10 mo)	RCV/SDA (rat coronavirus/ sialodacryoadenitis virus) *M. pul.* (24 mo)

Results

Results are presented in Table E1.

(a) MHV test was also performed by an immunofluorescence assay on sera from all moribund mice.
(b) On randomly selected controls only

TABLE E1. MURINE ANTIBODY DETERMINATIONS FOR RATS AND MICE IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER (a)

Interval (months)	Number of Animals	Positive Serologic Reaction for
RATS		
0	0/10	None positive
7	1/1	PVM
9	0/1	None positive
12	1/1	PVM
	1/1	RCV/SDA
13	0/1	None positive
15	0/1	None positive
16	1/3	PVM
17	1/1	PVM
24	7/10	PVM
	2/10	KRV
	2/10	RCV/SDA
MICE		
18	1/1	PVM
20-23	0/6	None positive
24	4/11	PVM
	2/11	MHV

(a) Blood samples were taken from moribund animals after the start of dosing and from the control animals just before they were killed; samples were sent to Microbiological Associates, Inc. (Bethesda, MD) for determination of antibody titers.

APPENDIX F

INGREDIENTS, NUTRIENT COMPOSITION, AND CONTAMINANT LEVELS IN NIH 07 RAT AND MOUSE RATION

Pellet Diet: April 1982 to April 1984

(Manufactured by Zeigler Bros., Inc., Gardners, PA)

TABLE F1. INGREDIENTS OF NIH 07 RAT AND MOUSE RATION (a)

Ingredients (b)	Percent by Weight
Ground #2 yellow shelled corn	24.50
Ground hard winter wheat	23.00
Soybean meal (49% protein)	12.00
Fish meal (60% protein)	10.00
Wheat middlings	10.00
Dried skim milk	5.00
Alfalfa meal (dehydrated, 17% protein)	4.00
Corn gluten meal (60% protein)	3.00
Soy oil	2.50
Dried brewer's yeast	2.00
Dry molasses	1.50
Dicalcium phosphate	1.25
Ground limestone	0.50
Salt	0.50
Premixes (vitamin and mineral)	0.25

(a) NCI, 1976; NIH, 1978
(b) Ingredients ground to pass through a U.S. Standard Screen No. 16 before being mixed

TABLE F2. VITAMINS AND MINERALS IN NIH 07 RAT AND MOUSE RATION (a)

	Amount	Source
Vitamins		
A	5,500,000 IU	Stabilized vitamin A palmitate or acetate
D_3	4,600,000 IU	D-activated animal sterol
K_3	2.8 g	Menadione
d-α-Tocopheryl acetate	20,000 IU	
Choline	560.0 g	Choline chloride
Folic acid	2.2 g	
Niacin	30.0 g	
d-Pantothenic acid	18.0 g	*d*-Calcium pantothenate
Riboflavin	3.4 g	
Thiamine	10.0 g	Thiamine mononitrate
B_{12}	4,000 µg	
Pyridoxine	1.7 g	Pyridoxine hydrochloride
Biotin	140.0 mg	*d*-Biotin
Minerals		
Iron	120.0 g	Iron sulfate
Manganese	60.0 g	Manganous oxide
Zinc	16.0 g	Zinc oxide
Copper	4.0 g	Copper sulfate
Iodine	1.4 g	Calcium iodate
Cobalt	0.4 g	Cobalt carbonate

(a) Per ton (2,000 lb) of finished product

TABLE F3. NUTRIENT COMPOSITION OF NIH 07 RAT AND MOUSE RATION

Nutrients	Mean ± Standard Deviation	Range	Number of Samples
Protein (percent by weight)	23.34 ± 1.13	22.1-26.3	18
Crude fat (percent by weight)	5.26 ± 0.46	4.4-6.2	18
Crude fiber (percent by weight)	3.47 ± 0.58	2.9-5.6	18
Ash (percent by weight)	6.44 ± 0.40	5.7-7.2	18
Amino Acids (percent of total diet)			
Arginine	1.320 ± 0.072	1.310-1.390	5
Cystine	0.319 ± 0.088	0.218-0.400	5
Glycine	1.146 ± 0.063	1.060-1.210	5
Histidine	0.571 ± 0.026	0.531-0.603	5
Isoleucine	0.914 ± 0.030	0.881-0.944	5
Leucine	1.946 ± 0.056	1.850-1.990	5
Lysine	1.280 ± 0.067	1.200-1.370	5
Methionine	0.436 ± 0.165	0.306-0.699	5
Phenylalanine	0.938 ± 0.158	0.665-1.05	5
Threonine	0.855 ± 0.035	0.824-0.898	5
Tryptophan	0.277 ± 0.221	0.156-0.671	5
Tyrosine	0.618 ± 0.086	0.564-0.769	5
Valine	1.108 ± 0.043	1.050-1.170	5
Essential Fatty Acids (percent of total diet)			
Linoleic	2.290 ± 0.313	1.83-2.52	5
Linolenic	0.258 ± 0.040	0.210-0.308	5
Vitamins			
Vitamin A (IU/kg)	12,472 ± 3,773	3,600-24,000	18
Vitamin D (IU/kg)	4,450 ± 1,382	3,000-6,300	4
α-Tocopherol (ppm)	43.58 ± 6.92	31.1-48.0	5
Thiamine (ppm)	16.94 ± 2.80	13.0-22.0	18
Riboflavin (ppm)	7.6 ± 0.85	6.10-8.2	5
Niacin (ppm)	97.8 ± 31.68	65.0-150.0	5
Pantothenic acid (ppm)	30.06 ± 4.31	23.0-34.0	5
Pyridoxine (ppm)	7.68 ± 1.31	5.60-8.8	5
Folic acid (ppm)	2.62 ± 0.89	1.80-3.7	5
Biotin (ppm)	0.254 ± 0.053	0.19-0.32	5
Vitamin B_{12} (ppb)	24.21 ± 12.66	10.6-38.0	5
Choline (ppm)	3,122 ± 416.8	2,400-3,430	5
Minerals			
Calcium (percent)	1.23 ± 0.12	0.95-1.42	18
Phosphorus (percent)	0.97 ± 0.05	0.90-1.10	18
Potassium (percent)	0.900 ± 0.098	0.772-0.971	3
Chloride (percent)	0.513 ± 0.114	0.380-0.635	5
Sodium (percent)	0.323 ± 0.043	0.258-0.371	5
Magnesium (percent)	0.167 ± 0.012	0.151-0.181	5
Sulfur (percent)	0.304 ± 0.064	0.268-0.420	5
Iron (ppm)	410.3 ± 94.04	262.0-523.0	5
Manganese (ppm)	90.29 ± 7.15	81.7-99.4	5
Zinc (ppm)	52.78 ± 4.94	46.1-58.2	5
Copper (ppm)	10.72 ± 2.76	8.09-15.39	5
Iodine (ppm)	2.95 ± 1.05	1.52-3.82	4
Chromium (ppm)	1.85 ± 0.25	1.44-2.09	5
Cobalt (ppm)	0.681 ± 0.14	0.490-0.780	4

TABLE F4. CONTAMINANT LEVELS IN NIH 07 RAT AND MOUSE RATION

Contaminants	Mean ± Standard Deviation	Range	Number of Samples
Arsenic (ppm)	0.51 ± 0.14	0.17-0.72	18
Cadmium (ppm) (a)	<0.10		18
Lead (ppm)	0.86 ± 0.73	0.33-3.37	18
Mercury (ppm) (a)	<0.05		18
Selenium (ppm)	0.31 ± 0.06	0.13-0.41	18
Aflatoxins (ppb)	<5.0		18
Nitrate nitrogen (ppm) (b)	3.31 ± 3.78	0.10-15.0	18
Nitrite nitrogen (ppm) (b)	2.18 ± 2.17	0.10-7.20	18
BHA (ppm) (c)	4.94 ± 5.41	2.00-17.0	18
BHT (ppm) (c)	2.89 ± 2.93	1.00-12.0	18
Aerobic plate count (CFU/g) (d)	38,111 ± 31,645	6,600-130,000	18
Coliform (MPN/g) (e)	47.72 ± 116.98	3.0-460	18
E. coli (MPN/g) (e)	≤3.00		18
Total nitrosamines (ppb) (f)	4.72 ± 2.79	1.85-9.30	18
N-Nitrosodimethylamine (ppb) (f)	3.66 ± 2.72	0.95-8.30	18
N-Nitrosopyrrolidine (ppb) (f)	1.06 ± 0.28	0.81-1.70	18
Pesticides (ppm)			
α-BHC (a,g)	<0.01		18
β-BHC (a)	<0.02		18
γ-BHC-Lindane (a)	<0.01		18
δ-BHC (a)	<0.01		18
Heptachlor (a)	<0.01		18
Aldrin (a)	<0.01		18
Heptachlor epoxide (a)	<0.01		18
DDE (a)	<0.01		18
DDD (a)	<0.01		18
DDT (a)	<0.01		18
HCB (a)	<0.01		18
Mirex (a)	<0.01		18
Methoxychlor (a)	<0.05		18
Dieldrin (a)	<0.01		18
Endrin (a)	<0.01		18
Telodrin (a)	<0.01		18
Chlordane (a)	<0.05		18
Toxaphene (a)	<0.1		18
Estimated PCBs (a)	<0.2		18
Ronnel (a)	<0.01		18
Ethion (a)	<0.02		18
Trithion (a)	<0.05		18
Diazinon (a)	<0.1		18
Methyl parathion (a)	<0.02		18
Ethyl parathion (a)	<0.02		18
Malathion (h)	0.07 ± 0.09	0.05-0.15	18
Endosulfan I (a)	<0.01		18
Endosulfan II (a)	<0.01		18
Endosulfan sulfate (a)	<0.03		18

(a) All values were less than the detection limit, given in the table as the mean.
(b) Sources of contamination: alfalfa, grains, and fish meal
(c) Sources of contamination: soy oil and fish meal
(d) CFU = colony-forming unit
(e) MPN = most probable number
(f) All values were corrected for percent recovery.
(g) BHC is hexachlorocyclohexane or benzene hexachloride.
(h) Nine lots contained more than 0.05 ppm.

APPENDIX G

CHEMICAL CHARACTERIZATION, ANALYSIS, AND GENERATION OF CHAMBER CONCENTRATIONS OF ALLYL GLYCIDYL ETHER FOR THE TOXICOLOGY STUDIES

APPENDIX G. CHEMICAL CHARACTERIZATION

PROCUREMENT AND CHARACTERIZATION OF ALLYL GLYCIDYL ETHER

Allyl glycidyl ether was obtained in four lots (Table G1) as a clear, colorless liquid from Alcolac, Inc. (Baltimore, MD). Purity and identity analyses were conducted at Midwest Research Institute (MRI) (Kansas City, MO). MRI reports on the analyses performed in support of the allyl glycidyl ether studies are on file at the National Institute of Environmental Health Sciences.

The identity of all lots was confirmed by spectroscopic analyses. The infrared and nuclear magnetic resonance spectra agreed with the literature spectra (Sadtler Standard Spectra) (a representative infrared spectrum is shown in Figure G1, and a representative nuclear magnetic resonance spectrum is shown in Figure G2). The ultraviolet/visible spectra were consistent with that expected for the structure of allyl glycidyl ether.

The purity of each lot was found to be approximately 99%, as determined by elemental analysis, Karl Fischer water analysis, titration of the epoxide group in chloroform with 0.1 N perchloric acid in the presence of excess tetrabutylammonium iodide with potentiometric monitoring, and gas chromatography. Gas chromatographic analysis was performed with flame ionization detection, with nitrogen as the carrier, a flow rate of 70 ml/minute, and either a 20% SP2100/0.1% Carbowax 1500 column (system 1) or a 10% Carbowax 20M-TPA column (system 2).

The results of elemental analysis for lot no. E337MO were slightly high for carbon and were in agreement with the theoretical values for hydrogen. Karl Fischer analysis indicated 0.066% water. Titration of the epoxide group indicated a purity of 98.7%. Gas chromatography with system 1 showed two impurities eluting after the major peak, with a combined area 0.22% that of the major peak. Three additional impurities were observed, with individual relative areas of less than 0.1%. System 2 indicated two impurities, one eluting before and one after the major peak, with a combined relative area of 0.25%; four additional impurities, with individual areas less than 0.1% that of the major peak, were also observed.

The results of elemental analysis for lot no. E584CI were in agreement with the theoretical values for carbon and hydrogen. Karl Fischer analysis indicated the presence of 0.24% water. Titration of the epoxide group indicated a purity of 98.7%. Gas chromatography with system 1 showed one impurity eluting before the major peak, with an area 0.17% that of the major peak. One additional impurity was observed, with a relative area of less than 0.1%. System 2 indicated two impurities, both eluting before the major peak, with a combined area 0.60% that of the major peak. One additional impurity was observed, with an area less than 0.1% that of the major peak.

TABLE G1. IDENTITY AND SOURCE OF ALLYL GLYCIDYL ETHER USED IN THE INHALATION STUDIES

Fourteen-Day Studies	Eight-Week and Thirteen-Week Studies	Two-Year Studies
Lot Numbers		
E337MO	E337MO; E584CI	E584CI; E83902; E839D2
Date of Initial Use		
9/13/80	E337MO--12/1/81	E584CI--6/21/82
Supplier		
Alcolac, Inc. (Baltimore, MD)	Alcolac, Inc. (Baltimore, MD)	Alcolac, Inc. (Baltimore, MD)

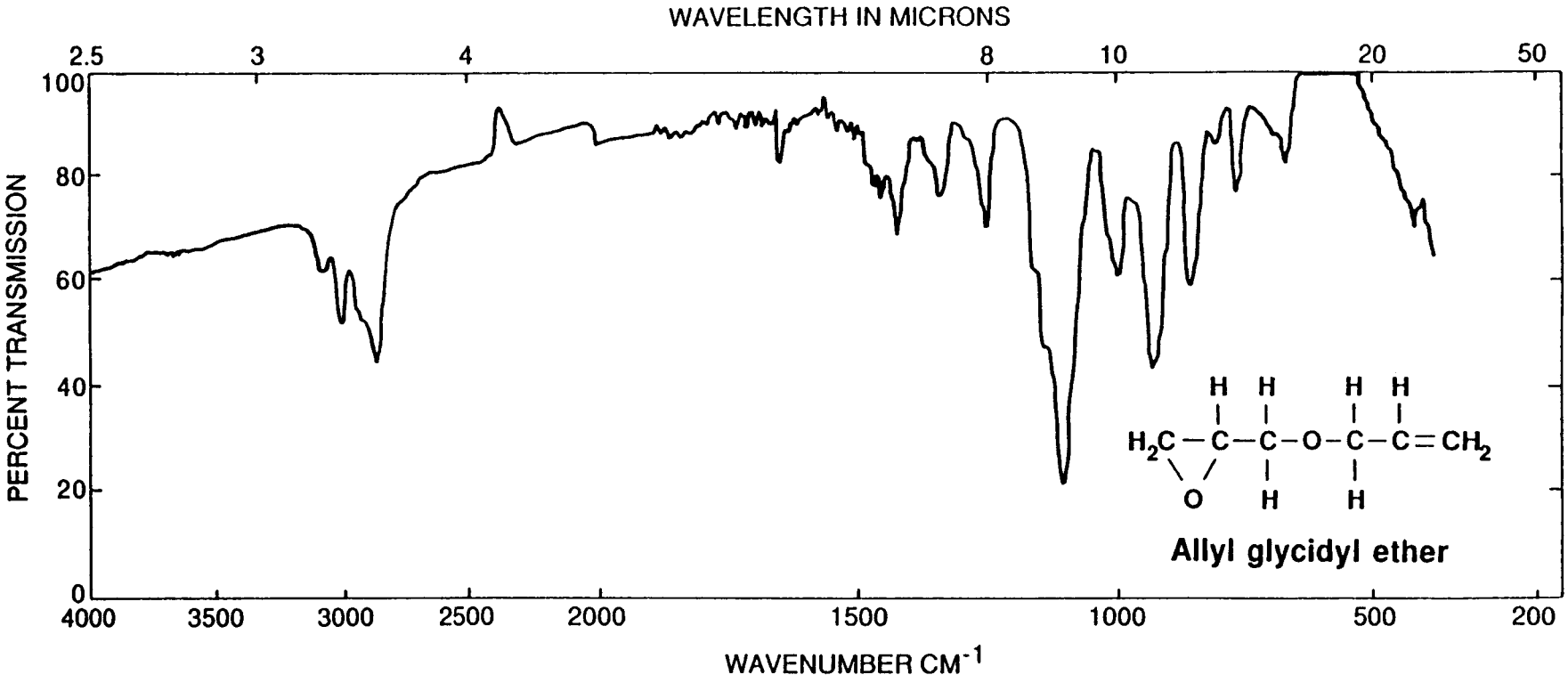

FIGURE G1. INFRARED ABSORPTION SPECTRUM OF ALLYL GLYCIDYL ETHER (LOT NO. E337MO)

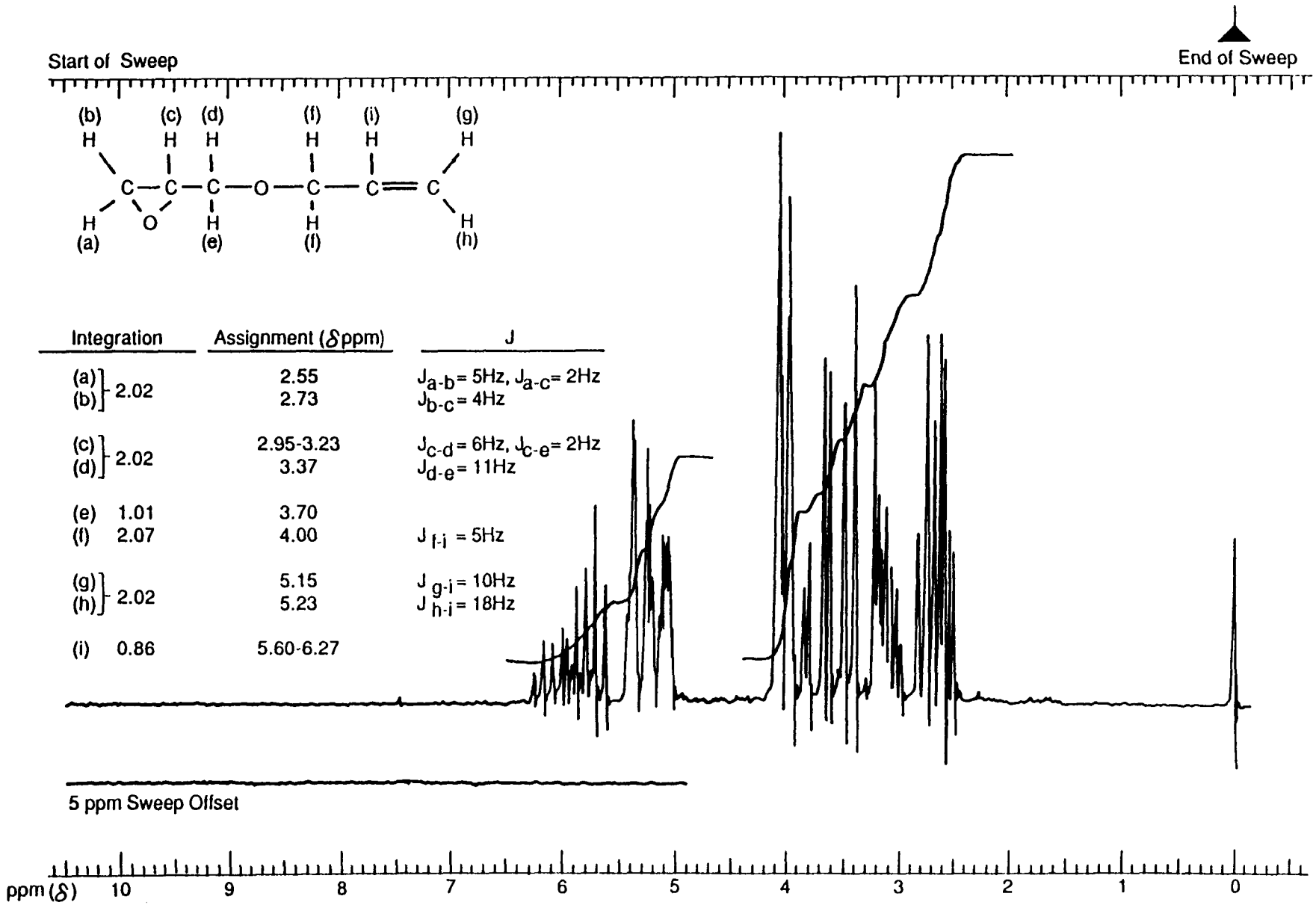

FIGURE G2. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF ALLYL GLYCIDYL ETHER (LOT NO. E337MO)

The results of elemental analysis for lot no. E83902 were in agreement with the theoretical values for carbon and hydrogen. Karl Fischer analysis indicated the presence of 0.015% water. Titration of the epoxide group indicated a purity of 97.8%. Gas chromatography with system 1 indicated two impurities, one eluting before and one after the major peak, with a combined area 0.22% that of the major peak. Four additional impurities were observed, with relative areas of less than 0.1%. System 2 indicated two impurities, both eluting before the major peak, with a combined area 0.78% that of the major peak. Four additional impurities were observed, with areas less than 0.1% that of the major peak.

The results of elemental analysis for lot no. E839D2 were in agreement with the theoretical values for carbon and hydrogen. Karl Fischer analysis indicated the presence of 0.07% water. Titration of the epoxide group indicated a purity of 98.1%. Gas chromatography with system 1 indicated two impurities, one eluting before and one after the major peak, with a combined area 0.23% that of the major peak. Eight additional impurities were observed, with relative areas of less than 0.1%. System 2 indicated three impurities, two eluting before the major peak and one after, with a combined area 0.91% that of the major peak. Three additional impurities were observed, with areas less than 0.1% that of the major peak.

Stability studies performed by gas chromatography, with the same column as previously described for system 2 and with tetradecane as an internal standard, indicated that allyl glycidyl ether was stable as a bulk chemical for 2 weeks when stored protected from light at temperatures up to 25° C. There was an indication of possible slight decomposition when the chemical was stored for 2 weeks at 60° C.

The bulk chemical was stored at less than 5° C throughout the studies. Periodic purity analysis of allyl glycidyl ether by gas chromatography, infrared spectroscopy (until April 1981), and nonaqueous acid/base titration (from April 1981) indicated no notable degradation of the study material throughout the studies. The purity was greater than 97%.

GENERATION AND MEASUREMENT OF CHAMBER CONCENTRATIONS

Vapor Generation System

No additional preparation of the liquid allyl glycidyl ether was necessary before introduction into the vapor generation system. The liquid was pumped from a stainless steel reservoir to a vaporizer by a stable micrometering pump with adjustable pump rates. For the 14-day and 13-week studies at concentrations from 10 ppm to 200 ppm and 2-year studies after week 40, the liquid was vaporized from a fine glass wick on the surface of a cylindrical vaporizer by an electric heater embedded in the cylinder (vapor-generating system 1) (Figure G3). For the 14-day and 2-year studies, the vaporizer surface temperatures were set at approximately 105° C and for the 13-week studies at approximately 90° C. Each cylindrical vaporizer was positioned in the fresh air duct leading directly into the exposure chamber. For the 13-week studies at exposure concentrations of 1 ppm or 4 ppm and for the first 39 weeks of the 2-year studies, liquid allyl glycidyl ether was drawn from the stainless steel reservoir through a three-way valve into a glass syringe large enough to contain the total amount necessary for a 6-hour exposure. The syringe was attached to a syringe pump unit, and the three-way valve was adjusted to allow flow of the liquid through an injection needle to a cotton wick positioned in the fresh air duct leading directly into the exposure chamber (vapor-generating system 2) (Figure G4). No additional heating was necessary to generate the vapor.

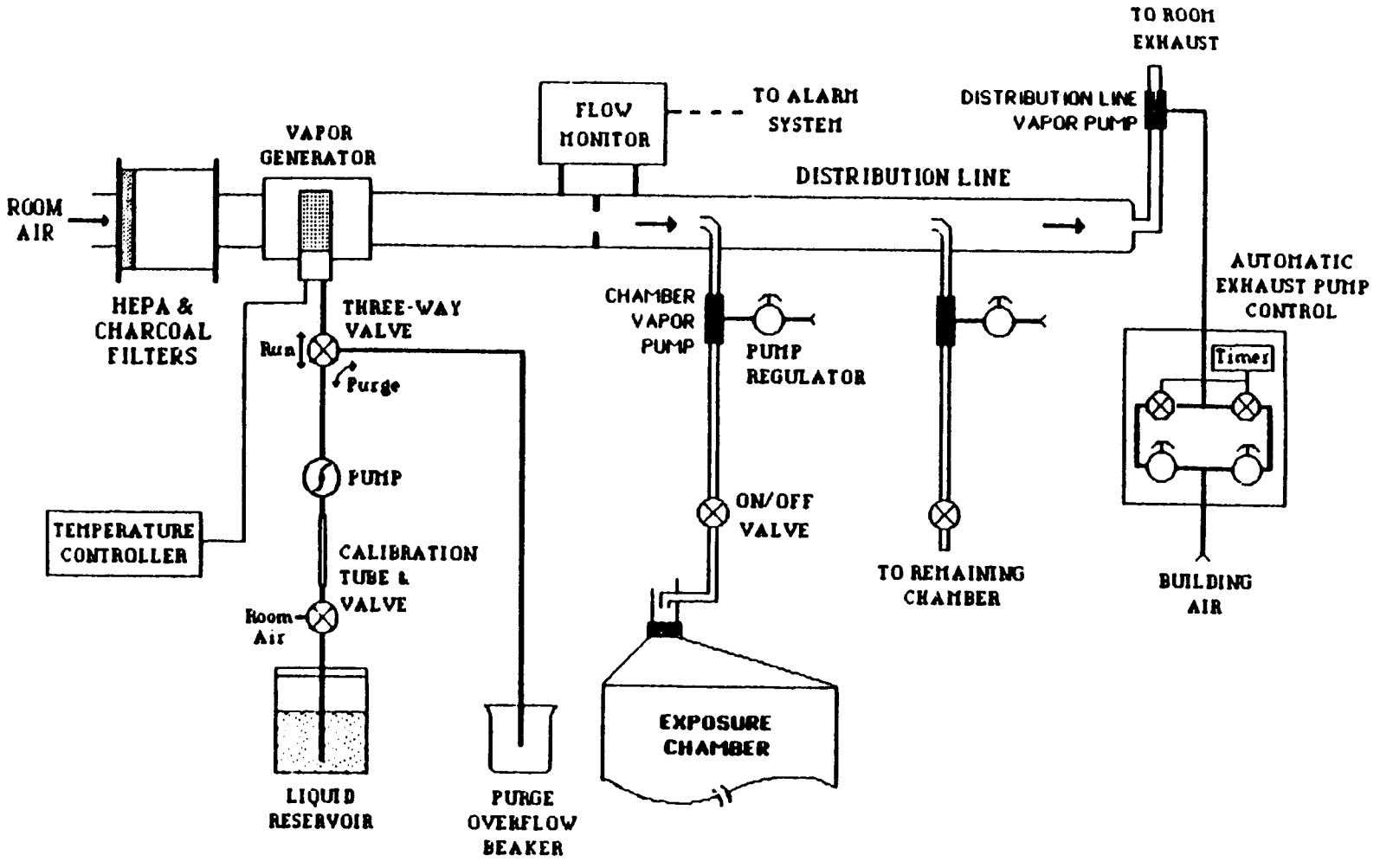

FIGURE G3. ALLYL GLYCIDYL ETHER GENERATION SYSTEM (SYSTEM 1)

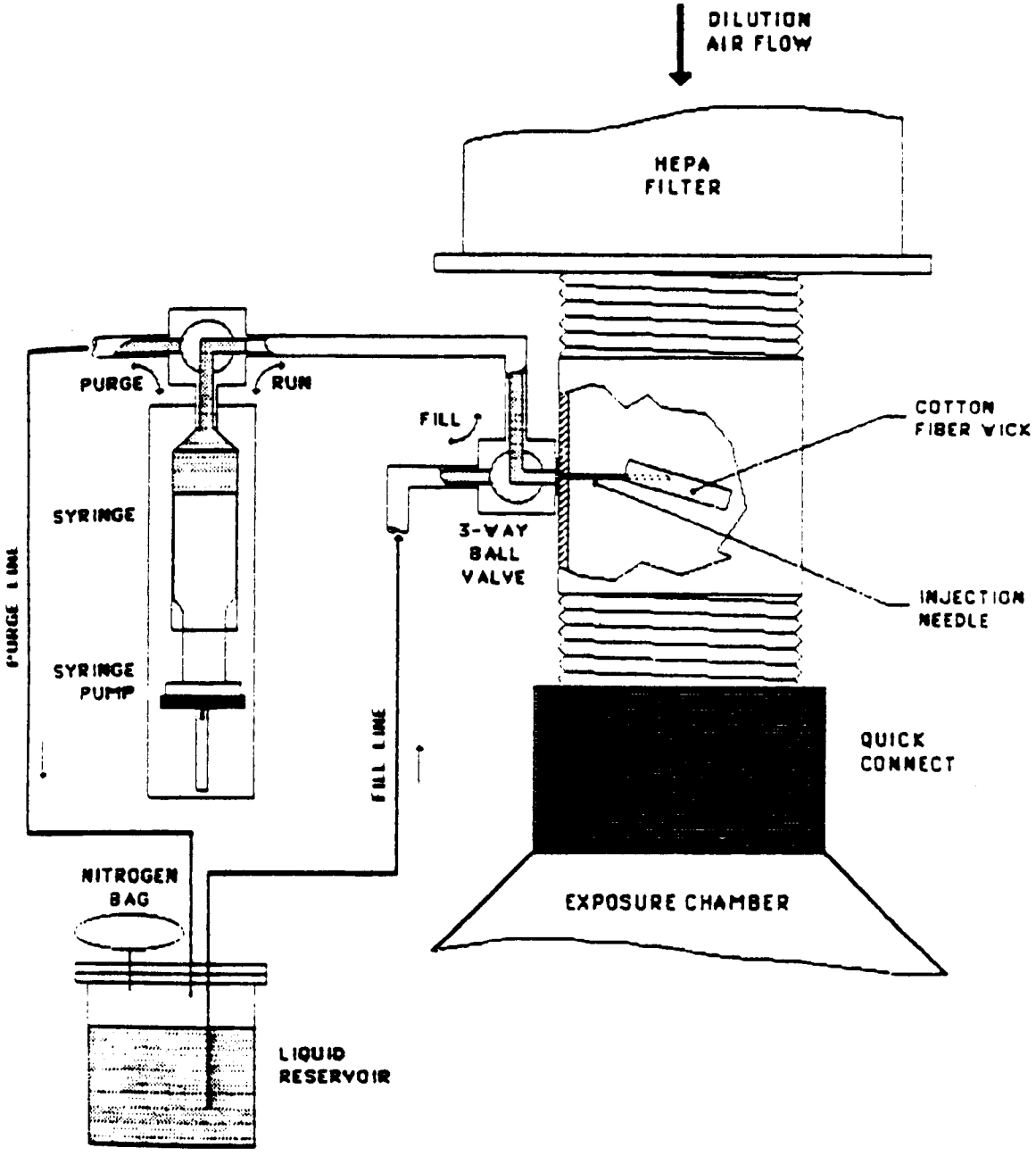

FIGURE G4. ALLYL GLYCIDYL ETHER GENERATION SYSTEM (SYSTEM 2)

Vapor Concentration Monitoring

Concentrations of allyl glycidyl ether in the chambers and the exposure room were measured by a gas chromatograph (HP 5840) equipped with a flame ionization detector. Calibration of the monitor was confirmed and corrected as necessary by checking the calibration against periodic assays of grab samples from the chambers. Generally, duplicate grab samples were obtained from each chamber by bubblers filled with *N,N*-dimethylformamide. On December 7, 1983, a small amount of *N,N*-dimethylformamide was accidentally introduced into the 5-ppm allyl glycidyl ether chamber when the bubbler sample was being collected. The maximum *N,N*-dimethylformamide concentration was approximately 6 ppm; maximum exposure time was 71 minutes. During the 14-day and 13-week studies, exposure concentrations were within ±10% of the target concentrations. Weekly mean exposure concentrations for the 2-year studies are presented in Figures G5 through G8. A summary of the chamber concentrations is presented in Table G2; Table G3 summarizes the distribution of mean daily concentrations.

TABLE G2. SUMMARY OF CHAMBER CONCENTRATIONS IN THE TWO-YEAR INHALATION STUDIES OF ALLYL GLYCIDYL ETHER

Target Concentration (ppm)	Total Number of Readings	Average Concentration (a) (ppm)
Rat chambers		
5	11,939	5.02 ± 0.37
10	11,919	9.95 ± 0.68
Mouse chambers		
5	11,818	5.03 ± 0.37
10	11,799	9.95 ± 0.68

(a) Mean ± standard deviation

TABLE G3. DISTRIBUTION OF MEAN DAILY CONCENTRATIONS OF ALLYL GLYCIDYL ETHER DURING THE TWO-YEAR INHALATION STUDIES

Range of Concentration (percent of target)	Number of Days Mean Within Specified Range	
	5 ppm	10 ppm
Rat chambers		
110-120	4	0
100-110	273	203
90-100	215	288
80-90	4	5
Mouse chambers		
110-120	4	0
100-110	272	200
90-100	211	286
80-90	4	5

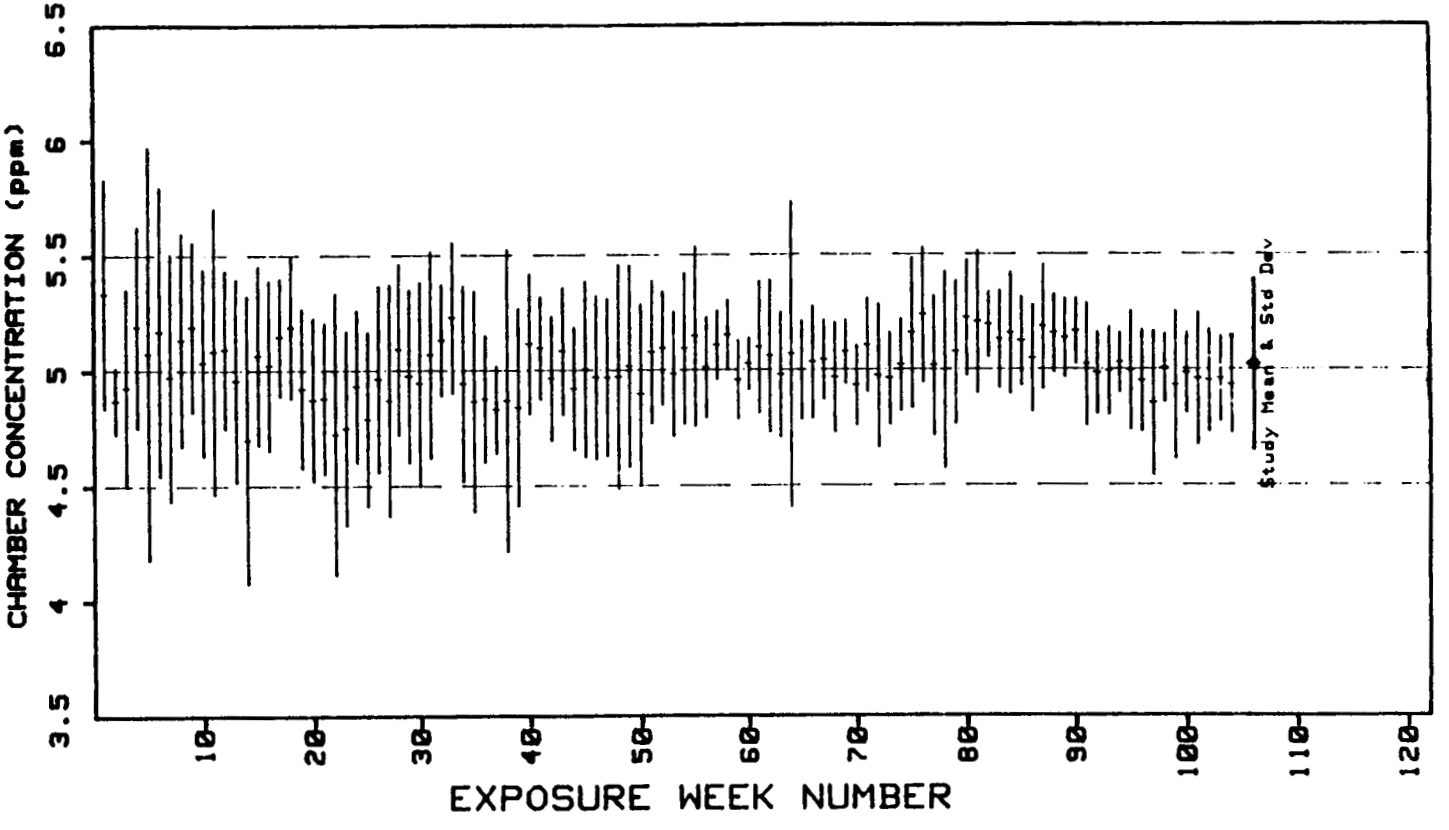

FIGURE G5. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION
IN THE 5-ppm ALLYL GLYCIDYL ETHER RAT EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

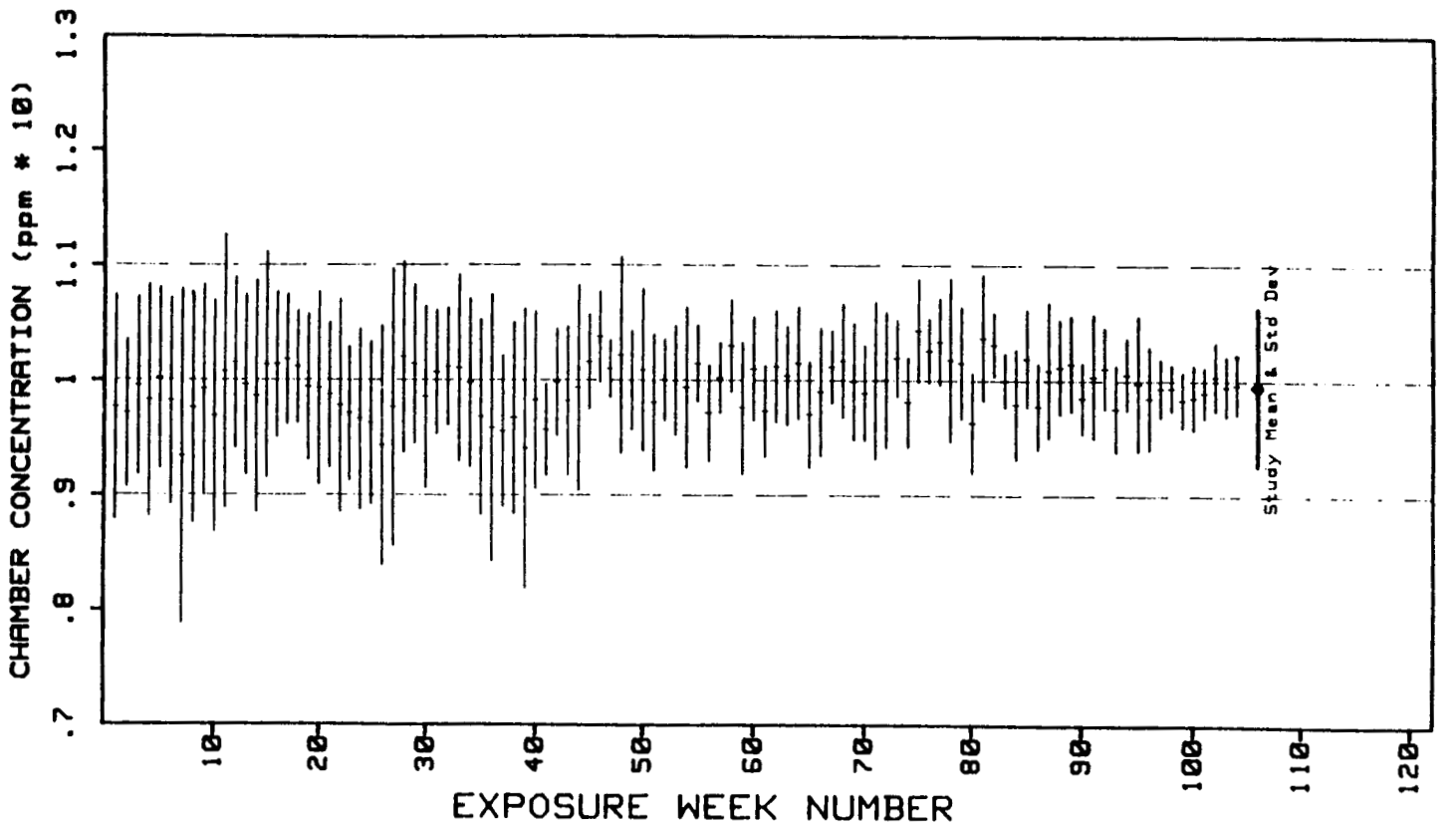

FIGURE G6. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION
IN THE 10-ppm ALLYL GLYCIDYL ETHER RAT EXPOSURE CHAMBER FOR ENTIRE 103-WEEK STUDIES

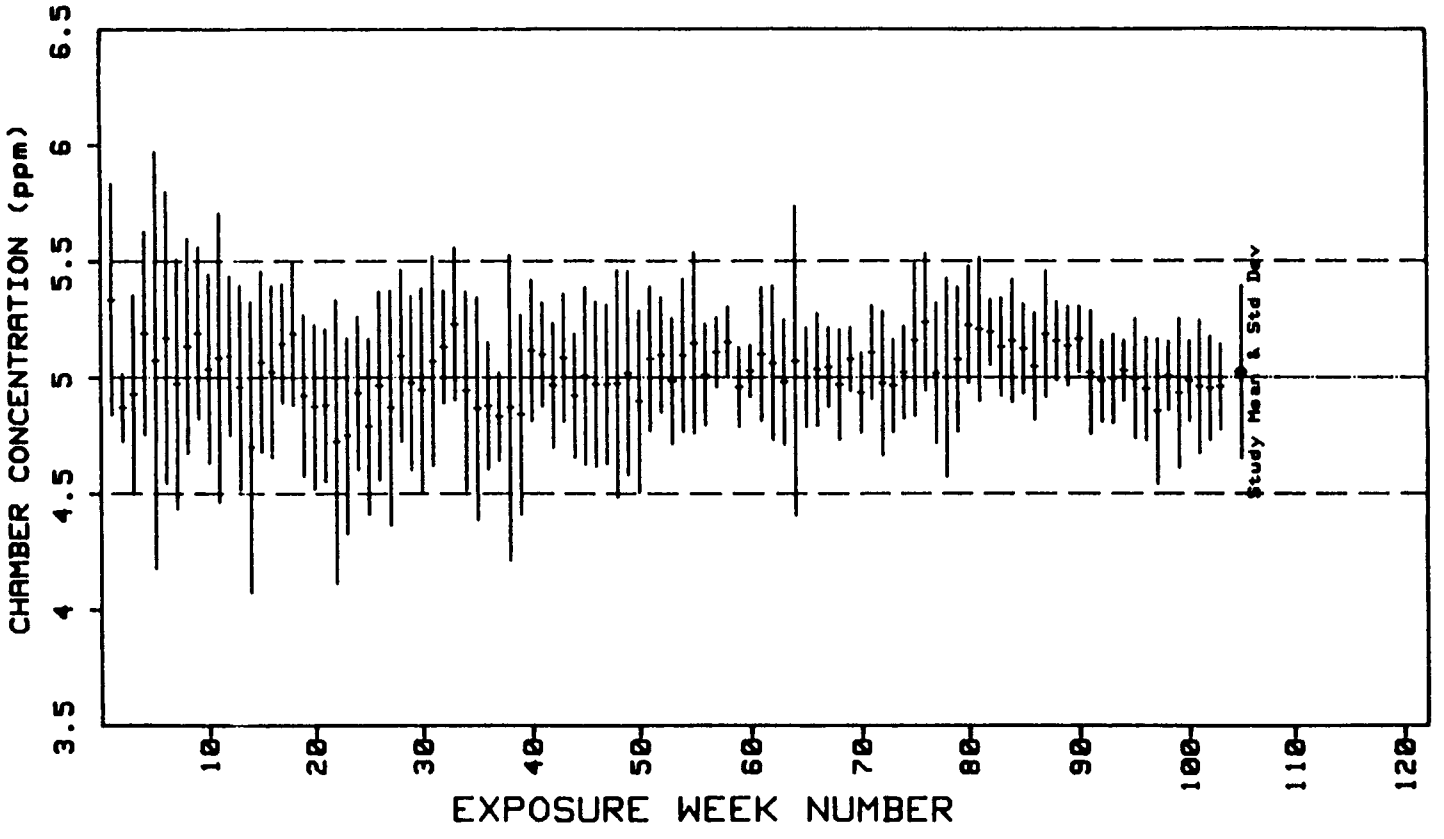

FIGURE G7. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION
IN THE 5-ppm ALLYL GLYCIDYL ETHER MICE EXPOSURE CHAMBER FOR ENTIRE 102-WEEK STUDIES

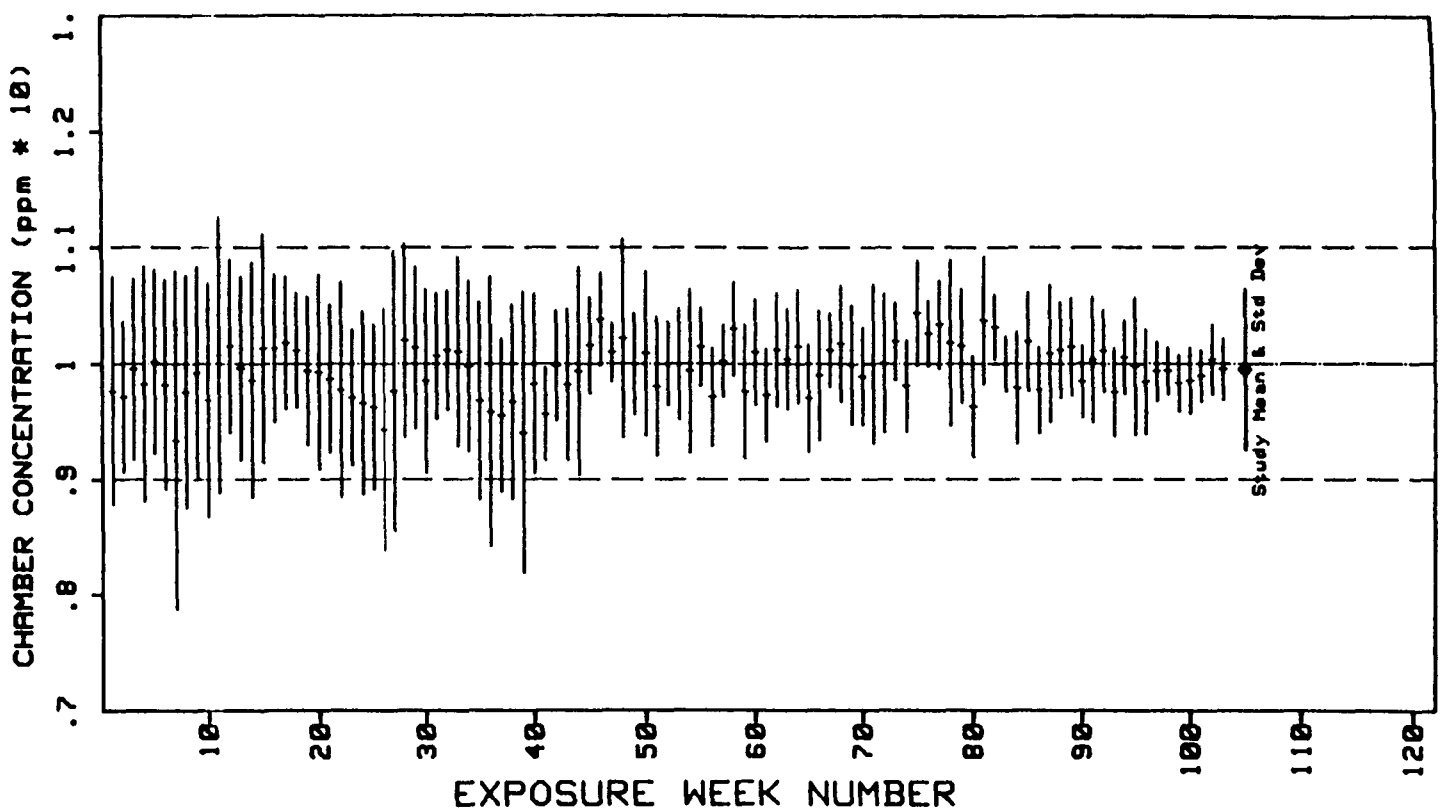

FIGURE G8. WEEKLY MEAN CONCENTRATION AND STANDARD DEVIATION
IN THE 10-ppm ALLYL GLYCIDYL ETHER MICE EXPOSURE CHAMBER FOR ENTIRE 102-WEEK STUDIES

Degradation Study of Allyl Glycidyl Ether in Chamber

Samples of allyl glycidyl ether exposure atmosphere were analyzed for the presence of potential degradation products. No evidence of any degradation products was detected by an HP 5840 gas chromatograph equipped with a flame ionization detector, a 10% Carbowax 20M-TPA column, and helium as the carrier.

Vapor Concentration Uniformity in Chamber

The uniformity of vapor concentration in each exposure chamber was measured before the start of the studies and was checked at intervals of approximately 3 months throughout the studies with the same HP 5840 gas chromatographic system previously described. In most instances, the vapor concentrations were within 10% of the mean target concentration values at all 12 positions sampled within the chamber and ranged from 58% to 112% of the target concentrations. Early in the studies, problems in uniformity with vapor-generating system 1 were solved by adjusting flow deflectors and by changing air-mixer designs. Problems with vapor-generating system 2 were solved by repairing door seals that had been leaking.

APPENDIX H

METHODS FOR STUDIES OF REPRODUCTIVE EFFECTS IN RATS AND MICE EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION

As part of the 13-week studies of allyl glycidyl ether, 20 additional animals of each sex and species were allocated randomly to the three highest dose groups and to the control groups. Additionally, three groups of 20 control males and 20 control females each were allocated as mates for the exposed animals.

The dosed animals were exposed for 6 hours per day, 5 days per week for 8 weeks. The day after the last exposure, all female rats were placed in stainless steel wire mesh-bottom cages, where they were housed individually throughout the breeding period and during the first 15 days of gestation. They were then maintained individually in solid-bottom plastic cages. Male rats were housed individually in stainless steel wire mesh-bottom cages until they were killed. Male and female mice were transferred to solid-bottom plastic cages the day after the last exposure and were maintained individually in these cages until they were killed.

Housing and maintenance conditions for control male and female rats and mice were identical to those for exposed animals throughout the studies. The animals were allowed free access to NIH 07 Rat and Mouse Ration in slot feeders and to water from the Richland, WA, municipal water supply in bottles affixed to the cages. Clean cages were provided each week. The chamber temperature was maintained between 69° F and 80° F. Relative humidity in the chamber ranged from 32% to 75%. The room was illuminated by fluorescent lights with a 12-hour electronically operated on/off cycle.

Mating Procedures

Rats: Cohabitation of male and female rats was initiated 2 days after the final exposure. A computer-derived randomization program was used to determine male-female pairings. A single male rat was placed in a cage with a single female rat at 3:00-4:00 p.m. and was removed the following morning at 6:30-7:30. Each female was lavaged with 0.9% saline, which was then examined microscopically for the presence of sperm. The day that sperm were detected was designated day 0 of gestation; no further cohabitation of this pair took place. Cohabitation and lavage for unmated pairs were repeated each day for a period of 7 days until sperm were detected. The day sperm were found was recorded for each male-female pair. Sperm-negative females were recorded as not having mated.

Mice: Two days after termination of exposure, cohabitation was initiated. A single male was paired with a single female according to a computer-derived randomization program. Each male was placed with the designated female at 3:00-4:00 p.m. and was removed the following morning at 6:30-7:30. Each female was immediately examined for the presence of a vaginal plug, which indicates that copulation has occurred. The day a plug was found was called day 0 of gestation; no further cohabitation of this pair took place. Cohabitation and examination for unmated pairs were repeated each day for a period of 7 days or until a vaginal plug was found. Females in which no plugs were seen were recorded as not having mated. Four mice became pregnant during the exposure period. Three control animals from the 13-week study were substituted for the pregnant control mice.

Rats and Mice: Half of the females in which copulation was detected were assigned to the group to be used for fetal examinations. The remainder were assigned to the group to be used for postnatal examinations. Females selected for the two examination groups were those whose days of mating were representative of those of all mated females at their exposure concentration. Postnatal observations were performed on offspring from pregnant females in which copulation was not detected.

Teratologic Evaluation

All rats and mice were killed by carbon dioxide, which allows for a more accurate assessment of fetal viability than does administration of sodium pentobarbital. The dams were weighed immediately, and the body weight and time of kill were recorded. The uterus and ovaries were removed and weighed. The ovaries were separated from the uterus, and the corpora lutea were counted. The nongravid uterus was stained with an aqueous solution of 10% ammonium sulfide to locate implantation sites. The rest of the maternal necropsy was conducted according to standard protocol. All maternal tissues were preserved in 10% normal-buffered formalin (NBF).

Live and dead fetuses and early, mid, and late resorption sites were counted in each uterine horn. The fetuses and placentas were then removed and numbered for identification. The fetuses were killed by an intraperitoneal injection of 0.05 ml of 50 mg/ml sodium pentobarbital. The sex, shape of head, limbs, and number of digits were noted, and the fetus was examined for gross external malformations. The mouth was opened to check for a cleft palate. The fetus and placenta were then weighed. A small incision was made in the abdomen, and each fetus was placed in an individual carton containing Bouin's fixative.

When all fetal examinations had been completed, the results were tabulated and classified as major malformations, minor anomalies, or common variants. Stunting was calculated by multiplying the mean body weight of all pups in a litter by 0.66, omitting the suspected stunted pup. If the suspect pup weighed less than this value, it was considered stunted.

Postnatal Observations

Pregnant females were observed twice per day before parturition. During the first 24 hours after birth, the pups were sexed, weighed, and examined for external abnormalities. This was repeated when the pups were 4 days old. On the 13th day post partum, the dams were weighed. When the pups were 21 days old, they and their dams were killed with carbon dioxide and weighed, and the sex of the pups was verified. The ovaries and uteruses of the dams were removed, and the ovaries were examined to enumerate corpora lutea. The uteruses were stained with 10% ammonium sulfide to display implantation sites. All necropsies, except those for 21-day-old mice, were performed according to standard protocol. To facilitate processing the large number of animals, the necropsy protocol was modified for mouse pups. The lungs, liver, spleen, and gastrointestinal tract were removed and placed in NBF. Next, a transverse incision was made in each kidney in situ. The skin on the skull was peeled back, and the calvarium was removed. The brain was gently raised to permit examination of the pituitary gland and then was repositioned in the skull. The mouse was then placed in NBF for fixation.

Sperm Morphology, Motility, and Numbers

Eight male rats and eight male mice from each group were killed with carbon dioxide 13 or 14 days after the end of exposure (4-12 days after mating). Both cauda epididymides were removed from each animal and placed in 0.1 ml of semen extender. Two or three cuts were made in each specimen to release some sperm into the extender. Approximately 0.01-0.02 ml was pipetted onto a glass slide and covered with a No. 1, 22-mm^2 coverslip. The sperm were immediately examined microscopically for evaluation of motility. The sample was scored from 0 (no motile sperm) to 4 (all sperm motile).

The cauda epididymides were then finely minced. Phosphate-buffered saline (PBS) was added to the specimens (mice, 1.9 ml; rats, 4.9 ml), and the cell suspensions were dispersed with siliconized pasteur pipets. Rat cell suspensions were diluted with PBS. Hemacytometers were loaded with duplicate

samples from each sperm cell specimen, and the sperm were counted promptly. The count was recorded on a form that also indicated the dilution used and the squares counted.

The original cell suspensions were filtered through an 80-µm stainless steel screen into a 15-ml plastic centrifuge tube. A sufficient volume of 1% Eosin Y was added to each filtrate to provide a final concentration of 0.1% Eosin Y. The sperm were stained for at least 30 minutes. Smears were then made on glass slides and air-dried overnight. The slides were then quickly dipped, first in 90% ethanol and then in absolute ethanol, and finally cleared in xylene. Permount was used to cover the slides with coverslips. Sperm were examined for abnormalities at 400× magnification.

APPENDIX I

RESULTS OF STUDIES OF REPRODUCTIVE EFFECTS IN OSBORNE-MENDEL RATS EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION

Two of 20 male rats exposed to 200 ppm died before the end of the 8-week studies of reproductive effects. The reproductive performance of males exposed to 200 ppm was found to be markedly impaired (Tables I2 and I3); the mating behavior of females was not affected at any exposure concentration. Small but statistically significant reductions were seen in the number of corpora lutea per dam and in the number of implantation sites per dam in females exposed to 200 ppm (Table I4). Fetal body weights, placental weights, maternal body weights, and weights of gravid uteri were not affected in exposed females (Table I5). The numbers of implantation sites per dam and live fetuses per litter were greatly reduced in dams mated with exposed males in the 30- and 100-ppm groups. None of the females mated with 200-ppm males in the fetal studies became pregnant, and no implantation sites for developing fetuses were found (Table I4). Very few malformations were observed in fetal offspring of exposed dams (Table I6). No abnormal fetuses were found in the relatively small number of fetuses available for examination which were sired by exposed males. No effects of exposure were seen on the offspring of exposed females. The number of live pups sired by any group of exposed males was significantly lower than that sired by controls (Tables I3, I7, and I8). Exposure had no effect on sperm motility or on number of sperm recovered from the cauda epididymis 13-14 days after the last exposure. The percentage of abnormal sperm was significantly increased in males exposed to 200 ppm (Table I9).

TABLE I1. MEAN BODY WEIGHTS OF RATS IN THE EIGHT-WEEK INHALATION STUDIES OF THE REPRODUCTIVE EFFECTS OF ALLYL GLYCIDYL ETHER (a)

Concentration (ppm)	Male	Female	
		Fetal Exam Groups (b)	Postnatal Exam Groups (c)
	Before exposure		
(d) 0	267	187	179
(e) 0	265	185	181
30	234	183	185
100	263	177	185
200	269	180	183
	End of exposure (f)		
(d) 0	419	260	247
(e) 0	414	257	247
30	352	240	244
100	337	226	232
200	296	214	216
	Termination (g)		
(d) 0	--	326	281
(e) 0	414	360	298
30	371	344	291
100	370	326	289
200	349	332	286

(a) Group mean body weight in grams
(b) Groups designated for fetal examination on day 19 of gestation
(c) Groups designated for postnatal examination on day 21 post partum
(d) Mates for exposed animals
(e) Mates for control animals
(f) Animals were weighed 1 day after the end of exposure.
(g) Males were killed 13-14 days after the end of exposure.

TABLE I2. SUMMARY OF PREGNANCY STATUS OF RATS AFTER INHALATION EXPOSURE FOR EIGHT WEEKS TO ALLYL GLYCIDYL ETHER

	Control	30 ppm	100 ppm	200 ppm
Results when males were exposed (a)				
Number of females examined	20	20	20	18
Percentage sperm-positive	75	90	85	78
Percentage pregnant, sperm-positive	100	**50	**23.5	**7
Percentage sperm-negative	25	10	15	22
Percentage pregnant, sperm-negative	0	0	0	0
Percentage of all females pregnant	75	45	**20	**6
Results when females were exposed (b)				
Number of females examined	20	20	20	20
Percentage sperm-positive	75	85	95	75
Percentage pregnant, sperm-positive	100	100	100	100
Percentage sperm-negative	25	15	5	25
Percentage pregnant, sperm-negative	0	67	100	40
Percentage of all females pregnant	75	95	*100	85

(a) Control female rats were mated with exposed male rats.
(b) Exposed female rats were mated with control male rats.
*$P<0.05$ vs. the controls by the Fisher exact test
**$P<0.01$ vs. the controls by the Fisher exact test

TABLE I3. SUMMARY OF REPRODUCTIVE PERFORMANCE OF RATS AFTER INHALATION EXPOSURE FOR EIGHT WEEKS TO ALLYL GLYCIDYL ETHER

Concentration (ppm)	Day of Mating	Results When Males Were Exposed (a)				Results When Females Were Exposed (b)			
		Copulations Detected (c)	No. of Females Impregnated	No. of Litters (d)	Total Pups/ Litter (e)	Copulations Detected (c)	No. of Females Impregnated	No. of Litters (d)	Total Pups/ Litter (e)
0	1	4/20	4	4	14.3 ± 3.1	4/20	4	4	14.3 ± 3.1
	2	3/16	3	3	14.3 ± 0.6	3/16	3	3	14.3 ± 0.6
	3	2/13	2	2	14.0 ± 1.4	2/13	2	2	14.0 ± 1.4
	4	4/11	4	4	13.5 ± 3.1	4/11	4	4	13.5 ± 3.1
	5	2/7	2	2	12.5 ± 2.1	2/7	2	2	12.5 ± 2.1
	6	0/5	--	--	--	0/5	--	--	--
	7	0/5	--	--	--	0/5	--	--	--
	Summary	15/20	15	15	13.8 ± 2.2	15/20	15	15	13.8 ± 2.2
30	1	2/20	1	1	6	5/20	5	5	13.8 ± 2.4
	2	7/18	2	2	1.5 ± 0.7	8/15	8	8	12.5 ± 2.2
	3	2/11	1	1	1	2/7	2	2	13.5 ± 3.5
	4	2/9	2	2	5.5 ± 6.4	1/5	1	1	12
	5	5/7	3	3	10.7 ± 3.2	1/4	1	1	15
	6	0/7	--	--	--	0/3	--	--	--
	7	0/7	--	--	--	0/3	--	--	--
	Undetected						2	2	
	Summary	18/20	9	9	5.9 ± 4.9	17/20	19	19	13.0 ± 2.1
100	1	1/20	0	--	--	5/20	5	5	11.6 ± 2.3
	2	3/19	0	--	--	8/15	8	8	13.4 ± 2.7
	3	7/16	2	2	1.0 ± 0.0	0/7	--	--	--
	4	2/9	0	--	--	1/7	1	0	--
	5	2/7	0	--	--	4/6	4	4	13.0 ± 2.4
	6	1/5	1	1	10	1/2	1	1	11
	7	1/4	1	1	10	0/1	--	--	--
	Undetected						1	1	13
	Summary	17/20	4	4	5.3 ± 4.9	19/20	20	19	12.7 ± 2.4
200	1	1/18	0	--	--	1/20	1	1	11
	2	1/17	0	--	--	7/19	7	7	13.0 ± 0.8
	3	3/16	0	--	--	5/12	5	5	12.8 ± 1.1
	4	2/13	0	--	--	0/7	--	--	--
	5	5/11	0	--	--	1/7	1	1	12
	6	2/6	1	1	8	1/6	1	1	10
	7	0/4	0	--	--	0/5	--	--	--
	Undetected						2	2	10.0 ± 0
	Summary	14/18	1	1	8	15/20	17	17	12.1 ± 1.5

(a) Data from control females mated with exposed males
(b) Data from exposed females mated with control males
(c) Number of copulations detected/number of females
(d) Litters examined at d 19 of gestation or within 24 h after birth
(e) Mean ± standard deviation

TABLE I4. EFFECT OF EIGHT-WEEK INHALATION EXPOSURE TO ALLYL GLYCIDYL ETHER ON THE SUBSEQUENT REPRODUCTIVE STATUS OF FEMALE RATS ON DAY NINETEEN OF GESTATION

	Control		30 ppm		100 ppm		200 ppm	
	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)
Number of corpora lutea per dam								
Exposed males (c)	8	16.6 ± 3.7	6	17.4 ± 4.0	4	15.8 ± 2.2	0	--
Exposed females (d)	8	16.6 ± 3.7	9	16.6 ± 2.1	10	15.0 ± 1.8	8	*13.5 ± 1.6
Number of implantation sites per dam								
Exposed males	8	15.0 ± 1.5	6	**5.7 ± 5.6	4	**5.2 ± 4.9	0	--
Exposed females	8	15.0 ± 1.5	9	15.0 ± 1.5	10	13.5 ± 1.6	8	*12.6 ± 1.7
Number of resorptions per litter								
Exposed males	8	1.0 ± 0.93	6	**0	4	**0	0	--
Exposed females	8	1.0 ± 0.93	9	1.33 ± 1.32	10	2.1 ± 4.31	8	0.5 ± 0.76
Percentage resorptions per implantation site								
Exposed males	8	7.1 ± 6.74	6	*0	4	*0	0	--
Exposed females	8	7.1 ± 6.74	9	9.1 ± 8.75	10	15.5 ± 31.0	8	3.9 ± 6.11
Number of live fetuses per litter								
Exposed males	8	14.0 ± 2.2	6	**5.7 ± 5.6	4	**5.2 ± 4.9	0	--
Exposed females	8	14.0 ± 2.2	9	13.7 ± 2.1	10	12.8 ± 2.1	8	12.1 ± 1.7
Number of dead fetuses per litter								
Exposed males	8	0	6	0	4	0	0	--
Exposed females	8	0	9	0	10	0	8	0
Percentage live fetuses per implantation site								
Exposed males	8	92.9 ± 6.74	6	*100.0 ± 0	4	*100.0 ± 0	0	--
Exposed females	8	92.9 ± 6.74	9	91.0 ± 8.75	10	84.5 ± 31.0	8	96.1 ± 6.11

(a) Number of dams or litters
(b) Mean ± standard deviation
(c) Results when control female rats were mated with exposed male rats
(d) Results when exposed female rats were mated with control male rats
*$P<0.05$ vs. the controls by Dunnett's test (Dunnett, 1980)
**$P<0.01$ vs. the controls by Dunnett's test (Dunnett, 1980)

TABLE I5. EFFECT OF EIGHT-WEEK INHALATION EXPOSURE (BEFORE MATING) TO ALLYL GLYCIDYL ETHER ON MATERNAL AND FETAL WEIGHTS OF RATS ON DAY NINETEEN OF GESTATION

	Control		30 ppm		100 ppm		200 ppm	
	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)
Results when males were exposed (c)								
Body weight of pregnant dams	8	360 ± 32	6	325 ± 38	4	336 ± 29	0	--
Weight of gravid uterus	8	62 ± 11	6	**28 ± 25	4	*25 ± 21	0	--
Extrauterine weight (d)	8	298 ± 22	6	297 ± 17	4	311 ± 15	0	--
Fetal body weight								
Male	8	2.44 ± 0.13	5	2.61 ± 0.21	2	2.41 ± 0.09	0	--
Female	8	2.30 ± 0.19	4	2.54 ± 0.12	4	2.41 ± 0.20	0	--
Males/litter (percent)	8	50.7 ± 5.0	6	56.5 ± 16.0	4	57.5 ± 21.0	0	--
Placental weight								
Male fetuses	8	0.55 ± 0.08	5	0.68 ± 0.22	2	0.54 ± 0.01	0	--
Female fetuses	8	0.57 ± 0.08	4	0.66 ± 0.23	4	0.80 ± 0.31	0	--
Results when females were exposed (e)								
Body weight of pregnant dams	8	360 ± 32	9	344 ± 39	9	334 ± 17	8	332 ± 31
Weight of gravid uterus	8	62 ± 11	9	60 ± 8	9	57 ± 8	8	56 ± 8
Extrauterine weight (d)	8	298 ± 22	9	284 ± 32	8	278 ± 14	8	276 ± 29
Fetal body weight								
Male	8	2.44 ± 0.13	9	2.33 ± 0.13	9	2.48 ± 0.17	8	2.46 ± 0.15
Female	8	2.30 ± 0.19	9	2.16 ± 0.20	9	2.33 ± 0.19	8	2.31 ± 0.15
Males/litter (percent)	8	50.7 ± 5.0	9	54.1 ± 5.0	9	47.2 ± 4.4	8	50.0 ± 4.0
Placental weight								
Male fetuses	8	0.55 ± 0.08	9	0.54 ± 0.05	9	0.56 ± 0.03	8	0.57 ± 0.05
Female fetuses	8	0.57 ± 0.08	9	0.56 ± 0.04	9	0.56 ± 0.04	8	0.61 ± 0.03

(a) Number of dams or litters
(b) Mean ± standard deviation
(c) Control female rats were mated with exposed male rats.
(d) Extragestational weight was calculated by subtracting the weight of the gravid uterus from the body weight of the pregnant dam.
(e) Exposed female rats were mated with control male rats.
*$P<0.05$ vs. the controls by Dunnett's test (Dunnett, 1980)
**$P<0.01$ vs. the controls by Dunnett's test (Dunnett, 1980)

TABLE I6. SUMMARY OF MALFORMATIONS, ANOMALIES, AND VARIATIONS IN OFFSPRING FROM RATS EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR EIGHT WEEKS (a)

	Control	30 ppm	100 ppm	200 ppm
Fetal (day 19 of gestation)				
Control				
Number of litters examined	8			
Number of offspring examined	112			
Major malformations				
Cleft palate	(b) 1 (12.5)			
Umbilical hernia	(c) 1 (12.5)			
Minor anomalies				
Fore limb flexure	(b) 1 (12.5)			
Results when males were exposed (d)				
Number of litters examined		6	4	0
Number of offspring examined		34	21	0
No abnormalities were observed				
Results when females were exposed (e)				
Number of litters examined		9	9	8
Number of offspring examined		123	114	97
Major malformations				
Cleft palate		(f) 1 (11.1)		
Minor anomalies				
Brachyury		(f) 1 (11.1)		
Ectrodactyly		(f) 1 (11.1)		
Variations (stunted)		(f) 1 (11.1)		1 (12.5)
Neonatal (day 1)				
Control				
Number of litters examined	6			
Number of offspring examined	69			
Major malformations				
Anophthalmia	(g) 1 (16.7)			
Results when males were exposed (d)				
Number of litters examined		2	0	1
Number of offspring examined		9	0	8
No abnormalities were observed				
Results when females were exposed (e)				
Number of litters examined		10	10	9
Number of offspring examined		115	112	107
Minor anomalies				
Kinked tail		1 (10.0)		
Variations (stunted)			1 (10.0)	

(a) Results are expressed as number of fetuses affected. Number in parentheses is percentage of litters affected.
(b) Same fetus; litter 6585, fetus 8F
(c) Litter 68, fetus 4F
(d) Control female rats were mated with exposed male rats.
(e) Exposed female rats were mated with control male rats.
(f) Same fetus; litter 3578, fetus 12M
(g) Missing right eye was noted at necropsy at 21 days of age but not at 1 or 4 days.

TABLE I7. REPRODUCTIVE STATUS OF MATERNAL RATS AND POSTNATAL SURVIVAL OF OFFSPRING OF RATS EXPOSED FOR EIGHT WEEKS (BEFORE MATING) TO ALLYL GLYCIDYL ETHER BY INHALATION

	Control		30 ppm		100 ppm		200 ppm	
	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)
Results when males were exposed (c)								
Length of gestation (days)	7	23.1 ± 0.9	3	23.7 ± 0.6	0	--	1	23
Implantation sites per dam	7	14.0 ± 4.6	5	*6.4 ± 5.7	0	--	1	10
Pups alive on day 1	7	11.6 ± 5.5	3	6.3 ± 4.0	0	--	1	8
Pups alive on day 4	7	8.9 ± 4.7	3	0.7 ± 1.2	0	--	1	8
Pups alive on day 21	7	8.9 ± 4.7	3	0.7 ± 1.2	0	--	1	8
Pups alive on day 1 per implantation site (percent)	7	74.2 ± 35.6	3	81.5 ± 17.0	0	--	1	80
Pups alive on day 4 per pups alive on day 1 (percent)	6	77.0 ± 17.7	3	33.3 ± 57.7	0	--	1	100.0
Pups alive on day 21 per pups alive on day 4 (percent)	6	100.0 ± 0.0	1	100.0 ± 0.0	0	--	1	100.0
Results when females were exposed (d)								
Length of gestation (days)	7	23.1 ± 0.9	8	22.6 ± 0.7	9	22.8 ± 0.4	7	22.7 ± 0.5
Implantation sites per dam	7	14.0 ± 4.6	10	15.0 ± 1.9	10	14.4 ± 1.7	9	13.6 ± 1.1
Pups alive on day 1	7	11.6 ± 5.5	10	12.4 ± 2.1	10	12.7 ± 2.7	9	12.1 ± 1.4
Pups alive on day 4	7	8.9 ± 4.7	10	11.3 ± 4.1	10	11.1 ± 4.0	9	11.9 ± 1.5
Pups alive on day 21	7	8.9 ± 4.7	10	11.2 ± 4.2	10	11.1 ± 4.0	9	11.9 ± 1.5
Pups alive on day 1 per implantation site (percent)	7	74.2 ± 35.6	10	83.4 ± 14.7	10	88.3 ± 15.6	9	89.4 ± 8.3
Pups alive on day 4 per pups alive on day 1 (percent)	6	77.0 ± 17.7	10	88.0 ± 31.6	10	84.6 ± 17.5	9	98.0 ± 3.9
Pups alive on day 21 per pups alive on day 4 (percent)	6	100.0 ± 0.0	10	99.0 ± 3.0	10	100.0 ± 0.0	9	100.0 ± 0.0

(a) Number of dams or litters
(b) Mean ± standard deviation
(c) Control female rats were mated with exposed male rats.
(d) Exposed female rats were mated with control male rats.
*$P<0.05$ vs. the controls by Dunnett's test (Dunnett, 1980); statistical analysis performed on length of gestation and implantation sites per dam only.

TABLE I8. MEAN BODY WEIGHTS OF OFFSPRING OF RATS EXPOSED FOR EIGHT WEEKS BY INHALATION TO ALLYL GLYCIDYL ETHER BEFORE MATING (a)

	Days Post Partum	Control Number (a)	Control Mean (b)	30 ppm Number (a)	30 ppm Mean (b)	100 ppm Number (a)	100 ppm Mean (b)	200 ppm Number (a)	200 ppm Mean (b)
Results when males were exposed (c)									
Male offspring	1	6	6.2 ± 0.3	2	6.6 ± 1.0	0	--	1	8.0
Female offspring	1	6	6.0 ± 0.4	2	6.3 ± 0.8	0	--	1	7.6
Male offspring	4	6	10.0 ± 0.5	1	10.1	0	--	1	12.8
Female offspring	4	6	9.7 ± 0.7	1	10.9	0	--	1	12.4
Male offspring	21	6	54.6 ± 9.0	1	65.0	0	--	1	65.2
Female offspring	21	6	52.1 ± 8.4	1	60.0	0	--	1	61.0
Results when females were exposed (d)									
Male offspring	1	6	6.2 ± 0.3	10	6.7 ± 0.5	10	6.7 ±0.4	9	*6.8 ± 0.5
Female offspring	1	6	6.0 ± 0.4	10	6.3 ± 0.5	10	6.5 ±0.3	9	6.5 ± 0.4
Male offspring	4	6	10.0 ± 0.5	9	9.8 ± 1.1	10	10.2 ±1.1	9	10.4 ± 0.7
Female offspring	4	6	9.7 ± 0.7	9	9.7 ± 0.8	10	9.8 ±1.4	9	9.8 ± 0.7
Male offspring	21	6	54.6 ± 9.0	9	48.8 ± 5.8	10	52.5 ±7.8	9	53.2 ± 4.6
Female offspring	21	6	52.1 ± 8.4	9	46.1 ± 5.4	10	50.0 ±8.7	9	49.4 ± 3.9

(a) Number of dams or litters
(b) Mean ± standard deviation in grams
(c) Control female rats were mated with exposed male rats.
(d) Exposed female rats were mated with control male rats.
*P<0.05 vs. the controls by Dunnett's test (Dunnett, 1980)

TABLE I9. SUMMARY OF ABNORMALITIES, MOTILITY, AND NUMBER OF SPERM FROM THE CAUDA EPIDIDYMIS OF MALE RATS EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR EIGHT WEEKS (a)

	Control	30 ppm	100 ppm	200 ppm
Abnormal sperm (percent)	0.64 ± 0.20	0.68 ± 0.25	0.81 ± 0.31	**1.11 ± 0.26
Motility (b)	+ + +	+ + +	+ + +	+ + +
Number of sperm/g cauda ($\times 10^8$)	4.05 ± 1.73	3.78 ± 1.56	3.13 ± 1.17	3.26 ± 0.93

(a) Mean ± standard deviation; specimens were obtained from eight rats in each group, 13-14 days after the last exposure.
(b) Scored on a scale of 0 (no motile sperm) to 4 (all sperm motile)
**P<0.01 vs. the controls by Dunnett's test (Dunnett, 1980)

APPENDIX J

RESULTS OF STUDIES OF REPRODUCTIVE EFFECTS IN MICE EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION

One of 20 male mice exposed to 30 ppm, 2/19 female mice exposed to 10 ppm, and 1/20 female control mice died before the end of the 8-week studies of reproductive effects. Three control mice and one mouse exposed to 10 ppm were removed from the study because of pregnancy during the exposure period; the controls were replaced with animals from the 13-week study. The reproductive performance of exposed males and females was unaffected (Tables J2 and J3). No effect on the number of implantation sites or the size of the litters was seen (Tables J7 and J8). No deficiencies in fetal or postnatal development in offspring were detected (Tables J4 through J8). After 17 days of gestation, exencephaly was seen in one fetus from a dam exposed to 4 ppm, in one fetus from a dam exposed to 10 ppm, and in one fetus sired by a male exposed to 10 ppm (Table J6). Hydronephrosis was seen in one pup of a female exposed to 10 ppm (Table J6). No other major malformations were seen in pups born to exposed females. Spina bifida was seen in one pup sired by a male exposed to 4 ppm. Exposure had no effect on the morphology, motility, or number of sperm recovered from the cauda epididymis 13-14 days after the last exposure (Table J9).

TABLE J1. MEAN BODY WEIGHTS OF MICE IN THE EIGHT-WEEK INHALATION STUDIES OF THE REPRODUCTIVE EFFECTS OF ALLYL GLYCIDYL ETHER (a)

Concentration (ppm)	Male	Female	
		Fetal Exam Groups (b)	Postnatal Exam Groups (c)
	Before exposure		
(d) 0	25.6	20.2	20.0
(e) 0	26.4	20.5	20.0
4	25.5	20.5	20.2
10	24.8	20.2	20.8
30	24.5	19.9	19.9
	End of exposure (f)		
(d) 0	30.5	25.8	25.5
(e) 0	29.5	26.2	26.2
4	28.1	24.6	25.4
10	26.5	24.0	24.3
30	23.9	21.4	21.7
	Termination (g)		
(d) 0	--	41.8	32.5
(e) 0	28.9	39.0	31.4
4	28.3	44.4	32.5
10	28.1	42.3	32.3
30	26.2	40.6	30.1

(a) Group mean body weight in grams
(b) Groups designated for fetal examination on day 17 of gestation
(c) Groups designated for postnatal examination on day 21 post partum
(d) Mates for exposed animals
(e) Mates for control animals
(f) Animals were weighed 1 day after the end of exposure.
(g) Males were killed 13-14 days after the end of exposure.

TABLE J2. SUMMARY OF PREGNANCY STATUS OF MICE AFTER INHALATION EXPOSURE FOR EIGHT WEEKS TO ALLYL GLYCIDYL ETHER

	Control	4 ppm	10 ppm	30 ppm
Results when males were exposed (a)				
Number of females examined	20	19	19	19
Percentage of female mice with plugs	65	68	84	*95
Percentage of female mice with plugs, pregnant	92	100	94	89
Percentage of female mice without plugs	35	32	16	*5
Percentage of female mice without plugs, pregnant	100	83	100	100
Percentage of female mice pregnant	95	95	95	90
Results when females were exposed (b)				
Number of females examined	20	20	17	20
Percentage of female mice with plugs	65	*95	59	85
Percentage of female mice with plugs, pregnant	92	95	100	71
Percentage of female mice without plugs	35	*5	41	15
Percentage of female mice without plugs, pregnant	100	0	86	100
Percentage of female mice pregnant	95	90	94	75

(a) Control female mice were mated with exposed male mice.
(b) Exposed female mice were mated with control male mice.
*$P<0.05$ vs. the controls by the Fisher exact test

TABLE J3. SUMMARY OF REPRODUCTIVE PERFORMANCE OF MICE AFTER INHALATION EXPOSURE FOR EIGHT WEEKS TO ALLYL GLYCIDYL ETHER

Concentration (ppm)	Day of Mating	Results When Males Were Exposed (a)				Results When Females Were Exposed (b)			
		Copulations Detected (e)	No. of Females Impregnated	No. of Litters (c)	Total Pups/ Litter (d)	Copulations Detected (e)	No. of Females Impregnated	No. of Litters (c)	Total Pups/ Litter (d)
0	1	6/20	5	3	7.3 ± 5.5	6/20	5	3	7.3 ± 5.5
	2	4/14	4	3	9.3 ± 0.6	4/14	4	3	9.3 ± 0.6
	3	3/10	3	3	8.0 ± 1.0	3/10	3	3	8.0 ± 1.0
	4	0/7	--	--	--	0/7	--	--	--
	5	0/7	--	--	--	0/7	--	--	--
	6	0/7	--	--	--	0/7	--	--	--
	7	0/7	--	--	--	0/7	--	--	--
	Undetected		7	7			7	7	
	Summary	13/20	19	16	8.7 ± 2.9	13/20	19	16	8.7 ± 2.9
4	1	7/19	7	7	9.0 ± 1.9	5/20	5	5	10.6 ± 1.3
	2	3/12	3	3	10.7 ± 1.5	7/15	7	7	8.4 ± 2.8
	3	1/9	1	1	10	6/8	5	5	10.8 ± 2.6
	4	2/8	2	2	8.5 ± 2.1	0/2	--	--	--
	5	0/6	--	--	--	0/2	--	--	--
	6	0/6	--	--	--	0/2	--	--	--
	7	0/6	--	--	--	1/2	1	1	11
	Undetected		5	5					
	Summary	13/19	18	18	9.4 ± 1.7	19/20	18	18	9.8 ± 2.5
10	1	5/19	5	5	7.6 ± 4.4	7/17	7	7	9.9 ± 3.9
	2	4/14	3	3	10.0 ± 1.0	1/10	1	1	11
	3	5/10	5	5	8.4 ± 0.9	2/9	2	2	10.5 ± 0.7
	4	1/5	1	1	10	0/7	--	--	--
	5	0/4	--	--	--	0/7	--	--	--
	6	0/4	--	--	--	0/7	--	--	--
	7	1/4	1	1	9	0/7	--	--	--
	Undetected		3	2	10.5 ± 2.1		6	6	8.5 ± 3.1
	Summary	16/19	18	17	8.8 ± 2.6	10/17	16	16	9.5 ± 3.2
30	1	6/19	4	4	10.5 ± 1.0	12/20	7	7	9.1 ± 3.8
	2	8/13	8	8	9.8 ± 0.9	5/8	5	4	10.0 ± 0.8
	3	1/5	1	1	11	0/3	--	--	--
	4	2/4	2	2	9.0 ± 0	0/3	--	--	--
	5	0/2	--	--	--	0/3	--	--	--
	6	1/2	1	1	10	0/3	--	--	--
	7	0/1	--	--	--	0/3	--	--	--
	Undetected		1	1	5		3	3	10.0 ± 0.0
	Summary	18/19	17	17	9.8 ± 1.7	17/20	15	14	9.6 ± 2.7

(a) Data from control females mated with exposed males
(b) Data from exposed females mated with control males
(c) Litters examined at d 17 of gestation or within 24 h after birth
(d) Mean ± standard deviation
(e) Number of copulations detected/number of females

TABLE J4. EFFECT OF EIGHT-WEEK INHALATION EXPOSURE TO ALLYL GLYCIDYL ETHER ON THE SUBSEQUENT REPRODUCTIVE STATUS OF FEMALE MICE ON DAY SEVENTEEN OF GESTATION

	Control		4 ppm		10 ppm		30 ppm	
	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)
Number of corpora lutea per dam								
Exposed males (c)	6	9.0 ± 3.9	7	11.4 ± 1.5	8	*12.4 ± 1.4	8	11.8 ± 1.2
Exposed females (d)	6	9.0 ± 3.9	10	12.3 ± 1.3	5	*13.8 ± 4.5	8	11.9 ± 2.1
Number of implantation sites per dam								
Exposed males (c)	6	8.3 ± 3.7	7	9.9 ± 1.9	8	8.4 ± 3.2	8	11.1 ± 1.2
Exposed females (d)	6	8.3 ± 3.7	10	11.1 ± 0.7	5	9.6 ± 4.9	8	9.6 ± 2.6
Number of resorptions per litter								
Exposed males (c)	6	0.8 ± 0.7	7	0.6 ± 0.5	8	0.6 ± 0.7	8	0.5 ± 0.5
Exposed females (d)	6	0.8 ± 0.7	10	0.5 ± 0.7	5	0.6 ± 0.9	8	0.5 ± 0.8
Percent resorptions per implantation site								
Exposed males (c)	6	23.0 ± 38.3	7	6.3 ± 5.4	8	9.1 ± 12.0	8	4.5 ± 4.8
Exposed females (d)	6	23.0 ± 38.3	10	4.6 ± 6.5	5	4.7 ± 7.0	8	4.5 ± 6.8
Number of live fetuses per litter								
Exposed males (c)	6	7.5 ± 3.7	7	9.3 ± 2.0	8	7.8 ± 3.2	8	10.6 ± 1.3
Exposed females (d)	6	7.5 ± 3.7	10	10.6 ± 1.1	5	9.0 ± 4.5	8	9.1 ± 3.4
Number of dead fetuses per litter								
Exposed males (c)	6	0	7	0	8	0	8	0
Exposed females (d)	6	0	10	0.1 ± 0.3	5	0	8	0
Percent live fetuses per implantation site								
Exposed males (c)	6	77.0 ± 38.3	7	93.7 ± 6.5	8	90.9 ± 12.0	8	95.5 ± 4.8
Exposed females (d)	6	77.0 ± 38.3	10	95.4 ± 6.5	5	92.3 ± 7.0	8	95.6 ± 6.8

(a) Number of dams or litters
(b) Mean ± standard deviation
(c) Results when control female mice were mated with exposed male mice
(d) Results when exposed female mice were mated with control male mice
*$P < 0.05$ vs. the controls by Dunnett's test (Dunnett, 1980)

TABLE J5. EFFECT OF EIGHT-WEEK INHALATION EXPOSURE (BEFORE MATING) TO ALLYL GLYCIDYL ETHER ON MATERNAL AND FETAL WEIGHTS OF MICE ON DAY SEVENTEEN OF GESTATION

	Control		4 ppm		10 ppm		30 ppm	
	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)
Results when males were exposed (c)								
Body weight of pregnant dams (grams)	5	41.7 ± 1.3	7	41.2 ± 4.4	8	40.2 ± 6.0	8	43.8 ± 2.4
Weight of gravid uterus (grams)	5	12.1 ± 0.5	7	12.5 ± 2.2	8	10.9 ± 4.0	8	14.3 ± 1.4
Extragestational weight (grams) (d)	5	29.4 ± 0.9	7	28.7 ± 2.7	8	29.3 ± 2.9	8	29.5 ± 1.4
Fetal body weight (grams)								
Male fetuses	5	0.95 ± 0.04	7	0.95 ± 0.10	8	0.98 ± 0.11	8	0.94 ± 0.04
Female fetuses	5	0.92 ± 0.08	7	0.92 ± 0.12	8	0.93 ± 0.11	8	0.89 ± 0.04
Males/litter (percent)	5	55.1 ± 13.4	7	61.1 ± 11.9	8	40.3 ± 20.6	8	48.5 ± 9.7
Placental weight (grams)								
Male fetuses	5	0.10 ± 0.01	7	0.10 ± 0.01	8	0.10 ± 0.01	8	0.10 ± 0.01
Female fetuses	5	0.09 ± 0.01	7	0.09 ± 0.01	8	0.09 ± 0.02	8	0.09 ± 0.01
Results when females were exposed (e)								
Body weight of pregnant dams (grams)	5	41.7 ± 1.3	10	44.4 ± 1.6	5	42.3 ± 7.6	8	40.6 ± 4.9
Weight of gravid uterus (grams)	5	12.1 ± 0.5	10	14.3 ± 1.1	5	12.4 ± 6.0	8	12.4 ± 4.5
Extragestational weight (grams) (d)	5	29.4 ± 0.9	10	30.1 ± 0.9	5	29.9 ± 2.0	8	28.3 ± 1.2
Fetal body weight (grams)								
Male fetuses	5	0.95 ± 0.04	10	0.95 ± 0.05	5	0.96 ± 0.07	7	0.98 ± 0.04
Female fetuses	5	0.92 ± 0.08	10	0.88 ± 0.06	5	0.90 ± 0.08	8	0.93 ± 0.03
Males/litter (percent)	5	55.1 ± 13.4	10	49.0 ± 16.0	5	69.1 ± 25.4	8	47.9 ± 24.7
Placental weight (grams)								
Male fetuses	5	0.10 ± 0.01	10	0.10 ± 0.01	5	0.12 ± 0.04	7	0.10 ± 0.01
Female fetuses	5	0.09 ± 0.01	10	0.09 ± 0.01	4	0.09 ± 0.01	8	0.09 ± 0.03

(a) Number of dams or litters
(b) Mean ± standard deviation; no significant differences were observed by the Fisher exact test.
(c) Control female mice were mated with exposed male mice.
(d) Extragestational weight was calculated by subtracting the weight of the gravid uterus from the body weight of the pregnant dam.
(e) Exposed female mice were mated with control male mice.

TABLE J6. SUMMARY OF MALFORMATIONS, ANOMALIES, AND VARIATIONS IN OFFSPRING FROM MICE EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR EIGHT WEEKS (a)

	Control	4 ppm	10 ppm	30 ppm
Fetal (day 17 of gestation)				
Control				
Number of litters examined	5			
Number of offspring examined	45			
No abnormalities were observed				
Results when males were exposed (b)				
Number of litters examined		7	8	9
Number of offspring examined		65	62	85
Major malformations				
Exencephaly			1 (12.5)	
Results when females were exposed (c)				
Number of litters examined		10	5	8
Number of offspring examined		105	45	74
Major malformations				
Exencephaly		1 (10.0)	1 (20.0)	
Minor anomalies				
Variations (stunted)		2 (20.0)		1 (12.5)
Neonatal (day 1)				
Control				
Number of litters examined	10			
Number of offspring examined	87			
Minor anomalies				
Variations (stunted)				1 (10.0)
Results when males were exposed (b)				
Number of litters examined		11	9	9
Number of offspring examined		108	88	83
Major malformations				
Spina bifida		1 (9.1)		
Minor anomalies				
Misshapen kidney			1 (11.1)	2 (22.2)
Unilateral renal agenesis			1 (11.1)	1 (11.1)
Variations (stunted)			1 (11.1)	
Results when females were exposed (c)				
Number of litters examined		7	11	6
Number of offspring examined		65	107	61
Major malformations				
Hydronephrosis			1 (9.1)	
Minor anomalies				
Unilateral renal agenesis				1 (16.7)

(a) Results are expressed as number of fetuses affected. Number in parentheses is percentage of litters affected.
(b) Control females were bred with exposed males.
(c) Exposed females were bred with control males.

TABLE J7. REPRODUCTIVE STATUS OF MATERNAL MICE AND POSTNATAL SURVIVAL OF OFFSPRING OF MICE EXPOSED FOR EIGHT WEEKS (BEFORE MATING) TO ALLYL GLYCIDYL ETHER BY INHALATION

	Control		4 ppm		10 ppm		30 ppm	
	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)	Number (a)	Mean (b)
Results when males were exposed (c)								
Length of gestation (days)	4	18.5 ± 1.0	6	18.2 ± 0.4	7	18.3 ± 0.5	8	18.3 ± 0.5
Implantation sites per dam	12	8.3 ± 3.8	11	11.0 ± 1.2	9	10.7 ± 1.7	9	10.8 ± 1.8
Pups alive on day 1	11	8.5 ± 3.5	11	9.8 ± 1.5	9	9.8 ± 1.5	9	9.2 ± 1.8
Pups alive on day 4	11	8.4 ± 3.8	11	9.4 ± 1.4	9	9.6 ± 1.2	9	9.2 ± 1.8
Pups alive on day 21	11	8.4 ± 3.8	11	9.4 ± 1.4	9	9.6 ± 1.2	9	8.6 ± 2.4
Pups alive on day 1 per implantation sites (percent)	11	95.3 ± 8.6	11	89.3 ± 9.9	9	92.5 ± 10.9	9	85.4 ± 9.5
Pups alive on day 4 per pups alive on day 1 (percent)	11	90.9 ± 30.2	11	96.6 ± 7.8	9	98.1 ± 5.6	9	100.0 ± 0.0
Pups alive on day 21 per pups alive on day 4 (percent)	10	100.0 ± 0.0	11	100.0 ± 0.0	9	100.0 ± 0.0	9	93.0 ± 18.4
Results when females were exposed (d)								
Length of gestation (days)	4	18.5 ± 1.0	8	18.5 ± 0.8	5	18.0 ± 0.0	3	18.0 ± 0.0
Implantation sites per dam	12	8.3 ± 3.8	8	9.2 ± 3.1	11	10.8 ± 2.9	7	10.3 ± 3.7
Pups alive on day 1	11	8.5 ± 3.5	7	9.7 ± 1.7	11	9.8 ± 2.6	6	10.2 ± 1.0
Pups alive on day 4	11	8.4 ± 3.8	7	9.4 ± 1.9	11	9.7 ± 2.7	6	10.2 ± 1.0
Pups alive on day 21	11	8.4 ± 3.8	7	9.3 ± 2.1	11	9.7 ± 2.7	6	10.2 ± 1.0
Pups alive on day 1 per implantation sites (percent)	11	95.3 ± 8.6	7	94.0 ± 10.3	11	91.3 ± 6.9	6	87.2 ± 6.8
Pups alive on day 4 per pups alive on day 1 (percent)	11	90.9 ± 30.2	7	96.8 ± 5.5	11	99.0 ± 3.4	6	100.0 ± 0.0
Pups alive on day 21 per pups alive on day 4 (percent)	10	100.0 ± 0.0	7	98.0 ± 5.4	11	100.0 ± 0.0	6	100.0 ± 0.0

(a) Number of dams or litters
(b) Mean ± standard deviation
(c) Control female mice were mated with exposed male mice.
(d) Exposed female mice were mated with control male mice.

TABLE J8. MEAN BODY WEIGHTS OF OFFSPRING OF MICE EXPOSED FOR EIGHT WEEKS BY INHALATION TO ALLYL GLYCIDYL ETHER BEFORE MATING

	Days Post Partum	Control Number (a)	Control Mean (b)	4 ppm Number (a)	4 ppm Mean (b)	10 ppm Number (a)	10 ppm Mean (b)	30 ppm Number (a)	30 ppm Mean (b)
Results when males were exposed (c)									
Male offspring	1	(d,e) 10	1.50 ± 0.25	11	1.45 ± 0.16	9	1.36 ± 0.11	9	1.48 ± 0.20
Female offspring	1	(e) 9	1.37 ± 0.25	11	1.40 ± 0.16	9	1.32 ± 0.11	9	1.40 ± 0.20
Male offspring	4	10	2.62 ± 0.44	11	2.66 ± 0.33	9	2.44 ± 0.27	9	2.75 ± 0.42
Female offspring	4	10	2.54 ± 0.53	11	2.62 ± 0.42	9	2.37 ± 0.32	9	2.63 ± 0.40
Male offspring	21	10	11.8 ± 1.1	11	11.9 ± 1.1	9	11.3 ± 1.1	9	12.4 ± 1.6
Female offspring	21	10	11.0 ± 1.2	11	11.4 ± 1.1	9	10.7 ± 1.2	9	11.6 ± 1.3
Results when females were exposed (f)									
Male offspring	1	(d,e) 10	1.50 ± 0.25	7	1.38 ± 0.11	11	1.46 ± 0.23	6	1.39 ± 0.10
Female offspring	1	(e) 9	1.37 ± 0.25	7	1.38 ± 0.10	11	1.36 ± 0.15	6	1.30 ± 0.08
Male offspring	4	10	2.62 ± 0.44	7	2.46 ± 0.22	11	2.52 ± 0.42	6	2.40 ± 0.17
Female offspring	4	10	2.54 ± 0.53	7	2.51 ± 0.27	11	2.41 ± 0.29	6	2.27 ± 0.16
Male offspring	21	10	11.8 ± 1.1	7	11.5 ± 1.2	11	11.9 ± 1.9	6	11.1 ± 1.0
Female offspring	21	10	11.0 ± 1.2	7	11.3 ± 1.3	11	11.1 ± 1.2	6	10.4 ± 0.9

(a) Number of litters
(b) Mean ± standard deviation in grams; no significant differences were observed by Dunnett's test (Dunnett, 1980).
(c) Control female mice were mated with exposed male mice.
(d) One litter was composed of a single male mouse that was found cannibalized on day 4.
(e) One litter was not weighed on day 1.
(f) Exposed female mice were mated with control male mice.

TABLE J9. SUMMARY OF ABNORMALITIES, MOTILITY, AND NUMBER OF SPERM FROM THE CAUDA EPIDIDYMIS OF MALE MICE EXPOSED TO ALLYL GLYCIDYL ETHER BY INHALATION FOR EIGHT WEEKS (a)

	Control	4 ppm	10 ppm	30 ppm
Abnormal sperm (percent)	0.91 ± 0.35	0.72 ± 0.49	0.72 ± 0.47	1.25 ± 0.27
Motility (b)	+ + +	+ + +	+ + +	+ + +
Number of sperm/g cauda ($\times 10^6$)	31.0 ± 13.1	29.5 ± 12.1	24.7 ± 11.3	25.5 ± 7.4

(a) Mean ± standard deviation; specimens were obtained from eight mice in each group. No significant differences were observed by Dunnett's test (Dunnett, 1980).
(b) Scored on a scale of 0 (no motile sperm) to 4 (all sperm motile)

APPENDIX K

GENETIC TOXICOLOGY

OF ALLYL GLYCIDYL ETHER

METHODS

Salmonella Protocol: Testing was performed as reported by Canter et al. (1986). Chemicals were sent to the laboratory as coded aliquots from Radian Corporation (Austin, TX). The study chemical was incubated with the *Salmonella typhimurium* tester strains (TA98, TA100, TA1535, and TA1537) either in solvent or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver) for 20 minutes at 37° C before the addition of soft agar supplemented with L-histidine and D-biotin and subsequent plating on minimal glucose agar plates. Incubation was continued for an additional 48 hours.

Chemicals were tested in four strains. Each test consisted of triplicate plates of concurrent positive and negative controls and of at least five doses of the study chemical. The high dose was limited by toxicity or solubility but did not exceed 10 mg/plate. All positive assays were repeated under the conditions that elicited the positive response.

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

Chinese Hamster Ovary Cytogenetics Assays: Testing was performed as reported by Galloway et al. (1985) and is described briefly below. Chemicals were sent to the laboratory as coded aliquots from Radian Corporation (Austin, TX). Chemicals were tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCEs) and chromosomal aberrations both in the presence and absence of Aroclor 1254-induced male Sprague Dawley rat liver S9 and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine (BrdU)-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least three doses of the study chemical; the high dose was limited by toxicity or solubility but did not exceed 100 µg/ml.

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

In the chromosomal aberration test without S9, cells were incubated in McCoy's 5A medium with the study chemical for 8 hours; colcemid was added, and incubation was continued for 2 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. For the chromosomal aberration test with S9, cells were treated with the study chemical and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 10 hours in fresh medium, with colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9.

For the SCE test, if significant chemical-induced cell cycle delay was seen, incubation time was lengthened to ensure a sufficient number of scorable cells. The harvest time for the chromosomal aberration test was based on the cell cycle information obtained in the SCE test; if cell cycle delay was anticipated, the incubation period was extended approximately 5 hours.

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

Statistical analyses were conducted on both the slopes of the dose-response curves and the individual dose points. An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001. Chromosomal aberration data are presented as percentage of cells with aberrations. As with SCEs, both the dose-response curve and individual dose points were statistically analyzed. A statistically significant ($P<0.003$) trend test or a significantly increased dose point ($P<0.05$) was sufficient to indicate a chemical effect.

Drosophila Melanogaster Protocol: The assays for gene mutation and chromosomal translocation induction were performed as described by Yoon et al. (1985). Study chemicals were supplied as coded aliquots from Radian Corporation (Austin, TX). Initially, study chemicals were assayed in the sex-linked recessive lethal (SLRL) test by feeding to adult Canton-S wild-type males that were no more than 24 hours old. If no response was obtained, the chemical was retested by injection into adult males. If either route of administration produced a positive result, the chemical was assayed for induction of reciprocal translocations (RTs) by the same method of exposure. If, because of the physical nature of the chemical, feeding experiments were not possible, injection was selected as the method of study chemical administration, and a positive result was followed by an RT test.

Toxicity tests attempted to set concentrations of study chemical at a level that would produce 30% mortality after 72 hours of feeding or 24 hours after injection, while keeping induced sterility at an acceptable level. For the SLRL test, exposure by feeding was done by allowing Canton-S males (10-20 flies per vial) to feed for 72 hours on a solution of the study chemical in 5% sucrose. In the injection experiments, 24- to 72-hour-old Canton-S males were given a solution of the chemical dissolved in 0.7% saline or peanut oil and allowed 24 hours to recover. Exposed males were mated to three *Basc* females for 3 days and given fresh females at 2-day intervals to produce three matings of 3, 2, and 2 days; sample sperm from successive matings were treated as successively earlier postmeiotic stages. F_1 heterozygous females were allowed to mate with their siblings and then were placed in individual vials. F_1 daughters from the same parental male were kept together to identify clusters. (A cluster occurs when a number of mutants from a given male result from a single spontaneous premeiotic mutation event and is identified when the number of mutants from that male exceeds the number predicted by a Poisson distribution.) If a cluster was identified, all data from the male in question were discarded. After 17 days, presumptive lethal mutations were identified as vials containing no wild-type males; these were retested. At least two experiments were performed for each study chemical, resulting in the testing of some 5,000 treated and 5,000 control chromosomes. The only exceptions occurred when the results of the first experiment were clearly positive (induced frequency of recessive lethal mutations equal to or greater than 1%); then, the second trial was run.

Recessive lethal data were analyzed by the normal test (Margolin et al., 1983). A test result was considered to be positive if the P value was less than 0.01 and the mutation frequency in the tested group was greater than 0.10% or if the P value was less than 0.05 and the frequency in the treatment group was greater than 0.15%. A test was considered to be inconclusive if (a) the P value was between 0.05 and 0.01 but the frequency in the treatment group was between 0.10% and 0.15% or (b) the P value was between 0.10 and 0.05 but the frequency in the treatment group was greater than 0.10%. A

result was considered to be negative if the P value was greater than 0.10 or if the frequency in the treatment group was less than 0.10%.

For the RT test, the exposure regimen was the same as that for the SLRL test except that small mass matings were used (10 males and 20 females). Exposed males were mated to X.Y,y;bw;st females for 3 days and discarded. The females were transferred to fresh medium every 3-4 days for a period of about 3 weeks to produce a total of six broods. The results of the SLRL test were used to narrow the germ-cell stage most likely to be affected by the chemical; for example, if earlier germ-cell stages seemed to exhibit increased sensitivity, mating of the males was continued and translocation tests were carried out from the offspring derived from these earlier germ cell stages. F_1 males were mated individually to X.Y,y;bw;st females and the progeny were examined for missing classes, which indicate the occurrence of a translocation in the parental male. Suspected RTs were retested. The translocation data were analyzed according to the conditional binomial (Kastenbaum and Bowman, 1970).

RESULTS

Allyl glycidyl ether (concentration range of 100-10,000 µg/plate) was mutagenic in *S. typhimurium* base-substitution strains TA100 and TA1535 when tested in a preincubation protocol in the presence and absence of Aroclor 1254-induced male Sprague Dawley rat or Syrian hamster liver S9; no mutagenic activity was observed in the frame-shift strains TA98 or TA1537 with or without S9 (Canter et al., 1986; Table K1). In cytogenetic tests with CHO cells, allyl glycidyl ether induced highly significant increases in SCEs and chromosomal aberrations both with and without Aroclor 1254-induced male Sprague Dawley rat liver S9 (Table K2). In the SCE test, cultures treated with the highest concentrations tested, with and without S9, required delayed harvest to offset chemical-induced cell cycle delay; however, positive responses in the assay were obtained at concentrations that allowed normal harvest times as well as in the cultures that exhibited delay. The protocol for the chromosomal aberration test was also modifed to allow for later harvest times. Allyl glycidyl ether induced a significant increase in sex-linked recessive lethal mutations in the germ cells of male Canton-S *D. melanogaster* fed a sucrose solution containing 5,500 ppm of the chemical (Table K4); however, this same treatment with allyl glycidyl ether did not induce reciprocal translocations in the germ cells of these flies (Yoon et al., 1985; Table K5).

TABLE K1. MUTAGENICITY OF ALLYL GLYCIDYL ETHER IN *SALMONELLA TYPHIMURIUM* (a)

Strain	Dose (µg/plate)	Revertants/Plate (b)					
		−S9		+10% S9 (hamster)		+10% S9 (rat)	
		Trial 1	Trial 2	Trial 1	Trial 2	Trial 1	Trial 2
TA100	0	105 ± 1.7	159 ± 9.0	105 ± 9.8	130 ± 5.8	116 ± 13.9	135 ± 5.8
	100	177 ± 2.9	211 ± 7.9	84 ± 10.7	137 ± 6.8	123 ± 1.5	143 ± 7.8
	333	326 ± 15.3	371 ± 9.0	147 ± 8.8	172 ± 0.9	161 ± 8.4	155 ± 10.7
	1,000	904 ± 198.3	814 ± 30.5	329 ± 14.3	399 ± 5.8	382 ± 13.6	417 ± 10.5
	3,333	2,178 ± 119.4	2,047 ± 79.8	1,382 ± 21.7	1,571 ± 14.9	1,478 ± 50.1	1,388 ± 150.7
	10,000	(c) 3,312 ± 135.3	(c) 3,431 ± 15.9	3,569 ± 85.7	(c) 3,705 ± 91.3	3,726 ± 133.3	(c) 3,654 ± 63.6
Trial summary		Positive	Positive	Positive	Positive	Positive	Positive
Positive control (d)		2,407 ± 63.5	2,397 ± 25.7	2,160 ± 50.6	1,491 ± 37.0	1,125 ± 41.3	395 ± 17.1
TA1535	0	23 ± 3.8	26 ± 2.7	10 ± 1.8	10 ± 1.5	18 ± 1.2	13 ± 2.3
	100	63 ± 10.2	54 ± 5.4	9 ± 1.2	17 ± 2.2	13 ± 0.6	17 ± 3.5
	333	125 ± 10.3	166 ± 1.0	27 ± 3.8	42 ± 5.2	19 ± 7.2	29 ± 2.1
	1,000	250 ± 45.1	347 ± 9.0	119 ± 9.1	195 ± 5.7	49 ± 9.8	128 ± 7.2
	3,333	759 ± 20.2	783 ± 22.0	444 ± 27.8	516 ± 12.0	442 ± 43.6	495 ± 12.2
	10,000	(c) 525 ± 84.6	(c) 1,019 ± 26.4	(c) 454 ± 15.3	(c) 577 ± 11.9	521 ± 33.2	(c) 406 ± 91.8
Trial summary		Positive	Positive	Positive	Positive	Positive	Positive
Positive control (d)		1,373 ± 108.5	1,604 ± 61.8	115 ± 13.6	139 ± 1.7	119 ± 0.7	63 ± 0.6

Strain	Dose (µg/plate)	−S9	+S9 (hamster)	+S9 (rat)
TA1537	0	7 ± 0.7	6 ± 0.0	7 ± 1.0
	100	7 ± 2.3	8 ± 1.5	10 ± 3.2
	333	8 ± 2.6	8 ± 1.0	7 ± 2.1
	1,000	8 ± 1.3	11 ± 2.2	4 ± 1.5
	3,333	9 ± 1.7	7 ± 0.6	5 ± 1.0
	10,000	(c) 5 ± 1.2	11 ± 0.9	(c) 10 ± 2.4
Trial summary		Negative	Negative	Negative
Positive control (d)		346 ± 115	76 ± 20.7	114 ± 13.2
TA98	0	16 ± 1.8	28 ± 2.3	29 ± 3.1
	100	18 ± 2.1	27 ± 3.6	28 ± 1.2
	333	19 ± 0.9	25 ± 2.7	27 ± 2.0
	1,000	18 ± 1.2	26 ± 1.5	31 ± 5.5
	3,333	(c) 17 ± 1.2	25 ± 5.8	29 ± 2.6
	10,000	Toxic	34 ± 5.5	30 ± 2.6
Trial summary		Negative	Negative	Negative
Positive control (d)		1,579 ± 37.9	970 ± 40.2	874 ± 39.3

(a) Study performed at EG&G Mason Research Institute. The detailed protocol and data are presented in Canter et al. (1986). Cells and study compound or solvent (dimethyl sulfoxide) were incubated in the absence of exogenous metabolic activation (−S9) or with Aroclor 1254-induced S9 from male Syrian hamster liver or male Sprague Dawley rat liver. High dose was limited by toxicity or solubility but did not exceed 10 mg/plate; 0 µg/plate dose is the solvent control.
(b) Revertants are presented as mean ± standard error from three plates.
(c) Slight toxicity
(d) Positive control; 2-aminoanthracene was used on all strains in the presence of S9. In the absence of metabolic activation, 4-nitro-*o*-phenylenediamine was used with TA98, sodium azide was used with TA100 and TA1535, and 9-aminoacridine was used with TA1537.

TABLE K2. INDUCTION OF SISTER CHROMATID EXCHANGES IN CHINESE HAMSTER OVARY CELLS BY ALLYL GLYCIDYL ETHER (a)

Compound	Dose (μg/ml)	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hours in BrdU	Relative SCEs/ Chromosome (percent) (b)
−S9 (c)								
Trial 1--Summary: Positive								
Dimethyl sulfoxide		50	1,017	423	0.41	8.5	25.5	
Allyl glycidyl ether	1	50	1,026	763	0.74	15.3	25.5	(d) 78.80
	3.3	50	1,033	921	0.89	18.4	25.5	(d) 114.36
	10	50	1,028	1,238	1.20	24.8	25.5	(d) 189.55
Mitomycin C	0.0015	50	1,033	737	0.71	14.7	25.5	(d) 71.54
	0.01	5	102	198	1.94	39.6	25.5	(d) 366.72
Trend test: P<0.001								
Trial 2--Summary: Positive								
Dimethyl sulfoxide		20	406	177	0.43	8.9	25.6	
Allyl glycidyl ether	30	20	405	586	1.44	29.3	25.6	(d) 231.89
	39.8	20	416	838	2.01	41.9	(e) 34.0	(d) 362.07
	50.2	20	416	932	2.24	46.6	(e) 34.0	(d) 413.90
Mitomycin C	0.0015	20	408	282	0.69	14.1	25.6	(d) 58.54
	0.01	5	98	188	1.91	37.6	25.6	(d) 340.03
Trend test: P<0.001								
+S9 (f)								
Trial 1--Summary: Positive								
Dimethyl sulfoxide		50	1,032	598	0.57	12.0	25.5	
Allyl glycidyl ether	3.3	50	1,043	777	0.74	15.5	25.5	(d) 28.56
	10	50	1,023	772	0.75	15.4	25.5	(d) 30.23
	33.4	50	1,032	1,010	0.97	20.2	(e) 33.3	(d) 68.90
Cyclophosphamide	0.4	50	1,030	943	0.91	18.9	25.5	(d) 58.00
	2	5	104	189	1.81	37.8	25.5	(d) 213.62
Trend test: P<0.001								
Trial 2--Summary: Positive								
Dimethyl sulfoxide		20	415	249	0.6	12.5	25.6	
Allyl glycidyl ether	60	20	413	367	0.88	18.4	(e) 34.0	(d) 48.10
	79.5	20	419	443	1.05	22.2	(e) 34.0	(d) 76.21
	100	20	414	465	1.12	23.3	(e) 34.0	(d) 87.20
Cyclophosphamide	0.4	20	415	466	1.12	23.3	25.6	(d) 87.15
	2	5	106	249	2.34	49.8	25.6	(d) 291.51
Trend test: P<0.001								

TABLE K2. INDUCTION OF SISTER CHROMATID EXCHANGES IN CHINESE HAMSTER OVARY CELLS BY ALLYL GLYCIDYL ETHER (Continued)

(a) Study performed at Litton Bionetics, Inc. SCE = sister chromatid exchange; BrdU = bromodeoxyuridine. A detailed description of the SCE protocol is presented by Galloway et al. (1985). Briefly, Chinese hamster ovary cells were incubated with study compound or solvent (dimethyl sulfoxide) as described in (c) and (e) below and cultured for sufficient time to reach second metaphase division. Cells were then collected by mitotic shake-off, fixed, air dried, and stained.
(b) Percentage change in the value of SCEs/chromosome for exposed culture compared with that for solvent control culture. An increase of 20% or more was considered to be a significant response.
(c) In the absence of S9, Chinese hamster ovary cells were incubated with study compound or solvent for 2 hours at 37° C. Then BrdU was added, and incubation was continued for 24 hours. Cells were washed, fresh medium containing BrdU and colcemid was added, and incubation was continued for 2-3 hours.
(d) More than a 20% increase over the solvent controls
(e) Because some chemicals induce a delay in the cell division cycle, harvest times are occasionally extended to maximize the proportion of second division cells available for analysis.
(f) In the presence of S9, cells were incubated with study compound or solvent for 2 hours at 37° C. Cells were then washed, and medium containing BrdU was added. Cells were incubated for a further 26 hours, with colcemid present for the final 2-3 hours. S9 was from the liver of Aroclor 1254-induced male Sprague Dawley rats.

TABLE K3. INDUCTION OF CHROMOSOMAL ABERRATIONS IN CHINESE HAMSTER OVARY CELLS BY ALLYL GLYCIDYL ETHER (a)

−S9 (b) Dose (µg/ml)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs	+S9 (c) Dose (µg/ml)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells with Abs
Trial 1--Harvest time: 21.3 hours (d)					Harvest time: 21.3 hours (d)				
Dimethyl sulfoxide					Dimethyl sulfoxide				
	100	2	0.02	2.0		100	3	0.03	3.0
Allyl glycidyl ether					Allyl glycidyl ether				
60	100	7	0.07	6.0	130.2	100	6	0.06	6.0
64.8	100	13	0.13	*11.0	150	100	17	0.17	*13.0
70.7	100	20	0.20	*14.0	176	25	62	2.48	*68.0
Summary: Positive					Summary: Positive				
Mitomycin C					Cyclophosphamide				
0.025	100	12	0.12	11.0	2.5	100	4	0.04	4.0
0.0625	25	17	0.68	36.0	12.5	25	8	0.32	28.0
Trend test (e): P<0.001					Trend test: P<0.001				
Trial 2--Harvest time: 20.5 hours (d)									
Dimethyl sulfoxide									
	50	3	0.06	4.0					
Allyl glycidyl ether									
74.7	50	25	0.50	*30.0					
80.0	50	9	0.18	12.0					
90.0	50	28	0.56	*30.0					
Summary: Positive									
Mitomycin C									
0.0250	50	5	0.10	8.0					
0.0625	25	8	0.32	28.0					
Trend test: P=0.004									

(a) Study performed at Litton Bionetics, Inc. Abs = aberrations. A detailed presentation of the technique for detecting chromosomal aberrations is found in Galloway et al. (1985). Briefly, Chinese hamster ovary cells were incubated with study compound or solvent (dimethyl sulfoxide) as indicated in (b) and (c). Cells were arrested in first metaphase by addition of colcemid and harvested by mitotic shake-off, fixed, and stained in 6% Giemsa.
(b) In the absence of S9, cells were incubated with study compound or solvent for 8-10 hours at 37° C. Cells were then washed, and fresh medium containing colcemid was added for an additional 2-3 hours followed by harvest.
(c) In the presence of S9, cells were incubated with study compound or solvent for 2 hours at 37° C. Cells were then washed, medium was added, and incubation was continued for 8-10 hours. Colcemid was added for the last 2-3 hours of incubation before harvest. S9 was from the liver of Aroclor 1254-induced male Sprague Dawley rats.
(d) Because of significant chemical-induced cell cycle delay, incubation time prior to addition of colcemid was lengthened to provide sufficient metaphases at harvest.
(e) Statistical analysis performed on the "percent aberrant cells" values.
*P<0.05

TABLE K4. INDUCTION OF SEX-LINKED RECESSIVE LETHAL MUTATIONS IN *DROSOPHILA MELANOGASTER* BY ALLYL GLYCIDYL ETHER (a)

Route of Exposure	Dose (ppm)	Incidence of Deaths (percent)	Incidence of Sterility (percent)	No. of Lethals/No. of X Chromosomes Tested			Overall Total (b)
				Mating 1	Mating 2	Mating 3	
Feeding	5,500	13	9	15/3,142	19/2,720	24/2,744	58/8,606 (0.67%)
	0			1/2,372	1/2,282	1/2,216	3/6,870 (0.04%)

(a) Study performed at Bowling Green State University. A detailed protocol of the sex-linked recessive lethal assay is presented by Yoon et al. (1985). Exposure by feeding was done by allowing 24-hour-old Canton-S males to feed for 3 days on a solution of the study chemical dissolved in 5% sucrose. Exposed males were mated to three *Basc* females for 3 days and given fresh females at 2-day intervals to produce three broods of 3, 2, and 2 days; sample sperm from successive matings were treated as spermatozoa (mating 1), spermatids (mating 2), and spermatocytes (mating 3). F_1 heterozygous females were crossed to their siblings and placed in individual vials. F_1 daughters from the same parental male were kept together to identify clusters; no clusters were found. After 17 days, presumptive lethal mutations were identified as vials containing no wild-type males; these were retested. Results were significant at the 5% level (Margolin et al., 1983).
(b) Combined total of number of lethal mutations/number of X chromosomes tested for three mating trials

TABLE K5. INDUCTION OF RECIPROCAL TRANSLOCATIONS IN *DROSOPHILA MELANOGASTER* BY ALLYL GLYCIDYL ETHER (a)

Route of Exposure	Dose (ppm)	Transfers Translocations/Total F_1 Tested					Total Number of Tests	Total Number of Translocations	Total Translocations (percent)
		1	2	3	4	5			
Feeding	5,500	0/1,169	0/1,117	0/1,196	0/1,125	0/996	5,693	0	0.00
Historical control	0						116,163	2	0.00

(a) Study performed at Bowling Green State University. A detailed protocol of the reciprocal translocation assay is presented by Yoon et al. (1985). Exposed males were mated to three X.Y,y;bw;st females for 3 days and discarded. The females were transferred to fresh medium every 3-4 days to produce a total of six cultures, and then they were discarded. In this manner, sample sperm from successive cultures were stored for increasing lengths of time. Individual F_1 males were backcrossed to X.Y,y;bw;st females, and the F_2 were screened for pseudolinkage. This procedure allows the recovery of translocations involving the Y, second, or third chromosomes in any combination. Presumptive translocations were retested. Results were not significant at the 5% level (Kastenbaum and Bowman, 1970).

APPENDIX L

AUDIT SUMMARY

APPENDIX L. AUDIT SUMMARY

The pathology specimens, experimental data, study documents, and draft (February 1989) of NTP Technical Report No. 376 for the 2-year studies of allyl glycidyl ether in rats and mice were audited for the National Institute of Environmental Health Sciences (NIEHS) at the National Toxicology Program (NTP) Archives by quality assurance contractors. The audit included review of:

(1) All records concerning animal receipt, quarantine, randomization, and disposition prior to study start.
(2) All inlife records including protocol, correspondence, animal identification, animal husbandry, environmental conditions, dosing, external masses, mortality, and serology.
(3) Body weight and clinical observation data; all data were scanned before individual data for a random 10% sample of animals in each study group were reviewed in detail.
(4) All study chemistry records.
(5) All postmortem records for individual animals concerning date of death, disposition code, condition code, tissue accountability, correlation of masses or clinical signs recorded at or near the last inlife observation with gross observations and microscopic diagnoses, consistency of data entry on necropsy record forms, and correlation between gross observations and microscopic diagnoses.
(6) Inventory for wet tissue bags from all animals and residual wet tissues from a random 20% sample of animals in each study group, plus other relevant cases, to evaluate the integrity of individual animal identity and the thoroughness of necropsy and trimming procedure performance.
(7) Blocks and slides of tissues from a random 20% sample of animals from each study group, plus animals with less than complete or correct identification, to examine for proper inventory, labeling, matching of tissue sections, and preservation.
(8) All microscopic diagnoses for a random 10% sample of animals, plus 100% of the changes in diagnoses made to preliminary pathology tables, to verify their incorporation into the final pathology tables.
(9) The extent of correlation between the data, factual information, and procedures for the 2-year studies presented in the preliminary draft of the Technical Report and the study records available at the NTP Archives.

Procedures and events for the exposure phase of the studies were documented adequately, with the exception that records needed to document part or all of the following were not at the Archives: chamber-room air change rate; room light cycle; type of cage, feeder, and cleaning agents used; and feed storage records. Review of the archival records indicated that protocol-specified procedures for animal care were followed adequately. Records that documented the generation, analysis, distribution, and delivery of doses to animals were accurate. Review of body weight records for mice showed that all recalculated mean values were correct.

Data entries on necropsy forms were made appropriately for rats and mice. The external masses recorded at the last inlife observation period correlated well with observations made at necropsy (104/108 in rats and 22/22 in mice correlated). The date of death recorded at necropsy for each unscheduled-death animal had matching entries in the inlife records for 166/190 rats and 55/61 mice; the majority of the discrepant date-of-death entries involved 1 day. All of the discrepancies could be attributed to transcription errors, and the influence on the survival-adjusted statistical analyses was gauged to be minimal. The reason for animal removal recorded among the inlife records was in agreement with the disposition code recorded at necropsy for 286/300 rats and 294/300 mice. Fifteen of the 20 mode-of-death discrepancies involved either moribund animals that died before they could be killed, animals that died during the termination period, or data entry errors that had no effect on overall survival values; however, discrepancies involving 2 rats suggested that the actual number of survivors for the high dose male and control female groups were 7 and 23 (rather than 8 and 24), respectively. The records included original observations to indicate that the deaths of one rat and two

mice were accidental rather than natural or by moribund kill; these discrepancies would affect the survival-adjusted statistical analyses only slightly. The condition code assigned to each animal at necropsy was consistent with gross observations and disposition code for all rats and mice.

An individual animal identifier (ear tag) was present and correct in the residual tissue bags for each of the 49 rats and 44 mice examined. A total of 8 untrimmed potential lesions were found in the wet tissues of 49 rats examined, and 1 was found in those of 44 mice examined. Intestinal segments (6-55 cm) were opened incompletely in 19/49 rats and 1/44 mice examined; however, no untrimmed potential lesions were evident by external examination, and all other organs had been opened or incised properly. Each gross observation made at necropsy had a corresponding microscopic diagnosis for all but seven in rats and six in mice. Blocks and slides were present and labeled correctly; corresponding tissue sections in blocks and on slides matched each other properly, with the possible exception of six questionable matches in mice. All post-Pathology Working Group changes in diagnoses had been incorporated in the final pathology tables. The P values for the incidences of tumors given in the Technical Report are the same as those in the final pathology tables at the Archives.

This summary describes general audit findings and the extent to which the data and factual information presented in the Technical Report are supported by records at the NTP Archives. Full details are presented in audit reports that are on file at the NIEHS.