NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 240

CARCINOGENESIS BIOASSAY OF PROPYL GALLATE

(CAS NO. 121-79-9)

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 July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP TECHNICAL REPORT
ON THE

CARCINOGENESIS BIOASSAY OF PROPYL GALLATE

(CAS NO. 121-79-9)

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

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

December 1982

NTP-81-42
NIH Publication No. 83-1796

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

NOTE TO THE READER

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

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

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

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).

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

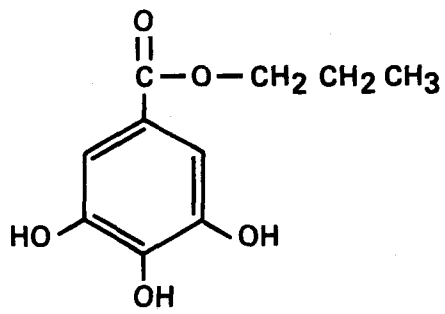
TABLE OF CONTENTS

TABLES

FIGURES

APPENDIXES

CARCINOGENESIS BIOASSAY OF PROPYL GALLATE



PROPYL GALLATE

CAS NO. 121-79-9
$C_{10}H_{12}O_5$ Mol. Wt. 212.20

ABSTRACT

A carcinogenesis bioassay of propyl gallate was conducted by feeding diets containing 6,000 or 12,000 ppm propyl gallate to groups of 50 F344/N rats and 50 B6C3F$_1$ mice of each sex for 103 weeks. Groups of 50 untreated rats and 50 untreated mice of each sex served as controls.

Survival of rats and mice was not adversely affected by propyl gallate, but mean body weights of dosed rats and mice of each sex were lower than those of the controls. At 104 weeks, mean body weights of low- and high-dose rats were 4% and 8% lower than those of the controls for males and 11% and 19% lower than those of the controls for females. Similarly, mean body weights of low- and high-dose mice were 5% and 8% lower than those of the controls for males and 11% (both dose groups) lower than those of the controls for females.

Thyroid follicular-cell adenomas or carcinomas (combined) occurred in male rats with a statistically significant ($P<0.05$) positive trend, but the incidences in the dosed groups were not statistically significant in direct comparisons with the control groups. Moreover, the incidence of high-dose male rats with follicular-cell tumors (3/50, 6%) was not statistically different from the historical control rate (14/584, 2.4%) for the laboratory that conducted this bioassay.

Rare tumors (an astrocytoma or a glioma) were found in the brains of two low-dose female rats. The incidence of all brain tumors in the Bioassay Program is only 0.86%. The absence of this tumor in the high-dose female rat group reduces the likelihood that this tumor is related to propyl gallate administration.

Increased incidences of hepatic cytoplasmic vacuolization and suppurative inflammation of the prostate were observed in dosed male rats. These findings were considered to be related to administration of propyl gallate.

Tumors (mostly benign) of the preputial gland, islet-cell tumors of the pancreas, and pheochromocytomas of the adrenal gland were observed with significantly ($P<0.05$) higher incidences in the low-dose male rats, but there was little evidence of an effect in the high-dose group. The incidences of male rats with tumors of the preputial gland were 1/50 (2%) for controls, 8/50 (16%) for the low-dose, and 0/50 (0%) for the high-dose group. Islet-cell tumors of the pancreas occurred in 2/50 (4%) control males, 9/50 (18%) low-dose males, and 4/50 (8%) for high-dose males. Pheochromocytomas of the adrenal gland were observed in 4/50 (8%) control males, 13/48 (25%) low-dose males, and 8/50 (16%) high-dose males.

Negative trends ($P<0.05$) were observed for leukemia in male rats (16/50, 7/50, 6/50) and for fibroadenomas of the mammary gland in female rats (11/50, 2/50, 5/50).

In male mice, malignant lymphoma was observed with a significantly ($P \leq 0.014$) positive trend (control, 1/50, 2%; low-dose, 3/49, 6%; high-dose, 8/50, 16%), and the incidence in the high-dose group was significantly ($P \leq 0.028$) higher than that observed in the concurrent controls. However, the high-dose incidence was not statistically different from the historical rate (60/640, 9.4%) for the laboratory that conducted this bioassay.

Adenomas of the liver in female mice occurred with a statistically significant ($P \leq 0.022$) positive trend, and the incidence in the high-dose group was significantly ($P \leq 0.039$) higher than that of the controls (0/50, 0%; 2/50, 4%; 5/49, 10%). The incidences of hepatocellular adenomas or carcinomas (combined) were similar in control and dosed groups (3/50, 6%; 3/50, 6%; 5/49, 10%).

Negative trends ($P < 0.05$) were obtained for fibromas of the skin or subcutaneous tissue in male mice (5/50, 1/49, 0/50).

Under the conditions of this bioassay, propyl gallate was not considered to be carcinogenic for F344/N rats, although there was evidence of an increased proportion of low-dose male rats with preputial gland tumors, islet-cell tumors of the pancreas, and pheochromocytomas of the adrenal glands; rare tumors of the brain occurred in two low-dose females. Propyl gallate was not considered to be carcinogenic for $B6C3F_1$ mice of either sex, although the increased incidence of malignant lymphoma in male mice may have been related to the dietary administration of propyl gallate.

CONTRIBUTORS

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

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

Dr. J. Prejean
Principal Investigator

Dr. D. Farnell
Pathologist

Dr. R. Thompson
Pathologist

Ms. R. James
Chemist

Ms. J. Belzer
Animal Care Supervisor

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

Dr. J. Keller
Director, Bioassay

Dr. S. Olin
Program Associate Director

Mr. E. Cremmins
Technical Editor

Ms. C. Dean
Production Editor

Dr. T. Griffin
Laboratory Operations Coordinator

Dr. A. Jacobs
Bioscience Writer

Dr. J. Joiner
Statistician

Ms. M. Levy
Technical Editor

Dr. P. Hildebrandt
Pathologist

Dr. W. Theriault
Reports Manager

Dr. J. Tomaszewski
Chemist

Mr. J. Warner
Statistician

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

Dr. Kamal Abdo (Chemical Manager)
Dr. G. Boorman
Dr. R. Chhabra
Dr. Michael P. Dieter
Dr. J. Fielding Douglas
Dr. Charles K. Grieshaber
Dr. Larry Hart
Dr. Joseph Haseman
Dr. James E. Huff
Dr. C. W. Jameson
Dr. John A. Moore
Dr. Ernest E. McConnell
Dr. Raymond Tennant

The pathology report and selected slides were evaluated in May, 1981 by the NTP Pathology Working Group, which was composed of Drs. G. Reznik, P. Hildebrandt (Tracor Jitco), and J. Ward.

The chemicals used in this bioassay of propyl gallate were analyzed by the Midwest Research Institute, 425 Volker Blvd., Kansas City, Missouri 64110, and reanalysis of the bulk chemical and analysis of formulated diets were performed by Southern Research Institute.

REVIEWERS

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

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

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

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

Ad Hoc Subcommittee Panel of Experts

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

Robert M. Elashoff, Ph.D. (Principal Reviewer)
University of California
at Los Angeles
Jonsson Comprehensive Cancer Center
Los Angeles, California

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

J. Michael Holland, Ph.D., D.V.M.
(Principal Reviewer)
Department of Biology
Oak Ridge National Laboratory
Oak Ridge, Tennessee

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

Robert A. Scala, Ph.D.
Exxon Corporation—REHD
East Millstone, New Jersey

Bernard Schwetz, Ph.D., D.V.M. (Principal Reviewer)
Toxicology Research Laboratory
Dow Chemical U.S.A.
Midland, Michigan

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

Stan D. Vesselinovitch, Ph.D.
Departments of Radiology and Pathology
University of Chicago
Chicago, Illinois

Mary Vore, Ph.D.
University of Kentucky
College of Medicine
Lexington, Kentucky

*Unable to attend December 16, 1981 meeting

SUMMARY OF PEER REVIEW COMMENTS ON THE BIOASSAY OF PROPYL GALLATE

On December 16, 1981, this carcinogenesis bioassay report on propyl gallate underwent peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9:00 a.m. in Conference Room A, Landow Building, 7910 Woodmont Avenue, Bethesda, Maryland.

Dr. Mirer, a principal reviewer for the report on the bioassay of propyl gallate, said that at least one type of neoplasm was found with a statistically significant trend or incidence in each test group: in male rats, thyroid follicular cell adenomas and carcinomas, adenomas of the preputial gland, and pheochromocytomas of the adrenal gland, and adenomas of the pancreatic islet cells; in female rats, adenomas of the mammary gland and endometrial stromal polyps; in male mice, malignant lymphomas; and in female mice, adenomas of the liver. Additionally, rare brain tumors were found in two low-dose female rats. He said that for each instance, the relationship of the increased incidence or trend to chemical administration was discounted because of the failure to exhibit a dose-response relationship or because results fell within the range of historical controls. Dr. Mirer proposed that the conclusion reflect these increases.

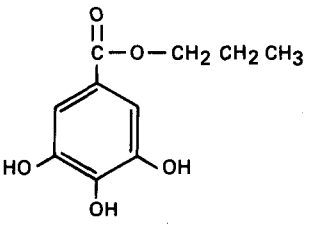
Dr. Mirer also commented that the anti-tumor effect cited in the literature for propyl gallate gives rise to speculation that the absence of a dose-response relationship for some of the glandular tumors in male and female rats is a biologically significant finding.

Dr. Elashoff, a second principal reviewer, commented on the endocrine organ tumors in rats, malignant lymphomas in male mice, and liver adenomas in female mice, as mentioned by Dr. Mirer. He noted that there was evidence of a fat metabolism disorder in low- and high-dose rats, and he asked if analysis should be limited to separate sites or expanded to include the pattern of elevated tumor incidence rates in glandular organs. Dr. McConnell, NTP, replied that he did not think there was any obvious biological significance to such a pattern.

Dr. Hitchchock asked for a vote on Dr. Mirer's amended conclusion: nine affirmative and one negative vote (Dr. Schwetz) with one abstention (Dr. Scala). Dr. Schwetz said he agreed with the conclusion of the report based in part on the occurrence of particular tumors in only one sex of one species, coupled with the lack of a dose-response relationship. He said there was not pharmacokinetic, pharmacologic, or endocrinologic evidence given to explain the inverse dose-response observed. Dr. Scala said that he did not have sufficient information to evaluate the amended conclusion, and asked that the two reviewers' critiques be supplied to the panel. Dr. Hitchcock said that final action on the report on propyl gallate would be deferred until the panel had the opportunity to review the critiques by Drs. Mirer and Elashoff along with meeting transcripts. This was accomplished by mail, and the Peer Review Panel members agreed with the modifications as suggested and circulated by Drs. Elashoff and Mirer. The revised report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

I. INTRODUCTION



PROPYL GALLATE

CAS NO. 121-79-9
$C_{10}H_{12}O_5$ Mol. Wt. 212.20

Propyl gallate (2,4,5 trihydroxybenzoic acid propyl ester; gallic acid propyl ester; Progallin P; Tennox PG) is a white to nearly white odorless powder having a slightly bitter taste (Food Chemicals Codex, 1981). Solutions of propyl gallate turn dark in the presence of iron or iron salts (Merck, 1968).

Propyl gallate has been used since 1948 as an antioxidant to stabilize cosmetics, food-packaging materials, and foods containing fats (LSRO, 1973). As an additive, it may be found in edible fats, oils, mayonnaise, shortening, baked goods, candy, dried meat, fresh pork sausage, and dried milk (Furia, 1972; Harshaw Chemical Co., 1975; LSRO, 1973), and it is used in hair grooming products, pressure-sensitive adhesives, lubricating oil additives, and transforming oils (Harshaw Chemical Co., 1975; Lauffer, 1972; Merck, 1968). Current production figures are not available (USITC, 1980), but approximately 67,339 kg was used in food in the United States during 1970 (LSRO, 1973).

The Food Chemicals Codex (1981) specifies that propyl gallate must be 98% pure when used as a food additive. Propyl gallate is an approved food additive which has been classified as "generally recognized as safe" by the U.S. Food & Drug Administration. Its use is subject to regulation under the Food and Cosmetics Act. The total permissible concentration of antioxidants (including propyl gallate) is 0.02% of the oil content of the food, and 100 ppm in chewing gum. It is approved for use in food packaging materials, provided that no more than 50 ppm can be recovered in the food (Federal Register, 1979; US CFR, 1976, 1977, 1979). The daily per capita intake of propyl gallate has been estimated to be 1.4 - 3.88 mg (LSRO, 1973).

Oral LD_{50} values of 3,800 mg/kg for albino rats and 2,000-3,500 mg/kg for mice (strain unspecified) have been reported for propyl gallate (Lehman et al., 1951; Orten et al., 1948). No toxic effects were observed in groups of 30-35 male or female albino mice fed diets containing 5,000 or 10,000 ppm propyl gallate for 90 days (Dacre, 1974). When rats (strain unspecified) were fed diets containing 5,000 or 10,000 ppm propyl gallate for 2 years, 10%-12% growth retardation was found in the groups receiving the high dose (Lehman et al., 1951). Reduced food intake and growth retardation were observed in albino rats fed diets containing 11,700 or 23,400 ppm propyl gallate for 71 and 43 weeks, respectively (Orten et al., 1948). Forty percent of the animals fed the higher dose died within 4 weeks; tubular damage was found in the kidneys of these animals. Other than growth retardation, no compound-related effects (gross or microscopic) were seen in the survivors.

Propyl gallate is metabolized in rats to gallic acid, which is further metabolized to 4-0-methyl gallic acid (Booth et al., 1959; Dacre, 1974). Tannic acid, found in tea, cocoa, and coffee, is also metabolized in rats to gallic acid (Archer et al., 1977; Booth et al., 1959). Humans consume considerable amounts of gallic acid as a consequence of their consumption of these foods (Singleton and Katzer, 1973). Pyrogallol detected in human urine was probably derived from gallic acid by decarboxylation in the digestive tract (Tempsett, 1958). Human subjects ingesting tannic acid excreted 3,4-dihydroxy- and 3-methoxy-4-hydroxybenzoic acid (Tempsett, 1959).

Propyl gallate was reported to retard growth of ascites tumors and hepatomas in mice given a single (180 mg) dose (Gorbacheva et al.,1966), and induction of mouse lung adenoma by morpholine and sodium nitrite was strongly inhibited by gallic acid (Mirvish et al., 1975).

Propyl gallate inhibited *in vitro* N-demethylation of various drugs, hydroxylation of aryl hydrocarbons, and biosynthesis of prostaglandin

E_2 and F_{2a} (McDonald-Gibson et al., 1976; Yang and Strickhart, 1974; Carpenter, 1981). Propyl gallate enhanced the mutagenicity of N-hydroxy-2-acetylaminofluorene and 4-nitroquinoline-1-oxide for *Salmonella typhimurium* TA 98 and TA 100; propyl gallate alone was not mutagenic for these two strains of *Salmonella typhimurium* (Rosin and Stich, 1980). Propyl gallate did not induce any mutagenic response in *S. typhimurium* (tester strains TA 98, 100, 1535, and 1537) with and without metabolic activation. Exogenous metabolic activation was provided by 9,000 x g liver supernatant (S-9) fractions from Aroclor 1254-induced male Sprague-Dawley rats and male Syrian golden hamsters (NTP, 1982). Gallic acid, a metabolite of propyl gallate, was not mutagenic for *Salmonella typhimurium* TA 98, TA 100, and TA 1537, with or without metabolic activation (Wang and Klemencic, 1979). Propyl gallate was not teratogenic for Wistar rats (Tanaka et al., 1979).

The Bioassay Program tested propyl gallate because of widespread human exposure through its use as a food additive and because a previous 2-year study (Lehman et al., 1951) was considered to be inadequate because of the small numbers (5-15 per dose group) of animals used.

II. MATERIALS AND METHODS

CHEMICAL ANALYSIS

PRECHRONIC STUDIES

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDIES

Study Design

Preparation of Test Diets

Clinical Examinations and Pathology

Data Recording and Statistical Methods

CHEMICAL ANALYSIS

Food-grade propyl gallate was obtained in two batches. Lot No. 2185, from Harshaw Chemical Co. (Philadelphia, PA), was used for the prechronic studies and the first 22 months of the chronic studies; and Lot No. 831, from Tennessee Eastman Co. (Kingsport, TN) was used for the last 2 months of the chronic studies.

Purity and identity analyses were performed at Midwest Research Institute. The results were consistent with the literature values for propyl gallate (Appendix E). The results of thin-layer, vapor-phase, and high-performance liquid chromatography indicated that each lot contained only one component. No gallic acid was detected in either lot. Propyl gallate was stored in the dark at 5°C. Southern Research Institute reanalyzed the chemical periodically throughout the studies by infrared and gas-liquid chromatography (using a 3% Dexsil 300 column) or high-performance liquid chromatography (using conditions similar to those described in Appendix E, Section F3). The results of these analyses indicated no change in composition.

Stability of propyl gallate mixed in feed and stored at various temperatures was tested. The results indicate that this compound is stable for 2 weeks at temperatures up to 45°C (Appendix F).

PRECHRONIC STUDIES

Male and female F344/N rats and B6C3F$_1$ mice used in the prechronic studies were obtained from Frederick Cancer Research Center (Frederick, MD). Animals were approximately 5 weeks old when the study began. Details of animal maintenance are presented in Table 1.

Doses for the single-dose study were prepared by mixing a weighed amount of propyl gallate and a solution of 20% ethanol in distilled water with a plunger attached to a high-speed drill until a suspension was obtained. In the 14-day study and the 13-week study, weighed quantities of propyl gallate and feed were shaken together by hand vigorously until a uniform mixture was obtained; this premix was then added to the remaining feed and mixed for 15 minutes in a Patterson-Kelly® twin-shell blender.

Single-Dose Study

Groups of five rats and five mice of each sex were given a single dose of propyl gallate (125, 250, 500, 1,000, or 2,000 mg/kg) in 20% ethanol in water by gavage. No controls were used. Animals were observed twice daily for mortality during the 15-day test period. Necropsies were not performed.

Fourteen-Day Study

Groups of five males and five females of each species were fed diets containing 6,000, 12,500, 25,000, 50,000, or 100,000 ppm propyl gallate for 14 days. No controls were used. Animals were observed twice daily for mortality and were weighed weekly. Necropsies were performed on all animals.

Thirteen-Week Study

Thirteen-week studies were conducted to evaluate the cumulative toxicity of propyl gallate, to identify potential target organs, and to determine the concentrations to be used in the 2-year studies.

Groups of 10 rats of either sex were fed diets containing 0, 1,500, 3,000, 6,000, 12,500, or 25,000 ppm propyl gallate; groups of 10 mice of either sex were fed diets containing 0, 800, 1,500, 3,000, 6,000, or 12,500 ppm. Animals were observed twice daily for mortality, and individual animals were weighed weekly.

At the end of the 13-week study, survivors were killed with carbon dioxide. Necropsies were performed on all animals not autolyzed or cannibalized. The following specimens were examined microscopically for animals in control and high-dose groups: gross lesions, tissue masses, abnormal lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, thymus, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duode-

num, jejunum, ileum, colon, cecum, mesenteric and mandibular lymph nodes, liver, gall bladder (mice), pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, and pituitary. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

CHRONIC STUDIES

Study Design

Three-week-old male and female F344/N rats and 5-week-old male and female B6C3F1 mice were obtained from Harlan Industries (Indianapolis, IN) and observed for 15 days. Animals were assigned to cages according to a table of random numbers, and cages were assigned to control and dosed groups according to a second table of random numbers. Rats were 5 weeks old and mice were 8 weeks old when the study began.

Groups of 50 rats and 50 mice of each sex were fed diets containing 0, 6,000, or 12,000 ppm propyl gallate for 103 weeks (Table 1). Rats and mice were housed in the same room; no other chemicals were being tested in that room.

Preparation of Test Diets

Samples of feed mixtures containing 99,000 ppm propyl gallate were analyzed at Midwest Research Institute and were found to be stable at temperatures up to 45°C (Appendix F). Test diets were formulated by mixing a small amount of feed and the required amount of propyl gallate in a plastic bag and then shaking vigorously by hand. This premix and the required amount of animal meal were then mixed for 15 minutes in a Patterson-Kelly® twin-shell blender equipped with an intensifier bar. Test diets were stored in the dark for no longer than 14 days (7 days at 5°C followed by no more than 7 days at 21°-23°C). The concentrations of propyl gallate were measured in 55 samples selected at random from test diets administered during the chronic study (Appendix G). The results of these analyses indicate that all diets were formulated correctly. Five of the 55 samples were reanalyzed at other laboratories, and the results for all but one sample confirmed the results from Southern Research Institute. There was no apparent reason for the different results obtained from one sample.

Clinical Examinations and Pathology

All animals were observed twice daily for morbidity and mortality. Clinical signs were recorded monthly. Body weights and feed consumption by cage were recorded every week 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 with carbon dioxide and necropsied.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following were examined microscopically: tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone, bone marrow, costochondral junction (rib), thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, mesenteric lymph nodes, liver, external and middle ear, gallbladder (mice), pancreas, spleen, kidneys, adrenals, eyes, urinary bladder, seminal vesicles/prostate/ testes or ovaries/uterus/vagina/fallopian tubes, nasal cavity, brain, pituitary, and spinal cord.

Necropsies were performed on all animals not autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to the number of animals that

were placed on study in each group. The classification of neoplastic nodules was done according to the recommendations of Squire and Levitt (1975) and the National Academy of Sciences (1980). When the pathology examination was completed, the slides, individual animal data records, and summary tables were sent to an independent quality assurance laboratory. Individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10% of the animals were evaluated by an experienced rodent pathologist. Slides of all target tissues and those on which the original and quality assurance pathologists disagreed were submitted to the Chairperson of the Pathology Working Group (PWG) for evaluation. Representative slides selected by the PWG Chairperson were reviewed blindly by the PWG's experienced rodent pathologists, who reached a consensus and compared their findings with the original diagnoses. When conflicts were found, the PWG sent the appropriate slides and their comments to the original pathologist for review. (This procedure has been described, in part, by Ward et al., 1978.) The final diagnosis represents a consensus of contractor pathologists and the NTP Pathology Working Group.

Data Recording and Statistical Methods

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

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

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

For the statistical analysis of tumor incidence data, two different methods of adjusting for intercurrent mortality were employed. Each used the classical methods for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high-and low-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, week 93 to the week before terminal kill, and the terminal kill period. The denominators of these proportions were the number of animals actually autopsied during the time interval. The individual time interval comparisons were then combined by the previously described methods to obtain a single overall result. (See Peto et al., 1980, for the computational details of both methods.)

In addition to these tests, one other set of statistical analyses was carried out and reported in the tables analyzing primary tumors; the Fisher's exact test for pairwise comparisons and the Cochran-Armitage linear trend test for dose-response trends (Armitage, 1971; Gart et al., 1979). 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.

TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Experimental Design				
Size of Test Groups	5 males and 5 females of each species	5 males and 5 females of each species	10 males and 10 females of each species	50 males and 50 females of each species
Doses	125, 250, 500, 1,000, or 2,000 mg/kg body weight propyl gallate in 20% ethanol in distilled water by gavage; each animal received 10 ml/kg body weight	6,000, 12,500, 25,000, 50,000, or 100,000 ppm propyl gallate in feed, available *ad libitum*	Rats: 0, 1,500, 3,000, 6,000, 12,500, or 25,000 ppm propyl gallate in feed, available *ad libitum* Mice: 0, 800, 1,500, 3,000, 6,000, or 12,500 ppm propyl gallate in feed, available *ad libitum*	0, 6,000, or 12,000 ppm propyl gallate in feed, available *ad libitum*
Duration of Dosing	Single dose; killed on day 16	14 days; killed on days 16-17	91 days; killed on days 92-96	721 days; killed on days 735-749
Type and Frequency of Observation	Observed twice daily for mortality and morbidity	Observed twice daily for mortality and morbidity	Observed twice daily for mortality and morbidity	Observed twice daily for signs of morbidity and mortality
Necropsy and Histological Examination	None performed	Necropsies were performed on all animals;	Necropsies were performed on all animals; all controls and all animals in the highest dose group were examined histologically	Necropsies were performed on all animals, and all animals were examined histologically
Animal and Animal Maintenance				
Species	F344/N rats; $B6C3F_1$ mice	F344/N rats; $B6C3F_1$ mice	F344/N rats; $B6C3F_1$ mice	F344/N rats; $B6C3F_1$ mice
Animal Source	Frederick Cancer Research Center, Frederick, MD	Same as single-dose study	Same as single-dose study	Harlan Industries Indianapolis, IN
Time Held Before Start of Test	Rats: 8 days Mice: 7 days	8 days	6 days	15 days

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

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Age When Placed on Study	5 weeks	5 weeks	5 weeks	Rats: 5 weeks Mice: 8 weeks
Age When Killed	7-8 weeks	7-8 weeks	18-19 weeks	Rats: 110-112 weeks Mice: 113-115 weeks
Method of Animal Distribution	Assigned to cage by sex and species according to a table of random numbers; then assigned to control and dosed groups according to a second table of random numbers	Same as single-dose study	Same as single-dose study	Same as single-dose study
Feed	Wayne Lab Blox® Allied Mills, Inc. Chicago, IL	Same as single-dose study	Same as single-dose study	Same as single-dose study
Bedding	Betta-Chips® Northeastern Products Corp. (Warrensburg, NY)	Betta-Chips® Northeastern Products Corp. (Warrensburg, NY); bedding changed twice weekly	Same as 14-day study	Same as 14-day study
Water	Tap water was available in bottles *ad libitum*	Rats: Same as single-dose Study Mice: Automatic watering system, Edstrom Industries (Waterford, WI)	Same as 14-day study for mice	Same as 14-day study for mice
Cages	Stainless steel, Hahn Roofing & Sheet Metal Co. (Birmingham, AL)	Stainless steel, Hahn Roofing & Sheet Metal Co. (Birmingham, AL); cages changed twice weekly	Polycarbonate; Lab Products, Inc. (Garfield, NJ); cages changed twice weekly	Same as 13-week study

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

	Single-Dose Study	14-Day Study	13-Week Study	Chronic Study
Cage Filters	Reemay spun-bonded polyester filters, Dupont style #2024, Snow Filtration (Cincinnati, OH)	Rats: disposable filter bonnets; Mice: Same as single-dose study	Same as single-dose study	Same as single-dose study
Animals per Cage	Five	Five	Five	Five
Animal Room Environment	20°-24°C; 38%-42% relative humidity; room air was changed 15 times per hour; 9 hours of fluorescent light per day	Rats: Same as single-dose study Mice: 21°-23°C; 40%-60% relative humidity; air was changed 15 times per hour; 12 hours of fluorescent light per day	21°-23°C; 40%-60% relative humidity; room air was changed 15 times per hour; 12 hours of fluorescent light per day	21°-23°C; 30%-60% relative humidity; room air was changed a minimum of 15 times per hour; 12 hours of fluorescent light per day
Other Chemicals on Test in the Same Room	D-Mannitol, stannous chloride, ziram, ethyl acrylate, allyl isothiocyanate, zearalenone	Rats: D-Mannitol, ziram, zearalenone Mice: Zearalenone	None	None
Chemical/Vehicle/ Feed Mixture				
Preparation	Weighed propyl gallate and a solution of 20% ethanol in distilled water were mixed with a plunger attached to a high speed drill until a suspension was obtained (mixing time was not recorded)	Weighed quantities of propyl gallate and feed were shaken together vigorously until a uniform mixture was obtained; this premix was then added to the remaining feed and mixed for 15 minutes in an 8-qt. Patterson-Kelly® Twin Shell blender	Same as 14-day study	Same as 14-day study, but premix was added added to the remaining feed and mixed in a 16-qt Patterson-Kelly® twin shell blender, equipped with a intensifier bar
Maximum Storage Time	Not stored	14 days	14 days	14 days
Storage Conditions	Not stored	Sealed plastic containers in animal treatment rooms	Same as 14-day study	Double-thickness plastic bags inside sealed, rigid plastic containers at 5°C for 1 week and at 22°C for the 2nd week

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

Single-Dose Study

Fourteen-Day Study

Thirteen-Week Study

CHRONIC STUDIES

Body Weights and Clinical Signs

Survival

Pathology and Statistical Analyses of Results

PRECHRONIC STUDIES

Single-Dose Study

One male rat receiving 1,000 mg/kg propyl gallate died (on day 5). No other deaths occurred, and no compound-related effects were observed.

Fourteen-Day Study

All rats receiving 100,000 ppm propyl gallate died, and one male receiving 50,000 ppm died (Table 2). Male rats administered 50,000 ppm lost weight. Weight gain by female rats receiving 50,000 ppm was less than 25% of that for groups receiving lower doses. However, feed consumption by male rats fed 50,000 was comparable with that of rats fed lower doses. Feed consumption by all dosed groups was higher than that seen in untreated controls of similar age and weight at this laboratory.

All rats receiving 100,000 ppm and 5/5 males and 2/5 females receiving 50,000 ppm had wet fur or a yellow-brown, crusty exudate in the genital region. This yellow-brown color may have been due to the reaction of propyl gallate or one of its metabolites with iron salts present in the exudate.

The results of this study led to the selection of 0, 1,500, 3,000, 6,000, 12,500, and 25,000 ppm dose levels of propyl gallate in feed for use in the 13-week study.

TABLE 2. SURVIVAL AND MEAN BODY WEIGHTS OF RATS FED DIETS CONTAINING PROPYL GALLATE FOR 14 DAYS

Dose (ppm)	Survival *(a)*	Mean Body Weights (grams)			Average Daily Feed Consumption (grams) *(c,d)*	Average Daily Feed Consumption (grams) *(e)*
		Initial	Final	Change *(b)*		
Males						
6,000	5/5	87.6 ± 3.2	145.4 ± 1.5	+57.8 ± 2.9	25.5	25.0
12,500	5/5	74.6 ± 3.9	136.8 ± 4.4	+62.2 ± 1.6	27.0	26.4
25,000	5/5	81.6 ± 3.7	128.4 ± 4.3	+46.8 ± 1.0	27.4	27.5
50,000	4/5	78.0 ± 3.4	74.3 ± 7.7	- 3.8 ± 4.6	26.6	34.6
100,000	0/5	*(f)*	*(f)*	*(f)*	23.8	
Females						
6,000	5/5	70.0 ± 2.9	108.0 ± 2.5	+38.0 ± 0.6	24.1	22.2
12,500	5/5	70.0 ± 3.6	104.4 ± 3.4	+34.4 ± 2.2	23.4	21.3
25,000	5/5	73.4 ± 2.3	103.4 ± 2.5	+30.0 ± 2.0	26.1	28.0
50,000	5/5	70.2 ± 3.7	77.4 ± 6.4	+ 7.2 ± 3.3	18.8	23.3
100,000	0/5	*(f)*	*(f)*	*(f)*	19.3	

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study
(b) Mean body weight change of the survivors of the group ± standard error of the mean
(c) Day 1 through day 7
(d) Average daily feed consumption by untreated rats of comparable age and weight at this laboratory is 16 grams for males and 12 grams for females.
(e) Day 7 through day 14
(f) No data are presented due to the 100% mortality in this group

Thirteen-Week Study

One female rat receiving 12,500 ppm and one control female died (Table 3). Males receiving 12,500 or 25,000 ppm and females receiving 25,000 ppm had weight gain depressions of 10% or more when compared with weight gains for controls. Feed consumption generally increased as the dose increased. All rats administered 25,000 ppm had dirty tails, suggestive of digestive tract disturbances.

The duodenal mucosa was reddish in 8/10 males and 6/10 females fed diets containing 25,000 ppm propyl gallate and the stomach wall was thickened in 4/10 males and 2/10 females receiving 25,000 ppm. At this same dietary concentration, necrosis and ulceration of the mucosal surface of the stomach and a moderate to severe granulomatous inflammatory response in the submucosa and muscular wall of the stomach were observed in 4/10 males and 1/10 females. No stomach or duodenal lesions were observed during histopathologic evaluations of male and female rats in the 6,000- and 12,500-ppm dose groups.

Doses of 6,000 and 12,000 ppm propyl gallate were selected for rats in the 2-year study because of the gastrointestinal effects observed in rats administered 25,000 ppm in the 13-week study.

TABLE 3. SURVIVAL, MEAN BODY WEIGHTS, AND FEED CONSUMPTION OF RATS FED DIETS CONTAINING PROPYL GALLATE FOR 13 WEEKS

Dose (ppm)	Survival *(a)*	Mean Body Weight (grams)			Weight Change Relative to Controls *(c)* (percent)	Average Daily Feed Consumption (grams)
		Initial	Final	Change *(b)*		
Males						
0	10/10	88.3 ±4.7	333.1 ± 10.5	+244.8 ±9.4		21.1
1,500	10/10	84.0 ±3.5	319.9 ± 5.0	+235.9 ± 4.8	- 3.6	21.2
3,000	10/10	82.6 ±3.3	325.5 ± .7	+242.9 ± 7.4	- 0.8	20.8
6,000	10/10	84.6 ±3.6	314.2 ± 6.1	+229.6 ± 4.3	- 6.2	22.9
12,500	10/10	82.5 ±3.5	301.1 ± 9.0	+218.6 ± 7.6	-10.7	26.5
25,000	10/10	76.4 ±2.4	275.4 ± 5.3	+199.0 ±5.5	-18.7	27.7
Females						
0	9/10	71.8 ±1.3	185.7 ± 2.4	+113.9 ± 2.6		12.1
1,500	10/10	71.3 ±1.9	181.9 ± 3.4	+110.6 ±3.0	- 2.9	12.7
3,000	10/10	72.9 ±1.9	188.6 ± 3.3	+115.7 ± 3.9	+ 1.6	13.6
6,000	10/10	71.6 ±2.6	183.4 ± 2.4	+111.8 ± 3.4	- 1.8	15.4
12,500	9/10	75.1 ±1.9	185.1 ± 4.0	+110.0 ± 3.3	- 3.4	18.7
25,000	10/10	73.7 ±1.2	173.5 ± 2.5	+ 99.8 ± 2.2	-12.4	22.3

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study.

(b) Mean body weight of survivors of the group ± standard error of the mean.

(c) Weight change of the dosed group relative to that of the controls =

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

CHRONIC STUDIES

Body Weights and Clinical Signs

Throughout the study, mean body weights of dosed rats of each sex were lower than those of the controls (Figure 1 and Table 4). At 104 weeks, mean body weights of low- and high-dose rats were 4% and 8% lower than those of the controls for males and 11% and 19% lower than those of the controls for females. The depression in mean body weight gain was dose related. The average daily feed consumption per rat by low- and high-dose rats was 94% and 98% that of the controls for males and 95% and 115% of that of the controls for females (Table 5). No compound-related clinical signs were observed.

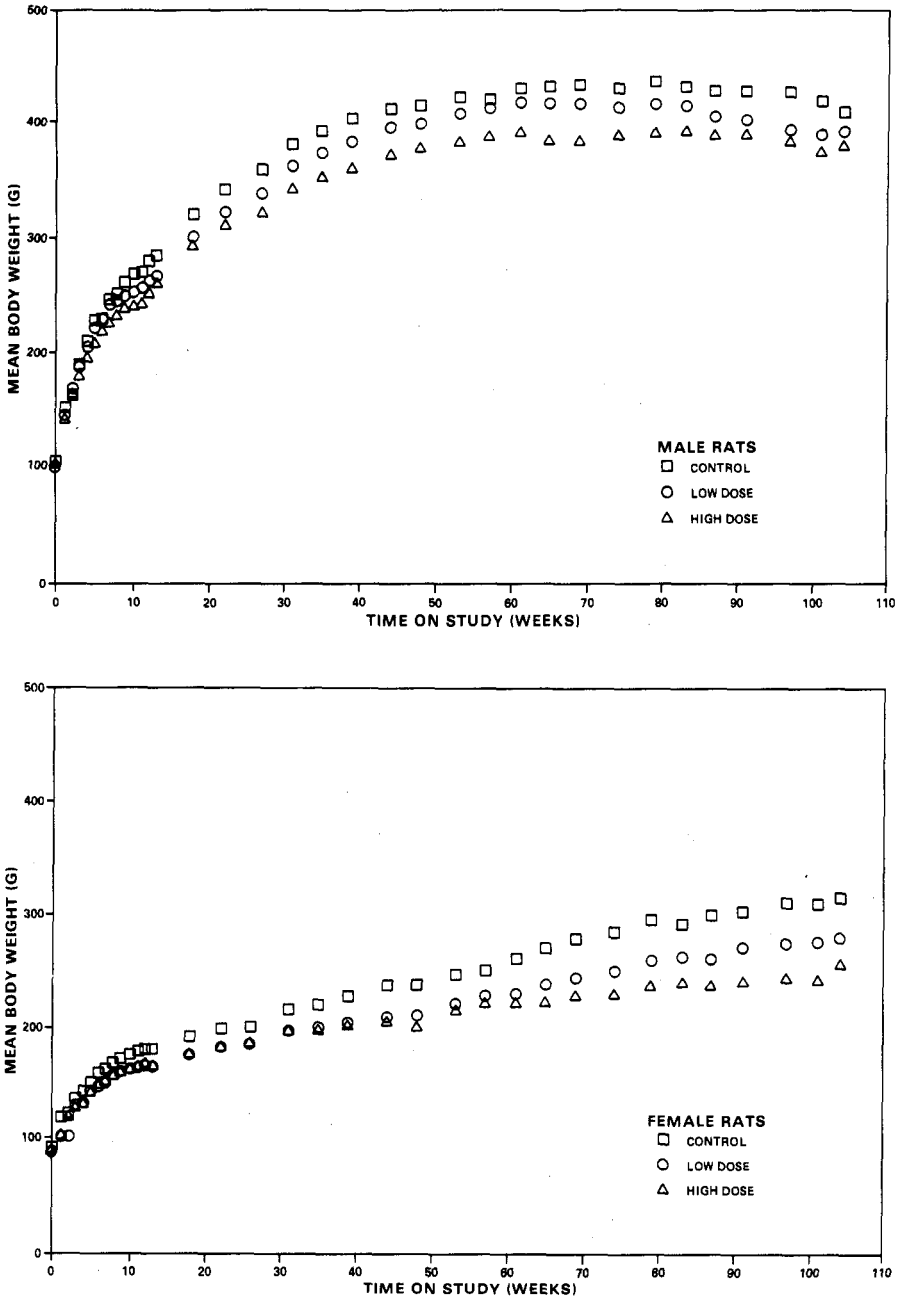


Figure 1. Growth Curves for Rats Fed Diets Containing Propyl Gallate

TABLE 4. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF RATS FED DIETS CONTAINING PROPYL GALLATE IN THE CHRONIC STUDY

	Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males					
0	104 *(b)*	99 *(b)*	103 *(b)*		
1	47	45	37	-4	-21
22	239	223	208	-7	-13
44	308	296	268	-4	-13
65	328	317	286	-3	-13
83	329	316	289	-4	-12
104	305	292	274	-4	-10
Final Body Weight	409	391	377	-4 *(c)*	-8 *(c)*
Females					
0 *(b)*	93 *(b)*	89 *(b)*	92 *(b)*		
1	24	23	21	-4	-13
22	106	94	91	-11	-14
44	146	122	114	-16	-22
65	179	150	132	-16	-26
83	205	175	149	-15	-27
104	222	191	164	-14	-26
Final Body Weight	315	280	256	-11 *(c)*	-19 *(c)*

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

(b) Initial weight

(c) Final body weight relative to controls (percent)

TABLE 5. FEED CONSUMPTION BY RATS RECEIVING PROPYL GALLATE IN THE CHRONIC STUDY

	Control	Low Dose		High Dose	
Week	Grams Feed/ Day *(a)*	Grams Feed/ Day *(a)*	Low/ Control *(b)*	Grams Feed/ Day *(a)*	High/ Control *(b)*
Males					
4 *(c)*					
22	15.0	14.0	0.9	16.0	1.1
44	17.0	15.0	0.9	15.0	0.9
65	16.4	15.5	0.9	15.4	0.9
83	17.6	16.6	0.9	15.5	0.9
104	16.5	16.4	1.0	19.7	1.2
Mean	16.5	15.5	0.9	16.3	1.0
SD *(d)*	1.0	1.1	0.0	1.9	0.1
CV *(e)*	6.1	7.1	0.0	11.7	10.0
Females					
4 *(c)*					
22	10.0	9.0	0.9	10.0	1.0
44	11.0	10.0	0.9	10.0	0.9
65	9.6	9.6	1.0	10.6	1.1
83	12.5	12.5	1.0	14.5	1.2
104	14.3	13.2	0.9	20.8	1.5
Mean	11.5	10.9	0.9	13.2	1.1
SD *(d)*	1.9	1.9	0.1	4.7	0.2
CV *(e)*	16.5	17.4	11.1	35.6	18.3

(a) Grams of feed consumed per animal per day.

(b) Grams of feed consumed per day by the dosed group divided by that for the controls.

(c) Feed consumption not measured

(d) Standard deviation

(e) Coefficient of variation = (standard deviation/mean) x 100

Survival

Estimates of the probabilities of survival of male and female rats fed diets containing 0, 6,000, or 12,000 ppm propyl gallate are shown by the Kaplan and Meier curves in Figure 2. No significant differences in survival were observed between groups of male rats or between groups of female rats. It is, however, noteworthy that survival during the last 10 months of the study was slightly better for high-dose rats than for low-dose or control rats of each sex.

In male rats, 39/50 (78%) of the controls, 38/50 (76%) of the low-dose group, and 44/50 (88%) of the high-dose group lived to the end of the study at 105-107 weeks. In female rats, 39/50 (78%) of the controls, 38/50 (76%) of the low-dose group, and 42/50 (84%) of the high-dose group lived to the end of the study at 105-107 weeks. These incidences include one control male that died during the terminal kill period.

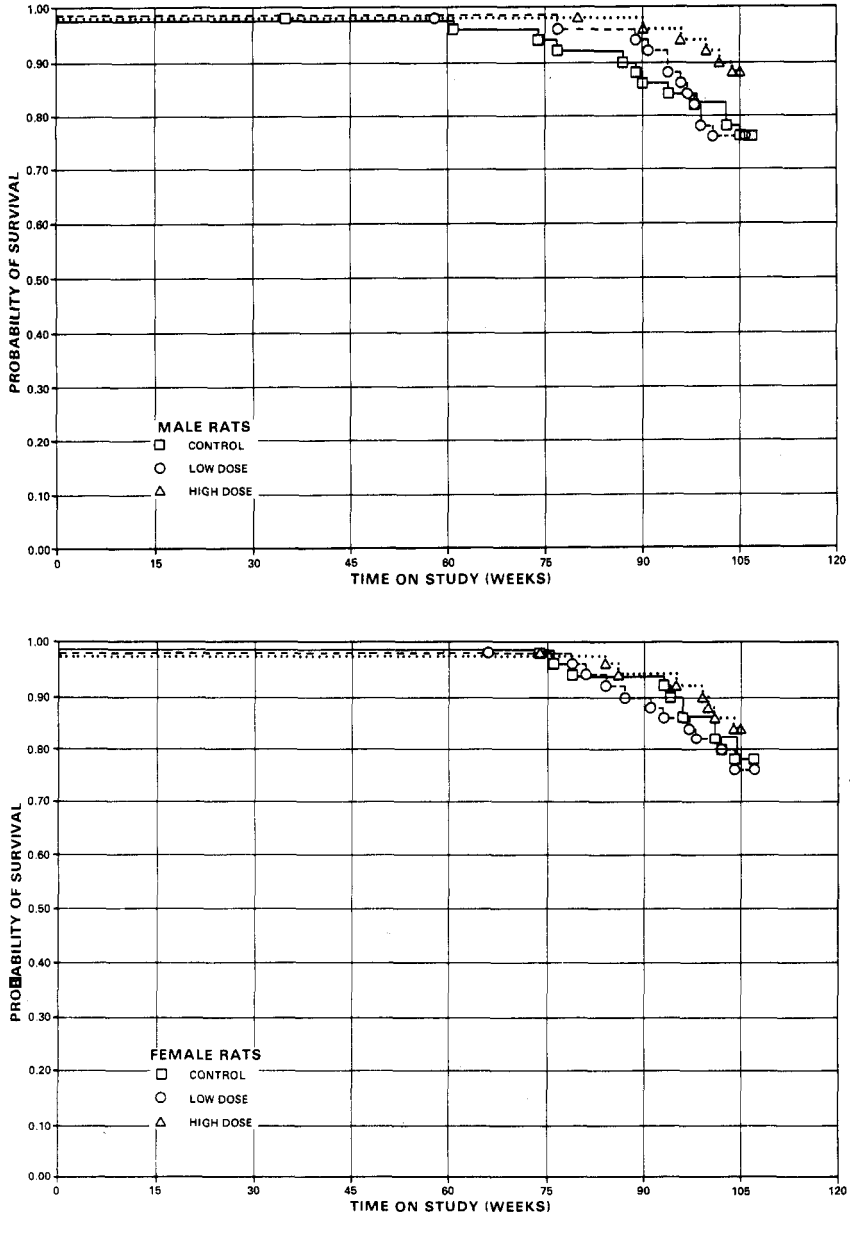


Figure 2. Survival Curves for Rats Fed Diets Containing Propyl Gallate

Pathology and Statistical Analyses of Results

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

Thyroid: Two follicular-cell carcinomas and one follicular-cell adenoma were found in high-dose male rats; none were observed in male controls, male low-dose rats, or female rats. The combined incidence of male rats with either follicular-cell adenomas or carcinomas was statistically significant ($P<0.05$) by the trend tests, but the incidence in the high-dose group was not statistically different from that in the control group in a direct comparison.

Mammary Gland: Three of 50 high-dose female rats had adenomas; none were observed in the control and low-dose groups. The tests for trend were all statistically significant ($P<0.05$), but the comparisons between the high-dose and control groups were not significant. The incidence of control females with fibroadenomas (11/50, 22%) was significantly higher ($P\leq0.011$) than that in the low-dose group (2/50, 4%) and somewhat higher than that observed in the high-dose group (5/50, 10%).

Preputial Gland: Adenomas, adenocarcinomas, or carcinomas (combined) were observed in 1/50 control males, 8/50 low-dose males, and 0/50 high-dose males. The tests between the low-dose and control groups were all significant ($P\leq0.040$), but there was no evidence of a positive dose response.

Pancreas: The combined incidence of islet-cell adenomas and carcinomas was higher in low-dose males than in control and high-dose males (control, 2/50, 4%; low-dose, 9/50, 18%; high-dose 4/50, 8%). The tests between the low-dose and control groups were all statistically significant ($P<0.05$), but neither the dose-response trend nor the high-dose effect was statistically significant.

Uterus: A statistically significant (P=0.049, incidental tumor test) positive trend was observed in the incidence of female rats with endometrial stromal polyps (6/50, 12%; 8/50, 16%; 13/50, 26%). However, none of the pairwise comparisons of incidence in either dose group with the control group were statistically significant.

Adrenal: Pheochromocytomas were observed in 4/50 control males, 13/48 low-dose males, and 8/50 high-dose males. The tests between the low-dose and control groups were all statistically significant ($P\leq0.017$), but no trend tests or comparisons between the high-dose and control groups were significant.

Brain: One low-dose female rat had an astrocytoma and another rat in the same group had a glioma.

Hematopoietic System: A negative trend was observed in the incidences of male rats with leukemia of the hematopoietic system (controls, 16/50, 32%; low-dose, 7/50, 14%; high-dose, 6/50, 12%). All tests for trend were significant ($P\leq0.009$), and the incidence in the high-dose group differed significantly from that in the controls ($P\leq0.015$). Hematopoietic tumors did not occur in significant proportions in female rats.

Liver: The incidences of dosed male rats with cytoplasmic vacuolization were higher than was the incidence in the controls (control, 4/50, 8%; low-dose, 22/50, 44%; high-dose, 22/50, 44%). The severity of this lesion ranged from mild/minimal to moderate. The vacuoles appeared to be composed primarily of glycogen, but fat was also present. The incidences of liver tumors were similar among groups (male: 2/50, 1/50, 1/50; female: 0/50, 1/50; 0/50).

Eye: An increased incidence of nonneoplastic lesions, consisting of retinopathy and cataract formation, was observed in high-dose male rats and low-dose female rats. Retinopathy was seen in 12/50 (24%) control males, 8/50 (16%) low-dose males, 35/50 (70%) high-dose males, 10/50 (20%) control females, 40/50 (80%) low-dose females, and 14/50 (28%) high-dose females. Cataract formation occurred in 12/50 (24%) control males, 4/50 (8%) low-dose males, 35/50 (70%) high-dose males, 8/50 (16%) control females, 39/50 (78%) low-dose females, and 13/50 (26%) high-dose females.

Prostate: Suppurative inflammation was observed at an increased incidence in high-dose male rats (controls, 17/50, 34%; low-dose, 18/46, 39%; high-dose, 30/50, 60%).

Kidney: Nephrosis was observed at an increased incidence in low-dose female rats (control, 8/50, 16%; low-dose, 28/50, 56%; high-dose, 4/50, 8%).

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

	Control	Low Dose	High Dose
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	16/50 (32%)	7/50 (14%)	6/50 (12%)
Adjusted *(c)*	36.1%	16.7%	13.6%
Terminal *(d)*	11/39 (28%)	4/38 (11%)	6/44 (14%)
Statistical Tests *(e)*			
Life Table	P=0.006N	P=0.041N	P=0.009N
Incidental Tumor Test	P=0.009N	P=0.023N	P=0.015N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.008N	P=0.028N	P=0.014N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	16/50 (32%)	8/50 (16%)	6/50 (12%)
Adjusted *(c)*	36.1%	18.4%	13.6%
Terminal *(d)*	11/39 (28%)	4/38 (11%)	6/44 (14%)
Statistical Tests *(e)*			
Life Table	P=0.006N	P=0.068N	P=0.009N
Incidental Tumor Test	P=0.011N	P=0.045N	P=0.015N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.009N	P=0.050N	P=0.014N
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	5/49 (10%)	8/48 (17%)	4/49 (8%)
Adjusted *(c)*	12.0%	19.9%	9.0%
Terminal *(d)*	3/38 (8%)	5/36 (14%)	3/43 (7%)
Statistical Tests *(e)*			
Life Table	P=0.358N	P=0.268	P=0.428N
Incidental Tumor Test	P=0.394N	P=0.371	P=0.477N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.438N	P=0.263	P=0.500N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	5/49 (10%)	10/48 (21%)	4/49 (8%)
Adjusted *(c)*	12.0%	23.1%	9.0%
Terminal *(d)*	3/38 (8%)	5/36 (14%)	3/43 (7%)
Statistical Tests *(e)*			
Life Table	P=0.360N	P=0.138	P=0.428N
Incidental Tumor Test	P=0.490N	P=0.160	P=0.477N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.441N	P=0.121	P=0.500N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	12/48 (25%)	8/50 (16%)
Adjusted *(c)*	9.8%	31.3%	17.4%
Terminal *(d)*	3/39 (8%)	11/37 (30%)	6/44 (14%)
Statistical Tests *(e)*			
Life Table	P=0.255	P=0.024	P=0.247
Incidental Tumor Test	P=0.232	P=0.030	P=0.221
Cochran-Armitage Trend, Fisher Exact Tests	P=0.172	P=0.022	P=0.178

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

	Control	Low Dose	High Dose
Adrenal: All Pheochromocytomas			
Tumor Rates			
Overall *(b)*	4/50 (8%)	13/48 (27%)	8/50 (16%)
Adjusted *(c)*	9.8%	34.0%	17.4%
Terminal *(d)*	3/39 (8%)	12/37 (32%)	6/44 (14%)
Statistical Tests *(e)*			
Life Table	P=0.262	P=0.013	P=0.247
Incidental Tumor Test	P=0.239	P=0.017	P=0.221
Cochran-Armitage Trend, Fisher Exact Tests	P=0.176	P=0.012	P=0.178
Thyroid: Follicular-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted *(c)*	0.0%	0.0%	6.6%
Terminal *(d)*	0/39 (0%)	0/38 (0%)	2/44 (5%)
Statistical Tests *(e)*			
Life Table	P=0.049	*(f)*	P=0.147
Incidental Tumor Test	P=0.038	*(f)*	P=0.138
Cochran-Armitage Trend, Fisher Exact Tests	P=0.037	*(f)*	P=0.121
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	2/50 (4%)	3/50 (6%)
Adjusted *(c)*	10.3%	5.3%	6.8%
Terminal *(d)*	4/39 (10%)	2/38 (5%)	3/44 (7%)
Statistical Tests *(e)*			
Life Table	P=0.358N	P=0.348N	P=0.434N
Incidental Tumor Test	P=0.358N	P=0.348N	P=0.434N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.417N	P=0.339N	P=0.500N
Thyroid: C-Cell Carcinoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	1/50 (2%)	1/50 (2%)
Adjusted *(c)*	7.4%	2.6%	2.3%
Terminal *(d)*	2/39 (5%)	1/38 (3%)	1/44 (2%)
Statistical Tests *(e)*			
Life Table	P=0.176N	P=0.313N	P=0.266N
Incidental Tumor Test	P=0.175N	P=0.253N	P=0.275N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.203N	P=0.309N	P=0.309N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	7/50 (14%)	3/50 (6%)	4/50 (8%)
Adjusted *(c)*	17.4%	7.9%	9.1%
Terminal *(d)*	6/39 (15%)	3/38 (8%)	4/44 (9%)
Statistical Tests *(e)*			
Life Table	P=0.149N	P=0.169N	P=0.199N
Incidental Tumor Test	P=0.149N	P=0.141N	P=0.204N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.196N	P=0.159N	P=0.262N

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

	Control	Low Dose	High Dose
Pancreatic Islets: Islet-Cell Adenoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	8/50 (16%)	2/50 (4%)
Adjusted *(c)*	0.0%	19.6%	4.5%
Terminal *(d)*	0/39 (0%)	6/38 (16%)	2/44 (5%)
Statistical Tests *(e)*			
Life Table	P=0.334	P=0.005	P=0.265
Incidental Tumor Test	P=0.318	P=0.009	P=0.265
Cochran-Armitage Trend, Fisher Exact Tests	P=0.274	P=0.003	P=0.247
Pancreatic Islets: Islet-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	2/50 (4%)	9/50 (18%)	4/50 (8%)
Adjusted *(c)*	5.1%	22.1%	9.1%
Terminal *(d)*	2/39 (5%)	7/38 (18%)	4/44 (9%)
Statistical Tests *(e)*			
Life Table	P=0.386	P=0.027	P=0.394
Incidental Tumor Test	P=0.374	P=0.040	P=0.394
Cochran-Armitage Trend, Fisher Exact Tests	P=0.309	P=0.026	P=0.339
Preputial Gland: Adenoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	5/50 (10%)	0/50 (0%)
Adjusted *(c)*	0.0%	12.6%	0.0%
Terminal *(d)*	0/39 (0%)	4/38 (11%)	0/44 (0%)
Statistical Tests *(e)*			
Life Table	P=0.564N	P=0.033	*(f)*
Incidental Tumor Test	P=0.574N	P=0.043	*(f)*
Cochran-Armitage Trend, Fisher Exact Tests	P=0.609	P=0.028	*(f)*
Preputial Gland: Adenoma, Adenocarcinoma, or Carcinoma			
Tumor Rates			
Overall *(b)*	1/50 (2%)	8/50 (16%)	0/50 (0%)
Adjusted *(c)*	2.6%	18.7%	0.0%
Terminal *(d)*	1/39 (3%)	4/38 (11%)	0/44 (0%)
Statistical Tests *(e)*			
Life Table	P=0.360N	P=0.021	P=0.476N
Incidental Tumor Test	P=0.375N	P=0.040	P=0.476N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.417N	P=0.015	P=0.500N
Testis: Interstitial-Cell Tumor			
Tumor Rates			
Overall *(b)*	47/50 (94%)	48/50 (96%)	50/50(100%)
Adjusted *(c)*	100.0%	100.0%	100.0%
Terminal *(d)*	39/39(100%)	38/38(100%)	44/44(100%)
Statistical Tests *(e)*			
Life Table	P=0.278N	P=0.425	P=0.323N
Incidental Tumor Test	P=0.450	P=0.657N	P=0.581
Cochran-Armitage Trend, Fisher Exact Tests	P=0.083	P=0.500	P=0.121

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

(a) Dosed groups received doses of 6,000 or 12,000 ppm of propyl gallate in the diet.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(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 prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).
(f) No statistical tests were done because there were no tumors observed in the dosed or untreated control group.

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

	Control	Low Dose	High Dose
Hematopoietic System: Undifferentiated Leukemia			
Tumor Rates			
Overall *(b)*	8/50 (16%)	5/50 (10%)	6/50 (12%)
Adjusted *(c)*	18.3%	12.3%	13.1%
Terminal *(d)*	5/39 (13%)	3/38 (8%)	3/42 (7%)
Statistical Tests *(e)*			
Life Table	P=0.295N	P=0.299N	P=0.352N
Incidental Tumor Test	P=0.402N	P=0.272N	P=0.444N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.326N	P=0.277N	P=0.387N
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	16/50 (32%)	14/49 (29%)	16/50 (32%)
Adjusted *(c)*	36.8%	31.9%	36.2%
Terminal *(d)*	12/39 (31%)	9/38 (24%)	14/42 (33%)
Statistical Tests *(e)*			
Life Table	P=0.460N	P=0.453N	P=0.497N
Incidental Tumor Test	P=0.513N	P=0.354N	P=0.573N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.543	P=0.440N	P=0.585
Pituitary: Carcinoma			
Tumor Rates			
Overall *(b)*	1/50 (2%)	3/49 (6%)	0/50 (0%)
Adjusted *(c)*	2.6%	7.6%	0.0%
Terminal *(d)*	1/39 (3%)	2/38 (5%)	0/42 (0%)
Statistical Tests *(e)*			
Life Table	P=0.359N	P=0.300	P=0.485N
Incidental Tumor Test	P=0.399N	P=0.275	P=0.485N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.379N	P=0.301	P=0.500N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	17/50 (34%)	17/49 (35%)	16/50 (32%)
Adjusted *(c)*	39.1%	38.2%	36.2%
Terminal *(d)*	13/39 (33%)	11/38 (29%)	14/42 (33%)
Statistical Tests *(e)*			
Life Table	P=0.377N	P=0.542	P=0.413N
Incidental Tumor Test	P=0.435N	P=0.544N	P=0.485N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.458N	P=0.555	P=0.500N
Adrenal: Pheochromocytoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	1/50 (2%)	3/50 (6%)
Adjusted *(c)*	9.8%	2.6%	7.1%
Terminal *(d)*	3/39 (8%)	1/38 (3%)	3/42 (7%)
Statistical Tests *(e)*			
Life Table	P=0.382N	P=0.191N	P=0.464N
Incidental Tumor Test	P=0.410N	P=0.206N	P=0.501N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.412N	P=0.181N	P=0.500N

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

	Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	8/48 (17%)	2/50 (4%)
Adjusted *(c)*	10.3%	20.7%	4.5%
Terminal *(d)*	4/39 (10%)	7/37 (16%)	1/42 (2%)
Statistical Tests *(e)*			
Life Table	P=0.269N	P=0.155	P=0.305N
Incidental Tumor Test	P=0.271N	P=0.204	P=0.345N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.304N	P=0.159	P=0.339N
Thyroid: C-Cell Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	6/50 (12%)	8/48 (17%)	3/50 (6%)
Adjusted *(c)*	15.4%	20.7%	6.8%
Terminal *(d)*	6/39 (15%)	7/37 (19%)	2/42 (5%)
Statistical Tests *(e)*			
Life Table	P=0.184N	P=0.346	P=0.209N
Incidental Tumor Test	P=0.185N	P=0.421	P=0.236N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.217N	P=0.355	P=0.243N
Mammary Gland: Fibroadenoma			
Tumor Rates			
Overall *(b)*	11/50 (22%)	2/50 (4%)	5/50 (10%)
Adjusted *(c)*	27.3%	5.3%	11.6%
Terminal *(d)*	10/39 (26%)	2/38 (5%)	4/42 (10%)
Statistical Tests *(e)*			
Life Table	P=0.036N	P=0.010N	P=0.067N
Incidental Tumor Test	P=0.044N	P=0.011N	P=0.084N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.046N	P=0.007N	P=0.086N
Mammary Gland: Adenoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted *(c)*	0.0%	0.0%	7.1%
Terminal *(d)*	0/39 (0%)	0/38 (0%)	3/42 (7%)
Statistical Tests *(e)*			
Life Table	P=0.043	(f)	P=0.135
Incidental Tumor Test	P=0.043	(f)	P=0.135
Cochran-Armitage Trend, Fisher Exact Tests	P=0.037	(f)	P=0.121
Preputial Gland: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	2/50 (4%)	1/50 (2%)	3/50 (6%)
Adjusted *(c)*	5.1%	2.5%	7.1%
Terminal *(d)*	2/39 (5%)	0/38 (0%)	3/42 (7%)
Statistical Tests *(e)*			
Life Table	P=0.430	P=0.506N	P=0.534
Incidental Tumor Test	P=0.394	P=0.539N	P=0.534
Cochran-Armitage Trend, Fisher Exact Tests	P=0.400	P=0.500N	P=0.500

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

	Control	Low Dose	High Dose
Uterus: Endometrial Stromal Polyp			
Tumor Rates			
Overall *(b)*	6/50 (12%)	8/50 (16%)	13/50 (26%)
Adjusted *(c)*	15.4%	20.3%	29.5%
Terminal *(d)*	6/39 (15%)	7/38 (18%)	11/42 (26%)
Statistical Tests *(e)*			
Life Table	P=0.067	P=0.367	P=0.090
Incidental Tumor Test	P=0.049	P=0.352	P=0.068
Cochran-Armitage Trend, Fisher Exact Tests	P=0.046	P=0.387	P=0.062
Uterus: Endometrial Stromal Polyp or Sarcoma			
Tumor Rates			
Overall *(b)*	7/50 (14%)	8/50 (16%)	14/50 (28%)
Adjusted *(c)*	17.5%	20.3%	31.1%
Terminal *(d)*	6/39 (15%)	7/38 (18%)	11/42 (26%)
Statistical Tests *(e)*			
Life Table	P=0.077	P=0.481	P=0.105
Incidental Tumor Test	P=0.046	P=0.450	P=0.060
Cochran-Armitage Trend, Fisher Exact Tests	P=0.050	P=0.500	P=0.070

(a) Dosed groups received doses of 6,000 or 12,000 ppm of propyl gallate in the diet.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(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 prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).
(f) No statistical tests were done because there were no tumors observed in the dosed or untreated control group.

PRECHRONIC STUDIES

Single-Dose Study

One of five male and 3/5 females receiving 2,000 mg/kg propyl gallate died within 2 hours of dosing; the survivors in this group were slightly inactive for 1 day after dosing. No deaths occurred among the 125, 250, 500, or 1,000 mg/kg groups, and no other compound-related effects were observed.

Fourteen-Day Study

All mice receiving 100,000 ppm and 4/5 males and 5/5 females receiving 50,000 ppm died (Table 8). Mean body weight gains by dosed male and female mice were inversely proportional to dose. Feed consumption was comparable for mice fed diets containing 6,000, 12,500, or 25,000 ppm propyl gallate. Four of the five male mice receiving 100,000 ppm and all female mice receiving 50,000 or 100,000 ppm had wet fur in the pelvic region.

Based on the results of this study, dose levels selected for the 13-week study were 0, 800, 1,500, 3,000, 6,000, and 12,500 ppm of propyl gallate in feed.

TABLE 8. SURVIVAL AND MEAN BODY WEIGHTS OF MICE FED DIETS CONTAINING PROPYL GALLATE FOR 14 DAYS

Dose (ppm)	Survival *(a)*	Mean Body Weights (grams)			Average Daily Feed Consumption (grams) *(c,d)*	Average Daily Feed Consumption (grams) *(e)*
		Initial	Final	Change *(b)*		
Males						
6,000	5/5	21.6 ±1.0	24.4 ± 0.5	+ 2.8 ± 0.6	7.9	8.8
12,500	5/5	21.6 ±1.0	23.6 ± 0.8	+ 2.0 ± 0.6	7.3	9.0
25,000	5/5	21.8 ±0.7	22.2 ±0.7	+ 0.4 ± 0.4	8.3	7.8
50,000	1/5	21.0	16.0	- 5.0	8.4	10.0
100,000	0/5	*(f)*	*(f)*	*(f)*	6.9	
Females						
6,000	5/5	16.2 ±0.2	18.6 ± 0.2	+ 2.4 ± 0.4	7.2	8.8
12,500	5/5	17.0 ±0.3	18.0 ± 0.6	+ 1.0 ± 0.3	7.0	7.7
25,000	5/5	17.4 ±1.1	17.4 ± 0.8	0.0 ± 0.6	7.9	7.1
50,000	0/5	*(f)*	*(f)*	*(f)*	8.4	8.0 *(g)*
100,000	0/5	*(f)*	*(f)*	*(f)*	8.2	

(a) Number surviving/number initially in the group. All calculations are based on those animals surviving to the end of the study.
(b) Mean body weight change of the survivors of the group ± standard error of the mean.
(c) Day 2 through day 7
(d) Average daily feed consumption by untreated mice of comparable age and weight at this laboratory is 8 grams for males and 7 grams for females.
(e) Day 7 through day 14
(f) No data are presented due to the 100% mortality in this group.
(g) Day 7 through day 13

Thirteen-Week Study

No mice died (Table 9). Weight gain in the dosed groups could not be meaningfully evaluated because controls were dehydrated as a result of a malfunction in the automatic watering system. Weight gain data were not used for selecting dose levels for the chronic study. No compound-related gross or microscopic pathologic effects were observed.

Doses of 6,000 and 12,000 ppm propyl gallate were selected for mice in the chronic study because of the weight gain depression seen in mice administered 25,000 ppm in the 14-day study.

TABLE 9. SURVIVAL, MEAN BODY WEIGHTS, AND FEED CONSUMPTION OF MICE FED DIETS CONTAINING PROPYL GALLATE FOR 13 WEEKS

Dose (ppm)	Survival *(a)*	Mean Body Weight (grams)			Weight Change Relative to Controls *(c)* (percent)	Average Daily Feed Consumption (grams)
		Initial	Final	Change *(b)*		
Males						
0	10/10	19.0 ± 0.6	31.3 ± 0.8	+12.3 ± 0.4		6.3
800	10/10	18.8 ± 0.5	30.7 ± 0.6	+11.9 ± 0.3	- 3.3	7.6
1,500	10/10	17.0 ± 0.3	29.9 ± 0.7	+12.9 ± 0.6	+ 4.9	7.4
3,000	10/10	18.5 ± 0.5	30.4 ± 0.6	+11.9 ± 0.7	- 3.3	7.3
6,000	10/10	18.8 ± 0.4	30.1 ± 0.7	+11.3 ± 0.5	- 8.1	7.5
12,500	10/10	18.5 ± 0.5	29.0 ± 0.6	+10.5 ± 0.4	-14.6	7.8
Females						
0	10/10	15.9 ± 0.5	22.9 ± 0.7	+7.0 ± 0.6		7.8
800	10/10	15.6 ± 0.3	23.9 ± 0.3	+8.3 ± 0.3	+18.6	7.9
1,500	10/10	15.4 ± 0.4	24.7 ± 0.4	+9.3 ± 0.2	+32.9	8.5
3,000	10/10	15.4 ± 0.4	23.5 ± 0.3	+8.1 ± 0.3	+15.7	7.9
6,000	10/10	15.0 ± 0.3	23.1 ± 0.5	+8.1 ± 0.4	+15.7	7.7
12,500	10/10	15.5 ± 0.5	23.0 ± 0.5	+7.5 ± 0.4	+ 7.1	7.6

(a) Number surviving/number initially in the group.

(b) Mean body weight change of the group ± standard error of the mean.

(c) Weight change of the dosed group relative to that of the controls ◘

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

CHRONIC STUDIES

Body Weights and Clinical Signs

Mean body weights of dosed mice of each sex were lower than those of the controls throughout most of the study (Figure 3 and Table 10). At 104 weeks, mean body weights of low- and high-dose male mice were 5% and 8% lower than those of the controls. Mean body weights of female mice of either dose group were 11% lower than those of the controls. The average daily feed consumption per mouse by low-and high-dose mice was 91% and 100% that of the controls for males and 109% and 106% for females (Table 11). No other compound-related clinical signs were observed.

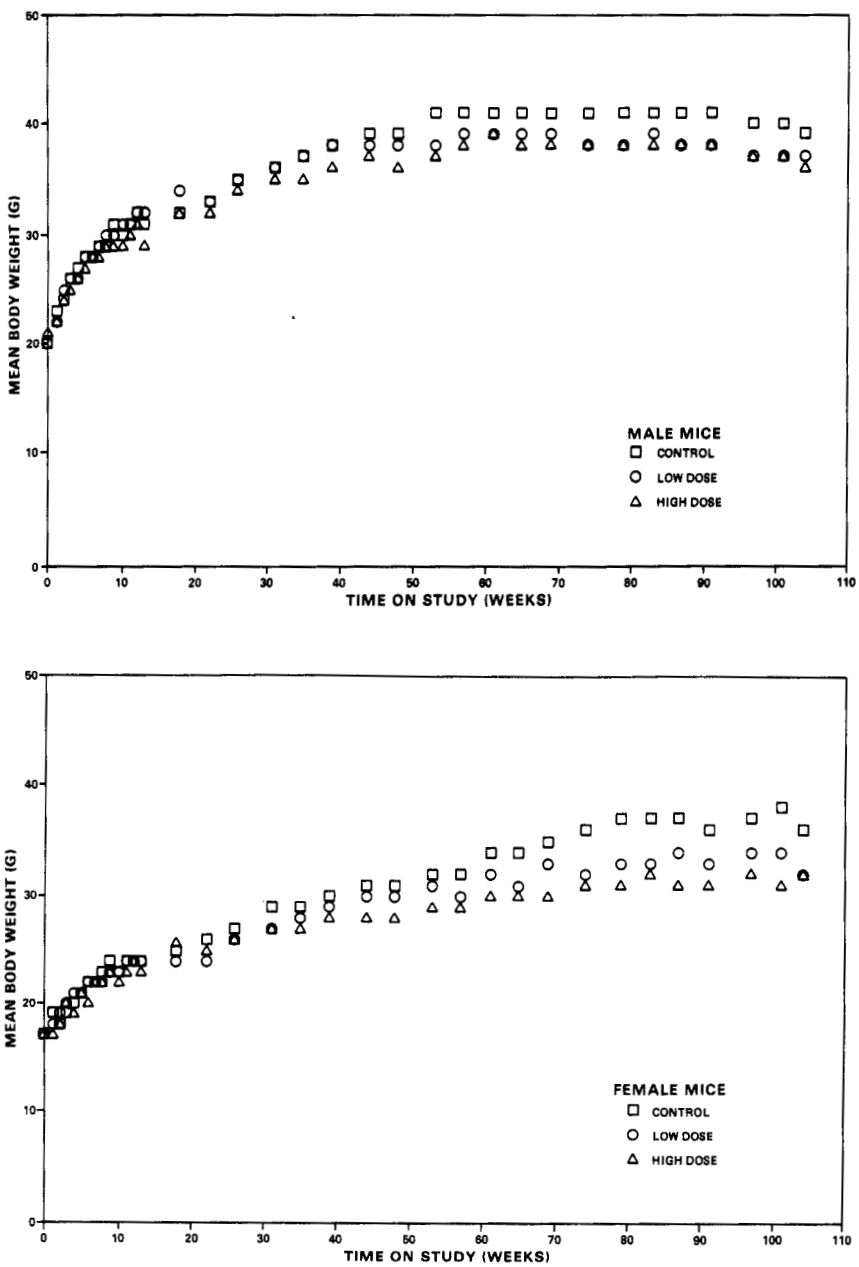


Figure 3. Growth Curves for Mice Fed Diets Containing Propyl Gallate

TABLE 10. CUMULATIVE MEAN BODY WEIGHT CHANGE (RELATIVE TO CONTROLS) OF MICE FED DIETS CONTAINING PROPYL GALLATE IN THE CHRONIC STUDY

	Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls *(a)* (Percent)	
Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Males					
0	20 *(b)*	20 *(b)*	21 *(b)*		
1	3	2	1	-33	-67
22	13	13	11	0	-15
44	19	18	16	-5	-16
65	21	19	17	-10	-19
83	21	19	17	-10	-19
104	19	17	15	-11	-21
Final Body Weight	39	37	36	-5 *(c)*	-8 *(c)*
Females					
0	17 *(b)*	17 *(b)*	17 *(b)*		
1	2	1	0	-50	-100
22	9	7	8	-22	-11
44	14	13	11	-7	-21
65	17	14	13	-18	-24
83	20	16	15	-20	-25
104	19	15	15	-21	-21
Final Body Weight	36	32	32	-11 *(c)*	-11 *(c)*

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

(b) Initial Weight

(c) Final body weight relative to controls (percent)

TABLE 11. FEED CONSUMPTION BY MICE RECEIVING PROPYL GALLATE IN THE CHRONIC STUDY

	Control	Low Dose		High Dose	
Week	Grams Feed/ Day *(a)*	Grams Feed/ Day *(a)*	Low/ Control *(b)*	Grams Feed/ Day *(a)*	High/ Control *(b)*
Males					
22	6.0	6.0	1.0	6.0	1.0
44	7.0	6.0	0.9	6.0	0.9
65	6.8	5.8	0.9	6.8	1.0
83	6.8	5.8	0.9	6.8	1.0
104	7.3	7.3	1.0	8.4	1.1
Mean	6.8	6.2	0.9	6.8	1.0
SD *(c)*	0.5	0.6	0.1	1.0	0.1
CV *(d)*	7.4	9.7	11.1	14.7	10.0
Females					
22	6.0	6.0	1.0	6.0	1.0
44	6.0	6.0	1.0	6.0	1.0
65	6.8	6.8	1.0	6.8	1.0
83	5.8	6.8	1.2	6.8	1.2
104	7.3	9.4	1.3	8.4	1.2
Mean	6.4	7.0	1.1	6.8	1.1
SD *(c)*	0.6	1.4	0.1	1.0	0.1
CV *(d)*	9.4	20.0	9.1	14.7	9.1

(a) Grams of feed consumed per animal per day.

(b) Grams of feed consumed per day by the dosed group divided by that for the controls.

(c) Standard deviation

(d) Coefficient of variation = (standard deviation/mean) x 100

Survival

Estimates of the probabilities of survival of male and female mice fed diets containing 0, 6,000, or 12,000 ppm propyl gallate are shown by the Kaplan and Meier curves in Figure 4. No significant differences in survival were observed between dosed groups of male mice or groups of female mice.

In male mice, 41/50 (82%) of the controls, 37/50 (74%) of the low-dose group, and 44/50 (88%) of the high-dose group lived to the end of the study at 105-107 weeks. In female mice, 37/50 (74%) of the controls, 34/50 (68%) of the low-dose group, and 38/50 (76%) of the high-dose group lived to the end of the study at 105-107 weeks. These incidences include one low-dose female that died during the terminal kill period.

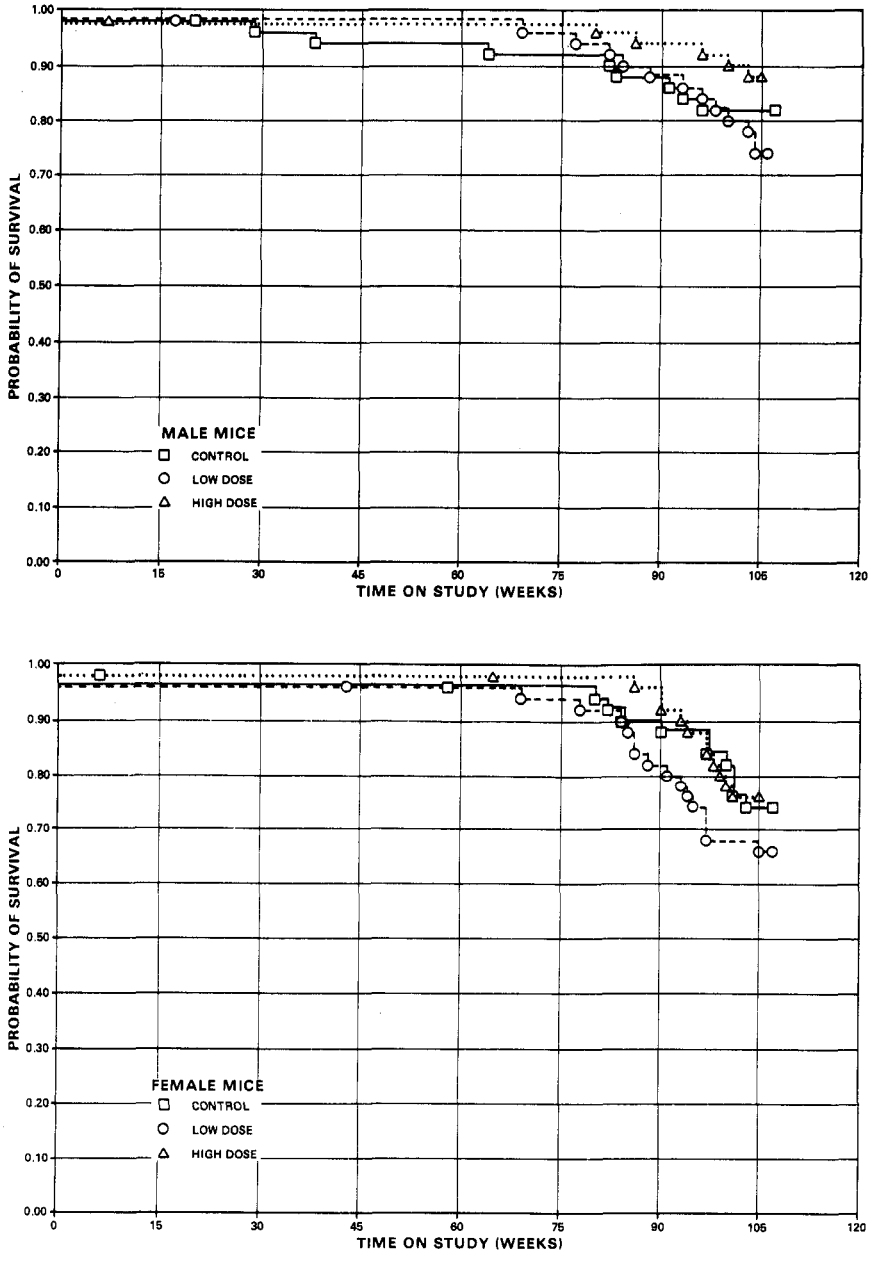


Figure 4. Survival Curves for Mice Fed Diets Containing Propyl Gallate

Pathology and Statistical Analyses of Results

Histopathologic findings on neoplasms occurring in mice are summarized in Appendix B, Tables B1 and B2; Tables B3 and B4 give the survival and tumor status for each individual animal in the male and female mouse studies, respectively. Findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2. Tables 12 and 13 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 in male mice were observed with a statistically significant ($P \leq 0.014$) positive trend (controls, 1/50, 2%; low-dose, 3/49, 6%; high-dose, 8/50, 16%). All tests between the high-dose and control groups were significant ($P \leq 0.028$). The incidence of male mice with malignant lymphoma, histiocytic type, occurred with a significant ($P \leq 0.02$) positive trend (control, 0/50, 0%; low-dose, 0/49, 0%; high-dose, 4/50, 8%); but statistical comparisons between high-dose males and controls were not significant.

Liver: The incidence of male mice with adenomas or carcinomas (combined) occurred with a significant ($P=0.043$, incidental tumor test) negative trend. Hepatocellular adenomas in female mice occurred with a significant ($P \leq 0.022$) positive trend (control, 0/50, 0%; low-dose, 2/50, 4%; high-dose, 5/49, 10%). The incidence of high-dose female mice with this tumor is significantly ($P \leq 0.039$) higher than that of the controls. The combined incidence of female mice with either adenomas or carcinomas was not significantly different from that of controls.

Pituitary: Low-dose female mice had fewer adenomas than did animals in the control group ($P \leq 0.035$), but no statistically significant results were obtained when the incidences of females with adenomas or carcinomas were combined.

Skin or Subcutaneous Tissue: Fibromas occurred in male mice with a negative trend ($P \leq 0.011$), and the incidence in the high-dose group was significantly ($P < 0.028$) reduced relative to controls (5/50, 1/49, 0/50).

Uterus: Endometrial stromal polyps or sarcomas occurred with a significant ($P < 0.038$) negative trend in female mice; none of the results of the individual group comparisons were significant.

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

	Control	Low Dose	High Dose
Skin or Subcutaneous Tissue: Fibroma			
Tumor Rates			
Overall *(b)*	5/50 (10%)	1/49 (2%)	0/50 (0%)
Adjusted *(c)*	12.2%	2.7%	0.0%
Terminal *(d)*	5/41 (12%)	1/37 (3%)	0/44 (0%)
Statistical Tests *(e)*			
Life Table	P=0.010N	P=0.128N	P=0.028N
Incidental Tumor Test	P=0.010N	P=0.128N	P=0.028N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.011N	P=0.107N	P=0.028N
Subcutaneous Tissue: Fibrosarcoma			
Tumor Rates			
Overall *(b)*	2/50 (4%)	3/49 (6%)	0/50 (0%)
Adjusted *(c)*	4.5%	7.7%	0.0%
Terminal *(d)*	0/41 (0%)	1/37 (3%)	0/44 (0%)
Statistical Tests *(e)*			
Life Table	P=0.189N	P=0.484	P=0.223N
Incidental Tumor Test	P=0.139N	P=0.581N	P=0.235N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.203N	P=0.490	P=0.247N
Lung: Alveolar/Bronchiolar Adenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	4/48 (8%)	5/50 (10%)
Adjusted *(c)*	7.0%	10.8%	11.4%
Terminal *(d)*	2/41 (5%)	4/37 (11%)	5/44 (11%)
Statistical Tests *(e)*			
Life Table	P=0.331	P=0.453	P=0.396
Incidental Tumor Test	P=0.312	P=0.453	P=0.363
Cochran-Armitage Trend, Fisher Exact Tests	P=0.292	P=0.477	P=0.357
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	4/50 (8%)	5/48 (10%)	5/50 (10%)
Adjusted *(c)*	9.4%	13.5%	11.4%
Terminal *(d)*	3/41 (7%)	5/37 (14%)	5/44 (11%)
Statistical Tests *(e)*			
Life Table	P=0.479	P=0.443	P=0.543
Incidental Tumor Test	P=0.459	P=0.443	P=0.511
Cochran-Armitage Trend, Fisher Exact Tests	P=0.433	P=0.474	P=0.500
Hematopoietic System: Malignant Lymphoma, Histiocytic Type			
Tumor Rates			
Overall *(b)*	0/50 (0%)	0/49 (0%)	4/50 (8%)
Adjusted *(c)*	0.0%	0.0%	8.9%
Terminal *(d)*	0/41 (0%)	0/37 (0%)	3/44 (7%)
Statistical Tests *(e)*			
Life Table	P=0.020	*(f)*	P=0.075
Incidental Tumor Test	P=0.016	*(f)*	P=0.086
Cochran-Armitage Trend, Fisher Exact Tests	P=0.015	*(f)*	P=0.059

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

	Control	Low Dose	High Dose
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Tumor Rates			
Overall *(b)*	0/50 (0%)	1/49 (2%)	3/50 (6%)
Adjusted *(c)*	0.0%	2.7%	6.8%
Terminal *(d)*	0/41 (0%)	1/37 (3%)	3/44 (7%)
Statistical Tests *(e)*			
Life Table	P=0.072	P=0.480	P=0.134
Incidental Tumor Test	P=0.072	P=0.480	P=0.134
Cochran-Armitage Trend, Fisher Exact Tests	P=0.061	P=0.495	P=0.121
Hematopoietic System: All Malignant Lymphoma			
Tumor Rates			
Overall *(b)*	1/50 (2%)	3/49 (6%)	8/50 (16%)
Adjusted *(c)*	2.4%	7.2%	17.4%
Terminal *(d)*	1/41 (2%)	1/37 (3%)	6/44 (14%)
Statistical Tests *(e)*			
Life Table	P=0.014	P=0.290	P=0.026
Incidental Tumor Test	P=0.009	P=0.387	P=0.028
Cochran-Armitage Trend, Fisher Exact Tests	P=0.009	P=0.301	P=0.015
Liver: Adenoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	4/49 (8%)	1/50 (2%)
Adjusted *(c)*	7.3%	10.1%	2.3%
Terminal *(d)*	3/41 (7%)	3/37 (8%)	1/44 (2%)
Statistical Tests *(e)*			
Life Table	P=0.230N	P=0.456	P=0.280N
Incidental Tumor Test	P=0.249N	P=0.453	P=0.280N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.253N	P=0.489	P=0.309N
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	14/50 (28%)	11/49 (22%)	9/50 (18%)
Adjusted *(c)*	32.5%	25.9%	19.5%
Terminal *(d)*	12/41 (29%)	6/37 (16%)	7/44 (16%)
Statistical Tests *(e)*			
Life Tablee	P=0.114N	P=0.406N	P=0.133N
Incidental Tumor Test	P=0.089N	P=0.139N	P=0.134N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.143N	P=0.343N	P=0.171N
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	17/50 (34%)	15/49 (31%)	10/50 (20%)
Adjusted *(c)*	39.4%	34.5%	21.6%
Terminal *(d)*	15/41 (37%)	9/37 (24%)	8/44 (18%)
Statistical Tests *(e)*			
Life Table	P=0.058N	P=0.516N	P=0.063N
Incidental Tumor Test	P=0.043N	P=0.244N	P=0.063N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.075N	P=0.442N	P=0.088N

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

	Control	Low Dose	High Dose
Adrenal: All Pheochromocytomas			
Tumor Rates			
Overall *(b)*	1/49 (2%)	3/47 (6%)	0/50 (0%)
Adjusted *(c)*	2.5%	7.1%	0.0%
Terminal *(d)*	1/40 (3%)	1/35 (3%)	0/44 (0%)
Statistical Tests *(e)*			
Life Table	P=0.351N	P=0.288	P=0.481N
Incidental Tumor Test	P=0.471N	P=0.342	P=0.481N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.373N	P=0.293	P=0.495N
Thyroid: Follicular Cell Adenoma			
Tumor Rates			
Overall *(b)*	3/49 (6%)	2/48 (4%)	0/49 (0%)
Adjusted *(c)*	7.5%	5.0%	0.0%
Terminal *(d)*	3/40 (8%)	1/37 (3%)	0/44 (0%)
Statistical Tests *(e)*			
Life Table	P=0.074N	P=0.526N	P=0.105N
Incidental Tumor Test	P=0.067N	P=0.436N	P=0.105N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.083N	P=0.510N	P=0.121N

(a) Dosed groups received doses of 6,000 or 12,000 ppm of propyl gallate in the diet.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(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 prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).
(f) No statistical tests were done because there were no tumors observed in the dosed or untreated control group.

TABLE 13. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)*

	Control	Low Dose	High Dose
Hematopoietic System: Malignant Lymphoma, Lymphocytic Type			
Tumor Rates			
Overall *(b)*	2/50 (4%)	1/50 (2%)	3/49 (6%)
Adjusted *(c)*	4.9%	2.9%	7.9%
Terminal *(d)*	1/37 (3%)	1/34 (3%)	3/38 (8%)
Statistical Tests *(e)*			
Life Table	P=0.410	P=0.539N	P=0.510
Incidental Tumor Test	P=0.420	P=0.537N	P=0.522
Cochran-Armitage Trend, Fisher Exact Tests	P=0.392	P=0.500N	P=0.490
Hematopoietic System: Malignant Lymphoma, Mixed Type			
Tumor Rates			
Overall *(b)*	4/50 (8%)	1/50 (2%)	3/49 (6%)
Adjusted *(c)*	9.6%	2.9%	7.9%
Terminal *(d)*	2/37 (5%)	1/34 (3%)	3/38 (8%)
Statistical Tests *(e)*			
Life Table	P=0.408N	P=0.214N	P=0.494N
Incidental Tumor Test	P=0.424N	P=0.183N	P=0.531N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.422N	P=0.181N	P=0.511N
Hematopoietic System: All Malignant Lymphomas			
Tumor Rates			
Overall *(b)*	8/50 (16%)	3/50 (6%)	6/49 (12%)
Adjusted *(c)*	19.3%	8.4%	15.8%
Terminal *(d)*	5/37 (14%)	2/34 (6%)	6/38 (16%)
Statistical Tests *(e)*			
Life Table	P=0.312N	P=0.144N	P=0.375N
Incidental Tumor Test	P=0.310N	P=0.121N	P=0.393N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.331N	P=0.100N	P=0.403N
Hematopoietic System: Lymphoma or Leukemia			
Tumor Rates			
Overall *(b)*	9/50 (18%)	5/50 (10%)	8/49 (16%)
Adjusted *(c)*	21.2%	13.6%	20.3%
Terminal *(d)*	5/37 (14%)	3/34 (9%)	7/38 (18%)
Statistical Tests *(e)*			
Life Table	P=0.436N	P=0.272N	P=0.489N
Incidental Tumor Test	P=0.416N	P=0.232N	P=0.490N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.461N	P=0.194N	P=0.518N
Liver: Adenoma			
Tumor Rates			
Overall *(b)*	0/50 (0%)	2/50 (4%)	5/49 (10%)
Adjusted *(c)*	0.0%	5.6%	12.7%
Terminal *(d)*	0/37 (0%)	1/34 (3%)	4/38 (11%)
Statistical Tests *(e)*			
Life Table	P=0.020	P=0.212	P=0.036
Incidental Tumor Test	P=0.022	P=0.214	P=0.039
Cochran-Armitage Trend, Fisher Exact Tests	P=0.016	P=0.247	P=0.027

TABLE 13. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

	Control	Low Dose	High Dose
Liver: Carcinoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	1/50 (2%)	0/49 (0%)
Adjusted *(c)*	8.1%	2.9%	0.0%
Terminal *(d)*	3/37 (8%)	1/34 (3%)	0/38 (0%)
Statistical Tests *(e)*			
Life Table	P=0.060N	P=0.335N	P=0.116N
Incidental Tumor Test	P=0.060N	P=0.335N	P=0.116N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.063N	P=0.309N	P=0.125N
Liver: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	3/50 (6%)	5/49 (10%)
Adjusted *(c)*	8.1%	8.4%	12.7%
Terminal *(d)*	3/37 (8%)	2/34 (6%)	4/38 (11%)
Statistical Tests *(e)*			
Life Table	P=0.297	P=0.616	P=0.368
Incidental Tumor Test	P=0.309	P=0.617	P=0.379
Cochran-Armitage Trend, Fisher Exact Tests	P=0.273	P=0.661	P=0.346
Pituitary: Adenoma			
Tumor Rates			
Overall *(b)*	5/48 (10%)	0/48 (0%)	2/49 (4%)
Adjusted *(c)*	14.3%	0.0%	5.3%
Terminal *(d)*	5/35 (14%)	0/34 (0%)	2/38 (5%)
Statistical Tests *(e)*			
Life Table	P=0.102N	P=0.035N	P=0.183N
Incidental Tumor Test	P=0.102N	P=0.035N	P=0.183N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.115N	P=0.028N	P=0.209N
Pituitary: Adenoma or Carcinoma			
Tumor Rates			
Overall *(b)*	6/48 (13%)	1/48 (2%)	2/49 (4%)
Adjusted *(c)*	17.1%	2.9%	5.3%
Terminal *(d)*	6/35 (17%)	1/34 (3%)	2/38 (5%)
Statistical Tests *(e)*			
Life Table	P=0.057N	P=0.061N	P=0.108N
Incidental Tumor Test	P=0.057N	P=0.061N	P=0.108N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.068N	P=0.056N	P=0.127N

TABLE 13. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE *(a)* (Continued)

	Control	Low Dose	High Dose
Uterus: Endometrial Stromal Polyp or Sarcoma			
Tumor Rates			
Overall *(b)*	3/50 (6%)	0/50 (0%)	0/49 (0%)
Adjusted *(c)*	8.1%	0.0%	0.0%
Terminal *(d)*	3/37 (8%)	0/34 (0%)	0/38 (0%)
Statistical Tests *(e)*			
Life Table	P=0.038N	P=0.136N	P=0.116N
Incidental Tumor Test	P=0.038N	P=0.136N	P=0.116N
Cochran-Armitage Trend, Fisher Exact Tests	P=0.038N	P=0.121N	P=0.125N

(a) Dosed groups received doses of 6,000 or 12,000 ppm of propyl gallate in the diet.
(b) Number of tumor bearing animals/number of animals examined at the site.
(c) Kaplan-Meier estimated lifetime tumor incidence after adjusting for intercurrent mortality.
(d) Observed tumor incidence at terminal kill.
(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 prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as non-fatal. The Cochran-Armitage and Fisher's exact tests compare directly the overall incidence rates. A negative trend or lower incidence is indicated by (N).

IV. DISCUSSION AND CONCLUSIONS

IV. DISCUSSION AND CONCLUSIONS

No compound-related histopathologic effects were observed in mice administered diets containing 800 - 12,500 ppm for 13 weeks. Feed consumption for female rats fed diets containing 25,000 ppm propyl gallate for 13 weeks was almost twice that of the controls, yet weight gain relative to controls was depressed 12%. Macroscopic gastrointestinal effects were observed in rats of each sex in the 25,000-ppm group. These effects consisted of a thickened stomach wall, reddened intestinal mucosa, and darkened mucosal surface of the stomach. Histologically, gastric lesions were characterized by ulceration and necrosis of the mucosal surface and by a moderate to severe granulomatous inflammatory response in the submucosa and muscular wall of the stomach. A previous study in which albino rats were fed diets containing 23,400 ppm propyl gallate reported that 40% of the animals died within the first 4 weeks and that tubular damage to the kidneys was observed (Orten et al., 1948). These earlier findings were not duplicated in the current 13-week study, possibly because of differences in animal husbandry, in the strain of rats, and in bioassay techniques.

In mice, weight gain depression was seen in animals fed diets containing 25,000 ppm propyl gallate for 14 days. Body weight data from the 13-week study could not be evaluated meaningfully because the controls were dehydrated when water was not available *ad libitum* due to a malfunction in the automatic watering system.

The doses selected for rats and mice on the chronic study were 6,000 and 12,000 ppm. The growth rates of dosed female rats and mice were more than 10% lower than those of controls. This finding agrees with the growth retardation observed in rats fed diets with 1.17% or 5% propyl gallate (Orten et al., 1948; Lehman et al., 1951). No significant differences in survival were observed between dosed or control rats or mice.

The incidences of dosed male rats with cytoplasmic vacuolization of the liver and of high-dose male rats with suppurative inflammation of the prostate were related to administration of propyl gallate. The presence of fat in vacuoles may be an indication of a disorder in fat metabolism. It is likely that propyl gallate administration to rats may result in methyl donors (e.g., choline) deficiency. This could occur since methyl groups are needed for the metabolism of this compound. Furthermore, choline deficiency in rats is known to interfere with the secretion of triglycerides in the form of low-density lipoprotein from the liver into the plasma (Mookerjea, 1971).

Rare tumors (an astrocytoma or a glioma) were found in the brain of two low-dose female rats. The incidence of all brain tumors in the Bioassay Program is only 0.86% and at this laboratory is 0.68% (Appendix H, Table H6). However, the presence of this tumor in the brain of low-dose female rats was not considered to be related to propyl gallate administration, since none of the high-dose female rats had this tumor.

Thyroid follicular-cell adenomas or carcinomas (combined) occurred in male rats with a statistically significant ($P<0.05$) positive trend, but the incidences in the dosed groups were not statistically significant in direct comparisons with the controls. Moreover, the incidence of high-dose male rats with follicular-cell tumors was quite low (3/50, 6%) and was not statistically significant relative to the historical control rate (14/584, 2.4%; Appendix H, Table H1) in the laboratory that conducted this bioassay.

The following tumors occurred in low-dose male rats at incidences significantly higher ($P<0.05$) than those in the controls but showed little evidence of an increase in high-dose males: adenomas (alone) and adenomas, adenocarcinomas, or carcinomas (combined) of the preputial gland, and adenomas (alone) and adenomas or carcinomas (combined) of the pancreatic islet cells, and pheochromocytomas of the adrenal gland. The historical control incidences of these tumors in the Bioassay Program are given in Appendix H (Tables H2, H3, and H4). Because there is no significant effect in the high-dose group, these increases are not considered to be clearly related to propyl gallate administration.

Adenomas in the mammary gland occurred in female rats with a statistically significant positive trend, but the incidence in the high-dose group was not significantly higher than that in the controls. Fibroadenomas in the mammary gland in female rats occurred with a statistically significant negative trend. Endometrial stromal polyps of the uterus occurred in female rats with a marginally significant positive trend ($P=0.049$, incidental tumor test), but the incidence in the high-dose group (13/50, 26%) was not significant relative to controls (6/50, 12%). The high-dose incidence falls within the overall historical control range (2/50, 4% to 18/49, 36%; Appendix H, Table H5), and this increase is not believed to be related to administration of propyl gallate.

IV. DISCUSSION AND CONCLUSIONS

Retinopathy and cataract formation occurred at increased incidences in high-dose male rats and low-dose female rats. At this bioassay laboratory, the incidence of eye lesions has been related to the distance of the animals from a fluorescent light source.

In male mice, malignant lymphoma was observed with significantly ($P \leq 0.028$) increased incidence in the high-dose group (16%) relative to concurrent controls (2%) and with a positive trend ($P < 0.014$). However, the high-dose incidence was not statistically significant ($P = 0.11$, Fisher's exact test) when compared with the historical rate (60/640, 9.4%; Appendix H, Table H7) for the laboratory that conducted this bioassay. This tumor was not observed in significant proportions in female mice. The increased incidence of malignant lymphomas in male mice was not clearly related to administration of propyl gallate.

Adenomas of the liver in female mice occurred with a statistically significant ($P \leq 0.022$) positive trend, with the incidence in the high-dose group being significantly ($P \leq 0.039$) higher than that in the controls. To date, the overall historical incidence is 104/3,127 (3.3%), with the group incidence ranging from 0/50 (0%) to 9/49 (18%) (Appendix H, Table H8). In addition, the combined incidence of hepatocellular adenomas or carcinomas was similar in dosed and control groups and hence the increased incidence of hepatocellular adenomas in the high-dose group was not considered to be related to propyl gallate administration.

No compound-related histopathologic effects were observed in previous 13- to 24-month feeding studies of propyl gallate (Dacre, 1974; Lehman et al., 1951; Orten et al., 1948); the doses administered in these studies were comparable to those used in the present study. The lack of compound-related histopathologic findings may be explained by the small number (5-15 per dose level) and/or the different strains of animals used. Growth retardation was observed in rats receiving diets with 1.17% or 5% propyl gallate (Orten et al., 1948; Lehman et al., 1951). Similar observations of growth retardation were made in the current chronic studies.

Although propyl gallate alone was not mutagenic for *Salmonella typhimurium,* propyl gallate given concurrently enhanced the mutagenicity of N-hydroxy-2-acetylaminofluorene for TA 98 and 4-nitroquinoline-1-oxide for TA 98 and 100. Mutagenic activity of N-methyl-N'-nitro-N-nitrosoguanidine, N-acetoxy-2-acetylaminofluorene, and aflatoxin B_1 was reduced or inhibited by propyl gallate (Rosin and Stich, 1980). Propyl gallate did not cause mutations in *S. typhimurium* strains TA 98, 100, 1535, and 1537 with and without exogenous metabolic activation (NTP unpublished results, 1982).

Conclusions: Under the conditions of this bioassay, propyl gallate was not considered to be carcinogenic for F344/N rats, although there was evidence of an increased proportion of low-dose male rats with preputial gland tumors, islet-cell tumors of the pancreas, and pheochromocytomas of the adrenal glands; rare tumors of the brain occurred in two low-dose females. Propyl gallate was not considered to be carcinogenic for B6C3F$_1$ mice of either sex, although the increased incidence of malignant lymphomas in male mice may have been related to the dietary administration of propyl gallate.

V. REFERENCES

V. REFERENCES

Archer, D.; Bukovic-Wess, J.; Smith, B., Suppression of macrophage-dependent T-lymphocyte function(s) by gallic acid, a food additive metabolite. Proc. Soc. Exp. Biol. Med. 156:465-469; 1977.

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, 1969.

Booth, A.; Masri, M.; Robbins, D.; Emerson, O.; Jones, F.; De Eds, F., The metabolic fate of gallic acid and related compounds. J. Biol. Chem. 234:3014-3016; 1959.

Carpenter, M., Antioxidant effect on the prostaglandin in endoperoxide synthethase product profile. Fed. Proc. 40(2):189-194; 1981.

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

Dacre, J., Long-term toxicity study of n-propyl gallate in mice, Food Cosmet. Toxicol. 12:125-129; 1974.

Fawcett, R.; Robinson, R., J. Chem. Soc. 2414-2422; 1927.

Federal Register, 44, No. 177:52825; 1979.

Food Chemicals Codex, 1981:257.

Furia, T., ed., Handbook of food additives. Cleveland: CRC Press, 1972:185-223.

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

Gorbacheva, L.; Kukushkina, G.; Petrov, O., Retardation of tumor growth and RNA biosynthesis by administration of phenolic compounds to tumor-bearing animals. In: Fenal' nye Soedin Ikh. Biol. Funkts; Mater Vses Simp. 1966: 345-348.

Harshaw Chemical Company, Bulletin 12775, 1975.

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

Lauffer, P., in Balsam, M.; Sagarin, E., eds., Cosmetics — science and technology. New York: John Wiley and Sons, Inc., 1972:376.

Lehman, A.; Fitzhugh, O.; Nelson, A.; Woodard, G., The pharmacological evaluation of antioxidants. Advances in Food Research 3:197-208; 1951.

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

LSRO, Life Sciences Research Office, Evaluation of the health aspects of propyl gallate as a food ingredient, SCOGS-11, January, 1973.

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

McDonald-Gibson, W.; Saeed, S.; Schneider, C., Local antinociceptive and topical anti-inflammatory effects of propyl gallate in rodents. Br. J. Pharmacol. 58:573-581; 1976.

Merck index, Rahway, New Jersey: Merck and Co., 1968; 877.

Mirvish, S.; Cardesa, A.; Wallace, L.; Shubik, P., Induction of mouse lung adenoma by amines or ureas plus nitrite and by nitroso compounds. Effect of ascorbate, gallic acid, thiocyanate and caffeine. J. Natl. Cancer Inst. 55(3): 633-636; 1975.

Mookerjea, S., Action of choline in lipoprotein metabolism. Fed. Proc. 30:143-150; 1971.

National Academy of Sciences, Histologic typing of liver tumors in the rat. J. Natl. Cancer Inst. 64:179; 1980.

NTP, NTP Technical Bulletin No. 6, National Toxicology Program, January 1982: 6.

Orten, J., Kuyper, A.; Smith, A., Studies on the toxicity of propyl gallate and of antioxidant mixtures containing propyl gallate. Food Technol. 2:308; 1948.

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, R. Montesano; H. Bartsch; L. Tomatis, eds. Geneva: World Health Organization. Supplement 2; 1980:311.

Pouchert, C., Aldrich library of infrared spectra, Aldrich Chemical Co., Inc., 1970:762.

V. REFERENCES

Rosin, M.; Stich, H., Enhancing and inhibiting effects of propyl gallate on carcinogen-induced mutagenesis. J. Environ. Pathol. Toxicol. 4:159-167; 1980.

Sadtler standard spectra, Philadephia: Sadtler Research Laboratories, IR No. 9163, NMR No. 18733.

Sedlacek, B., Fette, Seifen, Anstrichmittel 64: 683-687; 1962.

Singleton, V.; Katzer, F. In: Toxicants occurring naturally in foods, Committee on Food Protection, Food and Nutrition Board, National Research Council, National Academy of Sciences, Washington, D.C., 307; 1973.

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

Stahl, R., Thin-layer chromatography, 2nd ed., New York: Springer-Verlag, 1969:887; Spray No. 168A.

Tanaka, S.; Kawashima, K.; Nakaura, S.; Nagao, S.; Omori, Y., Shokuhin Eiseigaku Zasshi 20:378-384; 1979.

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

Tempsett, S., J. Pharm. Pharmacol, 10:157; 1958.

Tempsett, S., J. Pharm. Pharmacol. 11:32; 1959

USCFR, United States Code of Federal Regulations 21:121.2005, 1976; 21:121.1059, 1977; 21:573.1020; 1979.

USITC, United States International Trade Commission, Synthetic organic chemicals, United States production and sales 1979, USITC Publication 1099, Washington, D.C.: U.S. Government Printing Office, 1980.

Wang, C.; Klemencic, J., Mutagenicity and carcinogenicity of polyhydric phenols. Am. Assoc. Cancer Res. 20: 117; 1979.

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

Yang, C.; Strickhart, F., Inhibition of hepatic mixed function oxidase activity of propyl gallate. Biochem. Pharmacol. 23:3129-3138; 1974.

APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS FED DIETS CONTAINING PROPYL GALLATE

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS FED DIETS CONTAINING PROPYL GALLATE

	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)
SQUAMOUS CELL CARCINOMA	1 (2%)		
BASAL-CELL TUMOR	2 (4%)	2 (4%)	
SEBACEOUS ADENOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
BASAL-CELL CARCINOMA	1 (2%)		
ADENOCARCINOMA, NOS	1 (2%)		
FIBROMA	1 (2%)	1 (2%)	2 (4%)
FIBROSARCOMA		1 (2%)	1 (2%)
NEURILEMOMA, MALIGNANT		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)		
ALVEOLAR/BRONCHIOLAR CARCINOMA			1 (2%)
NEURILEMOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, MIXED TYPE		1 (2%)	
UNDIFFERENTIATED LEUKEMIA	16 (32%)	7 (14%)	6 (12%)
CIRCULATORY SYSTEM			
NONE			

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM			
*UPPER LIP	(50)	(50)	(50)
TRICHOEPITHELIOMA	1 (2%)		
*LOWER LIP	(50)	(50)	(50)
TRICHOEPITHELIOMA			1 (2%)
#PAROTID GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	2 (4%)	1 (2%)	1 (2%)
#PANCREAS	(50)	(50)	(50)
ACINAR-CELL ADENOMA	1 (2%)		
#GASTRIC MUCOSA	(50)	(50)	(50)
LEIOMYOSARCOMA		1 (2%)	
#JEJUNUM	(50)	(50)	(50)
LEIOMYOSARCOMA	1 (2%)		
#COLONIC SUBMUCOSA	(50)	(50)	(50)
FIBROMA	1 (2%)		

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
TUBULAR-CELL ADENOMA	1 (2%)	1 (2%)	
#KIDNEY/PELVIS	(50)	(50)	(50)
TRANSITIONAL-CELL CARCINOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(48)	(49)
CARCINOMA,NOS		2 (4%)	
ADENOMA, NOS	5 (10%)	8 (17%)	4 (8%)
#ADRENAL	(50)	(48)	(50)
CORTICAL ADENOMA	1 (2%)	2 (4%)	
CORTICAL CARCINOMA	1 (2%)		
PHEOCHROMOCYTOMA	4 (8%)	12 (25%)	8 (16%)
PHEOCHROMOCYTOMA, MALIGNANT		1 (2%)	
#THYROID	(50)	(50)	(50)
FOLLICULAR-CELL ADENOMA			1 (2%)
FOLLICULAR-CELL CARCINOMA			2 (4%)
C-CELL ADENOMA	4 (8%)	2 (4%)	3 (6%)
C-CELL CARCINOMA	3 (6%)	1 (2%)	1 (2%)
#PANCREATIC ISLETS	(50)	(50)	(50)
ISLET-CELL ADENOMA		8 (16%)	2 (4%)
ISLET-CELL CARCINOMA	2 (4%)	1 (2%)	2 (4%)

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA	2 (4%)		1 (2%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)		
ADENOMA, NOS		5 (10%)	
ADENOCARCINOMA, NOS		2 (4%)	
ADENOSQUAMOUS CARCINOMA		1 (2%)	
#TESTIS	(50)	(50)	(50)
INTERSTITIAL-CELL TUMOR	47 (94%)	48 (96%)	50 (100%)
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(50)
CARCINOMA, NOS, INVASIVE		1 (2%)	
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
SEBACEOUS ADENOCARCINOMA			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	VEHICLE CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(50)
PHEOCHROMOCYTOMA, INVASIVE		1 (2%)	
MESOTHELIOMA, MALIGNANT		1 (2%)	
*MESENTERY	(50)	(50)	(50)
MESOTHELIOMA BENIGN			1 (2%)
MESOTHELIOMA, NOS		1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
CORTICAL CARCINOMA, METASTATIC	1 (2%)		
SARCOMA, NOS			1 (2%)
MESOTHELIOMA, MALIGNANT	1 (2%)		
HEAD			
SQUAMOUS CELL CARCINOMA			1
SEBACEOUS ADENOCARCINOMA	1		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHə	3	3	1
MORIBUND SACRIFICE	9	9	5
SCHEDULED SACRIFICE	7		
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	31	33	44
ANIMAL MISSING			

ə INCLUDES AUTOLYZED ANIMALS

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

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	49	49	50
TOTAL PRIMARY TUMORS	104	112	91
TOTAL ANIMALS WITH BENIGN TUMORS	48	49	50
TOTAL BENIGN TUMORS	72	90	73
TOTAL ANIMALS WITH MALIGNANT TUMORS	23	16	16
TOTAL MALIGNANT TUMORS	30	20	17
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	2	
TOTAL SECONDARY TUMORS	2	3	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	2	2	1
TOTAL UNCERTAIN TUMORS	2	2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS FED DIETS CONTAINING PROPYL GALLATE

	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)
SQUAMOUS CELL PAPILLOMA		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
FIBROMA		1 (2%)	1 (2%)
FIBROSARCOMA	1 (2%)		
RESPIRATORY SYSTEM			
*NASOPHARYNX	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
UNDIFFERENTIATED LEUKEMIA	8 (16%)	5 (10%)	6 (12%)
#SPLEEN	(50)	(50)	(50)
LEIOMYOSARCOMA	1 (2%)		
CIRCULATORY SYSTEM			
NONE			
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA		1 (2%)	
NEOPLASTIC NODULE		1 (2%)	

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#ILEUM	(50)	(50)	(50)
LEIOMYOSARCOMA	1 (2%)		
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(49)	(50)
CARCINOMA,NOS	1 (2%)	3 (6%)	
ADENOMA, NOS	16 (32%)	14 (29%)	16 (32%)
#ADRENAL	(50)	(50)	(50)
CORTICAL ADENOMA	1 (2%)	1 (2%)	2 (4%)
PHEOCHROMOCYTOMA	4 (8%)	1 (2%)	3 (6%)
#THYROID	(50)	(48)	(50)
C-CELL ADENOMA	4 (8%)	8 (17%)	2 (4%)
C-CELL CARCINOMA	2 (4%)	1 (2%)	1 (2%)
#PANCREATIC ISLETS	(50)	(50)	(50)
ISLET-CELL CARCINOMA			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOMA, NOS			3 (6%)
ADENOCARCINOMA, NOS	1 (2%)	1 (2%)	
FIBROADENOMA	11 (22%)	2 (4%)	5 (10%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS			1 (2%)
ADENOMA, NOS	2 (4%)	1 (2%)	2 (4%)
#UTERUS	(50)	(50)	(50)
LEIOMYOMA	1 (2%)		
ENDOMETRIAL STROMAL POLYP	6 (12%)	8 (16%)	13 (26%)
ENDOMETRIAL STROMAL SARCOMA	1 (2%)		1 (2%)
#UTERUS/ENDOMETRIUM	(50)	(50)	(50)
ADENOMA, NOS			1 (2%)

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ADENOCARCINOMA, NOS			1 (2%)
#OVARY	(49)	(50)	(50)
GRANULOSA-CELL TUMOR	1 (2%)		
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
CARCINOMA, NOS, INVASIVE		1 (2%)	
GLIOMA, NOS		1 (2%)	
ASTROCYTOMA		1 (2%)	
#HYPOTHALAMUS	(50)	(50)	(49)
CARCINOMA, NOS, INVASIVE		1 (2%)	
SPECIAL SENSE ORGANS			
*EYELID	(50)	(50)	(50)
FIBROMA	1 (2%)		
*ZYMBAL'S GLAND	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL WALL	(50)	(50)	(50)
SARCOMA, NOS	1 (2%)		
ALL OTHER SYSTEMS			
HEAD			
CARCINOMA, NOS, INVASIVE		1	
LUMBOSACRAL REGION			
OSTEOSARCOMA			1

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

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	1	1	1
MORIBUND SACRIFICE	10	11	7
SCHEDULED SACRIFICE	2		
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	37	38	42
ANIMAL MISSING			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	38	34	36
TOTAL PRIMARY TUMORS	64	52	60
TOTAL ANIMALS WITH BENIGN TUMORS	32	27	31
TOTAL BENIGN TUMORS	46	37	48
TOTAL ANIMALS WITH MALIGNANT TUMORS	14	13	11
TOTAL MALIGNANT TUMORS	17	14	12
TOTAL ANIMALS WITH SECONDARY TUMORS#		4	
TOTAL SECONDARY TUMORS		4	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	1	
TOTAL UNCERTAIN TUMORS	1	1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE RATS IN THE 2-YEAR STUDY OF PROPYL GALLATE

CONTROL

ANIMAL NUMBER	50111	50112	50113	50114	50115	50116	50117	50118	50119	50120	50121	50122	50123	50124	50125	50126	50127	50128	50129	50130	50131	50132	50133	50134	50135
WEEKS ON STUDY	015	015	015	015	094	035	015	015	015	056	061	061	061	061	071	071	071	051	090	071	071	088	098	071	
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N
SQUAMOUS CELL CARCINOMA																									
BASAL-CELL TUMOR					X						X														
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N
BASAL-CELL CARCINOMA																									
ADENOCARCINOMA, NOS																X									
FIBROMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	•	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT																									
ALVEOLAR/BRONCHIOLAR ADENOMA	X																								
TRACHEA	+	−	+	−	+	+	+	−	−	−	−	−	−	+	+	−	+	−	+	+	−	+	+	+	−
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	−	−	+	−	+	+	−	+	−	+	+	−	+	+	+	+	+	−	−	+	+	+	−	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TRICHOEPITHELIOMA									X																
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																									
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE													X							X					
BILE DUCT	+	+	+	+	+	+	•	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ACINAR-CELL ADENOMA																X									
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOSARCOMA																									
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																									
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA																	X								
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOMA, NOS		X																			X	X	X		
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																				X					
CORTICAL CARCINOMA																									
PHEOCHROMOCYTOMA						X										X			X						
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA		X			X						X														X
C-CELL CARCINOMA																							X		
PARATHYROID	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	−	+		+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
ISLET-CELL CARCINOMA									X																
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROADENOMA																X									
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CARCINOMA,NOS			X																						
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
CORTICAL CARCINOMA, METASTATIC																				X					
MESOTHELIOMA, MALIGNANT																							X		
UNDIFFERENTIATED LEUKEMIA	X		X	X		X	X		X				X				X		X		X				X
HEAD NOS																									
SEBACEOUS ADENOCARCINOMA	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	52 26	52 27	52 28	52 29	53 30	53 31	53 32	53 33	53 41	53 35	53 36	53 37	53 38	53 39	54 01	54 11	54 12	54 33	54 41	54 45	54 61	54 77	54 84	54 91	55 01	TOTAL TISSUES TUMORS
WEEKS ON STUDY	10 07	10 07	10 07	10 07	10 07	09 01	10 07	10 03	08 89	10 07	10 07	11 07	10 07	07 74	07 77	10 07	10 07	10 07	10 07	10 07	10 07	10 07	10 07	10 07	10 07	
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
SQUAMOUS CELL CARCINOMA														X												1
BASAL-CELL TUMOR																										2
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
BASAL-CELL CARCINOMA							X																			1
ADENOCARCINOMA, NOS																										1
FIBROMA										X																1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA, METASTAT														X												1
ALVEOLAR/BRONCHIOLAR ADENOMA																		X								2
TRACHEA	+	-	-	-	-	-	+	-	-	+	+	+	-	-	-	-	-	-	+	+	-	+	-	-	+	23
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	-	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	-	36
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
																										•
DIGESTIVE SYSTEM																										
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
TRICHOEPITHELIOMA																										1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS																			X							1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																										2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ACINAR-CELL ADENOMA																										1
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	50
LEIOMYOSARCOMA																										1
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FIBROMA			X																							1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOMA																										1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS			X																							5
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA																							X			1
CORTICAL CARCINOMA																										1
PHEOCHROMOCYTOMA					X																					4
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA																		X								4
C-CELL CARCINOMA																								X		3
PARATHYROID	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	44
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL CARCINOMA										X																2
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROADENOMA													X													2
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	47
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
CARCINOMA,NOS																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
CORTICAL CARCINOMA, METASTATIC																										1
MESOTHELIOMA, MALIGNANT																										1
UNDIFFERENTIATED LEUKEMIA		X						X	X	X														X		16
HEAD NOS																										
SEBACEOUS ADENOCARCINOMA																										1

M ANIMALS NECROPSIED

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

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE RATS IN THE 2-YEAR STUDY OF PROPYL GALLATE

LOW DOSE

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	105	096	105	105	105	105	105	105	105	105	105	105	097	098	105	105	105	096	091	105	106	106	094	096	077
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+
BASAL-CELL TUMOR																									
SEBACEOUS ADENOMA																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+
FIBROMA				X																					
FIBROSARCOMA																									
NEURILEMOMA, MALIGNANT																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEURILEMOMA, METASTATIC																									
TRACHEA	+	+	-	+	+	+	+	+	+	+	+	+	-	+	+	+	-	-	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
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	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	-	+	+	+	+	+	+	+	-	+	+	+	+	-	-	-	-	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOSARCOMA																									
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TUBULAR-CELL ADENOMA																									
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									X
ADENOMA, NOS	X							X											X			X			
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																					X				
PHEOCHROMOCYTOMA		X		X								X			X							X		X	
PHEOCHROMOCYTOMA, MALIGNANT																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA									X																
C-CELL CARCINOMA																						X			
PARATHYROID	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA								X	X			X		X									X		
ISLET-CELL CARCINOMA																									
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	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							X				X		X				X								
ADENOCARCINOMA, NOS																			X				X		
ADENOSQUAMOUS CARCINOMA																									
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, INVASIVE																									X
BODY CAVITIES																									
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PHEOCHROMOCYTOMA, INVASIVE																									
MESOTHELIOMA, MALIGNANT														X											
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
MESOTHELIOMA, NOS													X												
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, MIXED TYPE																									
UNDIFFERENTIATED LEUKEMIA													X												

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

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

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

ANIMAL NUMBER	52616	52717	52818	52919	53101	53111	53212	53313	53414	53515	53616	53717	53818	53919	54010	54111	54212	54313	54414	54515	54616	54717	54818	54919	55010	TOTAL
WEEKS ON STUDY	100	106	106	091	106	106	106	106	106	106	111	106	106	106	106	099	106	106	106	105	106	107	094	089	106	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
BASAL-CELL TUMOR					X								X													2
SEBACEOUS ADENOMA					X																					1
SUBCUTANEOUS TISSUE	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
FIBROMA																				X						1
FIBROSARCOMA																										1
NEURILEMOMA, MALIGNANT		X																								1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEURILEMOMA, METASTATIC		X																								1
TRACHEA	+	+	+	-	-	+	+	+	+	-	-	-	+	-	+	-	-	+	+	+	-	+	+	+		37
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	-	+	+	+	-	-	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	38
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	+	+	+	-	+	-	+	-	-	-	-	-	-	-	+	+	+	+	+	+	+	+	+	+	+	35
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LEIOMYOSARCOMA			X																							1
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TUBULAR-CELL ADENOMA		X																								1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CARCINOMA,NOS																								X		2
ADENOMA, NOS						X	X									X							X			8
ADRENAL	+	+	+	+	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CORTICAL ADENOMA																				X						2
PHEOCHROMOCYTOMA								X								X		X	X	X		X				12
PHEOCHROMOCYTOMA, MALIGNANT		X																								1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA															X											2
C-CELL CARCINOMA																										1
PARATHYROID	+	-	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+		44
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA						X			X										X							8
ISLET-CELL CARCINOMA															X											1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	N	+	N	N	N	N	+	+	+	+	+	+	+	+	+	+	+	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	48
PROSTATE	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
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																						5
ADENOCARCINOMA, NOS																										2
ADENOSQUAMOUS CARCINOMA																X										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA, NOS, INVASIVE																										1
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PHEOCHROMOCYTOMA, INVASIVE		X																								1
MESOTHELIOMA, MALIGNANT																										1
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MESOTHELIOMA, NOS																										1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, MIXED TYPE																								X		1
UNDIFFERENTIATED LEUKEMIA		X			X			X			X		X		X											7

* ANIMALS NECROPSIED

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

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

TABLE A3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE RATS IN THE 2-YEAR STUDY OF PROPYL GALLATE

HIGH DOSE

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	105	109	105	105	109	080	105	096	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA																				X					
FIBROSARCOMA																							X		
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR CARCINOMA																	X								
TRACHEA	+	+	+	+	+	+	-	+	+	+	-	+	+	-	-	-	+	+	+	+	+	+	-	+	-
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	-	-	-	-	-	-	-	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TRICHOEPITHELIOMA				X																					
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASTIC NODULE					X																				
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	-	+	+
STOMACH	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
KIDNEY/PELVIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRANSITIONAL-CELL CARCINOMA																									
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
ADENOMA, NOS																		X					X		
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA		X																							
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA									X																
FOLLICULAR-CELL CARCINOMA			X																						
C-CELL ADENOMA																							X		
C-CELL CARCINOMA									X																
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ISLET-CELL ADENOMA													X												
ISLET-CELL CARCINOMA			X																						
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+
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	X	X
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	+	N	N	N	N	+	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SEBACEOUS ADENOCARCINOMA	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
MESOTHELIOMA BENIGN					X																				
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS								X																	
UNDIFFERENTIATED LEUKEMIA							X											X					X		
HEAD NOS																									
SQUAMOUS CELL CARCINOMA						X																			

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

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

ANIMAL NUMBER	52 26	52 27	52 28	52 29	53 30	53 31	53 32	53 33	53 34	53 35	53 36	53 37	53 38	53 39	54 40	54 41	54 42	54 43	54 44	54 45	54 46	54 47	54 48	54 49	55 01	TOTAL
WEEKS ON STUDY	10 05	10 05	10 05	10 05	10 04	09 00	10 05	10 05	10 02	10 05	10 01	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05	10 05	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	50*
FIBROMA																										2
FIBROSARCOMA						X																				1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
TRACHEA	-	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	+	+	+	-	+	-	+	-	-	35
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	•	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	-	+	+	+	+	+	+	-	-	+	+	-	-	+	+	+	+	+	+	+	-	35
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
ORAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
TRICHOEPITHELIOMA																										1
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NEOPLASTIC NODULE																										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	-	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	43
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
KIDNEY/PELVIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRANSITIONAL-CELL CARCINOMA							X																			1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS					X					X																4
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PHEOCHROMOCYTOMA	X			X	X		X		X			X	X													8
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FOLLICULAR-CELL ADENOMA																										1
FOLLICULAR-CELL CARCINOMA											X															2
C-CELL ADENOMA																X			X							3
C-CELL CARCINOMA																										1
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	48
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL ADENOMA								X																		2
ISLET-CELL CARCINOMA																									X	2
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	X	+	+	+	+	N	+	50*
FIBROADENOMA																			X							1
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
INTERSTITIAL-CELL TUMOR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	50
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
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*
SEBACEOUS ADENOCARCINOMA																										1
BODY CAVITIES																										
MESENTERY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MESOTHELIOMA BENIGN																										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*
SARCOMA, NOS																										1
UNDIFFERENTIATED LEUKEMIA				X										X									X			6
HEAD NOS																										
SQUAMOUS CELL CARCINOMA																										1

* ANIMALS NECROPSIED

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE RATS IN THE 2-YEAR STUDY OF PROPYL GALLATE

CONTROL

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	106	105	106	106	106	106	121	107	104	107	107	094	107	107	107	107	107	107	107	096	107	111	107	107	079
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA							X																		
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	•	+	+	+	
TRACHEA	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOSARCOMA																									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	−	−	+	−	+	+	−	+	−	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOSARCOMA														X											
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS	X							X				X	X	X			X		X	X	X				
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA																						X			
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA																			X				X		
C-CELL CARCINOMA														X							X				
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	−	+	+	−	
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																									
FIBROADENOMA			X													X		X	X		X			X	
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS				X																					
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LEIOMYOMA																									
ENDOMETRIAL STROMAL POLYP			X								X					X									
ENDOMETRIAL STROMAL SARCOMA									X																
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GRANULOSA-CELL TUMOR		X																							
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
EYE APPENDAGES	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
FIBROMA																X									
BODY CAVITIES																									
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
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	52606	52707	52808	52909	53010	53111	53212	53313	53414	53505	53606	53707	53808	53909	54010	54111	54212	54313	54414	54515	54616	54717	54818	54919	55010	TOTAL
WEEKS ON STUDY	107	107	107	107	107	107	107	107	107	076	107	107	107	107	107	107	107	101	105	107	093	107	074	107	096	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	N	+	+	+	+	+	50*
FIBROSARCOMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	-	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	-	+	45
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LEIOMYOSARCOMA																			X							1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	-	+	+	-	+	+	-	+	-	+	+	+	+	+	-	+	-	+	+	+	+	+	+	37
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LEIOMYOSARCOMA																										1
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA,NOS																			X							1
ADENOMA, NOS			X		X			X					X		X			X						X	16
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA													X													1
PHEOCHROMOCYTOMA				X											X				X							4
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA								X							X											4
C-CELL CARCINOMA																										2
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	45
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
ADENOCARCINOMA, NOS															X											1
FIBROADENOMA				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*
ADENOMA, NOS					X																					2
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LEIOMYOMA										X																1
ENDOMETRIAL STROMAL POLYP	X																X					X				6
ENDOMETRIAL STROMAL SARCOMA																										1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	49
GRANULOSA-CELL TUMOR																										1
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
EYE APPENDAGES	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
FIBROMA																										1
BODY CAVITIES																										
PERITONEUM	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SARCOMA, 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*
UNDIFFERENTIATED LEUKEMIA				X																	X			X		8

* ANIMALS NECROPSIED

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE RATS IN THE 2-YEAR STUDY OF PROPYL GALLATE

LOW DOSE

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	079	106	116	106	106	106	097	106	106	093	106	066	091	087	098	106	106	106	106	106	106	106	081	106	106
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	N	+	N	+	+	N
SQUAMOUS CELL PAPILLOMA				X																					
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	N	+	N	+	+	N
FIBROMA																				X					
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	-	+	+	+	+	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	-	+	+	+	+
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SQUAMOUS CELL CARCINOMA														X											
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	-	+	-	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SQUAMOUS CELL CARCINOMA, METASTAT														X											
NEOPLASTIC NODULE														X											
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	•	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
ADENOMA, NOS	X		X		X		X	X			X		X				X		X						X
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
PHEOCHROMOCYTOMA				X																					
THYROID	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
C-CELL ADENOMA						X								X					X	X					
C-CELL CARCINOMA						X																			
PARATHYROID	+	+	+	+	+	+	+	+	-	-	+	-	+	+	+	•	+	+	+	•	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																									
FIBROADENOMA			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
ADENOMA, NOS																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOMETRIAL STROMAL POLYP			X	X			X		X											X	X				
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA, NOS, INVASIVE																									
GLIOMA, NOS											X														
ASTROCYTOMA																									
SPECIAL SENSE ORGANS																									
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N
SQUAMOUS CELL CARCINOMA																									
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										
HEAD NOS																									
CARCINOMA, NOS, INVASIVE																									

+: 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) LOW DOSE

ANIMAL NUMBER	52 06	52 07	52 08	52 09	53 01	53 11	53 12	53 13	53 14	53 15	53 16	53 17	53 18	53 19	54 01	54 11	54 21	54 31	54 41	54 51	54 61	54 71	54 81	54 91	55 01	TOTAL
WEEKS ON STUDY	10 06	10 06	10 06	10 05	10 06	10 06	08 04	10 06	10 06	10 06	10 06	10 06	10 06	10 07	10 04	10 04	10 07	10 07	10 07	10 07	10 07	10 02	10 07	10 07	10 07	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
SQUAMOUS CELL PAPILLOMA																										1
SUBCUTANEOUS TISSUE	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	-	-	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	41
NASAL CAVITY	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
SQUAMOUS CELL CARCINOMA																										1
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	-	+	+	+	+	+	+	-	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	-	41
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SQUAMOUS CELL CARCINOMA, METASTAT																										1
NEOPLASTIC NODULE																										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	50M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	-	-	+	+	+	-	+	-	-	+	+	-	+	-	+	+	-	41
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA,NOS		X										X											X			3
ADENOMA, NOS							X									X				X	X					14
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA						X																				1
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
C-CELL ADENOMA	X				X	X							X													8
C-CELL CARCINOMA																										1
PARATHYROID	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	45
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
ADENOCARCINOMA, NOS		X																								1
FIBROADENOMA																		X								2
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS															X											1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOMETRIAL STROMAL POLYP			X																	X						8
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CARCINOMA, NOS, INVASIVE													X													2
GLIOMA, NOS																						X				1
ASTROCYTOMA			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	50M
SQUAMOUS CELL CARCINOMA																				X						1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
UNDIFFERENTIATED LEUKEMIA										X				X		X										5
HEAD NOS																										
CARCINOMA, NOS, INVASIVE		X																								1

M ANIMALS NECROPSIED

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

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

TABLE A4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE RATS IN THE 2-YEAR STUDY OF PROPYL GALLATE

HIGH DOSE

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524
WEEKS ON STUDY	105	104	105	105	105	105	095	105	105	105	105	105	105	105	105	105	105	105	095	105	105	105	105	105
INTEGUMENTARY SYSTEM																								
SUBCUTANEOUS TISSUE FIBROMA	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+ X	+	+	+	N	+
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
TRACHEA	-	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	-	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	-	-	+	-	+	-	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																								
PITUITARY ADENOMA, NOS	+	+	+	+	+	+	+	+ X	+ X	+	+ X	+	+	+	+	+ X	+	+	•	+	+ X	+	+ X	+ X
ADRENAL CORTICAL ADENOMA PHEOCHROMOCYTOMA	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+ X	+	+	+
THYROID C-CELL ADENOMA C-CELL CARCINOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS ISLET-CELL CARCINOMA	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND ADENOMA, NOS FIBROADENOMA	+	+	+	+	+	+ X X	+	+ X	+	N	+	+	+	+	+	+	+	+ X	+	+	+ X	+	+	+
PREPUTIAL/CLITORAL GLAND CARCINOMA,NOS ADENOMA, NOS	N	N	N X	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N	N	N	N X	N	N	N
UTERUS ADENOMA, NOS ADENOCARCINOMA, NOS ENDOMETRIAL STROMAL POLYP ENDOMETRIAL STROMAL SARCOMA	+	+ X	+ X	+	+	+	+	+ X	+	+	+	+	+ X	+	+ X	+	+	+	+	+ X	+	+	+	+
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																								
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS UNDIFFERENTIATED LEUKEMIA	N	N	N	N	N	N	N X	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
LUMBOSACRAL REGION OSTEOSARCOMA																								

+: 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	52606	52705	52809	52905	53011	53105	53212	53304	53411	53505	53605	53705	53811	53900	54007	54105	54211	54305	54411	54505	54611	54705	54811	54906	55010	TOTAL TISSUES TUMORS
WEEKS ON STUDY	105	105	099	105	105	105	105	084	105	105	105	105	105	100	074	105	105	105	105	105	105	101	105	086	105	
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	N	+	+	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	50*
FIBROMA																										1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+	-	41
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS	X	X		X					X	X			X							X		X			X	16
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA				X																						2
PHEOCHROMOCYTOMA						X	X																			3
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-CELL ADENOMA			X												X											2
C-CELL CARCINOMA																							X			1
PARATHYROID	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ISLET-CELL CARCINOMA																										1
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	50*
ADENOMA, NOS																										3
FIBROADENOMA	X												X										X			5
PREPUTIAL/CLITORAL GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
CARCINOMA,NOS																										1
ADENOMA, NOS																										2
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOMA, NOS																										1
ADENOCARCINOMA, NOS															X											1
ENDOMETRIAL STROMAL POLYP			X	X	X		X	X		X		X				X										13
ENDOMETRIAL STROMAL SARCOMA																							X			1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	49
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
UNDIFFERENTIATED LEUKEMIA			X		X	X												X				X				6
LUMBOSACRAL REGION																										
OSTEOSARCOMA													X													1

* ANIMALS NECROPSIED

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

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE FED DIETS CONTAINING PROPYL GALLATE

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS OF MALE MICE FED DIETS CONTAINING PROPYL GALLATE

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(50)
SARCOMA, NOS		1 (2%)	
FIBROMA	5 (10%)		
NEURILEMOMA	1 (2%)		
*SUBCUT TISSUE	(50)	(49)	(50)
SARCOMA, NOS		1 (2%)	1 (2%)
FIBROMA		1 (2%)	
FIBROSARCOMA	2 (4%)	3 (6%)	
NEURILEMOMA		1 (2%)	
NEURILEMOMA, MALIGNANT			1 (2%)
RESPIRATORY SYSTEM			
#LUNG/BRONCHIOLE	(50)	(48)	(50)
PAPILLARY ADENOMA			1 (2%)
#LUNG	(50)	(48)	(50)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	3 (6%)	4 (8%)	5 (10%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	1 (2%)	
PHEOCHROMOCYTOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(50)
MALIGNANT LYMPHOMA, NOS			1 (2%)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE		2 (4%)	
MALIGNANT LYMPHOMA, MIXED TYPE		1 (2%)	1 (2%)
#MESENTERIC L. NODE	(49)	(49)	(49)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			2 (4%)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#LIVER	(50)	(49)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE			2 (4%)
#PEYER'S PATCH	(48)	(49)	(49)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
CIRCULATORY SYSTEM			
#SPLEEN	(49)	(48)	(49)
HEMANGIOSARCOMA	1 (2%)	1 (2%)	1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(48)	(49)
SARCOMA, NOS	1 (2%)		
#LIVER	(50)	(49)	(50)
NEOPLASM, NOS		1 (2%)	
HEPATOCELLULAR ADENOMA	3 (6%)	4 (8%)	1 (2%)
HEPATOCELLULAR CARCINOMA	14 (28%)	11 (22%)	9 (18%)
#LARGE INTESTINE	(49)	(48)	(49)
MUCINOUS ADENOCARCINOMA	1 (2%)		
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#ADRENAL	(49)	(47)	(50)
CORTICAL ADENOMA			1 (2%)
PHEOCHROMOCYTOMA	1 (2%)	2 (4%)	
PHEOCHROMOCYTOMA, MALIGNANT		1 (2%)	
#THYROID	(49)	(48)	(49)
FOLLICULAR-CELL ADENOMA	3 (6%)	2 (4%)	

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
#TESTIS	(49)	(49)	(50)
INTERSTITIAL-CELL TUMOR		1 (2%)	1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(49)	(50)
ADENOMA, NOS	1 (2%)	1 (2%)	1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	5	7	4
MORIBUND SACRIFICE	4	6	2
SCHEDULED SACRIFICE	10		
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	31	37	44
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

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

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	29	31	22
TOTAL PRIMARY TUMORS	38	39	30
TOTAL ANIMALS WITH BENIGN TUMORS	15	13	10
TOTAL BENIGN TUMORS	17	16	10
TOTAL ANIMALS WITH MALIGNANT TUMORS	18	20	16
TOTAL MALIGNANT TUMORS	21	22	20
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	1	1
TOTAL SECONDARY TUMORS	1	1	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT		1	
TOTAL UNCERTAIN TUMORS		1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS OF FEMALE MICE FED DIETS CONTAINING PROPYL GALLATE

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

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#PEYER'S PATCH	(47)	(47)	(48)
MALIGNANT LYMPHOMA, MIXED TYPE			1 (2%)
#OVARY	(48)	(50)	(49)
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE			1 (2%)
CIRCULATORY SYSTEM			
#UTERUS	(50)	(50)	(49)
HEMANGIOSARCOMA			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(49)
HEPATOCELLULAR ADENOMA		2 (4%)	5 (10%)
HEPATOCELLULAR CARCINOMA	3 (6%)	1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
ADENOCARCINOMA, NOS, METASTATIC		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(48)	(49)
CARCINOMA,NOS	1 (2%)	1 (2%)	
ADENOMA, NOS	5 (10%)		2 (4%)
#ADRENAL	(50)	(49)	(49)
PHEOCHROMOCYTOMA		2 (4%)	
#ADRENAL CORTEX	(50)	(49)	(49)
SARCOMA, NOS	1 (2%)		
#THYROID	(49)	(47)	(48)
FOLLICULAR-CELL ADENOMA	1 (2%)		2 (4%)
#PANCREATIC ISLETS	(49)	(48)	(49)
ISLET-CELL ADENOMA			1 (2%)

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(49)
ADENOCARCINOMA, NOS	2 (4%)		
MIXED TUMOR, MALIGNANT	2 (4%)	1 (2%)	1 (2%)
#UTERUS	(50)	(50)	(49)
ENDOMETRIAL STROMAL POLYP	1 (2%)		
ENDOMETRIAL STROMAL SARCOMA	2 (4%)		
#CERVIX UTERI	(50)	(50)	(49)
SARCOMA, NOS			1 (2%)
#UTERUS/ENDOMETRIUM	(50)	(50)	(49)
CARCINOMA,NOS			1 (2%)
ADENOCARCINOMA, NOS		1 (2%)	
#OVARY	(48)	(50)	(49)
PAPILLARY CYSTADENOMA, NOS		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
EPENDYMOMA			1 (2%)
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(49)
ADENOMA, NOS	1 (2%)	2 (4%)	
MUSCULOSKELETAL SYSTEM			
*LUMBAR VERTEBRA	(50)	(50)	(49)
OSTEOSARCOMA	1 (2%)		
*MUSCLE OF BACK	(50)	(50)	(49)
RHABDOMYOSARCOMA			1 (2%)
*ABDOMINAL MUSCLE	(50)	(50)	(49)
FIBROSARCOMA	1 (2%)		
BODY CAVITIES			
NONE			

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

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(49)
SARCOMA, NOS		1 (2%)	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	6	8	4
MORIBUND SACRIFICE	7	9	8
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	37	33	38
ANIMAL MISSING			
@ INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	25	17	22
TOTAL PRIMARY TUMORS	32	18	27
TOTAL ANIMALS WITH BENIGN TUMORS	9	8	9
TOTAL BENIGN TUMORS	10	8	11
TOTAL ANIMALS WITH MALIGNANT TUMORS	20	10	15
TOTAL MALIGNANT TUMORS	22	10	16
TOTAL ANIMALS WITH SECONDARY TUMORS#	1	1	
TOTAL SECONDARY TUMORS	1	1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

CONTROL

ANIMAL NUMBER	50111	50112	50131	50145	50156	50167	50189	50192	50203	50215	50221	50235	50241	50256	50261	50271	50281	50291	50301	50311	50321	50331	50341	50351	50361	50371	50381	50394	50405
WEEKS ON STUDY	101	105	105	105	105	105	091	082	038	105	105	201	206	096	106	106	106	083	101	107	107	107	107	107	107	107	107	107	094
INTEGUMENTARY SYSTEM																													
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROMA	X																										X		
NEURILEMOMA																													
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																					X								X
RESPIRATORY SYSTEM																													
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									X				
ALVEOLAR/BRONCHIOLAR ADENOMA					X																X								
ALVEOLAR/BRONCHIOLAR CARCINOMA																									X				
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																													
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																				X									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																													
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																													
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																													
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																			X										
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA			X				X		X						X		X	X				X	X						
HEPATOCELLULAR CARCINOMA																													
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUCINOUS ADENOCARCINOMA																													
URINARY SYSTEM																													
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																													
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA													X																
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA		X																											
PARATHYROID	+	+	+	+	-	+	+	-	+	+	+	+	+	-	+	-	+	-	-	-	+	-	+	-	+	+	+	+	+
REPRODUCTIVE SYSTEM																													
MAMMARY GLAND	+	+	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																													
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																													
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS							X																						

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

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

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

ANIMAL NUMBER	52606	52707	52808	52909	53010	53111	53212	53313	53414	53515	53616	53717	53818	53919	54020	54121	54222	54323	54424	54525	54626	54727	54828	54929	55030	TOTAL
WEEKS ON STUDY	107	107	064	097	107	107	107	107	107	107	107	107	107	107	107	107	107	107	029	107	107	107	085	107	107	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	●	+	+	+	●	+	+	+	50*
FIBROMA													X	X									X			5
NEURILEMOMA																							X			1
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50*
FIBROSARCOMA																										2
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA																										1
ALVEOLAR/BRONCHIOLAR ADENOMA				X																						3
ALVEOLAR/BRONCHIOLAR CARCINOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	●	49
HEMANGIOSARCOMA																										1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	49
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																						X				1
THYMUS	+	-	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	46
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	49
SARCOMA, NOS																										1
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA					X					X																3
HEPATOCELLULAR CARCINOMA						X		X						X				X		X		X			X	14
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	50*
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MUCINOUS ADENOCARCINOMA			X																							1
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	46
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PHEOCHROMOCYTOMA																										1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	49
FOLLICULAR-CELL ADENOMA											X											X				3
PARATHYROID	+	+	-	+	-	-	-	-	+	-	-	+	-	+	-	-	+	+	+	-	-	+	+	-	-	27
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	N	N	+	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
TESTIS	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ADENOMA, NOS																										1

* ANIMALS NECROPSIED

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

LOW DOSE

ANIMAL NUMBER	5011	5012	5013	5014	5015	5016	5017	5018	5019	5020	5021	5022	5023	5024	5025	5026	5027	5028	5029	5030	5031	5032	5033	5034	5035
WEEKS ON STUDY	105	105	105	098	105	105	105	105	105	105	105	105	105	105	053	077	104	105	105	082	105	105	105	100	105
INTEGUMENTARY SYSTEM																									
SKIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	X	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS															X										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
FIBROMA										X															
FIBROSARCOMA																	X								
NEURILEMOMA																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA		X	X																						
ALVEOLAR/BRONCHIOLAR CARCINOMA																									
PHEOCHROMOCYTOMA, METASTATIC																X									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA				X																					
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NEOPLASM, NOS																								X	
HEPATOCELLULAR ADENOMA										X		X					X	X					X		X
HEPATOCELLULAR CARCINOMA																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
PHEOCHROMOCYTOMA																									
PHEOCHROMOCYTOMA, MALIGNANT																X									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FOLLICULAR-CELL ADENOMA																X									
PARATHYROID	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	+	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR																									
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
MALIGNANT LYMPHOMA, MIXED TYPE																									

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

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

ANIMAL NUMBER	52606	52707	52809	53001	53111	53202	53303	53404	53505	53606	53707	53808	53909	54010	54112	54203	54304	54405	54506	54607	54708	54809	55010	TOTAL
WEEKS ON STUDY	101	100	101	107	105	105	100	104	103	108	105	105	106	106	106	106	101	101	101	101	098	104	096	TISSUES TUMORS
INTEGUMENTARY SYSTEM																								
SKIN	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SARCOMA, NOS																								1
SUBCUTANEOUS TISSUE	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SARCOMA, NOS	X																							1
FIBROMA																								1
FIBROSARCOMA			X					X																3
NEURILEMOMA																		X						1
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ALVEOLAR/BRONCHIOLAR ADENOMA											X			X										4
ALVEOLAR/BRONCHIOLAR CARCINOMA																		X						1
PHEOCHROMOCYTOMA, METASTATIC																								1
TRACHEA	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SPLEEN	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMANGIOSARCOMA																								1
LYMPH NODES	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	48
CIRCULATORY SYSTEM																								
HEART	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	A	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	48
LIVER	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NEOPLASM, NOS														X										1
HEPATOCELLULAR ADENOMA										X									X		X			4
HEPATOCELLULAR CARCINOMA									X								X			X		X	X	11
BILE DUCT	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	A	+	+	+	+	N	+	+	+	+	N	+	N	+	+	+	+	+	N	+	49
PANCREAS	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LARGE INTESTINE	+	+	+	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																								
KIDNEY	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	A	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	45
ADRENAL	-	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
PHEOCHROMOCYTOMA										X											X			2
PHEOCHROMOCYTOMA, MALIGNANT																								1
THYROID	+	+	+	A	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
FOLLICULAR-CELL ADENOMA																				X				2
PARATHYROID	+	+	+	A	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+	+	-	42
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	N	+	N	A	N	N	+	N	N	N	N	N	N	+	N	N	N	N	+	N	+	N	N	N	49
TESTIS	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
INTERSTITIAL-CELL TUMOR								X																1
PROSTATE	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																								
BRAIN	+	+	+	A	+	+	+	+	+	+	●	+	+	+	●	+	+	+	+	+	+	+	+	49
SPECIAL SENSE ORGANS																								
HARDERIAN GLAND	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49
ADENOMA, NOS														X										1
ALL OTHER SYSTEMS																								
MULTIPLE ORGANS NOS	N	N	N	A	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	49
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE									X	X														2
MALIGNANT LYMPHOMA, MIXED TYPE											X													1

M ANIMALS NECROPSIED

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

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

TABLE B3.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

HIGH DOSE

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	105	096	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095	095
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SARCOMA, NOS																									
NEURILEMOMA, MALIGNANT																									
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA, METASTA																									
ALVEOLAR/BRONCHIOLAR ADENOMA		X								X							X			X				
PAPILLARY ADENOMA																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMANGIOSARCOMA																									
LYMPH NODES	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	X																								
MALIGNANT LYMPHOMA, MIXED TYPE																									
THYMUS	+	+	-	+	+	+	-	+	-	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA	X	X															X								
HEPATOCELLULAR CARCINOMA																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	N	N	+	+	N	+	N	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, MIXED TYPE																									
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CORTICAL ADENOMA																									
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	+	-	-	-	-	-	-	-	+	-	+	-	+	-	+	-	-	+	+	+	+	+	-	-
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N
TESTIS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
INTERSTITIAL-CELL TUMOR																									
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIGNANT LYMPHOMA, NOS			X																						
MALIGNANT LYMPHOMA, MIXED TYPE																									

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

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

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

ANIMAL NUMBER	526	527	528	529	530	531	532	533	534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549	550	TOTAL
WEEKS ON STUDY	105	105	105	105	105	105	080	007	105	105	105	105	105	105	105	105	103	105	086	105	105	105	105	105	100	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
SUBCUTANEOUS TISSUE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SARCOMA, NOS							X																			1
NEURILEMOMA, MALIGNANT																									X	1
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA, METASTA			X																							1
ALVEOLAR/BRONCHIOLAR ADENOMA					X	X																				5
PAPILLARY ADENOMA																										1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMANGIOSARCOMA									X																	1
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MALIG.LYMPHOMA, HISTIOCYTIC TYPE										X																2
MALIGNANT LYMPHOMA, MIXED TYPE											X															1
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	•	•	•	+	+	+	+	+	+	+	+	+	+	+	•	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA																X										1
HEPATOCELLULAR CARCINOMA			X	X		X			X										X						X	9
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																	X					X				2
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	N	+	N	+	+	+	+	+	N	50*
PANCREAS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MALIGNANT LYMPHOMA, MIXED TYPE	X																									1
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
PITUITARY	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	47
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
CORTICAL ADENOMA																							X			1
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	49
PARATHYROID	-	-	+	-	+	-	+	-	+	-	-	-	-	-	+	+	+	+	-	-	-	-	+	+	-	21
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			X																							1
PROSTATE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ADENOMA, NOS															X											1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
MALIGNANT LYMPHOMA, NOS																										1
MALIGNANT LYMPHOMA, MIXED TYPE							X																			1

* ANIMALS NECROPSIED

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

CONTROL

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	106	106	106	106	106	071	070	071	071	071	071	071	071	071	080	071	071	071	058	071	071	071	071	071	071
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																					X				
OSTEOSARCOMA, METASTATIC																									
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, MIXED TYPE																X									
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, MIXED TYPE					X																				
THYMUS	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR CARCINOMA																X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																							X		
ADENOMA, NOS																X									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+
SARCOMA, NOS															X										
THYROID	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	•	+	+	+	+
FOLLICULAR-CELL ADENOMA													X												
PARATHYROID	-	-	-	-	+	-	-	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N
ADENOCARCINOMA, NOS		X																							
MIXED TUMOR, MALIGNANT										X															
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROUS HISTIOCYTOMA																					X				
ENDOMETRIAL STROMAL POLYP		X																							
ENDOMETRIAL STROMAL SARCOMA																								X	
OVARY	-	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS																	X								
MUSCULOSKELETAL SYSTEM																									
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
OSTEOSARCOMA																									
MUSCLE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
FIBROSARCOMA																									
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																			X				X		
MALIGNANT LYMPHOMA, MIXED TYPE															X										
LYMPHOCYTIC LEUKEMIA							X																		

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

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

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

ANIMAL NUMBER	52606	52707	52808	52909	53010	53111	53212	53313	53414	53515	53616	53717	53818	53919	54010	54111	54212	54313	54414	54515	54616	54717	54818	54919	55020	TOTAL
WEEKS ON STUDY	107	082	011	097	107	107	084	107	107	107	107	107	107	107	107	107	107	107	106	090	107	107	107	107	097	TISSUES TUMORS
RESPIRATORY SYSTEM																										
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																										1
OSTEOSARCOMA, METASTATIC		X																								1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MALIGNANT LYMPHOMA, MIXED TYPE																										1
LYMPH NODES	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	49
MALIGNANT LYMPHOMA, MIXED TYPE																										1
THYMUS	+	+	+	+	+	+	•	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	+	47
CIRCULATORY SYSTEM																										
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR CARCINOMA							X																	X		3
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	N	N	N	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	50M
PANCREAS	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SMALL INTESTINE	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY BLADDER	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
CARCINOMA,NOS																										1
ADENOMA, NOS	X					X					X											X				5
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SARCOMA, NOS																										1
THYROID	•	+	+	+	+	+	+	+	+	+	+	+	+	+	~	+	+	+	+	+	+	+	+	+	+	49
FOLLICULAR-CELL ADENOMA																										1
PARATHYROID	+	+	+	+	+	+	-	+	+	+	-	-	-	~	-	•	+	~	-	+	-	-	-	+		32
REPRODUCTIVE SYSTEM																										
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	50M
ADENOCARCINOMA, NOS																							X			2
MIXED TUMOR, MALIGNANT			X																							2
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
FIBROUS HISTIOCYTOMA																										1
ENDOMETRIAL STROMAL POLYP																										1
ENDOMETRIAL STROMAL SARCOMA	X																									2
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
ADENOMA, NOS																										1
MUSCULOSKELETAL SYSTEM																										
BONE	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50M
OSTEOSARCOMA		X																								1
MUSCLE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50M
FIBROSARCOMA							X																			1
ALL OTHER SYSTEMS																										
MULTIPLE ORGANS NOS	N	N	M	N	N	N	N	N	N	N	N	N	N	N	N	N	X	N	N	N	N	N	N	N	X	50M
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																										2
MALIG.LYMPHOMA, HISTIOCYTIC TYPE																										2
MALIGNANT LYMPHOMA, MIXED TYPE			X																							2
LYMPHOCYTIC LEUKEMIA																										1

M ANIMALS NECROPSIED

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

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

LOW DOSE

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	106	106	106	106	091	106	106	069	106	106	106	106	106	106	106	106	106	106	084	106	106	106	097	086	106
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALVEOLAR/BRONCHIOLAR ADENOMA																		X							
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MALIGNANT LYMPHOMA, MIXED TYPE											X														
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEPATOCELLULAR ADENOMA																							X		
HEPATOCELLULAR CARCINOMA																X									
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS, METASTATIC																								X	
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CARCINOMA,NOS																									
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PHEOCHROMOCYTOMA																			X	X					
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
PARATHYROID	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	-	+	-	+	-	+	-	-	-	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+
MIXED TUMOR, MALIGNANT																									
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ADENOCARCINOMA, NOS																								X	
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
PAPILLARY CYSTADENOMA, NOS		X																							
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
ADENOMA, NOS	X																								
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
SARCOMA, NOS																									
MALIGNANT LYMPHOMA, NOS																									
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE							X																		
LEUKEMIA,NOS																									
LYMPHOCYTIC LEUKEMIA																						X			

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

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

ANIMAL NUMBER	52607	52707	52809	52906	53006	53111	53212	53308	53408	53504	53605	53706	53806	53906	54011	54202	54306	54408	54506	54611	54707	54809	54906	55001	TOTAL TISSUES TUMORS
WEEKS ON STUDY	11 06	10 67	10 96	11 06	10 68	08 84	08 85	08 43	04 43	04 35	09 07	10 06	10 66	09 51	07 81	10 66	10 61	08 66	10 65	11 05	10 76	10 67	10 77	09 73	
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALVEOLAR/BRONCHIOLAR ADENOMA																									1
TRACHEA	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPLEEN	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MALIGNANT LYMPHOMA, MIXED TYPE																									1
LYMPH NODES	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
THYMUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEPATOCELLULAR ADENOMA	X																								2
HEPATOCELLULAR CARCINOMA																									1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
GALLBLADDER & COMMON BILE DUCT	+	+	N	+	+	N	+	+	N	N	+	+	+	+	N	+	+	+	N	N	N	+	N	N	50*
PANCREAS	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
ESOPHAGUS	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	-	+	+	+	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	47
LARGE INTESTINE	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS, METASTATIC																									1
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																									
PITUITARY	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	48
CARCINOMA,NOS	X																								1
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	49
PHEOCHROMOCYTOMA																									2
THYROID	+	+	-	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
PARATHYROID	+	-	-	+	+	-	-	-	+	-	+	+	+	+	+	+	+	-	+	-	+	+	+	+	34
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND	+	+	N	+	+	+	+	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+	+	50*
MIXED TUMOR, MALIGNANT											X														1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ADENOCARCINOMA, NOS																									1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
PAPILLARY CYSTADENOMA, NOS																									1
NERVOUS SYSTEM																									
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																									
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
ADENOMA, NOS							X																		2
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	50*
SARCOMA, NOS																				X					1
MALIGNANT LYMPHOMA, NOS															X										1
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																									1
LEUKEMIA,NOS			X																						1
LYMPHOCYTIC LEUKEMIA																									1

* ANIMALS NECROPSIED

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

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

TABLE B4.

INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

HIGH DOSE

ANIMAL NUMBER	501	502	503	504	505	506	507	508	509	510	511	512	513	514	515	516	517	518	519	520	521	522	523	524	525
WEEKS ON STUDY	105	105	105	105	105	097	105	105	105	091	105	097	105	105	086	051	105	105	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
SUBCUTANEOUS TISSUE RHABDOMYOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
RESPIRATORY SYSTEM																									
LUNGS AND BRONCHI ALVEOLAR/BRONCHIOLAR ADENOMA ALVEOLAR/BRONCHIOLAR CARCINOMA	+	+ X	+	+	+	+	+	+	+	+ X	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
LIVER HEPATOCELLULAR ADENOMA LEUKEMIA,NOS	+			+ X	+	+	+	+	+	+ X	+	+	+ X	+	A	+ X	+	+	+	+	+	+	+	+	+
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	N	N	+	+	
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
STOMACH	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
SMALL INTESTINE MALIGNANT LYMPHOMA, MIXED TYPE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
LARGE INTESTINE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
URINARY BLADDER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
PITUITARY ADENOMA, NOS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+ X	+
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
THYROID FOLLICULAR-CELL ADENOMA	+ X	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
PARATHYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
PANCREATIC ISLETS ISLET-CELL ADENOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+ X	+	+
REPRODUCTIVE SYSTEM																									
MAMMARY GLAND MIXED TUMOR, MALIGNANT	+	+	+	+ X	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
UTERUS CARCINOMA,NOS SARCOMA, NOS HEMANGIOSARCOMA	+	+ X	+	+	+	+	+	+	+	+	+	+	+ X	+	A	+	+	+	+	+	+	+	+	+	+
OVARY MALIG.LYMPHOMA, LYMPHOCYTIC TYPE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
BRAIN EPENDYMOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
MUSCLE RHABDOMYOSARCOMA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
MULTIPLE ORGANS NOS MALIG.LYMPHOMA, LYMPHOCYTIC TYPE MALIGNANT LYMPHOMA, MIXED TYPE LYMPHOCYTIC LEUKEMIA	N	N	N	N X	N	N	N	N X	N	N	N	N	N X	N	A	N	N	N	N	N	N	N	N	N	N

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

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

ANIMAL NUMBER	52606	52707	52809	53001	53111	53205	53305	53405	53505	53605	53705	53805	53909	54001	54112	54205	54305	54405	54605	54705	54805	54905	55001	TOTAL
WEEKS ON STUDY	10 5	10 5	10 5	09 4	10 5	10 11	10 5	10 5	10 5	10 5	10 5	10 5	09 8	09 0	10 5	10 0	10 5	10 5	09 3	10 5	10 6	10 5	09 0	TISSUES TUMORS
INTEGUMENTARY SYSTEM																								
SUBCUTANEOUS TISSUE	+	+	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+ X	+	+	+	+	49M 1
RHABDOMYOSARCOMA																								
RESPIRATORY SYSTEM																								
LUNGS AND BRONCHI	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ALVEOLAR/BRONCHIOLAR ADENOMA																								1
ALVEOLAR/BRONCHIOLAR CARCINOMA																								1
TRACHEA	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																								
BONE MARROW	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	•	49
SPLEEN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LYMPH NODES	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYMUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	48
CIRCULATORY SYSTEM																								
HEART	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																								
SALIVARY GLAND	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
LIVER	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEPATOCELLULAR ADENOMA					X							X												5
LEUKEMIA,NOS																								1
BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
GALLBLADDER & COMMON BILE DUCT	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49M
PANCREAS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ESOPHAGUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
STOMACH	+	+	+	•	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
SMALL INTESTINE	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
MALIGNANT LYMPHOMA, MIXED TYPE									X															1
LARGE INTESTINE	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																								
KIDNEY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY BLADDER	+	+	+	+	+	+	+	+	+	•	+	+	+	+	+	+	+	+	•	+	+	+	+	49
ENDOCRINE SYSTEM																								
PITUITARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ADENOMA, NOS																			X					2
ADRENAL	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
THYROID	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	48
FOLLICULAR-CELL ADENOMA																			X					2
PARATHYROID	+	+	+	+	+	-	-	+	+	+	+	+	+	-	+	+	-	+	-	+	+	+	-	43
PANCREATIC ISLETS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
ISLET-CELL ADENOMA																								1
REPRODUCTIVE SYSTEM																								
MAMMARY GLAND	+	+	•	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49M
MIXED TUMOR, MALIGNANT																								1
UTERUS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
CARCINOMA,NOS																								1
SARCOMA, NOS			X																					1
HEMANGIOSARCOMA																								1
OVARY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																	X							1
NERVOUS SYSTEM																								
BRAIN	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
EPENDYMOMA																						X		1
MUSCULOSKELETAL SYSTEM																								
MUSCLE	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49M
RHABDOMYOSARCOMA																							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	49M
MALIG.LYMPHOMA, LYMPHOCYTIC TYPE																			X			X		2
MALIGNANT LYMPHOMA, MIXED TYPE																								2
LYMPHOCYTIC LEUKEMIA																								1

* ANIMALS NECROPSIED

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

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

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS FED DIETS CONTAINING PROPYL GALLATE

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS FED DIETS CONTAINING PROPYL GALLATE

	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)
CYST, NOS	1 (2%)		
EPIDERMAL INCLUSION CYST	2 (4%)	1 (2%)	1 (2%)
ULCER, NOS	1 (2%)		
FIBROSIS	2 (4%)		
RESPIRATORY SYSTEM			
#LUNG/BRONCHIOLE	(50)	(50)	(50)
HYPERPLASIA, FOCAL		1 (2%)	
HYPERPLASIA, ADENOMATOUS		1 (2%)	
#LUNG	(50)	(50)	(50)
CONGESTION, NOS		1 (2%)	
CONGESTION, CHRONIC PASSIVE		1 (2%)	
EDEMA, NOS		1 (2%)	
EDEMA, INTERSTITIAL		1 (2%)	
BRONCHOPNEUMONIA, ACUTE			1 (2%)
HYPERPLASIA, ALVEOLAR EPITHELIUM		2 (4%)	
METAPLASIA, OSSEOUS		2 (4%)	
#ALVEOLAR EPITHELIUM	(50)	(50)	(50)
HYPERPLASIA, ADENOMATOUS		2 (4%)	3 (6%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(50)	(50)
MYELOFIBROSIS	1 (2%)		
#SPLEEN	(50)	(49)	(50)
CONGESTION, NOS	1 (2%)		

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, GRANULOMATOUS		1 (2%)	
FIBROSIS, FOCAL	1 (2%)		1 (2%)
HEMATOPOIESIS	1 (2%)	3 (6%)	2 (4%)
#MANDIBULAR L. NODE	(50)	(50)	(50)
HYPERPLASIA, NOS	3 (6%)	1 (2%)	
#MESENTERIC L. NODE	(50)	(50)	(50)
ANGIECTASIS		1 (2%)	
#RENAL LYMPH NODE	(50)	(50)	(50)
HEMOSIDEROSIS			1 (2%)
ANGIECTASIS			4 (8%)
#INGUINAL LYMPH NODE	(50)	(50)	(50)
FIBROSIS			1 (2%)
HYPERPLASIA, NOS		1 (2%)	
#LUNG	(50)	(50)	(50)
LEUKOCYTOSIS, NOS		2 (4%)	
ERYTHROBLASTOSIS	1 (2%)		
#LIVER	(50)	(50)	(50)
LEUKOCYTOSIS, NOS	1 (2%)	5 (10%)	2 (4%)
ERYTHROBLASTOSIS	1 (2%)		
HEMATOPOIESIS		1 (2%)	
#KIDNEY	(50)	(50)	(50)
HYPERPLASIA, LYMPHOID		1 (2%)	
#ADRENAL	(50)	(48)	(50)
HEMATOPOIESIS		2 (4%)	
#ADRENAL CORTEX	(50)	(48)	(50)
HEMATOPOIESIS	2 (4%)		
#THYMUS	(36)	(38)	(35)
HYPERPLASIA, NOS	1 (3%)		
CIRCULATORY SYSTEM			
#HEART/ATRIUM	(50)	(50)	(50)
THROMBOSIS, NOS		2 (4%)	
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)	

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
FIBROSIS, FOCAL	18 (36%)	21 (42%)	23 (46%)
FIBROSIS, DIFFUSE	1 (2%)		
#PANCREAS	(50)	(50)	(50)
PERIARTERITIS	3 (6%)	5 (10%)	2 (4%)
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS	1 (2%)		2 (4%)
DIGESTIVE SYSTEM			
#PAROTID GLAND	(50)	(50)	(50)
ATROPHY, FOCAL		1 (2%)	
#LIVER	(50)	(50)	(50)
DEFORMITY, NOS	4 (8%)	2 (4%)	2 (4%)
CONGESTION, NOS		1 (2%)	
INFLAMMATION, FOCAL		1 (2%)	
EOSINOPHILIC INFILTRATE		1 (2%)	
INFLAMMATION, NECRO GRAN		1 (2%)	
DEGENERATION, CYSTIC	1 (2%)		
NECROSIS, CENTRAL		1 (2%)	
CYTOPLASMIC VACUOLIZATION	1 (2%)	2 (4%)	5 (10%)
NODULAR REGENERATION	1 (2%)	1 (2%)	1 (2%)
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, NOS		1 (2%)	
METAMORPHOSIS FATTY	1 (2%)	3 (6%)	2 (4%)
ATROPHY, NOS	5 (10%)	3 (6%)	
#LIVER/HEPATOCYTES	(50)	(50)	(50)
DEGENERATION, CYSTIC	5 (10%)		3 (6%)
CYTOPLASMIC VACUOLIZATION	3 (6%)	20 (40%)	17 (34%)
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	43 (86%)	37 (74%)	29 (58%)
HYPERPLASIA, FOCAL	2 (4%)		
#PANCREATIC ACINUS	(50)	(50)	(50)
ATROPHY, NOS		3 (6%)	
ATROPHY, FOCAL	17 (34%)	9 (18%)	13 (26%)
HYPERPLASIA, FOCAL	1 (2%)		
#GASTRIC FUNDAL GLAND	(50)	(50)	(50)
DILATATION, NOS	22 (44%)	22 (44%)	28 (56%)

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NOS	1 (2%)		
#COLON	(50)	(50)	(50)
NEMATODIASIS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
CYST, NOS	1 (2%)		
NEPHROSIS, NOS	47 (94%)	49 (98%)	48 (96%)
ENDOCRINE SYSTEM			
#PITUITARY	(49)	(48)	(49)
HYPERPLASIA, FOCAL	2 (4%)	3 (6%)	1 (2%)
#ANTERIOR PITUITARY	(49)	(48)	(49)
ANGIECTASIS	1 (2%)	2 (4%)	
#ADRENAL	(50)	(48)	(50)
ANGIECTASIS	1 (2%)		
#ADRENAL CORTEX	(50)	(48)	(50)
INFARCT, NOS			1 (2%)
CYTOPLASMIC VACUOLIZATION	5 (10%)	1 (2%)	1 (2%)
HYPERPLASIA, FOCAL	1 (2%)		
#ADRENAL MEDULLA	(50)	(48)	(50)
HEMATOMA, NOS			1 (2%)
NECROSIS, FOCAL	1 (2%)		
HYPERPLASIA, FOCAL	2 (4%)	5 (10%)	2 (4%)
#THYROID	(50)	(50)	(50)
CYSTIC FOLLICLES	2 (4%)		3 (6%)
DEGENERATION, CYSTIC	3 (6%)	10 (20%)	5 (10%)
HYPERPLASIA, C-CELL	3 (6%)	5 (10%)	1 (2%)
#PARATHYROID	(44)	(44)	(48)
HYPERPLASIA, NOS		2 (5%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC			1 (2%)
HYPERPLASIA, CYSTIC	1 (2%)		
CYSTIC DISEASE	13 (26%)	13 (26%)	10 (20%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CYSTIC DUCTS			3 (6%)
INFLAMMATION, NOS			1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)	10 (20%)	2 (4%)
HYPERPLASIA, CYSTIC	1 (2%)		
#PROSTATE	(50)	(46)	(50)
INFLAMMATION, NOS			2 (4%)
INFLAMMATION, SUPPURATIVE	17 (34%)	18 (39%)	30 (60%)
HYPERPLASIA, EPITHELIAL		1 (2%)	
*SEMINAL VESICLE	(50)	(50)	(50)
DILATATION, NOS			1 (2%)
#TESTIS	(50)	(50)	(50)
ATROPHY, NOS	42 (84%)	38 (76%)	39 (78%)
HYPERPLASIA, INTERSTITIAL CELL		1 (2%)	
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(50)
COMPRESSION	1 (2%)		1 (2%)
#HYPOTHALAMUS	(50)	(50)	(50)
COMPRESSION		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
HEMORRHAGE			2 (4%)
RETINOPATHY	12 (24%)	8 (16%)	35 (70%)
CATARACT	12 (24%)	4 (8%)	35 (70%)
*HARDERIAN GLAND	(50)	(50)	(50)
ECTOPIA	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			

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

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*ABDOMINAL WALL	(50)	(50)	(50)
ADHESION, NOS			1 (2%)
NECROSIS, FAT		1 (2%)	
*PERITONEUM	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
*PLEURA	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
*MESENTERY	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
INFLAMMATION, GRANULOMATOUS		1 (2%)	
NECROSIS, FAT	3 (6%)	4 (8%)	8 (16%)
ALL OTHER SYSTEMS			
OMENTUM			
NECROSIS, FAT	2		2
SPECIAL MORPHOLOGY SUMMARY			
NONE			

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

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS FED DIETS CONTAINING PROPYL GALLATE

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
INFLAMMATION, NOS			1 (2%)
ULCER, NOS	2 (4%)		
ULCER, CHRONIC		2 (4%)	
INFLAMMATION, CHRONIC FOCAL		1 (2%)	
FIBROSIS		1 (2%)	
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
VEGETABLE FOREIGN BODY			1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
#LUNG	(50)	(50)	(50)
CONGESTION, NOS	1 (2%)	2 (4%)	
INFLAMMATION, FOCAL		1 (2%)	
PNEUMONIA, ASPIRATION			2 (4%)
INFLAMMATION, FOCAL GRANULOMATOU	2 (4%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM			2 (4%)
#ALVEOLAR EPITHELIUM	(50)	(50)	(50)
HYPERPLASIA, ADENOMATOUS	1 (2%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(50)	(50)	(50)
MYELOFIBROSIS	1 (2%)		
#SPLEEN	(50)	(50)	(50)
INFARCT, NOS	1 (2%)		
HEMOSIDEROSIS	1 (2%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HEMATOPOIESIS	2 (4%)	1 (2%)	
#MANDIBULAR L. NODE	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)	2 (4%)	
HYPERPLASIA, CYSTIC		1 (2%)	
HYPERPLASIA, LYMPHOID			1 (2%)
#INGUINAL LYMPH NODE	(50)	(50)	(50)
HYPERPLASIA, NOS		1 (2%)	
#LUNG	(50)	(50)	(50)
LEUKOCYTOSIS, NOS		2 (4%)	
HYPERPLASIA, LYMPHOID		1 (2%)	
#LIVER	(50)	(50)	(50)
LEUKOCYTOSIS, NOS	3 (6%)	2 (4%)	1 (2%)
#CERVICAL MUCOUS MEMB	(50)	(50)	(50)
LEUKOCYTOSIS, NOS		1 (2%)	
CIRCULATORY SYSTEM			
#MYOCARDIUM	(50)	(50)	(50)
INFLAMMATION, FOCAL	2 (4%)		
FIBROSIS, FOCAL	4 (8%)	10 (20%)	10 (20%)
PERIARTERITIS	1 (2%)		
*MESENTERY	(50)	(50)	(50)
PERIARTERITIS	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
DEFORMITY, NOS	1 (2%)	2 (4%)	3 (6%)
CONGESTION, NOS		1 (2%)	
CHOLANGIOFIBROSIS		1 (2%)	
NECROSIS, FOCAL		1 (2%)	1 (2%)
METAMORPHOSIS FATTY	2 (4%)		
CYTOPLASMIC VACUOLIZATION	3 (6%)		2 (4%)
BASOPHILIC CYTO CHANGE	3 (6%)		
HYPERPLASIA, NOS			1 (2%)
NODULAR REGENERATION	1 (2%)	1 (2%)	
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
METAMORPHOSIS FATTY	4 (8%)	1 (2%)	

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ATROPHY, NOS		3 (6%)	1 (2%)
#LIVER/HEPATOCYTES	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION		4 (8%)	
BASOPHILIC CYTO CHANGE		3 (6%)	
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	13 (26%)	17 (34%)	16 (32%)
HYPERPLASIA, FOCAL			1 (2%)
#PANCREATIC ACINUS	(50)	(50)	(50)
ATROPHY, FOCAL	13 (26%)	3 (6%)	11 (22%)
#GASTRIC MUCOSA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
DEGENERATION, MUCOID		1 (2%)	
HYPERPLASIA, BASAL CELL			1 (2%)
#GASTRIC FUNDAL GLAND	(50)	(50)	(50)
DILATATION, NOS	26 (52%)	33 (66%)	35 (70%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
NEPHROSIS, NOS	8 (16%)	28 (56%)	4 (8%)
#KIDNEY/TUBULE	(50)	(50)	(50)
METAMORPHOSIS FATTY		1 (2%)	
PIGMENTATION, NOS	1 (2%)		
#URINARY BLADDER	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(49)	(50)
EMBRYONAL DUCT CYST		1 (2%)	
HEMORRHAGE	1 (2%)		
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL	5 (10%)	3 (6%)	1 (2%)
ANGIECTASIS	2 (4%)	3 (6%)	
#ANTERIOR PITUITARY	(50)	(49)	(50)
ANGIECTASIS	5 (10%)	4 (8%)	2 (4%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#ADRENAL	(50)	(50)	(50)
ANGIECTASIS	1 (2%)		
#ADRENAL CORTEX	(50)	(50)	(50)
METAMORPHOSIS FATTY	1 (2%)		
CYTOPLASMIC VACUOLIZATION	4 (8%)	3 (6%)	3 (6%)
ANGIECTASIS			1 (2%)
#ADRENAL MEDULLA	(50)	(50)	(50)
CYTOPLASMIC CHANGE, NOS		2 (4%)	
HYPERPLASIA, FOCAL		2 (4%)	1 (2%)
#THYROID	(50)	(48)	(50)
CYSTIC FOLLICLES	1 (2%)		
DEGENERATION, CYSTIC		1 (2%)	
HYPERPLASIA, C-CELL	5 (10%)	4 (8%)	3 (6%)
#PARATHYROID	(45)	(45)	(48)
HYPERPLASIA, FOCAL	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
CYSTIC DUCTS		1 (2%)	
INFLAMMATION, SUPPURATIVE	2 (4%)		
HYPERPLASIA, CYSTIC		1 (2%)	
ADENOSIS	1 (2%)		2 (4%)
CYSTIC DISEASE	37 (74%)	39 (78%)	32 (64%)
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)	1 (2%)	1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
HYPERPLASIA, CYSTIC			1 (2%)
*VAGINA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
*VAGINAL MUCOUS MEMBR	(50)	(50)	(50)
CYST, NOS			1 (2%)
#UTERUS	(50)	(50)	(50)
PROLAPSE		1 (2%)	
HYDROMETRA			1 (2%)

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HEMATOMA, NOS	1 (2%)	1 (2%)	
HEMATOMETRA			1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)		2 (4%)
#UTERUS/ENDOMETRIUM	(50)	(50)	(50)
HYPERPLASIA, CYSTIC	2 (4%)	1 (2%)	7 (14%)
HYPERPLASIA, STROMAL	1 (2%)		
#ENDOMETRIAL GLAND	(50)	(50)	(50)
DILATATION, NOS		4 (8%)	
#OVARY/PAROVARIAN	(49)	(50)	(50)
HEMORRHAGE		1 (2%)	
#OVARY	(49)	(50)	(50)
FOLLICULAR CYST, NOS		3 (6%)	3 (6%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
COMPRESSION		1 (2%)	
#INTERNAL CAPSULE	(50)	(50)	(49)
GLIOSIS	1 (2%)		
#HYPOTHALAMUS	(50)	(50)	(49)
COMPRESSION	3 (6%)	6 (12%)	1 (2%)
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
RETINOPATHY	10 (20%)	40 (80%)	14 (28%)
CATARACT	8 (16%)	39 (78%)	13 (26%)
*EYE/CORNEA	(50)	(50)	(50)
ULCER, NOS		1 (2%)	
*HARDERIAN GLAND	(50)	(50)	(50)
ECTOPIA	1 (2%)	1 (2%)	1 (2%)
*EXTERNAL EAR	(50)	(50)	(50)
ULCER, NOS	1 (2%)		

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

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, FOCAL	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*SKULL	(50)	(50)	(50)
HYPEROSTOSIS	1 (2%)		
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	4 (8%)	3 (6%)	2 (4%)
ALL OTHER SYSTEMS			
SOLE OF FOOT			
CALLUS	1		
OMENTUM			
NECROSIS, FAT	3	3	3
INFARCT HEMORRHAGIC	1		
VASCULARIZATION	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 PROPYL GALLATE

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE FED DIETS CONTAINING PROPYL GALLATE

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(49)	(50)
ULCER, NOS	1 (2%)	3 (6%)	
ULCER, FOCAL			2 (4%)
INFLAMMATION, CHRONIC	10 (20%)	4 (8%)	3 (6%)
INFLAMMATION, CHRONIC FOCAL	3 (6%)		1 (2%)
FIBROSIS	3 (6%)	2 (4%)	1 (2%)
HYPERPLASIA, BASAL CELL	1 (2%)		
*SUBCUT TISSUE	(50)	(49)	(50)
ABSCESS, NOS			1 (2%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC		1 (2%)	2 (4%)
INFLAMMATION, CHRONIC SUPPURATIV	3 (6%)		
ABSCESS, CHRONIC		1 (2%)	1 (2%)
RESPIRATORY SYSTEM			
#LUNG/BRONCHIOLE	(50)	(48)	(50)
HYPERPLASIA, NOS	1 (2%)		
#LUNG	(50)	(48)	(50)
CONGESTION, NOS	1 (2%)		
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		1 (2%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
INFLAMMATION, FOCAL GRANULOMATOU			1 (2%)
REACTION, FOREIGN BODY	1 (2%)		
CHOLESTEROL DEPOSIT		1 (2%)	1 (2%)
HYPERPLASIA, ADENOMATOUS	11 (22%)	8 (17%)	7 (14%)
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)		1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(50)
HYPERPLASIA, LYMPHOID	2 (4%)		2 (4%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#BONE MARROW	(50)	(49)	(50)
ATROPHY, NOS		2 (4%)	
HYPERPLASIA, GRANULOCYTIC	2 (4%)	1 (2%)	
#SPLEEN	(49)	(48)	(49)
FIBROSIS, FOCAL	1 (2%)		
AMYLOIDOSIS		1 (2%)	
ANGIECTASIS	2 (4%)		
HYPERPLASIA, LYMPHOID			2 (4%)
HEMATOPOIESIS	3 (6%)	5 (10%)	1 (2%)
#LYMPH NODE	(49)	(49)	(49)
ANGIECTASIS		1 (2%)	
#PANCREATIC L.NODE	(49)	(49)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)
#MESENTERIC L. NODE	(49)	(49)	(49)
HEMORRHAGE		1 (2%)	
ANGIECTASIS	1 (2%)	4 (8%)	2 (4%)
HYPERPLASIA, LYMPHOID			2 (4%)
HEMATOPOIESIS		2 (4%)	
#RENAL LYMPH NODE	(49)	(49)	(49)
INFLAMMATION, GRANULOMATOUS			1 (2%)
#AXILLARY LYMPH NODE	(49)	(49)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
#INGUINAL LYMPH NODE	(49)	(49)	(49)
HYPERPLASIA, LYMPHOID	2 (4%)	4 (8%)	2 (4%)
#LIVER	(50)	(49)	(50)
LEUKOCYTOSIS, NOS			1 (2%)
#PEYER'S PATCH	(48)	(49)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		2 (4%)
CIRCULATORY SYSTEM			
#MESENTERIC L. NODE	(49)	(49)	(49)
THROMBOSIS, NOS		1 (2%)	
#HEART	(48)	(49)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#AURICULAR APPENDAGE	(48)	(49)	(49)
THROMBUS, MURAL		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(49)	(50)
MINERALIZATION		1 (2%)	
CYST, NOS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		2 (4%)
INFLAMMATION, GRANULOMATOUS	1 (2%)		
NECROSIS, FOCAL	1 (2%)		
NECROSIS, COAGULATIVE	1 (2%)	6 (12%)	
NUCLEAR-SIZE ALTERATION		1 (2%)	
CYTOPLASMIC VACUOLIZATION	1 (2%)		
FOCAL CELLULAR CHANGE	1 (2%)		
ANGIECTASIS		1 (2%)	2 (4%)
#PANCREAS	(50)	(49)	(48)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
#SMALL INTESTINE	(48)	(49)	(49)
ULCER, FOCAL	1 (2%)		
#COLON	(49)	(48)	(49)
NEMATODIASIS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(50)
HYDRONEPHROSIS	1 (2%)		
PYELONEPHRITIS, NOS	2 (4%)	1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
INFLAMMATION, INTERSTITIAL	4 (8%)		
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC		3 (6%)	
INFLAMMATION, CHRONIC FOCAL			1 (2%)
NEPHROSIS, NOS		1 (2%)	
#KIDNEY/PELVIS	(50)	(49)	(50)
NECROSIS, MEDULLARY		1 (2%)	
#URINARY BLADDER	(50)	(49)	(49)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
*PROSTATIC URETHRA	(50)	(49)	(50)
HEMORRHAGE			1 (2%)
ENDOCRINE SYSTEM			
#ADRENAL CORTEX	(49)	(47)	(50)
HYPERTROPHY, FOCAL	1 (2%)		
HYPERPLASIA, FOCAL	1 (2%)		
#ADRENAL MEDULLA	(49)	(47)	(50)
HYPERPLASIA, FOCAL	1 (2%)	1 (2%)	
#THYROID	(49)	(48)	(49)
FOLLICULAR CYST, NOS			1 (2%)
DEGENERATION, CYSTIC	2 (4%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(49)	(50)
CYSTIC DUCTS	3 (6%)	6 (12%)	2 (4%)
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, NOS		3 (6%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		1 (2%)
INFLAMMATION, CHRONIC		2 (4%)	1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV	2 (4%)	1 (2%)	1 (2%)
ABSCESS, CHRONIC			1 (2%)
#PROSTATE	(50)	(49)	(50)
INFLAMMATION, SUPPURATIVE			1 (2%)
*SEMINAL VESICLE	(50)	(49)	(50)
INFLAMMATION, ACUTE SUPPURATIVE	1 (2%)		
INFLAMMATION, CHRONIC SUPPURATIV			1 (2%)
#TESTIS	(49)	(49)	(50)
GRANULOMA, SPERMATIC			1 (2%)
*EPIDIDYMIS	(50)	(49)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(49)	(50)
PERIVASCULAR CUFFING	1 (2%)		

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

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*EYE	(50)	(49)	(50)
PHTHISIS BULBI	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MESENTERY	(50)	(49)	(50)
NECROSIS, FAT		1 (2%)	
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	7	4	9
AUTOLYSIS/NO NECROPSY		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 PROPYL GALLATE

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	49
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	49
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(49)
INFLAMMATION, CHRONIC			1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(49)
EDEMA, NOS		1 (2%)	
INFLAMMATION, SUPPURATIVE		1 (2%)	1 (2%)
INFLAMMATION, GRANULOMATOUS			1 (2%)
INFLAMMATION, FOCAL GRANULOMATOU	1 (2%)		
CHOLESTEROL DEPOSIT	1 (2%)		1 (2%)
HYPERPLASIA, ADENOMATOUS	7 (14%)	5 (10%)	5 (10%)
HYPERPLASIA, ALVEOLAR EPITHELIUM			1 (2%)
#LUNG/ALVEOLI	(50)	(50)	(49)
HISTIOCYTOSIS		2 (4%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID	3 (6%)	2 (4%)	2 (4%)
#BONE MARROW	(50)	(50)	(49)
MYELOFIBROSIS	1 (2%)	3 (6%)	
#SPLEEN	(50)	(49)	(49)
ATROPHY, NOS			1 (2%)
ANGIECTASIS			1 (2%)
HYPERPLASIA, LYMPHOID	3 (6%)	6 (12%)	4 (8%)
HEMATOPOIESIS	4 (8%)	8 (16%)	5 (10%)
#MANDIBULAR L. NODE	(49)	(48)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#BRONCHIAL LYMPH NODE	(49)	(48)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)		
#MESENTERIC L. NODE	(49)	(48)	(49)
ANGIECTASIS		1 (2%)	
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	
#RENAL LYMPH NODE	(49)	(48)	(49)
ABSCESS, NOS		1 (2%)	
ANGIECTASIS	1 (2%)		
HYPERPLASIA, LYMPHOID		1 (2%)	
#LUNG	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID	1 (2%)	1 (2%)	
#LIVER	(50)	(50)	(49)
HYPERPLASIA, LYMPHOID			1 (2%)
HEMATOPOIESIS	1 (2%)	1 (2%)	2 (4%)
#PEYER'S PATCH	(47)	(47)	(48)
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	
#THYMUS	(47)	(49)	(48)
NECROSIS, NOS		1 (2%)	
CIRCULATORY SYSTEM			
#MYOCARDIUM	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, CHRONIC			1 (2%)
#CARDIAC VALVE	(50)	(50)	(49)
ENDOCARDITIS, BACTERIAL			1 (2%)
#UTERUS	(50)	(50)	(49)
THROMBUS, ORGANIZED	1 (2%)		
#THYROID	(49)	(47)	(48)
PERIARTERITIS			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR	2 (4%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	1 (2%)	4 (8%)
ABSCESS, CHRONIC		1 (2%)	
NECROSIS, COAGULATIVE	1 (2%)		2 (4%)
NUCLEAR-SIZE ALTERATION			1 (2%)
ANGIECTASIS		1 (2%)	
#PANCREAS	(49)	(48)	(49)
CYSTIC DUCTS	1 (2%)	1 (2%)	4 (8%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV			1 (2%)
#PANCREATIC ACINUS	(49)	(48)	(49)
ATROPHY, NOS	2 (4%)		
ATROPHY, FOCAL			1 (2%)
#STOMACH	(50)	(49)	(49)
ULCER, FOCAL	1 (2%)		
#GASTRIC MUCOSA	(50)	(49)	(49)
ULCER, FOCAL	1 (2%)		
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(49)
HYDRONEPHROSIS		1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)	1 (2%)	
PYELONEPHRITIS DIFFUSE		1 (2%)	
INFLAMMATION, INTERSTITIAL	4 (8%)	1 (2%)	2 (4%)
INFLAMMATION, SUPPURATIVE		1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	
GLOMERULONEPHRITIS PROLIFERATIVE		1 (2%)	1 (2%)
PERIVASCULAR CUFFING	2 (4%)	1 (2%)	1 (2%)
AMYLOIDOSIS	1 (2%)		
METAPLASIA, OSSEOUS		1 (2%)	1 (2%)
#KIDNEY/PELVIS	(50)	(50)	(49)
LYMPHOCYTIC INFLAMMATORY INFILTR	4 (8%)	2 (4%)	1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(48)	(48)	(49)
INFLAMMATION, NOS	1 (2%)		

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HYPERPLASIA, NOS		1 (2%)	1 (2%)
HYPERPLASIA, FOCAL	5 (10%)	3 (6%)	3 (6%)
ANGIECTASIS	4 (8%)		3 (6%)
#ADRENAL	(50)	(49)	(49)
ATROPHY, NOS			1 (2%)
ANGIECTASIS			1 (2%)
#THYROID	(49)	(47)	(48)
CYSTIC FOLLICLES			1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	1 (2%)	
DEGENERATION, CYSTIC	1 (2%)	1 (2%)	
HYPERPLASIA, FOLLICULAR-CELL	1 (2%)		
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(49)
CYSTIC DUCTS	1 (2%)	1 (2%)	1 (2%)
#UTERUS	(50)	(50)	(49)
PYOMETRA	2 (4%)		
#UTERUS/ENDOMETRIUM	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	6 (12%)	1 (2%)	6 (12%)
ABSCESS, NOS			1 (2%)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
HYPERPLASIA, EPITHELIAL	2 (4%)		
HYPERPLASIA, CYSTIC	41 (82%)	44 (88%)	40 (82%)
#OVARY/OVIDUCT	(50)	(50)	(49)
CYST, NOS			1 (2%)
#OVARY	(48)	(50)	(49)
CYSTIC FOLLICLES	2 (4%)	6 (12%)	2 (4%)
FOLLICULAR CYST, NOS	1 (2%)		1 (2%)
INFLAMMATION, SUPPURATIVE			1 (2%)
ABSCESS, NOS			1 (2%)
INFLAMMATION, CHRONIC SUPPURATIV			2 (4%)
ABSCESS, CHRONIC	6 (13%)	6 (12%)	9 (18%)
#OVARY/FOLLICLE	(48)	(50)	(49)
HEMORRHAGE		1 (2%)	

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
#BRAIN/MENINGES	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	1 (2%)	1 (2%)	
PERIVASCULAR CUFFING	2 (4%)		
#BRAIN	(50)	(50)	(49)
ABSCESS, NOS		1 (2%)	
#CEREBRAL CORTEX	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#BRAIN/THALAMUS	(50)	(50)	(49)
PSAMMOMA BODIES	1 (2%)		
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(49)
FIBROUS OSTEODYSTROPHY	4 (8%)	6 (12%)	8 (16%)
*FEMUR	(50)	(50)	(49)
FIBROUS OSTEODYSTROPHY	1 (2%)		1 (2%)
*ABDOMINAL MUSCLE	(50)	(50)	(49)
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE	2 (4%)	3 (6%)	
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, CHRONIC SUPPURATIV		1 (2%)	1 (2%)
ADHESION, NOS		1 (2%)	
*MESENTERY	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)

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

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, CHRONIC SUPPURATIV	1 (2%)		
NECROSIS, FAT	3 (6%)	1 (2%)	
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
INFLAMMATION, GRANULOMATOUS			1 (2%)
HEAD			
INFLAMMATION, SUPPURATIVE	1		
BROAD LIGAMENT			
HEMORRHAGIC CYST	1		
ABSCESS, CHRONIC	1		
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	1	2	
AUTOLYSIS/NO NECROPSY			1

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

APPENDIX E

ANALYSIS OF PROPYL GALLATE (LOT NO. 2185; LOT NO. 831) MIDWEST RESEARCH INSTITUTE

APPENDIX E

A. ELEMENTAL ANALYSIS

Element	C	H
Theory	56.60	5.70
Lot No. 2185:		
Determined	56.39	5.72
	56.50	5.61
Lot No. 831:		
Determined	56.92	5.76
	56.77	5.87

B. WATER ANALYSIS (Karl Fisher)

Lot No. 2185:

$1.3 \pm 0.1(\delta)\%$

Lot No. 831:

$0.04 \pm 0.02(\delta)$

C. MELTING POINT

Determined	Literature Values
Lot. No. 2185:	
m.p. 148 to 150°C (visual capillary) 149° to 150° with endotherms at 66° to 69°C and 146° to 148°C (Du Pont 900 DTA)	147° to 148°C (Fawcett and Robinson, 1927)
Lot No. 831:	
m.p.: 147° to 149°C (visual, capillary, Buchi 510 mp apparatus)	

D. THIN-LAYER CHROMATOGRAPHY

Plates: Silica Gel 60 F-254

Amount Spotted: 1,10 and 30μl of a 10 mg/ml solution of propyl gallate and 30μl of propyl gallate (Lot 2185) in 95% ethanol.

Ref. Standard: 1μl of a 10 mg/ml solution of resorcinol in 95% ethanol (1μl of a 10 mg/ml solution of gallic acid in 95% ethanol spotted as a check for presence of gallic acid in compound)

Visualization: Visible light, ultraviolet (254 nm and 366 nm) and 5% ethanolic molybdophosphoric acid spray, heated to 110°C until spots form (~20 min) (Stahl, 1969). Methyl red spray used on System 3.

APPENDIX E

1. Solvent System I: 95% ethanol/H_2O (90:10)

Spot intensity	R_f	R_{st}	Visualization			
			Visible Light	Spray	UV_{254}	UV_{366}
Lot No. 831 (major)	0.70	0.96	beige	blue	pink	yellow
Lot No. 2185 (major)	0.70	0.96	beige	blue	pink	yellow
Reference	0.72	nd	blue	pink	nd	
Gallic acid	0.66	0.91	beige	blue	pink	nd

2. Solvent System 2: 2-propanol/acetic acid (90:10)

Spot intensity	R_f	R_{st}	Visualization			
			Visible Light	Spray	UV_{254}	UV_{366}
Lot No. 831						
major	0.65	0.94	beige	blue	pink	yellow
slight trace	origin	nd	nd	pink	nd	
Lot No. 2185						
major	0.65	0.94	beige	blue	pink	yellow
slight trace	origin	nd	nd	pink	nd	
Reference	0.70	nd	blue	pink	nd	
Gallic acid	0.66	0.95	beige	blue	pink	nd

To detect the possible presence of gallic acid in the sample, 1μl of a 10 mg/ml solution of gallic acid was spotted concomitant with 300μg of Lot 831 and Lot 2185 of propyl gallate using a chromatographic system capable of increased separation of the two compounds (System 3, below). Visualization of spots with 254 nm ultraviolet light and methyl red reagent indicated no detectable free acid in either of the two batches.

3. Solvent System 3: Carbon tetrachloride; ethylene glycol monoethyl ether: acetic acid (75:15:10)

Spot intensity	R_f	R_{st}	Visualization			
			Visible Light	Spray	UV_{254}	UV_{366}
Lot No. 831						
major	0.49	0.94	beige	red	pink	yellow
slight trace	origin	nd	nd	pink	nd	
Lot No. 2185						
major	0.49	0.94	beige	red	pink	yellow
slight trace	origin	nd	nd	pink	nd	
Reference	0.51	nd	red	pink	nd	
Gallic acid	0.29	0.56	beige	red	pink	nd

E. VAPOR-PHASE CHROMATOGRAPHY

1. System 1, Lot 2185

Instrument: Tracor MT 220
Detector: Flame ionization
Column: 3% Dexsil 400, 1.8 m x 2 mm I.D.
Oven Temperature Program: 5 min. at 125°C, then 125° to 245°C 10°C/min.
Results: One homogeneous peak, retention time 13.4 min.

2. System 2, Lot 2185

Instrument: Tracor MT 220
Detector: Flame ionization
Column: 3% OV-17, 1.8 m x 2 mm I.D.
Oven Temperature Program: 5 min. at 150°C, then 150° to 245°C at 10°C/min.
Results: One homogeneous peak, retention time 11.4 min.

F. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

1. System 1, Lot 2185

Instrument: Waters ALC 202 with Model 660 Solvent Programmer
Detector: Ultraviolet, 254 nm
Column: μ-Porasil, 300 x 4 mm I.D.
Solvent: Tetrahydrofuran:hexane (70:30), isocratic
Flow Rate: 2 ml/min.
Results: One homogeneous peak, retention time 2.1 min.

2. System 2, Lot 2185

Instrument: Waters ALC 202 with Model 660 Solvent Programmer
Detector: Ultraviolet, 254 nm
Column: C_{18} μ-Bondapak, 300 x 4 mm I.D.
Solvent Program: 5% to 100% Methanol in 1% aqueous acetic acid, 10 min.
Program No.: 6
Flow Rate: 2 ml/min.
Results: One homogeneous peak, 6.8 min.

3. Instrumental System, Lot 831

Pump(s): Waters 6000A
Programmer: Waters 660
Detector: Waters 440
Injector: Waters U6K
Detection: Ultraviolet, 254 nm
Column: Waters μ-Bondapak C_{18}, 300 x 3.9 mm I.D.
Guard Column: Whatman CO:PELL ODS, 72 x 2.3 mm I.D.
Solvent System:

a. Water with 1% (v:v) acetic acid
b. Methanol with 1% (v:v) acetic acid

Program: 62% A:38%B, isocratic
Flow Rate: 1 ml/min.
Samples Injected: Solutions (25μl) of 1 mg propyl gallate/ml Solvent b filtered.

Results: Major peak and one impurity with a peak area of 0.38% of the major peak area, before the major peak. Two other peaks were observed before the major peak with individual areas <0.1% of the major peak area.

Peak No.	Retention Time (min.)	Retention Time (Relative to Major Peak)	Area (Percent of Major Peak)
1	9.25	0.51	0.38
2	18.25	1.00	100

Lot No. 2185 was analyzed using this same system and only one small impurity (<0.1%) was observed before the major peak.

The major peaks of lots 2185 and 831 were compared using an internal standard (propiophenone). The major peak of Lot No. 831 was 121.0±0.2% of the major peak of Lot No. 2185. Lot No. 2185 had evidently absorbed moisture during storage, as a Karl Fisher titration indicated 15.90±1.04% water.

G. SPECTRAL DATA

1. Infrared
Instrument: Beckman IR-12

Spectrum consistent with literature (Pouchert, 1970; Sadtler Standard Spectra)

a. Lot 2185

Cell: 1.2% in potassium bromide pellet
Results: See Figure 5

Instrument: Beckman IR-12

Spectrum consistent with literature reference (Pouchert, 1970; Sadtler Standard Spectra)

b. Lot 831

Cell: 1% in potassium bromide pellet

Results: See Figure 6

2. Ultraviolet/Visible
Instrument: Cary 118

Literature Values (Sedlacek, 1962)

a. Lot 2185

λ max (nm)	$\varepsilon \times 10^{-3}$	λ max (nm)	$\varepsilon \times 10^{-3}$
276	10.51 ± 0.06 (δ)	271	8.23
218	26.5 ± 0.2 (δ)	220	9.89

No maximum observed between 350 and 800 nm (visible range) but a gradual increase in absorbance toward the short wavelength end.
Concentration: 1 mg/ml
Solvent: 95% Ethanol

Solvent: 72% Ethanol

b. lot 831

λ max (nm)	$\varepsilon \times 10^{-3}$	λ max (nm)	$\varepsilon \times 10^{-3}$
372 (shoulder)	0.00157 ± 0012 (δ)	271	8.234
331 (shoulder)	1.334 ± 0.042 (δ)	220	9.889
277	10.13 ± 0.08 (δ)		
218	26.01 ± 0.36 (δ)		

Solvent: 95% ethanol

Solvent: 72% ethanol

3. Nuclear Magnetic Resonance
Instrument: Varian HA-100
Solvent: CD_3OD with internal tetramethylsilane
Assignments (See Figures 7 and 8)

No literature spectrum found

a. Lot 2185
(1) t, δ 1.00 ppm (J_{ab} = 7 Hz)
(2) m, δ 1.74 ppm (J_{bc} = 7 Hz)
(3) t, δ 4.20 ppm
(4) s, δ 5.10 ppm
(5) s, δ 7.16 ppm

Integration Ratios
(1) 3.19
(2) 2.01
(3) 1.97
(4) HDO and OH
(5) 1.83

b. Lot 831
(1) t, δ 1.00 ppm (J_{ab} = 7 Hz)
(2) m, δ 1.74 ppm (J_{bc} = 7 Hz)
(3) t, δ 4.20 ppm
(4) s, δ 5.10 ppm
(5) s, δ 7.16 ppm

Integration Ratios
(1) 3.19
(2) 2.01
(3) 1.97
(4) HDO and OH
(5) 1.83

No literature spectrum found.

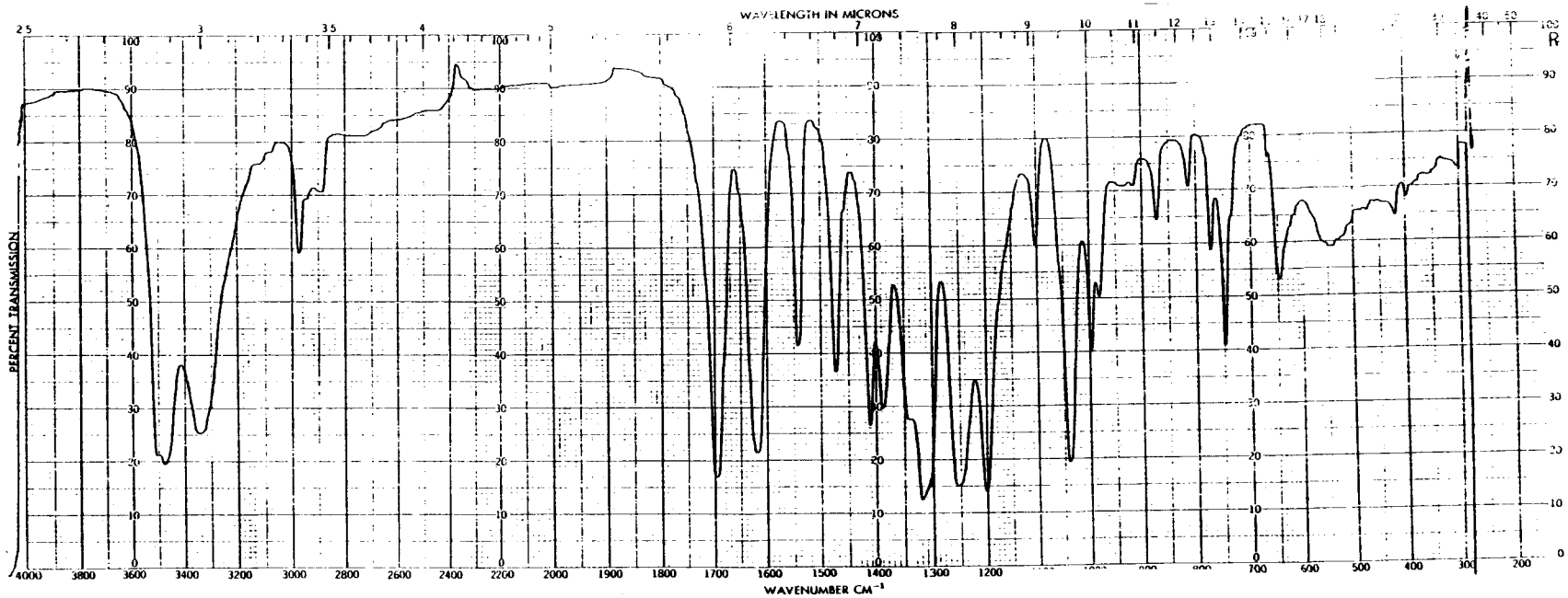


Figure 5. Infrared Absorption Spectrum of Propyl Gallate (Lot No. 2185)

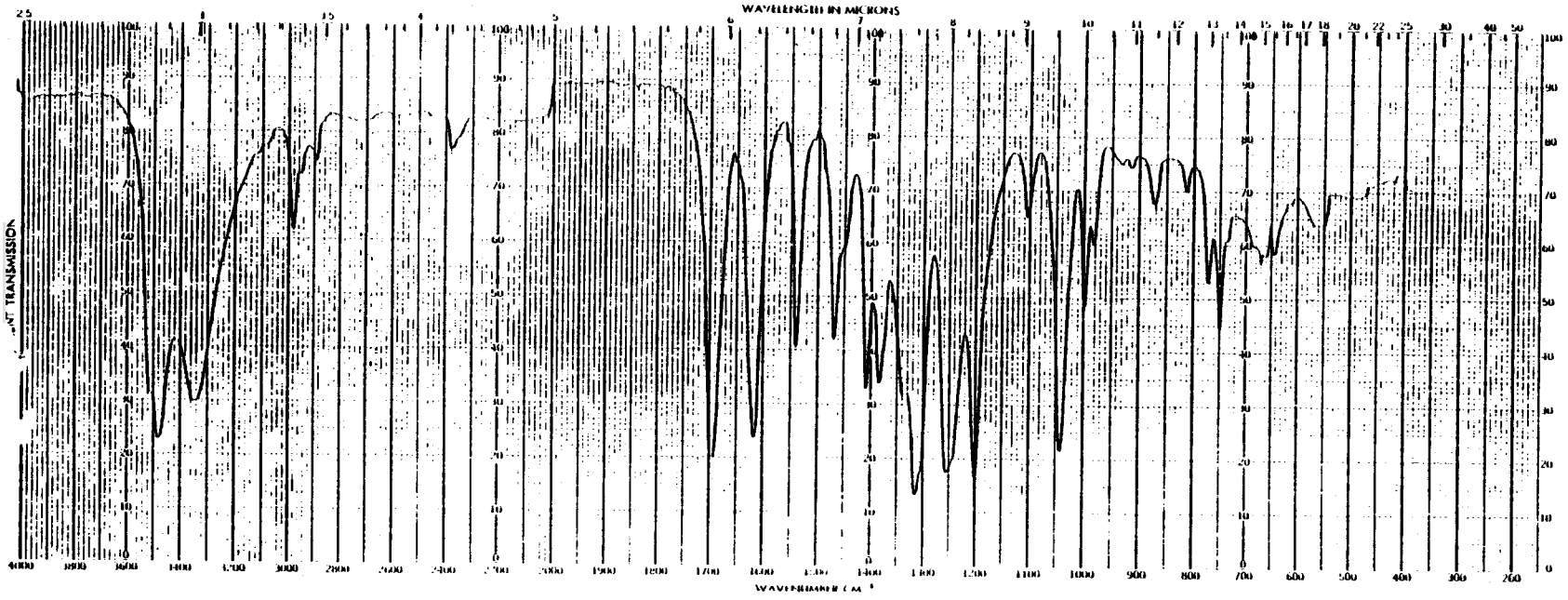


Figure 6. Infrared Absorption Spectrum of Propyl Gallate (Lot No. 831)

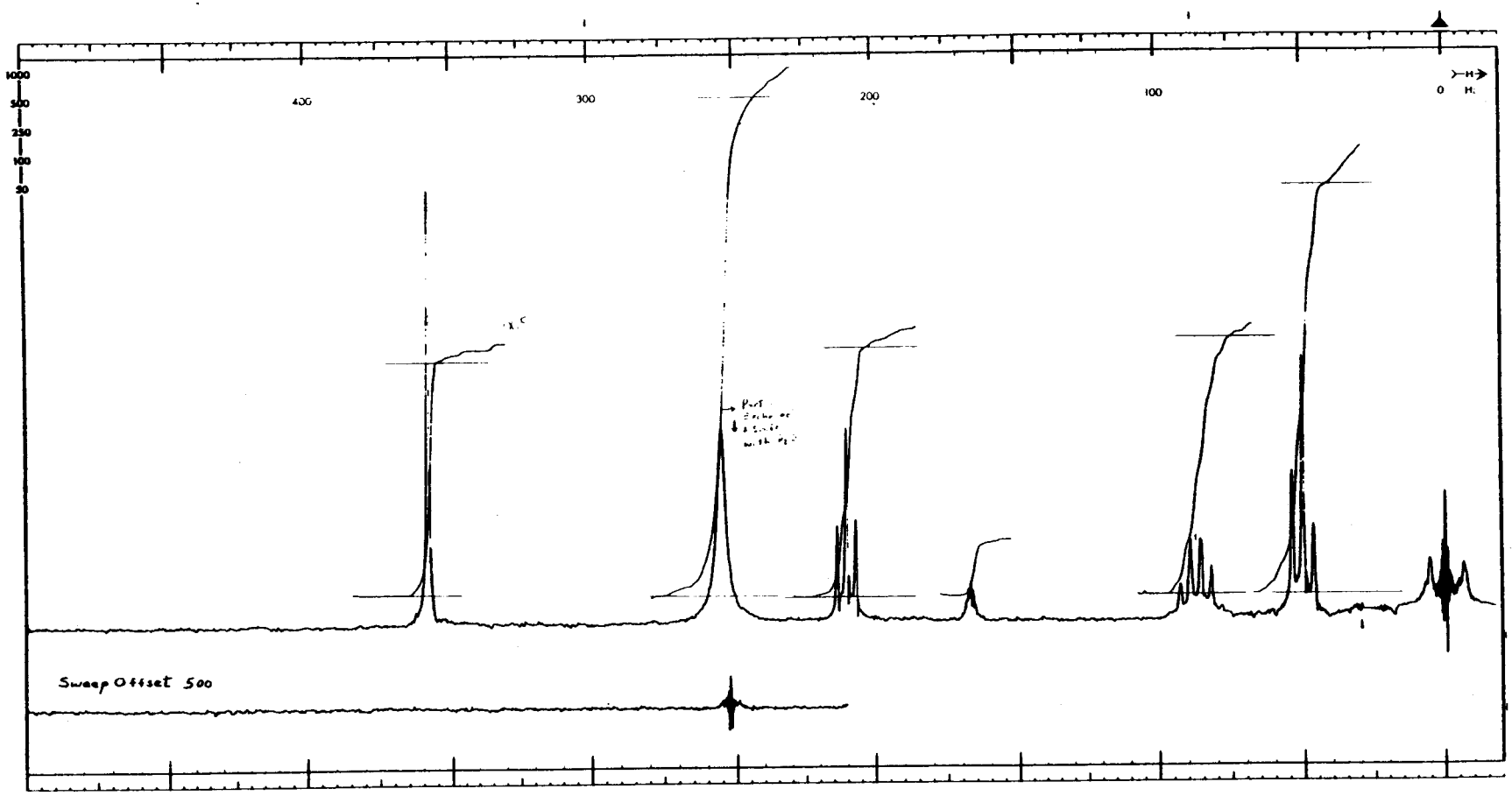


Figure 7. Nuclear Magnetic Resonance Spectrum of Propyl Gallate (Lot No. 2185)

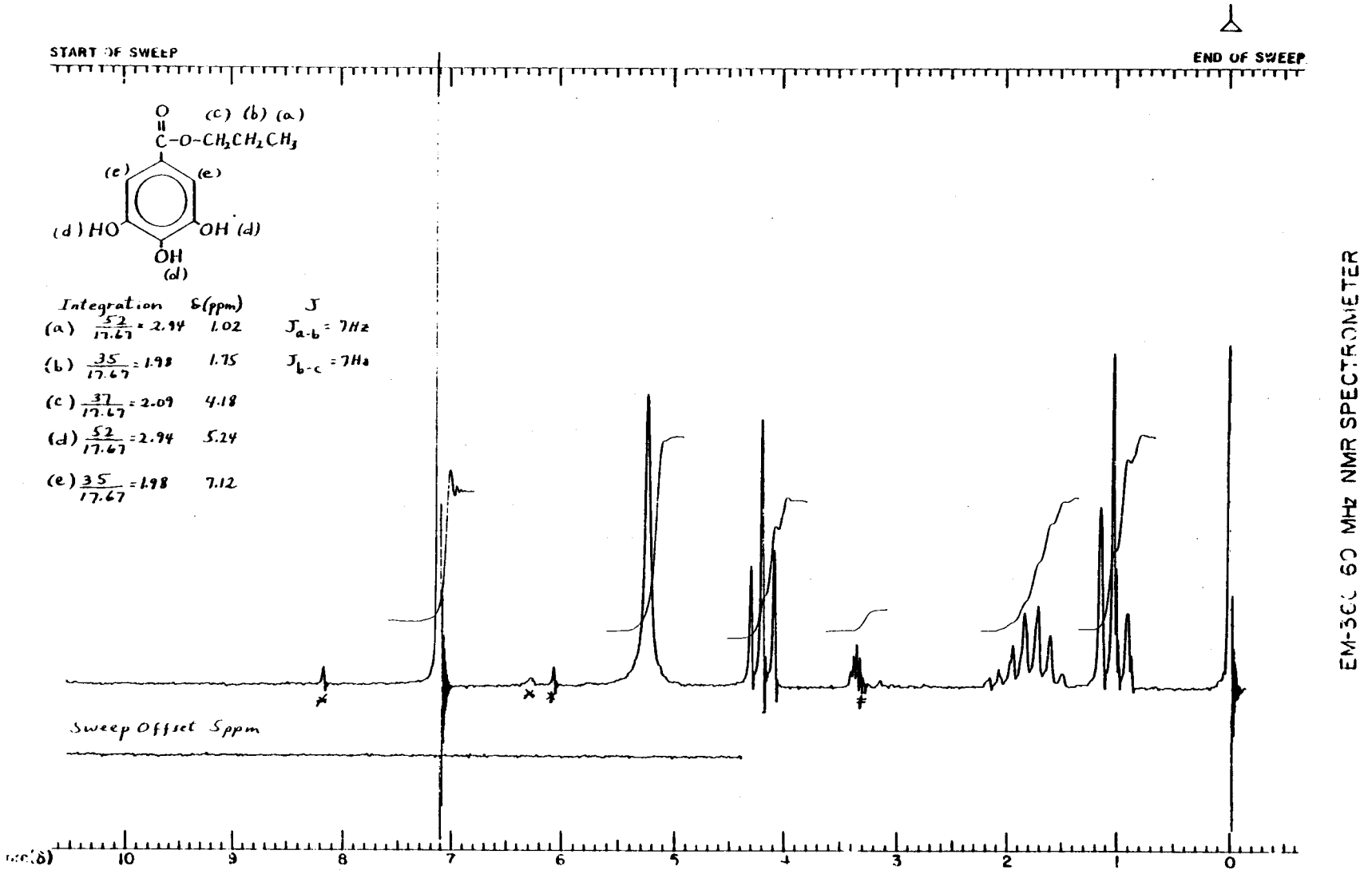


Figure 8. Nuclear Magnetic Resonance Spectrum of Propyl Gallate (Lot No. 831)

APPENDIX F

ANALYSIS OF FORMULATED DIETS FOR STABILITY OF PROPYL GALLATE MIDWEST RESEARCH INSTITUTE

APPENDIX F

A. MIXING AND STORAGE

Propyl gallate (2.48862 g) and Wayne Lab-Blox® Rodent Feed (22.71815 g) were mixed for 15 minutes using a mortar and pestle. Samples of the mix were then removed and stored for 2 weeks at -20°, 5°, 25°, and 45°C, respectively.

B. EXTRACTION AND ANALYSIS PROCEDURES

The samples were mixed with methanol in an ultrasonic vibratory bath and then were triturated with the methanol using a Polytron® mixer. The resulting mixture was centrifuged and the supernatant solution decanted. The remaining feed residue was reextracted with fresh methanol. The supernatant solutions were combined and diluted to working volume for analysis by ultraviolet absorption spectrophotometry on a Cary 118 spectrophotometer at 276 nm.

C. RESULTS

Temperature (°C)	Average (%)
45	9.2 ± 0.4
25	9.4 ± 0.4
5	9.8 ± 0.4
-20	10.0 ± 0.4

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

D. CONCLUSION

Propyl gallate mixed with feed is stable for 2 weeks at temperatures of up to 45°C.

APPENDIX G

ANALYSIS OF FORMULATED DIETS FOR CONCENTRATIONS OF PROPYL GALLATE

Two-gram samples of the chemical/feed mixtures were weighed into sample tubes and mixed with 29 ml of methanol. These mixtures were triturated for 2 minutes with the polytron blender and filtered using a millipore filtering apparatus with a fiberglass filter. The feed residue was then stirred with 20 ml of fresh methanol and filtered. This process was repeated with another 20 ml of methanol. The combined extracts were then diluted to a volume of 100 ml.

These extracts were analyzed by ultraviolet absorption spectroscopy. Two-milliliter aliquots of the extracts were diluted to a volume of 50 ml with methanol. The absorbance of the samples was then read at 276 nm and compared to a standard ultraviolet absorption curve for propyl gallate.

Control feed and spiked control feed were analyzed by the same procedure. Correction for absorption of the control feed was applied to the chemical/feed samples and spiked control feed.

Results are presented in Table G1.

TABLE G1. ANALYSIS OF FORMULATED DIETS FOR CONCENTRATIONS OF PROPYL GALLATE

Date Mixed	Date Used	Concentration *(a)* of Propyl Gallate in Feed for target concentration of	
		6,000 ppm	12,000 ppm
08/15/78	Week of 08/16 and 08/23	6,100	11,900
		5,900	
09/14/78	Week of 09/15 and 09/22	6,100	11,300
10/10/78	Week of 10/11 and 10/18	5,900	11,100
11/08/78	Week of 11/09 and 11/16	6,500	11,800
		5,800 *(b)*	
12/06/78	Week of 12/07 and 12/14	6,600	11,800
		6,100	11,800
01/03/79	Week of 01/04 and 01/11	5,600	12,000
01/31/79	Week of 02/01 and 02/08	5,500	11,300
02/28/79	Week of 03/01 and 03/08	5,500	11,200
		4,670 *(b)*	
03/28/79	Week of 03/30 and 04/07	5,500	10,900
04/25/79	Week of 04/26 and 05/01	5,400	11,100
05/29/79	Week of 06/01 and 06/08	6,000	12,000
06/20/79	Week of 06/21 and 06/28	5,600	11,200
07/18/79	Week of 07/19 and 07/26	5,900	11,800
		6,300	12,000
08/15/79	Week of 08/16 and 08/23	5,600	11,400
		6,300 *(c)*	
09/12/79	Week of 09/13 and 09/20	5,000	11,400
10/10/79	Week of 10/11 and 10/18	5,700	11,600
11/07/79	Week of 11/08 and 11/15	5,500	11,100
12/05/79	Week of 12/06 and 12/13	5,500	11,200
01/02/80	Week of 01/03 and 01/10	5,700	11,200
			11,300 *(b)*
01/30/80	Week of 02/01 and 02/08	5,800	12,000
02/27/80	Week of 02/28 and 03/05	5,700	11,200
03/26/80	Week of 03/27 and 04/03	5,860	11,900
04/23/80	Week of 04/24 and 05/01	5,700	12,000
05/21/80	Week of 05/22 and 05/29		11,100
05/28/80	Week of 05/29 and 06/05	5,950	
06/18/80	Week of 06/19 and 06/26	5,800	11,800
		5,740 *(b)*	
Mean (ppm)		5,795	11,522
Standard deviation		341	370
Coefficient of variation (%)		5.8	3.2
Range (ppm)		5,400-6,600	10,900-12,000
Number of samples		28	27

(a) The data presented are the average of the results of duplicate analyses.
(b) Analysis by Midwest Research Institute
(c) Analysis by Raltech Scientific Services

APPENDIX H

HISTORICAL INCIDENCES OF SELECTED TUMORS IN F344/N RATS AND $B6C3F_1$ MICE IN THE BIOASSAY PROGRAM

TABLE H1. HISTORICAL INCIDENCE OF THYROID TUMORS IN UNTREATED CONTROL MALE F344/N RATS *(a)*

Laboratory	Follicular-Cell Adenoma	Follicular-Cell Carcinoma	Follicular-Cell Adenoma or Carcinoma
Battelle	4/287 (1.4%)	3/287 (1.0%)	7/287 (2.4%)
Dow	0/89 (0.0%)	2/89 (2.2%)	2/89 (2.2%)
Frederick	2/462 (0.4%)	4/462 (0.9%)	6/462 (1.3%)
Gulf South	2/93 (2.2%)	2/93 (2.2%)	4/93 (4.3%)
Hazleton	2/192 (1.0%)	1/192 (0.5%)	3/192 (1.6%)
Litton	3/703 (0.4%)	4/703 (0.6%)	7/703 (1.0%)
Mason	3/989 (0.3%)	3/989 (0.3%)	6/989 (0.6%)
Papanicolaou	2/44 (4.5%)	0/44 (0.0%)	2/44 (4.5%)
Southern	8/584 (1.4%)	6/584 (1.0%)	14/584 (2.4%)
Total	26/3443 (0.8%)	25/3443 (0.7%)	51/3443 (1.5%)
Overall Historical Range			
High	2/44	1/37	4/89
Low	0/53	0/53	0/53

(a) Data as of June 15, 1981 for studies of at least 104 weeks. Range is presented for groups of 35 or more animals.

TABLE H2. HISTORICAL INCIDENCE OF PREPUTIAL GLAND TUMORS IN UNTREATED CONTROL MALE F344/N RATS *(a)*

Laboratory	Adenoma	Carcinoma	Adenocarcinoma
Battelle	4/290 (1.4%)	4/290 (1.4%)	5/290 (1.7%)
Dow	1/100 (1.0%)	7/100 (7.0%)	0/100 (0.0%)
Frederick	2/467 (0.4%)	0/467 (0.0%)	0/467 (0.0%)
Gulf South	1/97 (1.0%)	0/97 (0.0%)	0/97 (0.0%)
Hazleton	15/198 (7.6%)	0/198 (0.0%)	0/198 (0.0%)
Litton	9/789 (1.1%)	11/789 (1.4%)	2/789 (0.3%)
Mason	19/1066 (1.8%)	28/1066 (2.6%)	0/1066 (0.0%)
Papanicolaou	0/50 (0.0%)	4/50 (8.0%)	0/50 (0.0%)
Southern	10/591 (1.7%)	7/591 (1.2%)	1/591 (0.2%)
Total	61/3648 (1.7%)	61/3648 (1.7%)	8/3648 (0.2%)
Overall Historical Range			
High	6/50	8/50	3/50
Low	0/90	0/90	0/54

(a) Data as of June 15, 1981 for studies of at least 104 weeks. Range is presented for groups of 35 or more animals.

TABLE H3. HISTORICAL INCIDENCE OF ADRENAL TUMORS IN UNTREATED CONTROL MALE F344/N RATS *(a)*

Laboratory	Pheochromocytoma	Malignant Pheochromocytoma
Battelle	48/286 (16.8%)	4/286 (1.4%)
Dow	9/99 (9.1%)	1/99 (1.0%)
Frederick	50/465 (10.8%)	3/465 (0.6%)
Gulf South	9/93 (9.7%)	0/93 (0.0%)
Hazleton	25/194 (12.9%)	1/194 (0.5%)
Litton	101/773 (13.1%)	1/773 (0.1%)
Mason	156/1045 (14.9%)	14/1045 (1.3%)
Papanicolaou	2/45 (4.4%)	1/45 (2.2%)
Southern	64/586 (10.9%)	8/586 (1.4%)
Total	464/3586 (12.9%)	33/3586 (0.9%)
Overall Historical Range		
High	18/50	4/48
Low	2/50	0/50

(a) Data as of June 15, 1981 for studies of at least 104 weeks. Range is presented for groups of 35 or more animals.

TABLE H4. HISTORICAL INCIDENCE OF PANCREATIC ISLET-CELL TUMORS IN UNTREATED CONTROL MALE F344/N RATS *(a)*

Laboratory	Islet-Cell Adenoma	Islet-Cell Carcinoma
Battelle	5/282 (1.8%)	7/282 (2.5%)
Dow	7/97 (7.2%)	0/97 (0.0%)
Frederick	20/447 (4.5%)	1/447 (0.2%)
Gulf South	9/94 (9.6%)	1/94 (1.1%)
Hazleton	8/195 (4.1%)	1/195 (0.5%)
Litton	29/755 (3.8%)	7/755 (0.9%)
Mason	36/999 (3.6%)	6/999 (0.6%)
Papanicolaou	1/46 (2.2%)	0/46 (0.0%)
Southern	19/586 (3.2%)	12/586 (2.0%)
Total	134/3501 (3.8%)	35/3501 (1.0%)
Overall Historical Range		
High	6/49	3/44
Low	0/88	0/50

(a) Data as of June 15, 1981, for studies of at least 104 weeks. The range is presented for groups of 35 or more animals.

TABLE H5. HISTORICAL INCIDENCE OF UTERINE TUMORS IN UNTREATED CONTROL FEMALE F344/N RATS *(a)*

Laboratory	Endometrial Stromal Polyp	Endometrial Stromal Sarcoma
Battelle	65/286 (22.7%)	1/286 (0.3%)
Dow	11/100 (11.0%)	0/100 (0.0%)
Frederick	73/517 (14.1%)	1/517 (0.2%)
Gulf South	8/85 (9.4%)	0/85 (0.0%)
Hazleton	28/197 (14.2%)	2/197 (1.0%)
Litton	114/759 (15.0%)	3/759 (0.4%)
Mason	232/1097 (21.1%)	9/1097 (0.8%)
Papanicolaou	11/45 (24.4%)	0/45 (0.0%)
Southern	90/587 (15.3%)	8/587 (1.4%)
Total	632/3673 (17.2%)	24/3673 (0.7%)
Overall Historical Range		
High	18/49	3/50
Low	2/50	0/87

(a) Data as of June 15, 1981 for studies of at least 104 weeks. Range is presented for groups of 35 or more animals.

TABLE H6. HISTORICAL INCIDENCE OF BRAIN TUMORS IN UNTREATED CONTROL FEMALE F344/N RATS *(a)*

Laboratory	Tumor	Incidence (Percent)
Battelle	Ependymona	1/288 (0.35%)
	Astrocytoma	1/288 (0.35%)
	Glioma	1/288 (0.35%)
	Oligodendroglioma	1/288 (0.35%)
Dow	None	0/98 (0%)
Frederick	Ependymona	1/518 (0.19%)
	Astrocytoma	3/518 (0.58%)
	Oligodendroglioma	1/518 (0.19%)
Gulf South	None	0/100 (0%)
Hazleton	None	0/200 (0%)
Litton	Meningioma	1/766 (0.13%)
	Glioma	2/766 (0.26%)
	Astrocytoma	2/766 (0.26%)
Mason	Glioma	2/1107 (0.18%)
	Astrocytoma	7/1107 (0.63%)
	Meningioma	1/1107 (0.09%)
	Oligodendroglioma	2/1107 (0.18%)
	Neoplasm, NOS	1/1107 (0.09%)
	Carcinoma, NOS	1/1107 (0.09%)
Papanicolaou	None	0/48 (0%)
Southern	Oligodendroglioma	1/586 (0.17%)
	Astrocytoma	2/586 (0.34%)
	Meningioma	1/586 (0.17%)
Total		32/3711 (0.86%)

(a) Data as of June 15, 1981 for studies of at least 104 weeks.

TABLE H7. HISTORICAL INCIDENCE OF HEMATOPOIETIC TUMORS IN UNTREATED CONTROL MALE B6C3F$_1$ MICE *(a)*

Laboratory	Histiocytic Lymphoma	All Malignant Lymphoma	Lymphoma or Leukemia
Battelle	21/348 (6.0%)	45/348 (12.9%)	49/348 (14.1%)
Dow	4/99 (4.0%)	17/99 (17.2%)	18/99 (18.2%)
Frederick	7/407 (1.7%)	46/407 (11.3%)	48/407 (11.8%)
Gulf South	0/48 (0.0%)	6/48 (12.5%)	11/48 (22.9%)
Hazleton	5/49 (10.2%)	7/49 (14.3%)	7/49 (14.3%)
Litton	9/507 (1.8%)	44/507 (8.7%)	47/507 (9.3%)
Mason	12/852 (1.4%)	127/852 (14.9%)	129/852 (15.1%)
Southern	21/640 (3.3%)	60/640 (9.4%)	65/640 (10.2%)
Total	79/2950 (2.7%)	352/2950 (11.9%)	374/2950 (12.7%)
Overall Historical Range			
High	5/49	13/39	13/39
Low	0/50	1/50	1/50

(a) Data as of June 15, 1981 for studies of at least 104 weeks. Range is presented for groups of 35 or more animals.

TABLE H8. HISTORICAL INCIDENCE OF LIVER TUMORS IN UNTREATED CONTROL FEMALE B6C3F$_1$ MICE *(a)*

Laboratory	Adenoma	Carcinoma	Combined
Battelle	5/348 (1.4%)	21/348 (6.0%)	25/348 (7.2%)
Dow	3/98 (3.1%)	5/98 (5.1%)	7/98 (7.1%)
Frederick	10/431 (2.3%)	13/431 (3.0%)	22/431 (5.1%)
Gulf South	8/134 (6.0%)	5/134 (3.7%)	13/134 (9.7%)
Hazleton	1/100 (1.0%)	4/100 (4.0%)	5/100 (5.0%)
Litton	21/512 (4.1%)	11/512 (2.1%)	32/512 (6.3%)
Mason	38/859 (4.4%)	40/859 (4.7%)	77/859 (9.0%)
Southern	18/645 (2.8%)	21/645 (3.3%)	38/645 (5.9%)
Total	104/3127 (3.3%)	120/3127 (3.8%)	219/3127 (7.0%)
Overall Historical Range			
High	9/49	7/48	10/49
Low	0/50	0/50	0/50

(a) Data as of June 15, 1981 for studies of at least 104 weeks. Range is presented for groups of 35 or more animals.

☆ U.S. GOVERNMENT PRINTING OFFICE: 1983-381-132:758