NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 216

CARCINOGENESIS BIOASSAY OF 11-AMINOUNDECANOIC ACID

(CAS NO. 2432-99-7)

IN F344 RATS AND B6C3F$_1$ MICE

(FEED 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 June 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP Technical Report
on the

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

May 1982

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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NOTE TO THE READER

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

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

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 (702-487-4650).

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, North Carolina 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.

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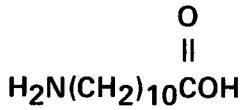

11-AMINOUNDECANOIC ACID

ABSTRACT

A carcinogenesis bioassay of 11-aminoundecanoic acid was carried out by administering diets containing 7,500 or 15,000 ppm of 11-aminoundecanoic acid to F344 rats and B6C3F1 mice. Groups of 50 rats and 50 mice of either sex were administered the test chemical for 104 weeks (rats) or 103 weeks (mice). Controls consisted of 50 untreated rats and 50 untreated mice of each sex.

Nonneoplastic effects included dose-related decreases in mean body weight gain and survival for male rats and for mice of each sex; a dose-related increased incidence of hyperplasia of the transitional epithelium of the kidney and urinary bladder in rats of each sex; and mineralization of the kidney in dosed mice of each sex.

Neoplastic nodules of the liver in dosed male rats (control 1/50, 2%; low dose 9/50, 18%; high dose 8/50, 16%: $P < 0.01$) and transitional-cell carcinomas of the urinary bladder in high-dose male rats (control 0/48, 0%; low dose 0/48, 0%; high dose 7/49, 14%: $P < 0.01$) were observed at significantly increased incidences compared with controls. Malignant lymphomas occurred at a significantly ($P < 0.05$) increased rate in low-dose male mice (control 2/50, 4%; low dose 9/50, 18%; high dose 4/50, 8%).

Under the conditions of this bioassay, 11-aminoundecanoic acid was carcinogenic for male F344 rats, inducing neoplastic nodules in the liver and transitional-cell carcinomas in the urinary bladder. The test chemical was not carcinogenic for female F344 rats. No clear evidence was found for the carcinogenicity of 11-aminoundecanoic acid in B6C3F1 mice of either sex, although the increase in malignant lymphoma in male mice may have been associated with administration of 11-aminoundecanoic acid.

CONTRIBUTORS

The bioassay of 11-aminoundecanoic acid was conducted at Litton Bionetics, Inc., under a subcontract to Tracor Jitco, Inc., the prime contractor for the Carcinogenesis Testing Program. The prechronic study was started in May 1976 and finished in August 1976; the chronic study was begun in February 1977 and completed in March 1979.

Principal Contributors at Litton Bionetics, Inc.
5516 Nicholson Lane
Kensington, Maryland 20795
(Conducted bioassay and evaluated tissues)

Dr. R. Cardy, Pathologist
Dr. E. Gordon, Principal Investigator
Dr. J. Moe, Pathologist
Mr. H. Paulin, Chemist
Mr. J. Sheldon, Animal Care Supervisor
Dr. B. Zook, Pathologist

Principal Contributors at Tracor Jitco
1776 East Jefferson Street
Rockville, Maryland 20852
(Prepared Preliminary Summary Report)

Dr. John Keller, Director, Bioassay Program
Dr. Abigail C. Jacobs, Bioscience Writer
Dr. James R. Joiner, Statistician
Dr. Steve S. Olin, Program Associate Director
Dr. Michael Stedham, Pathologist
Dr. William D. Theriault, Reports Manager
Mr. John Warner, Statistician

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

Dr. J. Fielding Douglas
Dr. June K. Dunnick (Chemical Manager)
Dr. Charles K. Grieshaber
Dr. Larry Hart
Dr. William V. Hartwell
Dr. Joseph Haseman
Dr. James E. Huff
Dr. C. W. Jameson
Dr. Mary Kornreich
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 by the NTP Pathology Working Group, which included Drs. G. Reznik, M. Stedham, and S. Stinson.

The chemicals used in this bioassay of 11-aminoundecanoic acid were analyzed by the Midwest Research Institute, 425 Volker Blvd., Kansas City, Missouri 64110; reanalysis of the bulk chemical and analysis of formulated diets were done by Litton Bionetics, Inc.

REVIEWERS

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

Margaret Hitchcock, Ph.D (Chairperson)
Pharmacology/Toxicology
John B. Pierce Foundation Laboratory
New Haven, Connecticut

Curtis Harper, Ph.D.
Associate Professor of Pharmacology
University of North Carolina
Chapel Hill, North Carolina

Thomas Shepard, M.D.
University of Washington
School of Medicine
Seattle, Washington

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

Ad Hoc Subcommittee Panel of Experts

James Swenberg, Ph.D. (Principal Reviewer)
Chief of Pathology
Chemical Industry Institute of Toxicology
Research Triangle Park, North Carolina

Frank Mirer, Ph.D. (Principal Reviewer)
United Auto Workers
International Union
Detroit, Michigan

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

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

Charles Irving, Ph.D.
Veterans Administration Hospital
Cancer Research Laboratory
Memphis, Tennessee

Sheldon Murphy, Ph.D.
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.
Toxicology Research Laboratory
Dow Chemical U.S.A.
Midland, Michigan

Roy Shore, Ph.D.
Statistics
New York University Medical Center
New York, New York

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

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*Unable to attend February 18, 1981 meeting

SUMMARY OF PEER REVIEW COMMENTS ON THE BIOASSAY OF 11-AMINOUNDECANOIC ACID

On February 18, 1981, this carcinogenesis bioassay report on 11-aminoundecanoic acid underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Report Review Subcommittee and associated Panel of Experts at an open meeting held in Building 31C, National Institutes of Health, Bethesda, Maryland.

Dr. Swenberg, a principal reviewer for the report on the bioassay of 11-aminoundecanoic acid, agreed with the conclusion that, under the conditions of the bioassay, 11-aminoundecanoic acid was carcinogenic for male F344 rats, inducing increased incidences of neoplastic nodules in the liver and transitional-cell carcinomas in the urinary bladder. The test chemical was not carcinogenic for female F344 rats. No clear evidence of carcinogenicity was demonstrated in B6C3F1 mice of either sex. Other effects included a dose-related decrease in mean body weight gain and survival for male rats and for mice of each sex, hyperplasia of the transitional epithelium of the kidney and urinary bladder in rats of each sex, and mineralization of the kidney in mice of each sex.

Dr. Swenberg stated that if early mortality in high-dose mice groups was due to toxicity then the high dose exceeded the maximum tolerated dose. If this were the case, the low dose group represented a maximum tolerated dose and the study is valid and not compromised. He said that more information on toxicity and cause of death would be preferable, particularly for the early deaths in the high dose male rats and mice.

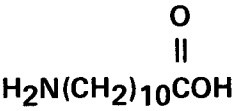
As another principal reviewer, Dr. Mirer, also agreed with the conclusions of the report. He noted that no transitional-cell carcinomas of the urinary bladder were observed in control male rats, and that this tumor is very rare in historical controls. He commented that compound-related toxicity in male mice (less than 50% survival) may have prevented the appearance of late developing tumors. Thus, this high mortality combined with a borderline statistically elevated incidence of lymphomas suggest that 11-aminoundecanoic acid was not adequately tested for carcinogenicity in male mice.

Dr. Shore questioned the word "clear" in the statement in the conclusions that "No clear evidence was found for the carcinogenicity of 11-aminoundecanoic acid in B6C3F1 mice of either sex." The qualifier derives from the finding of a statistically significant increase in malignant lymphoma in low-dose male mice but not in high-dose mice. After considerable discussion, Dr. Moore (NTP) proposed adding a clause to the statement such as, "although a significant incidence of malignant lymphoma in low-dose male mice may have been associated with chemical administration."

Dr. Swenberg moved that the report on the bioassay of 11-aminoundecanoic acid be accepted after minor changes and corrections described in the reviewers' comments and during the discussion are made. Dr. Mirer seconded the motion and the report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION



11-AMINOUNDECANOIC ACID

11-Aminoundecanoic acid (CAS No. 2432-99-7) is the monomer used in the manufacture of the polyamide, nylon-11. 11-Aminoundecanoic acid is synthesized through a series of reactions from ricinoleic acid isolated from castor bean oil (Hampel and Hawley, 1973; Hawley, 1977).

Nylon-11 is used in automobile parts, industrial fabrics (e.g., filter bags, work clothes, and netting), and brushes because of its resistance to vibration and shock and its stability when in contact with fuels (Kirk-Othmer, 1979). Nylon-11 resins are approved by the U.S. Food and Drug Administration for use in food contact films (U.S. CFR, 1977).

11-Aminoundecanoic acid is not produced in the United States, and specific production figures are not available for either 11-aminoundecanoic acid or nylon-11. The amount of nylon-11 used in the United States accounts for less than 1% of the nylon in use in this country. Nylon-11 is used more widely in France, Italy, and Brazil (Hampel and Hawley, 1973; Hawley, 1977).

11-Aminoundecanoic acid was one of a series of monomers assigned for testing by the Carcinogenesis Testing Program because of possible worker exposure and the absence of previous studies for carcinogenicity or other biological properties.

II. METHODS AND MATERIALS

CHEMICAL ANALYSIS

PRECHRONIC STUDIES

Single-Dose Study

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CHRONIC STUDY

Study Design

Source and Specifications of Test Animals

Animal Maintenance

Preparation of Test Diets

Clinical Examinations and Pathology

Data Recording and Statistical Methdods

CHEMICAL ANALYSIS

White crystalline 11-aminoundecanoic acid was obtained as a single batch (Lot No 503) from Rilsan Corporation (Glenrock, NJ) and was found to be 99 13% ± 0 03 (δ)% pure by titration of the amine (Midwest Research Institute), the elemental analyses were in agreement with the theoretical values (Appendix E) Results of thin-layer chromatography indicated one trace impurity or one trace and one slight impurity, depending on the solvent system used The infrared and nuclear magnetic resonance spectra were consistent with the structure

PRECHRONIC STUDIES

Single-Dose Study

Male and female F344 rats were obtained from Frederick Cancer Research Center (Frederick, MD), quarantined, and held for approximately 2 months before the test began Animals were approximately 11 weeks old when placed on study Mice were not used in the single-dose study

Groups of five male F344 rats were administered a single dose of 11-aminoundecanoic acid (14,700 or 21,500 mg/kg body weight) in corn oil by gavage and groups of five female rats received doses of 6,810, 10,000, 14,700, or 21,500 mg/kg by the same route All animals were observed for mortality for 14 days

Animals were housed two or three per cage and received water and feed *ad libitum* during the observation period Details of animal maintenance are presented in Table 1

Animals were observed for mortality every 30 minutes for the first 8 hours on the day of dosing and then daily for 14 days Weights were taken on the day of dosing and then on days 7 and 14 Gross necropsies were performed on all animals that died during the study and on those surviving to day 14

Fourteen-Day Study

Male and female F344 rats and B6C3F1 mice were obtained from Frederick Cancer Research Institute, quarantined, and held for approximately 3 months before the study began Animals were approximately 15 weeks old when placed on study

Groups of five males and five females of each species were fed diets containing 0, 5,000, 10,000, 15,000, 20,000, or 30,000 ppm 11-aminoundecanoic acid for 2 weeks Test diets were prepared several days before the start of the study by mixing the test chemical and ground Purina® Lab Chow in a Patterson-Kelly® Twin Shell Blender Diets were refrigerated until use

Animals were housed two or three per cage and received water and feed *ad libitum* Details of animal maintenance are presented in Table 1 The rats and mice were observed daily for mortality and were weighed weekly Gross necropsies were performed on all animals at the end of the 14-day study

Thirteen-Week Study

Subchronic studies were conducted to determine the concentrations to be used in the chronic studies

Three-week-old male and female F344 rats and B6C3F1 mice were obtained from the NCI Frederick Cancer Research Center, observed for 2 weeks, and then randomized by weight and assigned to test groups so that average cage weights were approximately equal for all animals of the same sex and species

Rats and mice were housed four per cage in polycarbonate cages covered with nonwoven polyester filter sheets (Table 1) Racks and filters were replaced once every 2 weeks Cages and bedding were replaced twice per week, and water bottles were replaced three times per week

Test diets consisted of Purina® Lab Chow and the required amount of 11-aminoundecanoic acid (Lot No 503) The analytical procedures described in the chronic study were used Control diets consisted of Purina® Lab Chow Dosed feed, control diets, and bottled water (acidified with hydrochloric acid to pH 2 5 for bacterial control) were available *ad libitum*

Diets containing 0, 9,000, 12,000, 15,000, 18,000, 20,000 (mice), or 21,000 ppm (rats) 11-aminoundecanoic acid were fed for 13 weeks to groups of 12 male and 12 female rats and to groups of 10 male and 10 female mice

II. METHODS AND MATERIALS: PRECHRONIC STUDIES

Table 1. SOURCES AND DESCRIPTIONS OF MATERIALS USED FOR ANIMAL MAINTENANCE IN THE PRECHRONIC AND CHRONIC STUDIES

Item	Description	Source
Air Filter	AG-55 Ameriglass Roughing Filter	American Air Filter (Louisville, KY)
Air Filter	HEPA-100	American Air Filter (Louisville, KY)
Animal Feed	Purina® Lab Chow	Ralston Purina Co (Richmond, IN)
Bedding	Absorb-dri® hardwood chips	Lab Products, Inc (Garfield, NJ)
Cages	Polycarbonate	Lab Products, Inc (Garfield, NJ)
Filter Sheets	Nonwoven polyester	Snow Filtration (Cincinnati, OH)

Animals were checked for mortality and signs of morbidity twice daily Those animals that were judged moribund were killed and necropsied Each animal was given a clinical examination weekly, including palpation for tissue masses or swelling Body weight and feed consumption data were collected weekly

At the end of the 91-day study, survivors were killed with carbon dioxide and necropsies were performed on animals that survived to the end of the study and on all animals found dead, unless precluded in whole or in part by autolysis or cannibalization Thus, the number of animals from which particular organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group The following specimens were examined for control and high-dose groups gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity, brain, pituitary, and spinal cord Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin

Histopathologic examination for all other dosed groups was limited to the kidneys and liver, except for male and female rats administered 12,000 ppm The kidneys, liver, lungs, and heart of animals in the 12,000-ppm groups were examined histopathologically

CHRONIC STUDY

Study Design

Diets containing 7,500 or 15,000 ppm 11-aminoundecanoic acid were fed to groups of 50 rats or mice of either sex for 104 weeks (rats) or 103 weeks (mice) Controls consisted of groups of 50 untreated rats and 50 untreated mice of either sex (Table 2) Rats and mice were approximately 5 weeks old when placed on study

Source and Specifications of Test Animals

Three-week-old male and female F344 rats and B6C3F1 mice were obtained from the NCI Frederick Cancer Research Center (Frederick, MD), observed for 2 weeks, and randomly assigned to individual cages The cages were then randomly assigned to control and dosed groups

Animal Maintenance

Rats and mice were housed five per cage in polycarbonate cages covered with nonwoven polyester filter sheets (Table 1) Racks and filters were changed once every 2 weeks Cages, bedding, and glass water bottles (equipped with stainless steel sipper tubes) were replaced twice per week Dosed feed, control diets, and tap water (acidified with hydrochloric acid to pH 2 5 for bacterial control) were available *ad libitum* Stainless steel feed containers were changed once per week

The temperature in the animal rooms was 22°-26°C and the humidity was 30%-70% Incoming air was first filtered through AG-55 Ameriglass roughing filters and then through HEPA-100 filters to remove particulate matter Ten changes of room air per hour were provided Fluorescent lighting provided illumination 12 hours per day

Rats fed 11-aminoundecanoic acid were housed in a room with rats on feeding studies of 2,6-dichloro-p-phenylenediamine (CAS No 609-20-1) (NTP TR 219, 1982) Mice fed 11-aminoundecanoic acid were housed in rooms with mice on feeding studies of caprolactam (CAS No 105-60-2) (NTP TR 214, Rev 1982), bisphenol A (CAS No 80-05-7) (NTP TR 215, 1982), and 2,6-dichloro-p-phenylenediamine (CAS No 609-20-1) (NTP TR 219, 1982)

Preparation of Test Diets

Test diets were prepared by first mixing a small amount of Purina® Lab Chow (Table 1) and the required amount of 11-aminoundecanoic acid (Lot No 503) with a mortar and pestle and then adding this premix to the required amount of animal meal and mixing for 20 minutes in a Patterson-Kelly® twin shell blender equipped with an intensifier bar Prepared diets containing 100,000 ppm 11-aminoundecanoic acid were analyzed at Midwest Research Institute and were found to be stable for 2 weeks at temperatures up to 45°C (Appendix F) Test diets were stored in the dark at 4°C for no longer than 2 weeks Control animals were fed Purina® Lab Chow

Dosed feed samples from the chronic studies were analyzed The mean concentration of 11-aminoundecanoic acid (± standard deviation) in nine randomly selected dosed feed samples containing a target level of 7,500 ppm was 7,597 ±416 ppm (Appendix G) The mean concentration of 11-aminoundecanoic acid in eight samples containing a target level of 15,000 ppm was 14,701 ± 618 ppm

Clinical Examinations and Pathology

All animals were observed twice daily for signs of toxicity Clinical signs were recorded monthly Body weights and feed consumption by cage were recorded every 2 weeks for the first 13 weeks and monthly thereafter 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 The average feed consumption per animal was calculated by dividing the total feed consumption measured for all cages by the number of surviving animals in the group Moribund animals and animals that survived to the end of the bioassay were killed using 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, sciatic nerve, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes,

Table 2. EXPERIMENTAL DESIGN OF CHRONIC FEEDING STUDIES WITH 11-AMINOUNDECANOIC ACID IN RATS AND MICE

Test Group	Initial No. of Animals	11-Aminoundecanoic Acid (ppm)	Weeks on Study	
			Dosed	Not Dosed
MALE RATS				
Control	50	0	0	109
Low-Dose	50	7,500	104	5
High-Dose	50	15,000	104	5
FEMALE RATS				
Control	50	0	0	109
Low-Dose	50	7,500	104	5
High-Dose	50	15,000	104	5
MALE MICE				
Control	50	0	0	109
Low-Dose	50	7,500	103	5-6
High-Dose	50	15,000	103	5-6
FEMALE MICE				
Control	50	0	0	109
Low-Dose	50	7,500	103	5-6
High-Dose	50	15,000	103	5-6

liver, gallbladder (mice), pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles/prostate/testes or ovaries/uterus, nasal cavity, brain, pituitary, and spinal cord. Special staining techniques were used as necessary.

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 cannibalization. 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 classification of neoplastic nodules was done according to the recommendations of Squire and Levitt (1975), and the National Academy of Sciences (1980). 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.

II. METHODS AND MATERIALS: CHRONIC STUDY

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-dosed 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, 93-108 weeks, and 109 weeks (when all surviving animals were killed) 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) These 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

III. RESULTS

RATS

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

MICE

PRECHRONIC STUDIES

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

RATS

PRECHRONIC STUDIES

Single-Dose Study

Rats were observed for 14 days and, at the end of the 14-day observation period, survival was 100% in females administered 6,810 or 10,000 mg/kg and in males administered 14,700 or 21,500 mg/kg. Deaths occurred in 1/5 females administered 14,700 mg/kg and in 5/5 females administered 21,500 mg/kg; depressions in mean body weight were observed in males and females at these doses.

Fourteen-Day Study

All animals survived to the end of the dosing period. No compound associated effects were observed in rats fed 0-15,000 ppm, but groups of male and female rats fed 20,000 or 30,000 ppm had depressions in mean body weight gain compared with controls. Daily food consumption data were not collected.

Thirteen-Week Study

One of 12 female rats fed the 18,000-ppm diet died at day 9. Mean body weight gain in male rats fed diets containing 18,000 or 21,000 ppm 11-aminoundecanoic acid was depressed 13% and 14%, respectively (Table 3). Multifocal tubular mineralization of the kidneys was noted in 70%-100% of all groups of female rats administered 11-aminoundecanoic acid (Table 4). The severity of the mineralization was dose related. Transitional-cell hyperplasia was found in the kidneys of 1/10 male rats fed 21,000 ppm, in 6/10 females fed 21,000 ppm, and in 2/9 females fed 18,000 ppm 11-aminoundecanoic acid. Hyperplasias of the renal pelvis were seen in 2/9 females fed 18,000 ppm and in 1/10 males and 6/10 females fed 21,000 ppm.

Because of compound-related effects, including transitional cell hyperplasia in the kidneys and body weight depression, doses for rats in the chronic study were set at 7,500 and 15,000 ppm.

Table 3. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID FOR 13 WEEKS

Dose (ppm)	Survival (*a*)	Mean Body Weights (grams)			Weight Change Relative to Control (*c*) (Percent)
		Initial	Final (*b*)	Change	
MALE					
0	12/12	114	298	+184	
9,000	12/12	114	298	+184	0
12,000	12/12	113	298	+185	0
15,000	12/12	114	283	+169	- 8
18,000	12/12	114	275	+161	-13
21,000	12/12	114	273	+159	-14
FEMALE					
0	12/12	91	172	+ 81	
9,000	12/12	92	183	+ 91	+12
12,000	12/12	92	182	+ 90	+11
15,000	12/12	92	180	+ 88	+ 9
18,000	11/12	91	178	+ 87	+ 7
21,000	12/12	91	177	+ 86	+ 6

(a) Number surviving/number per group

(b) Weights taken at week 12 are used as final weights.

(c) Weight Change Relative to Controls =

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

Table 4. NUMBER OF RATS WITH MINERALIZATION OR HYPERPLASIA OF THE KIDNEY OR RENAL PELVIS IN THE 13-WEEK STUDY

Dose (ppm)	Number of Animals with Mineralization of the Kidney	Number of Animals with Transitional-Cell Hyperplasia of the Kidney	Number of Animals with Hyperplasia of the Renal Pelvis
Male			
0	0/10	—	—
9,000	0/10	—	—
12,000	0/10	—	—
15,000	0/10	—	—
18,000	0/10	—	—
21,000	0/10	1/10	1/10
Female			
0	0/10	—	—
9,000	7/10	—	—
12,000	7/10	—	—
15,000	10/10	—	—
18,000	9/9	2/9	2/9
21,000	8/10	6/10	6/10

CHRONIC STUDIES

Body Weights and Clinical Signs

Throughout the last year of the study, mean body weights of high-dose rats of either sex were lower than those of the controls (Figure 1 and Table 5). The average daily feed consumption per rat by low- and high-dose rats was 98% and 88% that of the controls for males and 88% and 86% for females (Table 6). No compound-related clinical signs were observed.

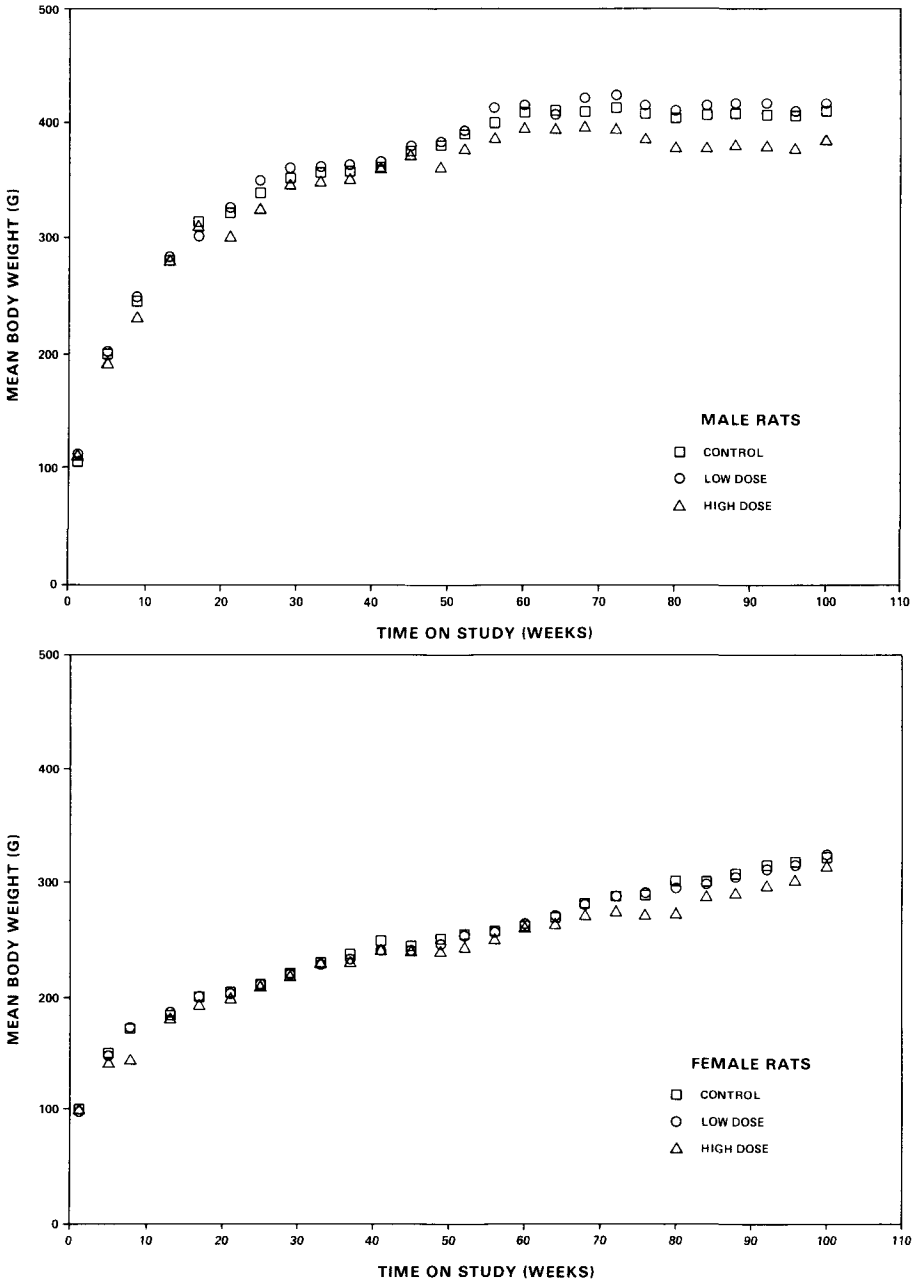

Figure 1. Growth Curves for Rats Fed Diets Containing 11-Aminoundecanoic Acid

Table 5. CUMULATIVE MEAN BODY WEIGHT CHANGE OF RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

		Cumulative Mean Body Weight Change (grams)			Percent Weight Change Relative to Controls *(a)*	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
MALE						
	1	105 *(b)*	112 *(b)*	110 *(b)*		
	5	+ 94	+ 90	+ 81	-4	-14
	25	+233	+237	+215	+2	- 8
	45	+270	+267	+260	-1	- 4
	64	+307	+295	+285	-4	- 7
	84	+302	+304	+267	+1	-12
	100	+307	+306	+275	0	-10
FEMALE						
	1	99 *(b)*	97 *(b)*	98 *(b)*		
	5	+ 51	+ 51	+ 42	0	-18
	25	+114	+116	+112	+2	- 2
	45	+146	+144	+142	-1	- 3
	64	+170	+173	+166	+2	- 2
	84	+201	+201	+189	0	- 6
	100	+222	+226	+216	+2	- 3

(a) Percent Weight Change Relative to Controls =

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

(b) Initial weight

Table 6 AVERAGE DAILY FEED CONSUMPTION (IN GRAMS) PER RAT IN THE CHRONIC STUDY

				Low Dose		High Dose
	Week	Control	Low Dose	Control	High Dose	Control
MALE	8	30	27	0 9	21	0 7
	24	23	25	1 1	22	1 0
	36	24	24	1 0	24	1 0
	48	23	23	1 0	21	0 9
	60	26	25	1 0	24	0 9
	72	30	30	1 0	25	0 8
	84	32	30	0 9	27	0 8
	96	27	27	1 0	25	0 9
FEMALE	8	18	17	0 9	16	0 9
	24	16	14	0 9	15	0 9
	36	18	17	0 9	17	0 9
	48	18	14	0 8	13	0 7
	60	21	18	0 9	16	0 8
	72	20	18	0 9	18	0 9
	84	24	20	0 8	20	0 8
	96	23	21	0 9	21	0 9

Survival

Estimates of the probabilities of survival of male and female rats administered 11-aminoundecanoic acid in feed at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 2 The Tarone test indicated a linear trend (P = 0 036) in the mortality of male rats in positive relation to the dose levels No significant trend was observed in the mortality of the female groups

In male rats, 39/50 (78%) of the control group, 37 50 (74%) of the low-dose group, and 30/50 (60%) of the high-dose group lived to the end of the study at 109 weeks In female rats, 38/50 (76%) of the control group, 32/50 (64%) of the low-dose group, and 42/50 (84%) of the high-dose group lived to the end of the study at 109 weeks The cause of death of animals dying during the study was not determined

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2, findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2 Appendix Tables A3 and A4 give the survival and tumor status for each individual animal in the male rat and female rat studies, respectively

A variety of tumors was found in control and dosed groups, including leukemias, pituitary chromophobe adenomas, interstitial-cell tumors, pheochromocytomas, mammary fibroadenomas, and lesser incidences of other neoplasms

Tables 7 and 8 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups

Urinary Bladder Transitional-cell carcinomas of the urinary bladder were observed in a significantly increased incidence ($P<0.01$) in the high-dose group of male rats (controls, 0/48, 0%, low-dose, 0/48, 0%, high-dose, 7/49, 14%) These tumors generally tended to grow toward the lumen of the bladder, often forming papillary processes These tumors had a large number of anaplastic cells, mitotic activity, and areas of focal necrosis Invasion of the basement membrane and underlying tissues was often seen in malignant tumors, however, no vascular invasion or metastases were observed Transitional-cell carcinomas of the urinary bladder were not observed in any of the three female rat groups

Focal or diffuse hyperplasia of the transitional epithelium of the urinary bladder was observed with a significantly ($P < 0.01$) increased incidence in high-dose male rats (controls, 0/48, 0%, low-dose, 2/48, 4%, high-dose, 20/49, 41%) These lesions were also observed with increased incidence in dosed female rats (controls, 4/49, 8%, low-dose, 12/47, 26%, high-dose, 9/48, 19%), but only in the low-dose group was this increase statistically significant ($P < 0.05$) (Table 9)

An increased incidence of calculi of the urinary bladder was seen in males in the high-dose group (controls, 1/48, 2%, low-dose, 1/48, 2%, high-dose, 5/49, 10%) However, these calculi were not found in any of the animals for which transitional-cell carcinomas were seen

Kidneys Focal or diffuse hyperplasia of the transitional epithelium of the kidney was observed with significantly ($P < 0.01$) increased incidence in high-dose male rats (controls, 0/50, 0%, low-dose, 4/50, 8%, high-dose 15/50, 30%) and female rats (controls, 0/49, 0%, low-dose 5/50, 10%, high-dose, 34/50, 68%) administered 11-aminoundecanoic acid The increased incidence in low-dose female rats was also statistically significant ($P < 0.05$) (Table 9) None was seen in the controls Foci of calcification in the renal cortex and medulla, especially at the cortico-medullary junction and tip of the medulla, were common lesions in dosed female rats Nonneoplastic kidney lesions (e g , chronic nephropathy), commonly seen in aging rats, were observed in all groups

Liver Neoplastic nodules occurred with a significantly increased incidence ($P<0.01$) in dosed male rats (controls, 1/50, 2%, low-dose, 9/50, 18%, high-dose, 8/50, 16%) The neoplastic nodules were not life shortening The slight increase in neoplastic nodules observed in female rats was not statistically significant Hepatocellular carcinomas were also observed in two high-dose male rats and one low-dose male rat

Mammary Gland Fibroadenomas showed an increased incidence ($P<0.05$) in the low-dose male rat group (controls, 0/50, 0%, low-dose, 5/50, 10%, high-dose, 2/50, 4%) The slight increase at the high dose was not statistically significant

Hematopoietic System: A significantly decreased incidence ($P<0.05$) of leukemia was observed in male rats administered 11-aminoundecanoic acid (control, 14/50, 28%; low-dose, 4/50, 8%; high-dose, 5/50, 10%).

Subcutaneous Tissue: A decreasing trend ($P<0.05$) was seen in neurofibromas of the subcutaneous tissue of male rats (control, 3/50, 6%; low-dose, 0/50, 0%; high-dose, 0/50, 0%).

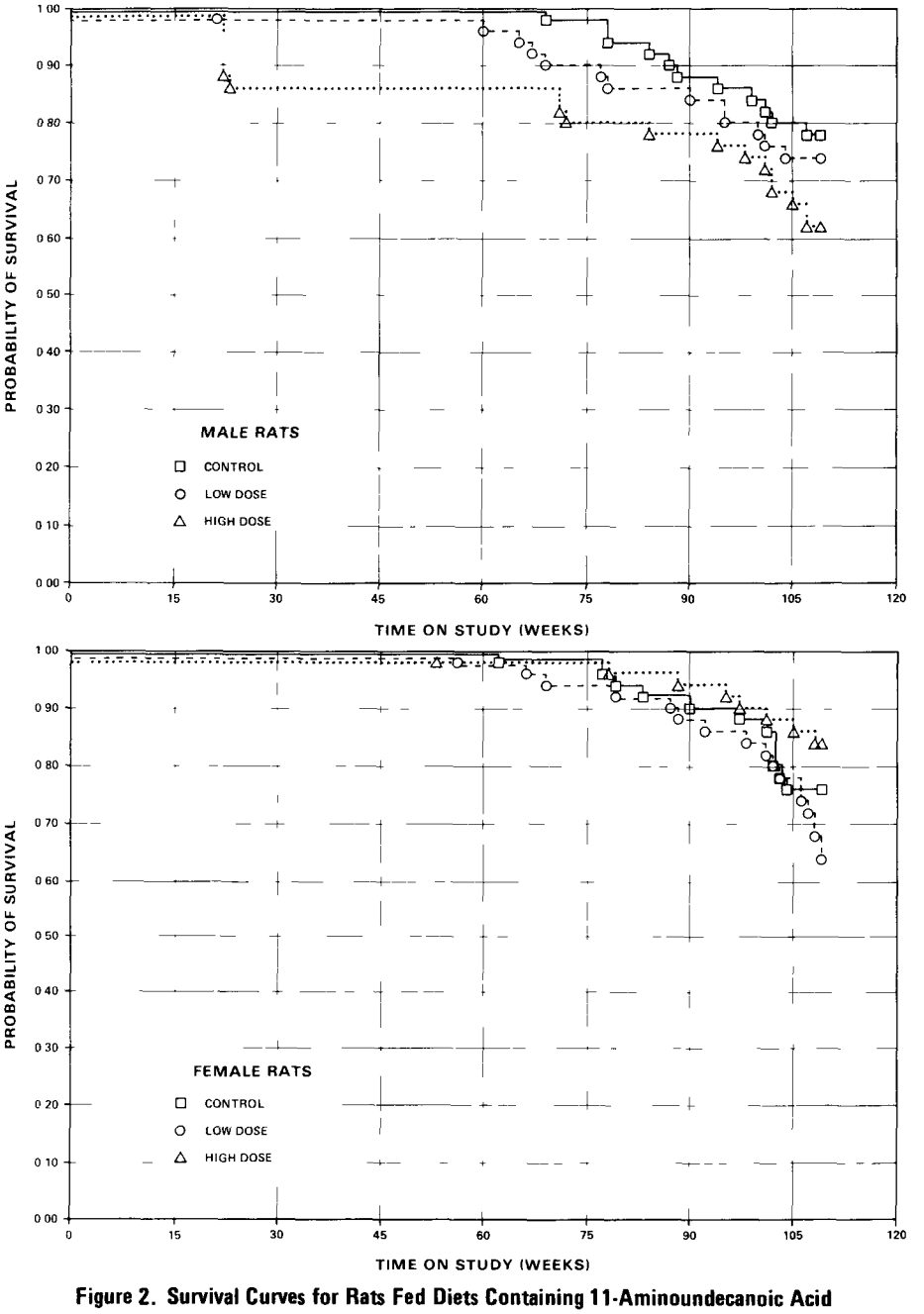

Figure 2. Survival Curves for Rats Fed Diets Containing 11-Aminoundecanoic Acid

Table 7. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)*

Topography: Morphology:	Control	Low Dose	High Dose
Subcutaneous Tissue: Fibroma			
Tumor Rates			
Overall *(b)*	1/50(2)	1/50(2)	3/50(6)
Adjusted *(c)*	0 025	0 027	0 088
Terminal *(d)*	0/39(0)	1/37(3)	2/30(7)
Statistical Tests *(e)*			
Life Table	P=0 094	P=0 746	P=0 236
Incidental Tumor Test	P=0 122	P=0 754	P=0 310
Cochran-Armitage Trend, Fisher Exact Tests	P=0 202	P=0 753	P=0 309
Subcutaneous Tissue: Neurofibroma			
Tumor Rates			
Overall *(b)*	3/50(6)	0/50(0)	0/50(0)
Adjusted *(c)*	0 077	0 000	0 000
Terminal *(d)*	3/39(8)	0/37(0)	0/30(0)
Statistical Tests *(e)*			
Life Table	P=0 023N	P=0 131N	P=0 171N
Incidental Tumor Test	P=0 023N	P=0 131N	P=0 171N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 037N	P=0 121N	P=0 121N
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(b)*	0/50(0)	4/50(8)	1/50(2)
Adjusted *(c)*	0 000	0 103	0 028
Terminal *(d)*	0/39(0)	3/37(8)	0/30(0)
Statistical Tests *(e)*			
Life Table	P=0 228	P=0 059	P=0 474
Incidental Tumor Test	P=0 320	P=0 060	P=0 617
Cochran-Armitage Trend, Fisher Exact Tests	P=0 391	P=0 059	P=0 500
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	12/50(24)	4/50(8)	4 50(8)
Adjusted *(c)*	0 284	0 099	0 114
Terminal *(d)*	9/39(23)	3/37(8)	1/30(3)
Statistical Tests *(e)*			
Life Table	P=0 028N	P=0 040N	P=0 084N
Incidental Tumor Test	P=0 003N	P=0 054N	P=0 016N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 014N	P=0 027N	P=0 027N

Table 7. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

Topography: Morphology:	Control	Low Dose	High Dose
Hematopoietic System: Leukemia			
Tumor Rates			
Overall *(b)*	14/50(28)	4/50(8)	5/50(10)
Adjusted *(c)*	0 322	0 099	0 136
Terminal *(d)*	10/39(26)	3/37(8)	1/30(3)
Statistical Tests *(e)*			
Life Table	P=0 023N	P=0 016N	P=0 075N
Incidental Tumor Test	P=0 003N	P=0 017N	P=0 020N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 009N	P=0 009N	P=0 020N
Liver: Neoplastic Nodule			
Tumor Rates			
Overall *(b)*	1/50(2)	9/50(18)	8/50(16)
Adjusted *(c)*	0 026	0 237	0 258
Terminal *(d)*	1/39(3)	8/37(22)	7/30(23)
Statistical Tests *(e)*			
Life Table	P=0 004	P=0 008	P=0 006
Incidental Tumor Test	P=0 006	P=0 008	P=0 008
Cochran-Armitage Trend, Fisher Exact Tests	P=0 023	P=0 008	P=0 015
Liver: Neoplastic Nodule or Carcinoma			
Tumor Rates			
Overall *(b)*	1/50(2)	10/50(20)	10/50(20)
Adjusted *(c)*	0 026	0 255	0 298
Terminal *(d)*	1/39(3)	8/37(22)	7/30(23)
Statistical Tests *(e)*			
Life Table	P=0 001	P=0 005	P=0 002
Incidental Tumor Test	P=0 002	P=0 003	P=0 004
Cochran-Armitage Trend, Fisher Exact Tests	P=0 007	P=0 004	P=0 004
Urinary Bladder: Transitional-Cell Carcinoma			
Tumor Rates			
Overall *(b)*	0/48(0)	0/48(0)	7/49(14)
Adjusted *(c)*	0 000	0 000	0 196
Terminal *(d)*	0/39(0)	0/37(0)	3/30(10)
Statistical Tests *(e)*			
Life Table	P<0 001	*(f)*	P=0 005
Incidental Tumor Test	P<0 001	*(f)*	P=0 017
Cochran-Armitage Trend, Fisher Exact Tests	P=0 001	*(f)*	P=0 007

Table 7. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

Topography: Morphology:	Control	Low Dose	High Dose
Pituitary: Chromophobe Adenoma			
Tumor Rates			
Overall *(b)*	3/48(6)	6/47(13)	5/47(11)
Adjusted *(c)*	0 079	0.159	0.156
Terminal *(d)*	3/38(8)	4/35(11)	4/30(13)
Statistical Tests *(e)*			
Life Table	P=0.153	P=0.209	P=0 242
Incidental Tumor Test	P=0.207	P=0.212	P=0.277
Cochran-Armitage Trend, Fisher Exact Tests	P=0 292	P=0 232	P=0.345
Adrenal: All Pheochromocytomas			
Tumor Rates			
Overall *(b)*	10/50(20)	12/50(24)	13/49(27)
Adjusted *(c)*	0 212	0.316	0.404
Terminal *(d)*	4/39(10)	11/37(30)	11/30(37)
Statistical Tests *(e)*			
Life Table	P=0.091	P=0.354	P=0.145
Incidental Tumor Test	P=0.081	P=0.290	P=0.120
Cochran-Armitage Trend, Fisher Exact Tests	P=0 259	P=0.405	P=0.298
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	6/42(14)	1/43(2)	3/42(7)
Adjusted *(c)*	0.194	0.029	0.111
Terminal *(d)*	6/31(19)	1/34(3)	3/27(11)
Statistical Tests *(e)*			
Life Table	P=0 141N	P=0 043N	P=0.309N
Incidental Tumor Test	P=0.141N	P=0.043N	P=0.309N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.157N	P=0.051N	P=0.241N
Testis: Interstitial-Cell Tumor			
Tumor Rates			
Overall *(b)*	45/50(90)	43/50(86)	40/50(80)
Adjusted *(c)*	0.978	1.000	1.000
Terminal *(d)*	38/39(97)	37/37(100)	30/30(100)
Statistical Tests *(e)*			
Life Table	P=0.101	P=0.568	P=0.159
Incidental Tumor Test	P=0 221	P=0.584	P=0.530
Cochran-Armitage Trend, Fisher Exact Tests	P=0.103N	P=0.380N	P=0.131N

Table 7. ANALYSIS OF PRIMARY TUMORS IN MALE RATS *(a)* (Continued)

Topography: Morphology:	Control	Low Dose	High Dose
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	0/50(0)	5/50(10)	2/50(4)
Adjusted *(c)*	0 000	0 132	0 067
Terminal *(d)*	0/39(0)	4/37(11)	2/30(7)
Statistical Tests *(e)*			
Life Table	P=0 109	P=0 030	P=0 183
Incidental Tumor Test	P=0 136	P=0 031	P=0 183
Cochran-Armitage Trend, Fisher Exact Tests	P=0 239	P=0 028	P=0 247

(a) Dosed groups received doses of 7,500 or 15,000 ppm of 11-aminoundecanoic acid in the diet

(b) Number of tumor-bearing animals/number of animals examined at the site (percent)

(c) Kaplan-Meier estimated lifetime tumor incidence (proportion) after adjusting for intercurrent mortality

(d) Observed tumor incidence in surviving animals killed at the end of the 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)

(f) The configuration of tumor incidences precludes use of this statistic

Table 8. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)*

Topography: Morphology:	Control	Low Dose	High Dose
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	11/50(22)	12/50(24)	6/50(12)
Adjusted *(c)*	0 240	0 294	0 127
Terminal *(d)*	4/38(11)	7/34(21)	2/42(5)
Statistical Tests *(e)*			
Life Table	P=0 094N	P=0 437	P=0 132N
Incidental Tumor Test	P=0 145N	P=0 582N	P=0 260N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 128N	P=0 500	P=0 143N
Hematopoietic System: Leukemia			
Tumor Rates			
Overall *(b)*	11/50(22)	14/50(28)	6/50(12)
Adjusted *(c)*	0 240	0 330	0 127
Terminal *(d)*	4/38(11)	7/34(21)	2/42(5)
Statistical Tests *(e)*			
Life Table	P=0 100N	P=0 283	P=0 132N
Incidental Tumor Test	P=0 158N	P=0 442	P=0 260N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 134N	P=0 322	P=0 143N
Hematopoietic System: Leukemia or Lymphoma			
Tumor Rates			
Overall *(b)*	13/50(26)	15/50(30)	6/50(12)
Adjusted *(c)*	0 285	0 355	0 127
Terminal *(d)*	6/38(16)	8/34(24)	2/42(5)
Statistical Tests *(e)*			
Life Table	P=0 046N	P=0 350	P=0 060N
Incidental Tumor Test	P=0 068N	P=0 521N	P=0 118N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 061N	P=0 412	P=0 062N
Liver: Neoplastic Nodule			
Tumor Rates			
Overall *(b)*	4/50(8)	5/50(10)	6/50(12)
Adjusted *(c)*	0 105	0 147	0 143
Terminal *(d)*	4/38(11)	5/34(15)	6/42(14)
Statistical Tests *(e)*			
Life Table	P=0 313	P=0 430	P=0 433
Incidental Tumor Test	P=0 313	P=0 430	P=0 433
Cochran-Armitage Trend, Fisher Exact Tests	P=0 309	P=0 500	P=0 370

Table 8. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

Topography: Morphology:	Control	Low Dose	High Dose
Liver: Neoplastic Nodule or Carcinoma			
Tumor Rates			
Overall *(b)*	5/50(10)	5/50(10)	6/50(12)
Adjusted *(c)*	0 132	0 147	0 143
Terminal *(d)*	5/38(13)	5/34(15)	6 42(14)
Statistical Tests *(e)*			
Life Table	P=0 444	P=0 560	P=0 570
Incidental Tumor Test	P=0 444	P=0 560	P=0 570
Cochran-Armitage Trend, Fisher Exact Tests	P=0 436	P=0 630	P=0 500
Pituitary: Chromophobe Adenoma			
Tumor Rates			
Overall *(b)*	21 50(42)	19/50(38)	18/49(37)
Adjusted *(c)*	0 509	0 445	0 408
Terminal *(d)*	18/38(47)	11/34(32)	16/42(38)
Statistical Tests *(e)*			
Life Table	P=0 182N	P=0 559N	P=0 222N
Incidental Tumor Test	P=0 305N	P=0 434N	P=0 311N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 332N	P=0 419N	P=0 371N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	3/48(6)	2 50(4)	2 49(4)
Adjusted *(c)*	0 073	0 059	0 049
Terminal *(d)*	1/38(3)	2/34(6)	2/41(5)
Statistical Tests *(e)*			
Life Table	P=0 296N	P=0 534N	P=0 471N
Incidental Tumor Test	P=0 327N	P=0 485N	P=0 540N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 397N	P=0 480N	P=0 490N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/45(9)	2 45(4)	3 45(7)
Adjusted *(c)*	0 111	0 069	0 081
Terminal *(d)*	2/33(6)	2 29(7)	3 37(8)
Statistical Tests *(e)*			
Life Table	P=0 294N	P=0 383N	P=0 446N
Incidental Tumor Test	P=0 323N	P=0 338N	P=0 507N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 417N	P=0 338N	P=0 500N

Table 8. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS *(a)* (Continued)

Topography: Morphology:	Control	Low Dose	High Dose
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	11 50(22)	10/50(20)	11/50(22)
Adjusted *(c)*	0 289	0 282	0 255
Terminal *(d)*	11 38(29)	9/34(26)	10/42(24)
Statistical Tests *(e)*			
Life Table	P=0 398N	P=0 588	P=0 494N
Incidental Tumor Test	P=0 417N	P=0 599N	P=0 511N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 548	P=0 500N	P=0 595
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(b)*	15/50(30)	12/48(25)	10/50(20)
Adjusted *(c)*	0 382	0 328	0 238
Terminal *(d)*	14/38(37)	10/34(29)	10/42(24)
Statistical Tests *(e)*			
Life Table	P=0 076N	P=0 445N	P=0 110N
Incidental Tumor Test	P=0 095N	P=0 407N	P=0 132N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 150N	P=0 372N	P=0 178N

(a) Dosed groups received doses of 7,500 or 15,000 ppm of 11-aminoundecanoic acid in the diet

(b) Number of tumor bearing animals/number of animals examined at the site (percent)

(c) Kaplan-Meier estimated lifetime tumor incidence (proportion) after adjusting for intercurrent mortality

(d) Observed tumor incidence in surviving animals killed at the end of the 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 9. INCIDENCE OF TUMORS AND PROLIFERATIVE LESIONS OF TRANSITIONAL CELLS IN RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	Males			Females		
	Control	Low Dose	High Dose	Control	Low Dose	High Dose
Kidney						
Tissues Examined	50	50	50	49	50	50
Hyperplasia	0	4 (8%)	15 (30%) *(a)*	0	5 (10%) *(b)*	34 (68%) *(a)*
Papilloma	0	0	0	0	0	0
Carcinoma	0	0	1 (2%)	0	0	2 (4%)
Urinary Bladder						
Tissues Examined	48	48	49	49	47	48
Hyperplasia	0	2 (4%)	20 (41%) *(a)*	4 (8%)	12 (26%) *(b)*	9 (19%)
Papilloma	0	0	1 (2%)	0	0	1 (2%)
Carcinoma	0	0	7 (14%) *(a)*	0	0	0

(a) $P < 0.01$ (Fisher's exact tests) relative to controls

(b) $P < 0.05$ (Fisher's exact tests) relative to controls

MICE

PRECHRONIC STUDIES

Fourteen-Day Study

All animals survived to the end of the dosing period. No compound-associated effects were observed in mice at any dose level (5,000-30,000 ppm).

Thirteen-Week Study

Deaths occurred in 2/10 males and 2/10 females administered 15,000 ppm, 4/10 males and 2/10 females receiving 18,000 ppm, and 3/10 males receiving 20,000 ppm (Table 10). The cause of death of animals dying during the study was not determined Mean body weight gain was depressed 20% in male mice receiving 15,000 ppm, but only 10% in male mice receiving 18,000 or 20,000 ppm Mean body weight gain was depressed by more than 10% in female mice fed diets containing 18,000-20,000 ppm 11-aminoundecanoic acid Focal mineralization of the kidney was noted in males that received 15,000-20,000 ppm and in females that received 15,000-18,000 ppm, particularly in those mice that died (Table 11)

Doses for mice in the chronic study were set at 7,500 and 15,000 ppm

Table 10. DOSAGE, SURVIVAL, AND MEAN BODY WEIGHTS OF MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID FOR 13 WEEKS

Dose (ppm)	Survival *(a)*	Mean Body Weights (grams)			Weight Change Relative to Control *(c)* (Percent)
		Initial	Final *(b)*	Change	
MALE					
0	10/10	20	30	+10	
9,000	10/10	20	31	+11	+10
12,000	10/10	20	30	+10	0
15,000	8/10	20	28	+ 8	-20
18,000	6/10	20	29	+ 9	-10
20,000	7/10	20	29	+ 9	-10
FEMALE					
0	10/10	17	25	+ 8	
9,000	10/10	17	25	+ 8	0
12,000	10/10	17	25	+ 8	0
15,000	8/10	17	25	+ 8	0
18,000	8/10	17	24	+ 7	-13
20,000	10/10	17	23	+ 6	-25

(a) Number surviving/number per group

(b) Weights taken at week 12 are used as final weights

(c) Weight Change Relative to Controls =

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

Table 11. NUMBER OF MICE WITH MINERALIZATION OF THE KIDNEY IN THE 13-WEEK STUDY

Dose (ppm)	Number of Animals with Mineralization of the Kidney	Number of Animals with Mineralization that Died Before End of Study
Male		
0	0/10	0/0
9,000	0/10	0/0
15,000	2/10	1/2
18,000	4/10	3/4
20,000	2/10	2/3
Female		
0	0/10	0/0
9,000	0/10	0/0
15,000	1/10	1/2
18,000	2/10	2/2
20,000	0/10	0/0

CHRONIC STUDIES

Body Weights and Clinical Signs

Mean body weights of dosed mice of either sex were lower than those of the controls throughout the study, and the depressions in mean body weight gain were dose related (Figure 3 and Table 12). The average daily feed consumption per mouse by low- and high-dose mice was 110% and 123% that of the controls for males and 110% and 97% for females. No other compound-related clinical signs were observed (Table 13).

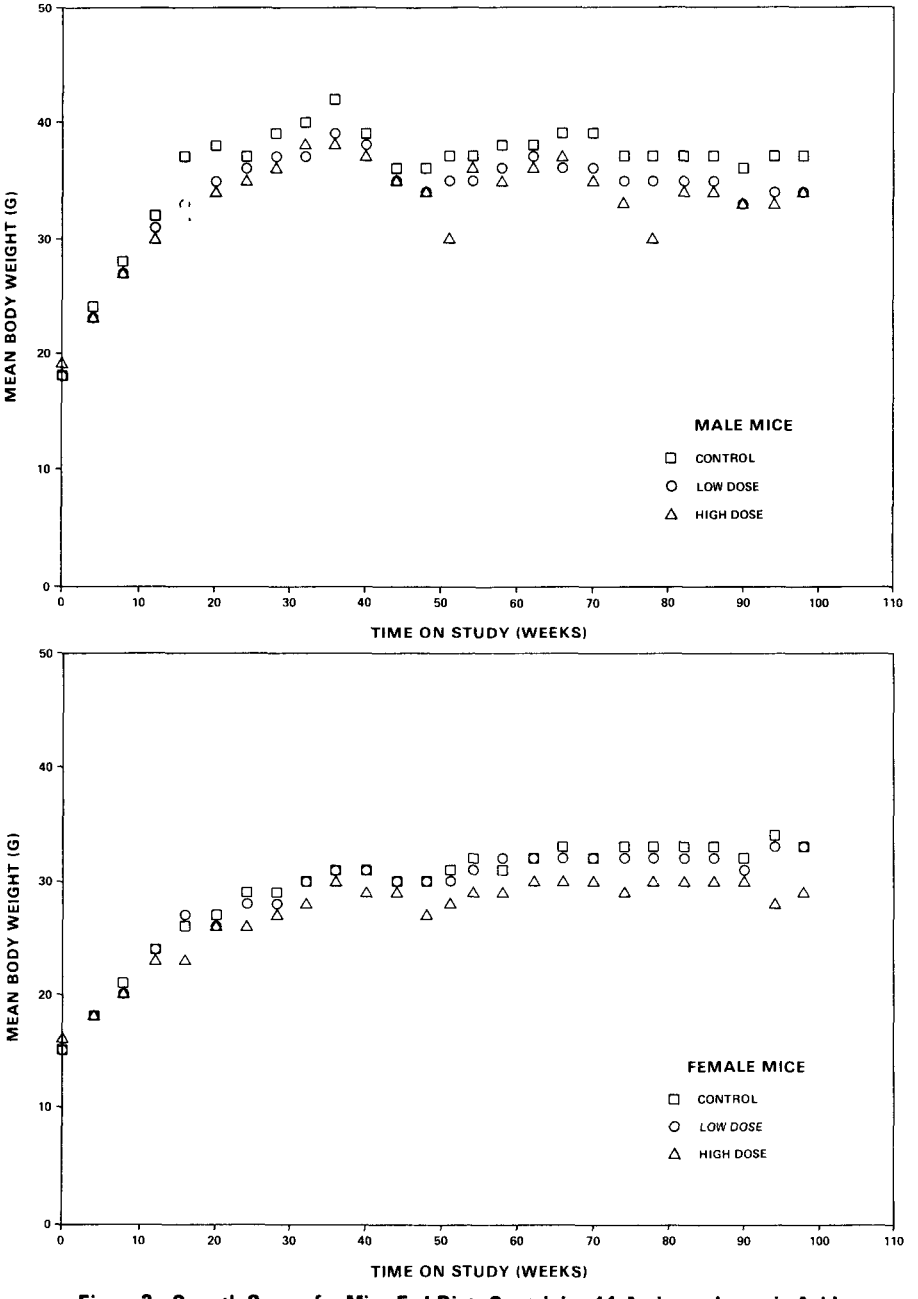

Figure 3. Growth Curves for Mice Fed Diets Containing 11-Aminoundecanoic Acid

Table 12. CUMULATIVE MEAN BODY WEIGHT CHANGE OF MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

		Cumulative Mean Body Weight Change (grams)			Percent Weight Change Relative to Controls *(a)*	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
MALE						
	1	18 *(b)*	18 *(b)*	19 *(b)*		
	4	+ 6	+ 5	+ 4	-17	-33
	24	+19	+18	+16	- 5	-16
	44	+18	+17	+16	- 6	-11
	62	+20	+19	+17	- 5	-15
	82	+19	+17	+15	-11	-21
	98	+19	+16	+15	-16	-21
FEMALE						
	1	15 *(b)*	15 *(b)*	16 *(b)*		
	4	+ 3	+ 3	+ 2	0	-33
	24	+14	+13	+10	- 7	-29
	44	+15	+15	+13	0	-13
	62	+17	+17	+14	0	-18
	82	+18	+17	+14	- 6	-22
	98	+18	+18	+13	0	-28

(a) Percent Weight Change Relative to Controls =

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

(b) Initial weight

Table 13. AVERAGE DAILY FEED CONSUMPTION (IN GRAMS) PER MOUSE IN THE CHRONIC STUDY

				Low Dose		High Dose
	Week	Control	Low Dose	Control	High Dose	Control
MALES	8	6	6	1 0	7	1 2
	24	6	5	0 8	6	1 0
	36	6	8	1 3	6	1 0
	48	5	6	1 2	6	1 2
	60	4	5	1 3	7	1 8
	72	4	4	1 0	5	1 3
	85	5	6	1 2	6	1 2
	97	4	4	1 0	6	1 5
FEMALES	8	7	8	1 1	6	0 9
	24	4	6	1 5	5	1 3
	36	-	9	-	9	-
	48	6	8	1 3	6	1 0
	60	6	6	1 0	6	1 0
	72	6	5	0 8	5	0 8
	85	6	4	0 7	4	0 7
	97	4	6	1 5	6	1 5

Survival

Estimates of the probabilities of survival of male and female mice administered 11-aminoundecanoic acid in feed at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 4. The Tarone test indicated a significant ($P<0.001$), positive, dose-related linear trend in mortality in both male and female groups. Two female mice, one from the low-dose and one from the high-dose groups, were missing.

In male mice, 37/50 (74%) of the control group, 34/50 (68%) of the low-dose group, and 18/50 (36%) of the high-dose group lived to the end of the study at 109 weeks. In female mice, 42/50 (84%) of the control group, 37/49 (76%) of the low-dose group, and 25/49 (51%) of the high-dose group lived to the end of the study at 109 weeks. The cause of death of animals dying during the study was not determined.

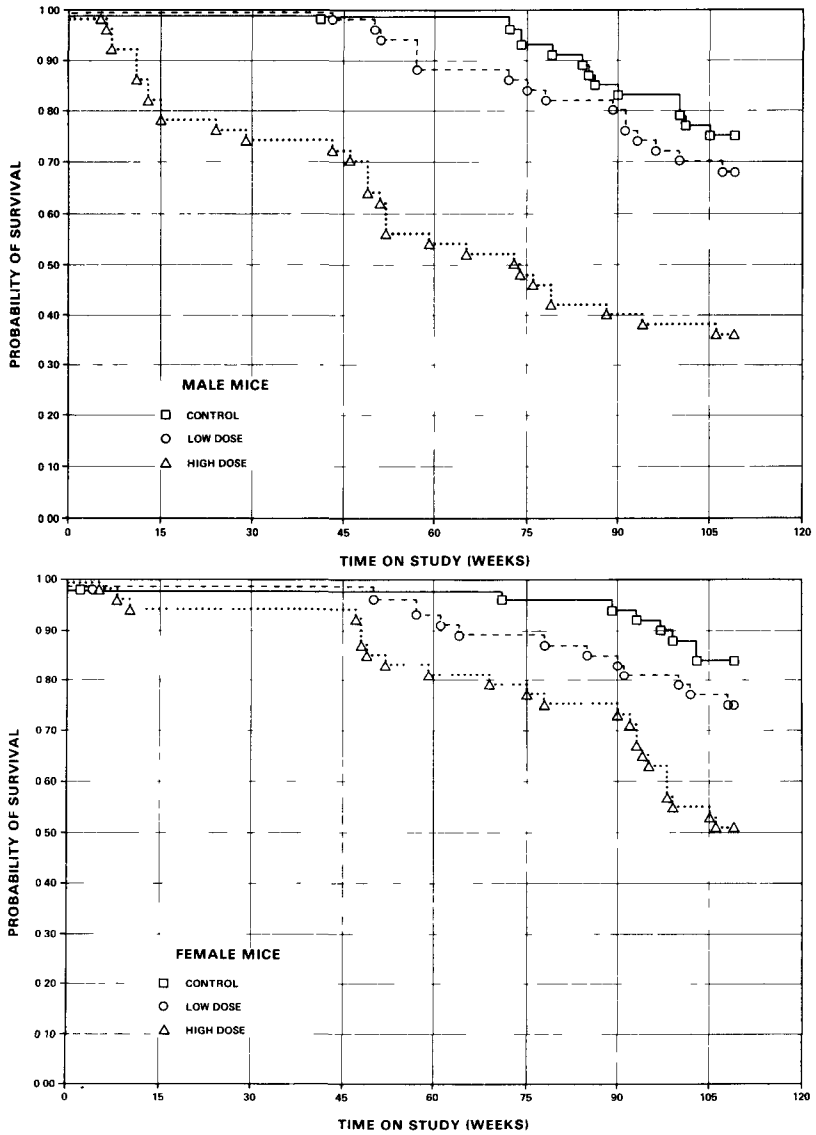

Figure 4. Survival Curves for Mice Fed Diets Containing 11-Aminoundecanoic Acid

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in mice are summarized in Table 14 and Appendix B, Tables B1 and B2; findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2. Tables B3 and B4 give the survival and tumor status for each individual animal in the male and female mouse studies, respectively.

Tables 15 and 16 contain the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups.

Hematopoietic System: Malignant lymphomas occurred with a significant ($P<0.05$) increasing trend in male mice, as shown in Table 14 (control, 2/50, 4%; low-dose, 9/50, 18%, high-dose, 4/50, 8%). The increase was statistically significant ($P<0.05$) at the low dose but not at the high dose. In most of the affected mice, two or more organs were involved in the neoplastic process. For female mice, a slight increase in malignant lymphomas was not statistically significant. If the results of the two sexes are combined, then the increasing trend is significant ($P<0.05$) by a life table analysis but not by an incidental tumor test.

Kidneys: The incidence of mineralization of the kidneys or kidney medulla was significantly ($P < 0.01$) increased in high-dose male mice (controls, 0/50, 0%; low-dose, 4/50, 8%; high-dose, 11/49, 22%), and in dosed female mice (controls, 0/50, 0%; low-dose, 8/49, 16%; high-dose, 9/49, 18%) fed 11-aminoundecanoic acid.

Liver: Hepatocellular vacuolization was observed with significantly ($P < 0.05$) increased incidence in high-dose male mice (controls, 2/50, 4%; low-dose, 2/50, 4%; high-dose 10/49, 20%) and in dosed female mice (controls, 0/50, 0%; low-dose, 5/49, 10%; high-dose, 6/49, 12%) fed 11-aminoundecanoic acid.

Table 14. INCIDENCE OF MALIGNANT LYMPHOMAS IN MALE MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID IN THE CHRONIC STUDY

	Control	Low Dose	High Dose
Multiple Organs	2 (4%)	6 (12%)	4 (8%)
Localized			
Spleen	—	1 (2%)	—
Lymph Node	—	1 (2%)	—
Thymus	—	1 (2%)	—
Total	2 (4%)	9 (18%)	4 (8%)

Table 15. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)*

Topography: Morphology:	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(b)*	10/50(20)	3/50(6)	4/46(9)
Adjusted *(c)*	0 262	0 088	0 222
Terminal *(d)*	9/37(24)	3/34(9)	4/18(22)
Statistical Tests *(e)*			
Life Table	P=0 205N	P=0 051N	P=0 482N
Incidental Tumor Test	P=0 202N	P=0 049N	P=0 478N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 055N	P=0 036N	P=0 100N
Hematopoietic System: Malignant Lymphoma			
Tumor Rates			
Overall *(b)*	2/50(4)	9/50(18)	4/50(8)
Adjusted *(c)*	0 049	0 243	0 181
Terminal *(d)*	1/37(3)	6/34(18)	1/18(6)
Statistical Tests *(e)*			
Life Table	P=0 036	P=0 022	P=0 097
Incidental Tumor Test	P=0 044	P=0 017	P=0 175
Cochran-Armitage Trend, Fisher Exact Tests	P=0 309	P=0 026	P=0 339
Circulatory System: Hemangiosarcoma			
Tumor Rates			
Overall *(b)*	2/50(4)	3/50(6)	0/50(0)
Adjusted *(c)*	0 054	0 081	0 000
Terminal *(d)*	2/37(5)	2/34(6)	0/18(0)
Statistical Tests *(e)*			
Life Table	P=0 284N	P=0 463	P=0 407N
Incidental Tumor Test	P=0 201N	P=0 561	P=0 407N
Cochran-Armitage Trend, Fisher Exact Tests	P=0 203N	P=0 500	P=0 247N
Liver: Adenoma			
Tumor Rates			
Overall *(b)*	1/50(2)	3/50(6)	3/49(6)
Adjusted *(c)*	0 024	0 088	0 140
Terminal *(d)*	0/37(0)	3/34(9)	2/18(11)
Statistical Tests *(e)*			
Life Table	P=0 041	P=0 273	P=0 114
Incidental Tumor Test	P=0 093	P=0 284	P=0 243
Cochran-Armitage Trend, Fisher Exact Tests	P=0 232	P=0 309	P=0 301

Table 15. ANALYSIS OF PRIMARY TUMORS IN MALE MICE *(a)* (Continued)

Topography: Morphology:	Control	Low Dose	High Dose
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	16/50(32)	16/50(32)	9/49(18)
Adjusted *(c)*	0.379	0.415	0.377
Terminal *(d)*	11/37(30)	12/34(35)	4/18(22)
Statistical Tests *(e)*			
Life Table	P=0.347	P=0.473	P=0.449
Incidental Tumor Test	P=0.466	P=0.459	P=0.579N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.081N	P=0.585	P=0.091N
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	17/50(34)	18/50(36)	12/49(24)
Adjusted *(c)*	0.394	0.469	0.483
Terminal *(d)*	11/37(30)	14/34(41)	6/18(33)
Statistical Tests *(e)*			
Life Table	P=0.140	P=0.386	P=0.203
Incidental Tumor Test	P=0.258	P=0.368	P=0.405
Cochran-Armitage Trend, Fisher Exact Tests	P=0.184N	P=0.500	P=0.207N

(a) Dosed groups received doses of 7,500 or 15,000 ppm of 11-aminoundecanoic acid in the diet.

(b) Number of tumor bearing animals/number of animals examined at the site (percent).

(c) Kaplan-Meier estimated lifetime tumor incidence (proportion) after adjusting for intercurrent mortality.

(d) Observed tumor incidence in surviving animals killed at the end of the 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 16. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)*

Topography: Morphology:	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(b)*	2/50(4)	3/49(6)	3/49(6)
Adjusted *(c)*	0 048	0 081	0 120
Terminal *(d)*	2/42(5)	3/37(8)	3/25(12)
Statistical Tests *(e)*			
Life Table	P=0 141	P=0 442	P=0 272
Incidental Tumor Test	P=0 141	P=0 442	P=0 272
Cochran-Armitage Trend, Fisher Exact Tests	P=0 403	P=0 490	P=0 490
Hematopoietic System: Malignant Lymphoma			
Tumor Rates			
Overall *(b)*	9/50(18)	10/49(20)	10/49(20)
Adjusted *(c)*	0 203	0 250	0 327
Terminal *(d)*	7/42(17)	7/37(19)	5 25(20)
Statistical Tests *(e)*			
Life Table	P=0 089	P=0 384	P=0 137
Incidental Tumor Test	P=0 339	P=0 434	P=0 424
Cochran-Armitage Trend, Fisher Exact Tests	P=0 430	P=0 480	P=0 480
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	7/50(14)	8/49(16)	5/49(10)
Adjusted *(c)*	0 162	0 202	0 176
Terminal *(d)*	6/42(14)	6/37(16)	3 25(12)
Statistical Tests *(e)*			
Life Table	P=0 374	P=0 399	P=0 515
Incidental Tumor Test	P=0 395N	P=0 415	P=0 502N
Cochran-Armitage Trend Fisher Exact Tests	P=0 344N	P=0 483	P=0 394N
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	5/50(10)	7 49(14)	4/49(8)
Adjusted *(c)*	0 116	0 176	0 139
Terminal *(d)*	4 42(10)	5 37(14)	2 25(8)
Statistical Tests *(e)*			
Life Table	P=0 320	P=0 299	P=0 484
Incidental Tumor Test	P=0 430N	P=0 313	P=0 537N
Cochran-Armitage Trend Fisher Exact Tests	P=0 450N	P=0 365	P=0 513N

Table 16. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

Topography: Morphology:	Control	Low Dose	High Dose
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	3/42(7)	5/39(13)	2/41(5)
Adjusted *(c)*	0.083	0.167	0.087
Terminal *(d)*	3/36(8)	5/30(17)	2/23(9)
Statistical Tests *(e)*			
Life Table	P=0.424	P=0.258	P=0.665
Incidental Tumor Test	P=0.424	P=0.258	P=0.665
Cochran-Armitage Trend, Fisher Exact Tests	P=0.434N	P=0.315	P=0.512N
Mammary Gland: Adenocarcinoma			
Tumor Rates			
Overall *(b)*	6/50(12)	1/49(2)	2/49(4)
Adjusted *(c)*	0.138	0.027	0.077
Terminal *(d)*	5/42(12)	1/37(3)	1/25(4)
Statistical Tests *(e)*			
Life Table	P=0.132N	P=0.083N	P=0.347N
Incidental Tumor Test	P=0.073N	P=0.094N	P=0.206N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.075N	P=0.059N	P=0.141N

(a) Dosed groups received doses of 7,500 or 15,000 ppm of 11-aminoundecanoic acid in the diet.

(b) Number of tumor bearing animals/number of animals examined at the site (percent).

(c) Kaplan-Meier estimated lifetime tumor incidence (proportion) after adjusting for intercurrent mortality.

(d) Observed tumor incidence in surviving animals killed at the end of the 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 carcinogenesis bioassay of 11-aminoundecanoic acid was conducted in F344 rats and B6C3F1 mice

The probable cause(s) of death in the high-dose male rats and in the high-dose mice of either sex was not determined, this poor survival rate, particularly for the mice (male, 36%, female, 51%) was due most likely to compound-related toxicity

11-Aminoundecanoic acid was carcinogenic for male F344 rats (Table 7), causing liver and urinary bladder tumors Transitional-cell carcinomas of the urinary bladder were observed in a significantly increased incidence ($P<0.01$) in the high-dose group of male rats (controls, 0/48, 0%, low-dose, 0/48, 0%, high-dose, 7/49, 14%) Urinary bladder tumors are rare in untreated male F344 rats in the Bioassay Program (Goodman et al , 1979, Sacksteder, 1976, Sass et al , 1975) In 3,512 untreated male F344 rats observed in the NCI/NTP Bioassay Program, there is a 0 02% incidence of undifferentiated carcinoma and a 0 11% incidence of transitional-cell papilloma of the urinary bladder Transitional-cell carcinomas of the urinary bladder have not been seen in any untreated F344 male rats (0/780) examined at Litton Bionetics as part of the Bioassay Program

Neoplastic nodules of the liver also occurred with a significant, dose-related ($P<0.01$) increase in male rats (controls, 1/50, 2%, low-dose, 9/50, 18%, and high-dose, 8/50, 16%) The historical incidence of this tumor in untreated male F344 rats in the Bioassay Program is 1 62% (57/3,512), and at Litton Bionetics, 1 79% (14/780) The occurrence of neoplastic nodules is considered to be a manifestation of the carcinogenesis process (NAS, 1980) Female rats fed diets containing 11-aminoundecanoic acid did not show evidence of compound related tumor development in the urinary bladder or liver or at any other site

Additional evidence of urinary tract toxicity was seen in rats An increased incidence of calculi of the urinary bladder was seen in males in the high-dose group (controls, 1/48, 2%, low-dose, 1/48, 2%, high-dose, 5/49, 10%) The rats with calculi were not the ones that had tumors of the urinary bladder Hyperplasia of the transitional epithelium of the kidney and bladder was associated with the administration of 11-aminoundecanoic acid in male and female rats (Table 9) In particular, hyperplasia was associated with calculi of the urinary bladder in 2/5 high-dose males For the 20 high-dose male rats with hyperplasia of the urinary bladder, 7 of these had transitional-cell carcinomas and 1 other had a papilloma, the remaining 12 had hyperplasia in the apparent absence of urinary bladder tumors Hyperplasia of the renal pelvis was also observed in the 13-week subchronic study in 2/9 females that received 18,000 ppm and in 1/10 males and 6/10 females that received 21,000 ppm

Leukemia was observed in male rats at the following incidences controls, 14/50, 28%, low-dose, 4/50, 8%, and high-dose, 5/50, 10% Control F344 male rats at Litton Bionetics have a mean incidence of leukemia of 14% (111/780, range 0%-44%)

No clear evidence was found for the carcinogenicity of 11-aminoundecanoic acid in mice Mean body weights for dosed mice of either sex were lower than those of the controls throughout the study There was a significant ($P<0.001$), positive, dose-related linear trend in mortality in both male and female groups Early mortality in the high-dose male and female mice groups reduced the sensitivity of the bioassay for detecting increases in the incidence of late developing tumors

Malignant lymphomas occurred with a statistically significant ($P<0.05$), increase in low-dose male mice but not in the high-dose group (controls, 2/50, 4%, low-dose, 9/50, 18%, and high-dose, 4/50, 8%) The incidence of malignant lymphomas in untreated male B6C3F1 mice in this laboratory is 9% (44/507) (range 0%-20%) Malignant lymphomas in dosed male mice are not clearly associated with the administration of 11-aminoundecanoic acid because of the variable incidence of this tumor historically and the lack of a statistically significant effect at the high dose

Evidence for renal toxicity was also seen in mice Mineralization in the kidney was seen in dosed mice of either sex in both the subchronic and chronic studies

11-Aminoundecanoic acid was tested in the same room with other chemicals undergoing carcinogenesis bioassay feeding studies—rats 2,6-dichloro-p-phenylenediamine, mice bisphenol A, caprolactam, and 2,6-dichloro-p-phenylenediamine Abbreviated results from these three studies are given for comparative purposes Bisphenol A (NTP TR 215, 1982) was not carcinogenic for F344 rats or B6C3F1 mice of either sex, yet, the increased incidences of leukemia in male rats (control 13/50, low dose

12/50, high dose 23/50*) and lymphoma in male mice (control 2/49, low dose 8/50*, high dose 3/50) may have been associated with the administration of bisphenol A Caprolactam (NTP TR 214, Rev 1982) was not carcinogenic for F344 rats or B6C3F1 mice of either sex 2,6-Dichloro-p-phenylenediamine (NTP TR 219, 1982) was not carcinogenic for F344 rats and was carcinogenic for B6C3F1 mice, causing an increased incidence of hepatocellular adenomas (male control 4/50, low dose 7/50, high dose 15/50*) and hepatocellular adenomas and carcinomas combined (female control 6/50, low dose 6/50, high dose 16/50*)

Although chemical cross-contamination among groups cannot be excluded completely, the responses in the separate testing experiments persuade that any adjacent chemical effect was absent or minimal The results of these other studies support the conclusion that in male rats 11-aminoundecanoic acid caused transition-cell carcinomas of the urinary bladder and neoplastic nodules of the liver, additionally, in male mice an association may exist between the occurrence of malignant lymphoma (low dose) and administration of 11-aminoundecanoic acid These data stand independently because the bisphenol A exposed animals and the caprolactam exposed groups did not show any definite compound-related tumor development and because 2,6-dichloro-p-phenylenediamine induced liver tumors distinctly in mice The apparent correlative association between the 11-aminoundecanoic acid-induced and the bisphenol A-caused marginal increase in lymphomas in low dose male B6C3F1 mice may or may not be real and significant

Conclusions Under the conditions of this bioassay, 11-aminoundecanoic acid was carcinogenic for male F344 rats, inducing neoplastic nodules in the liver and transitional-cell carcinomas in the urinary bladder The test chemical was not carcinogenic for female F344 rats No clear evidence was found for the carcinogenicity of 11-aminoundecanoic acid in B6C3F1 mice of either sex, although the increase in malignant lymphoma in male mice may have been associated with the administration of 11-aminoundecanoic acid

*Increase is statistically significant ($P < 0.05$) relative to controls

V. REFERENCES

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

Berenblum, I , ed , Carcinogenicity 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

Gart, J , Chu, K , Tarone, R , Statistical issues in interpretation of chronic bioassay tests for carcinogenicity J Natl Cancer Inst 62(4) 957, 1979

Goodman, D , Ward, J , Squire, R , Chu, K , Linhart, M , Neoplastic and nonneoplastic lesions in aging F344 rats Toxicol Appl Pharmacol 48 237-248, 1979

Hampel, C , Hawley, G , ed , The encyclopedia of chemistry New York Van Nostrand Reinhold Co , 1973 874-875

Hawley, G , ed , The condensed chemical dictionary New York Van Nostrand Reinhold Co , 1977 628-629

Kaplan, E L , Meier, P , Nonparametric estimation of incomplete observations J Amer Stat Assoc 53 457-481, 1958

Kirk-Othmer encyclopedia of chemical technology, 3rd ed New York John Wiley & Sons, Inc 5 6-7, 1979

Linhart, M S , Cooper, J A , Martin, R L , Page, N P , Peters, J A , 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 Natl Cancer Inst 22 719-748, 1959

NAS, National Academy of Sciences Histologic typing of liver tumors of the rat J Natl Cancer Inst 64 179, 1980

NTP, National Toxicology Program Carcinogenesis bioassay of bisphenol A, U S Dept of Health and Human Services, Public Health Service, National Institutes of Health, 1982, TR 215

NTP, National Toxicology Program Carcinogenesis bioassay of caprolactam, U S Dept of Health and Human Services, Public Health Service, National Institutes of Health, Rev 1982, TR 214

NTP, National Toxicology Program Carcinogenesis bioassay of 2,6-dichloro-p-phenylenediamine, U S Dept of Health and Human Services, Public Health Service, National Institutes of Health, 1982, TR 219

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

Rekhter, M A , Nesterova, I P , Uch Zap Kishinevsk Univ 68 82, 1963

Sacksteder, M , Brief communication occurrence of spontaneous tumors in the germ free F344 rat J Natl Cancer Inst 57(6) 1371-1373, 1976

Sadtler Research Laboratories Sadtler standard spectra Philadelphia Sadtler Research Laboratories, IR No 15268

Sass, B , Rabstein, L , Madison, R , Nims, R , Peters, R , Kelloff, G , Incidence of spontaneous neoplasms in F344 rats throughout the natural lifespan J Natl Cancer Inst 54(6) 1449-1453, 1975

Squire, R , Levitt, M , Report of a workshop on classification of specific hepatocellular lesions in rats Cancer Res 35 3214, 1975

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

U S Code of Federal Regulations 21 177 1500 and 179 45, 1977

Ward, J M , Goodman, D G , Griesemer, R A , Hardisty, J F , Schueler, R L , Squire, R A , Strandberg, J D , Quality assurance for pathology in rodent carcinogenesis tests J Environ Path Toxicol 2 371-378, 1978

APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED 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	2 (4%)	1 (2%)	
SQUAMOUS CELL CARCINOMA	1 (2%)	1 (2%)	
TRICHOEPITHELIOMA	1 (2%)	1 (2%)	
SEBACEOUS ADENOMA			1 (2%)
NEUROFIBROSARCOMA	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS		1 (2%)	
FIBROMA	1 (2%)	1 (2%)	3 (6%)
FIBROSARCOMA	1 (2%)	2 (4%)	
LIPOMA		1 (2%)	
NEUROFIBROMA	3 (6%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR ADENOMA		4 (8%)	1 (2%)
PHEOCHROMOCYTOMA, METASTATIC	1 (2%)		
FIBROSARCOMA, METASTATIC	1 (2%)		
OSTEOSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
LEUKEMIA,NOS	2 (4%)		1 (2%)
UNDIFFERENTIATED LEUKEMIA	10 (20%)	3 (6%)	4 (8%)
#SPLEEN	(50)	(50)	(50)
UNDIFFERENTIATED LEUKEMIA	2 (4%)	1 (2%)	
CIRCULATORY SYSTEM			
NONE			

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(47)	(49)
FIBROSARCOMA		1 (2%)	
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	1 (2%)	9 (18%)	8 (16%)
HEPATOCELLULAR CARCINOMA		1 (2%)	2 (4%)
#STOMACH	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
#DUODENUM	(49)	(50)	(50)
ADENOCARCINOMA, NOS			1 (2%)
#COLON	(50)	(50)	(50)
ADENOCARCINOMA, NOS			1 (2%)
ADENOMATOUS POLYP, NOS			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
TRANSITIONAL-CELL CARCINOMA			1 (2%)
#URINARY BLADDER	(48)	(48)	(49)
TRANSITIONAL-CELL PAPILLOMA			1 (2%)
TRANSITIONAL-CELL CARCINOMA			7 (14%)
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(47)	(47)
CHROMOPHOBE ADENOMA	3 (6%)	6 (13%)	5 (11%)
#ADRENAL	(50)	(50)	(49)
CORTICAL ADENOMA			1 (2%)
PHEOCHROMOCYTOMA	9 (18%)	12 (24%)	13 (27%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)		
#THYROID	(42)	(43)	(42)
C-CELL ADENOMA	6 (14%)	1 (2%)	1 (2%)
C-CELL CARCINOMA			2 (5%)
#PANCREATIC ISLETS	(50)	(46)	(50)
ISLET-CELL ADENOMA		1 (2%)	1 (2%)

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS		1 (2%)	
FIBROADENOMA		5 (10%)	2 (4%)
*PREPUCE	(50)	(50)	(50)
SEBACEOUS ADENOCARCINOMA	1 (2%)		
*PREPUTIAL GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
ADENOMA, NOS	1 (2%)	1 (2%)	
SEBACEOUS ADENOCARCINOMA	1 (2%)		
#TESTIS	(50)	(50)	(50)
INTERSTITIAL-CELL TUMOR	45 (90%)	43 (86%)	40 (80%)
NERVOUS SYSTEM			
#CEREBRUM	(50)	(49)	(49)
OLIGODENDROGLIOMA		1 (2%)	
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MEDIASTINUM	(50)	(50)	(50)
LIPOMA		1 (2%)	
*ABDOMINAL CAVITY	(50)	(50)	(50)
MESOTHELIOMA, MALIGNANT		1 (2%)	
*PERITONEUM	(50)	(50)	(50)
MESOTHELIOMA, NOS		2 (4%)	

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)		1 (2%)
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
MESOTHELIOMA, METASTATIC		1 (2%)	
LEG			
OSTEOSARCOMA		1	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	6	13
MORIBUND SACRIFICE	6	7	7
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	39	37	30
ANIMAL MISSING			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	49	48	42
TOTAL PRIMARY TUMORS	94	105	98
TOTAL ANIMALS WITH BENIGN TUMORS	48	43	41
TOTAL BENIGN TUMORS	71	78	70
TOTAL ANIMALS WITH MALIGNANT TUMORS	18	14	17
TOTAL MALIGNANT TUMORS	21	16	19
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	2	
TOTAL SECONDARY TUMORS	2	2	
TOTAL ANIMALS WITH TUMORS UNCERTAIN- BENIGN OR MALIGNANT	2	10	9
TOTAL UNCERTAIN TUMORS	2	11	9
TOTAL ANIMALS WITH TUMORS UNCERTAIN- PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED 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%)		2 (4%)
SQUAMOUS CELL CARCINOMA	1 (2%)		
BASAL-CELL TUMOR			1 (2%)
TRICHOEPITHELIOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
NEUROFIBROMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(49)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
LEUKEMIA,NOS		2 (4%)	
UNDIFFERENTIATED LEUKEMIA	11 (22%)	11 (22%)	6 (12%)
#SPLEEN	(50)	(49)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
UNDIFFERENTIATED LEUKEMIA		1 (2%)	
#LYMPH NODE	(50)	(50)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
#MESENTERIC L. NODE	(50)	(50)	(49)
OSTEOSARCOMA, METASTATIC			1 (2%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#THYMUS	(43)	(39)	(36)
THYMOMA	1 (2%)		
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(49)	(49)
ADENOMA, NOS		1 (2%)	
#PAROTID DUCT	(50)	(49)	(49)
ADENOMA, NOS	1 (2%)		
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	4 (8%)	5 (10%)	6 (12%)
HEPATOCELLULAR CARCINOMA	2 (4%)		
#STOMACH	(50)	(50)	(48)
SQUAMOUS CELL CARCINOMA	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(49)	(50)	(50)
TRANSITIONAL-CELL CARCINOMA			2 (4%)
#URINARY BLADDER	(49)	(47)	(48)
TRANSITIONAL-CELL PAPILLOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)	1 (2%)	
CHROMOPHOBE ADENOMA	21 (42%)	19 (38%)	18 (37%)
CHROMOPHOBE CARCINOMA		1 (2%)	
#ADRENAL	(48)	(50)	(49)
CORTICAL ADENOMA		1 (2%)	
PHEOCHROMOCYTOMA	3 (6%)	2 (4%)	2 (4%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#THYROID	(45)	(45)	(45)
C-CELL ADENOMA	3 (7%)	2 (4%)	3 (7%)
C-CELL CARCINOMA	1 (2%)		
#PANCREATIC ISLETS	(50)	(50)	(50)
ISLET-CELL ADENOMA			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
ADENOMA, NOS		1 (2%)	
PAPILLARY ADENOMA		1 (2%)	
FIBROADENOMA	11 (22%)	10 (20%)	11 (22%)
*PREPUTIAL GLAND	(50)	(50)	(50)
SEBACEOUS ADENOCARCINOMA		1 (2%)	
*VULVA	(50)	(50)	(50)
PAPILLOMA, NOS			1 (2%)
*CLITORAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)		
SQUAMOUS CELL CARCINOMA			1 (2%)
ADENOMA, NOS	1 (2%)		
SEBACEOUS ADENOCARCINOMA		1 (2%)	
#UTERUS	(50)	(48)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
SARCOMA, NOS		1 (2%)	
LEIOMYOSARCOMA		1 (2%)	
ENDOMETRIAL STROMAL POLYP	15 (30%)	12 (25%)	10 (20%)
#OVARY	(50)	(50)	(50)
GRANULOSA-CELL TUMOR	1 (2%)		
OSTEOSARCOMA		1 (2%)	
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(49)	(50)
MENINGIOMA			1 (2%)
SPECIAL SENSE ORGANS			
NONE			

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
LIPOMA	1 (2%)		
ALL OTHER SYSTEMS			
LEG			
OSTEOSARCOMA			1
SOLE OF FOOT			
SQUAMOUS CELL CARCINOMA		1	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	4	5	3
MORIBUND SACRIFICE	8	13	5
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	38	32	42
ANIMAL MISSING			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	46	47	37
TOTAL PRIMARY TUMORS	86	80	67
TOTAL ANIMALS WITH BENIGN TUMORS	38	38	31
TOTAL BENIGN TUMORS	60	53	51
TOTAL ANIMALS WITH MALIGNANT TUMORS	17	20	9
TOTAL MALIGNANT TUMORS	21	22	10
TOTAL ANIMALS WITH SECONDARY TUMORS#	1		1
TOTAL SECONDARY TUMORS	1		1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	4	5	6
TOTAL UNCERTAIN TUMORS	5	5	6
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

CONTROL

ANIMAL NUMBER	0011	0023	0031	0045	0046	0047	0048	0049	0050	0051	0052	0053	0054	0055	0056	0057	0058	0059	0060	0061	0062	0063	0064	0065
WEEKS ON STUDY	109	088	109	078	109	109	109	099	109	078	109	109	167	159	169	084	109	109	109	109	109	109	469	109
INTEGUMENTARY SYSTEM																								
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																	X							
SQUAMOUS CELL CARCINOMA																								
TRICHOEPITHELIOMA												X												
NEUROFIBROSARCOMA																								
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA													X											
FIBROSARCOMA													X											
NEUROFIBROMA															X									
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA, METASTATIC																							X	
FIBROSARCOMA, METASTATIC													X											
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
UNDIFFERENTIATED LEUKEMIA																								
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	-	+
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE																								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
CHROMOPHOBE ADENOMA																X						X		
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA		X	X	X	X								X				X	X						
PHEOCHROMOCYTOMA, MALIGNANT																							X	
THYROID	-	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	-	+	+	-
C-CELL ADENOMA																								
PARATHYROID	-	+	+	+	-	+	+	+	+	+	-	-	-	+	+	+	-	+	+	-	+	+	-	+
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X		X		X	X	X	X	X	X	X	X	X	X	X			X	X	X		X	X	X
PROSTATE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PENIS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SEBACEOUS ADENOCARCINOMA									X															
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																			X					
ADENOMA, NOS																								
SEBACEOUS ADENOCARCINOMA																								
BODY CAVITIES																								
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																								
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA, NOS																							X	
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) 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	109	109	101	094	109	087	109	109	109	109	109	109	109	109	109	109	109	109	109	102	109	109	109	109	109	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
PAPILLOMA, NOS																	X									2
SQUAMOUS CELL CARCINOMA																			X							1
TRICHOEPITHELIOMA																										1
NEUROFIBROSARCOMA																								X		1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
FIBROMA																										1
FIBROSARCOMA																										1
NEUROFIBROMA					X						X															3
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA, METASTATIC																										1
FIBROSARCOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
UNDIFFERENTIATED LEUKEMIA					X				X																	2
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	42
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
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	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CHROMOPHOBE ADENOMA												X														3
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA				X		X																				9
PHEOCHROMOCYTOMA, MALIGNANT																										1
THYROID	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	42
C-CELL ADENOMA					X			X							X			X			X				X	6
PARATHYROID	+	-	+	+	+	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	36
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
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	X	45
PROSTATE	+	+	+	+	+	-	+	-	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	45
PENIS	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*
SEBACEOUS ADENOCARCINOMA																										1
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*
SQUAMOUS CELL CARCINOMA																										1
ADENOMA, NOS							X																			1
SEBACEOUS ADENOCARCINOMA																				X						1
BODY CAVITIES																										
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
MESOTHELIOMA, 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*
LEUKEMIA,NOS																	X									2
UNDIFFERENTIATED LEUKEMIA			X					X								X		X		X					X	10

\+ 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

* ANIMALS NECROPSIED

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

LOW DOSE

ANIMAL NUMBER	0001	0002	0003	0004	0005	0006	0007	0008	0009	0010	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0021	0022	0023	0024	0025
WEEKS ON STUDY	077	067	011	091	099	099	099	099	099	091	060	099	099	099	099	090	099	099	099	099	116	099	269	099	099
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																									
SQUAMOUS CELL CARCINOMA					X																				X
TRICHOEPITHELIOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA NOS																						X			
FIBROMA															X										
FIBROSARCOMA																									
LIPOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA													X												
OSTEOSARCOMA, METASTATIC																X									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
UNDIFFERENTIATED LEUKEMIA																				X					
LYMPH NODES	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	-	-	-	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	-	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA			X																						
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE								X		X										X		X			
HEPATOCELLULAR CARCINOMA																X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	-	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA					X																				
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+
CHROMOPHOBE ADENOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA									X	X			X							X			X		
THYROID	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA				X																					
PARATHYROID	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	-	+	+
PANCREATIC ISLETS	+	-	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+
ADENOCARCINOMA, NOS																									
FIBROADENOMA					X																			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
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
ADENOMA, NOS																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
OLIGODENDROGLIOMA																									
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
SQUAMOUS CELL CARCINOMA																									
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
LIPOMA																									
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
MESOTHELIOMA, NOS					X																				
MESOTHELIOMA, MALIGNANT											X														
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MESOTHELIOMA, METASTATIC											X														
UNDIFFERENTIATED LEUKEMIA						X																			
LEG NOS																									
OSTEOSARCOMA																X									

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

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

ANIMAL NUMBER	0246	0247	0248	0249	0330	0311	0312	0335	0341	0355	0356	0357	0358	0359	0400	0401	0402	0403	0404	0405	0406	0407	0408	0409	0500	TOTAL
WEEKS ON STUDY	1109	1009	0211	1009	0091	1001	1009	0955	1009	1004	1109	0651	1009	1009	0708	1009	1009	1009	1009	0955	1009	1009	1009	1009	1009	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
PAPILLOMA, NOS																							X			1
SQUAMOUS CELL CARCINOMA																										1
TRICHOEPITHELIOMA																										1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
SARCOMA, NOS																										1
FIBROMA																										1
FIBROSARCOMA								X												X						2
LIPOMA	X																									1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA								X					X			X										4
OSTEOSARCOMA, METASTATIC																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
UNDIFFERENTIATED LEUKEMIA																										1
LYMPH NODES	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYMUS	+	+	-	+	+	+	+	-	+	+	+	-	+	+	-	+	+	+	+	+	-	-	+	+	+	38
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	47
FIBROSARCOMA																										1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE	X									X						X								X		9
HEPATOCELLULAR CARCINOMA																									X	1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																										1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
CHROMOPHOBE ADENOMA				X		X	X	X			X											X				6
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA	X			X					X	X	X									X				X		12
THYROID	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	-	+	+	+	-	+	+	43
C-CELL ADENOMA																										1
PARATHYROID	+	-	+	+	+	+	+	-	+	-	-	-	+	+	+	-	+	+	-	+	+	+	-	+	+	36
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ISLET-CELL ADENOMA									X																	1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	50*
ADENOCARCINOMA, NOS									X																	1
FIBROADENOMA							X			X						X										5
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	43
PROSTATE	+	+	+	+	+	-	+	-	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	39
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
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
OLIGODENDROGLIOMA															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	50*
SQUAMOUS CELL CARCINOMA												X														1
BODY CAVITIES																										
MEDIASTINUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N	50*
LIPOMA																										1
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MESOTHELIOMA, NOS	X																									2
MESOTHELIOMA, MALIGNANT																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MESOTHELIOMA, METASTATIC																										1
UNDIFFERENTIATED LEUKEMIA			X																	X						3
LEG NOS																										1
OSTEOSARCOMA																										

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

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

* ANIMALS NECROPSIED

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

HIGH DOSE

ANIMAL NUMBER	0011	0023	0034	0045	0056	0067	0078	0089	0090	0110	0121	0132	0143	0154	0165	0176	0187	0198	0202	0213	0224	0235	0246	0255
WEEKS ON STUDY	109	109	091	071	102	108	091	105	094	109	091	091	084	109	109	109	087	109	092	091	101	091	091	072
INTEGUMENTARY SYSTEM																								
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SEBACEOUS ADENOMA																				X				
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																			X					
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA					X																			
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	–	+	+	+	–	–	+	–	+	–	+	+	+	+	+	–	+	–	+	+	–
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE						X					X					X			X					
HEPATOCELLULAR CARCINOMA																				X				
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																								
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																								
ADENOMATOUS POLYP, NOS																								
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL CARCINOMA														X										
URINARY BLADDER	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL PAPILLOMA			X																					
TRANSITIONAL-CELL CARCINOMA		X		X		X											X			X		X		
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CHROMOPHOBE ADENOMA									X															
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																					X			
PHEOCHROMOCYTOMA						X				X		X			X	X	X					X		
THYROID	+	–	+	+	–	+	+	–	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	–
C-CELL ADENOMA	X																							
C-CELL CARCINOMA													X											
PARATHYROID	–	–	–	+	–	+	–	+	–	–	+	+	–	+	+	+	+	+	–	+	+	–	–	–
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA													X											
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA																								
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PROSTATE	+	+	+	+	+	+	+	–	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
BODY CAVITIES																								
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MESOTHELIOMA, NOS																								
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LEUKEMIA,NOS													X											
UNDIFFERENTIATED LEUKEMIA								X	X									X					X	

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

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	098	109	109	109	109	107	109	109	109	109	109	109	022	022	022	109	109	022	022	231	091	109	109	109	109	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50✱
SEBACEOUS ADENOMA																									1	1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50✱
FIBROMA			X				X																			3
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	+	+	+	+	-	+	-	+	+	+	-	+	-	-	-	+	+	-	-	-	+	+	+	+	+	33
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE					X					X						X					X					8
HEPATOCELLULAR CARCINOMA	X																									2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	50✱
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	48
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS								X																		1
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS																	X									1
ADENOMATOUS POLYP, NOS																									X	1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRANSITIONAL-CELL CARCINOMA																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRANSITIONAL-CELL PAPILLOMA																										1
TRANSITIONAL-CELL CARCINOMA			X																							7
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
CHROMOPHOBE ADENOMA				X								X				X							X			5
ADRENAL	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA					X				X							X	X				X		X			13
THYROID	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	42
C-CELL ADENOMA																										1
C-CELL CARCINOMA																							X			2
PARATHYROID	+	+	+	+	+	+	+	+	-	+	-	-	-	-	+	+	-	+	+	+	+	-	+	-	+	30
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	N	N	N	+	+	N	N	N	+	+	+	+	+	50✱
FIBROADENOMA			X					X																		2
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X		X	X	X		X				X	X				X	X	X	X	X	40
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	-	+	+	+	44
BODY CAVITIES																										
TUNICA VAGINALIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50✱
MESOTHELIOMA, 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✱
LEUKEMIA,NOS																										1
UNDIFFERENTIATED LEUKEMIA																										4

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

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

✱ ANIMALS NECROPSIED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

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	109	109	109	109	102	109	090	109	091	109	109	083	109	109	109	091	109	109	031	091	109	091	109	091	109
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																									
SQUAMOUS CELL CARCINOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																	X								
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS								X																	
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
THYMUS	+	+	+	+	+	+	-	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+
THYMOMA																									
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS			X																						
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE	X									X											X				
HEPATOCELLULAR CARCINOMA																	X				X				
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS											X														
CHROMOPHOBE ADENOMA		X							X				X				X	X		X	X			X	X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
C-CELL ADENOMA	X													X											
C-CELL CARCINOMA																			X						
PARATHYROID	+	+	+	-	+	+	-	+	-	-	-	+	+	-	+	+	+	-	-	+	-	-	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA																									
FIBROADENOMA						X						X					X						X		
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS																									
ADENOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS									X																
ENDOMETRIAL STROMAL POLYP			X	X		X	X		X		X		X									X			
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR										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	N	N	N
LIPOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
UNDIFFERENTIATED LEUKEMIA					X											X			X		X	X			

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

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

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

ANIMAL NUMBER	0264	0279	0289	0299	0301	0311	0321	0331	0341	0351	0361	0371	0381	0391	0401	0411	0422	0433	0441	0455	0466	0477	0488	0499	0500	TOTAL
WEEKS ON STUDY	1009	1079	1109	1109	1102	1104	1089	1109	1109	1109	1089	1109	1109	1109	1102	1109	1109	0977	1109	1109	1062	1089	0977	1101	1109	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
PAPILLOMA, NOS							X																			1
SQUAMOUS CELL CARCINOMA																							X			1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																										1
ALVEOLAR/BRONCHIOLAR ADENOMA					X																					1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIGNANT LYMPHOMA, NOS																										1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIGNANT LYMPHOMA, NOS									X																	1
THYMUS	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	-	+	+	43
THYMOMA													X													1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																										1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE							X																			4
HEPATOCELLULAR CARCINOMA																										2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA																								X		1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+		49
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+		49
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																										1
CHROMOPHOBE ADENOMA	X		X		X				X	X	X					X	X	X	X	X		X				21
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	48
PHEOCHROMOCYTOMA						X								X										X		3
THYROID	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	45
C-CELL ADENOMA					X																					3
C-CELL CARCINOMA																										1
PARATHYROID	+	-	-	+	+	+	+	+	+	+	+	-	+	+	+	-	+	-	-	+	-	-	+	+		29
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+		50*
SQUAMOUS CELL CARCINOMA											X															1
FIBROADENOMA	X			X			X	X			X								X			X				11
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		50*
CARCINOMA,NOS									X																	1
ADENOMA, NOS																			X							1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
ADENOCARCINOMA, NOS																										1
ENDOMETRIAL STROMAL POLYP	X						X	X		X		X		X						X						15
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
GRANULOSA-CELL TUMOR																										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		50*
LIPOMA			X																							1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N		50*
UNDIFFERENTIATED LEUKEMIA		X				X				X						X					X		X			11

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

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

* ANIMALS NECROPSIED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

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	109	109	107	011	079	056	091	091	102	091	091	091	091	088	091	086	069	091	091	091	066	098	091	092	109
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
TRICHOEPITHELIOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
NEUROFIBROMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
UNDIFFERENTIATED LEUKEMIA																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	−	−	+	+	+	+	+	+	−	−	+	−	−	−	−	+	−	+	+	−	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
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	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS																									
CHROMOPHOBE ADENOMA			X	X					X		X	X			X			X		X		X		X	X
CHROMOPHOBE CARCINOMA																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA									X																
PHEOCHROMOCYTOMA								X					X												
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA																							X		
PARATHYROID	−	−	−	+	−	−	−	+	−	+	−	+	−	+	+	+	+	+	+	+	+	−	−	−	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+
ADENOMA, NOS								X																	
PAPILLARY ADENOMA																									
FIBROADENOMA							X					X										X			
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SEBACEOUS ADENOCARCINOMA					X																				
UTERUS	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS														X											
LEIOMYOSARCOMA																									
ENDOMETRIAL STROMAL POLYP		X			X		X			X	X						X								X
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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
MALIGNANT LYMPHOMA, NOS																									
LEUKEMIA,NOS			X	X																					
UNDIFFERENTIATED LEUKEMIA	X	X												X	X		X	X	X			X			
SOLE OF FOOT																			X						
SQUAMOUS CELL CARCINOMA																									

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

C NO TISSUE INFORMATION SUBMITTED
A NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
M AUTOLYSIS
B ANIMAL MISSING
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	109	108	87	109	109	106	109	109	109	109	109	109	108	109	109	103	109	109	109	109	109	109	109	109	109	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
TRICHOEPITHELIOMA							X																			1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
NEUROFIBROMA								X																		1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																				X						1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
UNDIFFERENTIATED LEUKEMIA				X																						1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS				X																						1
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	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS														X												1
CHROMOPHOBE ADENOMA		X	X					X				X				X		X					X		X	19
CHROMOPHOBE CARCINOMA						X																				1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA																										2
THYROID	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	-	+	+	+	+	-	+	45
C-CELL ADENOMA												X														2
PARATHYROID	+	-	+	+	+	-	+	+	+	+	-	+	+	-	-	+	+	-	-	+	+	-	+	-	+	29
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
ADENOMA, NOS																										1
PAPILLARY ADENOMA		X																								1
FIBROADENOMA											X	X						X		X	X			X		X	10
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*
SEBACEOUS ADENOCARCINOMA	X																									2
UTERUS	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SARCOMA, NOS																										1
LEIOMYOSARCOMA																		X								1
ENDOMETRIAL STROMAL POLYP	X							X				X				X								X		12
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
OSTEOSARCOMA																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, NOS	X																									1
LEUKEMIA, NOS																										2
UNDIFFERENTIATED LEUKEMIA								X				X									X					11
SOLE OF FOOT																										
SQUAMOUS CELL CARCINOMA																										1

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

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

* ANIMALS NECROPSIED

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

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	109	091	091	091	091	091	091	091	088	091	091	078	091	091	095	091	091	091	091	091	091	053	091	091	097
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																							X		
BASAL-CELL TUMOR																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
OSTEOSARCOMA, METASTATIC							X																		
THYMUS	+	-	+	-	+	-	-	+	+	+	+	-	+	-	-	+	+	+	+	+	+	-	+	+	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE					X			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	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL CARCINOMA																									X
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL PAPILLOMA		X																							
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
CHROMOPHOBE ADENOMA			X						X					X								X		X	X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA								X																	
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
C-CELL ADENOMA		X	X							X															
PARATHYROID	+	-	+	+	-	+	+	-	+	-	+	+	+	-	-	+	+	-	+	-	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA								X																	
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA										X															X
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA																									
FEMALE EXTERNAL GENITALIA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLOMA, NOS																					X				
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP			X															X		X	X				
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MENINGIOMA																						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
UNDIFFERENTIATED LEUKEMIA	X	X										X													X
LEG NOS																									
OSTEOSARCOMA							X																		

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

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

ANIMAL NUMBER	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	0 8 8	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 5	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	1 0 9	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
PAPILLOMA, NOS																			X							2
BASAL-CELL TUMOR																								X		1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
TRACHEA	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	48
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
OSTEOSARCOMA, METASTATIC																										1
THYMUS	+	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	–	+	–	–	+	+	+	+	36
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE										X								X								6
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
ESOPHAGUS	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	50
TRANSITIONAL-CELL CARCINOMA																										2
URINARY BLADDER	+	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
TRANSITIONAL-CELL PAPILLOMA																										1
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CHROMOPHOBE ADENOMA			X				X		X	X	X		X		X			X			X	X	X	X		18
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PHEOCHROMOCYTOMA				X																						2
THYROID	+	+	+	+	–	+	+	+	+	–	–	+	+	+	+	+	+	+	+	–	+	+	+	+	45
C-CELL ADENOMA																										3
PARATHYROID	–	+	+	+	–	–	+	+	–	+	–	–	+	+	–	+	+	+	+	–	–	–	+	+	+	32
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
FIBROADENOMA	X		X				X			X	X	X	X					X					X			11
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SQUAMOUS CELL CARCINOMA																								X		1
FEMALE EXTERNAL GENITALIA	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*
PAPILLOMA, NOS																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP						X			X	X	X				X					X						10
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MENINGIOMA																										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										6
LEG NOS																										
OSTEOSARCOMA																										1

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

* ANIMALS NECROPSIED

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 FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
NONE			
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(46)
HEPATOCELLULAR CARCINOMA, METAST	3 (6%)	2 (4%)	1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	10 (20%)	3 (6%)	4 (9%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	2 (4%)	6 (12%)	4 (8%)
#SPLEEN	(50)	(47)	(47)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#LYMPH NODE	(33)	(43)	(32)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#THYMUS	(24)	(25)	(17)
MALIGNANT LYMPHOMA, NOS		1 (4%)	
CIRCULATORY SYSTEM			
*SKIN	(50)	(50)	(50)
HEMANGIOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
HEMANGIOMA	1 (2%)		
#SPLEEN	(50)	(47)	(47)
HEMANGIOSARCOMA		3 (6%)	

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#HEART	(50)	(50)	(49)
HEMANGIOSARCOMA	1 (2%)		
#LIVER	(50)	(50)	(49)
HEMANGIOSARCOMA	1 (2%)	1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(49)
HEPATOCELLULAR ADENOMA	1 (2%)	3 (6%)	3 (6%)
HEPATOCELLULAR CARCINOMA	16 (32%)	16 (32%)	9 (18%)
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#ADRENAL	(44)	(48)	(42)
CORTICAL ADENOMA	1 (2%)		
PHEOCHROMOCYTOMA	1 (2%)		
#THYROID	(47)	(42)	(36)
FOLLICULAR-CELL ADENOMA	1 (2%)	1 (2%)	1 (3%)
REPRODUCTIVE SYSTEM			
#TESTIS	(49)	(50)	(47)
INTERSTITIAL-CELL TUMOR		1 (2%)	1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	7	12	28
MORIBUND SACRIFICE	5	4	4
SCHEDULED SACRIFICE	1		
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	37	34	18
ANIMAL MISSING			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	30	29	18
TOTAL PRIMARY TUMORS	36	39	22
TOTAL ANIMALS WITH BENIGN TUMORS	15	8	9
TOTAL BENIGN TUMORS	16	10	9
TOTAL ANIMALS WITH MALIGNANT TUMORS	19	25	12
TOTAL MALIGNANT TUMORS	20	29	13
TOTAL ANIMALS WITH SECONDARY TUMORS#	3	2	1
TOTAL SECONDARY TUMORS	3	2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING		1	1
ANIMALS NECROPSIED	50	49	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(49)
PAPILLOMA, NOS	1 (2%)		
NEUROFIBROSARCOMA	1 (2%)		
*SUBCUT TISSUE	(50)	(49)	(49)
OSTEOSARCOMA		1 (2%)	
NEUROFIBROSARCOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(49)	(49)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	3 (6%)	3 (6%)
OSTEOSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(49)
MALIGNANT LYMPHOMA, NOS	7 (14%)	10 (20%)	9 (18%)
#SPLEEN	(50)	(49)	(47)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
#SMALL INTESTINE	(49)	(49)	(47)
MALIGNANT LYMPHOMA, NOS			1 (2%)
#KIDNEY	(50)	(49)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
CIRCULATORY SYSTEM			
*SUBCUT TISSUE	(50)	(49)	(49)
HEMANGIOMA			1 (2%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#SPLEEN	(50)	(49)	(47)
HEMANGIOSARCOMA	2 (4%)		
#OVARY	(46)	(46)	(45)
HEMANGIOMA		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(49)
HEPATOCELLULAR ADENOMA	2 (4%)	1 (2%)	1 (2%)
HEPATOCELLULAR CARCINOMA	5 (10%)	7 (14%)	4 (8%)
OSTEOSARCOMA, METASTATIC		1 (2%)	
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(42)	(39)	(41)
ADENOMA, NOS	3 (7%)	5 (13%)	2 (5%)
#ADRENAL	(47)	(46)	(48)
CORTICAL ADENOMA		1 (2%)	
PHEOCHROMOCYTOMA		1 (2%)	1 (2%)
#THYROID	(37)	(41)	(40)
FOLLICULAR-CELL ADENOMA	1 (3%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(49)	(49)
ADENOCARCINOMA, NOS	6 (12%)	1 (2%)	2 (4%)
*VULVA	(50)	(49)	(49)
PAPILLOMA, NOS	1 (2%)		
#UTERUS	(48)	(49)	(49)
ADENOCARCINOMA, NOS	1 (2%)		
#OVARY/OVIDUCT	(48)	(49)	(49)
PAPILLARY ADENOMA			1 (2%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#OVARY	(46)	(46)	(45)
TERATOMA, BENIGN			1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(49)	(49)
ADENOMA, NOS		2 (4%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	4	8	19
MORIBUND SACRIFICE	4	4	5
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	42	37	25
ANIMAL MISSING		1	1
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	28	27	19
TOTAL PRIMARY TUMORS	34	34	26
TOTAL ANIMALS WITH BENIGN TUMORS	10	13	9
TOTAL BENIGN TUMORS	10	14	10
TOTAL ANIMALS WITH MALIGNANT TUMORS	21	20	13
TOTAL MALIGNANT TUMORS	24	20	16
TOTAL ANIMALS WITH SECONDARY TUMORS#		1	
TOTAL SECONDARY TUMORS		2	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

CONTROL

ANIMAL NUMBER	001	002	003	004	005	006	007	008	009	011	011	012	013	014	015	016	017	018	019	022	022	023	024	025
WEEKS ON STUDY	109	109	109	109	091	099	109	041	072	045	099	099	099	099	099	099	089	099	099	099	090	099	000	099
INTEGUMENTARY SYSTEM																								
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N
HEMANGIOMA																								
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA		X	X																					
ALVEOLAR/BRONCHIOLAR ADENOMA			X			X										X						X		
TRACHEA	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	-	-	+	-	+	-	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-
THYMUS	+	-	-	+	-	+	+	+	-	-	-	+	+	-	-	+	+	+	+	+	-	-	+	-	+
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA					X																			
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																								
HEPATOCELLULAR CARCINOMA		X	X													X	X	X				X	X	
HEMANGIOSARCOMA																								
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
STOMACH	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																								
PITUITARY	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	-	+	+
ADRENAL	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-
CORTICAL ADENOMA	X																							+
PHEOCHROMOCYTOMA										X														
THYROID	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
FOLLICULAR-CELL ADENOMA																								
PARATHYROID	+	-	+	-	-	+	+	-	-	-	-	-	-	-	+	-	-	-	-	-	+	-	-	-
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
SPECIAL SENSE ORGANS																								
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	X	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
MALIGNANT LYMPHOMA, 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) CONTROL

ANIMAL NUMBER	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	TOTAL TISSUES TUMORS
WEEKS ON STUDY	1 0 9	1 0 1 1	1 0 7 4	1 0 9 1	1 0 9 1	1 0 9 1	1 0 8 4	1 0 9 1	1 0 9 1	1 0 5 1	1 0 9 1	1 0 9 1	1 0 7 9	1 0 9 1	1 0 8 5	1 0 0 1	1 0 9 1	1 0 8 6	1 0 9 1	1 0 9 1	1 0 9 1	1 0 9 1	1 0 9 1	1 0 9 1	1 0 9 1	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOMA				X																						1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																			X							3
ALVEOLAR/BRONCHIOLAR ADENOMA								X						X		X					X		X		X	10
TRACHEA	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	45
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	47
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	−	−	+	+	−	+	−	+	+	−	+	−	−	+	+	+	−	+	−	−	+	+	+	+	33
THYMUS	−	−	−	−	+	−	+	−	+	−	+	−	−	−	−	−	+	−	+	+	−	+	+	+	−	24
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA																										1
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA																X										1
HEPATOCELLULAR CARCINOMA		X		X		X	X			X		X			X			X						X		16
HEMANGIOSARCOMA									X																	1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	50
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
STOMACH	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	−	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	46
LARGE INTESTINE	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+		42
ADRENAL	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	−	+	+	+	+	+	+	+	−	44
CORTICAL ADENOMA																										1
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	47
FOLLICULAR-CELL ADENOMA	X																									1
PARATHYROID	−	−	−	−	−	+	+	−	−	+	+	−	+	+	−	−	+	−	+	+	−	−	+	+	−	17
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	50
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
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
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50
MALIGNANT LYMPHOMA, NOS															X		X									2

+: 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

* ANIMALS NECROPSIED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

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	043	101	109	109	091	075	109	109	091	091	091	091	091	109	091	091	091	091	091	091	057	091	091	091	109
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+
HEMANGIOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									
ALVEOLAR/BRONCHIOLAR ADENOMA								X						X											
TRACHEA	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
HEMANGIOSARCOMA						X		X			X														
MALIGNANT LYMPHOMA, NOS													X												
LYMPH NODES	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
THYMUS	-	-	+	+	-	+	+	+	+	+	-	+	+	+	+	+	-	+	-	-	-	+	-	+	+
MALIGNANT LYMPHOMA, NOS																									
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA											X								X						
HEPATOCELLULAR CARCINOMA				X	X			X								X		X	X			X			
HEMANGIOSARCOMA						X																			
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	+	+	+	N	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	+
ADRENAL	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
THYROID	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	-	+	+	+
FOLLICULAR-CELL ADENOMA																								X	
PARATHYROID	-	-	+	-	-	+	+	+	+	+	-	-	-	-	+	+	-	+	-	-	-	-	+	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR														X											
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS														X											
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS		X						X														X	X		

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	057	072	093	109	109	109	109	050	107	109	051	109	057	109	078	109	109	089	096	109	109	091	109	109	109	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
HEMANGIOMA																						X				1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																		X	X							2
ALVEOLAR/BRONCHIOLAR ADENOMA																X										3
TRACHEA	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	43
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	-	+	+	+	+	~	+	+	43
SPLEEN	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMANGIOSARCOMA																										3
MALIGNANT LYMPHOMA, NOS																										1
LYMPH NODES	-	+	+	+	+	-	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	43
MALIGNANT LYMPHOMA, NOS																	X									1
THYMUS	-	-	-	-	-	+	+	-	+	-	-	-	-	+	-	-	+	+	-	+	+	-	~	-	+	25
MALIGNANT LYMPHOMA, NOS						X																				1
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	-	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+		47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA																	X									3
HEPATOCELLULAR CARCINOMA				X			X					X		X	X			X	X		X			X		16
HEMANGIOSARCOMA																										1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	50*
PANCREAS	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	~	+	+	46
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	-	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	44
ENDOCRINE SYSTEM																										
PITUITARY	-	-	+	+	+	+	+	+	+	+	+	+	-	+	-	-	+	+	-	+	+	+	+	+	+	40
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYROID	-	+	-	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	42
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	-	-	-	-	-	+	+	-	+	-	-	-	+	+	-	-	+	-	-	+	-	-	~	+	-	18
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR																										1
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	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
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, NOS			X						X																	6

+: 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

* ANIMALS NECROPSIED

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

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	109	109	109	074	097	043	096	013	109	046	091	051	091	091	051	094	011	091	095	049	052	091	049	097	052
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	A	+
HEPATOCELLULAR CARCINOMA, METASTA																									
ALVEOLAR/BRONCHIOLAR ADENOMA									X																
TRACHEA	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	A	+
SPLEEN	+	+	+	A	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
LYMPH NODES	+	+	+	A	-	+	+	-	+	+	+	+	+	-	+	-	+	+	A	+	+	+	-	A	+
THYMUS	-	+	+	A	+	-	-	-	+	-	-	-	+	-	-	+	+	-	A	-	-	-	-	A	-
CIRCULATORY SYSTEM																									
HEART	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
LIVER	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA	X											X													
HEPATOCELLULAR CARCINOMA									X																
BILE DUCT	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	N	+	N	+	+	+	N	+	+
PANCREAS	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
ESOPHAGUS	+	+	+	A	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
SMALL INTESTINE	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
LARGE INTESTINE	-	+	-	A	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	A	-
URINARY SYSTEM																									
KIDNEY	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	A	-	+	-	+	+	+	+	-	+	+	+	+	-	+	+	-	+	-	-	A	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	A	+	+	+	+	+	+	-	+	+	-	+	+	-	+	+	+	-	-	-	A	-
ADRENAL	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	-	+	-	A	-
THYROID	+	+	+	A	+	-	-	+	+	+	+	+	+	+	+	-	+	+	A	+	+	+	+	A	-
FOLLICULAR-CELL ADENOMA														X											
PARATHYROID	-	-	-	A	-	-	+	+	+	-	-	-	+	+	-	-	+	+	A	-	-	-	+	A	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+
INTERSTITIAL-CELL TUMOR																									
PROSTATE	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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																									

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	109	065	011	052	073	016	015	079	024	088	109	091	049	011	109	091	091	013	091	091	076	109	109	059	079	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
HEPATOCELLULAR CARCINOMA, METASTA																									X	1
ALVEOLAR/BRONCHIOLAR ADENOMA	X											X			X											4
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	-	+	+	44
HEMATOPOIETIC SYSTEM																										
BONE MARROW	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	-	+	+	-	41
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	+	+	+	+	-	+	+	-	+	+	-	-	+	-	+	+	-	-	+	-	+	-	+	+	-	32
THYMUS	+	-	-	-	-	-	-	-	-	-	+	-	-	+	+	+	+	-	+	+	-	+	+	-	-	17
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA																				X						3
HEPATOCELLULAR CARCINOMA		X						X		X		X							X		X		X		X	9
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	+	N	N		50*
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	46
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	47
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	-	45
LARGE INTESTINE	-	+	+	+	-	+	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	+	-	37
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	39
ENDOCRINE SYSTEM																										
PITUITARY	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	38
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	42
THYROID	-	+	+	+	+	+	+	+	+	-	+	-	-	-	+	+	+	+	+	+	+	+	-	-	+	36
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	-	-	+	-	-	+	-	+	+	-	-	-	-	-	-	+	-	-	-	-	+	+	-	-	-	16
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
TESTIS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
INTERSTITIAL-CELL TUMOR																	X									1
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, NOS					X	X				X					X											4

\+ 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

* ANIMALS NECROPSIED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

CONTROL

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0020	0111	0112	0113	0114	0115	0116	0117	0118	0119	0120	0201	0202	0203	0204	0205
WEEKS ON STUDY	091	091	091	091	071	091	091	091	091	093	091	091	091	089	021	091	091	091	091	091	091	091	091	093	089
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLOMA, NOS																									
NEUROFIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																				X					
TRACHEA	-	+	+	+	+	+	+	-	+	+	-	+	+	+	-	+	-	+	+	+	+	+	+	+	-
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA									X																
MALIGNANT LYMPHOMA, NOS									X																
LYMPH NODES	+	-	-	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	-	+	-	+	+
THYMUS	-	+	-	+	-	+	+	-	+	+	-	-	+	-	+	+	-	+	-	+	+	+	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA				X																					
HEPATOCELLULAR CARCINOMA						X				X	X														
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	-	+	+	+	-	+	+	-	+	+	-	+	+	+	-	+	-	-	+	+	+	+	-	-	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, NOS																									
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	-	+	-	+	-	+	+	+	-	+	+	+	+	-	+	+	+	+	+	-	+	+
ADENOMA, NOS																								X	
ADRENAL	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
THYROID	-	+	+	+	+	-	+	-	+	-	-	+	+	+	+	+	-	+	+	+	+	+	+	+	-
FOLLICULAR-CELL ADENOMA																X									
PARATHYROID	-	+	-	-	+	-	+	-	-	-	-	+	+	-	-	+	-	+	-	+	-	-	-	+	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	N	N	+
ADENOCARCINOMA, NOS													X												X
FEMALE EXTERNAL GENITALIA	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PAPILLOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS				X																					
OVARY	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS														X						X		X	X		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) CONTROL

ANIMAL NUMBER	02 26	02 27	02 28	02 29	03 30	03 31	03 32	03 33	03 34	03 35	03 36	03 37	03 38	03 39	04 01	04 11	04 21	04 31	04 41	04 45	04 46	04 47	04 48	04 49	05 00	TOTAL
WEEKS ON STUDY	100 99	090 99	100 99	100 99	100 99	100 99	100 99	100 99	100 99	100 99	100 99	100 99	093 99	100 99	100 99	100 99	093 77	100 99	100 99	100 99	100 99	100 99	100 99	100 99	110 99	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+		50*
PAPILLOMA, NOS																					X					1
NEUROFIBROSARCOMA		X																								1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA												X														2
TRACHEA	+	+	+	+	-	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	39
HEMATOPOIETIC SYSTEM																										
BONE MARROW	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMANGIOSARCOMA																		X								2
MALIGNANT LYMPHOMA, NOS																										1
LYMPH NODES	+	-	-	-	-	+	+	+	+	+	-	+	+	+	+	+	+	+	-	-	+	-	+	+	+	35
THYMUS	+	+	+	+	+	+	-	-	-	-	+	+	-	-	+	+	-	+	+	+	+	-	+	-	-	30
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA																							X			2
HEPATOCELLULAR CARCINOMA																					X				X	5
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	-	+	+	-	+		+	+	+	+	-	+	+	+	+	+	+	-	+	-		35
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIGNANT LYMPHOMA, NOS						X																				1
URINARY BLADDER	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	42
ADENOMA, NOS									X											X						3
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
THYROID	+	-	+	+	-	+	+	-	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	37
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	-	-	+	-	-	+	-	-	-	-	-	+	-	+	-	+	-	-	+	-	-	+	-	-	-	16
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	50*
ADENOCARCINOMA, NOS				X								X						X					X			6
FEMALE EXTERNAL GENITALIA	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*
PAPILLOMA, NOS														X												1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	48
ADENOCARCINOMA, NOS																										1
OVARY	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+		46
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, NOS	X						X																			2

\+ 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

* ANIMALS NECROPSIED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

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	109	109	109	091	090	109	108	091	091	091	092	091	091	091	091	091	091	091	091	091	091	091	091	091	109
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+
OSTEOSARCOMA																									
NEUROFIBROSARCOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA						X													X						
OSTEOSARCOMA, METASTATIC																									
TRACHEA	+	+	+	+	-	+	-	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+
THYMUS	+	+	+	+	-	+	+	-	+	+	+	+	+	-	+	+	-	+	-	-	+	+	+	-	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																				X					
HEPATOCELLULAR CARCINOMA	X																X	X	X						
OSTEOSARCOMA, METASTATIC																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	N	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	-	+	-
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	-	-	+	+	+
ADENOMA, NOS	X							X				X		X											
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	-	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA																									
THYROID	+	+	+	+	-	+	-	+	+	+	-	+	+	-	+	+	+	-	+	+	+	-	+	+	
PARATHYROID	-	-	+	+	-	+	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+	+	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	N	+	+
ADENOCARCINOMA, NOS																				X					
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
OVARY	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOMA				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								X								X									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS				X			X				X			X						X				X	

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	049	050	TOTAL
WEEKS ON STUDY	109	109	050	109	100	109	109	091	101	064	109	078	109	109	085	057	061	109	041	041	109	091	109	109	109	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49*
OSTEOSARCOMA										X																1
NEUROFIBROSARCOMA																	X									1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA							X																			3
OSTEOSARCOMA, METASTATIC										X																1
TRACHEA	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	M	+	+	+	+	+	42
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	44
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
LYMPH NODES	–	+	+	+	–	–	+	+	+	+	+	–	–	+	+	+	+	+	–	M	+	–	+	+	+	38
THYMUS	+	–	–	–	–	+	–	+	+	+	+	–	+	+	+	–	–	+	–	M	+	+	+	+	–	32
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA																										1
HEPATOCELLULAR CARCINOMA					X			X							X											7
OSTEOSARCOMA, METASTATIC										X																1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	44
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	M	+	+	+	+	+	48
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	M	+	+	+	–	+	45
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	–	–	+	+	+	+	+	–	+	+	+	+	+	+	+	–	M	+	+	+	–	+	39
ADENOMA, NOS													X													5
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	46
CORTICAL ADENOMA	X																									1
PHEOCHROMOCYTOMA					X																					1
THYROID	+	–	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	M	+	+	+	+	+	41
PARATHYROID	–	–	–	–	+	–	–	–	–	–	–	–	+	+	–	+	+	–	+	M	–	–	+	–	+	15
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	+	+	+	+	+	N	+	+	N	+	+	+	+	N	N	N	+	N	M	+	N	+	+	+	49*
ADENOCARCINOMA, NOS																										1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	–	+	+	M	+	+	+	+	+	46
HEMANGIOMA																										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	M	N	N	N	N	N	49*
ADENOMA, NOS																										2
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	M	N	N	N	N	N	49*
MALIGNANT LYMPHOMA, NOS				X							X							X			X					10

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

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

* ANIMALS NECROPSIED

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE 2-YEAR STUDY OF 11-AMINOUNDECANOIC ACID

HIGH DOSE

ANIMAL NUMBER	0011	0012	0013	0014	0015	0016	0017	0018	0019	0110	0111	0112	0113	0114	0115	0116	0117	0118	0119	0120	0121	0122	0123	0124	0125
WEEKS ON STUDY	109	092	093	096	098	098	098	098	099	100	109	104	109	109	109	095	109	106	109	092	099	095	091	095	109
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE HEMANGIOMA	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA	+	+	M	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	M	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
SPLEEN	+	+	M	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	M	+	−	+	−	+	+	+	−	+	+	+	+	+	−	−	−	+	−	−	+	+	+
THYMUS	−	−	M	−	−	−	−	+	−	+	−	−	+	+	+	−	−	+	+	+	+	−	+	−	+
CIRCULATORY SYSTEM																									
HEART	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	M	+	+	−	+	+	+	+	+	+	+	+	+	−	−	+	−	+	+	−	−	+	+
LIVER HEPATOCELLULAR ADENOMA HEPATOCELLULAR CARCINOMA	+	+	M	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+ X	+ X	+	+	+	+	+
BILE DUCT	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	M	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	N	+	+
PANCREAS	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE MALIGNANT LYMPHOMA, NOS	+	+	M	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	−	+	+	−	+	+	+
LARGE INTESTINE	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS	+	+	M	+	+	−	+	+	+	+	+	+	+	+	−	+ X	+	+	−	+	+	−	+	+	+
ADRENAL PHEOCHROMOCYTOMA	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+
THYROID	+	+	M	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+
PARATHYROID	+	+	M	−	+	−	−	−	+	+	+	−	−	−	−	−	−	+	+	−	+	−	−	+	−
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND ADENOCARCINOMA, NOS	+	+	M	+	N	N	N	+	+	+	+	N	+	+	+ X	+	N	+	+ X	N	+	+	+	+	+
UTERUS PAPILLARY ADENOMA	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+
OVARY TERATOMA, BENIGN	+	+	M	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+ X	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS MALIGNANT LYMPHOMA, NOS	N X	N	M	N X	N	N	N	N X	N	N	N	N	N	N	N X	N X	N	N	N X	N	N	N	N	N	N

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

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

ANIMAL NUMBER	026	027	028	029	030	031	032	033	034	035	036	037	038	039	040	041	042	043	044	045	046	047	048	050	TOTAL
WEEKS ON STUDY	008	052	078	091	098	109	109	093	094	109	101	090	090	094	090	110	047	091	091	091	091	091	091	005	TISSUES TUMORS
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49*
HEMANGIOMA							X																		1
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA						X									X										3
TRACHEA	-	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	+	+	43
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	47
SPLEEN	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LYMPH NODES	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	38
THYMUS	-	-	+	-	-	-	-	-	+	+	+	-	+	-	+	-	+	+	-	+	-	+	+	-	22
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																									
SALIVARY GLAND	-	+	+	+	-	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	39
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA																									1
HEPATOCELLULAR CARCINOMA			X			X																			4
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	N	N	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	49*
PANCREAS	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
ESOPHAGUS	-	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	46
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
MALIGNANT LYMPHOMA, NOS																									1
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	46
ENDOCRINE SYSTEM																									
PITUITARY	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	41
ADENOMA NOS																	X								2
ADRENAL	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PHEOCHROMOCYTOMA																									1
THYROID	-	+	+	+	+	+	-	+	+	-	+	+	+	-	+	+	+	+	+	-	+	+	-	+	40
PARATHYROID	-	+	+	+	+	+	+	-	+	-	-	-	-	-	-	-	-	+	+	+	-	+	-	-	21
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	+	+	+	+	+	+	N	+	N	+	+	N	+	+	N	+	+	N	N	+	+	+	49*
ADENOCARCINOMA, NOS																									2
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PAPILLARY ADENOMA																									1
OVARY	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	45
TERATOMA, BENIGN																									
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	49*
MALIGNANT LYMPHOMA, NOS					X										X					X					5

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

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

* ANIMALS NECROPSIED

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED 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	1 (2%)	1 (2%)	2 (4%)
ABSCESS, NOS			1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
CUTANEOUS HORN	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
DEFORMITY, NOS			1 (2%)
EDEMA, NOS	1 (2%)		
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#LUNG	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
PNEUMONIA, ASPIRATION		2 (4%)	
ALVEOLAR MACROPHAGES		1 (2%)	
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)		
HEMATOPOIETIC SYSTEM			
#MANDIBULAR L. NODE	(50)	(48)	(49)
HYPERPLASIA, RETICULUM CELL		1 (2%)	
#COLON	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID	1 (2%)	2 (4%)	
#THYMUS	(42)	(38)	(33)
HYPERPLASIA, RETICULUM CELL			1 (3%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
#LUNG	(50)	(50)	(50)
PERIARTERITIS	1 (2%)		
#HEART/ATRIUM	(50)	(50)	(50)
THROMBOSIS, NOS	2 (4%)	3 (6%)	
#AURICULAR APPENDAGE	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, NOS			1 (2%)
INFLAMMATION, CHRONIC	2 (4%)		
FIBROSIS		1 (2%)	
*AORTA	(50)	(50)	(50)
MEDIAL CALCIFICATION			1 (2%)
*PULMONARY ARTERY	(50)	(50)	(50)
MEDIAL CALCIFICATION	14 (28%)	11 (22%)	13 (26%)
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS		2 (4%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
HERNIA, NOS		1 (2%)	
GRANULOMA, NOS	9 (18%)	15 (30%)	4 (8%)
NECROSIS, FOCAL	1 (2%)	1 (2%)	1 (2%)
METAMORPHOSIS FATTY	2 (4%)	1 (2%)	2 (4%)
CYTOPLASMIC VACUOLIZATION	1 (2%)	14 (28%)	5 (10%)
BASOPHILIC CYTO CHANGE		2 (4%)	4 (8%)
FOCAL CELLULAR CHANGE		2 (4%)	3 (6%)
EOSINOPHILIC CYTO CHANGE		4 (8%)	
CLEAR-CELL CHANGE	1 (2%)	4 (8%)	5 (10%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, NOS		1 (2%)	
#LIVER/HEPATOCYTES	(50)	(50)	(50)
NECROSIS, NOS			1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
#BILE DUCT	(50)	(50)	(50)
INFLAMMATION, FOCAL	1 (2%)		
HYPERPLASIA, NOS	4 (8%)		1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		
#PANCREAS	(50)	(46)	(50)
INFLAMMATION, NOS		1 (2%)	
ATROPHY, NOS	2 (4%)	2 (4%)	3 (6%)
ATROPHY, FOCAL	1 (2%)		
#STOMACH	(50)	(50)	(50)
INFLAMMATION, ACUTE			3 (6%)
HYPERPLASIA, EPITHELIAL			1 (2%)
HYPERKERATOSIS	1 (2%)		
#DUODENUM	(49)	(50)	(50)
POLYP		1 (2%)	
#COLON	(50)	(50)	(50)
NEMATODIASIS			2 (4%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
HYDRONEPHROSIS		1 (2%)	
NEPHROPATHY, TOXIC	1 (2%)		
GLOMERULOSCLEROSIS, NOS	32 (64%)	35 (70%)	27 (54%)
CALCIFICATION, FOCAL		1 (2%)	2 (4%)
#KIDNEY/PELVIS	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL		4 (8%)	15 (30%)
#URINARY BLADDER	(48)	(48)	(49)
CALCULUS, NOS	1 (2%)	1 (2%)	5 (10%)
HYPERPLASIA, EPITHELIAL		2 (4%)	20 (41%)
*URETHRA	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(47)	(47)
CYST, NOS		3 (6%)	1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
GRANULOMA, FOREIGN BODY	1 (2%)		
HYPERPLASIA, CHROMOPHOBE-CELL	1 (2%)	1 (2%)	3 (6%)
#ADRENAL	(50)	(50)	(49)
EDEMA, NOS		1 (2%)	
METAMORPHOSIS FATTY	1 (2%)	1 (2%)	1 (2%)
#ADRENAL MEDULLA	(50)	(50)	(49)
HYPERPLASIA, NOS		3 (6%)	3 (6%)
#THYROID	(42)	(43)	(42)
CYST, NOS			1 (2%)
HYPERPLASIA, C-CELL	4 (10%)	2 (5%)	3 (7%)
#PARATHYROID	(36)	(36)	(30)
HYPERPLASIA, NOS	1 (3%)	1 (3%)	1 (3%)
#PANCREATIC ISLETS	(50)	(46)	(50)
HYPERPLASIA, NOS	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
CYST, NOS			1 (2%)
LACTATION	1 (2%)		1 (2%)
*PREPUCE	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)		
*PREPUTIAL GLAND	(50)	(50)	(50)
DISTENTION	1 (2%)		
CYSTIC DUCTS		1 (2%)	
INFLAMMATION, CHRONIC		1 (2%)	
HYPERPLASIA, NOS		1 (2%)	
#PROSTATE	(45)	(39)	(44)
INFLAMMATION, SUPPURATIVE		2 (5%)	
*SEMINAL VESICLE	(50)	(50)	(50)
INFLAMMATION, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
GRANULOMA, NOS			1 (2%)
GRANULOMA, SPERMATIC		1 (2%)	
#TESTIS	(50)	(50)	(50)
ATROPHY, NOS	1 (2%)	1 (2%)	3 (6%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, INTERSTITIAL CELL	1 (2%)		1 (2%)
*EPIDIDYMIS	(50)	(50)	(50)
DEGENERATION, NOS			1 (2%)
*SCROTUM	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		
NERVOUS SYSTEM			
#CEREBELLUM	(50)	(49)	(49)
HEMORRHAGE		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
CATARACT	8 (16%)	9 (18%)	5 (10%)
*EYE ANTERIOR CHAMBER	(50)	(50)	(50)
FIBROSIS		1 (2%)	
*EYE/CORNEA	(50)	(50)	(50)
INFLAMMATION, NOS	1 (2%)		
ULCER, NOS	1 (2%)		
INFLAMMATION, SUPPURATIVE	1 (2%)		
SCAR	1 (2%)		
DEGENERATION, HYALINE		2 (4%)	1 (2%)
*EYE/RETINA	(50)	(50)	(50)
ATROPHY, NOS	8 (16%)	9 (18%)	5 (10%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
ACCESSORY SPLEEN		1 (2%)	
NECROSIS, FAT		1 (2%)	
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, FOCAL			1 (2%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		3 (6%)
ALL OTHER SYSTEMS			
TAIL			
HEMORRHAGIC CYST			1
ADIPOSE TISSUE			
NECROSIS, NOS		1	
OMENTUM			
NECROSIS, FAT			1
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED			5

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

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED 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, NOS	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(49)
PNEUMONIA, ASPIRATION	2 (4%)		
PNEUMONIA, CHRONIC MURINE		1 (2%)	
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(50)	(49)	(48)
HYPOPLASIA, NOS	2 (4%)		5 (10%)
#SPLEEN	(50)	(49)	(50)
HYPERPLASIA, NODULAR		2 (4%)	1 (2%)
#LIVER	(50)	(50)	(50)
HYPERPLASIA, RETICULUM CELL	1 (2%)		
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(50)
DILATATION, NOS		1 (2%)	
FIBROELASTOSIS ENDOCARDIAL			1 (2%)
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, NOS	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
FIBROSIS		1 (2%)	1 (2%)
*CORONARY ARTERY	(50)	(50)	(50)
THROMBUS, CANALIZED			1 (2%)
*PULMONARY ARTERY	(50)	(50)	(50)
MINERALIZATION		1 (2%)	1 (2%)
MEDIAL CALCIFICATION	10 (20%)	11 (22%)	8 (16%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
HERNIA, NOS		1 (2%)	
GRANULOMA, NOS	21 (42%)	26 (52%)	27 (54%)
NECROSIS, FOCAL		1 (2%)	
METAMORPHOSIS FATTY	8 (16%)	10 (20%)	
CYTOPLASMIC VACUOLIZATION			3 (6%)
BASOPHILIC CYTO CHANGE	3 (6%)	1 (2%)	5 (10%)
FOCAL CELLULAR CHANGE			1 (2%)
EOSINOPHILIC CYTO CHANGE		2 (4%)	
CLEAR-CELL CHANGE	1 (2%)	3 (6%)	
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, NOS			1 (2%)
METAMORPHOSIS FATTY		1 (2%)	
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS		1 (2%)	
#PANCREAS	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
FIBROSIS, FOCAL		1 (2%)	1 (2%)
ATROPHY, NOS	3 (6%)		
ATROPHY, FOCAL	1 (2%)		
#STOMACH	(50)	(50)	(48)
ULCER, NOS	1 (2%)		
INFLAMMATION, ACUTE			1 (2%)
HYPERKERATOSIS	1 (2%)	1 (2%)	
#GASTRIC MUCOSA	(50)	(50)	(48)
CYST, NOS	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(49)	(50)	(50)
MINERALIZATION		1 (2%)	

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
CYST, NOS			3 (6%)
NEPHROSIS, TOXIC		1 (2%)	
GLOMERULOSCLEROSIS, NOS	4 (8%)	1 (2%)	12 (24%)
METAMORPHOSIS FATTY	1 (2%)		
CALCIFICATION, NOS			3 (6%)
CALCIFICATION, FOCAL	3 (6%)	18 (36%)	26 (52%)
#KIDNEY/MEDULLA	(49)	(50)	(50)
CYST, NOS			1 (2%)
#KIDNEY/PELVIS	(49)	(50)	(50)
DEGENERATION, MUCOID			1 (2%)
HYPERPLASIA, EPITHELIAL		5 (10%)	34 (68%)
#URINARY BLADDER	(49)	(47)	(48)
ULCER, NOS			1 (2%)
HYPERPLASIA, EPITHELIAL	4 (8%)	12 (26%)	9 (19%)
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(50)	(49)
CYST, NOS	1 (2%)		1 (2%)
HEMATOMA, NOS			1 (2%)
HEMORRHAGIC CYST	1 (2%)		
HYPERPLASIA, CHROMOPHOBE-CELL	1 (2%)	2 (4%)	4 (8%)
ANGIECTASIS		1 (2%)	
#ADRENAL	(48)	(50)	(49)
NECROSIS, CORTICAL		2 (4%)	
METAMORPHOSIS FATTY	5 (10%)	2 (4%)	1 (2%)
LIPOIDOSIS		1 (2%)	
#ADRENAL CORTEX	(48)	(50)	(49)
HYPERPLASIA, NODULAR	1 (2%)		
#ADRENAL MEDULLA	(48)	(50)	(49)
HYPERPLASIA, NOS	1 (2%)		1 (2%)
#THYROID	(45)	(45)	(45)
HYPERPLASIA, C-CELL	5 (11%)	5 (11%)	4 (9%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
CYST, NOS			1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
LACTATION	13 (26%)	10 (20%)	11 (22%)
*CLITORAL GLAND	(50)	(50)	(50)
HYPERPLASIA, NOS			1 (2%)
*VAGINA	(50)	(50)	(50)
POLYP		1 (2%)	
#UTERUS	(50)	(48)	(50)
CYST, NOS		1 (2%)	
HEMORRHAGIC CYST			1 (2%)
HYPERPLASIA, EPITHELIAL	1 (2%)		
#UTERUS/ENDOMETRIUM	(50)	(48)	(50)
CYST, NOS			4 (8%)
HYPERPLASIA, CYSTIC	1 (2%)	2 (4%)	1 (2%)
HYPERPLASIA, STROMAL	1 (2%)		
#OVARY/OVIDUCT	(50)	(48)	(50)
ABSCESS, NOS		1 (2%)	
#OVARY	(50)	(50)	(50)
CYST, NOS	1 (2%)		3 (6%)
ATROPHY, NOS	1 (2%)		
NERVOUS SYSTEM			
#BRAIN	(50)	(49)	(50)
HYDROCEPHALUS, NOS	1 (2%)		
SCAR		1 (2%)	
ATROPHY, PRESSURE	3 (6%)	6 (12%)	3 (6%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
SYNECHIA, ANTERIOR		1 (2%)	
SYNECHIA, POSTERIOR	1 (2%)		
CATARACT	12 (24%)	8 (16%)	8 (16%)
*SCLERA	(50)	(50)	(50)
CALCIFICATION, NOS			1 (2%)
CALCIFICATION, FOCAL		1 (2%)	
*EYE/CORNEA	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	2 (4%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
DEGENERATION, HYALINE	4 (8%)		
KERATOCONUS		1 (2%)	
*EYE/RETINA	(50)	(50)	(50)
DEGENERATION, NOS	2 (4%)		
ATROPHY, NOS	10 (20%)	7 (14%)	7 (14%)
*EYE/CRYSTALLINE LENS	(50)	(50)	(50)
CATARACT			1 (2%)
*EYE/CONJUNCTIVA	(50)	(50)	(50)
INFLAMMATION, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(50)
HYPEROSTOSIS		1 (2%)	
*SKELETAL MUSCLE	(50)	(50)	(50)
CALCIFICATION, NOS	1 (2%)		
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
STEATITIS	1 (2%)	1 (2%)	
NECROSIS, FAT			2 (4%)
*PLEURA	(50)	(50)	(50)
INFLAMMATION, CHRONIC FOCAL			1 (2%)
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)	4 (8%)	1 (2%)
ALL OTHER SYSTEMS			
DIAPHRAGM			
HERNIA, NOS		1	
SPECIAL MORPHOLOGY SUMMARY			
NONE			

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

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
HYPERKERATOSIS	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
ABSCESS, NOS		1 (2%)	
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, GRANULOMATOUS		1 (2%)	
RESPIRATORY SYSTEM			
*LARYNX	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)		
#TRACHEA	(45)	(43)	(44)
INFLAMMATION, SUPPURATIVE			1 (2%)
#LUNG	(50)	(50)	(46)
MINERALIZATION		2 (4%)	
CONGESTION, NOS	2 (4%)	4 (8%)	9 (20%)
EDEMA, NOS	1 (2%)		
HEMORRHAGE			1 (2%)
SEQUESTRATION	1 (2%)		
HISTIOCYTOSIS	3 (6%)		
HEMATOPOIETIC SYSTEM			
#SPLEEN	(50)	(47)	(47)
CONGESTION, NOS	1 (2%)	1 (2%)	
PLASMACYTOSIS	1 (2%)		

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, LYMPHOID	5 (10%)	3 (6%)	4 (9%)
HEMATOPOIESIS	7 (14%)	5 (11%)	3 (6%)
#MESENTERIC L. NODE	(33)	(43)	(32)
CONGESTION, NOS		1 (2%)	
EDEMA, NOS	1 (3%)		
HEMORRHAGE	14 (42%)	10 (23%)	4 (13%)
HEMOSIDEROSIS			1 (3%)
PLASMACYTOSIS	1 (3%)	1 (2%)	
HYPERPLASIA, LYMPHOID	9 (27%)	3 (7%)	
#INGUINAL LYMPH NODE	(33)	(43)	(32)
PLASMACYTOSIS	3 (9%)		
HYPERPLASIA, LYMPHOID	3 (9%)		
#LUNG	(50)	(50)	(46)
PLASMACYTOSIS	1 (2%)		
#LIVER	(50)	(50)	(49)
HEMATOPOIESIS	1 (2%)		
#PEYER'S PATCH	(46)	(50)	(45)
HYPERPLASIA, LYMPHOID			1 (2%)
#THYMUS	(24)	(25)	(17)
EDEMA, NOS		1 (4%)	
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
PERIARTERITIS		1 (2%)	
#MESENTERIC L. NODE	(33)	(43)	(32)
THROMBOSIS, NOS	1 (3%)		
#HEART	(50)	(50)	(49)
MINERALIZATION		1 (2%)	
FIBROSIS	1 (2%)		
DEGENERATION, NOS	3 (6%)	1 (2%)	
*AORTA	(50)	(50)	(50)
MINERALIZATION		2 (4%)	2 (4%)
#LIVER	(50)	(50)	(49)
THROMBUS, FIBRIN			1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*MESENTERY	(50)	(50)	(50)
THROMBUS, FIBRIN	1 (2%)		
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(47)	(48)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
NECROSIS, NOS		1 (2%)	
#LIVER	(50)	(50)	(49)
MINERALIZATION	1 (2%)		
INFLAMMATION, SUPPURATIVE	1 (2%)		
INFLAMMATION, NECROTIZING		1 (2%)	
ABSCESS, NOS	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	
GRANULOMA, NOS			1 (2%)
INFLAMMATION, PYOGRANULOMATOUS		3 (6%)	
DEGENERATION, NOS			1 (2%)
NECROSIS, NOS	2 (4%)		
NECROSIS, COAGULATIVE	1 (2%)		
CYTOPLASMIC VACUOLIZATION	2 (4%)	2 (4%)	10 (20%)
FOCAL CELLULAR CHANGE			1 (2%)
ATROPHY, NOS			1 (2%)
ANGIECTASIS			1 (2%)
#LIVER/CENTRILOBULAR	(50)	(50)	(49)
NECROSIS, NOS	1 (2%)		
CYTOPLASMIC VACUOLIZATION	1 (2%)		
ATROPHY, NOS			1 (2%)
*GALLBLADDER	(50)	(50)	(50)
INFLAMMATION, NECROTIZING		1 (2%)	
#PANCREAS	(50)	(48)	(47)
CYST, NOS	1 (2%)		
ATROPHY, NOS		1 (2%)	
#STOMACH	(48)	(48)	(47)
MINERALIZATION			6 (13%)
INFLAMMATION ACUTE AND CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, EPITHELIAL	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
MINERALIZATION		4 (8%)	11 (22%)
HYDRONEPHROSIS		1 (2%)	
POLYCYSTIC KIDNEY			1 (2%)
PYELONEPHRITIS SUPPURATIVE	1 (2%)		
INFLAMMATION, CHRONIC	38 (76%)	35 (70%)	21 (43%)
NECROSIS, MEDULLARY			3 (6%)
CYTOPLASMIC VACUOLIZATION			1 (2%)
ATROPHY, NOS	1 (2%)	4 (8%)	3 (6%)
#KIDNEY/TUBULE	(50)	(50)	(49)
NECROSIS, NOS	1 (2%)		
#KIDNEY/PELVIS	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
#URINARY BLADDER	(48)	(44)	(39)
INFLAMMATION, SUPPURATIVE			1 (3%)
INFLAMMATION, CHRONIC	17 (35%)	17 (39%)	4 (10%)
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		
HYPERPLASIA, EPITHELIAL	1 (2%)		
ENDOCRINE SYSTEM			
#ADRENAL	(44)	(48)	(42)
FOCAL CELLULAR CHANGE		1 (2%)	1 (2%)
#THYROID	(47)	(42)	(36)
LYMPHOCYTIC INFLAMMATORY INFILTR			2 (6%)
HYPERPLASIA, FOLLICULAR-CELL		1 (2%)	1 (3%)
REPRODUCTIVE SYSTEM			
*PREPUCE	(50)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
*PREPUTIAL GLAND	(50)	(50)	(50)
DILATATION/DUCTS	4 (8%)	1 (2%)	5 (10%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	2 (4%)
INFLAMMATION, CHRONIC SUPPURATIV	2 (4%)		
INFLAMMATION, GRANULOMATOUS	2 (4%)		1 (2%)
INFLAMMATION, PYOGRANULOMATOUS			2 (4%)
#PROSTATE	(49)	(50)	(48)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)	3 (6%)	
INFLAMMATION, SUPPURATIVE	1 (2%)		
INFLAMMATION, ACUTE		1 (2%)	
#TESTIS	(49)	(50)	(47)
MINERALIZATION	2 (4%)	2 (4%)	
CYST, NOS		1 (2%)	
ATROPHY, NOS	2 (4%)		1 (2%)
#TESTIS/TUBULE	(49)	(50)	(47)
MINERALIZATION		1 (2%)	
*EPIDIDYMIS	(50)	(50)	(50)
LYMPHOCYTIC INFLAMMATORY INFILTR	3 (6%)	1 (2%)	1 (2%)
GRANULOMA, SPERMATIC			1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
CATARACT		1 (2%)	
*EYE/RETINA	(50)	(50)	(50)
DETACHMENT		1 (2%)	
ATROPHY, NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*STERNUM	(50)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
NECROSIS, NOS		1 (2%)	
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC			1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
*PLEURA	(50)	(50)	(50)
INFLAMMATION ACUTE AND CHRONIC		1 (2%)	
*PERICARDIUM	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
*MESENTERY	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
MINERALIZATION		2 (4%)	5 (10%)
INFLAMMATION, ACUTE	1 (2%)		
ABSCESS, NOS	1 (2%)		
INFLAMMATION ACUTE AND CHRONIC	1 (2%)		
SITE UNKNOWN			
MINERALIZATION			1
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED		1	
AUTO/NECROPSY/HISTO PERF			2
AUTO/NECROPSY/NO HISTO			1

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

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE FED DIETS CONTAINING 11-AMINOUNDECANOIC ACID

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING		1	1
ANIMALS NECROPSIED	50	49	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(49)
INFLAMMATION, CHRONIC	1 (2%)	2 (4%)	
HYPERKERATOSIS	1 (2%)	1 (2%)	
ACANTHOSIS	2 (4%)		
RESPIRATORY SYSTEM			
#TRACHEA	(39)	(42)	(43)
INFLAMMATION, FIBRINOUS	1 (3%)		
#LUNG	(50)	(49)	(49)
MINERALIZATION		1 (2%)	4 (8%)
CONGESTION, NOS		2 (4%)	5 (10%)
EDEMA, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)		
HYPERPLASIA, NOS	1 (2%)		
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(46)	(44)	(47)
HEMOSIDEROSIS		1 (2%)	
GRANULOPOIESIS		1 (2%)	1 (2%)
#SPLEEN	(50)	(49)	(47)
HEMOSIDEROSIS			1 (2%)
HYPERPLASIA, LYMPHOID	5 (10%)	4 (8%)	3 (6%)
HEMATOPOIESIS	5 (10%)	3 (6%)	3 (6%)
#LYMPH NODE	(35)	(38)	(38)
CONGESTION, NOS	1 (3%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
HEMORRHAGE		1 (3%)	
PLASMACYTOSIS	1 (3%)		
#MANDIBULAR L. NODE	(35)	(38)	(38)
HEMOSIDEROSIS			1 (3%)
HYPERPLASIA, LYMPHOID		1 (3%)	
#ABDOMINAL LYMPH NODE	(35)	(38)	(38)
HYPERPLASIA, LYMPHOID	1 (3%)		
#LUMBAR LYMPH NODE	(35)	(38)	(38)
EDEMA, NOS	1 (3%)		
HEMOSIDEROSIS	1 (3%)		
#MESENTERIC L. NODE	(35)	(38)	(38)
HEMORRHAGE	1 (3%)	1 (3%)	2 (5%)
HYPERPLASIA, LYMPHOID	1 (3%)		
#THYMUS	(30)	(32)	(22)
INFLAMMATION, SUPPURATIVE		1 (3%)	
NECROSIS, CORTICAL			1 (5%)
CIRCULATORY SYSTEM			
#HEART	(50)	(49)	(49)
MINERALIZATION	3 (6%)		2 (4%)
INFLAMMATION ACUTE AND CHRONIC			1 (2%)
DEGENERATION, NOS		1 (2%)	
NECROSIS, NOS			1 (2%)
*AORTA	(50)	(49)	(49)
MINERALIZATION		1 (2%)	2 (4%)
#UTERUS	(48)	(49)	(49)
THROMBUS, FIBRIN		1 (2%)	
DIGESTIVE SYSTEM			
*TONGUE	(50)	(49)	(49)
INFLAMMATION, GRANULOMATOUS			1 (2%)
#LIVER	(50)	(49)	(49)
CONGESTION, NOS		1 (2%)	

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, NOS	1 (2%)		
INFLAMMATION ACUTE AND CHRONIC	1 (2%)		
INFLAMMATION, GRANULOMATOUS		1 (2%)	1 (2%)
INFLAMMATION, PYOGRANULOMATOUS	1 (2%)		
NECROSIS, NOS	1 (2%)		
INFARCT, NOS			1 (2%)
CYTOPLASMIC VACUOLIZATION		5 (10%)	6 (12%)
FOCAL CELLULAR CHANGE	1 (2%)		1 (2%)
#PANCREAS	(50)	(49)	(47)
DILATATION/DUCTS			2 (4%)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	1 (2%)
ATROPHY, NOS	1 (2%)		3 (6%)
#STOMACH	(50)	(48)	(49)
MINERALIZATION			4 (8%)
INFLAMMATION, SUPPURATIVE			1 (2%)
HYPERPLASIA, ADENOMATOUS	1 (2%)		
HYPERKERATOSIS	1 (2%)	2 (4%)	
#FORESTOMACH	(50)	(48)	(49)
HYPERPLASIA, NOS	1 (2%)		
#COLON	(50)	(45)	(47)
EDEMA, NOS	1 (2%)		1 (2%)
INFLAMMATION, SEROUS	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(49)
MINERALIZATION		6 (12%)	9 (18%)
INFLAMMATION, CHRONIC	36 (72%)	36 (73%)	32 (65%)
SCLEROSIS			1 (2%)
NECROSIS, MEDULLARY		4 (8%)	1 (2%)
CYTOPLASMIC VACUOLIZATION		1 (2%)	
ATROPHY, NOS		4 (8%)	4 (8%)
#KIDNEY/MEDULLA	(50)	(49)	(49)
MINERALIZATION		2 (4%)	
SCLEROSIS			1 (2%)
DEGENERATION, NOS		1 (2%)	
#URINARY BLADDER	(49)	(48)	(46)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC	40 (82%)	32 (67%)	28 (61%)
INFLAMMATION, PYOGRANULOMATOUS			1 (2%)
ENDOCRINE SYSTEM			
#ADRENAL	(47)	(46)	(48)
CYST, NOS	1 (2%)		
DEGENERATION, LIPOID		1 (2%)	
AMYLOIDOSIS		1 (2%)	
#THYROID	(37)	(41)	(40)
LYMPHOCYTIC INFLAMMATORY INFILTR	2 (5%)	1 (2%)	
HYPERPLASIA, FOLLICULAR-CELL	1 (3%)	1 (2%)	
#PARATHYROID	(16)	(15)	(21)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (7%)	
REPRODUCTIVE SYSTEM			
#UTERUS	(48)	(49)	(49)
HYDROMETRA			1 (2%)
ABSCESS, NOS			1 (2%)
#UTERUS/ENDOMETRIUM	(48)	(49)	(49)
CYST, NOS			1 (2%)
HYPERPLASIA, CYSTIC	40 (83%)	34 (69%)	23 (47%)
#OVARY	(46)	(46)	(45)
CYST, NOS	16 (35%)	19 (41%)	7 (16%)
HEMORRHAGE			1 (2%)
HEMATOMA, NOS		1 (2%)	1 (2%)
HEMORRHAGIC CYST			1 (2%)
NERVOUS SYSTEM			
#BRAIN/MENINGES	(49)	(49)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR	3 (6%)	1 (2%)	3 (6%)
#BRAIN	(49)	(49)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR	2 (4%)	2 (4%)	1 (2%)
SPECIAL SENSE ORGANS			
NONE			

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	UNTREATED CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MEDIASTINUM	(50)	(49)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
NECROSIS, FAT		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(49)	(49)
MINERALIZATION			3 (6%)
SPECIAL MORPHOLOGY SUMMARY			
ANIMAL MISSING/NO NECROPSY		1	1

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

APPENDIX E

ANALYSIS OF 11-AMINOUNDECANOIC ACID
MIDWEST RESEARCH INSTITUTE

APPENDIX E

A. ELEMENTAL ANALYSIS

Element	C	H	N
Theory	65 63	11 52	6 96
Determined	65 54	11 46	6 95
	65 71	11 60	6 97

B. WATER ANALYSIS

(Karl Fisher) 0 5% ±0 1 (δ)%

C. TITRATION OF AMINO GROUP WITH PERCHLORIC ACID IN GLACIAL ACETIC ACID

99 13% ±0 03 (δ)%

D. MELTING POINT

Determined	Literature Values
190°-191°C, dec (Dupont 900DTA)	184°-185°C (Rekhter and Nesterova, 1963)
188°-189°C, dec (visual, capillary)	

E. THIN-LAYER CHROMATOGRAPHY

Plates Silica gel 60

Ref Standard L-phenylalanine

Amount spotted 100 and 300 μg

System 1 Phenol water formic acid (72 28 1)

Visualization Ninhydrin

R_f 0 83 (trace), 0 66

R_{st} 1 4, 1 1

System 2 Chloroform methanol water ammonium hydroxide (45 45 4 6)

R_f 0 94 (slight trace), 0 88 (trace), 0 48 (major)

R_{st} 1 8, 1 7, 0 91

F. HIGH-PRESSURE LIQUID CHROMATOGRAPHY

Derivation procedure The amino acid was suspended in 0 5M aqueous sodium bicarbonate buffer and an equivalent amount of 10 mM 5-(dimethylamino)naphthalene sulphonyl chloride (dansyl chloride) solution in acetonitrile was added The resulting solution was incubated at 37°C for 1 hour and then diluted with 50% aqueous acetonitrile This resulting solution was analyzed by high-pressure liquid chromatography, using the following system

Instrument Waters ALC202, with Model 660 Solvent Programmer

Column μBondapak C_{18}, 30 cm x 4 mm I D

Detector UV-254 nm

Solvent 37% acetonitrile in 0 01M aqueous sodium bicarbonate

Flow 1 ml/min

Results A single peak with retention time of 7 5 minutes was detected in the samples

APPENDIX E

G. SPECTRAI DATA

	Literature Values
(1) Infrared	
Instrument Beckman IR-12	Consistent with literature spectrum (Sadtler Research Laboratories)
Cell 1% KBr pellet	
Results (See Figure 5)	
(2) Ultraviolet/Visible	
Instrument Cary 118	No literature values found
Results No absorbance detected between 350 and 800 nm (visible range) No maximum between 200 and 350 nm (ultraviolet range), however, the absorbance increases from 250 nm to the instrument cutoff at 220 nm	
Concentration 1 2 mg/ml	
Solvent 0 1N HCl	
(3) Nuclear Magnetic Resonance	
Instrument Varian HA-100	No literature spectrum found
Solvent Deuterated trifluoroacetic acid with internal tetramethylsilane	
Assignments (See Figure 6)	
(a) s, δ 1 35 ppm, (b) m, δ 1 54 to 1 94 ppm, (c) t, δ 2 46 ppm, J_{bc} = 7Hz, (d) m, δ 3 01 to 3 35 ppm, (e) s, 6 29 to 6 84 ppm	
Integration ratios	
(a) 13 2, (b) 3 7, (c) 1 8, (d) 1 4, (e) 0 5	

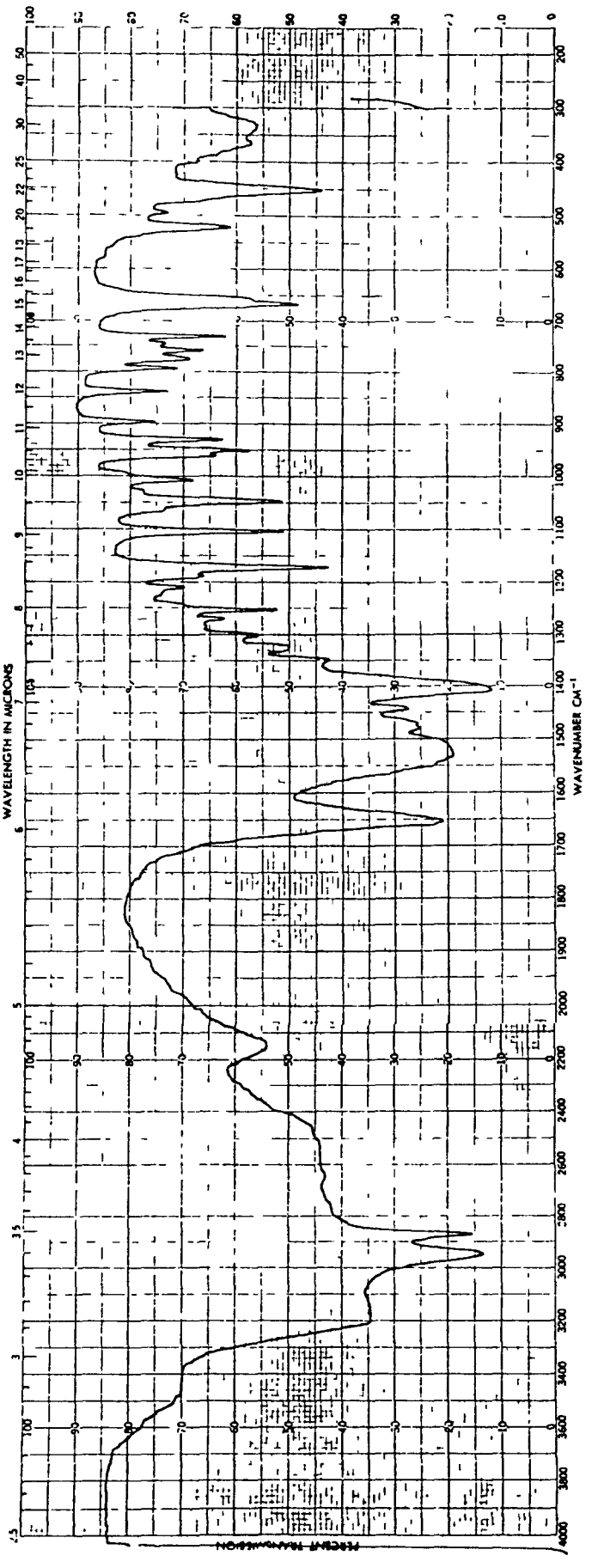

Figure 5. Infrared Absorption Spectrum 11-Aminoundecanoic Acid

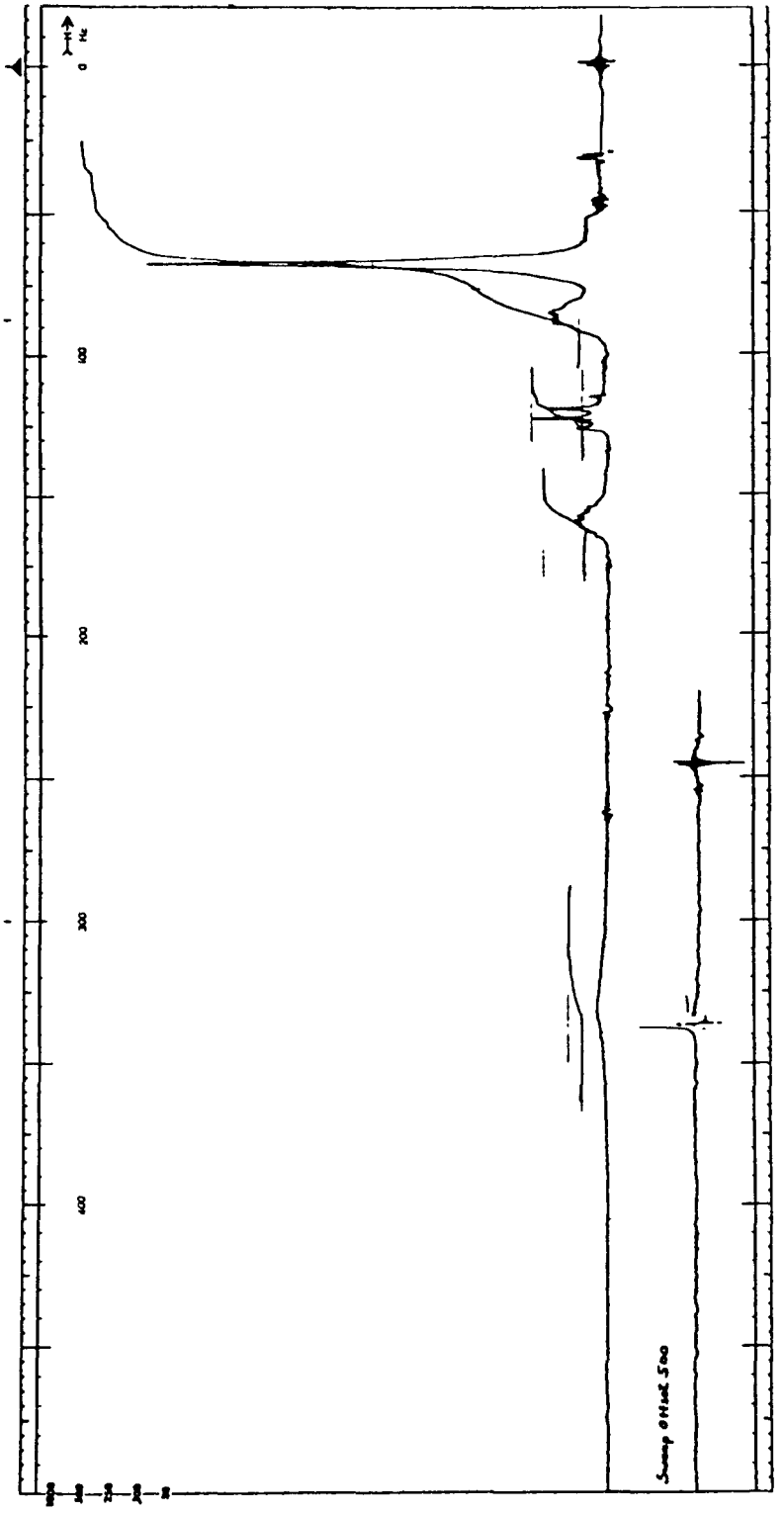

Figure 6. Nuclear Magnetic Resonance Spectrum 11-Aminoundecanoic Acid

APPENDIX F

ANALYSIS OF FORMULATED DIETS FOR STABILITY OF 11-AMINOUNDECANOIC ACID MIDWEST RESEARCH INSTITUTE

APPENDIX F

1. MIXING AND STORAGE: 11-Aminoundecanoic acid (20 g) and Wayne Lab Blox® Rodent feed (180 g) were mixed in a mortar. Samples of the mixture were then removed and stored for 2 weeks at -20°, 5°, 25°, and 45°C. These samples were extracted and analyzed by the high-pressure liquid chromatographic method described below.

2. PROCEDURES FOR EXTRACTION AND ANALYSIS: Samples of the chemical/feed mixtures were triturated three times with 0.1N nitric acid using a Polytron® mixer, and the combined mixtures were centrifuged. The supernatant solutions were separated and neutralized to approximately pH7 with 0.35N sodium hydroxide solution and then buffered by adding solid sodium bicarbonate (to make the solution 0.5M in $NaHCO_3$). This solution was then treated with an equivalent amount of 10 mM 5-(dimethylamino)naphthalene sulphonyl chloride (dansyl chloride) solution in acetonitrile. The resulting solution was incubated at 37°C for 1 hour and then diluted with 50% aqueous acetonitrile. This resulting solution was analyzed by high-pressure liquid chromatography, using the following system:

Instrument: Waters ALC202, with Model 660 Solvent Programmer

Column: μBondapak C_{18}, 30 cm x 4 mm I.D.

Detector: UV-254 nm

Solvent: 37% acetonitrile in 0.01M aqueous sodium bicarbonate

Flow: 1 ml/min

3. RESULTS:

Temperature (°C)	Average % Compound Recovered
-20	9.8 ±0.4
5	9.8 ±0.4
25	10.1 ±0.4
45	10.6 ±0.4

There is no significant difference between the samples stored at the various temperatures.

4. CONCLUSION: 11-Aminoundecanoic acid mixed with feed is stable for two weeks at temperatures up to 45°C.

APPENDIX G

ANALYSIS OF FORMULATED DIETS FOR CONCENTRATIONS OF 11-AMINOUNDECANOIC ACID LITTON BIONETICS, INC.

APPENDIX G

A 5-g portion of feed was extracted with three 40-ml portions of 0.1N nitric acid. After the mixture was shaken for 10 minutes on an automatic shaker and centrifuged for 10 minutes at 1,500 rpm, the supernatant was filtered through glass wool into a 200-ml volumetric flask. The total extract was diluted to volume with additional dilute nitric acid. A 1.0- to 2.0-ml aliquot of the extract was transferred to a test tube; 0.1N nitric acid was added, if necessary, to make the final volume 2.0 ml in all cases. A reference standard was prepared by pipetting 2.0 ml of the 0.1N nitric acid containing 375 μg aminoundecanoic acid into a test tube. To both the sample and the standard were added 5.0 ml of 0.5M $NaHCO_3$ and 5.0 ml of 10 mM dansyl chloride in acetonitrile. The tubes were incubated for 1 hour at 37°C and allowed to cool. Two milliliters of acetonitrile were added and the volume adjusted to 15 ml with 50% acetonitrile/water.

Analysis was performed with a Waters Model No. 204 high-pressure liquid chromatograph with a UV detector at 254 nm. The column was stainless steel, 25 cm x 4.6 mm I.D., packed with μBondapak/C_{18}. The solvent system was 37% acetonitrile in 0.01M aqueous sodium bicarbonate at a flow rate of 2.0 ml/min. The amount of test compound in the feed was calculated by reference to a calibration curve obtained by analysis of the reference standard in the same manner. Control feed and control feed treated with a known amount of aminoundecanoic acid were analyzed concurrently to correct for possible feed background and method recovery.

Table G-1. ANALYSIS OF FORMULATED DIETS

		Concentration *(b)* of 11-Aminoundecanoic Acid in Feed for Target Concentration	
Date Mixed *(a)*	**Date Used (week of)**	**7,500 ppm**	**15,000 ppm**
11/12/77	11/15 - 11/22	7,951	15,135
		7,805	13,833
		7,146	
12/12/77	12/14 - 12/21		14,411
2/23/78	2/25 - 3/1	6,892	
4/06/78	4/8 - 4/15		14,561
5/19/78	5/22 - 5/29		14,879
7/28/78	8/1 - 8/8	8,028	14,628
		7,930	
8/31/78	9/1 - 9/8	7,517	
9/14/78	9/16 - 9/23		15,884
10/26/78	10/28 - 11/4		14,278
11/09/78	11/11 - 11/18	7,232	
12/21/78	12/23 - 12/30	7,874	
Mean (ppm)		7,597	14,701
Standard deviation		416	618
Coefficient of variation (%)		5.5	4.2
Range (ppm)		6,892-8,028	13,833-15,884
Number of samples		9	8

(a) 2/2/77 was the start date for rats and 2/1/77 was the start date for mice.

(b) The data presented are the average of the results of duplicate analyses.

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