NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 234

CARCINOGENESIS BIOASSAY OF ALLYL ISOTHIOCYANATE

(CAS NO. 57-06-7)

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

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

NATIONAL TOXICOLOGY PROGRAM

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

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

NTP TECHNICAL REPORT
ON THE

CARCINOGENESIS BIOASSAY OF ALLYL ISOTHIOCYANATE (CAS NO. 57-06-7) IN F344/N RATS AND B6C3F$_1$ MICE (GAVAGE STUDY)

NATIONAL TOXICOLOGY PROGRAM
Box 12233
Research Triangle Park
North Carolina 27709
and
Bethesda, Maryland 20205

October 1982

NTP-81-36
NIH Publication No. 83-1790

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

NOTE TO THE READER

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

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

Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room A-306, Landow Building, Bethesda, MD 20205 (301-496-1152) or at Research Triangle Park, NC 27709 (919-541-3991).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP.

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650).

Single copies of this carcinogenesis bioassay technical report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

TABLE OF CONTENTS

Page

Abstract 7
Contributors 8
Reviewers 10
Summary of Peer Review Comments 11

I. Introduction 13
II. Materials and Methods 17
Chemical Analysis 18
Dosage Preparation 18
Prechronic Studies 18
Single-Dose Study 18
Fourteen-Day Study 19
Thirteen-Week Study 19
Chronic Study 19
Study Design 19
Clinical Examinations and Pathology 19
Data Recording and Statistical Methods 20
III. Results 25
Rats 26
Prechronic Studies 26
Single-Dose Study 26
Fourteen-Day Study 26
Thirteen-Week Study 27
Chronic Study 28
Body Weights and Clinical Signs 28
Survival 29
Pathology and Statistical Analyses of Results 30
Mice 40
Prechronic Studies 40
Single-Dose Study 40
Fourteen-Day Study 40
Thirteen-Week Study 40
Chronic Study 42
Body Weights and Clinical Signs 42
Survival 43
Pathology and Statistical Analyses of Results 44
IV. Discussion and Conclusions 51
V. References 55

TABLES

Table 1 Experimental Design and Materials and Methods 21
Table 2 Dosage, Survival, and Mean Body Weights of Rats Receiving Allyl Isothiocyanate by Gavage for 14 Days 26
Table 3 Incidence of Compound-Related Effects Observed in Rats at Necropsy in the 14-Day Study of Allyl Isothiocyanate 27
Table 4 Dosage, Survival, and Mean Body Weights of Rats Administered Allyl Isothiocyanate by Gavage for 13 Weeks 27
Table 5 Incidence of Rats with Bladder Lesions in the Chronic Study with Allyl Isothiocyanate 30
Table 6 Analysis of Primary Tumors in Male Rats 31
Table 7 Analysis of Primary Tumors in Female Rats 36
Table 8 Dosage and Survival of Mice Administered a Single Dose of Allyl Isothiocyanate in Corn Oil by Gavage 40

Table 9 Dosage, Survival, and Mean Body Weights of Mice Receiving Allyl Isothiocyanate by Gavage for 14 Days 41
Table 10 Dosage, Survival, and Mean Body Weights of Mice Administered Allyl Isothiocyanate by Gavage for 13 Weeks 41
Table 11 Analysis of Primary Tumors in Male Mice 45
Table 12 Analysis of Primary Tumors in Female Mice 47

FIGURES

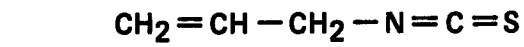
Figure 1 Growth Curves for Rats Administered Allyl Isothiocyanate by Gavage 28
Figure 2 Survival Curves for Rats Administered Allyl Isothiocyanate by Gavage 29
Figure 3 Growth Curves for Mice Administered Allyl Isothiocyanate by Gavage 42
Figure 4 Survival Curves for Mice Administered Allyl Isothiocyanate by Gavage 43
Figure 5 Infrared Absorption Spectrum of Allyl Isothiocyanate (Lot No. 532251) 135
Figure 6 Nuclear Magnetic Resonance Spectrum of Allyl Isothiocyanate (Lot No. 532251) 136

APPENDIXES

Appendix A Summary of the Incidence of Neoplasms in Rats Administered Allyl Isothiocyanate by Gavage 59
Table A1 Summary of the Incidence of Neoplasms in Male Rats Administered Allyl Isothiocyanate in Corn Oil by Gavage 60
Table A2 Summary of the Incidence of Neoplasms in Female Rats Administered Allyl Isothiocyanate in Corn Oil by Gavage 65
Table A3 Individual Animal Tumor Pathology of Male Rats in the 2-Year Study of Allyl Isothiocyanate 68
Table A4 Individual Animal Tumor Pathology of Female Rats in the 2-Year Study of Allyl Isothiocyanate 74
Appendix B Summary of the Incidence of Neoplasms in Mice Administered Allyl Isothiocyanate by Gavage 81
Table B1 Summary of the Incidence of Neoplasms in Male Mice Administered Allyl Isothiocyanate in Corn Oil by Gavage 82
Table B2 Summary of the Incidence of Neoplasms in Female Mice Administered Allyl Isothiocyanate in Corn Oil by Gavage 86
Table B3 Individual Animal Tumor Pathology of Male Mice in the 2-Year Study of Allyl Isothiocyanate 90
Table B4 Individual Animal Tumor Pathology of Female Mice in the 2-Year Study of Allyl Isothiocyanate 96
Appendix C Summary of the Incidence of Nonneoplastic Lesions in Rats Administered Allyl Isothiocyanate by Gavage 103
Table C1 Summary of the Incidence of Nonneoplastic Lesions in Male Rats Administered Allyl Isothiocyanate in Corn Oil by Gavage 104
Table C2 Summary of the Incidence of Nonneoplastic Lesions in Female Rats Administered Allyl Isothiocyanate in Corn Oil by Gavage 110

Appendix D Summary of the Incidence of Nonneoplastic Lesions in Mice Administered Allyl Isothiocyanate by Gavage 115
Table D1 Summary of the Incidence of Nonneoplastic Lesions in Male Mice Administered Allyl Isothiocyanate in Corn Oil by Gavage 116
Table D2 Summary of the Incidence of Nonneoplastic Lesions in Female Mice Administered Allyl Isothiocyanate in Corn Oil by Gavage 122
Appendix E Analysis of Allyl Isothiocyanate Lot No. 532251 (Midwest Research Institute) 131
Appendix F Analysis of Allyl Isothiocyanate in Corn Oil for Stability of Allyl Isothiocyanate 137
Appendix G Analysis of Allyl Isothiocyanate in Corn Oil for Concentrations of Allyl Isothiocyanate 139
Table G1 Analysis of Allyl Isothiocyanate in Corn Oil for Concentrations of Allyl Isothiocyanate 140
Appendix H Cumulative Mean Body Weight Change of Rats and Mice Administered Allyl Isothiocyanate by Gavage in the Chronic Study 141
Table H1 Cumulative Mean Body Weight Change (Relative to Controls) of Rats Administered Allyl Isothiocyanate by Gavage 142
Table H2 Cumulative Mean Body Weight Change (Relative to Controls) of Mice Administered Allyl Isothiocyanate by Gavage 142

CARCINOGENESIS BIOASSAY OF ALLYL ISOTHIOCYANATE



ALLYL ISOTHIOCYANATE

CAS NO. 57-06-7
C_4H_5NS Mol. Wt. 99.16

ABSTRACT

A 2-year carcinogenesis bioassay of food-grade allyl isothiocyanate (greater than 93% purity), a flavoring agent, was conducted by administering 12 or 25 mg/kg allyl isothiocyanate in corn oil five times per week by gavage to groups of 50 F344/N rats and 50 B6C3F1 mice of each sex for 103 weeks. Groups of 50 rats and 50 mice of each sex received corn oil alone and served as vehicle controls.

A single-dose study, a 14-day study, and a 13-week study were performed before the chronic study was conducted. Pathologic findings seen in the 14-day study at 50 mg/kg included a thickened mucosal surface of the stomach in rats and mice and a thickened urinary bladder wall in male mice. No gross or microscopic lesions were seen at the highest dose level (25 mg/kg) in the 13-week study.

In the chronic study, survival of dosed and control rats of each sex was comparable. Throughout the study, the mean body weights of high-dose male rats were lower than those of the controls, while during the last half of the study the mean body weights of the low-dose and high-dose female rats were higher than the mean body weights of the control animals. Final body weights in control and dosed groups were comparable.

Transitional-cell papillomas in the urinary bladder occurred in dosed male rats with a statistically significant trend ($P<0.05$; controls, 0/49, 0%; low-dose, 2/49, 4%; high-dose, 4/49, 8%). This tumor has not been observed among 568 untreated male control F344/N rats at this laboratory. The incidence of transitional-cell papillomas in male vehicle control rats in all laboratories in the NCI/NTP Bioassay Program is 1/994 (0.1%). Epithelial hyperplasia in the urinary bladder was also observed at increased incidences in dosed male rats (0/49, 1/49, 6/49). The hyperplasia did not occur in the same animals that had papillomas.

Fibrosarcomas in the subcutaneous tissue occurred in female rats with a statistically significant positive trend ($P<0.05$; controls, 0/50, 0%; low-dose, 0/50, 0%; high-dose, 3/50, 6%), but the incidence in the high-dose group was not significant when compared with that in the control group. The historical incidence of this lesion is 1/591 (0.2%) in untreated control female F344/N rats at this laboratory and 9/999 (0.9%) in female gavage control rats in all laboratories in the Bioassay Program.

Survival of control and dosed female mice, although comparable, was unusually low. Mean body weights of high-dose mice of each sex were higher than those of the controls throughout most of the study. Final body weights in control and dosed groups were comparable. The mice probably did not receive the maximum tolerated dose of allyl isothiocyanate.

The increased incidence of cytoplasmic vacuolization in the liver of dosed male mice was related to administration of allyl isothiocyanate (controls, 2/49, 4%; low-dose, 8/49, 16%; high-dose, 13/50, 26%).

Under the conditions of this bioassay, allyl isothiocyanate was carcinogenic for male F344/N rats, causing transitional-cell papillomas in the urinary bladder. Evidence for associating allyl isothiocyanate with subcutaneous fibrosarcomas in female F344/N rats was equivocal. Allyl isothiocyanate was not carcinogenic for B6C3F1 mice of either sex.

CONTRIBUTORS

The bioassay of allyl isothiocyanate was conducted at Southern Research Institute under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The chronic study was begun in March 1978 and completed in April 1980.

Principal Contributors at Southern Research Institute
Southern Research Institute
2000 Ninth Avenue South
Birmingham, Alabama 35255
(Conducted bioassay and evaluated tissues)

Dr. J. D. Prejean
Principal Investigator

Dr. D. Giles
Pathologist

Dr. D. R. Farnell
Pathologist

Dr. R. B. Thompson
Pathologist

Dr. J. C. Peckham
Pathologist

Ms. L. Burford
Chemist

Ms. R. James
Chemist

Mrs. J. Belzer
Animal Care and Chemical Administration

Mr. J. Bowers
Animal Care and Chemical Administration

Mr. I. Brown
Animal Care and Chemical Administration

Principal Contributors at Tracor Jitco
Tracor Jitco, Inc.
1776 East Jefferson Street
Rockville, Maryland 20852
(Prepared preliminary summary report)

Dr. J. Keller
Director, Bioassay

Mr. E. Cremmins
Technical Editor

Ms. C. E. Dean
Production Editor

Dr. A. Jacobs
Bioscience Writer

Dr. J. Joiner
Statistician

Ms. M. Levy
Technical Editor

Dr. S. Olin
Program Associate Director

Ms. L. Scheer
Production Editor

Dr. M. Stedham
Pathologist

Dr. W. Theriault
Reports Manager

Dr. J. Tomaszewski
Chemist

Mr. J. Warner
Statistician

Principal Contributors at the National Toxicology Program,
National Institute of Environmental Health Sciences
National Toxicology Program
Box 12233
Research Triangle Park
North Carolina 27709
and
Landow Building
Bethesda, Maryland 20205
(Evaluated the experiment, interpreted
results, and reported findings)

Dr. June K. Dunnick (Chemical Manager)
Dr. J. Fielding Douglas
Dr. Charles K. Grieshaber
Dr. Larry Hart
Dr. Joseph Haseman
Dr. James E. Huff
Dr. C. W. Jameson
Dr. Ernest E. McConnell
Dr. John A. Moore
Dr. Sherman F. Stinson
Dr. Raymond Tennant
Dr. Jerrold M. Ward

The pathology report and selected slides were evaluated on February 18, 1981 by the NTP Pathology Working Group, which included Drs. J. Ward, D. Goodman (Clement Associates), R. Kovatch (Tracor Jitco), S. Stinson, G. Reznik, G. Boorman, E. McConnell, and B. Gupta.

The chemicals used in this bioassay of allyl isothiocyanate were analyzed by the Midwest Research Institute, 425 Volker Blvd., Kansas City, Missouri 64110, and analysis of the corn oil mixtures and reanalysis of the bulk chemical were done by Southern Research Institute.

REVIEWERS

National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee

Margaret Hitchcock, Ph.D. (Chairperson and Principal Reviewer)
John B. Pierce Foundation Laboratory
New Haven, Connecticut

Curtis Harper, Ph.D.
University of North Carolina
School of Medicine
Chapel Hill, North Carolina

Alice Whittemore, Ph.D. *
Stanford University
School of Medicine
Palo Alto, California

Ad Hoc Subcommittee Panel of Experts

Gary Williams, M.D. (Principal Reviewer)
Chief of Experimental Pathology
American Health Foundation
Valhalla, New York

Norman Breslow, Ph.D.
University of Washington
School of Biostatistics
Seattle, Washington

Joseph Highland, Ph.D. *
Environmental Defense Fund
Washington, D.C.

Frank Mirer, Ph.D.
International Union
United Auto Workers
Detroit, Michigan

Sheldon D. Murphy, Ph.D. *
Professor of Toxicology
University of Texas Medical School
Houston, Texas

Svend Nielsen, D.V.M., Ph.D. *
Professor of Pathology
The University of Connecticut
Storrs, Connecticut

Bernard Schwetz, Ph.D. *
Dow Chemical U.S.A.
Toxicology Research Laboratory
Midland, Michigan

Roy Shore, Ph.D.
New York University Medical Center
Health Survey Unit
New York, New York

James Swenberg, D.V.M., Ph.D.
Chemical Industry Institute
of Toxicology
Research Triangle Park,
North Carolina

*Unable to attend June 23, 1981 meeting

SUMMARY OF PEER REVIEW COMMENTS ON THE BIOASSAY OF ALLYL ISOTHIOCYANATE

On June 23, 1981, this carcinogenesis bioassay report on allyl isothiocyanate underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts at an open meeting held in Building 101, National Institute of Environmental Health Sciences, Research Triangle Park, NC.

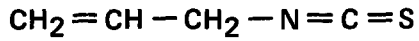
Dr. Williams, as a principal reviewer for the report on the bioassay of allyl isothiocyanate, agreed with the conclusions that, under the conditions of the bioassay, allyl isothiocyanate was carcinogenic to male F344/N rats, causing transitional-cell papillomas in the urinary bladder. Evidence for associating allyl isothiocyanate with subcutaneous fibrosarcomas in female rats was equivocal. The chemical was not carcinogenic for B6C3F1 mice of either sex. He stated that the discussion should emphasize that this compound was associated with only a low incidence of benign bladder tumors under conditions of exposure that are known to affect the physiology of urine excretion.

As the second principal reviewer, Dr. Hitchcock said there was quite low survival in control and high-dose female mice and suggested that some explanation should have been given for this. She noted the incidence of eye lesions which may have been due to groups of rats being housed near the light source without rotation of cages. Dr. Shore asked whether attention could be given to balancing cage position in the room. Dr. G. Boorman, NTP, replied that one problem with cage rotation is that it may enhance the chances for gavage errors; he further stated that the NTP was investigating this recurring phenomenon and would consider the option of cage rotation as well as reduced light intensity. Dr. Hitchcock asked that recent negative results with *Salmonella* be mentioned. Dr. Swenberg said that the discussion should include comment that allyl isothiocyanate may possibly be working as a tumor promoter.

Dr. Williams moved that the report on the bioassay of allyl isothiocyanate be accepted. Dr. Hitchcock accepted the motion, and the report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION



ALLYL ISOTHIOCYANATE

CAS NO. 57-06-7
C_4H_5NS Mol. Wt. 99.16

Allyl isothiocyanate is the major component in volatile oil of mustard, a flavoring agent prepared from seeds of black mustard (*Brassica nigra*) (Life Sciences Research Office, 1975). Synthetically prepared allyl isothiocyanate and volatile oil of mustard are approved by the U.S. Food and Drug Administration for use as flavoring agents (U.S. CFR, 1979); the Food Chemicals Codex (1972) specifies that the oil should contain not less than 93% allyl isothiocyanate. Allyl isothiocyanate is also found in cabbage, broccoli, kale, cauliflower, and horseradish (Mitchell and Jordan, 1974; Life Sciences Research Office, 1975; Hall, 1973).

Volatile oil of mustard is used in pickling spices and imitation pineapple flavoring (Kirk-Othmer, 1966). Allyl isothiocyanate may be present in the following foods: syrups (10-88 ppm), meats (87 ppm), condiments (52 ppm), baked goods (5.2 ppm), candy, ice cream, and ices (0.50 ppm), and nonalcoholic beverages (0.02-0.50 ppm) (Life Sciences Research Office, 1975). Allyl isothiocyanate is also used as a denaturant for alcohol and as a medicinal counter-irritant (Merck Index, 1976; Kirk-Othmer, 1965).

Approximately 33,000 pounds of allyl isothiocyanate were used by the food industry in the United States in 1970 (Life Sciences Research Office, 1975). The amount of synthetic allyl isothiocyanate produced in 1979 exceeded 1,000 pounds, but specific production figures are not available (USITC, 1979). Thirty-two thousand metric tons of mustard seed were imported into the United States in 1978 (Kirk-Othmer, 1980).

The oral LD_{50} value of allyl isothiocyanate is reported to be 339 mg/kg for Osborne-Mendel rats (Jenner et al., 1964) and 490 mg/kg for male rats of an unspecified strain (Vernot et al., 1977). The subcutaneous LD_{50} value for white mice is 80 mg/kg (Klesse and Lukoschek, 1955).

Administration of allyl isothiocyanate has been shown to affect various functions and organs in the rat. Radioiodine uptake by the thyroid was depressed and the relative weight of the thyroid was increased in male Wistar rats administered 2-to 5-mg doses of allyl isothiocyanate by gavage daily for 1 to 60 days (Langer and Greer, 1968; Langer and Stole, 1965). Hyperplastic areas were observed in the thyroid of female Holtzman rats 12 days after they received two 100 mg/kg subcutaneous doses of allyl isothiocyanate (Nishie and Daxenbichler, 1980). The blood coagulation time for male Sprague-Dawley rats given daily 0.5 mg intraperitoneal injections of allyl isothiocyanate for 30 days was 60% of the value for controls (Muztar et al., 1979b). A twofold increase in urine volume, an increase in the total amount of uric acid, creatinine, and glucose excreted during a 24-hour period, and an increase in the concentration of uric acid in the urine compared with that of controls were observed in male Sprague-Dawley rats fed diets containing 100 or 300 ppm allyl isothiocyanate (Muztar et al., 1979a; Muztar et al., 1979b).

Epithelial hyperplasia of the nonglandular portion of the stomach, with acute to subacute ulcers 2 to 6.5 mm in diameter, was observed in all Osborne-Mendel rats of either sex administered 50 mg/kg allyl isothiocyanate by gavage for 20 days and in 50% of the rats receiving 20 mg/kg. Minor inflammatory foci were observed in the liver of rats receiving the higher dose (Hagan et al., 1967).

Allyl isothiocyanate was not mutagenic in *Bacillus subtilis* H17 and M45, *Escherichia coli* WP2, or *Salmonella typhimurium* TA 98, 100, 1535, or 1537 (with or without metabolic activation) (Oda et al., 1978; Eder et al., 1980; NTP, 1981). Allyl isothiocyanate was fetotoxic for Holtzman rats (Nishie and Daxenbichler, 1980),

but was not found to be teratogenic in Wistar rats (Ruddick et al., 1976).

The Food and Drug Administration has prepared three reviews on oil of mustard (90% allyl isothiocyanate), a food additive generally recognized as safe (NTIS, 1972; NTIS, 1973; NTIS, 1975). These reviews emphasize the lack of data on the carcinogenicity and toxicity of these substances. The FDA cites some evidence for increased fetal deaths and resorptions in rodents when oil of mustard is administered at 28.0 mg/kg for 10 consecutive days (from days 6 to 15 of gestation) to pregnant mice (albino CD-1 outbred mice). Other teratology studies in rats, hamsters, and rabbits were considered negative (NTIS, 1973). A select committee of the Federation of American Societies for Experimental Biology (FASEB) stated that "more definitive toxicological studies" on oil of mustard were warranted. Using the data available in 1975, FASEB concluded that there was no indication that allyl isothiocyanate was a hazard to the public at levels currently used in food (NTIS, 1973).

The NCI/NTP Bioassay Program tested allyl isothiocyanate because it is a widely used food additive that had not been tested for carcinogenicity.

II. MATERIALS AND METHODS

CHEMICAL ANALYSIS

DOSAGE PREPARATION

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Study Design

Clinical Examinations and Pathology

Data Recording and Statistical Methods

CHEMICAL ANALYSIS

Food-grade allyl isothiocyanate (CAS No. 57-06-7), greater than 93% allyl isothiocyanate, was obtained from Arsynco, Inc. (Carestadt, NJ) in a single batch (Lot No. 532251).

The results of the analyses performed at Midwest Research Institute (Appendix E) indicated the following: elemental analyses agreed with theoretical values; gas-liquid chromatography on two different systems detected at least six minor impurities with areas totaling less than 1% of the major peak; thin-layer chromatography in two systems detected only one spot; the infrared and ultraviolet spectra were consistent with the structure and spectra reported in the literature (Sadtler Research Laboratories); and the nuclear magnetic resonance spectrum was consistent with the structure. The nuclear magnetic resonance spectrum indicated the presence of a minor impurity that could be the thiocyanate. The identity of this minor impurity was not pursued.

Southern Research Institute analyzed the chemical periodically throughout the study by gas-liquid chromatography and infrared spectroscopy. The results indicated no breakdown of the bulk material during the study.

DOSAGE PREPARATION

Dosage mixtures of allyl isothiocyanate were prepared daily in the single-dose and 14-day studies and were prepared weekly in the 13-week and chronic studies. Mixtures were obtained by pipetting the appropriate amount of the chemical in a beaker and dissolving it in a small amount of corn oil. This stock solution was diluted with additional corn oil to the desired final volume. Concentrations of the test substance were based on the volume of the chemical in relation to the volume of corn oil.

Analysis of the stability of allyl isothiocyanate in corn oil was performed at Midwest Research Institute by assaying samples of corn oil mixtures containing 0.05% test chemical that had been stored at room temperature for 7 days (Appendix F). The corn oil/allyl isothiocyanate solutions were then diluted with anhydrous ethyl ether, and the concentration of the test chemical was determined by vapor-phase chromatography. Allyl isothiocyanate was found to be stable in corn oil for 7 days at room temperature with a recovery of 99.5%. Selected batches of corn oil gavage mixtures administered during the chronic study were analyzed at Southern Research Institute to determine the adequacy of preparation; differences between the mean sample concentration and the targeted concentration were 0.01% (v/v) or less (Table G1).

Four samples of corn oil gavage mixtures prepared and analyzed at Southern Research Institute were shipped to either Midwest Research Institute or Raltech Scientific Services, Inc., for referee analysis of allyl isothiocyanate. The results from the three laboratories were in agreement.

PRECHRONIC STUDIES

Single-Dose Study

Groups of five F344/N rats of each sex were administered a single dose of allyl isothiocyanate (25, 50, 100, 200, or 400 mg/kg body weight) in corn oil by gavage. Groups of five B6C3F1 mice of each sex received 50, 100, 200, 400, or 800 mg/kg allyl isothiocyanate by the same route. No controls were used.

Animals were observed twice daily for 16 days. Weights were taken on the day of dosing and then on day 15. The peritoneal cavities were examined in male mice administered 200, 400, or 800 mg/kg and in female mice administered 100, 200, or 400 mg/kg.

Further details of the study are presented in Table 1.

Fourteen-Day Study

Groups of five F344/N rats of either sex were administered 25, 50, 100, 200, or 400 mg/kg allyl isothiocyanate in corn oil by gavage for 14 consecutive days (Table 1). Groups of B6C3F1 mice received 3, 6, 12, 25, or 50 mg/kg by the same route. No controls were used.

Rats and mice were observed twice daily and were weighed on days 1 and 15 of the study. Gross necropsies were performed on all animals.

Thirteen-Week Study

Thirteen-week studies were conducted to evaluate the cumulative toxicity of allyl isothiocyanate and to determine the doses to be used in the chronic studies.

Groups of 10 rats and mice of each sex received 1.5, 3, 6, 12, or 25 mg/kg allyl isothiocyanate by gavage 5 days per week for 13 weeks (Table 1). Vehicle controls received corn oil alone.

All animals were checked for mortality and clinical signs of toxicity and morbidity twice daily. Moribund animals were killed and necropsied. Individual animals were weighed weekly.

From days 92 to 96, survivors were killed with carbon dioxide. Necropsies were performed on animals that survived to day 92 and on all animals found dead, unless precluded in whole or part by autolysis or cannibalism. The following specimens were examined histologically in vehicle-control and high-dose groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, bone marrow, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, cecum, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, thymus, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, and pituitary. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

CHRONIC STUDY

Study Design

Groups of 50 rats and 50 mice of each sex received 12 or 25 mg/kg allyl isothiocyanate in corn oil by gavage 5 times per week (Monday through Friday) for 103 weeks (Table 1). Groups of 50 rats and 50 mice of each sex received corn oil on the same schedule and served as vehicle controls.

Control and dosed groups were of the same strain, sex, and age range and were from the same source and shipment. All animals were housed in the same room, and no other chemicals were on test in that room. Neither cages nor racks were rotated. The animal cages were housed on two racks, each rack having six levels. On one rack, high-dose males were on the top two levels, high-dose females were on the middle two levels, and low-dose males were on the bottom two levels. On the other rack, low-dose females were placed on the top two levels, control males were on the middle two levels, and control females were on the bottom two levels. All aspects of animal care and maintenance were similar. Animals were randomized to control and dosed groups as described in Table 1. Chronic studies for rats and mice began in March 1978.

Clinical Examinations and Pathology

All animals were observed twice daily for signs of morbidity and mortality. Clinical signs and body weights by cage were recorded every 4 weeks. The mean body weight of each group was calculated by dividing the total weight of all animals in the group by the number of surviving animals in the group. Moribund animals and animals that survived to the end of the bioassay were killed with carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, bone marrow, femur, thymus, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/ uterus, brain, and pituitary. Oil Red O on frozen sections was used to more clearly

define the nature of cytoplasmic vacuolization in the livers of male mice.

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

The pathology report and selected slides were evaluated by the NTP Pathology Working Group as described by Ward et al. (1978). The diagnoses represent a consensus of contracting pathologists and the NTP Pathology Working Group.

Data Recording and Statistical Methods

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

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

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

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

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

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

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

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Experimental Design				
Size of Test Groups	5 males, 5 females of each species	5 males, 5 females of each species	10 males, 10 females of each species	50 males, 50 females of each species
Doses	Rats: 25, 50, 100, 200, or 400 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight Mice: 50, 100, 200, 400, or 800 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight.	Rats: 25, 50, 100, 200, or 400 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight Mice: 3, 6, 12, 25, or 50 mg/kg body weight allyl isothiocyanate in corn oil; volume: 10 ml/kg body weight	Rats and mice: 1.5, 3, 6, 12, or 25 mg/kg body weight allyl isothiocyanate in corn oil; vehicle control, corn oil only, volume: rats, 5 ml/kg body weight; mice, 10 ml/kg body weight	Rats and mice: low dose 12 mg/kg body weight allyl isothiocyanate in corn oil; high dose 25 mg/kg body weight allyl isothiocyanate in corn oil; vehicle control: corn oil; volume: rats, 5 ml/kg body weight; mice, 10 ml/kg body weight
Duration of Dosing	Rats and mice: single dose; killed on day 16	Rats: 14 consecutive days; killed on days 16-17 Mice: 14 consecutive days; killed on days 17-31	Rats and mice: 13 weeks, 5 days per week; killed on days 92-96	Rats and mice: 103 weeks; 5 days per week; killed at week 104-106
Type and Frequency of Observation	Observed twice daily for mortality	Observed twice daily for mortality	Observed twice daily for morbidity and mortality	Observed twice daily for morbidity and mortality
Necropsy and Histologic Examination	Peritoneal cavity examined in male mice receiving 200, 400, or 800 mg/kg and in female mice receiving 100, 200, or 400 mg/kg	All animals necropsied	Gross necropsy performed on all animals; histologic examination performed on all vehicle controls and all animals receiving 25 mg/kg	Gross necropsy and histologic examination performed on all animals

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

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Animals and Animal Maintenance				
Species	F344/N Rats; B6C3F1 Mice	F344/N Rats; B6C3F1 Mice	F344/N Rats; B6C3F1 Mice	F344/N Rats; B6C3F1 Mice
Animal Source	Frederick Cancer Research Center (Frederick, MD)	Same as single-dose study	Same as single-dose study	Harlan Industries, Inc. (Indianapolis, IN)
Time Held Before Start of Test	Rats: 9 days Mice: 8 days	Rats: 8 days Mice: 8 days	Rats: 5 days Mice: 5 days	Rats: 16 days Mice: 16 days
Age When Placed on Study	35 days old	35 days old	35 days old	Rats: 39 days old Mice: 57 days old
Age When Killed	51 days old	Rats: 51-52 days old Mice: 52-66 days old	127-131 days old	Rats: 767 days old Mice: 785 days old
Method of Animal Distribution	Randomized to cages using table of random numbers; cages randomized to test groups using another table of random numbers	Same as single-dose study	Same as single-dose study	Same as single-dose study
Feed	Wayne Lab Blox®, Allied Mills, Inc. (Chicago, IL) Available *ad libitum*	Same as single-dose study	Same as single-dose study	Same as single-dose study
Bedding	Beta Chips®, hardwood chips, Northeastern Products Corp. (Warrensburg, NY)	Same as single-dose study	Same as single-dose study	Same as single-dose study
Water	Tap water in glass bottles available *ad libitum*	Same as single-dose study	Tap water via automatic system, Edstrom Industries, Inc. (Waterford, WI)	Same as 13-week study
Cages	Stainless steel, Hahn Roofing and Sheet Metal Co. (Birmingham, AL)	Same as single-dose study	Polycarbonate Lab Products, Inc. (Garfield, NJ)	Same as 13-week study

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

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Animals and Animal Maintenance				
Animals Per Cage	5	5	5	5
Cage Filters	Fiberglass	Fiberglass	Disposable spun-bonded Polyester Dupont #2024 Snow Filtration Co. (Cincinnati, OH)	Same as 13-week study
Animal Room Environment	23° ± 3°C; humidity uncontrolled; 15 air changes per hr. 9 hrs fluorescent light	Same as single-dose study	23°±3°C; humidity uncontrolled; 15 air changes per hr. 12 hrs fluorescent light	23°±3°C; humidity uncontrolled; 15 air changes per hr. 12 hrs fluorescent light
Other Chemicals on Test in Same Room	Rats and mice: ethyl acrylate, eugenol, D-mannitol;	Rats: ethyl acrylate, eugenol, D-mannitol; Mice: ethyl acrylate, eugenol, D-mannitol; stannous chloride, ziram, propyl gallate, zearalenone	None	None
Chemical/Vehicle Mixture				
Preparation	Allyl isothiocyanate mixed with Mazola® corn oil to concentration of highest dose (stock mixture); stock mixture diluted with corn oil to make other doses	Same as single-dose study	Same as single-dose study	Same as single-dose study
Frequency of Preparation	Mixture prepared daily	Mixture prepared daily	Mixture prepared once each week	Mixture prepared once each week
Storage Conditions		Excess mixture discarded		Dosing mixture stored at 5°C for no longer than 10 days

III. RESULTS

RATS

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDY

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

PRECHRONIC STUDIES

Single-Dose Study

All animals survived to the end of the 16-day observation period. The following average weight increases over the initial weight (on day 0) were measured:

Dose (mg/kg)	Weight Increase (Percent)	
	Males	Females
25	69	40
50	58	45
100	61	44
200	50	38
400	31	20

Other signs of toxicity seen in male rats receiving 200-400 mg/kg included inactivity, watery eyes, and ruffled fur. All signs were gone by day 9 in the 400 mg/kg group and by day 3 in the 200 mg/kg group. Female rats also exhibited inactivity and ruffled fur. Since no rats died during the course of those studies, the highest dose for the 14-day study was set at 400 mg/kg.

Fourteen-Day Study

All rats administered 200 or 400 mg/kg allyl isothiocyanate died before the end of the study (Table 2). Animals administered 100 mg/kg gained less weight than did animals receiving lower doses. A thickened mucosal surface of the stomach was seen in groups of males and females administered 50-400 mg/kg, and adhesion of the stomach to the peritoneum was observed in groups of male rats receiving 50-400 mg/kg and in groups of female rats receiving 100-400 mg/kg (Table 3).

Toxic signs were seen at all dose levels. These signs included inactivity and ruffled fur and were most severe at the 400 mg/kg dose level. Due to the toxicity and pathologic effects observed, the highest dose for the 13-week study was set at 25 mg/kg.

TABLE 2. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF RATS RECEIVING ALLYL ISOTHIOCYANATE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weight (grams)		
		Initial	Final	Change *(b)*
Males				
25	5/5	96.6 ± 5.0	147.0 ± 6.6	+50.4 ± 2.8
50	5/5	85.8 ± 3.9	127.2 ± 4.1	+41.4 ± 2.3
100	5/5	92.8 ± 7.1	113.0 ± 6.1	+20.2 ± 2.2
200	0/5*(c)*	*(d)*	*(d)*	*(d)*
400	0/5*(e)*	*(d)*	*(d)*	*(d)*
Females				
25	5/5	82.6 ± 2.7	113.2 ± 1.7	+30.6 ± 2.3
50	5/5	77.4 ± 3.5	105.6 ± 3.2	+28.2 ± 2.6
100	5/5	84.8 ± 3.0	105.8 ± 3.8	+21.0 ± 2.7
200	0/5*(f)*	*(d)*	*(d)*	*(d)*
400	0/5*(g)*	*(d)*	*(d)*	*(d)*

(a) Number surviving/number initially in the group. All calculations refer only to the survivors of each group.
(b) Mean weight change of the survivors of the group ± standard error of the mean.
(c) Days of death: 2, 2, 3, 8, 9
(d) No data are presented due to the 100% mortality in this group.
(e) Days of death: 2, 2, 2, 2, 4
(f) Days of death: 2, 2, 6, 8, 9
(g) Days of death: 2, 2, 2, 2, 3

TABLE 3. INCIDENCE OF COMPOUND-RELATED EFFECTS OBSERVED IN RATS AT NECROPSY IN THE 14-DAY STUDY OF ALLYL ISOTHIOCYANATE

Dose (mg/kg)	Thickened Mucosal Surface of Stomach	Adhesion of Stomach to Peritoneum
Males		
25	0/5	0/5
50	5/5	1/5
100	5/5	4/5
200	4/5*(a)*	5/5*(a)*
400	1/5*(a)*	3/5*(a)*
Females		
25	0/5	0/5
50	5/5	0/5
100	5/5	2/5
200	3/5*(a)*	4/5*(a)*
400	3/5*(a)*	4/5*(a)*

(a) See Table 2 for days of death.

Thirteen-Week Study

No compound-related deaths or histopathologic effects in the stomach or other tissues were observed. Mean body weight gains of control and dosed groups were comparable (Table 4). In this study, the highest dose level (25 mg/kg) had no effect on either male or female F344/N rats.

Doses of 12 and 25 mg/kg allyl isothiocyanate, administered five times per week by gavage, were selected for rats in the chronic study because compound-related gross pathologic effects were observed in the 14-day study at 50 mg/kg.

TABLE 4. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE FOR 13 WEEKS

Dose (mg/kg) *(a)*	Survival *(b)*	Mean Body Weight (grams)			Weight Change Relative to Controls *(d)* (Percent)
		Initial	Final	Change *(c)*	
Males					
0*(e)*	10/10	65.4 ± 3.4	309.8 ± 5.4	+244.4 ± 3.8	
1.5	10/10	65.9 ± 2.8	322.5 ± 6.2	+256.6 ± 4.8	+5.0
3	10/10	67.2 ± 2.6	321.0 ± 5.2	+253.8 ± 4.2	+3.8
6	10/10	67.2 ± 3.9	318.4 ± 5.4	+251.2 ± 4.9	+2.8
12	10/10	66.9 ± 2.9	314.5 ± 5.4	+247.6 ± 4.8	+1.3
25	10/10	66.7 ± 4.4	303.4 ± 8.8	+236.7 ± 7.5	-3.2
Females					
0*(e)*	10/10	56.1 ± 1.8	191.9 ± 3.1	+135.8 ± 4.1	
1.5	10/10	60.0 ± 2.1	194.7 ± 4.4	+134.7 ± 5.1	-0.8
3	10/10	64.0 ± 2.3	196.4 ± 4.0	+132.4 ± 4.1	-2.5
6	10/10	60.8 ± 2.4	195.3 ± 3.6	+134.5 ± 2.1	-1.0
12	10/10	59.8 ± 1.9	191.4 ± 3.0	+131.6 ± 3.8	-3.1
25	10/10	62.6 ± 2.7	192.9 ± 4.4	+130.3 ± 3.3	-4.1

(a) Allyl isothiocyanate in corn oil was administered 5 days per week.
(b) Number surviving/number initially in the group.
(c) Mean weight change of the group ± standard error of the mean.
(d) Weight change of the dosed group relative to that of the controls ◘

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

(e) Vehicle controls received corn oil alone.

CHRONIC STUDY

Body Weights and Clinical Signs

Throughout the study, the mean body weights of high-dose male rats were lower than those of the controls, and during the last half of the study the mean body weights of both low- and high-dose female rats were higher than those of the controls (Figure 1, and Appendix H, Table H1). No compound-related clinical signs were observed.

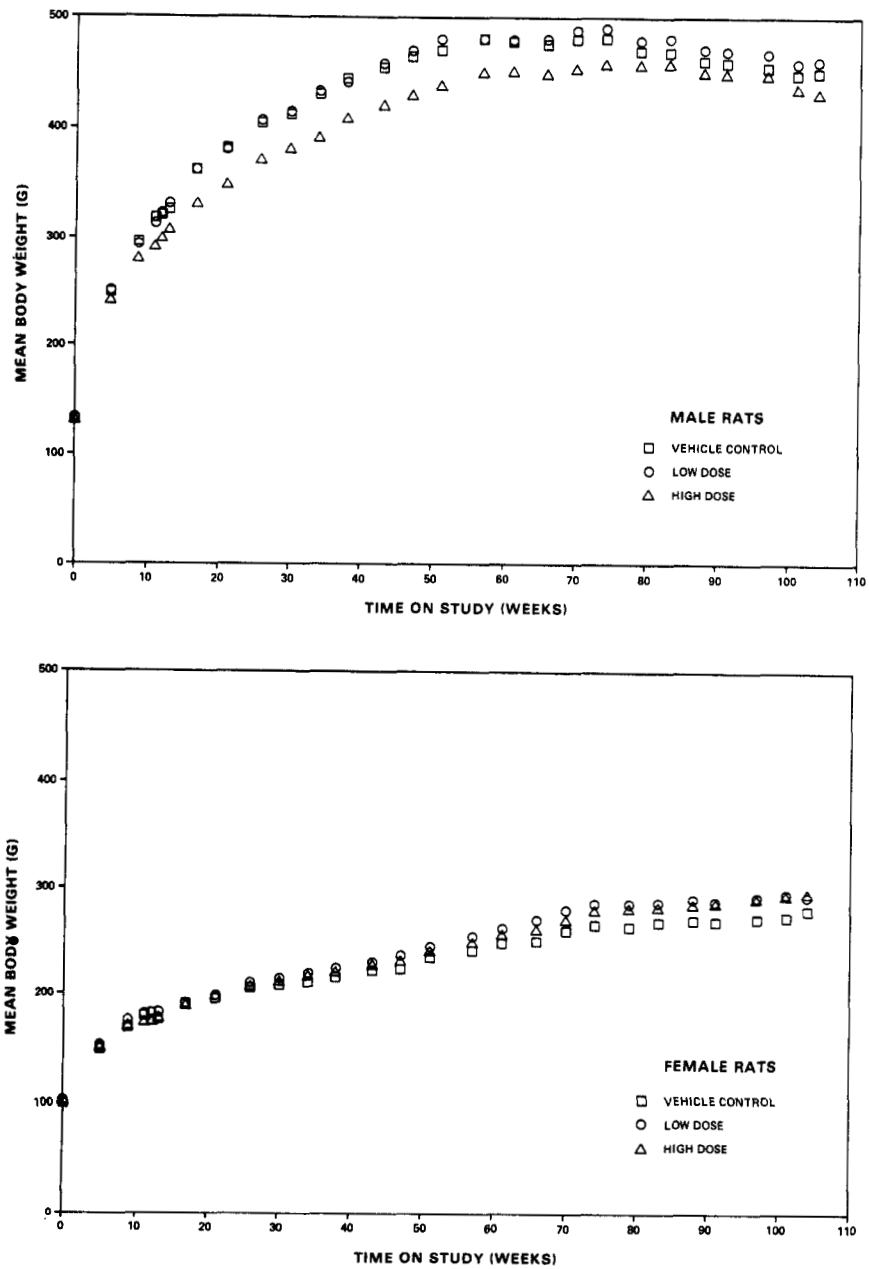


Figure 1. Growth Curves for Rats Administered Allyl Isothiocyanate by Gavage.

Survival

Estimates of the probabilities of survival of male and female rats administered allyl isothiocyanate by gavage at the doses of this bioassay, together with those of the control groups, are shown by the Kaplan and Meier curves in Figure 2. Two male rats were accidentally killed, one in the low-dose group at week 54 and one in the high-dose group at week 68. Two female rats in the low-dose group were accidentally killed at week 54. These deaths were due to gavage error. No significant differences in survival were observed. One control male, one low-dose male, and two low-dose females died during weeks 104-106. In the statistical analyses reported in Tables 6 and 7, no distinction was made between these animals and those killed during the termination period.

In male rats, 37/50 (74%) of the controls, 32/50 (64%) of the low-dose, and 33/50 (66%) of the high-dose group lived to the termination period of the study at 104-106 weeks. In female rats, 35/50 (70%) of the controls, 29/50 (58%) of the low-dose, and 33/50 (66%) of the high-dose group lived to the end of the study at 104-106 weeks.

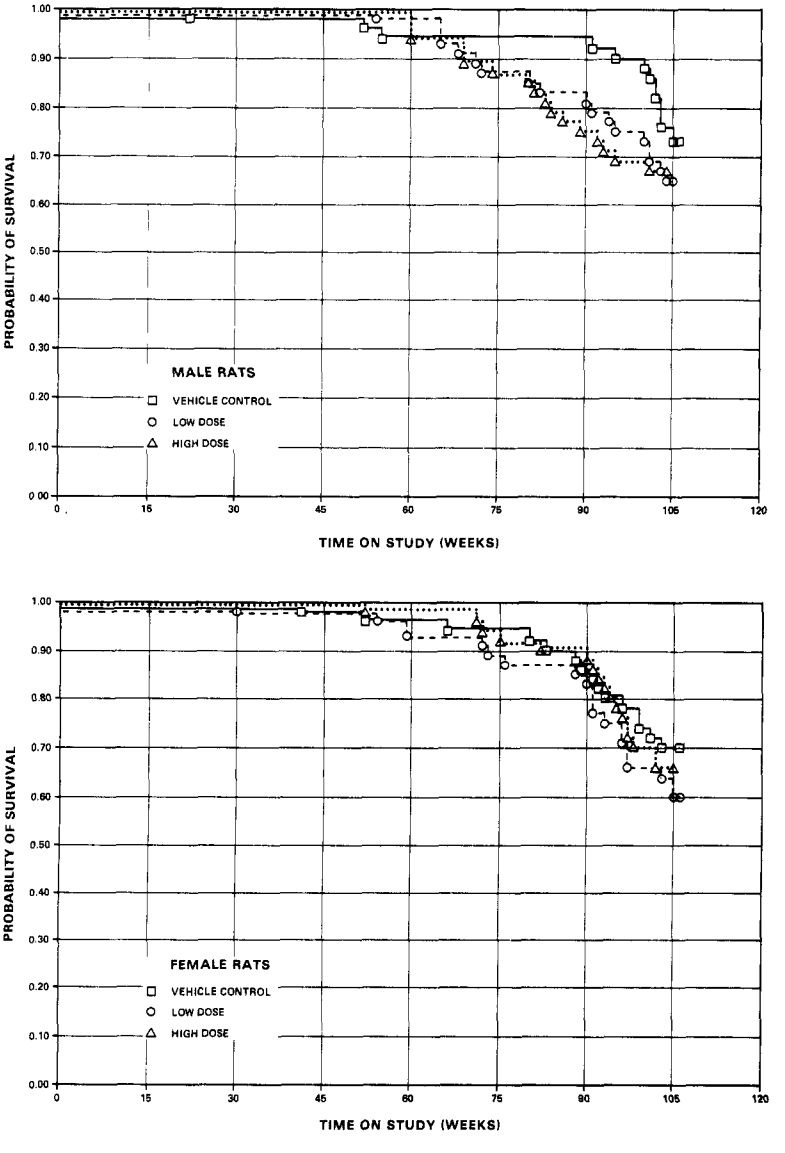


Figure 2. Survival Curves for Rats Administered Allyl Isothiocyanate by Gavage.

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; Tables A3 and A4 give the survival and tumor status for each individual animal in the male rat and female rat studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2. Tables 6 and 7 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Subcutaneous Tissue: Fibrosarcomas were observed in 3/50 (6%) high-dose female rats; none were seen in the control and low-dose groups. The results of all three trend tests were significant ($P<0.05$), but comparisons between the high-dose and control groups were not significant.

Hematopoietic System: Leukemia was observed in dosed male rats with a statistically significant positive trend ($P<0.05$; incidence: control, 2/50, 4%; low-dose 6/50, 12%; high-dose, 8/50, 16%). The incidence in the male high-dose group was significantly higher ($P<0.05$) than that in the control group. This leukemia, designated here as undifferentiated leukemia, is the typical leukemia of F344/N rats and is variously described as mononuclear cell leukemia. Fischer rat leukemia, or monocytic leukemia.

Urinary Bladder: Transitional-cell papillomas occurred in dosed male rats with a statistically significant ($P<0.05$) positive trend. Incidences in the control, low-dose, and high-dose groups were 0/49 (0%), 2/49 (4%), and 4/49 (8%). One female rat in the high-dose group had this lesion; the results in female rats were not significant. Epithelial hyperplasia was seen in 1/49 (2%) low-dose and 6/49 (12%) high-dose male rats. Both the overall trend and the increase at the high dose were statistically significant ($P<0.05$). Incidences of bladder lesions are given in Table 5.

Three of the tumors were large polypoid masses. The other lesions were small. Two of the large papillomas had a prominent myxomatous stroma. The hyperplasias were focal and small; a few were associated with mild inflammation. Urinary calculi were not observed in any animals in this study.

Eye: An increased incidence of nonneoplastic lesions consisting of retinopathy and cataract formation was observed in high-dose male rats and in low-dose female rats. Retinopathy was seen in 9/50 (18%) control males, 6/50 (12%) low-dose males, 39/50 (78%) high-dose males, 4/50 (8%) control females, 35/50 (70%) low-dose females, and 11/50 (22%) high-dose females. Cataract formation was observed in 7/50 (14%) control males, 6/50 (12%) low-dose males, 13/50 (26%) high-dose males, 2/50 (4%) control females, 33/50 (66%) low-dose females, and 9/50 (18%) high-dose females. The incidence of retinopathy and cataract formation correlated with the placement of the cages. The animals that occupied the two top levels of the racks (i.e., high-dose males and low-dose females) had the highest incidence of eye effects.

TABLE 5. INCIDENCE OF RATS WITH BLADDER LESIONS IN THE CHRONIC STUDY WITH ALLYL ISOTHIOCYANATE

	Incidence					
	Males			Females		
	Vehicle Control	Low Dose	High Dose	Vehicle Control	Low Dose	High Dose
Animals examined	49	49	49	49	49	50
Lesion:						
Transitional-Cell Papilloma	0	2	4	0	0	1
Epithelial Hyperplasia	0	1	6 *(a)*	0	0	1
Nodular Hyperplasia	0	0	1	0	0	0

(a) None of these animals had papillomas.

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Skin: Squamous Cell Papilloma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	0/50 (0%)	4/50 (8%)
Adjusted *(c)*	7.6%	0.0%	12.1%
Terminal *(d)*	2/38 (5%)	0/33 (0%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.331	P=0.152N	P=0.418
Incidental Tumor Test	P=0.292	P=0.159N	P=0.364
Cochran-Armitage Trend, Fisher Exact Tests	P=0.393	P=0.121N	P=0.500
Skin: Squamous Cell Papilloma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	0/50 (0%)	6/50 (12%)
Adjusted *(c)*	10.1%	0.0%	17.2%
Terminal *(d)*	3/38 (8%)	0/33 (0%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.203N	P=0.086N	P=0.284
Incidental Tumor Test	P=0.234N	P=0.090N	P=0.331
Cochran-Armitage Trend, Fisher Exact Tests	P=0.260	P=0.059N	P=0.370
Subcutaneous Tissue: Fibrosarcoma			
Tumor Rates			
Overall *(b)*	5/50 (10%)	5/50 (10%)	1/50 (2%)
Adjusted *(c)*	12.5%	14.1%	2.8%
Terminal *(d)*	4/38 (11%)	4/33 (12%)	0/33 (0%)
Statistical Tests *(e)*			
Life Table	P=0.133N	P=0.542	P=0.154N
Incidental Tumor Test	P=0.123N	P=0.628N	P=0.215N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.088N	P=0.630	P=0.102N
Subcutaneous Tissue: All Sarcomas			
Tumor Rates			
Overall *(b)*	6/50 (12%)	8/50 (16%)	2/50 (4%)
Adjusted *(c)*	14.5%	20.5%	5.1%
Terminal *(d)*	4/38 (11%)	5/33 (15%)	0/33 (0%)
Statistical Tests *(e)*			
Life Table	P=0.189N	P=0.304	P=0.209N
Incidental Tumor Test	P=0.088N	P=0.540	P=0.198N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.124N	P=0.387	P=0.134N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	3/49 (6%)	2/49 (4%)	3/48 (6%)
Adjusted *(c)*	7.2%	6.3%	8.8%
Terminal *(d)*	1/37 (3%)	2/32 (6%)	2/31 (6%)
Statistical Tests *(e)*			
Life Table	P=0.512	P=0.556N	P=0.590
Incidental Tumor Test	P=0.545N	P=0.426N	P=0.541N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.577	P=0.500N	P=0.651

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	2/50 (4%)	6/50 (12%)	8/50 (16%)
Adjusted *(c)*	4.7%	17.1%	21.6%
Terminal *(d)*	0/38 (0%)	4/33 (12%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.024	P=0.093	P=0.030
Incidental Tumor Test	P=0.006	P=0.070	P=0.009
Cochran-Armitage Trend, Fisher Exact Tests	P=0.039	P=0.134	P=0.046
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	2/50 (4%)	7/50 (14%)	8/50 (16%)
Adjusted *(c)*	4.7%	19.1%	21.6%
Terminal *(d)*	0/38 (0%)	4/33 (12%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.027	P=0.054	P=0.030
Incidental Tumor Test	P=0.011	P=0.060	P=0.009
Cochran-Armitage Trend, Fisher Exact Tests	P=0.044	P=0.080	P=0.046
Liver: Neoplastic Nodule			
Tumor Rates			
Overall *(b)*	2/50 (4%)	0/50 (0%)	5/50 (10%)
Adjusted *(c)*	5.3%	0.0%	15.2%
Terminal *(d)*	2/38 (5%)	0/33 (0%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.085	P=0.270N	P=0.162
Incidental Tumor Test	P=0.085	P=0.270N	P=0.162
Cochran-Armitage Trend, Fisher Exact Tests	P=0.112	P=0.247N	P=0.218
Urinary Bladder: Transitional-Cell Papilloma			
Tumor Rates			
Overall *(b)*	0/49 (0%)	2/49 (4%)	4/49 (8%)
Adjusted *(c)*	0.0%	5.5%	12.1%
Terminal *(d)*	0/37 (0%)	1/32 (3%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.030	P=0.209	P=0.049
Incidental Tumor Test	P=0.048	P=0.356	P=0.049
Cochran-Armitage Trend, Fisher Exact Tests	P=0.038	P=0.247	P=0.059
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	7/47 (15%)	12/49 (24%)	4/49 (8%)
Adjusted *(c)*	18.0%	30.6%	11.7%
Terminal *(d)*	5/36 (14%)	6/32 (19%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.326N	P=0.107	P=0.336N
Incidental Tumor Test	P=0.270N	P=0.236	P=0.462N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.204N	P=0.178	P=0.238N

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	7/47 (15%)	13/49 (27%)	4/49 (8%)
Adjusted *(c)*	18.0%	33.3%	11.7%
Terminal *(d)*	5/36 (14%)	7/32 (22%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.329N	P=0.071	P=0.336N
Incidental Tumor Test	P=0.275N	P=0.162	P=0.462N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.205N	P=0.124	P=0.238N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	16/50 (32%)	15/50 (30%)	11/50 (22%)
Adjusted *(c)*	39.7%	40.8%	33.3%
Terminal *(d)*	14/38 (37%)	12/33 (36%)	11/33 (33%)
Statistical Tests *(e)*			
Life Table	P=0.293N	P=0.483	P=0.322N
Incidental Tumor Test	P=0.260N	P=0.580N	P=0.376N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.158N	P=0.500N	P=0.184N
Adrenal: Pheochromocytoma or Malignant Pheochromocytoma			
Tumor Rates			
Overall *(b)*	17/50 (34%)	15/50 (30%)	11/50 (22%)
Adjusted *(c)*	41.1%	40.8%	33.3%
Terminal *(d)*	14/38 (37%)	12/33 (36%)	11/33 (33%)
Statistical Tests *(e)*			
Life Table	P=0.231N	P=0.557	P=0.258N
Incidental Tumor Test	P=0.213N	P=0.505N	P=0.330N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.113N	P=0.415N	P=0.133N
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	6/48 (13%)	10/50 (20%)	5/50 (10%)
Adjusted *(c)*	16.7%	29.1%	14.6%
Terminal *(d)*	6/36 (17%)	9/33 (27%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.511N	P=0.151	P=0.570N
Incidental Tumor Test	P=0.470N	P=0.194	P=0.614N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.400N	P=0.233	P=0.471N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	8/48 (17%)	11/50 (22%)	7/50 (14%)
Adjusted *(c)*	21.4%	30.7%	20.5%
Terminal *(d)*	7/36 (19%)	9/33 (27%)	6/33 (18%)
Statistical Tests *(e)*			
Life Table	P=0.530N	P=0.235	P=0.587N
Incidental Tumor Test	P=0.474N	P=0.348	P=0.560
Cochran-Armitage Trend, Fisher Exact Tests	P=0.404N	P=0.341	P=0.465N

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Pancreatic Islets: Islet-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/50 (4%)	1/49 (2%)
Adjusted *(c)*	7.9%	6.1%	3.0%
Terminal *(d)*	3/38 (8%)	2/33 (6%)	1/33 (3%)
Statistical Tests *(e)*			
Life Table	P=0.272N	P=0.564N	P=0.356N
Incidental Tumor Test	P=0.272N	P=0.564N	P=0.356N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.232N	P=0.500N	P=0.316N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	3/50 (6%)	3/50 (6%)
Adjusted *(c)*	7.4%	9.1%	9.1%
Terminal *(d)*	2/38 (5%)	3/33 (9%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.508	P=0.591	P=0.584
Incidental Tumor Test	P=0.474	P=0.584	P=0.533
Cochran-Armitage Trend, Fisher Exact Tests	P=0.586	P=0.661	P=0.661
Preputial Gland: Adenocarcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	1/50 (2%)	1/50 (2%)
Adjusted *(c)*	10.5%	3.0%	3.0%
Terminal *(d)*	4/38 (11%)	1/33 (3%)	1/33 (3%)
Statistical Tests *(e)*			
Life Table	P=0.137N	P=0.223N	P=0.223N
Incidental Tumor Test	P=0.137N	P=0.223N	P=0.223N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.108N	P=0.181N	P=0.181N
Preputial Gland: Carcinoma or Adenocarcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	2/50 (4%)	2/50 (4%)
Adjusted *(c)*	10.5%	6.1%	6.1%
Terminal *(d)*	4/38 (11%)	2/33 (6%)	2/33 (6%)
Statistical Tests *(e)*			
Life Table	P=0.316N	P=0.403N	P=0.403N
Incidental Tumor Test	P=0.316N	P=0.403N	P=0.403N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.260N	P=0.339N	P=0.339N
Testis: Interstitial-Cell Tumor			
Tumor Rates			
Overall *(b)*	45/50 (90%)	45/50 (90%)	49/49 (100%)
Adjusted *(c)*	97.8%	95.7%	100.0%
Terminal *(d)*	37/38 (97%)	31/33 (94%)	33/33 (100%)
Statistical Tests *(e)*			
Life Table	P=0.024	P=0.146	P=0.023
Incidental Tumor Test	P=0.066	P=0.596N	P=0.068
Cochran-Armitage Trend, Fisher Exact Tests	P=0.036	P=0.630	P=0.030

TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) 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 control. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)*

	Vehicle Control	Low Dose	High Dose
Subcutaneous Tissue: Fibrosarcoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted *(c)*	0.0%	0.0%	8.1%
Terminal *(d)*	0/35 (0%)	0/31 (0%)	2/33 (6%)
Statistical Tests *(e)*			
Life Table	P=0.037	*(f)*	P=0.116
Incidental Tumor Test	P=0.028	*(f)*	P=0.094
Cochran-Armitage Trend, Fisher Exact Tests	P=0.036	*(f)*	P=0.121
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	1/50 (2%)	0/50 (0%)	3/50 (6%)
Adjusted *(c)*	2.9%	0.0%	7.4%
Terminal *(d)*	1/35 (3%)	0/31 (0%)	1/33 (3%)
Statistical Tests *(e)*			
Life Table	P=0.174	P=0.524N	P=0.301
Incidental Tumor Test	P=0.125	P=0.524N	P=0.223
Cochran-Armitage Trend, Fisher Exact Tests	P=0.171	P=0.500N	P=0.309
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	7/50 (14%)	9/50 (18%)	11/50 (22%)
Adjusted *(c)*	16.6%	23.8%	26.1%
Terminal *(d)*	3/35 (9%)	4/31 (13%)	4/33 (12%)
Statistical Tests *(e)*			
Life Table	P=0.192	P=0.318	P=0.219
Incidental Tumor Test	P=0.186	P=0.373	P=0.291
Cochran-Armitage Trend, Fisher Exact Tests	P=0.184	P=0.393	P=0.218
Hematopoietic System: All Leukemia			
Tumor Rates			
Overall *(b)*	7/50 (14%)	9/50 (18%)	12/50 (24%)
Adjusted *(c)*	16.6%	23.8%	28.6%
Terminal *(d)*	3/35 (9%)	4/31 (13%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.136	P=0.318	P=0.159
Incidental Tumor Test	P=0.124	P=0.373	P=0.210
Cochran-Armitage Trend, Fisher Exact Tests	P=0.125	P=0.393	P=0.154
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	8/50 (14%)	9/50 (18%)	14/50 (28%)
Adjusted *(c)*	19.2%	23.8%	31.6%
Terminal *(d)*	4/35 (11%)	4/31 (13%)	5/33 (15%)
Statistical Tests *(e)*			
Life Table	P=0.101	P=0.410	P=0.125
Incidental Tumor Test	P=0.096	P=0.479	P=0.206
Cochran-Armitage Trend, Fisher Exact Tests	P=0.087	P=0.500	P=0.114

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

Topography:Morphology	Vehicle Control	Low Dose	High Dose
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	17/49(35%)	10/50(20%)	13/50(26%)
Adjusted *(c)*	44.3%	29.8%	36.7%
Terminal *(d)*	13/34(38%)	8/31(26%)	11/33(33%)
Statistical Tests *(e)*			
Life Table	P=0.247N	P=0.145N	P=0.283N
Incidental Tumor Test	P=0.241N	P=0.139N	P=0.279N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.207N	P=0.078N	P=0.235N
Pituitary: Carcinoma			
Tumor Rates			
Overall *(b)*	0/49(0%)	3/50(6%)	2/50(4%)
Adjusted *(c)*	0.0%	9.7%	6.1%
Terminal *(d)*	0/34(0%)	3/31(10%)	2/33(6%)
Statistical Tests *(e)*			
Life Table	P=0.208	P=0.105	P=0.231
Incidental Tumor Test	P=0.208	P=0.105	P=0.231
Cochran-Armitage Trend, Fisher Exact Tests	P=0.219	P=0.125	P=0.253
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	17/49(35%)	13/50(26%)	15/50(30%)
Adjusted *(c)*	44.3%	38.9%	42.5%
Terminal *(d)*	13/34(38%)	11/31(35%)	13/33(39%)
Statistical Tests *(e)*			
Life Table	P=0.407N	P=0.360N	P=0.446N
Incidental Tumor Test	P=0.404N	P=0.359N	P=0.447N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.355N	P=0.235N	P=0.388N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	1/50(2%)	2/50(4%)	3/50(6%)
Adjusted *(c)*	2.3%	6.5%	9.1%
Terminal *(d)*	0/35(0%)	2/31(6%)	3/33(9%)
Statistical Tests *(e)*			
Life Table	P=0.216	P=0.464	P=0.293
Incidental Tumor Test	P=0.194	P=0.451	P=0.256
Cochran-Armitage Trend, Fisher Exact Tests	P=0.226	P=0.500	P=0.309
Adrenal: Pheochromocytoma and Malignant Pheochromocytoma			
Tumor Rates			
Overall *(b)*	2/50(4%)	2/50(4%)	3/50(6%)
Adjusted *(c)*	5.1%	6.5%	9.1%
Terminal *(d)*	1/35(3%)	2/31(6%)	3/33(9%)
Statistical Tests *(e)*			
Life Table	P=0.390	P=0.654	P=0.481
Incidental Tumor Test	P=0.364	P=0.644	P=0.442
Cochran-Armitage Trend, Fisher Exact Tests	P=0.408	P=0.691	P=0.500

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	10/50 (20%)	8/48 (17%)	6/50 (12%)
Adjusted *(c)*	28.6%	26.1%	18.2%
Terminal *(d)*	10/35 (29%)	7/29 (24%)	6/33 (18%)
Statistical Tests *(e)*			
Life Table	P=0.200N	P=0.570N	P=0.236N
Incidental Tumor Test	P=0.211N	P=0.574N	P=0.236N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.173N	P=0.435N	P=0.207N
Thyroid: C-Cell Carcinoma			
Tumor Rates			
Overall *(b)*	2/50 (4%)	2/48 (4%)	3/50 (6%)
Adjusted *(c)*	5.7%	6.9%	9.1%
Terminal *(d)*	2/35 (6%)	2/29 (7%)	3/33 (9%)
Statistical Tests *(e)*			
Life Table	P=0.385	P=0.626	P=0.473
Incidental Tumor Test	P=0.385	P=0.626	P=0.473
Cochran-Armitage Trend, Fisher Exact Tests	P=0.409	P=0.676	P=0.500
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	12/50 (24%)	10/48 (21%)	9/50 (18%)
Adjusted *(c)*	34.3%	32.8%	27.3%
Terminal *(d)*	12/35 (34%)	9/29 (31%)	9/33 (27%)
Statistical Tests *(e)*			
Life Table	P=0.314N	P=0.598	P=0.359N
Incidental Tumor Test	P=0.327N	P=0.595	P=0.359N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.272N	P=0.447N	P=0.312N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	8/50 (16%)	14/50 (28%)	11/50 (22%)
Adjusted *(c)*	21.8%	39.7%	30.7%
Terminal *(d)*	7/35 (20%)	11/31 (35%)	9/33 (27%)
Statistical Tests *(e)*			
Life Table	P=0.247	P=0.068	P=0.264
Incidental Tumor Test	P=0.246	P=0.115	P=0.246
Cochran-Armitage Trend, Fisher Exact Tests	P=0.285	P=0.114	P=0.306
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(b)*	14/50 (28%)	15/49 (31%)	16/50 (32%)
Adjusted *(c)*	38.9%	44.8%	42.4%
Terminal *(d)*	13/35 (37%)	13/31 (42%)	12/33 (36%)
Statistical Tests *(e)*			
Life Table	P=0.311	P=0.346	P=0.347
Incidental Tumor Test	P=0.374	P=0.420	P=0.400
Cochran-Armitage Trend, Fisher Exact Tests	P=0.375	P=0.474	P=0.414

TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) 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 control. The life table analysis regards tumors in animals dying before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).
(f) No test was performed because there was no incidence in the low-dose or vehicle control group.

PRECHRONIC STUDIES

Single-Dose Study

Two of five males receiving 400 mg/kg and 4/5 males and 5/5 females receiving 800 mg/kg died (Table 8). The following average weight increases over the initial weight (on day 0) were calculated at the end of the 16th day for the surviving male and female mice:

Dose (mg/kg)	Weight Increase (Percent)	
	Males	Females
50	2	18
100	17	22
200	24	13
400	21	11
800	38	—

Male and female mice exhibited a transient, dose-related toxicity which was most marked in the 100, 200, 400, and 800 mg/kg groups. This included inactivity, drooping eyelids, and ruffled fur.

The peritoneal cavities were examined in male mice administered 200, 400, or 800 mg/kg and in female mice administered 100, 200, or 400 mg/kg. The lower third of the mucosal surface of the stomach was thickened and necrotic. The stomach adhered to the peritoneal wall in male mice administered 400 or 800 mg/kg and in female mice administered 200 or 400 mg/kg. The severity of these effects was dose related.

The highest dosage levels producing no deaths were 200 mg/kg in the males and 400 mg/kg in the females. In addition, the 100, 200, 400, and 800 mg/kg levels produced toxicity. For these reasons, the highest dose level in the 14-day study was set at 50 mg/kg.

Fourteen-Day Study

One male mouse administered 50 mg/kg died (Table 9). A thickened area of mucosa in the nonglandular region of the stomach was observed in 4/5 males and 5/5 females administered 50 mg/kg. A thickened urinary bladder wall was seen in 4/5 males and 1/5 females administered 50 mg/kg. The average weight gain in the experimental groups varied from 3% to 16%.

No other signs of toxicity were observed. Due to the stomach and bladder lesions observed at the 50 mg/kg dose, the highest dose set for the 13-week study was 25 mg/kg.

Thirteen-Week Study

No compound-related deaths or histopathologic effects in the stomach or other tissues were observed. Mean body weight gains of control and dosed groups were comparable (Table 10). The highest dose level (25 mg/kg) had no effect on male or female B6C3F1 mice.

Doses of 12 and 25 mg/kg allyl isothiocyanate, administered five times per week by gavage, were selected for mice in the chronic study because compound-related effects were observed in the 14-day study at 50 mg/kg.

TABLE 8. DOSAGE AND SURVIVAL OF MICE ADMINISTERED A SINGLE DOSE OF ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

Dose (mg/kg)	Survival *(a)*	
	Males	Females
50	5/5	5/5
100	5/5	5/5
200	5/5	5/5
400	3/5 *(b)*	5/5
800	1/5 *(c)*	0/5 *(d)*

(a) Number surviving/number initially in the group.
(b) Deaths occurred on days 1 and 14.
(c) Two animals died on day 1 and two animals on day 2.
(d) Four animals died on day 1 and one animal on day 2.

TABLE 9. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF MICE RECEIVING ALLYL ISOTHIOCYANATE BY GAVAGE FOR 14 DAYS

Dose (mg/kg)	Survival *(a)*	Mean Body Weight (grams)		
		Initial	Final	Change *(b)*
Males				
3	5/5	20.2 ± 0.4	21.0 ± 0.7	+0.8 ± 0.5
6	5/5	20.6 ± 0.2	22.6 ± 0.7	+2.0 ± 0.5
12	5/5	20.2 ± 0.7	21.0 ± 1.0	+0.8 ± 0.4
25	5/5	19.8 ± 0.5	21.8 ± 0.7	+2.0 ± 0.5
50	4/5 *(c)*	20.5 ± 0.7	23.8 ± 0.5	+3.3 ± 0.8
Females				
3	5/5	17.4 ± 0.4	19.0 ± 0.3	+1.6 ± 0.5
6	5/5	16.6 ± 0.2	18.8 ± 0.7	+2.2 ± 0.7
12	5/5	17.8 ± 0.5	18.4 ± 0.4	+0.6 ± 0.2
25	5/5	16.8 ± 0.4	18.4 ± 0.2	+1.6 ± 0.5
50	5/5	17.6 ± 0.5	18.0 ± 0.9	+0.4 ± 1.0

(a) Number surviving/number initially in the group. All calculations refer only to the survivors of each group.
(b) Mean weight change of the survivors of the group ± standard error of the mean.
(c) Death occurred on day 15, the day after administration of the test material was discontinued.

TABLE 10. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE FOR 13 WEEKS

Dose *(a)* (mg/kg)	Survival *(b)*	Mean Body Weight (grams)			Weight Change Relative to Controls *(d)* (Percent)
		Initial	Final	Change *(c)*	
Males					
0*(e)*	10/10	18.7 ±0.5	32.4 ±0.6	+13.7 ±0.5	
1.5	9/10 *(f)*	19.4 ±0.3	34.1 ±1.1	+14.7 ±1.1	+ 7.3
3	10/10	18.2 ±0.6	33.4 ±1.1	+15.2 ±0.8	+10.9
6	10/10	18.7 ±0.7	35.0 ±0.8	+16.3 ±0.8	+19.0
12	9/10 *(f)*	20.1 ±0.5	32.8 ±0.4	+12.7 ±0.4	- 7.3
25	10/10	19.9 ±0.4	35.2 ±0.6	+15.3 ±0.8	+11.7
Females					
0*(e)*	10/10	16.1 ±0.4	25.3 ±0.3	+9.2 ±0.4	
1.5	10/10	15.6 ±0.3	24.3 ±0.5	+8.7 ±0.7	- 5.4
3	8/10 *(f)*	16.4 ±0.5	24.5 ±0.6	+8.1 ±0.2	-12.0
6	9/10 *(f)*	16.6 ±0.4	25.2 ±0.6	+8.6 ±0.5	- 6.5
12	9/10 *(f)*	16.9 ±0.5	25.9 ±0.8	+9.0 ±0.7	- 2.2
25	10/10	15.9 ±0.4	24.5 ±0.5	+8.6 ±0.3	- 6.5

(a) Allyl isothiocyanate in corn oil was administered 5 days per week.
(b) Number surviving/number initially in the group. All calculations refer only to the survivors of each group.
(c) Mean weight change of the survivors of the group ± standard error of the mean.
(d) Weight change of the dosed group relative to that of the controls =

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

(e) Vehicle controls received corn oil alone.
(f) Death was a result of gavage error.

CHRONIC STUDY

Body Weights and Clinical Signs

Throughout most of the study, mean body weights of high-dose male and female mice were higher than those of the vehicle controls (Figure 3, Appendix H, Table H2).

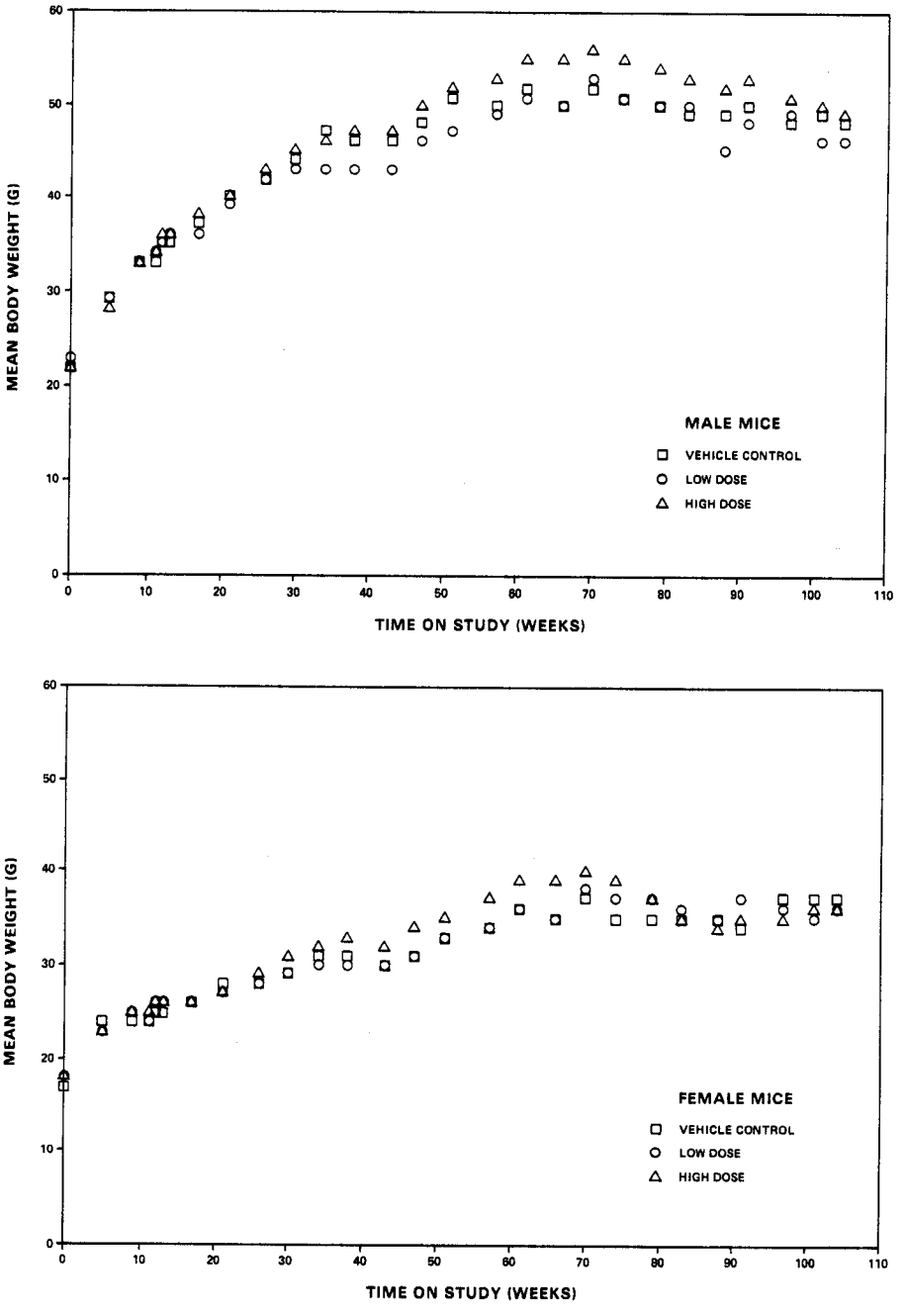


Figure 3. Growth Curves for Mice Administered Allyl Isothiocyanate by Gavage.

Survival

Estimates of the probabilities of survival of male and female mice administered allyl isothiocyanate by gavage at the doses of this bioassay, together with those of the control groups, are shown by the Kaplan and Meier curves in Figure 4. No significant differences in survival were observed between any groups of either sex. The survival in control female mice was consistently lower than the survival in either dosed group after week 40. One control male, one low-dose

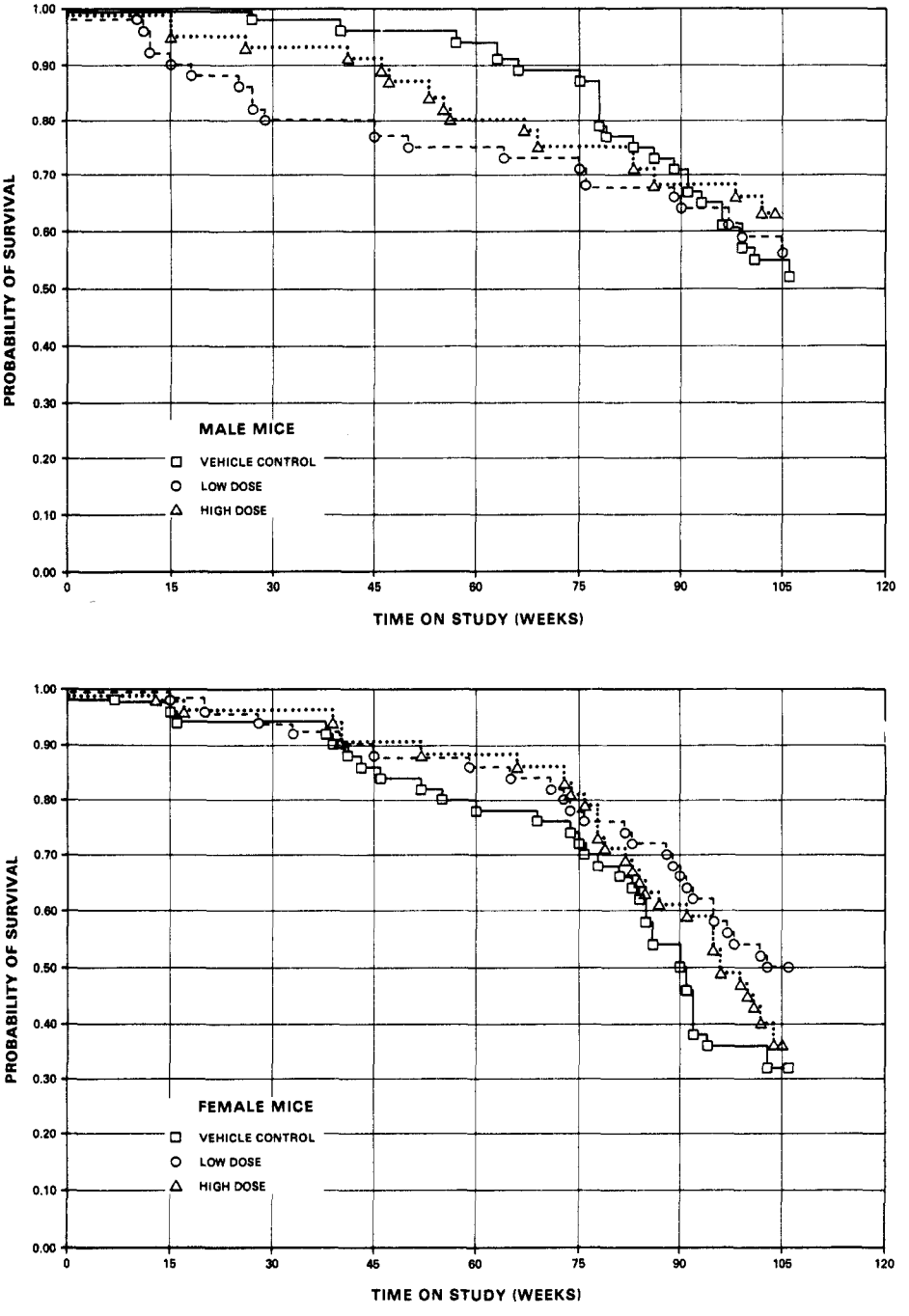


Figure 4. Survival Curves for Mice Administered Allyl Isothiocyanate by Gavage.

male, and two high-dose female mice died during weeks 104-106. In the statistical analyses reported in Tables 11 and 12, no distinction was made between these animals and those killed during this termination period. One control male (at week 41), six low-dose males (at weeks 42, 48, 56, 59, 60, and 65), seven high-dose males (at weeks 6, 20, 29, 31, 35, 62, and 65), and one high-dose female (at week 60) were accidentally killed (due to gavage error) during the study.

In male mice, 26/50 (52%) of the controls, 24/50 (48%) of the low-dose, and 27/50 (54%) of the high-dose group lived to the termination period of the study at 104-106 weeks. In female mice, 16/50 (32%) of the controls, 25/50 (50%) of the low-dose, and 18/50 (36%) of the high-dose group lived to the termination period of the study at 104-106 weeks. Suppurative inflammation of the peritoneum, uterus, or multiple organs was seen in many of the female mice that died before 104 weeks (13/34 controls, 6/25 low-dose, 12/30 high-dose). These lesions are suggestive of generalized infection and may have been causative in these early deaths.

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in mice are summarized in Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status for each individual animal in the male and female mouse studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2. Tables 11 and 12 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Liver: A significant, ($P<0.01$) dose-related increase in cytoplasmic vacuolization was observed in male mice (control 2/49, 4%; low-dose, 8/49, 16%; high-dose, 13/50, 26%). The distribution of these vacuoles was not consistent, but most livers had some centrilobular component. In other male mice with cytoplasmic vacuolization, the distribution was more consistently centrilobular. The vacuoles contained fat as determined by special stains of frozen sections. The degree of severity was similiar in the three groups.

TABLE 11. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma without Carcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	3/50 (6%)	4/50 (8%)
Adjusted *(c)*	14.8%	10.6%	14.3%
Terminal *(d)*	4/27 (15%)	2/25 (8%)	3/27 (11%)
Statistical Tests *(e)*			
Life Table	P=0.435	P=0.557N	P=0.643N
Incidental Tumor Test	P=0.509	P=0.547N	P=0.575
Cochran-Armitage Trend, Fisher Exact Tests	P=0.575	P=0.500N	P=0.643
Lung: Alveolar/Bronchiolar Carcinoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	1/50 (2%)	3/50 (6%)
Adjusted *(c)*	0.0%	4.0%	10.3%
Terminal *(d)*	0/27 (0%)	1/25 (4%)	2/27 (7%)
Statistical Tests *(e)*			
Life Table	P=0.060	P=0.485	P=0.113
Incidental Tumor Test	P=0.048	P=0.485	P=0.084
Cochran-Armitage Trend, Fisher Exact Tests	P=0.061	P=0.500	P=0.121
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	4/50 (8%)	7/50 (14%)
Adjusted *(c)*	14.8%	14.5%	23.9%
Terminal *(d)*	4/27 (15%)	3/25 (12%)	5/27 (19%)
Statistical Tests *(e)*			
Life Table	P=0.191	P=0.588	P=0.253
Incidental Tumor Test	P=0.143	P=0.598	P=0.176
Cochran-Armitage Trend, Fisher Exact Tests	P=0.201	P=0.643	P=0.262
Hematopoietic System: Lymphoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/50 (4%)	0/50 (0%)
Adjusted *(c)*	8.9%	7.7%	0.0%
Terminal *(d)*	1/27 (4%)	1/25 (4%)	0/27 (0%)
Statistical Tests *(e)*			
Life Table	P=0.104N	P=0.576N	P=0.148N
Incidental Tumor Test	P=0.175N	P=0.661	P=0.194N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.083N	P=0.500N	P=0.121N
Liver: Adenoma without Carcinoma			
Tumor Rates			
Overall *(b)*	8/49 (16%)	5/49 (10%)	9/50 (18%)
Adjusted *(c)*	28.0%	18.7%	31.3%
Terminal *(d)*	7/27 (26%)	4/25 (16%)	8/27 (30%)
Statistical Tests *(e)*			
Life Table	P=0.411	P=0.349N	P=0.482
Incidental Tumor Test	P=0.439	P=0.378N	P=0.540
Cochran-Armitage Trend, Fisher Exact Tests	P=0.453	P=0.276N	P=0.518

TABLE 11. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	13/49 (27%)	9/49 (18%)	10/50 (20%)
Adjusted *(c)*	35.3%	29.4%	35.7%
Terminal *(d)*	5/27 (19%)	5/25 (20%)	9/27 (33%)
Statistical Tests *(e)*			
Life Table	P=0.356N	P=0.408N	P=0.385N
Incidental Tumor Test	P=0.534N	P=0.580N	P=0.597
Cochran-Armitage Trend, Fisher Exact Tests	P=0.261N	P=0.234N	P=0.298N
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	21/49 (43%)	14/49 (29%)	19/50 (38%)
Adjusted *(c)*	57.2%	45.4%	65.2%
Terminal *(d)*	12/27 (44%)	9/25 (36%)	17/27 (63%)
Statistical Tests *(e)*			
Life Table	P=0.476N	P=0.259N	P=0.490N
Incidental Tumor Test	P=0.469	P=0.392N	P=0.529
Cochran-Armitage Trend, Fisher Exact Tests	P=0.362N	P=0.103N	P=0.387N
Thyroid: Follicular-Cell Adenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/45 (4%)	1/50 (2%)
Adjusted *(c)*	11.1%	7.2%	3.7%
Terminal *(d)*	3/27 (11%)	1/24 (4%)	1/27 (4%)
Statistical Tests *(e)*			
Life Table	P=0.242N	P=0.576N	P=0.303N
Incidental Tumor Test	P=0.236N	P=0.569N	P=0.303N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.228N	P=0.550N	P=0.309N
Harderian Gland: Adenoma or Cystadenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	1/50 (2%)	1/50 (2%)
Adjusted *(c)*	10.0%	4.0%	3.7%
Terminal *(d)*	2/27 (7%)	1/25 (4%)	1/27 (4%)
Statistical Tests *(e)*			
Life Table	P=0.224N	P=0.346N	P=0.325N
Incidental Tumor Test	P=0.258N	P=0.420N	P=0.366N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.210N	P=0.309N	P=0.309N

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) 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 before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

TABLE 12. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)*

	Vehicle Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Carcinoma			
Tumor Rates			
Overall *(b)*	0/47 (0%)	2/49 (4%)	3/49 (6%)
Adjusted *(c)*	0.0%	7.1%	11.8%
Terminal *(d)*	0/16 (0%)	0/25 (0%)	1/20 (5%)
Statistical Tests *(e)*			
Life Table	P=0.119	P=0.337	P=0.194
Incidental Tumor Test	P=0.247	P=0.395	P=0.281
Cochran-Armitage Trend, Fisher Exact Tests	P=0.091	P=0.258	P=0.129
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	2/47 (4%)	2/49 (4%)	3/49 (6%)
Adjusted *(c)*	7.9%	7.1%	11.8%
Terminal *(d)*	0/16 (0%)	0/25 (0%)	1/20 (5%)
Statistical Tests *(e)*			
Life Table	P=0.510	P=0.559N	P=0.626
Incidental Tumor Test	P=0.594	P=0.697N	P=0.600
Cochran-Armitage Trend, Fisher Exact Tests	P=0.425	P=0.676N	P=0.520
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Tumor Rates			
Overall *(b)*	3/50 (6%)	2/50 (4%)	1/49 (2%)
Adjusted *(c)*	13.6%	5.8%	5.0%
Terminal *(d)*	1/16 (6%)	0/25 (0%)	1/20 (5%)
Statistical Tests *(e)*			
Life Table	P=0.166N	P=0.354N	P=0.241N
Incidental Tumor Test	P=0.277N	P=0.604N	P=0.397N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.232N	P=0.500N	P=0.316N
Hematopoietic System: Lymphoma			
Tumor Rates			
Overall *(b)*	5/50 (10%)	4/50 (8%)	4/49 (8%)
Adjusted *(c)*	21.3%	11.7%	17.9%
Terminal *(d)*	1/16 (6%)	1/25 (4%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.326N	P=0.320N	P=0.375N
Incidental Tumor Test	P=0.393N	P=0.562N	P=0.448N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.447N	P=0.500N	P=0.513N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	5/50 (10%)	4/50 (8%)	6/49 (12%)
Adjusted *(c)*	21.3%	11.7%	24.6%
Terminal *(d)*	1/16 (6%)	1/25 (4%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.559	P=0.320N	P=0.593N
Incidental Tumor Test	P=0.559	P=0.562N	P=0.589N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.418	P=0.500N	P=0.486

TABLE 12. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

	Vehicle Control	Low Dose	High Dose
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	2/50 (4%)	3/49 (6%)	1/49 (2%)
Adjusted *(c)*	12.5%	10.9%	2.9%
Terminal *(d)*	2/16 (13%)	2/25 (8%)	0/20 (0%)
Statistical Tests *(e)*			
Life Table	P=0.325N	P=0.675N	P=0.445N
Incidental Tumor Test	P=0.453N	P=0.597	P=0.534N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.404N	P=0.490	P=0.508N
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	3/47 (6%)	3/45 (7%)	4/44 (9%)
Adjusted *(c)*	18.8%	11.0%	17.9%
Terminal *(d)*	3/16 (19%)	2/25 (8%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.535	P=0.465N	P=0.643
Incidental Tumor Test	P=0.493	P=0.561N	P=0.635N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.388	P=0.641	P=0.463
Pituitary: Carcinoma			
Tumor Rates			
Overall *(b)*	3/47 (6%)	3/45 (7%)	0/44 (0%)
Adjusted *(c)*	18.8%	12.0%	0.0%
Terminal *(d)*	3/16 (19%)	3/25 (12%)	0/20 (0%)
Statistical Tests *(e)*			
Life Table	P=0.054N	P=0.444N	P=0.081N
Incidental Tumor Test	P=0.054N	P=0.444N	P=0.081N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.112N	P=0.641	P=0.133N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	6/47 (13%)	6/45 (13%)	4/44 (9%)
Adjusted *(c)*	37.5%	22.6%	17.9%
Terminal *(d)*	6/16 (38%)	5/25 (20%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.176N	P=0.304N	P=0.212N
Incidental Tumor Test	P=0.200N	P=0.371N	P=0.183N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.354N	P=0.589	P=0.413N
Thyroid: Follicular-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	1/48 (2%)	3/47 (6%)	3/47 (6%)
Adjusted *(c)*	6.3%	12.5%	15.0%
Terminal *(d)*	1/16 (6%)	3/24 (12%)	3/20 (15%)
Statistical Tests *(e)*			
Life Table	P=0.302	P=0.458	P=0.385
Incidental Tumor Test	P=0.302	P=0.458	P=0.385
Cochran-Armitage Trend, Fisher Exact Tests	P=0.238	P=0.300	P=0.300

TABLE 12. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

(a) Dosed groups received doses of 12 or 25 mg/kg of allyl isothiocyanate by gavage.
(b) Number of tumor-bearing animals/number of animals examined at the site (percent).
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence in surviving animals killed at end of study.
(e) 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 before the end of the study as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend is indicated by (N).

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

A 2-year carcinogenesis bioassay of allyl isothiocyanate was conducted in F344/N rats and B6C3F1 mice. Doses of 12 or 25 mg/kg allyl isothiocyanate, administered 5 times per week by gavage, were selected for the chronic study since the 50 mg/kg dose administered in the 14-day study produced thickening of the mucosal surface of the stomach in male and female rats and mice, adherence of the stomach to the peritoneum in male rats, and a thickened urinary bladder wall in male mice. A dose of 25 mg/kg produced no gross lesions when administered for 14 consecutive days or when administered 5 times per week for 13 weeks, and all animals survived this dose.

Survival of dosed and control rats was comparable in the chronic study. Throughout the study, the mean body weights of high-dose male rats were lower than those of controls, and during the last half of the study the mean body weights of high-dose female rats were higher than the control values.

Transitional-cell papillomas of the urinary bladder occurred in dosed male rats with a statistically significant positive trend ($P<0.05$; incidence: control, 0/49, 0%; low-dose, 2/49, 4%; high-dose, 4/49, 8%). This benign urinary bladder tumor has not been observed among 568 untreated male control F344/N rats at this laboratory. The incidence of transitional-cell papillomas in male vehicle control rats in all laboratories in the NCI/NTP Bioassay Program is 1/994 (0.1%).

Epithelial hyperplasia was also seen at an increased incidence ($P<0.05$) in the urinary bladder of dosed male rats (control, 0/49, 0%; low-dose, 1/49, 2%; high-dose, 6/49, 12%). This hyperplasia did not occur in the animals that had transitional-cell papillomas. No urinary bladder calculi were seen in male rats.

Fibrosarcomas of the subcutaneous tissue occurred in female rats with a statistically significant positive trend ($P<0.05$; incidence: control, 0/50, 0%; low-dose, 0/50, 0%; high-dose, 3/50, 6%). The incidence in the high-dose group was not significant in comparison with the control group, and the evidence for the association of fibrosarcomas with administration of allyl isothiocyanate is considered equivocal. This tumor has been observed in 1/591 (0.2%) of the untreated female control F344/N rats at this laboratory and in 9/999 (0.9%) of the female vehicle control rats in all laboratories in the NCI/NTP Bioassay Program.

Retinopathy and cataract formation occurred at increased incidence in high-dose male rats and in low-dose female rats. This eye toxicity occurred most frequently in animals placed at the top of the racks, a position that gives maximum light exposure. Other chemicals assayed in a similar manner, such as stannous chloride (NTP, 1982), also showed a correlation between eye toxicity and rack position. However, not all NTP bioassays have shown a correlation between rack placement and eye toxicity. From these incidental observations it is not possible to determine whether a causative relationship exists for light exposure, allyl isothiocyanate administration, and eye defects.

Leukemia occurred in dosed male rats with a statistically significant positive trend ($P<0.05$; incidence: control, 2/50, 4%; low-dose, 6/50, 12%; high-dose, 8/50, 16%). The incidence in the high-dose group was significantly higher than that in the controls ($P<0.05$). However, this observed incidence was not statistically different from the historical incidence in male gavage controls in all laboratories in the Bioassay Program (96/999, 10%). No significant increases were observed for leukemia in female rats (7/50, 9/50, 12/50), or for lymphoma in male and female mice. Consequently, this increase is not considered to be the result of allyl isothiocyanate administration.

Survival of control and dosed female mice was comparable but lower than that usually seen at this laboratory, and the decreased survival may have reduced the incidence of late-appearing tumors in these groups. Suppurative inflammation of the peritoneum, uterus, or multiple organs was found in about one third of the female mice that died before the terminal kill, suggesting that an infection may have been a contributing factor to the decreased survival. Mean body weights of high-dose male and female mice were higher than those of controls throughout most of the study, and the animals may have been able to tolerate higher doses of allyl isothiocyanate.

The incidences of liver tumors in dosed male and female mice were not statistically significant. However, cytoplasmic vacuolization in the liver of dosed male mice was related to administration of allyl isothiocyanate (controls, 2/49, 4%; low-dose, 8/49, 16%; high-dose, 13/50, 26%).

The mechanism of action of allyl isothiocyanate is not known. Other unsaturated compounds, such as haloolefins, are thought to be metabolized *in vivo* to active epoxides (Eder et al., 1980). It

has been suggested that some haloolefins containing an allylic group may act as alkylating agents (Eder et al., 1980). Thiocyanate, which may be metabolically derived from isothiocyanate (White et al., 1978), has been shown to promote nitrosation of amines (Edwards et al., 1979; Fan and Tannenbaum, 1973). Isothiocyanates can react with an alcohol or an amine to give a thiocarbamate or thiourea (March, 1977). It is not known if any of these reactions were involved in producing the "ultimate carcinogen." An alternative mechanism of action for allyl isothiocyanate is as a promoter (Pitot and Sirica, 1980). Allyl isothiocyanate might enhance or stimulate the neoplastic growth of cells already initiated in the bladder cells, rather than initiate the first alteration itself. Allyl isothiocyanate was not mutagenic with or without activation in the Ames assay using strains TA 98, 100, 1535, and 1537 (NTP, 1981).

Other studies have shown that allyl isothiocyanate increases urine excretion (Muztar et al., 1979b). Williams (1974) has shown that allyl isothiocyanate and other isothiocyanates are directly toxic to cells grown in culture. These other toxic effects of allyl isothiocyanate were not measured in this bioassay. Whether they have an association with the carcinogenic effect observed in this study is not known.

Conclusions: Under the conditions of this bioassay, allyl isothiocyanate was carcinogenic for male F344/N rats, causing transitional-cell papillomas of the urinary bladder. Evidence for associating allyl isothiocyanate with subcutaneous fibrosarcomas in female F344/N rats was equivocal. Allyl isothiocyanate was not carcinogenic for B6C3F1 mice of either sex.

V. REFERENCES

V. REFERENCES

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

Berenblum, I. ed., Carcinogencity testing: a report of the panel on carcinogenicity of the Cancer Research Commission of UICC. Geneva: International Union Against Cancer, Vol. 2; 1969.

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

Eder, E.; Neudecker, T.; Lutz, D.; Henschler, D., Mutagenic potential of allyl and allylic compounds. Biochem. Pharmacol. 29:993-998; 1980.

Edwards, G.; Whong, W-Z.; Speciner, N., Intrahepatic mutagenesis assay: a sensitive method for detecting n-nitrosomorpholine and *in vivo* nitrosation of morpholine. Mutat. Res. 64:415-423; 1979.

Fan, T-Y.; Tannenbaum, S., Factors influencing the rate of formation of nitrosomorpholine from morpholine and nitrite: acceleration by thiocyanate and other anions. J. Agric. Food Chem. 21:237-240; 1973.

Food Chemicals Codex, 1972: 31-32.

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

Hagan, E., Hansen, W.; Fitzhugh, O.; Jenner, P.; Jones, W.; Taylor, J.; Long, E.; Nelson, A.; Brouwer, J., Food flavourings and compounds of related structure. II. Subacute and chronic toxicity. Food Cosmet. Toxicol. 5:141; 1967.

Hall, R., Toxicants occurring naturally in spices and flavors. In: Toxicants occuring naturally in foods. Washington, DC: National Academy of Science; 1973:448-451.

Jenner, P.; Hagan E.; Taylor, J.; Cook, E.; Fitzhugh, O., Food flavourings and compounds of related structure. I. Acute oral toxicity. Food Cosmet. Toxicol. 2:327-343; 1964.

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

Kirk-Othmer encyclopedia of chemical technology. New York: Interscience Publishers; Vol. 8, 1965:450.

Kirk-Othmer encyclopedia of chemical technology. New York; Interscience Publishers; Vol. 9, 1966:356.

Kirk-Othmer encyclopedia of chemical technology. New York: Interscience Publishers, Vol. 10, 1980:473.

Klesse, P.; Lukoschek, P., Untersuchungen ueber die bakteriostatische Wirksamkeit einiger Senfoele. Arzneim. Forsch. 5:505-507; 1955.

Langer, P.; Greer, M., Antithyroid activity of some naturally occurring isothiocyanates *in vitro*. Metabolism 17:569-605; 1968.

Langer, P.; Stole, V., Goitrogenic activity of allyl isothiocyanate — a widespread natural oil. Endocrinology 76:151-155; 1965.

Life Sciences Research Office, Evaluation of the health aspects of mustard and oil of mustard as food ingredients. Bethesda, MD: Life Sciences Research Office. SCOGS-16, 1975.

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

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

March, J., Advanced organic chemistry. New York: McGraw-Hill Book Co.; 1977: 813, 823.

Merck Index, 9th ed. Rahway, NJ: Merck and Co.; 1976: 292.

Mitchell, J.; Jordan, W., Allergic contact dermatitis from the radish *Raphanus Sativus*. Br. J. Dermat. 91:183-189; 1974.

Muztar, A.; Ahmad, P.; Huque, T.; Slinger, S., A study of the chemical binding of allyl isothiocyanate with thyroxine and of the effect of allyl isothiocyanate on lipid metabolism in the rat. Can. J. Physiol. Pharmacol. 57:385-389; 1979a.

Muztar, A.; Huque, T.; Ahmad, P.; Slinger, S., Effect of allyl isothiocyanate on plasma and urinary concentrations of some biochemical entities in the rat. Can. J. Physiol. Pharmacol. 57:504-509; 1979b.

Nishie, K.; Daxenbichler, M., Toxicology of glucosinolates, related compounds (nitriles, R-goitrin, isothiocyanates) and vitamin U found in cruciferae. Food Cosmet. Toxicol. 18:159-172; 1980.

NTIS, National Technical Information Service, PB Report 221 215. GRAS (generally recognized as safe) food ingredients—oil of mustard and allyl isothiocyanate. Maspeth, NY: Food and Drug Research Labs., Inc.; FDABF GRAS 015; October 1972.

V. REFERENCES

NTIS, National Technical Information Service, PB Report 223 812. Teratogenic evaluation of FDA 71-26 (oil of mustard). Maspeth, NY: Food and Drug Research Labs., Inc.; FDABF GRAS, FDA 17-260; June 1973.

NTIS, National Technical Information Service, PB Report 254 528. Evaluation of the health aspects of mustard and oil of mustard as food ingredients. Federation of American Societies for Experimental Biology; 1975.

NTP, National Toxicology Program, NTP Technical Bulletin, Issue 5:9, August 1981.

NTP, National Toxicology Program, NTP Technical Report on the carcinogenesis bioassay of stannous chloride, NTP TR 231, Department of Health and Human Services, Research Triangle Park, North Carolina, 1982.

Oda, Y.; Hamano, Y.; Inoue, K.; Yamamoto, H.; Niihara, T.; Kunita, N., Mutagenicity of food flavours in bacteria. Osaka-Furitsu Koshu Eisei Kenkyu Hokoku, Shokuhin eisei hen 9:177-181; 1978.

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

Pitot, H.; Sirica, A., The stages of initiation and promotion in hepatocarcinogenesis. Biochem. Biophys. Acta 605:191-215, 1980.

Ruddick, J.; Newsome, W.; Nash, L., Correlation of teratogenicity and molecular structure: ethylene thiourea and related compounds. Teratology 13:263-266; 1976.

Sadtler Research Laboratories, Sadtler Standard Spectra. Philadelphia: Sadtler Research Laboratories; IR No. 1603; UV No. 459; NMR No. 3155.

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

Timmermans, M.; Hennault-Roland, J. Chem. Phys. 29:564-565; 1922.

U.S. CFR, U.S. Code of Federal Regulations, 21CFR:172, 515; 1979.

USITC, United States International Trade Commission, Synthetic organic chemicals: United States production and sales. Washington, DC: U.S. Government Printing Office; 1979; USITC Publication No. *1001*.

Vernot, E.; MacEwen, J.; Haun, C.; Kinkead, E., Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions. Toxicol. Appl. Pharmacol. 42:417-423; 1977.

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

White, A.; Handler, P.; Smith, E.; Hill, R.; Lehman, I., eds., Principles of biochemistry. New York: McGraw-Hill Book Co.; 1978: 1208.

Williams, G., Direct toxicity of alpha-naphthylisothiocyanate in cell culture. Chem-Biol. Interact. 8:363-369; 1974.

APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
PAPILLOMA, NOS			1 (2%)
SQUAMOUS CELL PAPILLOMA	3 (6%)		4 (8%)
SQUAMOUS CELL CARCINOMA	1 (2%)		2 (4%)
BASAL-CELL TUMOR	1 (2%)		
BASAL-CELL CARCINOMA		1 (2%)	
ADNEXAL ADENOMA	1 (2%)		
KERATOACANTHOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS	1 (2%)	3 (6%)	1 (2%)
FIBROMA	2 (4%)	2 (4%)	2 (4%)
FIBROSARCOMA	5 (10%)	5 (10%)	1 (2%)
FIBROUS HISTIOCYTOMA, MALIGNANT	1 (2%)	2 (4%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(49)	(48)
SQUAMOUS CELL CARCINOMA, UNC PRI			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	2 (4%)	1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		2 (4%)
SARCOMA, NOS, UNC PRIM OR META			1 (2%)
FIBROSARCOMA, METASTATIC		1 (2%)	
FIBROUS HISTIOCYTOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
UNDIFFERENTIATED LEUKEMIA	2 (4%)	6 (12%)	8 (16%)
#SPLEEN	(50)	(49)	(50)
HISTIOCYTOMA, METASTATIC		1 (2%)	

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(49)	(50)
HEMANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	2 (4%)		5 (10%)
#PANCREAS	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)		
#DUODENUM	(48)	(49)	(47)
MUCINOUS ADENOCARCINOMA			1 (2%)
#ILEUM	(48)	(49)	(47)
OSTEOSARCOMA			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
TUBULAR-CELL ADENOMA		1 (2%)	
#URINARY BLADDER	(49)	(49)	(49)
TRANSITIONAL-CELL PAPILLOMA		2 (4%)	4 (8%)
LIPOMA		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(49)	(49)
CARCINOMA,NOS		1 (2%)	
ADENOMA, NOS	7 (15%)	12 (24%)	4 (8%)
#ADRENAL	(50)	(50)	(50)
CORTICAL ADENOMA	1 (2%)		
PHEOCHROMOCYTOMA	16 (32%)	15 (30%)	11 (22%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)	1 (2%)	
GANGLIONEUROMA		1 (2%)	
#THYROID	(48)	(50)	(50)
FOLLICULAR-CELL CARCINOMA	1 (2%)		1 (2%)

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
C-CELL ADENOMA	6 (13%)	10 (20%)	5 (10%)
C-CELL CARCINOMA	2 (4%)	1 (2%)	2 (4%)
#PANCREATIC ISLETS	(50)	(50)	(49)
ISLET-CELL ADENOMA	2 (4%)	2 (4%)	1 (2%)
ISLET-CELL CARCINOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA	3 (6%)	3 (6%)	3 (6%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS		1 (2%)	1 (2%)
ADENOMA, NOS			
ADENOCARCINOMA, NOS	4 (8%)	1 (2%)	1 (2%)
CYSTADENOMA, NOS		1 (2%)	
#TESTIS	(50)	(50)	(49)
INTERSTITIAL-CELL TUMOR	45 (90%)	45 (90%)	49 (100%)
NERVOUS SYSTEM			
#BRAIN	(50)	(49)	(50)
GLIOMA, NOS			1 (2%)
ASTROCYTOMA	2 (4%)		
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
ADENOMA, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
OSTEOMA		1 (2%)	
BODY CAVITIES			
*THORAX	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, METASTA	1 (2%)		

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*ABDOMINAL WALL	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
*MESENTERY	(50)	(50)	(50)
MESOTHELIOMA, NOS		1 (2%)	
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS			1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, METASTA			1 (2%)
SARCOMA, NOS			1 (2%)
FIBROUS HISTIOCYTOMA, METASTATIC	1 (2%)		
MESOTHELIOMA, NOS		1 (2%)	
MESOTHELIOMA, MALIGNANT		1 (2%)	1 (2%)
TAIL			
OSTEOSARCOMA		1	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	3	4	7
MORIBUND SACRIFICE	10	13	9
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED		1	1
TERMINAL SACRIFICE	32	32	33
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	48	50	49
TOTAL PRIMARY TUMORS	114	128	118
TOTAL ANIMALS WITH BENIGN TUMORS	47	49	49
TOTAL BENIGN TUMORS	90	99	86
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	25	21
TOTAL MALIGNANT TUMORS	22	27	24
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	3	1
TOTAL SECONDARY TUMORS	2	3	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	2	6
TOTAL UNCERTAIN TUMORS	2	2	6
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			2
TOTAL UNCERTAIN TUMORS			2

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

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
BASAL-CELL TUMOR	1 (2%)		
SARCOMA, NOS			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS			
FIBROMA		2 (4%)	
FIBROSARCOMA			3 (6%)
FIBROUS HISTIOCYTOMA, MALIGNANT	1 (2%)		
OSTEOSARCOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR ADENOMA			1 (2%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		2 (4%)
C-CELL CARCINOMA, METASTATIC	1 (2%)		
FIBROUS HISTIOCYTOMA, METASTATIC	1 (2%)		
CARCINOSARCOMA			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, UNDIFFER-TYPE			1 (2%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)
LEUKEMIA,NOS			1 (2%)
UNDIFFERENTIATED LEUKEMIA	7 (14%)	9 (18%)	11 (22%)
#SPLEEN	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
*TONGUE	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
#SALIVARY GLAND	(50)	(50)	(48)
ADENOMA, NOS	1 (2%)		
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE			1 (2%)
FIBROUS HISTIOCYTOMA, METASTATIC	1 (2%)		
#PANCREAS	(49)	(49)	(50)
ADENOMA, NOS			1 (2%)
URINARY SYSTEM			
#URINARY BLADDER	(49)	(49)	(50)
TRANSITIONAL-CELL PAPILLOMA			1 (2%)
ENDOMETRIAL STROMAL SARCOMA, MET			

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(50)	(50)
CARCINOMA,NOS		3 (6%)	2 (4%)
ADENOMA, NOS	17 (35%)	10 (20%)	13 (26%)
#ADRENAL	(50)	(50)	(50)
CORTICAL ADENOMA	2 (4%)	2 (4%)	2 (4%)
PHEOCHROMOCYTOMA	1 (2%)	2 (4%)	3 (6%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)		
GANGLIONEUROMA	1 (2%)		
#THYROID	(50)	(48)	(50)
FOLLICULAR-CELL CARCINOMA		1 (2%)	
C-CELL ADENOMA	10 (20%)	8 (17%)	6 (12%)
C-CELL CARCINOMA	2 (4%)	2 (4%)	3 (6%)
#PANCREATIC ISLETS	(49)	(49)	(50)
ISLET-CELL ADENOMA	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)		2 (4%)
FIBROADENOMA	8 (16%)	14 (28%)	11 (22%)
*CLITORAL GLAND	(50)	(50)	(50)
ADENOMA, NOS		1 (2%)	
*VAGINA	(50)	(50)	(50)
SARCOMA, NOS			
FIBROMA			1 (2%)
#UTERUS	(50)	(49)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
LEIOMYOMA			1 (2%)
ENDOMETRIAL STROMAL POLYP	14 (28%)	15 (31%)	16 (32%)
ENDOMETRIAL STROMAL SARCOMA	1 (2%)		
#CERVIX UTERI	(50)	(49)	(50)
SARCOMA, NOS			
#OVARY	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)		
NERVOUS SYSTEM			
#CEREBRAL VENTRICLE	(50)	(50)	(50)
ASTROCYTOMA		1 (2%)	
#BRAIN	(50)	(50)	(50)
ASTROCYTOMA	1 (2%)		
#BRAIN/THALAMUS	(50)	(50)	(50)
GLIOMA, NOS			1 (2%)
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
BASAL-CELL CARCINOMA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(50)	(50)
LIPOMA	1 (2%)		

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, INVASIV			1 (2%)
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	6	12	5
MORIBUND SACRIFICE	9	7	12
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED		2	
TERMINAL SACRIFICE	30	29	33
ANIMAL MISSING			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	42	43	42
TOTAL PRIMARY TUMORS	77	72	86
TOTAL ANIMALS WITH BENIGN TUMORS	37	32	33
TOTAL BENIGN TUMORS	58	54	56
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	16	25
TOTAL MALIGNANT TUMORS	19	18	29
TOTAL ANIMALS WITH SECONDARY TUMORS#	2		1
TOTAL SECONDARY TUMORS	3		1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			1
TOTAL UNCERTAIN TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	104	104	104	111	106	091	106	061	106	106	061	106	106	106	052	102	102	103	106	095	106	106	106
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	N	N	+
SQUAMOUS CELL PAPILLOMA																			X						
SQUAMOUS CELL CARCINOMA																									
BASAL-CELL TUMOR																									
ADNEXAL ADENOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	N	N	+
SARCOMA, NOS						X																			
FIBROMA							X																		
FIBROSARCOMA																					X		X		
FIBROUS HISTIOCYTOMA, MALIGNANT									X																
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE		X																					X		
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS										X															
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS									X										X			X			
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																			X						
PHEOCHROMOCYTOMA				X		X				X	X							X		X	X		X		X
PHEOCHROMOCYTOMA, MALIGNANT																	X								
THYROID	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																									
C-CELL ADENOMA										X															
C-CELL CARCINOMA						X																			
PARATHYROID	+	+	-	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	N	+	+	N	+
FIBROADENOMA												X													
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X		X	X	X	X	X	X		X		X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOCARCINOMA, NOS			X																					X	
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																									
BODY CAVITIES																									
PLEURA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALVEOLAR/BRONCHIOLAR CA, METASTAT																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROUS HISTIOCYTOMA, METASTATIC									X																
UNDIFFERENTIATED LEUKEMIA																			X						

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	106	106	106	106	106	106	106	105	106	106	106	102	106	105	106	106	106	100	106	106	106	103	106	106	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	50 M
SQUAMOUS CELL PAPILLOMA																				X					X	3
SQUAMOUS CELL CARCINOMA	X																									1
BASAL-CELL TUMOR																								X		1
ADNEXAL ADENOMA																			X							1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	50 M
SARCOMA, NOS																										1
FIBROMA			X																							2
FIBROSARCOMA	X																	X								5
FIBROUS HISTIOCYTOMA, MALIGNANT																									X	1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA											X													X		2
ALVEOLAR/BRONCHIOLAR CARCINOMA									X																	1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	●	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																										2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	+	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	50 M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																										1
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
ENDOCRINE SYSTEM																										
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	47
ADENOMA, NOS			X											X					X	X						7
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA	X			X		X					X		X			X				X						16
PHEOCHROMOCYTOMA, MALIGNANT																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
FOLLICULAR-CELL CARCINOMA																		X								1
C-CELL ADENOMA			X		X					X						X				X						6
C-CELL CARCINOMA																								X		2
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	-	+	-	+	+	-	+	+	+	42
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA													X								X					2
ISLET-CELL CARCINOMA				X																						1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	50 M
FIBROADENOMA																	X	X								3
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	45
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50 M
ADENOCARCINOMA, NOS																				X				X		4
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA							X											X								2
BODY CAVITIES																										
PLEURA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50 M
ALVEOLAR/BRONCHIOLAR CA, METASTAT									X																	1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50 M
FIBROUS HISTIOCYTOMA, METASTATIC																										1
UNDIFFERENTIATED LEUKEMIA							X																			2

M ANIMALS NECROPSIED

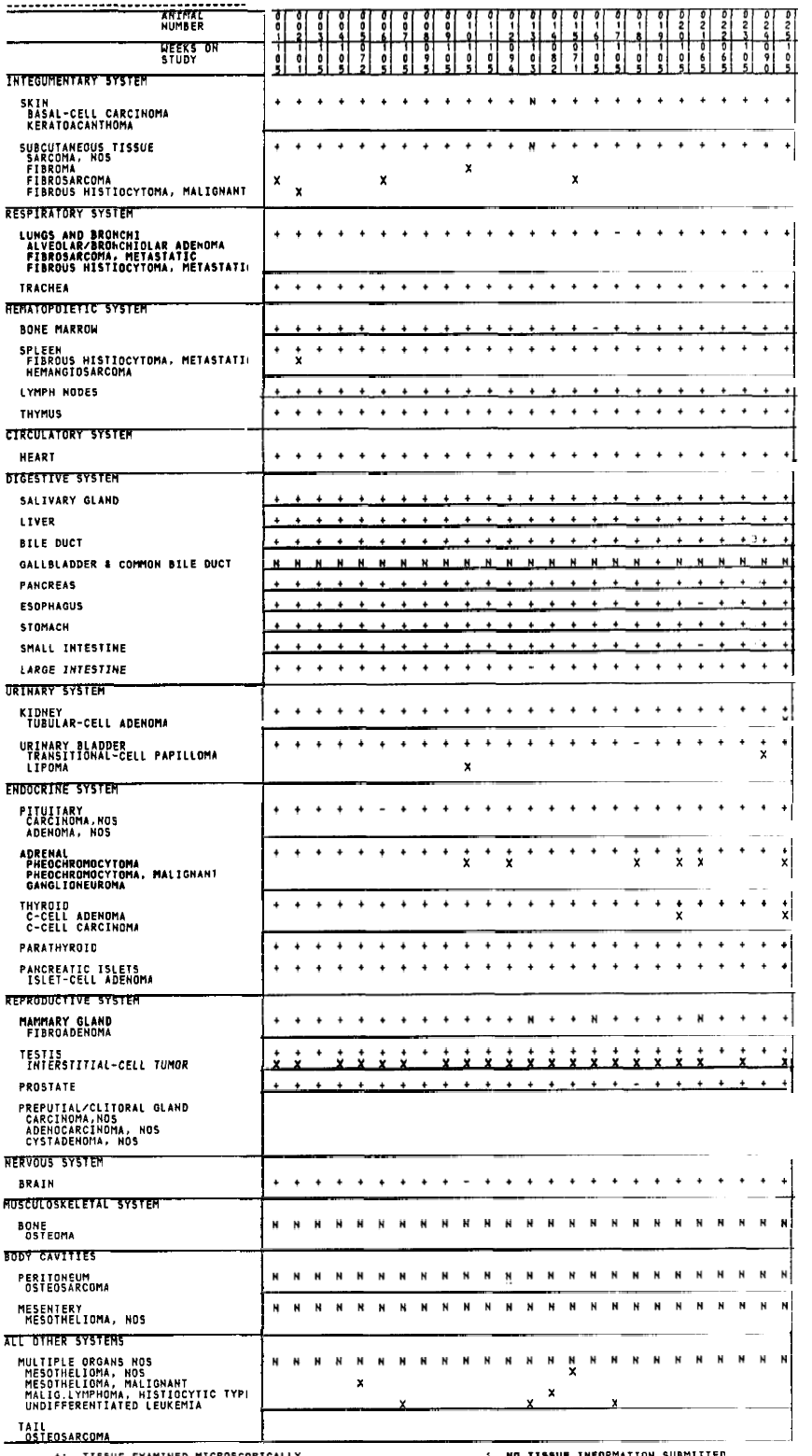
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

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

TABLE A3.

INDIVIDUAL ANIMAL T JMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUI Y OF ALLYL ISOTHIOCYANATE

LOW DOSE



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

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	105	085	104	068	095	095	100	095	054	095	095	095	095	054	095	095	095	095	095	091	095	095	080	011	095	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
BASAL-CELL CARCINOMA										X																1
KERATOACANTHOMA																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
SARCOMA, NOS	X			X					X																	3
FIBROMA												X														2
FIBROSARCOMA			X					X																		5
FIBROUS HISTIOCYTOMA, MALIGNANT											X															2
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA						X									X											1
FIBROSARCOMA, METASTATIC			X																							1
FIBROUS HISTIOCYTOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	49
FIBROUS HISTIOCYTOMA, METASTATIC																										1
HEMANGIOSARCOMA																										
LYMPH NODES																										
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOMA																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRANSITIONAL-CELL PAPILLOMA									X																	2
LIPOMA																										1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA,NOS																										1
ADENOMA, NOS							X				X		X		X					X	X		X			12
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA	X	X											X					X	X	X	X	X			X	15
PHEOCHROMOCYTOMA, MALIGNANT																										2
GANGLIONEUROMA																										
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA		X	X		X			X			X										X	X			X	10
C-CELL CARCINOMA																										1
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA													X									X				2
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROADENOMA		X				X																				3
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	45
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
CARCINOMA,NOS																	X									1
ADENOCARCINOMA, NOS																									X	1
CYSTADENOMA, NOS																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MUSCULOSKELETAL SYSTEM																										
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
OSTEOMA							X																			1
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
OSTEOSARCOMA																										1
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N	N	50M
MESOTHELIOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MESOTHELIOMA, NOS																										1
MESOTHELIOMA, MALIGNANT																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
UNDIFFERENTIATED LEUKEMIA			X		X																			X		6
TAIL																										
OSTEOSARCOMA																										

M ANIMALS NECROPSIED

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

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE

ANIMAL NUMBER	0011	0021	0031	0041	0051	0061	0071	0081	0091	0101	0111	0121	0131	0141	0151	0161	0171	0181	0191	0201	0211	0221	0231	0241	0251
WEEKS ON STUDY	074	084	080	104	104	104	184	044	060	044	095	044	044	044	084	069	089	044	044	044	044	069	044	044	083
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS		X																							
SQUAMOUS CELL PAPILLOMA													X												
SQUAMOUS CELL CARCINOMA		X																							
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									X
FIBROMA							X							X											
FIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, UNC PRIM												X													
ALVEOLAR/BRONCHIOLAR ADENOMA										X															
ALVEOLAR/BRONCHIOLAR CARCINOMA																							X		
SARCOMA, NOS, UNC PRIM OR META														X											
TRACHEA	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE					X								X							X					
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUCINOUS ADENOCARCINOMA																									
OSTEOSARCOMA																									
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL PAPILLOMA													X											X	
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
ADENOMA, NOS											X											X			
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA					X	X						X	X	X						X					
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																	X								
C-CELL ADENOMA											X							X						X	
C-CELL CARCINOMA															X							X			
PARATHYROID	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
FIBROADENOMA							X																		
TESTIS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS											X														
ADENOCARCINOMA, NOS																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GLIOMA, NOS																									
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																								X	
BODY CAVITIES																									
TUNICA VAGINALIS	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALVEOLAR/BRONCHIOLAR CA, METASTAT																									
SARCOMA, NOS																									
MESOTHELIOMA, MALIGNANT																									
UNDIFFERENTIATED LEUKEMIA								X			X		X									X			

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

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	104	104	104	104	041	068	104	060	104	093	086	104	104	104	104	060	081	104	084	011	104	092	104	104	104	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	50M
PAPILLOMA, NOS																										1
SQUAMOUS CELL PAPILLOMA												X	X											X		4
SQUAMOUS CELL CARCINOMA																	X									2
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	50M
SARCOMA, NOS																										1
FIBROMA																										2
FIBROSARCOMA										X																1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	48
SQUAMOUS CELL CARCINOMA, UNC PRIM																										1
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
ALVEOLAR/BRONCHIOLAR CARCINOMA																	X									2
SARCOMA, NOS, UNC PRIM OR META																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE													X												X	5
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
MUCINOUS ADENOCARCINOMA															X											1
OSTEOSARCOMA																						X				1
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRANSITIONAL-CELL PAPILLOMA																		X					X			4
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS		X																X								4
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA	X						X							X							X			X		11
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FOLLICULAR-CELL CARCINOMA																										1
C-CELL ADENOMA														X				X								5
C-CELL CARCINOMA																										2
PARATHYROID	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	45
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	49
ISLET-CELL ADENOMA																							X			1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	50M
FIBROADENOMA	X						X																			3
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	49
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
CARCINOMA,NOS																										1
ADENOCARCINOMA, NOS																							X			1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GLIOMA, NOS										X																1
SPECIAL SENSE ORGANS																										
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																										1
BODY CAVITIES																										
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
MESOTHELIOMA, NOS				X																						1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	M	N	N	N	N	N	N	N	N	N	50M
ALVEOLAR/BRONCHIOLAR CA, METASTAT																X										1
SARCOMA, NOS																			X							1
MESOTHELIOMA, MALIGNANT										X																1
UNDIFFERENTIATED LEUKEMIA			X										X			X				X						8

M ANIMALS NECROPSIED

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	106	104	104	052	106	099	091	106	103	106	105	106	106	106	106	099	091	106	106	106	106	106	106	106
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BASAL-CELL TUMOR																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROUS HISTIOCYTOMA, MALIGNANT																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA																	X								
C-CELL CARCINOMA, METASTATIC																									
FIBROUS HISTIOCYTOMA, METASTATIC													X												
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL PAPILLOMA																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROUS HISTIOCYTOMA, METASTATIC																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS			X	X						X	X			X		X	X			X		X		X	X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA							X																		
PHEOCHROMOCYTOMA									X																
PHEOCHROMOCYTOMA, MALIGNANT																									
GANGLIONEUROMA																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA	X		X	X			X			X													X	X	
C-CELL CARCINOMA																									
PARATHYROID	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																	X								
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+
ADENOCARCINOMA, NOS																	X								
FIBROADENOMA			X		X		X																	X	
UTERUS			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																									
ENDOMETRIAL STROMAL POLYP							X				X	X	X	X			X								
ENDOMETRIAL STROMAL SARCOMA																									
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA																									
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
BASAL-CELL CARCINOMA																									
MUSCULOSKELETAL SYSTEM																									
MUSCLE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIPOMA				X																					
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE													X												
UNDIFFERENTIATED LEUKEMIA								X												X					

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

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

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

ANIMAL NUMBER	0256	0267	0285	0290	0301	0312	0331	0335	0336	0337	0338	0391	0401	0411	0423	0433	0441	0445	0466	0477	0488	0499	0500	TOTAL
WEEKS ON STUDY	106	106	106	080	088	106	096	106	106	106	106	106	092	093	083	106	106	041	106	083	106	106		TISSUES TUMORS
INTEGUMENTARY SYSTEM																								
SKIN	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
BASAL-CELL TUMOR																								
SUBCUTANEOUS TISSUE	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
FIBROUS HISTIOCYTOMA, MALIGNANT				X																				1
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR CARCINOMA																								1
C-CELL CARCINOMA, METASTATIC																								1
FIBROUS HISTIOCYTOMA, METASTATIC																								1
TRACHEA																								
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	49
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																								
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL PAPILLOMA																								1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																								1
LIVER																							+	50
FIBROUS HISTIOCYTOMA, METASTATIC																								1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS						X		X						X						X	X	X		17
ADRENAL																								
CORTICAL ADENOMA																								
PHEOCHROMOCYTOMA																								
PHEOCHROMOCYTOMA, MALIGNANT																								
GANGLIONEUROMA																								
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA													X				X	X						10
C-CELL CARCINOMA																								
PARATHYROID																								
PANCREATIC ISLETS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ISLET-CELL ADENOMA																								1
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
ADENOCARCINOMA, NOS																								1
FIBROADENOMA										X							X			X	X			8
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS													X											1
ENDOMETRIAL STROMAL POLYP	X		X							X	X	X	X				X						X	14
ENDOMETRIAL STROMAL SARCOMA											X													1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS		X																						1
NERVOUS SYSTEM																								
BRAIN																								50
ASTROCYTOMA																								1
SPECIAL SENSE ORGANS																								
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
BASAL-CELL CARCINOMA																								1
MUSCULOSKELETAL SYSTEM																								
MUSCLE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
LIPOMA																								1
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS																								
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																								
DIFFERENTIATED LEUKEMIA																								

* ANIMALS NECROPSIED

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

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

LOW DOSE

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0110	0111	0112	0113	0114	0115	0116	0117	0118	0119	0120	0121	0122	0123	0124	0125
WEEKS ON STUDY	105	105	059	072	096	095	105	105	105	106	080	106	106	054	106	106	106	091	054	106	106	106	106	106	105
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																				X					
OSTEOSARCOMA				X																					
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
OSTEOSARCOMA				X																					
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
PANCREAS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS														X	X								X		
ADENOMA, NOS																					X				
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA																								X	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL CARCINOMA																	+								
C-CELL ADENOMA	X	X					X				X								X						
C-CELL CARCINOMA										X				X											
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA		X					X	X	X		X										X				X
PREPUTIAL/CLITORAL 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
ADENOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP		X	X			X	X		X		X		X						X						X
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ASTROCYTOMA					X																				
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
UNDIFFERENTIATED LEUKEMIA																			X		X	X			

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

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	097	091	105	106	103	054	076	096	106	090	106	106	106	106	073	106	106	106	091	106	106	106	106	088	093	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	N	+	+	+	50
FIBROMA					X																					2
OSTEOSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
OSTEOSARCOMA																										1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS																										3
ADENOMA, NOS	X		X						X			X	X				X	X	X	X						10
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA							X																			2
PHEOCHROMOCYTOMA									X												X					2
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	48
FOLLICULAR-CELL CARCINOMA																										1
C-CELL ADENOMA		X							X			X									X					8
C-CELL CARCINOMA																										2
PARATHYROID	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	-	-	+	+	+	+	-	+	+	+	45
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	N	+	+	+	50
FIBROADENOMA							X				X	X	X								X	X			X	14
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
ADENOMA, NOS					X																					1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	49
ENDOMETRIAL STROMAL POLYP			X									X	X	X								X	X			15
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ASTROCYTOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
UNDIFFERENTIATED LEUKEMIA	X	X								X					X			X							X	9

* ANIMALS NECROPSIED

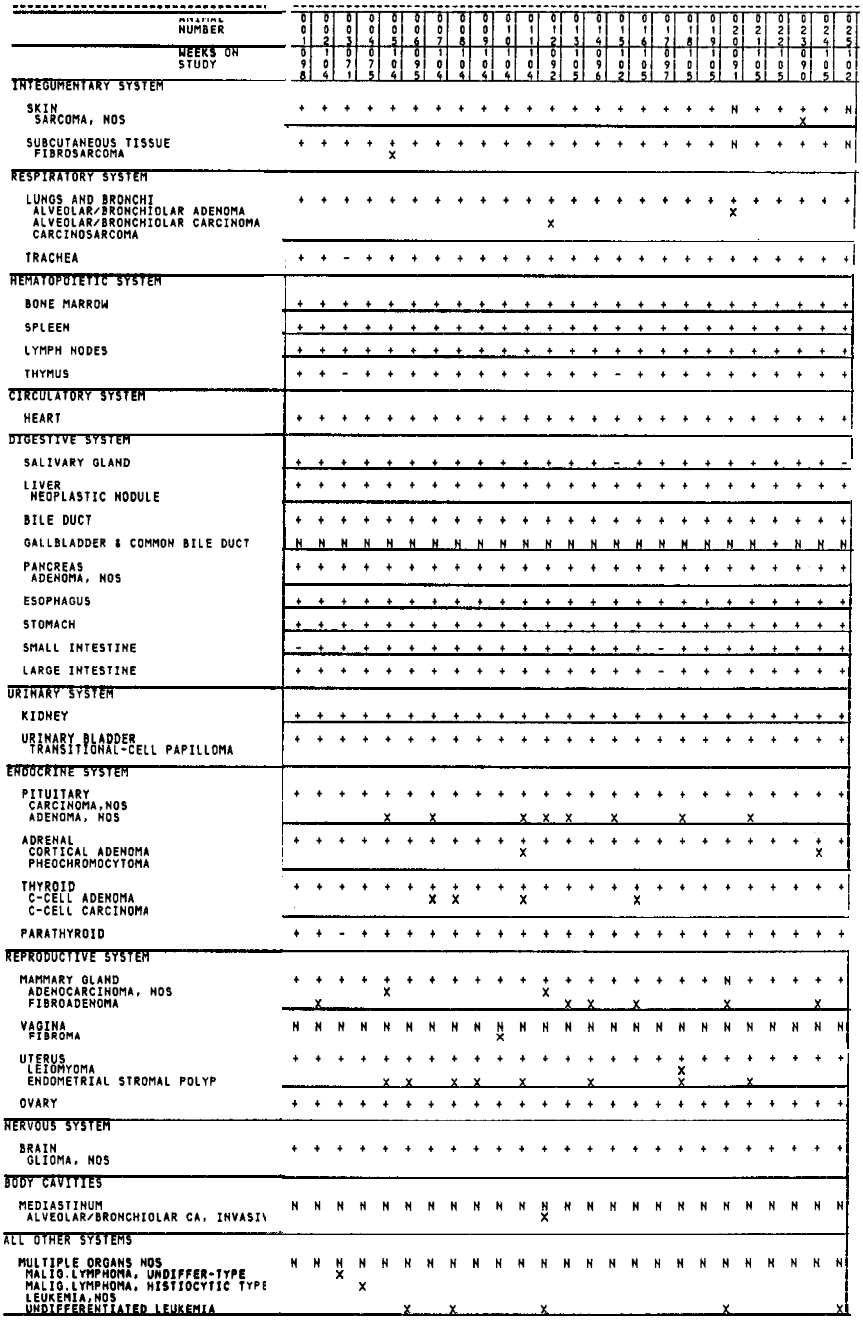
+: TISSUE EXAMINED MICROSCOPICALLY
-: REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
X: TUMOR INCIDENCE
N: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE



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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	072	105	093	105	105	097	105	105	052	105	105	105	105	105	105	105	105	105	105	105	105	105	094	082	105	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	50
SARCOMA, NOS																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	50
FIBROSARCOMA						X																		X		3
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
ALVEOLAR/BRONCHIOLAR CARCINOMA					X																					2
CARCINOSARCOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	47
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE								X																		1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS						X																				1
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRANSITIONAL-CELL PAPILLOMA																X										1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS																X							X			2
ADENOMA, NOS					X				X		X											X			X	13
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA																										2
PHEOCHROMOCYTOMA				X					X																	3
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA								X																	X	6
C-CELL CARCINOMA		X													X				X							3
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	47
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS																										2
FIBROADENOMA					X							X	X			X	X									11
VAGINA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
FIBROMA																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LEIOMYOMA																										1
ENDOMETRIAL STROMAL POLYP							X	X					X	X	X				X		X			X		16
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GLIOMA, NOS										X																1
BODY CAVITIES																										
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
ALVEOLAR/BRONCHIOLAR CA, INVASIVE																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MALIG.LYMPHOMA, UNDIFFER-TYPE																										1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										1
LEUKEMIA,NOS																			X							1
UNDIFFERENTIATED LEUKEMIA	X		X				X				X										X			X		11

M ANIMALS NECROPSIED

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

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

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
PAPILLOMA, NOS	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
HEPATOCELLULAR CARCINOMA, METAST	5 (10%)	2 (4%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	4 (8%)	3 (6%)	5 (10%)
ALVEOLAR/BRONCHIOLAR CARCINOMA		1 (2%)	3 (6%)
SARCOMA, NOS, METASTATIC			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2 (4%)		
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)	2 (4%)	
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
HEMANGIOSARCOMA	1 (2%)		1 (2%)
#SPLEEN	(49)	(48)	(50)
HEMANGIOSARCOMA	1 (2%)	1 (2%)	1 (2%)
#MYOCARDIUM	(50)	(50)	(50)
HEMANGIOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(50)
BILE DUCT CARCINOMA			1 (2%)

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEPATOCELLULAR ADENOMA	9 (18%)	6 (12%)	12 (24%)
HEPATOCELLULAR CARCINOMA	13 (27%)	9 (18%)	10 (20%)
MIXED HEPATO/CHOLANGIO CARCINOMA			1 (2%)
#STOMACH	(49)	(48)	(48)
SQUAMOUS CELL CARCINOMA			1 (2%)
#JEJUNUM	(45)	(42)	(45)
CARCINOMA,NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY/CORTEX	(49)	(49)	(50)
ADENOMA, NOS			
ENDOCRINE SYSTEM			
#ADRENAL	(47)	(49)	(50)
PHEOCHROMOCYTOMA			
#THYROID	(50)	(45)	(50)
FOLLICULAR-CELL ADENOMA	3 (6%)	2 (4%)	1 (2%)
REPRODUCTIVE SYSTEM			
NONE			
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS	2 (4%)	1 (2%)	1 (2%)
CYSTADENOMA, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR CA, INVASIV			
ALVEOLAR/BRONCHIOLAR CA, METASTA			1 (2%)
*MESENTERY	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)		
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
FIBROSARCOMA			1 (2%)
HEAD			
SARCOMA, NOS			1
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHa	14	17	10
MORIBUND SACRIFICE	9	3	6
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED	1	6	7
TERMINAL SACRIFICE	21	24	27
ANIMAL MISSING			

a INCLUDES AUTOLYZED ANIMALS

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	33	22	26
TOTAL PRIMARY TUMORS	39	27	39
TOTAL ANIMALS WITH BENIGN TUMORS	18	12	18
TOTAL BENIGN TUMORS	20	13	19
TOTAL ANIMALS WITH MALIGNANT TUMORS	18	14	17
TOTAL MALIGNANT TUMORS	18	14	20
TOTAL ANIMALS WITH SECONDARY TUMORS#	6	2	3
TOTAL SECONDARY TUMORS	6	2	3
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1		
TOTAL UNCERTAIN TUMORS	1		
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(49)
FIBROUS HISTIOCYTOMA, MALIGNANT			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(49)
MALIGNANT MELANOMA		1 (2%)	
FIBROUS HISTIOCYTOMA, MALIGNANT			1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(47)	(49)	(49)
SQUAMOUS CELL CARCINOMA, METASTA			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	1 (2%)	
ALVEOLAR/BRONCHIOLAR CARCINOMA		2 (4%)	3 (6%)
OSTEOSARCOMA, METASTATIC			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)	1 (2%)	
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	3 (6%)	2 (4%)	1 (2%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		2 (4%)
MALIGNANT LYMPHOMA, MIXED TYPE			
LYMPHOCYTIC LEUKEMIA			1 (2%)
#SPLEEN	(47)	(48)	(49)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#MESENTERIC L. NODE	(50)	(47)	(49)
MALIGNANT LYMPHOMA, MIXED TYPE		1 (2%)	
#LIVER	(50)	(49)	(49)
KUPFFER-CELL SARCOMA			1 (2%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
UNDIFFERENTIATED LEUKEMIA			1 (2%)
CIRCULATORY SYSTEM			
*SKIN	(50)	(50)	(49)
HEMANGIOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(49)
HEMANGIOSARCOMA	1 (2%)		
LYMPHANGIOMA			1 (2%)
#SPLEEN	(47)	(48)	(49)
HEMANGIOSARCOMA			1 (2%)
*MESENTERY	(50)	(50)	(49)
HEMANGIOMA		1 (2%)	
#UTERUS	(50)	(47)	(49)
HEMANGIOSARCOMA	1 (2%)		
#OVARY	(49)	(44)	(48)
HEMANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEPATOCELLULAR ADENOMA	2 (4%)	1 (2%)	
HEPATOCELLULAR CARCINOMA		2 (4%)	1 (2%)
#STOMACH	(47)	(47)	(49)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
SQUAMOUS CELL CARCINOMA			
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(45)	(44)
CARCINOMA,NOS	3 (6%)	3 (7%)	

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ADENOMA, NOS	3 (6%)	3 (7%)	4 (9%)
ACIDOPHIL CARCINOMA	1 (2%)		
#THYROID	(48)	(47)	(47)
FOLLICULAR-CELL ADENOMA	1 (2%)	3 (6%)	1 (2%)
FOLLICULAR-CELL CARCINOMA			2 (4%)
#PANCREATIC ISLETS	(47)	(45)	(49)
ISLET-CELL ADENOMA		1 (2%)	
ISLET-CELL CARCINOMA			
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)		
ADENOCARCINOMA, NOS	1 (2%)	1 (2%)	1 (2%)
#UTERUS	(50)	(47)	(49)
SQUAMOUS CELL CARCINOMA			1 (2%)
ADENOCARCINOMA, NOS		1 (2%)	
ENDOMETRIAL STROMAL POLYP	2 (4%)		
#OVARY	(49)	(44)	(48)
TERATOMA, NOS			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
ACIDOPHIL CARCINOMA, INVASIVE	1 (2%)		
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)	1 (2%)	
CYSTADENOMA, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*FEMUR	(50)	(50)	(49)
OSTEOSARCOMA			1 (2%)
BODY CAVITIES			
NONE			

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	22	15	16
MORIBUND SACRIFICE	12	10	15
SCHEDULED SACRIFICE	5		
ACCIDENTALLY KILLED			1
TERMINAL SACRIFICE	11	25	18
ANIMAL MISSING			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	18	20	20
TOTAL PRIMARY TUMORS	25	28	26
TOTAL ANIMALS WITH BENIGN TUMORS	11	11	6
TOTAL BENIGN TUMORS	13	13	6
TOTAL ANIMALS WITH MALIGNANT TUMORS	10	14	15
TOTAL MALIGNANT TUMORS	12	15	19
TOTAL ANIMALS WITH SECONDARY TUMORS#	1		2
TOTAL SECONDARY TUMORS	1		2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			1
TOTAL UNCERTAIN TUMORS			1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

VEHICLE CONTROL

ANIMAL NUMBER	0012	0023	0034	0045	0056	0067	0078	0089	0110	0112	0136	0147	0158	0169	0179	0181	0192	0201	0212	0223	0234	0245
WEEKS ON STUDY	099	096	078	074	084	044	041	044	046	078	086	079	066	066	044	019	041	089	066	066	077	066
INTEGUMENTARY SYSTEM																						
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS								X														
RESPIRATORY SYSTEM																						
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA	X																			X	X	
ALVEOLAR/BRONCHIOLAR ADENOMA						X																
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																						
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA									X													
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+
CIRCULATORY SYSTEM																						
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																						
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA									X													X
HEPATOCELLULAR CARCINOMA	X	X	X		X											X				X		
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
GALLBLADDER & COMMON BILE DUCT	N	N	+	+	+	+	+	+	+	+	N	+	+	+	+	N	N	+	N	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
URINARY SYSTEM																						
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																						
PITUITARY	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA						X									X			X				
PARATHYROID	+	+	+	+	+	+	+	+	-	+	-	+	+	-	+	+	+	+	-	+	+	+
REPRODUCTIVE SYSTEM																						
MAMMARY GLAND	N	N	+	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	+
TESTIS	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																						
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																						
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																			X			
CYSTADENOMA, NOS																		X				
BODY CAVITIES																						
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, NOS																X						
ALL OTHER SYSTEMS																						
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEPATOCELLULAR CARCINOMA, METASTA																X						
HEMANGIOSARCOMA																		X				
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																						
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																						

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

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

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 10	03 11	03 12	03 33	03 34	03 35	03 36	03 37	03 38	03 39	04 00	04 11	04 12	04 13	04 14	04 15	04 16	04 17	04 18	04 19	05 00	TOTAL
WEEKS ON STUDY	05 07	10 06	10 06	10 06	10 06	07 05	09 01	07 08	10 06	09 03	07 08	10 06	09 11	10 06	10 06	10 06	06 05	04 11	10 06	08 03	09 06	10 06	06 03	10 06	10 08	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PAPILLOMA, NOS																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA										X	X															5
ALVEOLAR/BRONCHIOLAR ADENOMA				X										X										X		4
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
HEMANGIOSARCOMA																										1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	50
THYMUS	-	+	+	+	+	-	+	+	+	-	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	41
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA			X		X		X		X					X	X	X										9
HEPATOCELLULAR CARCINOMA						X				X	X		X		X					X						13
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	50
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	45
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	46
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	47
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FOLLICULAR-CELL ADENOMA																										3
PARATHYROID	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	-	-	-	+	+	+	+	+	+	+	40
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	N	N	N	N	N	N	N	+	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	50
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
ADENOMA, NOS																						X				2
CYSTADENOMA, NOS																										1
BODY CAVITIES																										
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MESOTHELIOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
HEPATOCELLULAR CARCINOMA, METASTA																										1
HEMANGIOSARCOMA																										1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE												X									X					2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE								X																		1

* ANIMALS NECROPSIED

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

LOW DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	012	105	105	105	207	105	105	105	105	075	018	105	051	042	105	059	097	105	105	060	099	105	105	027	011
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA									X										X						
ALVEOLAR/BRONCHIOLAR ADENOMA																X									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																	X								
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA												X													
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA			X							X		X													
HEPATOCELLULAR CARCINOMA																X			X	X					
BILE DUCT	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	+	+	+	+	N	+	+	N	+	+	N	N	+	N	+	+	+	+	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-
CARCINOMA, NOS															X										
LARGE INTESTINE	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-
FOLLICULAR-CELL ADENOMA																				X					
PARATHYROID	-	-	-	-	+	-	+	+	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	+	N	N	+	N	N	N	N	N	N	N	+	N	+	N	N	N	+	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, HISTIOCYTIC TYPE						X															X				

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	105	105	076	025	105	105	056	065	045	012	105	105	029	105	090	064	050	108	089	051	105	105	048	045	105	
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA														X												2
ALVEOLAR/BRONCHIOLAR ADENOMA	X																									3
ALVEOLAR/BRONCHIOLAR CARCINOMA											X															1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMANGIOSARCOMA																										1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOMA																										1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA					X																X			X		6
HEPATOCELLULAR CARCINOMA								X				X		X					X		X				X	9
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	N	N	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	50M
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	42
CARCINOMA,NOS																										1
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYROID	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
FOLLICULAR-CELL ADENOMA																					X					2
PARATHYROID	+	+	-	-	+	+	-	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	36
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	+	+	N	N	N	+	N	N	N	N	+	N	+	N	50M
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																									X	1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										2

M ANIMALS NECROPSIED

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	015	062	041	104	015	104	104	104	104	029	104	035	056	104	104	006	047	041	053	104	104	104	104
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
ALVEOLAR/BRONCHIOLAR CARCINOMA										X															
SARCOMA, NOS, METASTATIC																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT CARCINOMA																									
HEPATOCELLULAR ADENOMA						X				X													X	X	X
HEPATOCELLULAR CARCINOMA	X					X		X			X		X				X	X					X		
MIXED HEPATO/CHOLANGIO CARCINOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	N	N	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
SMALL INTESTINE	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA													X												
PARATHYROID	+	-	+	+	-	-	-	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	+	N	N	+	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS	X																								
BODY CAVITIES																									
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ALVEOLAR/BRONCHIOLAR CA, METASTAT																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA, METASTAT																									
FIBROSARCOMA																									
HEMANGIOSARCOMA																									
HEAD NOS																									
SARCOMA, NOS																									

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

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

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

ANIMAL NUMBER	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	TOTAL
WEEKS ON STUDY	1 0 4	0 8 3	0 8 6	0 8 6	0 6 5	0 4	0 2 0	1 0 4	0 9 8	1 0 0	1 0 3	1 0 4	1 0 4	0 4 6	0 5 5	0 6 7	1 0 4	1 0 2	1 0 2	1 0 4	1 0 4	1 0 4	1 0 6	1 0 9	1 0 4	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA		X											X					X				X			X	5
ALVEOLAR/BRONCHIOLAR CARCINOMA		X					X																			3
SARCOMA, NOS, METASTATIC									X																	1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA																	X									1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
THYMUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	-	+	+	+	46
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT CARCINOMA																		X								1
HEPATOCELLULAR ADENOMA									X				X	X			X			X	X		X			12
HEPATOCELLULAR CARCINOMA																	X	X								10
MIXED HEPATO/CHOLANGIO CARCINOMA		X																								1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	+	N	+	+	+	N	+	+	+	N	N	+	+	N	+	+	+	+	N	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	-	+	46
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	48
SQUAMOUS CELL CARCINOMA				X																						1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	45
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	46
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	+	-	+	+	+	-	-	+	+	-	-	+	+	+	-	-	+	+	+	+	+	+	+	+	+	35
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	+	50*
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ADENOMA, NOS																										1
BODY CAVITIES																										
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ALVEOLAR/BRONCHIOLAR CA, METASTAT		X																								1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA, METASTAT				X																						1
FIBROSARCOMA																									X	1
HEMANGIOSARCOMA			X																							1
HEAD NOS																										
SARCOMA, NOS									X																	1

* ANIMALS NECROPSIED

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

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

VEHICLE CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	104	104	104	104	104	078	104	083	081	075	046	091	059	069	007	006	006	006	038	086	092	033	115	055	103
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																	X								
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	+	+	N	+	N	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS							X										X								
ADENOMA, NOS			X																						
ACIDOPHIL CARCINOMA	X																								
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA			X																						
PARATHYROID	-	+	+	-	-	+	-	-	-	+	-	+	-	+	-	+	-	+	-	+	+	+	-	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																						X			
ADENOCARCINOMA, NOS																X									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP						X																			
HEMANGIOSARCOMA																	X								
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ACIDOPHIL CARCINOMA, INVASIVE	X																								
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
CYSTADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																						X			
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE												X													
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL TISSUES TUMORS
WEEKS ON STUDY	106	106	106	106	091	084	043	106	076	060	092	016	074	086	094	090	085	091	086	052	106	106	092	085	092	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
HEMANGIOSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	47
ALVEOLAR/BRONCHIOLAR ADENOMA					X											X										2
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	-	+	44
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA																					X	X				2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	N	+	N	N	+	N	+	+	N	+	+	+	N	+	+	+	+	+	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	47
SMALL INTESTINE	+	+	+	+	+	-	+	+	-	-	+	+	+	-	+	+	-	+	+	+	+	+	+	+	-	40
LARGE INTESTINE	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	-	42
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	47
CARCINOMA,NOS		X																								3
ADENOMA, NOS	X		X																							3
ACIDOPHIL CARCINOMA																										1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYROID	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	+	+	-	+	+	+	+	-	+	-	-	-	+	+	+	+	-	+	+	+	+	-	+	+	-	30
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
ADENOMA, NOS																										1
ADENOCARCINOMA, NOS																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP					X																					2
HEMANGIOSARCOMA																										1
OVARY	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ACIDOPHIL CARCINOMA, INVASIVE																										1
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ADENOMA, NOS																			X							1
CYSTADENOMA, NOS								X																		1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, NOS																										1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																						X	X			3
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																			X							1

* ANIMALS NECROPSIED

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

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

LOW DOSE

ANIMAL NUMBER	0 0 1	0 0 2	0 0 3	0 0 4	0 0 5	0 0 6	0 0 7	0 0 8	0 0 9	0 1 0	0 1 1	0 1 2	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 2 1	0 2 2	0 2 3	0 2 4	0 2 5
WEEKS ON STUDY	0 9 1	0 9 5	0 5 9	0 7 3	0 2 8	0 9 5	0 9 5	0 8 5	1 0 3	0 9 5	0 9 5	0 9 5	0 9 5	0 9 7	0 9 5	1 0 3	0 9 5	0 9 5	0 7 4	0 7 6	0 9 5	0 9 5	1 0 1	0 9 5	0 9 5
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
MALIGNANT MELANOMA													X												
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
MALIGNANT LYMPHOMA, MIXED TYPE												X													
THYMUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
HEPATOCELLULAR ADENOMA																					X				
HEPATOCELLULAR CARCINOMA													X												
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+
PANCREAS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
SQUAMOUS CELL PAPILLOMA																					X				
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
CARCINOMA,NOS	X	X					X					X					X								X
ADENOMA, NOS																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	-	+
FOLLICULAR-CELL ADENOMA							X					X													
PARATHYROID	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	A	-	+
PANCREATIC ISLETS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	A	+	+
ISLET-CELL ADENOMA																	X								
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+
ADENOCARCINOMA, NOS		X																							
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+
ADENOCARCINOMA, NOS																									
OVARY	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	A	+	+
HEMANGIOSARCOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
BODY CAVITIES																									
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
HEMANGIOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS																									
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																X									

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

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

ANIMAL NUMBER / WEEKS ON STUDY	TOTAL TISSUES / TUMORS
INTEGUMENTARY SYSTEM	
SKIN	50
HEMANGIOMA	1
SUBCUTANEOUS TISSUE	50
MALIGNANT MELANOMA	1
RESPIRATORY SYSTEM	
LUNGS AND BRONCHI	49
ALVEOLAR/BRONCHIOLAR ADENOMA	1
ALVEOLAR/BRONCHIOLAR CARCINOMA	2
TRACHEA	47
HEMATOPOIETIC SYSTEM	
BONE MARROW	49
SPLEEN	48
LYMPH NODES	47
MALIGNANT LYMPHOMA, MIXED TYPE	1
THYMUS	45
CIRCULATORY SYSTEM	
HEART	50
DIGESTIVE SYSTEM	
SALIVARY GLAND	49
LIVER	49
HEPATOCELLULAR ADENOMA	1
HEPATOCELLULAR CARCINOMA	2
BILE DUCT	49
GALLBLADDER & COMMON BILE DUCT	50
PANCREAS	45
ESOPHAGUS	50
STOMACH	47
SQUAMOUS CELL PAPILLOMA	1
SMALL INTESTINE	44
LARGE INTESTINE	45
URINARY SYSTEM	
KIDNEY	48
URINARY BLADDER	47
ENDOCRINE SYSTEM	
PITUITARY	45
CARCINOMA,NOS	3
ADENOMA, NOS	3
ADRENAL	47
THYROID	47
FOLLICULAR-CELL ADENOMA	3
PARATHYROID	48
PANCREATIC ISLETS	45
ISLET-CELL ADENOMA	1
REPRODUCTIVE SYSTEM	
MAMMARY GLAND	50
ADENOCARCINOMA, NOS	1
UTERUS	47
ADENOCARCINOMA, NOS	1
OVARY	44
HEMANGIOSARCOMA	1
NERVOUS SYSTEM	
BRAIN	50
SPECIAL SENSE ORGANS	
HARDERIAN GLAND	50
ADENOMA, NOS	1
BODY CAVITIES	
MESENTERY	50
HEMANGIOMA	1
ALL OTHER SYSTEMS	
MULTIPLE ORGANS NOS	50
MALIGNANT LYMPHOMA, NOS	1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	2

M ANIMALS NECROPSIED

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF ALLYL ISOTHIOCYANATE

HIGH DOSE

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	010	011	012	013	014	015	016	017	018	019	020	021	022	023	024	025
WEEKS ON STUDY	066	095	104	104	076	095	087	101	078	104	082	096	104	091	093	096	091	104	078	040	041	082	104	078	104
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROUS HISTIOCYTOMA, MALIGNANT																									
LYMPHANGIOMA																	X								
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																									
ALVEOLAR/BRONCHIOLAR CARCINOMA						X							X			X									
OSTEOSARCOMA, METASTATIC																			X						
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																				X					
MALIGNANT LYMPHOMA, MIXED TYPE																				X					
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA																									
KUPFFER-CELL SARCOMA																									
UNDIFFERENTIATED LEUKEMIA																						X			
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	N	+	+	N	+	+	N	+	+	+	+	+	N	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS														X		X									X
ADRENAL	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																									
FOLLICULAR-CELL CARCINOMA											X			X											
PARATHYROID	-	-	+	+	-	-	-	+	+	+	-	+	+	-	-	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS															X										
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
OVARY	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TERATOMA, NOS														X											
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA																			X						
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROUS HISTIOCYTOMA, MALIGNANT																									
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE															X		X								
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																			X						
LYMPHOCYTIC LEUKEMIA						X																			

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

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

ANIMAL NUMBER	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	TOTAL
WEEKS ON STUDY	1 0 1	0 9 1	1 0 4	1 0 4	0 8 3	0 7 9	0 1 3	0 1 7	1 0 4	1 0 4	1 0 4	0 7 4	0 4 0	0 5 2	1 0 4	0 6 0	1 0 4	1 0 4	1 0 4	0 7 3	1 0 5	1 0 5	0 8 4	0 8 5	1 0 5	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
FIBROUS HISTIOCYTOMA, MALIGNANT														X												1
LYMPHANGIOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
SQUAMOUS CELL CARCINOMA, METASTAT																							X			1
ALVEOLAR/BRONCHIOLAR CARCINOMA																										3
OSTEOSARCOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMANGIOSARCOMA																										1
MALIGNANT LYMPHOMA, MIXED TYPE																										1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	-	+	-	+	+	+	+	+	44
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR CARCINOMA					X																					1
KUPFFER-CELL SARCOMA																					X					1
UNDIFFERENTIATED LEUKEMIA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	N	+	+	+	N	A	+	+	+	+	+	+	+	+	+	+	N	+	49M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	A	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	A	+	+	-	+	+	+	-	+	+	-	-	+	44
ADENOMA, NOS															X											4
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	A	+	-	+	+	+	+	+	+	+	+	+	+	47
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	47
FOLLICULAR-CELL ADENOMA																			X							1
FOLLICULAR-CELL CARCINOMA																										2
PARATHYROID	+	+	-	+	+	+	-	-	+	+	+	+	A	+	+	+	+	+	+	-	+	+	+	+	+	37
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49M
ADENOCARCINOMA, NOS																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
SQUAMOUS CELL CARCINOMA																							X			1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	48
TERATOMA, NOS																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	49
MUSCULOSKELETAL SYSTEM																										
BONE	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	49M
OSTEOSARCOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	49M
FIBROUS HISTIOCYTOMA, MALIGNANT																			X							1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE									X																	1
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										2
LYMPHOCYTIC LEUKEMIA																										1

M ANIMALS NECROPSIED

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

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

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	3 (6%)	1 (2%)	3 (6%)
*SUBCUT TISSUE	(50)	(50)	(50)
HEMATOMA, NOS		1 (2%)	
GRANULOMA, FOREIGN BODY	1 (2%)		
FIBROSIS	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(49)	(49)	(48)
EDEMA, NOS	1 (2%)		
PNEUMONIA, ASPIRATION	1 (2%)		4 (8%)
INFLAMMATION, SUPPURATIVE	2 (4%)		
BRONCHOPNEUMONIA, CHRONIC			
CHOLESTEROL DEPOSIT			1 (2%)
HYPERPLASIA, ADENOMATOUS			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM		3 (6%)	1 (2%)
METAPLASIA, OSSEOUS			1 (2%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(48)	(49)	(50)
HYPERPLASIA, NOS	2 (4%)		
MYELOFIBROSIS	1 (2%)		
#SPLEEN	(50)	(49)	(50)
CONGESTION, NOS	2 (4%)		
FIBROSIS, MULTIFOCAL	1 (2%)		
METAMORPHOSIS FATTY	1 (2%)		
HEMOSIDEROSIS	20 (40%)	20 (41%)	7 (14%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANGIECTASIS	1 (2%)		
HYPERPLASIA, LYMPHOID	2 (4%)		
HEMATOPOIESIS	1 (2%)	2 (4%)	
#LYMPH NODE	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)		
#MANDIBULAR L. NODE	(50)	(50)	(50)
HYPERPLASIA, PLASMA CELL		1 (2%)	
#MESENTERIC L. NODE	(50)	(50)	(50)
HEMORRHAGE, CHRONIC			
INFLAMMATION, GRANULOMATOUS			
ANGIECTASIS	1 (2%)		
#INGUINAL LYMPH NODE	(50)	(50)	(50)
HYPERPLASIA, DIFFUSE			
#PANCREAS	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(50)
MINERALIZATION	1 (2%)		
INFLAMMATION, CHRONIC			
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	1 (2%)
FIBROSIS, FOCAL	23 (46%)	23 (46%)	19 (38%)
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC		2 (4%)	5 (10%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
*DESCENDING THORACIC	(50)	(50)	(50)
ARTERIOSCLEROSIS, NOS	1 (2%)		
*MESENTERIC ARTERY	(50)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
#PANCREAS	(50)	(50)	(49)
PERIARTERITIS			
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(50)	(50)
FIBROSIS, FOCAL		1 (2%)	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ATROPHY, FOCAL		1 (2%)	
#LIVER	(50)	(50)	(50)
CONGESTION, ACUTE			1 (2%)
INFLAMMATION, GRANULOMATOUS			1 (2%)
NECROSIS, ZONAL	1 (2%)		
CYTOPLASMIC VACUOLIZATION	2 (4%)		
CYTOLOGIC ALTERATION, NOS	3 (6%)	4 (8%)	1 (2%)
ANGIECTASIS			2 (4%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION		1 (2%)	
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	11 (22%)	32 (64%)	10 (20%)
HYPERPLASIA, FOCAL	14 (28%)	1 (2%)	1 (2%)
#PANCREAS	(50)	(50)	(49)
CYST, NOS			1 (2%)
ATROPHY, FOCAL	4 (8%)	5 (10%)	1 (2%)
#PANCREATIC ACINUS	(50)	(50)	(49)
ATROPHY, NOS	1 (2%)		
#GASTRIC SUBMUCOSA	(49)	(50)	(49)
FIBROSIS		1 (2%)	
#COLON	(48)	(49)	(49)
PARASITISM		1 (2%)	1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
INFLAMMATION, CHRONIC	40 (80%)	23 (46%)	20 (40%)
NEPHROSIS, NOS		1 (2%)	1 (2%)
PIGMENTATION, NOS		1 (2%)	
#KIDNEY/TUBULE	(50)	(50)	(50)
DEGENERATION, HYALINE	1 (2%)		
#URINARY BLADDER	(49)	(49)	(49)
INFLAMMATION, HEMORRHAGIC			
HYPERPLASIA, NODULAR			1 (2%)
HYPERPLASIA, EPITHELIAL		1 (2%)	6 (12%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(49)	(49)
ANGIECTASIS		1 (2%)	1 (2%)
#ADRENAL	(50)	(50)	(50)
CYST, NOS		1 (2%)	
CYTOPLASMIC VACUOLIZATION		1 (2%)	
#ADRENAL CORTEX	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION		2 (4%)	
ANGIECTASIS	1 (2%)		
#ADRENAL MEDULLA	(50)	(50)	(50)
NECROSIS, NOS		1 (2%)	
HYPERPLASIA, FOCAL	2 (4%)		
#THYROID	(48)	(50)	(50)
CYSTIC FOLLICLES	7 (15%)	1 (2%)	1 (2%)
HYPERPLASIA, C-CELL		3 (6%)	
#PARATHYROID	(42)	(50)	(45)
HYPERPLASIA, NOS			
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
CYSTIC DUCTS	13 (26%)	15 (30%)	6 (12%)
HYPERPLASIA, NOS			1 (2%)
ADENOSIS	3 (6%)		
*PENIS	(50)	(50)	(50)
PROLAPSE	1 (2%)		
*PREPUTIAL GLAND	(50)	(50)	(50)
CYST, NOS		1 (2%)	2 (4%)
CYSTIC DUCTS	6 (12%)	3 (6%)	1 (2%)
INFLAMMATION, ACUTE			
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
INFLAMMATION ACUTE AND CHRONIC			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	
HYPERPLASIA, NOS			
HYPERPLASIA, CYSTIC			

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PROSTATE	(49)	(49)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE	10 (20%)	4 (8%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL			
#PROSTATIC GLAND	(49)	(49)	(49)
ABSCESS, CHRONIC		1 (2%)	
*SEMINAL VESICLE	(50)	(50)	(50)
DILATATION, NOS		1 (2%)	1 (2%)
CYST, NOS			
INFLAMMATION, ACUTE FOCAL			
GRANULOMA, SPERMATIC			
#TESTIS	(50)	(50)	(49)
ATROPHY, NOS		1 (2%)	
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(49)	(50)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
#HYPOTHALAMUS	(50)	(49)	(50)
HEMORRHAGE			
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
RETINOPATHY	9 (18%)	6 (12%)	39 (78%)
CATARACT	7 (14%)	6 (12%)	13 (26%)
MUSCULOSKELETAL SYSTEM			
*SKELETAL MUSCLE	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)		
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
NECROSIS, FAT	14 (28%)	9 (18%)	8 (16%)
ANGIECTASIS			1 (2%)
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NONE			

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

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			
INFLAMMATION, ACUTE FOCAL		1 (2%)	
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST			1 (2%)
CONGESTION, NOS		1 (2%)	
HEMORRHAGE		2 (4%)	
PROTEINOSIS, ALVEOLAR		1 (2%)	
CHOLESTEROL DEPOSIT	1 (2%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM			
HEMATOPOIETIC SYSTEM			
#SPLEEN	(50)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
FIBROSIS, FOCAL	1 (2%)		
HEMOSIDEROSIS	30 (60%)	30 (60%)	27 (54%)
ANGIECTASIS			1 (2%)
HEMATOPOIESIS	1 (2%)	1 (2%)	
#MEDIASTINAL L.NODE	(50)	(50)	(50)
HEMOSIDEROSIS	1 (2%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#PANCREATIC L.NODE	(50)	(50)	(50)
ANGIECTASIS			
#PEYER'S PATCH	(49)	(48)	(48)
HYPERPLASIA, LYMPHOID			1 (2%)
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL	1 (2%)	1 (2%)	1 (2%)
FIBROSIS, FOCAL	10 (20%)	8 (16%)	8 (16%)
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC		2 (4%)	
*MESENTERIC ARTERY	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS		1 (2%)	
#KIDNEY/GLOMERULUS	(50)	(50)	(50)
EMBOLISM, NOS		1 (2%)	
#ADRENAL	(50)	(50)	(50)
EMBOLISM, NOS		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
NECROSIS, FOCAL		1 (2%)	
NECROSIS, ZONAL		1 (2%)	
CYTOPLASMIC VACUOLIZATION			
CYTOLOGIC ALTERATION, NOS	3 (6%)	2 (4%)	3 (6%)
HYPERPLASIA, NOS			1 (2%)
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	8 (16%)	21 (42%)	23 (46%)
HYPERPLASIA, FOCAL	12 (24%)	4 (8%)	1 (2%)
#PANCREAS	(49)	(49)	(50)
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
FIBROSIS, FOCAL	1 (2%)		
ATROPHY, NOS		1 (2%)	1 (2%)
ATROPHY, FOCAL	3 (6%)	3 (6%)	1 (2%)
#COLON	(49)	(47)	(49)
PARASITISM	1 (2%)		1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)	2 (4%)	
FIBROSIS, FOCAL	1 (2%)	1 (2%)	
NEPHROSIS, NOS			1 (2%)
PIGMENTATION, NOS		1 (2%)	
#URINARY BLADDER	(49)	(49)	(50)
HYPERPLASIA, EPITHELIAL			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(50)	(50)
CYST, NOS	1 (2%)		
HEMOSIDEROSIS	1 (2%)		
ANGIECTASIS	2 (4%)	3 (6%)	1 (2%)
#ADRENAL	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION			2 (4%)
ANGIECTASIS		1 (2%)	
#ADRENAL CORTEX	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION	5 (10%)	6 (12%)	3 (6%)
ANGIECTASIS			1 (2%)
#THYROID	(50)	(48)	(50)
ULTIMOBRANCHIAL CYST			1 (2%)
CYSTIC FOLLICLES	2 (4%)	1 (2%)	
FOLLICULAR CYST, NOS			
ATROPHY, CYSTIC		1 (2%)	
HYPERPLASIA, EPITHELIAL			1 (2%)
HYPERPLASIA, C-CELL		1 (2%)	1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
CYSTIC DUCTS	30 (60%)	30 (60%)	36 (72%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NOS			3 (6%)
HYPERPLASIA, CYSTIC			5 (10%)
ADENOSIS	5 (10%)	9 (18%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
CYSTIC DUCTS	1 (2%)	6 (12%)	2 (4%)
INFLAMMATION, ACUTE SUPPURATIVE		3 (6%)	1 (2%)
HYPERPLASIA, NOS	1 (2%)	1 (2%)	1 (2%)
*CLITORAL GLAND	(50)	(50)	(50)
CYST, NOS		1 (2%)	
CYSTIC DUCTS		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE			1 (2%)
#UTERUS	(50)	(49)	(50)
HEMATOMETRA	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, EPITHELIAL			1 (2%)
ANGIECTASIS			
#UTERUS/ENDOMETRIUM	(50)	(49)	(50)
EDEMA, NOS		1 (2%)	
HEMATOMETRA		2 (4%)	
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE			3 (6%)
HYPERPLASIA, NOS	1 (2%)		2 (4%)
HYPERPLASIA, CYSTIC	9 (18%)	5 (10%)	
#ENDOMETRIAL GLAND	(50)	(49)	(50)
HYPERPLASIA, CYSTIC		1 (2%)	
#OVARY	(50)	(50)	(50)
CYST, NOS	3 (6%)		1 (2%)
FOLLICULAR CYST, NOS		1 (2%)	
NERVOUS SYSTEM			
#CEREBRAL VENTRICLE	(50)	(50)	(50)
HYDROCEPHALUS, NOS			1 (2%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
RETINOPATHY	4 (8%)	35 (70%)	11 (22%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
CATARACT	2 (4%)	33 (66%)	9 (18%)
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS		1 (2%)	
*EYELID	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*STERNUM	(50)	(50)	(50)
CYST, NOS			
BODY CAVITIES			
*MEDIASTINAL PLEURA	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
*MESENTERY	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
HEMORRHAGE			
FIBROSIS, FOCAL		1 (2%)	
NECROSIS, FAT	8 (16%)	18 (36%)	13 (26%)
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	3	1	

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

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
ULCER, FOCAL			
INFLAMMATION, ACUTE/CHRONIC			
INFLAMMATION, CHRONIC		1 (2%)	
FIBROSIS			
FIBROSIS, FOCAL	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV			2 (4%)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS	1 (2%)		
NECROSIS, FOCAL			
NECROSIS, FAT			3 (6%)
FOREIGN MATERIAL, NOS		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG/BRONCHIOLE	(50)	(50)	(50)
HYPERPLASIA, NOS	2 (4%)		1 (2%)
#LUNG	(50)	(50)	(50)
EDEMA, NOS			1 (2%)
HEMORRHAGE	2 (4%)		
BRONCHOPNEUMONIA, FOCAL	2 (4%)		
LYMPHOCYTIC INFLAMMATORY INFILTR			
INFLAMMATION, INTERSTITIAL	1 (2%)		1 (2%)
BRONCHOPNEUMONIA SUPPURATIVE		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
PNEUMONIA, CHRONIC MURINE	3 (6%)		1 (2%)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
INFLAMMATION, GRANULOMATOUS	1 (2%)	2 (4%)	

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, FOCAL GRANULOMATOU	3 (6%)		
REACTION, FOREIGN BODY	1 (2%)		
CHOLESTEROL DEPOSIT		2 (4%)	
HYPERPLASIA, ADENOMATOUS	8 (16%)	12 (24%)	15 (30%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	3 (6%)	1 (2%)	2 (4%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
HYPERPLASIA, HEMATOPOIETIC	1 (2%)		
HYPERPLASIA, LYMPHOID	1 (2%)		
#SPLEEN	(49)	(48)	(50)
ANGIECTASIS		1 (2%)	
HYPERPLASIA, LYMPHOID	1 (2%)		
HEMATOPOIESIS	2 (4%)		1 (2%)
#MANDIBULAR L. NODE	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)
#MESENTERIC L. NODE	(50)	(49)	(49)
HEMORRHAGE	2 (4%)		
ANGIECTASIS	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	2 (4%)
HEMATOPOIESIS			
#INGUINAL LYMPH NODE	(50)	(49)	(49)
HYPERPLASIA, LYMPHOID	2 (4%)		1 (2%)
#LUNG/BRONCHUS	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID			
#PEYER'S PATCH	(45)	(42)	(45)
HYPERPLASIA, LYMPHOID	5 (11%)	4 (10%)	2 (4%)
#THYMUS	(41)	(48)	(46)
CYST, NOS	1 (2%)		
ATROPHY, NOS			1 (2%)
HYPERPLASIA, LYMPHOID		1 (2%)	
CIRCULATORY SYSTEM			
#ILIAC LYMPH NODE	(50)	(49)	(49)
LYMPHANGIECTASIS			

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#AURICULAR APPENDAGE	(50)	(50)	(50)
PERIARTERITIS			
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, NECROTIZING			1 (2%)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
INFLAMMATION, CHRONIC FOCAL	2 (4%)		
*BLOOD VESSEL	(50)	(50)	(50)
DEGENERATION PIGMENTARY	1 (2%)		
*AORTA	(50)	(50)	(50)
CALCIFICATION, FOCAL	1 (2%)		
#LIVER	(49)	(49)	(50)
THROMBOSIS, NOS	1 (2%)		
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS			1 (2%)
#KIDNEY	(49)	(49)	(50)
PERIARTERITIS	1 (2%)		1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(49)	(50)
HEMORRHAGE	1 (2%)		
INFLAMMATION, GRANULOMATOUS	1 (2%)		
FIBROSIS, FOCAL			1 (2%)
CHOLESTEROL DEPOSIT	1 (2%)		
#LIVER	(49)	(49)	(50)
INFLAMMATION, ACUTE FIBRINOUS	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		
NECROSIS, NOS			1 (2%)
NECROSIS, COAGULATIVE	1 (2%)	1 (2%)	1 (2%)
CYTOPLASMIC CHANGE, NOS			
CYTOPLASMIC VACUOLIZATION		4 (8%)	10 (20%)
FOCAL CELLULAR CHANGE	2 (4%)	1 (2%)	2 (4%)
HYPERPLASIA, FOCAL	1 (2%)		
#LIVER/CENTRILOBULAR	(49)	(49)	(50)
CYTOPLASMIC VACUOLIZATION	2 (4%)	4 (8%)	3 (6%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
*GALLBLADDER	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)		
#BILE DUCT	(49)	(49)	(50)
CYST, NOS		1 (2%)	
#ESOPHAGUS	(50)	(50)	(49)
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, GRANULOMATOUS	3 (6%)	1 (2%)	1 (2%)
#GASTRIC MUCOSA	(49)	(48)	(48)
EPIDERMAL INCLUSION CYST	1 (2%)		
#ILEUM	(45)	(42)	(45)
DIVERTICULUM		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(49)	(49)	(50)
PYELONEPHRITIS, FOCAL	1 (2%)		
INFLAMMATION, INTERSTITIAL	1 (2%)		2 (4%)
PYELONEPHRITIS, ACUTE/CHRONIC			
NEPHROPATHY	3 (6%)		
DEGENERATION PIGMENTARY	1 (2%)		
NEPHROSIS, NOS		1 (2%)	
METAPLASIA, OSSEOUS			1 (2%)
#KIDNEY/PELVIS	(49)	(49)	(50)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(46)	(46)
CYST, NOS	1 (2%)		
#ADRENAL	(47)	(49)	(50)
CYTOLOGIC ALTERATION, NOS			
#ADRENAL MEDULLA	(47)	(49)	(50)
HYPERPLASIA, NOS			1 (2%)
#THYROID	(50)	(45)	(50)
CYSTIC FOLLICLES		1 (2%)	1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FOLLICULAR CYST, NOS	2 (4%)		
INFLAMMATION, SUPPURATIVE	1 (2%)		
REACTION, FOREIGN BODY	1 (2%)		
DEGENERATION, CYSTIC	1 (2%)		
HYPERPLASIA, FOLLICULAR-CELL			1 (2%)
#THYROID FOLLICLE	(50)	(45)	(50)
HYPERPLASIA, CYSTIC	1 (2%)		
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST		1 (2%)	
CYSTIC DUCTS	2 (4%)	2 (4%)	6 (12%)
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, NOS		1 (2%)	
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)	1 (2%)	1 (2%)
#PROSTATE	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
HYPERPLASIA, EPITHELIAL			1 (2%)
#TESTIS	(50)	(50)	(50)
NECROSIS, FOCAL	1 (2%)		
ATROPHY, NOS	1 (2%)		
HYPERPLASIA, INTERSTITIAL CELL		1 (2%)	
*EPIDIDYMIS	(50)	(50)	(50)
ULCER, NOS		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
CORPORA AMYLACEA		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
ATROPHY, NOS	1 (2%)		
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)		

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
*INTERCOSTAL MUSCLE	(50)	(50)	(50)
INFLAMMATION, NECROTIZING		1 (2%)	
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)	1 (2%)	
*PERICARDIUM	(50)	(50)	(50)
EDEMA, NOS		1 (2%)	
REACTION, FOREIGN BODY		1 (2%)	
NECROSIS, FAT		1 (2%)	
*MESENTERY	(50)	(50)	(50)
HEMORRHAGIC CYST	1 (2%)		
STEATITIS	2 (4%)		2 (4%)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
NECROSIS, FAT	2 (4%)	1 (2%)	3 (6%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
ULCER, FOCAL			1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
OMENTUM			
STEATITIS	1		
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED		10	5
AUTO/NECROPSY/NO HISTO			

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

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE ADMINISTERED ALLYL ISOTHIOCYANATE IN CORN OIL BY GAVAGE

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(49)
EPIDERMAL INCLUSION CYST			1 (2%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(49)
ABSCESS, NOS		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
REACTION, FOREIGN BODY		1 (2%)	
INFLAMMATION, PYOGRANULOMATOUS		1 (2%)	
CHOLESTEROL DEPOSIT		1 (2%)	1 (2%)
RESPIRATORY SYSTEM			
#TRACHEA	(47)	(47)	(48)
PENETRATING WOUND		1 (2%)	
#LUNG/BRONCHIOLE	(47)	(49)	(49)
HYPERPLASIA, NOS		1 (2%)	
#LUNG	(47)	(49)	(49)
HEMORRHAGE		1 (2%)	1 (2%)
INFLAMMATION, INTERSTITIAL			2 (4%)
PNEUMONIA, ASPIRATION		1 (2%)	
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
BRONCHOPNEUMONIA SUPPURATIVE			1 (2%)
PNEUMONIA, CHRONIC MURINE	4 (9%)		2 (4%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU			2 (4%)
CHOLESTEROL DEPOSIT		1 (2%)	1 (2%)
HYPERPLASIA, ADENOMATOUS	3 (6%)	2 (4%)	3 (6%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)	2 (4%)	1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
*MULTIPLE ORGANS	(50)	(50)	(49)
HYPERPLASIA, HEMATOPOIETIC	3 (6%)		
HYPERPLASIA, LYMPHOID	2 (4%)		1 (2%)
HEMATOPOIESIS		1 (2%)	
#BONE MARROW	(49)	(49)	(49)
HYPERPLASIA, NOS	2 (4%)	2 (4%)	1 (2%)
MYELOFIBROSIS		4 (8%)	
HYPERPLASIA, HEMATOPOIETIC		2 (4%)	1 (2%)
HYPERPLASIA, GRANULOCYTIC		1 (2%)	4 (8%)
HYPERPLASIA, RETICULUM CELL	1 (2%)		
#SPLEEN	(47)	(48)	(49)
HYPERPLASIA, NOS		1 (2%)	
HYPERPLASIA, HEMATOPOIETIC			1 (2%)
HYPERPLASIA, LYMPHOID	2 (4%)	4 (8%)	2 (4%)
HEMATOPOIESIS	3 (6%)	10 (21%)	5 (10%)
MYELOPOIESIS			
#SPLENIC CAPSULE	(47)	(48)	(49)
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
#LYMPH NODE	(50)	(47)	(49)
HYPERPLASIA, NOS	1 (2%)		
#MANDIBULAR L. NODE	(50)	(47)	(49)
HYPERPLASIA, LYMPHOID		1 (2%)	
#CERVICAL LYMPH NODE	(50)	(47)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)
#PANCREATIC L.NODE	(50)	(47)	(49)
HYPERPLASIA, NOS			1 (2%)
#MESENTERIC L. NODE	(50)	(47)	(49)
HEMORRHAGIC CYST		1 (2%)	
INFLAMMATION, GRANULOMATOUS		1 (2%)	
#RENAL LYMPH NODE	(50)	(47)	(49)
HYPERPLASIA, NOS	1 (2%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, LYMPHOID		3 (6%)	
#ILIAC LYMPH NODE	(50)	(47)	(49)
ANGIECTASIS			
#LUNG/BRONCHUS	(47)	(49)	(49)
HYPERPLASIA, LYMPHOID			
#LUNG	(47)	(49)	(49)
HYPERPLASIA, LYMPHOID		1 (2%)	1 (2%)
#LIVER	(50)	(49)	(49)
LEUKOCYTOSIS, NOS	1 (2%)		
HEMATOPOIESIS	1 (2%)	4 (8%)	1 (2%)
MYELOPOIESIS			
#PEYER'S PATCH	(40)	(44)	(47)
HYPERPLASIA, LYMPHOID	1 (3%)		
#KIDNEY	(50)	(48)	(49)
PLASMACYTOSIS		1 (2%)	
HYPERPLASIA, LYMPHOID			1 (2%)
#THYMUS	(44)	(45)	(44)
INFLAMMATION, CHRONIC		1 (2%)	
ATROPHY, NOS			1 (2%)
HYPERPLASIA, LYMPHOID		1 (2%)	
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(49)
PERIARTERITIS		1 (2%)	
#ENDOCARDIUM	(49)	(50)	(49)
FIBROSIS, FOCAL			1 (2%)
*AORTA	(50)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
*CORONARY ARTERY	(50)	(50)	(49)
INFLAMMATION, NECROTIZING			1 (2%)
HYPERTROPHY, FOCAL			1 (2%)
#PANCREAS	(47)	(45)	(49)
PERIARTERITIS			1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
#OVARY	(49)	(44)	(48)
THROMBOSIS, NOS		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEMORRHAGIC CYST	1 (2%)		
INFLAMMATION, NOS			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	3 (6%)	2 (4%)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
NECROSIS, FOCAL	1 (2%)		
NUCLEAR ENLARGEMENT	1 (2%)		
INCLUSION, NUCLEAR	1 (2%)		
CYTOPLASMIC CHANGE, NOS			
CYTOPLASMIC VACUOLIZATION		1 (2%)	1 (2%)
FOCAL CELLULAR CHANGE		1 (2%)	1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		
*GALLBLADDER	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#PANCREAS	(47)	(45)	(49)
CYSTIC DUCTS		2 (4%)	
EDEMA, NOS			1 (2%)
INFLAMMATION, INTERSTITIAL		1 (2%)	
INFLAMMATION, SUPPURATIVE		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		
NECROSIS, FAT		1 (2%)	
ATROPHY, NOS			1 (2%)
*OROPHARYNX	(50)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
#ESOPHAGUS	(49)	(50)	(49)
PENETRATING WOUND		1 (2%)	
INFLAMMATION ACUTE AND CHRONIC			1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	
INFLAMMATION, GRANULOMATOUS	5 (10%)		
#CARDIAC STOMACH	(47)	(47)	(49)
ULCER, NOS			1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, BASAL CELL	1 (2%)		
#INTESTINAL VILLUS	(40)	(44)	(47)
CYTOPLASMIC VACUOLIZATION			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(48)	(49)
HYDRONEPHROSIS			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
INFLAMMATION, INTERSTITIAL		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)		
NEPHROPATHY	1 (2%)		1 (2%)
NECROSIS, MEDULLARY		1 (2%)	
HYPOPLASIA, NOS			1 (2%)
#KIDNEY/PELVIS	(50)	(48)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR			
INFLAMMATION, NECROTIZING	1 (2%)	1 (2%)	
#URINARY BLADDER	(47)	(47)	(47)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(47)	(45)	(44)
HYPERPLASIA, NOS	3 (6%)		
HYPERPLASIA, FOCAL			3 (7%)
ANGIECTASIS	1 (2%)	2 (4%)	
#THYROID	(48)	(47)	(47)
CYSTIC FOLLICLES	1 (2%)		1 (2%)
FOLLICULAR CYST, NOS			2 (4%)
DEGENERATION, CYSTIC	2 (4%)		
HYPERPLASIA, FOLLICULAR-CELL	1 (2%)		
#THYROID FOLLICLE	(48)	(47)	(47)
MULTIPLE CYSTS		1 (2%)	
HYPERPLASIA, PAPILLARY			1 (2%)
HYPERPLASIA, CYSTIC	1 (2%)		1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(49)
CYSTIC DUCTS	4 (8%)	3 (6%)	2 (4%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
FIBROSIS	1 (2%)		
HYPERPLASIA, NOS		2 (4%)	
*MAMMARY LOBULE	(50)	(50)	(49)
HYPERPLASIA, NOS	1 (2%)		
#UTERUS	(50)	(47)	(49)
HYDROMETRA		1 (2%)	
CYST, NOS	1 (2%)		1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
PYOMETRA	2 (4%)	1 (2%)	1 (2%)
ENDOMETRIAL POLYP		1 (2%)	
ANGIECTASIS	1 (2%)		
#UTERUS/ENDOMETRIUM	(50)	(47)	(49)
CYST, NOS	5 (10%)	3 (6%)	4 (8%)
INFLAMMATION, SUPPURATIVE	1 (2%)	3 (6%)	3 (6%)
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, CYSTIC	5 (10%)	2 (4%)	8 (16%)
HYPERPLASIA, ADENOMATOUS			
ANGIECTASIS			1 (2%)
#ENDOMETRIAL GLAND	(50)	(47)	(49)
HYPERPLASIA, CYSTIC	18 (36%)	25 (53%)	14 (29%)
#OVARY	(49)	(44)	(48)
CYST, NOS	2 (4%)	1 (2%)	3 (6%)
CYSTIC FOLLICLES	1 (2%)		
FOLLICULAR CYST, NOS		1 (2%)	
HEMATOMA, NOS	1 (2%)		
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, CHRONIC	4 (8%)	2 (5%)	3 (6%)
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	1 (2%)		
#BRAIN	(50)	(50)	(49)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
CORPORA AMYLACEA			
#BRAIN/THALAMUS	(50)	(50)	(49)
PSAMMOMA BODIES	1 (2%)		1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(49)
PHTHISIS BULBI		1 (2%)	
*MIDDLE EAR	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	2 (4%)	1 (2%)	
INFLAMMATION, CHRONIC SUPPURATIV			1 (2%)
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(49)
FIBROUS DYSPLASIA	1 (2%)		
*CORTEX OF BONE	(50)	(50)	(49)
FIBROUS OSTEODYSTROPHY			3 (6%)
HYPERPLASIA, NOS		1 (2%)	
BODY CAVITIES			
*THORACIC CAVITY	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
REACTION, FOREIGN BODY			1 (2%)
*MEDIASTINUM	(50)	(50)	(49)
INFLAMMATION, GRANULOMATOUS	2 (4%)		1 (2%)
*PERITONEUM	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	1 (2%)		1 (2%)
INFLAMMATION, FIBRINOUS	1 (2%)		
INFLAMMATION, ACUTE SUPPURATIVE	2 (4%)		
INFLAMMATION, CHRONIC			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		2 (4%)
ABSCESS, CHRONIC	1 (2%)		
NECROSIS, FAT			1 (2%)
*PLEURA	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
*MEDIASTINAL PLEURA	(50)	(50)	(49)
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
REACTION, FOREIGN BODY		1 (2%)	
*MESENTERY	(50)	(50)	(49)
STEATITIS		1 (2%)	1 (2%)
INFLAMMATION, NECROTIZING	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC SUPPURATIV	2 (4%)		
NECROSIS, FAT	1 (2%)	3 (6%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR			
INFLAMMATION, SUPPURATIVE	9 (18%)	5 (10%)	4 (8%)
INFLAMMATION, ACUTE FIBRINOUS			
HYPERPLASIA, NOS		1 (2%)	
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	3	3	2
AUTO/NECROPSY/HISTO PERF		1	
AUTOLYSIS/NO NECROPSY			1

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

APPENDIX E

ANALYSIS OF ALLYL ISOTHIOCYANATE
LOT NO. 532251
(MIDWEST RESEARCH INSTITUTE)

APPENDIX E

A. ELEMENTAL ANALYSIS

Element	C	H	N	S
Theory	48.45	5.08	14.13	32.34
Determined	48.52	5.08	14.10	32.13
	48.56	5.13	14.18	32.27

B. BOILING POINT

Determined

151°C at 746.3 mm (visual, micro boiling point tube) 148° to 152°C (Dupont 900DTA)

Literature Values

152.05°C at 760 mm (Timmermans and Hennault-Roland, 1922)

C. DENSITY

Determined

d_{22}^{23}:1.016

Literature Value

d_4^{30}:1.00811 (variation 0.000103/°C) (Timmermans and Hennault-Roland, 1922)

D. REFRACTIVE INDEX

Determined

n_D^{20} 1.5315 ± 0.0002 (δ)

Literature Value

n_D^{17} 1.5336 (Timmermans and Hennault-Roland, 1922)

E. THIN-LAYER CHROMATOGRAPHY

Plates: Silica Gel 60 F254
Amount spotted: 100 and 300 μg

Ref. Standard: 1,1,3,3-Tetramethylthiourea
Visualization: Ultraviolet (254 nm), and I_2 vapor

System 1: 95% Ethanol
R_f: 0.86
R_{st}: 1.13

System 2: Chloroform:1,4-Dioxane (95:5)
R_f: 0.55
R_{st}: 0.61

APPENDIX E

F. VAPOR-PHASE CHROMATOGRAPHY

1. System 1

Instrument: Bendix 2500
Detector: Flame ionization
Column: Chromosorb 102, 1.8 m x 4 mm I.D.
Inlet temperature: 225°C
Detector temperature: 270°C
Oven temperature program: 2 min. at 150°C, then 150° to 200°C at 10°/min.
Results: Major peak and four impurities

Peak	Retention Time (min.)	Retention Time (Relative to Allyl Isothiocyanate)	Area (Relative to Allyl Isothiocyanate)
1	3.5	0.21	0.007
2	8.6	0.52	0.04
3	9.3	0.56	0.07
4	16.6	1.00	100
5	20.3	1.22	0.2

2. System 2

Instrument: Bendix 2500
Detector: Flame ionization
Column: 10% Carbowax 20 M, on 80/100 Chromosorb W (AW), 1.8 m x 4 mm I.D.
Inlet temperature: 225°C
Detector temperature: 270°C
Oven temperature program: 5 min. at 50°C, then 50° to 125°C at 10°C/min.
Results: Major peak and six impurities

Peak	Retention Time (min.)	Retention Time (Relative to Allyl Isothiocyanate)	Area (Relative to Allyl Isothiocyanate)
1	1.0	0.07	0.006
2	4.9	0.36	0.3
3	10.6	0.78	0.08
4	12.8	0.95	Shoulder 0.1%
5	13.5	1.00	100
6	15.2	1.13	0.5
7	16.0	1.19	0.04

APPENDIX E

G. SPECTRAL DATA

1. Infrared

Instrument: Beckman IR-12
Cell: Neat, sodium chloride plates
Results: See Figure 5

Consistent with literature spectrum (Sadtler Research Laboratories)

2. Ultraviolet/Visible

Instrument: Cary 118

Determined literature values (Sadtler Research Laboratories)

λ max (nm)	$\varepsilon \times 10^{-2}$	λ max (nm)	$\varepsilon \times 10^{-2}$
249	10.40 ± 0.01 (δ)	247	8.30

No absorbance between 350 and 800 nm (visible range) at a concentration of 1 mg/ml
Solvent: Hexane

(Calculated from graph of spectrum)

3. Nuclear Magnetic Resonance

Solvent: Dioxane

Instrument: Varian HA-100
Solvent: Chloroform-d with internal tetramethylsilane
Assignments (See Figure 6)

Identical to literature spectrum (Sadtler Research Laboratories)

(a) } d^2 δ 4.17 ppm
(b) } d
(c) m, δ 5.31 ppm
(d) m, δ 5.42 ppm
(e) t^4, δ 5.92 ppm
(f) d, δ 3.59 ppm (impurity, possibly thiocyanate)

J_{ae} = 4.7 Hz, J_{be} = 4.7 Hz, J_{ad} = 3.2 Hz, J_{cd} ◻ 1.5 Hz, J_{ce} ◻ 10 Hz, J_{de} = 17.5 Hz

Integration Ratios:

(a) } 1.82
(b) }
(c) } 2.00
(d) }
(e) 1.17
(f) 0.06

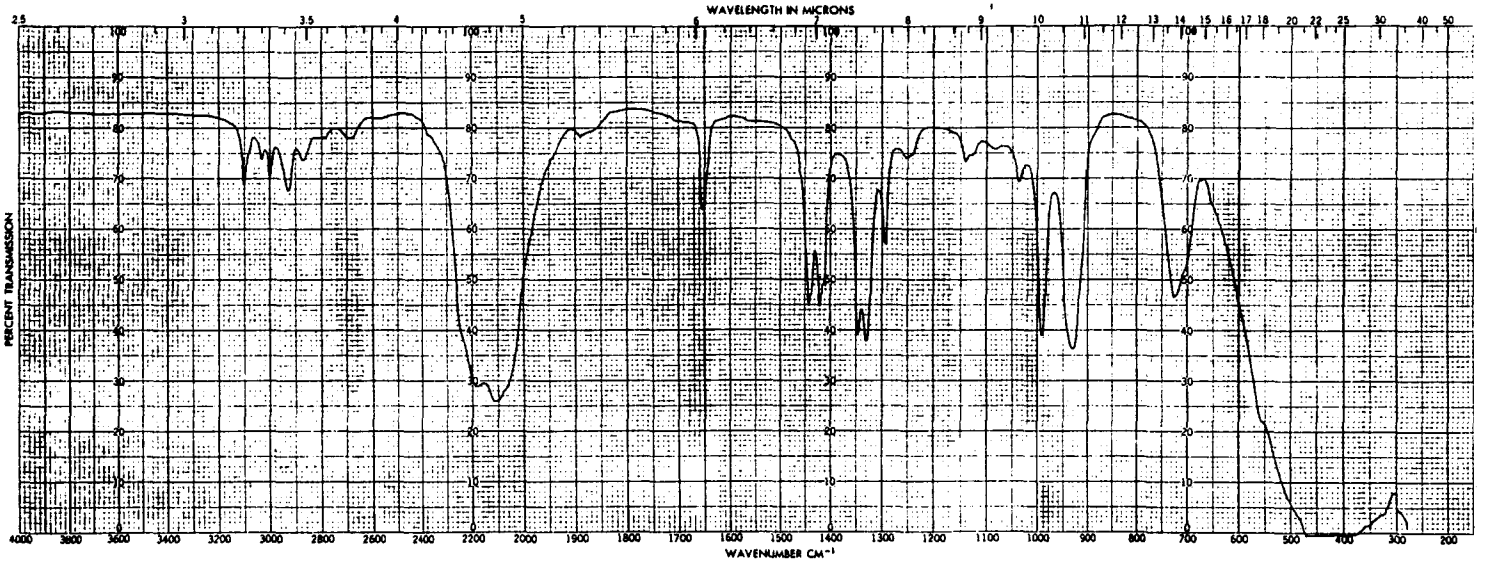


Figure 5. Infrared Absorption Spectrum of Allyl Isothiocyanate (Lot No. 532251)

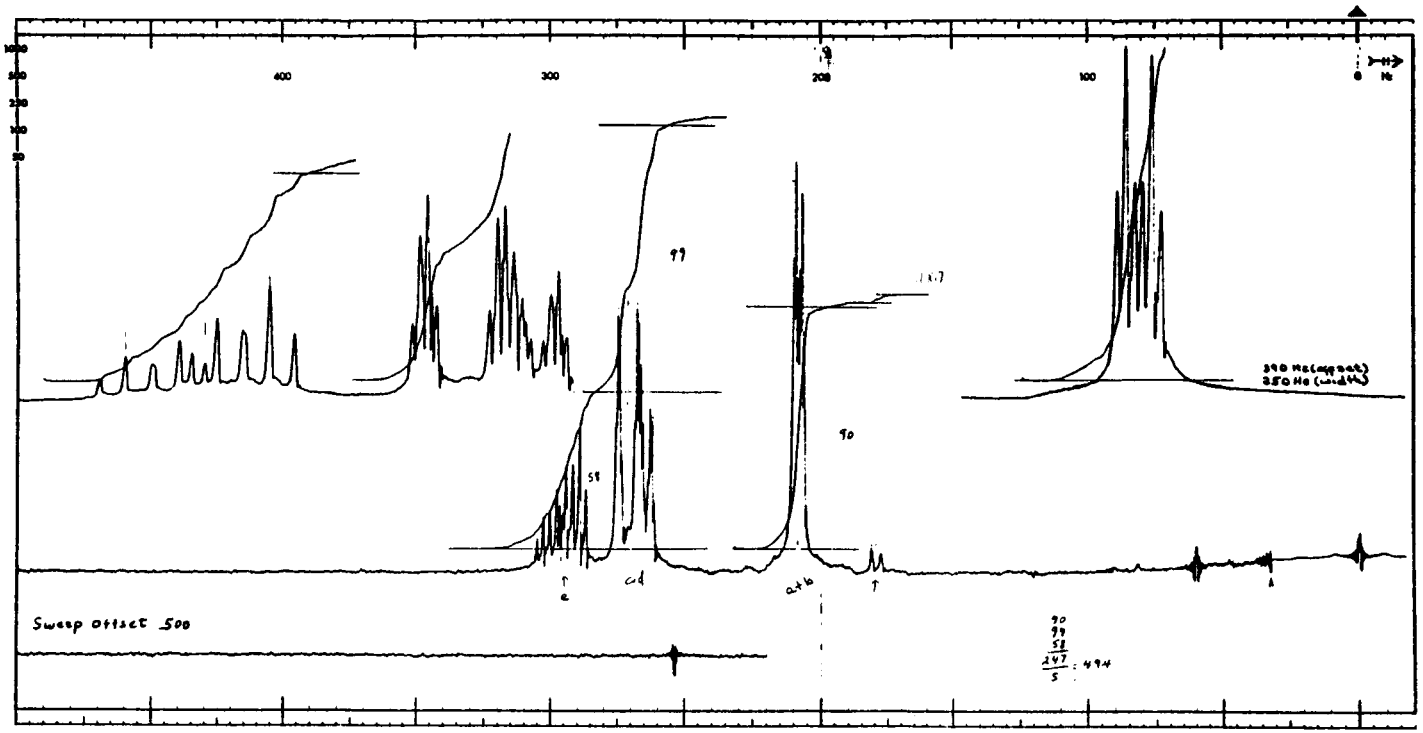


Figure 6. Nuclear Magnetic Resonance Spectrum of Allyl Isothiocyanate (Lot No. 532251)

APPENDIX F

ANALYSIS OF ALLYL ISOTHIOCYANATE IN CORN OIL FOR STABILITY OF ALLYL ISOTHIOCYANATE

APPENDIX F

A. PREPARATION OF SAMPLE AND STORAGE

A 26-μl aliquot of allyl isothiocyanate (26.90 mg) was placed in a 50-ml volumetric flask containing 50 ml corn oil, shaken, and placed in an ultrasonic vibrator bath for 30 seconds. The flask was stored at room temperature for 7 days with no effort made to protect the solution from light.

B. DILUTION AND ANALYSIS

1. Procedure

A 1.84-ml aliquot of the above stock solution (allyl isothiocyanate in corn oil) was pipetted into a small septum vial and 2 ml of anhydrous ethyl ether containing decane (15.63 mg decane in 50 ml ether) was added. The septum vial was sealed and mixed on a vortex mixer for 1 minute and placed in an ultrasonic vibrator bath for 2 minutes. The ether-corn oil mixture was analyzed by vapor-phase chromatography.

Note: Solvents which were immiscible with corn oil, such as alcohols, were not used due to their reactivity with allyl isothiocyanate. Therefore, dilution rather than extraction was used.

2. Instrumental Parameters

Instrument: Bendix 2500 with Hewlett-Packard 3380A automatic recorder/integrator
Detector: Flame ionization
Column: 20% SP2100/0.1% Carbowax 1500 on 100/120 Supelcoport, 1.8 m × 4 mm I.D., glass
Oven temperature: 90°C, isothermal
Inlet temperature: 130°C
Detector temperature: 285°C
Carrier gas: Nitrogen
Carrier flow rate: 50 cc/min
Sample injected: 5 μl

C. QUALITY ASSURANCE PROCEDURES

Analysis was performed in duplicate using decane as an internal standard. Linearity studies were done at two concentration levels (0.26 mg/ml and 0.13 mg/ml or 0.026% and 0.013%) to determine the relative weight response of compound versus internal standard (decane).

D. RESULTS

Day	Theoretical Percent (Chemical/Vehicle)	Determined Percent (Chemical/Vehicle)	Percent D/T × 100
0	0.02578	0.02578 ± 0.00081	100 ± 3
1	0.02578	0.02656 ± 0.00039	103 ± 2
2	0.02578	0.02480 ± 0.00031	96 ± 1
3	0.02578	0.02533 ± 0.00025	98 ± 1
4	0.02578	0.02455 ± 0.00084	95 ± 3
7	0.02578	0.02566	99.54

Retention time: Compound (4.7 min.), internal standard (11.7 min.)
Response of allyl isothiocyanate in corn oil versus that of allyl isothiocyanate in ether: 93.1 ± 0.3%
Linearity: $RWR \frac{\text{compound}}{\text{internal standard}}$ = 0.70 ± 0.03 at two concentration levels (0.026% and 0.013%).

E. CONCLUSION

The variation in the analysis is within the error of the method. Therefore, allyl isothiocynate is stable in corn oil at 0.05% concentration when stored at room temperature for 7 days without protection from light.

APPENDIX G

ANALYSIS OF ALLYL ISOTHIOCYANATE IN CORN OIL FOR CONCENTRATIONS OF ALLYL ISOTHIOCYANATE

APPENDIX G

Allyl isothiocyanate in corn oil mixtures was analyzed directly by vapor-phase chromatography. Extractions were not performed on the samples since corn oil does not interfere with the analysis. Gas chromatography conditions were as follows:

Column:	3% OV-17 on 80/100 Supelcoport, 1.8 m x 2 mm I.D., glass
Detection:	Flame Ionization
Temperatures:	Inlet, 250°C Oven, 75°C, isothermal Detector, 275°C
Retention Time:	1.1 min.
Injection Size:	1 μl

There was no correction for work-up loss since samples were injected without any work-up. Reference samples of allyl isothiocyanate were prepared in corn oil and analyzed under the same conditions.

Results: See Table G1.

TABLE G1. ANALYSIS OF ALLYL ISOTHIOCYANATE IN CORN OIL FOR CONCENTRATIONS OF ALLYL ISOTHIOCYANATE

Date Mixed *(a)*	Used During Week of:	Concentration *(b)* of Allyl Isothiocyanate for Target Concentration of			
		0.12% (v/v)	0.24% (v/v)	0.25% (v/v)	0.50% (v/v)
04/10/78	04/11/78	0.10	0.23	0.25	0.48
05/05/78	05/06/78			0.25	0.48
06/07/78	06/08/78			0.25	0.48
07/05/78	07/06/78	0.12	0.24		
08/16/78	08/17/78			0.25	0.50
09/13/78	09/14/78	0.11	0.25		
10/11/78	10/12/78				0.50
11/09/78	11/10/78			0.24	
12/06/78	12/08/78				0.48
01/04/79	01/05/79			0.25	
02/01/79	02/02/79				0.47
03/01/79	03/02/79			0.25	
03/29/79	03/30/79				0.51
04/26/79	04/27/79			0.24	
05/24/79	05/25/79				0.53
06/21/79	06/22/79			0.24	
07/19/79	07/20/79				0.49
08/16/79	08/17/79			0.24	
09/13/79	09/14/79				0.46
10/11/79	10/12/79			0.24	
11/08/79	11/09/79				0.51
12/06/79	12/08/79			0.23	
01/03/80	01/04/80				0.51
02/01/80	02/02/80	0.11	0.26		
02/28/80	02/29/80			0.27	0.52
Mean (%)		0.11	0.25	0.25	0.49
Standard Deviation		0.01	0.01	0.01	0.02
Coefficient of variation (%)		9.1	4.0	4.0	2.0
Range (%,)		0.10-0.12	0.23-0.26	0.23-0.27	0.46-0.53
Number of samples		4	4	13	14

(a) Start dates were March 1978 for rats and mice.
(b) The data presented are the average of duplicate analyses.

APPENDIX H

CUMULATIVE MEAN BODY WEIGHT CHANGE OF RATS AND MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE IN THE CHRONIC STUDY

TABLE H1. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF RATS ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males	0	133 *(b)*	134 *(b)*	133 *(b)*		
	5	115	115	108	0	- 6
	26	272	273	237	0	-13
	47	332	336	296	+ 1	-11
	79	337	345	324	+ 2	- 4
	104	317	326	298	+ 3	- 6
		450 *(c)*	460 *(c)*	431 *(c)*	+ 2 *(d)*	- 4 *(d)*
Females	0	99 *(b)*	102 *(b)*	100 *(b)*		
	5	48	51	50	+ 6	+ 4
	26	107	109	107	+ 2	0
	47	125	134	132	+ 7	+ 6
	79	166	184	180	+11	+ 8
	104	180	191	195	+ 6	+ 8
		279 *(c)*	293 *(c)*	295 *(c)*	+ 5 *(d)*	+ 6 *(d)*

(a) Weight change of the dosed group relative to that of the controls = $\frac{\text{Weight Change (Dosed Group) - Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$

(b) Initial weight.

(c) Mean body weight at week 104.

(d) Mean body weight at week 104 relative to controls.

TABLE H2. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF MICE ADMINISTERED ALLYL ISOTHIOCYANATE BY GAVAGE

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males	0	22 *(b)*	23 *(b)*	22 *(b)*		
	5	7	6	6	-14	-14
	26	20	19	21	- 5	+ 5
	47	26	23	28	-12	+ 8
	79	28	27	32	- 4	+14
	104	26	23	27	-12	+ 4
		48 *(c)*	46 *(c)*	49 *(c)*	- 4 *(d)*	+ 2 *(d)*
Females	0	17 *(b)*	18 *(b)*	18 *(b)*		
	5	7	5	5	-29	-29
	26	11	10	11	- 9	0
	47	14	13	16	- 7	+14
	79	18	19	19	+ 6	+ 6
	104	20	18	18	-10	-10
		37 *(c)*	36 *(c)*	36 *(c)*	- 3 *(d)*	- 3 *(d)*

(a) Weight change of the dosed group relative to that of the controls = $\frac{\text{Weight Change (Dosed Group) - Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$

(b) Initial weight.

(c) Mean body weight at week 104.

(d) Mean body weight at week 104 relative to controls.

☆ U.S. GOVERNMENT PRINTING OFFICE: 1982-381-132:703

NIH Publication No. 83-1790
October 1982

NIH Publication No. 83-1790
October 1982