CARCINOGENESIS BIOASSAY OF PROPYL GALLATE (CAS NO. 121-79-9) IN F344 RATS AND B6C3F1 MICE (FEED STUDY)
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 B6C3F1 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

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstract</td>
<td>7</td>
</tr>
<tr>
<td>Contributors</td>
<td>9</td>
</tr>
<tr>
<td>Reviewers</td>
<td>11</td>
</tr>
<tr>
<td>Summary of Peer Review Comments</td>
<td>12</td>
</tr>
<tr>
<td>I. Introduction</td>
<td>13</td>
</tr>
<tr>
<td>II. Materials and Methods</td>
<td>17</td>
</tr>
<tr>
<td>Chemical Analysis</td>
<td>18</td>
</tr>
<tr>
<td>Prechronic Studies</td>
<td>18</td>
</tr>
<tr>
<td>Single-Dose Study</td>
<td>18</td>
</tr>
<tr>
<td>Fourteen-Day Study</td>
<td>18</td>
</tr>
<tr>
<td>Thirteen-Week Study</td>
<td>18</td>
</tr>
<tr>
<td>Chronic Studies</td>
<td>19</td>
</tr>
<tr>
<td>Study Design</td>
<td>19</td>
</tr>
<tr>
<td>Preparation of Test Diets</td>
<td>19</td>
</tr>
<tr>
<td>Clinical Examinations and Pathology</td>
<td>19</td>
</tr>
<tr>
<td>Data Recording and Statistical Methods</td>
<td>20</td>
</tr>
<tr>
<td>III. Results</td>
<td>25</td>
</tr>
<tr>
<td>Rats</td>
<td>26</td>
</tr>
<tr>
<td>Prechronic Studies</td>
<td>26</td>
</tr>
<tr>
<td>Single-Dose Study</td>
<td>26</td>
</tr>
<tr>
<td>Fourteen-Day Study</td>
<td>26</td>
</tr>
<tr>
<td>Thirteen-Week Study</td>
<td>27</td>
</tr>
<tr>
<td>Chronic Studies</td>
<td>28</td>
</tr>
<tr>
<td>Body Weights and Clinical Signs</td>
<td>28</td>
</tr>
<tr>
<td>Survival</td>
<td>30</td>
</tr>
<tr>
<td>Pathology and Statistical Analyses of Results</td>
<td>31</td>
</tr>
<tr>
<td>Mice</td>
<td>39</td>
</tr>
<tr>
<td>Prechronic Studies</td>
<td>39</td>
</tr>
<tr>
<td>Single-Dose Study</td>
<td>39</td>
</tr>
<tr>
<td>Fourteen-Day Study</td>
<td>39</td>
</tr>
<tr>
<td>Thirteen-Week Study</td>
<td>40</td>
</tr>
<tr>
<td>Chronic Studies</td>
<td>41</td>
</tr>
<tr>
<td>Body Weights and Clinical Signs</td>
<td>41</td>
</tr>
<tr>
<td>Survival</td>
<td>43</td>
</tr>
<tr>
<td>Pathology and Statistical Analyses of Results</td>
<td>44</td>
</tr>
<tr>
<td>IV. Discussion and Conclusions</td>
<td>51</td>
</tr>
<tr>
<td>V. References</td>
<td>55</td>
</tr>
</tbody>
</table>

## TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td>Experimental Design and Materials and Methods</td>
<td>22</td>
</tr>
<tr>
<td>Table 2</td>
<td>Survival and Mean Body Weights of Rats Fed Diets Containing Propyl Gallate for 14 Days</td>
<td>26</td>
</tr>
<tr>
<td>Table 3</td>
<td>Survival, Mean Body Weights, and Feed Consumption of Rats Fed Diets Containing Propyl Gallate for 13 Weeks</td>
<td>27</td>
</tr>
<tr>
<td>Table 4</td>
<td>Cumulative Mean Body Weight Change (Relative to Controls) of Rats Fed Diets Containing Propyl Gallate in the Chronic Study</td>
<td>29</td>
</tr>
<tr>
<td>Table 5</td>
<td>Feed Consumption by Rats Receiving Propyl Gallate in the Chronic Study</td>
<td>29</td>
</tr>
</tbody>
</table>
Table 6 Analysis of Primary Tumors in Male Rats ........................................ 32
Table 7 Analysis of Primary Tumors in Female Rats ........................................ 36
Table 8 Survival and Mean Body Weights of Mice Fed Diets Containing Propyl Gallate for 14 Days .......................................................... 39
Table 9 Survival, Mean Body Weights, and Feed Consumption of Mice Fed Diets Containing Propyl Gallate for 13 Weeks .................................. 40
Table 10 Cumulative Mean Body Weight Change (Relative to Controls) of Mice Fed Diets Containing Propyl Gallate in the Chronic Study .................. 42
Table 11 Feed Consumption by Mice Receiving Propyl Gallate in the Chronic Study .......................................................... 42
Table 12 Analysis of Primary Tumors in Male Mice ........................................ 45
Table 13 Analysis of Primary Tumors in Female Mice ........................................ 48

FIGURES

Figure 1 Growth Curves for Rats Fed Diets Containing Propyl Gallate .................. 28
Figure 2 Survival Curves for Rats Fed Diets Containing Propyl Gallate .................. 30
Figure 3 Growth Curves for Mice Fed Diets Containing Propyl Gallate .................. 41
Figure 4 Survival Curves for Mice Fed Diets Containing Propyl Gallate .................. 43
Figure 5 Infrared Absorption Spectrum of Propyl Gallate (Lot No. 2185) ............... 137
Figure 6 Infrared Absorption Spectrum of Propyl Gallate (Lot No. 831) ............... 138
Figure 7 Nuclear Magnetic Resonance Spectrum of Propyl Gallate (Lot No. 2185) ... 139
Figure 8 Nuclear Magnetic Resonance Spectrum of Propyl Gallate (Lot No. 831) .... 140

APPENDIXES

Appendix A Summary of the Incidence of Neoplasms in Rats Fed Diets Containing Propyl Gallate .......................................................... 59
Table A1 Summary of the Incidence of Neoplasms in Male Rats Fed Diets Containing Propyl Gallate .......................................................... 60
Table A2 Summary of the Incidence of Neoplasms in Female Rats Fed Diets Containing Propyl Gallate .......................................................... 66
Table A3 Individual Animal Tumor Pathology Tables of Male Rats in the 2-Year Study of Propyl Gallate .......................................................... 70
Table A4 Individual Animal Tumor Pathology Tables of Female Rats in the 2-Year Study of Propyl Gallate .......................................................... 76
Appendix B Summary of the Incidence of Neoplasms in Mice Fed Diets Containing Propyl Gallate .......................................................... 83
Table B1 Summary of the Incidence of Neoplasms in Male Mice Fed Diets Containing Propyl Gallate .......................................................... 84
Table B2 Summary of the Incidence of Neoplasms in Female Mice Fed Diets Containing Propyl Gallate .......................................................... 88
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 B6C3F1 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≤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≤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≤0.022) positive trend, and the incidence in the high-dose group was significantly (P≤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 B6C3F1 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. Joseph Haseman
Dr. G. Boorman                  Dr. James E. Huff
Dr. R. Chhabra                  Dr. C. W. Jameson
Dr. Michael P. Dieter           Dr. John A. Moore
Dr. J. Fielding Douglas         Dr. Ernest E. McConnell
Dr. Charles K. Grieshaber       Dr. Raymond Tennant
Dr. Larry Hart

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. Hitchcock 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
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 LD50 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-O-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.
I. INTRODUCTION

E2 and F2a (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
II. MATERIALS AND METHODS—CHEMICAL ANALYSIS

CHEMICAL ANALYSIS

Food-grade propyl gallate was obtained in two batches. Lot No. 2185, from Harshaw Chemical Co. (Philadelphia, PA), was used for the pre-chronic 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 B6C3F1 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-
II. MATERIALS AND METHODS—CHRONIC STUDIES

num, jejunum, ileum, colon, cecum, mesenteric
and mandibular lymph nodes, liver, gall bladder
(mice), pancreas, spleen, kidneys, adrenals, urina-
ary bladder, seminal vesicles/prostate/testes or
ovaries/uterus, brain, and pituitary. Tissues were
preserved in 10% neutral buffered formalin, em-
bedded 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 (Indian-
apolis, 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°C–23°C).
The concentrations of propyl gallate were mea-
sured in 55 samples selected at random from test
diets administered during the chronic study
(Appendix G). The results of these analyses indi-
cate that all diets were formulated correctly. Five
of the 55 samples were reanalyzed at other lab-
oratories, 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 con-
sumption 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 con-
sumption 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, abnor-
mal 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), pan-
creas, spleen, kidneys, adrenals, eyes, urinary
bladder, seminal vesicles/prostate/testes or ova-
ries/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

Propyl Gallate
II. MATERIALS AND METHODS—CHRONIC STUDIES

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.)
II. MATERIALS AND METHODS—CHRONIC STUDIES

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>
<thead>
<tr>
<th>TABLE 1. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Experimental Design</strong></td>
</tr>
<tr>
<td>Size of Test Groups</td>
</tr>
<tr>
<td>5 males and 5 females of each species</td>
</tr>
<tr>
<td>Doses</td>
</tr>
<tr>
<td>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</td>
</tr>
<tr>
<td>Duration of Dosing</td>
</tr>
<tr>
<td>Single dose; killed on day 16</td>
</tr>
<tr>
<td>Type and Frequency of Observation</td>
</tr>
<tr>
<td>Observed twice daily for mortality and morbidity</td>
</tr>
<tr>
<td>Necropsy and Histological Examination</td>
</tr>
<tr>
<td>None performed</td>
</tr>
<tr>
<td><strong>Animal and Animal Maintenance</strong></td>
</tr>
<tr>
<td>Species</td>
</tr>
<tr>
<td>F344/N rats; B6C3F1 mice</td>
</tr>
<tr>
<td>Animal Source</td>
</tr>
<tr>
<td>Frederick Cancer Research Center, Frederick, MD</td>
</tr>
<tr>
<td>Time Held Before Start of Test</td>
</tr>
<tr>
<td>Rats: 8 days</td>
</tr>
<tr>
<td>Mice: 7 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Single-Dose Study</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>5 males and 5 females of each species</td>
</tr>
<tr>
<td>Doses</td>
</tr>
<tr>
<td>6,000, 12,500, 25,000, 50,000, or 100,000 ppm propyl gallate in feed, available ad libitum</td>
</tr>
<tr>
<td>Duration of Dosing</td>
</tr>
<tr>
<td>14 days; killed on days 16</td>
</tr>
<tr>
<td>Type and Frequency of Observation</td>
</tr>
<tr>
<td>Observed twice daily for mortality and morbidity</td>
</tr>
<tr>
<td>Necropsy and Histological Examination</td>
</tr>
<tr>
<td>Necropsies were performed on all animals;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>14-Day Study</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>10 males and 10 females of each species</td>
</tr>
<tr>
<td>Doses</td>
</tr>
<tr>
<td>Rats: 0, 1,500, 3,000, 6,000, 12,500, or 25,000 ppm propyl gallate in feed, available ad libitum</td>
</tr>
<tr>
<td>Mice: 0, 800, 1,500, 3,000, 6,000, or 12,500 ppm propyl gallate in feed, available ad libitum</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>13-Week Study</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>50 males and 50 females of each species</td>
</tr>
<tr>
<td>Doses</td>
</tr>
<tr>
<td>Same as single-dose study</td>
</tr>
<tr>
<td>Duration of Dosing</td>
</tr>
<tr>
<td>91 days; killed on days 92-96</td>
</tr>
<tr>
<td>Type and Frequency of Observation</td>
</tr>
<tr>
<td>Observed twice daily for mortality and morbidity</td>
</tr>
<tr>
<td>Necropsy and Histological Examination</td>
</tr>
<tr>
<td>Necropsies were performed on all animals;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Chronic Study</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>15 days</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Chronic Study</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>0, 6,000, or 12,000 ppm propyl gallate in feed, available ad libitum</td>
</tr>
<tr>
<td>Duration of Dosing</td>
</tr>
<tr>
<td>721 days; killed on days 735-749</td>
</tr>
<tr>
<td>Type and Frequency of Observation</td>
</tr>
<tr>
<td>Observed twice daily for signs of morbidity and mortality</td>
</tr>
<tr>
<td>Necropsy and Histological Examination</td>
</tr>
<tr>
<td>Necropsies were performed on all animals, and all animals were examined histologically</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Animal and Animal Maintenance</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Species</td>
</tr>
<tr>
<td>F344/N rats; B6C3F1 mice</td>
</tr>
<tr>
<td>Animal Source</td>
</tr>
<tr>
<td>Frederick Cancer Research Center, Frederick, MD</td>
</tr>
<tr>
<td>Time Held Before Start of Test</td>
</tr>
<tr>
<td>Rats: 8 days</td>
</tr>
<tr>
<td>Mice: 7 days</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th></th>
<th>Single-Dose Study</th>
<th>14-Day Study</th>
<th>13-Week Study</th>
<th>Chronic Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age When Placed on Study</td>
<td>5 weeks</td>
<td>5 weeks</td>
<td>5 weeks</td>
<td>Rats: 5 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mice: 8 weeks</td>
</tr>
<tr>
<td>Age When Killed</td>
<td>7-8 weeks</td>
<td>7-8 weeks</td>
<td>18-19 weeks</td>
<td>Rats: 110-112 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mice: 113-115 weeks</td>
</tr>
<tr>
<td>Method of Animal</td>
<td>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</td>
<td>Same as single-dose study</td>
<td>Same as single-dose study</td>
<td>Same as single-dose study</td>
</tr>
<tr>
<td>Distribution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feed</td>
<td>Wayne Lab Blox®</td>
<td></td>
<td></td>
<td>Same as single-dose study</td>
</tr>
<tr>
<td></td>
<td>Allied Mills, Inc.</td>
<td></td>
<td></td>
<td>Same as single-dose study</td>
</tr>
<tr>
<td></td>
<td>Chicago, IL</td>
<td></td>
<td></td>
<td>Same as single-dose study</td>
</tr>
<tr>
<td>Bedding</td>
<td>Betta-Chips®</td>
<td></td>
<td></td>
<td>Same as 14-day study</td>
</tr>
<tr>
<td></td>
<td>Northeastern Products Corp.</td>
<td></td>
<td></td>
<td>Same as 14-day study</td>
</tr>
<tr>
<td></td>
<td>(Warrensburg, NY)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>Tap water was available in bottles <em>ad libitum</em></td>
<td>Rats: Same as single-dose study</td>
<td>Same as 14-day study for mice</td>
<td>Same as 14-day study for mice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mice: Automatic watering system, Edstrom Industries (Waterford, WI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cages</td>
<td>Stainless steel, Hahn Roofing &amp; Sheet Metal Co. (Birmingham, AL)</td>
<td>Stainless steel, Hahn Roofing &amp; Sheet Metal Co. (Birmingham, AL); cages changed twice weekly</td>
<td>Polycarbonate; Lab Products, Inc. (Garfield, NJ); cages changed twice weekly</td>
<td>Same as 13-week study</td>
</tr>
<tr>
<td>Cage Filters</td>
<td>Single-Dose Study</td>
<td>14-Day Study</td>
<td>13-Week Study</td>
<td>Chronic Study</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------</td>
<td>-------------</td>
<td>---------------</td>
<td>---------------</td>
</tr>
<tr>
<td><strong>Cage Filters</strong></td>
<td>Reemay spun-bonded polyester filters, Dupont style #2024, Snow Filtration (Cincinnati, OH)</td>
<td>Rats: disposable filter bonnets; Mice: Same as single-dose study</td>
<td>Same as single-dose study</td>
<td>Same as single-dose study</td>
</tr>
<tr>
<td>Animals per Cage</td>
<td>Five</td>
<td>Five</td>
<td>Five</td>
<td>Five</td>
</tr>
<tr>
<td>Animal Room Environment</td>
<td>20°-24°C; 38%-42% relative humidity; room air was changed 15 times per hour; 9 hours of fluorescent light per day</td>
<td>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</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Other Chemicals on Test in the Same Room</td>
<td>D-Mannitol, stannous chloride, ziram, ethyl acrylate, allyl isothiocyanate, zearalenone</td>
<td>Rats: D-Mannitol, ziram, zearalenone Mice: Zearalenone</td>
<td>Same as 14-day study</td>
<td>Same as 14-day study, but premix was added to the remaining feed and mixed in a 16-qt Patterson-Kelly® twin shell blender, equipped with a intensifier bar</td>
</tr>
<tr>
<td>Chemical/Vehicle/Feed Mixture</td>
<td>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)</td>
<td>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</td>
<td>Same as 14-day study</td>
<td>Double-thickness plastic bags inside sealed, rigid plastic containers at 5°C for 1 week and at 22°C for the 2nd week</td>
</tr>
<tr>
<td>Maximum Storage Time</td>
<td>Not stored</td>
<td>14 days</td>
<td>14 days</td>
<td>14 days</td>
</tr>
<tr>
<td>Storage Conditions</td>
<td>Not stored</td>
<td>Sealed plastic containers in animal treatment rooms</td>
<td>Same as 14-day study</td>
<td>None</td>
</tr>
</tbody>
</table>
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
III. RESULTS: RATS—PRECHRONIC STUDIES

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>
<thead>
<tr>
<th>Dose (ppm)</th>
<th>Survival (a)</th>
<th>Mean Body Weights (grams)</th>
<th>Average Daily Feed Consumption (grams) (c,d)</th>
<th>Average Daily Feed Consumption (grams) (e)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>Change (b)</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6,000</td>
<td>5/5</td>
<td>87.6 ± 3.2</td>
<td>145.4 ± 1.5</td>
<td>+57.8 ± 2.9</td>
</tr>
<tr>
<td>12,500</td>
<td>5/5</td>
<td>74.6 ± 3.9</td>
<td>136.8 ± 4.4</td>
<td>+62.2 ± 1.6</td>
</tr>
<tr>
<td>25,000</td>
<td>5/5</td>
<td>81.6 ± 3.7</td>
<td>128.4 ± 4.3</td>
<td>+46.8 ± 1.0</td>
</tr>
<tr>
<td>50,000</td>
<td>4/5</td>
<td>78.0 ± 3.4</td>
<td>74.3 ± 7.7</td>
<td>3.8 ± 4.6</td>
</tr>
<tr>
<td>100,000</td>
<td>0/5</td>
<td>(f)</td>
<td>(f)</td>
<td>(f)</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6,000</td>
<td>5/5</td>
<td>70.0 ± 2.9</td>
<td>108.0 ± 2.3</td>
<td>+38.0 ± 0.6</td>
</tr>
<tr>
<td>12,500</td>
<td>5/5</td>
<td>70.0 ± 3.6</td>
<td>104.4 ± 3.4</td>
<td>+34.4 ± 2.2</td>
</tr>
<tr>
<td>25,000</td>
<td>5/5</td>
<td>73.4 ± 2.3</td>
<td>103.4 ± 2.5</td>
<td>+30.0 ± 2.0</td>
</tr>
<tr>
<td>50,000</td>
<td>5/5</td>
<td>70.2 ± 3.7</td>
<td>77.4 ± 6.4</td>
<td>7.2 ± 3.3</td>
</tr>
<tr>
<td>100,000</td>
<td>0/5</td>
<td>(f)</td>
<td>(f)</td>
<td>(f)</td>
</tr>
</tbody>
</table>

(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.

Propyl Gallate 26
III. RESULTS: RATS—PRECHRONIC STUDIES

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>
<thead>
<tr>
<th>TABLE 3. SURVIVAL, MEAN BODY WEIGHTS, AND FEED CONSUMPTION OF RATS FED DIETS CONTAINING PROPYL GALLATE FOR 13 WEEKS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose (ppm)</strong></td>
</tr>
<tr>
<td><strong>Initial</strong></td>
</tr>
<tr>
<td><strong>Males</strong></td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1,500</td>
</tr>
<tr>
<td>3,000</td>
</tr>
<tr>
<td>6,000</td>
</tr>
<tr>
<td>12,500</td>
</tr>
<tr>
<td>25,000</td>
</tr>
<tr>
<td><strong>Females</strong></td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1,500</td>
</tr>
<tr>
<td>3,000</td>
</tr>
<tr>
<td>6,000</td>
</tr>
<tr>
<td>12,500</td>
</tr>
<tr>
<td>25,000</td>
</tr>
</tbody>
</table>

(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 = Weight Change (Dosed Group) – Weight Change (Control Group) x 100

Weight Change (Control Group)
III. RESULTS: RATS—CHRONIC STUDIES

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

<table>
<thead>
<tr>
<th>Week No.</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
<th>Weight Change Relative to Controls (a) (Percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Body Weight Change (grams)</td>
<td>Mean Body Weight Change (grams)</td>
<td>Mean Body Weight Change (grams)</td>
<td>Low Dose</td>
</tr>
<tr>
<td>Males</td>
<td>104 (b)</td>
<td>99 (b)</td>
<td>103 (b)</td>
<td>-4</td>
</tr>
<tr>
<td></td>
<td>47</td>
<td>45</td>
<td>37</td>
<td>-7</td>
</tr>
<tr>
<td></td>
<td>239</td>
<td>223</td>
<td>208</td>
<td>-3</td>
</tr>
<tr>
<td></td>
<td>308</td>
<td>296</td>
<td>268</td>
<td>-4</td>
</tr>
<tr>
<td></td>
<td>328</td>
<td>317</td>
<td>289</td>
<td>-4</td>
</tr>
<tr>
<td>Final Body Weight</td>
<td>409</td>
<td>391</td>
<td>377</td>
<td>-4 (c)</td>
</tr>
</tbody>
</table>

Females

<table>
<thead>
<tr>
<th>Week No.</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
<th>Weight Change Relative to Controls (a) (Percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Body Weight Change (grams)</td>
<td>Mean Body Weight Change (grams)</td>
<td>Mean Body Weight Change (grams)</td>
<td>Low Dose</td>
</tr>
<tr>
<td></td>
<td>93 (b)</td>
<td>89 (b)</td>
<td>92 (b)</td>
<td>-4</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>23</td>
<td>21</td>
<td>-11</td>
</tr>
<tr>
<td></td>
<td>146</td>
<td>122</td>
<td>114</td>
<td>-16</td>
</tr>
<tr>
<td></td>
<td>179</td>
<td>150</td>
<td>132</td>
<td>-16</td>
</tr>
<tr>
<td></td>
<td>205</td>
<td>175</td>
<td>149</td>
<td>-15</td>
</tr>
<tr>
<td>Final Body Weight</td>
<td>315</td>
<td>280</td>
<td>256</td>
<td>-11 (c)</td>
</tr>
</tbody>
</table>

(a) Weight change of the dosed group relative to that of the controls = Weight Change (Dosed Group) - Weight Change (Control Group) x 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

<table>
<thead>
<tr>
<th>Week</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grams</td>
<td>Grams</td>
<td>Grams</td>
</tr>
<tr>
<td></td>
<td>Feed/</td>
<td>Feed/</td>
<td>Feed/</td>
</tr>
<tr>
<td></td>
<td>Day (a)</td>
<td>Low/</td>
<td>High/</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b)</td>
<td>(b)</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 (c)</td>
<td>15.0</td>
<td>14.0</td>
<td>16.0</td>
</tr>
<tr>
<td>22</td>
<td>17.0</td>
<td>15.0</td>
<td>15.0</td>
</tr>
<tr>
<td>44</td>
<td>16.4</td>
<td>16.6</td>
<td>16.4</td>
</tr>
<tr>
<td>83</td>
<td>16.5</td>
<td>16.4</td>
<td>19.7</td>
</tr>
<tr>
<td>Mean</td>
<td>16.5</td>
<td>15.5</td>
<td>16.3</td>
</tr>
<tr>
<td>SD</td>
<td>1.0</td>
<td>1.1</td>
<td>1.9</td>
</tr>
<tr>
<td>CV (e)</td>
<td>6.1</td>
<td>7.1</td>
<td>11.7</td>
</tr>
</tbody>
</table>

Females

<table>
<thead>
<tr>
<th>Week</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grams</td>
<td>Grams</td>
<td>Grams</td>
</tr>
<tr>
<td></td>
<td>Feed/</td>
<td>Feed/</td>
<td>Feed/</td>
</tr>
<tr>
<td></td>
<td>Day (a)</td>
<td>Low/</td>
<td>High/</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>Control</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b)</td>
<td>(b)</td>
</tr>
<tr>
<td>4 (c)</td>
<td>10.0</td>
<td>9.0</td>
<td>10.0</td>
</tr>
<tr>
<td>22</td>
<td>11.0</td>
<td>10.0</td>
<td>10.0</td>
</tr>
<tr>
<td>44</td>
<td>9.6</td>
<td>9.6</td>
<td>10.6</td>
</tr>
<tr>
<td>83</td>
<td>12.5</td>
<td>12.5</td>
<td>14.5</td>
</tr>
<tr>
<td>Mean</td>
<td>11.5</td>
<td>10.9</td>
<td>13.2</td>
</tr>
<tr>
<td>SD</td>
<td>1.9</td>
<td>1.9</td>
<td>4.7</td>
</tr>
<tr>
<td>CV (e)</td>
<td>16.5</td>
<td>17.4</td>
<td>35.6</td>
</tr>
</tbody>
</table>

(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
III. RESULTS: RATS—CHRONIC STUDIES

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 (\(P\leq 0.011\)) 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 (\(P\leq 0.040\)), 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.

**Adren:** 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 (\(P\leq 0.017\)), 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 (\(P\leq 0.009\)), and the incidence in the high-dose group differed significantly from that in the controls (\(P\leq 0.015\)). 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, 8/50 (16%) control females, 39/50 (78%) low-dose females, and 13/50 (26%) high-dose females.

**Kidney:** Nephrosis 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%).
<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematopoietic System: Undifferentiated Leukemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>16/50 (32%)</td>
<td>7/50 (14%)</td>
<td>6/50 (12%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>36.1%</td>
<td>16.7%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>11/39 (28%)</td>
<td>4/38 (11%)</td>
<td>6/44 (14%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.006N</td>
<td>P=0.041N</td>
<td>P=0.009N</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.009N</td>
<td>P=0.023N</td>
<td>P=0.015N</td>
</tr>
<tr>
<td>Cochran-Armitage Trend,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fisher Exact Tests</td>
<td>P=0.008N</td>
<td>P=0.028N</td>
<td>P=0.014N</td>
</tr>
<tr>
<td><strong>Hematopoietic System: Lymphoma or Leukemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>16/50 (32%)</td>
<td>8/50 (16%)</td>
<td>6/50 (12%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>36.1%</td>
<td>18.4%</td>
<td>13.6%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>11/39 (28%)</td>
<td>4/38 (11%)</td>
<td>6/44 (14%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.006N</td>
<td>P=0.068N</td>
<td>P=0.009N</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.011N</td>
<td>P=0.045N</td>
<td>P=0.015N</td>
</tr>
<tr>
<td>Cochran-Armitage Trend,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fisher Exact Tests</td>
<td>P=0.009N</td>
<td>P=0.050N</td>
<td>P=0.014N</td>
</tr>
<tr>
<td><strong>Pituitary: Adenoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>5/49 (10%)</td>
<td>8/48 (17%)</td>
<td>4/49 (8%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>12.0%</td>
<td>19.9%</td>
<td>9.0%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>3/38 (8%)</td>
<td>5/36 (14%)</td>
<td>3/43 (7%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.358N</td>
<td>P=0.268</td>
<td>P=0.428N</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.394N</td>
<td>P=0.371</td>
<td>P=0.477N</td>
</tr>
<tr>
<td>Cochran-Armitage Trend,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fisher Exact Tests</td>
<td>P=0.438N</td>
<td>P=0.263</td>
<td>P=0.500N</td>
</tr>
<tr>
<td><strong>Pituitary: Adenoma or Carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>5/49 (10%)</td>
<td>10/48 (21%)</td>
<td>4/49 (8%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>12.0%</td>
<td>23.1%</td>
<td>9.0%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>3/38 (8%)</td>
<td>5/36 (14%)</td>
<td>3/43 (7%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.360N</td>
<td>P=0.138</td>
<td>P=0.428N</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.490N</td>
<td>P=0.160</td>
<td>P=0.477N</td>
</tr>
<tr>
<td>Cochran-Armitage Trend,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fisher Exact Tests</td>
<td>P=0.441N</td>
<td>P=0.121</td>
<td>P=0.500N</td>
</tr>
<tr>
<td><strong>Adrenal: Pheochromocytoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>4/50 (8%)</td>
<td>12/48 (25%)</td>
<td>8/50 (16%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>9.8%</td>
<td>31.3%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>3/39 (8%)</td>
<td>11/37 (30%)</td>
<td>6/44 (14%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.255</td>
<td>P=0.024</td>
<td>P=0.247</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.232</td>
<td>P=0.030</td>
<td>P=0.221</td>
</tr>
<tr>
<td>Cochran-Armitage Trend,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fisher Exact Tests</td>
<td>P=0.172</td>
<td>P=0.022</td>
<td>P=0.178</td>
</tr>
<tr>
<td>TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS (a) (Continued)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adrenal: All Pheochromocytomas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>4/50 (8%)</td>
<td>13/48 (27%)</td>
<td>8/50 (16%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>9.8%</td>
<td>34.0%</td>
<td>17.4%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>3/39 (8%)</td>
<td>12/37 (32%)</td>
<td>6/44 (14%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.262</td>
<td>P=0.013</td>
<td>P=0.247</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.239</td>
<td>P=0.017</td>
<td>P=0.221</td>
</tr>
<tr>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.176</td>
<td>P=0.012</td>
<td>P=0.178</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thyroid: Follicular-Cell Adenoma or Carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>0/50 (0%)</td>
<td>0/50 (0%)</td>
<td>3/50 (6%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>0.0%</td>
<td>0.0%</td>
<td>6.6%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>0/39 (0%)</td>
<td>0/38 (0%)</td>
<td>2/44 (5%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.049</td>
<td>(f)</td>
<td>P=0.147</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.038</td>
<td>(f)</td>
<td>P=0.138</td>
</tr>
<tr>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.037</td>
<td>(f)</td>
<td>P=0.121</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thyroid: C-Cell Adenoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>4/50 (8%)</td>
<td>2/50 (4%)</td>
<td>3/50 (6%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>10.3%</td>
<td>5.3%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>4/39 (10%)</td>
<td>2/38 (5%)</td>
<td>3/44 (7%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.358N</td>
<td>P=0.348N</td>
<td>P=0.434N</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.358N</td>
<td>P=0.348N</td>
<td>P=0.434N</td>
</tr>
<tr>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.417N</td>
<td>P=0.339N</td>
<td>P=0.500N</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thyroid: C-Cell Carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>3/50 (6%)</td>
<td>1/50 (2%)</td>
<td>1/50 (2%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>7.4%</td>
<td>2.6%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>2/39 (5%)</td>
<td>1/38 (3%)</td>
<td>1/44 (2%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.176N</td>
<td>P=0.313N</td>
<td>P=0.266N</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.175N</td>
<td>P=0.253N</td>
<td>P=0.275N</td>
</tr>
<tr>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.203N</td>
<td>P=0.309N</td>
<td>P=0.309N</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thyroid: C-Cell Adenoma or Carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>7/50 (14%)</td>
<td>3/50 (6%)</td>
<td>4/50 (8%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>17.4%</td>
<td>7.9%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>6/39 (15%)</td>
<td>3/38 (8%)</td>
<td>4/44 (9%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.149N</td>
<td>P=0.169N</td>
<td>P=0.199N</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.149N</td>
<td>P=0.141N</td>
<td>P=0.204N</td>
</tr>
<tr>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.196N</td>
<td>P=0.159N</td>
<td>P=0.262N</td>
</tr>
</tbody>
</table>

33 Propyl Gallate
TABLE 6. ANALYSIS OF PRIMARY TUMORS IN MALE RATS (a) (Continued)

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

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

Propyl Gallate 36
TABLE 7. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS (a) (Continued)

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

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

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uterus: Endometrial Stromal Polyp</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>6/50 (12%)</td>
<td>8/50 (16%)</td>
<td>13/50 (26%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>15.4%</td>
<td>20.3%</td>
<td>29.5%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>6/39 (15%)</td>
<td>7/38 (18%)</td>
<td>11/42 (26%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td>Life Table</td>
<td>Incidental Tumor Test</td>
<td>Cochran-Armitage Trend,</td>
</tr>
<tr>
<td></td>
<td>P=0.067</td>
<td>P=0.367</td>
<td>P=0.090</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Uterus: Endometrial Stromal Polyp or Sarcoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>7/50 (14%)</td>
<td>8/50 (16%)</td>
<td>14/50 (28%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>17.5%</td>
<td>20.3%</td>
<td>31.1%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>6/39 (15%)</td>
<td>7/38 (18%)</td>
<td>11/42 (26%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td>Life Table</td>
<td>Incidental Tumor Test</td>
<td>Cochran-Armitage Trend,</td>
</tr>
<tr>
<td></td>
<td>P=0.077</td>
<td>P=0.481</td>
<td>P=0.105</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(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.
III. RESULTS: MICE—PRECHRONIC STUDIES

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 WEIGHS OF MICE FED DIETS CONTAINING PROPYL GALLATE FOR 14 DAYS

<table>
<thead>
<tr>
<th>Dose (ppm)</th>
<th>Survival (a)</th>
<th>Mean Body Weights (grams)</th>
<th>Average Daily Feed Consumption (grams) (c,d)</th>
<th>Average Daily Feed Consumption (grams) (e)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>Change (b)</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6,000</td>
<td>5/5</td>
<td>21.6 ±1.0</td>
<td>24.4 ± 0.5</td>
<td>+ 2.8 ± 0.6</td>
</tr>
<tr>
<td>12,500</td>
<td>5/5</td>
<td>21.6 ±1.0</td>
<td>23.6 ± 0.8</td>
<td>+ 2.0 ± 0.6</td>
</tr>
<tr>
<td>25,000</td>
<td>5/5</td>
<td>21.8 ±0.7</td>
<td>22.2 ±0.7</td>
<td>+ 0.4 ±0.4</td>
</tr>
<tr>
<td>50,000</td>
<td>1/5</td>
<td>21.0</td>
<td>16.0</td>
<td>- 5.0</td>
</tr>
<tr>
<td>100,000</td>
<td>0/5</td>
<td>(f)</td>
<td>(f)</td>
<td>(f)</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6,000</td>
<td>5/5</td>
<td>16.2 ±0.2</td>
<td>18.6 ± 0.2</td>
<td>+ 2.4 ± 0.4</td>
</tr>
<tr>
<td>12,500</td>
<td>5/5</td>
<td>17.0 ±0.3</td>
<td>18.0 ± 0.6</td>
<td>+ 1.0 ± 0.3</td>
</tr>
<tr>
<td>25,000</td>
<td>5/5</td>
<td>17.4 ±1.1</td>
<td>17.4 ± 0.8</td>
<td>0.0 ±0.6</td>
</tr>
<tr>
<td>50,000</td>
<td>0/5</td>
<td>(f)</td>
<td>(f)</td>
<td>(f)</td>
</tr>
<tr>
<td>100,000</td>
<td>0/5</td>
<td>(f)</td>
<td>(f)</td>
<td>(f)</td>
</tr>
</tbody>
</table>

(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
III. RESULTS: MICE—PRECHRONIC STUDIES

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

<table>
<thead>
<tr>
<th>Dose (ppm)</th>
<th>Survival (a)</th>
<th>Mean Body Weight (grams)</th>
<th>Weight Change Relative to Controls (c) (percent)</th>
<th>Average Daily Feed Consumption (grams)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>Change (b)</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10/10</td>
<td>19.0 ± 0.6</td>
<td>31.3 ± 0.8</td>
<td>+12.3 ± 0.4</td>
</tr>
<tr>
<td>800</td>
<td>10/10</td>
<td>18.8 ± 0.5</td>
<td>30.7 ± 0.6</td>
<td>+11.9 ± 0.3</td>
</tr>
<tr>
<td>1,500</td>
<td>10/10</td>
<td>17.0 ± 0.3</td>
<td>29.9 ± 0.7</td>
<td>+12.9 ± 0.6</td>
</tr>
<tr>
<td>3,000</td>
<td>10/10</td>
<td>18.5 ± 0.5</td>
<td>30.4 ± 0.6</td>
<td>+11.9 ± 0.7</td>
</tr>
<tr>
<td>6,000</td>
<td>10/10</td>
<td>18.8 ± 0.4</td>
<td>30.1 ± 0.7</td>
<td>+11.3 ± 0.5</td>
</tr>
<tr>
<td>12,500</td>
<td>10/10</td>
<td>18.5 ± 0.5</td>
<td>29.0 ± 0.6</td>
<td>+10.5 ± 0.4</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10/10</td>
<td>15.9 ± 0.5</td>
<td>22.9 ± 0.7</td>
<td>+7.0 ± 0.6</td>
</tr>
<tr>
<td>800</td>
<td>10/10</td>
<td>15.6 ± 0.3</td>
<td>23.9 ± 0.3</td>
<td>+8.3 ± 0.3</td>
</tr>
<tr>
<td>1,500</td>
<td>10/10</td>
<td>15.4 ± 0.4</td>
<td>24.7 ± 0.4</td>
<td>+9.3 ± 0.2</td>
</tr>
<tr>
<td>3,000</td>
<td>10/10</td>
<td>15.4 ± 0.4</td>
<td>23.5 ± 0.3</td>
<td>+8.1 ± 0.3</td>
</tr>
<tr>
<td>6,000</td>
<td>10/10</td>
<td>15.0 ± 0.3</td>
<td>23.1 ± 0.5</td>
<td>+8.1 ± 0.4</td>
</tr>
<tr>
<td>12,500</td>
<td>10/10</td>
<td>15.5 ± 0.5</td>
<td>23.0 ± 0.5</td>
<td>+7.5 ± 0.4</td>
</tr>
</tbody>
</table>

(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

\[
\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100
\]
III. RESULTS: MICE—CHRONIC STUDIES

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

<table>
<thead>
<tr>
<th>Week No.</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
<th>Weight Change Relative to Controls (Percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Body Weight Change (grams)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>20 (b)</td>
<td>20 (b)</td>
<td>21 (b)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>-33</td>
</tr>
<tr>
<td>22</td>
<td>13</td>
<td>13</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>44</td>
<td>19</td>
<td>18</td>
<td>16</td>
<td>-5</td>
</tr>
<tr>
<td>65</td>
<td>21</td>
<td>19</td>
<td>17</td>
<td>-10</td>
</tr>
<tr>
<td>83</td>
<td>21</td>
<td>19</td>
<td>17</td>
<td>-10</td>
</tr>
<tr>
<td>104</td>
<td>19</td>
<td>17</td>
<td>15</td>
<td>-11</td>
</tr>
</tbody>
</table>

Final Body Weight
Males: 39 37 36
Females: 36 32 32

(a) Weight change of the dosed group relative to that of the controls = 
Weight Change (Dosed Group) - Weight Change (Control Group) / Weight Change (Control Group) x 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

<table>
<thead>
<tr>
<th>Week</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grams Feed/Day (a)</td>
<td>Grams Feed/Day (a)</td>
<td>Low/Control (b)</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>6.0</td>
<td>6.0</td>
<td>1.0</td>
</tr>
<tr>
<td>44</td>
<td>7.0</td>
<td>6.0</td>
<td>0.9</td>
</tr>
<tr>
<td>65</td>
<td>6.8</td>
<td>5.8</td>
<td>0.9</td>
</tr>
<tr>
<td>83</td>
<td>7.3</td>
<td>7.3</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Mean: 6.8 6.2 0.9
SD (c): 0.5 0.6 0.1
CV (d): 7.4 9.7 11.1

Females: 6.0 6.0 1.0
6.0 6.0 1.0
6.8 6.8 1.0
6.8 6.8 1.0
7.3 9.4 1.3
8.4 1.2

Mean: 6.4 7.0 1.1
SD (c): 0.6 1.4 0.1
CV (d): 9.4 20.0 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

Propyl Gallate 42
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.
III. RESULTS: MICE—CHRONIC STUDIES

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≤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<0.028). The incidence of male mice with malignant lymphoma, histiocytic type, occurred with a significant (P≤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≤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≤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≤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<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)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5/50 (10%)</td>
<td>1/49 (2%)</td>
</tr>
<tr>
<td>Skin or Subcutaneous Tissue: Fibroma</td>
<td></td>
<td>12.2%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td>5/41 (12%)</td>
<td>1/37 (3%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td>Life Table</td>
<td>P=0.010N</td>
<td>P=0.128N</td>
</tr>
<tr>
<td></td>
<td>Incidental Tumor Test</td>
<td>P=0.010N</td>
<td>P=0.128N</td>
</tr>
<tr>
<td></td>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.011N</td>
<td>P=0.107N</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Tissue: Fibrosarcoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td>2/50 (4%)</td>
<td>3/49 (6%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td>Life Table</td>
<td>P=0.189N</td>
<td>P=0.484</td>
</tr>
<tr>
<td></td>
<td>Incidental Tumor Test</td>
<td>P=0.139N</td>
<td>P=0.581N</td>
</tr>
<tr>
<td></td>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.203N</td>
<td>P=0.490</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung: Alveolar/Bronchiolar Adenoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td>3/50 (6%)</td>
<td>4/48 (8%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td>Life Table</td>
<td>P=0.331</td>
<td>P=0.453</td>
</tr>
<tr>
<td></td>
<td>Incidental Tumor Test</td>
<td>P=0.312</td>
<td>P=0.453</td>
</tr>
<tr>
<td></td>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.292</td>
<td>P=0.477</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung: Alveolar/Bronchiolar Adenoma or Carcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td>4/50 (8%)</td>
<td>5/48 (10%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td>Life Table</td>
<td>P=0.479</td>
<td>P=0.443</td>
</tr>
<tr>
<td></td>
<td>Incidental Tumor Test</td>
<td>P=0.459</td>
<td>P=0.443</td>
</tr>
<tr>
<td></td>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.433</td>
<td>P=0.474</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematopoietic System: Malignant Lymphoma, Histiocytic Type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Rates</td>
<td></td>
<td>0/50 (0%)</td>
<td>0/49 (0%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td>Life Table</td>
<td>P=0.020</td>
<td>(f)</td>
</tr>
<tr>
<td></td>
<td>Incidental Tumor Test</td>
<td>P=0.016</td>
<td>(f)</td>
</tr>
<tr>
<td></td>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.015</td>
<td>(f)</td>
</tr>
</tbody>
</table>

45 Propyl Gallate
TABLE 12. ANALYSIS OF PRIMARY TUMORS IN MALE MICE (a) (Continued)

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

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

(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)

<table>
<thead>
<tr>
<th>Hematopoietic System: Malignant Lymphoma, Lymphocytic Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor Rates</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall (b)</td>
<td>2/50 (4%)</td>
<td>1/50 (2%)</td>
<td>3/49 (6%)</td>
</tr>
<tr>
<td>Adjusted (c)</td>
<td>4.9%</td>
<td>2.9%</td>
<td>7.9%</td>
</tr>
<tr>
<td>Terminal (d)</td>
<td>1/37 (3%)</td>
<td>1/34 (3%)</td>
<td>3/38 (8%)</td>
</tr>
<tr>
<td>Statistical Tests (e)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Table</td>
<td>P=0.410</td>
<td>P=0.539N</td>
<td>P=0.510</td>
</tr>
<tr>
<td>Incidental Tumor Test</td>
<td>P=0.420</td>
<td>P=0.537N</td>
<td>P=0.522</td>
</tr>
<tr>
<td>Cochran-Armitage Trend, Fisher Exact Tests</td>
<td>P=0.392</td>
<td>P=0.500N</td>
<td>P=0.490</td>
</tr>
</tbody>
</table>

| 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   |

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

Propyl Gallate
### TABLE 13. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE (a) (Continued)

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

(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%. Macromolecular gastrointestinal effects were observed in rats of each sex in the 25,000-ppm group. These effects consisted of a thickened stomach wall, redened 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 suppurrative 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 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 incideneces 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 ($P<0.028$) 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 ($P<0.022$) positive trend, with the incidence in the high-dose group being significantly ($P<0.039$) 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-acetylamino-fluorene, 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 B6C3F1 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


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


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


V. REFERENCES


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


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


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**

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANIMALS INITIALLY IN STUDY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS NECROPSIED</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS EXAMINED HISTOPATHOLOGICALLY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

### INTEGUMENTARY SYSTEM

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Squamous Cell Carcinoma</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>Basal-Cell Tumor</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Sebaceous Adenoma</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcut Tissue</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Basal-Cell Carcinoma</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Adenocarcinoma, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Fibroma</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurilemma, Malignant</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### RESPIRATORY SYSTEM

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Squamous Cell Carcinoma, Metastatic</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Alveolar/Bronchiolar Adenoma</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar/Bronchiolar Carcinoma</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Neurilemma, Metastatic</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### HEMATOPOIETIC SYSTEM

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Organs</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Malignant Lymphoma, Mixed Type</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated Leukemia</td>
<td>16 (32%)</td>
<td>7 (14%)</td>
<td>6 (12%)</td>
</tr>
</tbody>
</table>

### CIRCULATORY SYSTEM

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

*# NUMBER OF ANIMALS NECROPSIED
<table>
<thead>
<tr>
<th>Digestive System</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Lip Tetarcheptileiomal</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Lower Lip Tetarcheptileiomal</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Parotid Gland Adenocarcinoma, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Liver Neoplastic Nodule</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Pancreas Acinar-Cell Carcinoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Gastric Mucosa Leiomyosarcoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Jejunum Leiomyosarcoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Colonic Submucosa Fibroma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
* Number of animals necropsied
<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>URINARY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney Tubular-Cell Adenoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Kidney/Pelvis Transitional-Cell Carcinoma</td>
<td>(50)</td>
<td>(50)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>ENDOCRINE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary Carcinoma, NOS</td>
<td>(49)</td>
<td>(43)</td>
<td>(49)</td>
</tr>
<tr>
<td>Pituitary Adenoma, NOS</td>
<td>5 (10%)</td>
<td>8 (17%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Adrenal Cortical Adenoma</td>
<td>(50)</td>
<td>(48)</td>
<td>(50)</td>
</tr>
<tr>
<td>Adrenal Cortical Carcinoma</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>Adrenal Pheochromocytoma</td>
<td>4 (8%)</td>
<td>12 (25%)</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Adrenal Pheochromocytoma, Malignant</td>
<td>4 (8%)</td>
<td>12 (25%)</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Thyroid Follicular-Cell Adenoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Thyroid Follicular-Cell Carcinoma</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid C-Cell Adenoma</td>
<td>4 (8%)</td>
<td>2 (4%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Thyroid C-Cell Carcinoma</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Pancreatic Islets</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Islet-Cell Adenoma</td>
<td>2 (4%)</td>
<td>8 (16%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Islet-Cell Carcinoma</td>
<td></td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>

* Number of animals with tissue examined microscopically

# Number of animals necropsied
<table>
<thead>
<tr>
<th>TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>REPRODUCTIVE SYSTEM</strong></td>
</tr>
<tr>
<td><em>MAMMARY GLAND</em>*</td>
</tr>
<tr>
<td>FIBROADENOMA</td>
</tr>
<tr>
<td>2 (4%)</td>
</tr>
<tr>
<td>1 (2%)</td>
</tr>
<tr>
<td><em>PREPUTIAL GLAND</em>*</td>
</tr>
<tr>
<td>CARCINOMA, NOS</td>
</tr>
<tr>
<td>1 (2%)</td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
</tr>
<tr>
<td>5 (10%)</td>
</tr>
<tr>
<td>ADENOCARCINOMA, NOS</td>
</tr>
<tr>
<td>2 (4%)</td>
</tr>
<tr>
<td>ADENOSQUAMOUS CARCINOMA</td>
</tr>
<tr>
<td>1 (2%)</td>
</tr>
<tr>
<td><em>TESTIS</em>*</td>
</tr>
<tr>
<td>INTERSTITIAL-CELL TUMOR</td>
</tr>
<tr>
<td>47 (94%)</td>
</tr>
<tr>
<td>48 (96%)</td>
</tr>
<tr>
<td>50 (100%)</td>
</tr>
<tr>
<td><strong>NERVOUS SYSTEM</strong></td>
</tr>
<tr>
<td><em>BRAIN/MENINGES</em>*</td>
</tr>
<tr>
<td>CARCINOMA, NOS, INVASIVE</td>
</tr>
<tr>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>SPECIAL SENSE ORGANS</strong></td>
</tr>
<tr>
<td><em>ZYMBA'S GLAND</em>*</td>
</tr>
<tr>
<td>SEBACEOUS ADENOCARCINOMA</td>
</tr>
<tr>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>MUSCULOSKELETAL SYSTEM</strong></td>
</tr>
<tr>
<td>NONE</td>
</tr>
<tr>
<td><strong>NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY</strong></td>
</tr>
<tr>
<td><strong>NUMBER OF ANIMALS NECROPSIED</strong></td>
</tr>
</tbody>
</table>

63 Propyl Gallate
TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

<table>
<thead>
<tr>
<th></th>
<th>VEHICLE CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BODY CAVITIES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PERITONEUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>PHAEOCHROMOCYTOMA, INVASIVE</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>MIESOTHELIOMA, MALIGNANT</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIESOTHELIOMA BENEIGN</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>MIESOTHELIOMA, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td><strong>ALL OTHER SYSTEMS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MULTIPLE ORGANS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>CORTICAL CARCINOMA, METASTATIC</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>SARCOMA, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>MIESOTHELIOMA, MALIGNANT</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEAD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SQUAMOUS CELL CARCINOMA</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>SEBACEOUS ADENDOCARCINOMA</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ANIMAL DISPOSITION SUMMARY**

<table>
<thead>
<tr>
<th>ANIMALS INITIALLY IN STUDY</th>
<th>VEHICLE CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NATURAL DEATH</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>MORIBUND SACRIFICE</td>
<td>9</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>SCHEDULED SACRIFICE</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACCIDENTALLY KILLED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TERMINAL SACRIFICE</td>
<td>31</td>
<td>33</td>
<td>44</td>
</tr>
<tr>
<td>ANIMAL MISSING</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2 INCLUDES AUTOLYZED ANIMALS.

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

* NUMBER OF ANIMALS NECROPSIED
### TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

<table>
<thead>
<tr>
<th>Tumor Summary</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Animals with Primary Tumors</strong></td>
<td>49</td>
<td>49</td>
<td>50</td>
</tr>
<tr>
<td><strong>Total Primary Tumors</strong></td>
<td>104</td>
<td>112</td>
<td>91</td>
</tr>
<tr>
<td><strong>Total Animals with Benign Tumors</strong></td>
<td>48</td>
<td>49</td>
<td>50</td>
</tr>
<tr>
<td><strong>Total Benign Tumors</strong></td>
<td>72</td>
<td>90</td>
<td>73</td>
</tr>
<tr>
<td><strong>Total Animals with Malignant Tumors</strong></td>
<td>23</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td><strong>Total Malignant Tumors</strong></td>
<td>30</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td><strong>Total Animals with Secondary Tumors</strong></td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total Secondary Tumors</strong></td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Total Animals with Tumors Uncertain-Benign or Malignant</strong></td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total Uncertain Tumors</strong></td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

*Primary Tumors: All Tumors Except Secondary Tumors
Secondary Tumors: Metastatic Tumors or Tumors Invasive into an Adjacent Organ*
<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANIMALS INITIALLY IN STUDY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS NECROPSIED</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS EXAMINED HISTOPATHOLOGICALLY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td><strong>INTEGUMENTARY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SKIN</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>SQUAMOUS CELL PAPILLOMA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SUBCUT TISSUE</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>FIBROMA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIBROSARCOMA</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RESPIRATORY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NASOPHARYNX</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>SQUAMOUS CELL CARCINOMA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HEMATOPOIETIC SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MULTIPLE ORGANS</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>UNDIFFERENTIATED LEUKEMIA</td>
<td>8 (16%)</td>
<td>5 (10%)</td>
<td>6 (12%)</td>
</tr>
<tr>
<td><strong>SPLNE</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>LEIMYOSARCOMA</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NONE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LIVER</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>SQUAMOUS CELL CARCINOMA, METASTA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEOPLASTIC NODULE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED
# TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>#ILEUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>URINARY SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NONE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENDOCRINE SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#PITUITARY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Adenoma, NOS</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>16 (32%)</td>
</tr>
<tr>
<td>#ADRENAL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical Adenoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Phaeochromocytoma</td>
<td>4 (8%)</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>#THYROID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-Cell Adenoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>C-Cell Carcinoma</td>
<td>4 (8%)</td>
<td>8 (17%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>#PANCREATIC ISLETS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Islet-Cell Carcinoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td></td>
<td>4 (8%)</td>
<td>8 (17%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#MAMMARY GLAND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Adenocarcinoma, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>11 (22%)</td>
<td>2 (4%)</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>#PREPUTIAL GLAND</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Adenoma, NOS</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>#UTERUS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leiomyoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Endometrial Stromal Polyp</td>
<td>6 (12%)</td>
<td>8 (16%)</td>
<td>13 (26%)</td>
</tr>
<tr>
<td>Endometrial Stromal Sarcoma</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>#UTERUS/ENDOMETRIUM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

# NUMBER OF ANIMALS NECROPSIED

67 Propyl Gallate
<table>
<thead>
<tr>
<th>Tissue Area</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>#OVARY</strong></td>
<td>(49)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Granulosa-Cell Tumor</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>NERVOUS SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#BRAIN</td>
<td></td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>Carcinoma, NOS, Invasive</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Glioma, NOS</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Astrocytoma</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>#HYPOTHALAMUS</td>
<td></td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>Carcinoma, NOS, Invasive</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td><strong>SPECIAL SENSE ORGANS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#EYELID</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Fibroma</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#ZYMBAI'S GLAND</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Squamous Cell Carcinoma</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td><strong>MUSCULOSKELETAL SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BODY CAVITIES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#ABDOMINAL WALL</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Sarcoma, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>ALL OTHER SYSTEMS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma, NOS, Invasive</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>LUMBOSACRAL REGION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
* Number of animals necropsied
### TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANIMAL DISPOSITION SUMMARY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animals Initially in Study</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Natural Death</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Moribund Sacrifice</td>
<td>10</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Scheduled Sacrifice</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accidentally Killed</td>
<td>37</td>
<td>38</td>
<td>42</td>
</tr>
<tr>
<td>Animal Missing</td>
<td>11</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td><strong>TOTAL ANIMALS WITH PRIMARY TUMORS</strong></td>
<td>38</td>
<td>34</td>
<td>36</td>
</tr>
<tr>
<td>Total Primary Tumors</td>
<td>54</td>
<td>52</td>
<td>60</td>
</tr>
<tr>
<td><strong>TOTAL ANIMALS WITH BENIGN TUMORS</strong></td>
<td>32</td>
<td>27</td>
<td>31</td>
</tr>
<tr>
<td>Total Benign Tumors</td>
<td>46</td>
<td>37</td>
<td>48</td>
</tr>
<tr>
<td><strong>TOTAL ANIMALS WITH MALIGNANT TUMORS</strong></td>
<td>14</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Total Malignant Tumors</td>
<td>17</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td><strong>TOTAL ANIMALS WITH SECONDARY TUMORS</strong></td>
<td>4</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Total Secondary Tumors</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT</strong></td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total Uncertain Tumors</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIIMARY OR METASTATIC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Uncertain Tumors</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS

# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

---

69

Propyl Gallate
## TABLE A3.
### INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE RATS IN THE 2-YEAR STUDY OF PROPYL GALLATE

#### CONTROL

| Weeks on Study | 0 | 2 | 4 | 6 | 8 | 10 | 12 | 14 | 16 | 18 | 20 | 22 | 24 | 26 | 28 | 30 | 32 | 34 | 36 | 38 | 40 | 42 |
|----------------|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| **INTERDIGESTIVE SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Skin | | | | | | | | | | | | | | | | | | | | | | | | |
| Squamous Cell Carcinoma | X | | | | | | | | | | | | | | | | | | | | | | | |
| Basal-Cell Tumor | X | | | | | | | | | | | | | | | | | | | | | | | |
| Subcutaneous Tissue | | | | | | | | | | | | | | | | | | | | | | | | |
| Basal-Cell Carcinoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenocarcinoma, Malignant | | | | | | | | | | | | | | | | | | | | | | | | |
| Peyer’s Patches | | | | | | | | | | | | | | | | | | | | | | | | |
| **RESPIRATORY SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Lungs and Bronchi | | | | | | | | | | | | | | | | | | | | | | | | |
| Squamous Cell Carcinoma, Malignant | | | | | | | | | | | | | | | | | | | | | | | | |
| Alveolar/Bronchiolar Adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| **Hepatopancreatic System** | | | | | | | | | | | | | | | | | | | | | | | | |
| Bone Marrow | | | | | | | | | | | | | | | | | | | | | | | | |
| Spleen | | | | | | | | | | | | | | | | | | | | | | | | |
| Lymph Nodes | | | | | | | | | | | | | | | | | | | | | | | | |
| Thymus | | | | | | | | | | | | | | | | | | | | | | | | |
| **DENTAL SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Oral Cavity | | | | | | | | | | | | | | | | | | | | | | | | |
| Trichoblastoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Salivary Gland | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenocarcinoma, Malignant | | | | | | | | | | | | | | | | | | | | | | | | |
| **LIVER** | | | | | | | | | | | | | | | | | | | | | | | | |
| Biliary System | | | | | | | | | | | | | | | | | | | | | | | | |
| Gallbladder & Common Bile Duct | | | | | | | | | | | | | | | | | | | | | | | | |
| Pancreas | | | | | | | | | | | | | | | | | | | | | | | | |
| Acinar-Cell Adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| Esophagus | | | | | | | | | | | | | | | | | | | | | | | | |
| **CIRCULATORY SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Heart | | | | | | | | | | | | | | | | | | | | | | | | |
| **DIGESTIVE SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Oral Cavity | | | | | | | | | | | | | | | | | | | | | | | | |
| Teledentition | | | | | | | | | | | | | | | | | | | | | | | | |
| Salivary Gland | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenocarcinoma, Malignant | | | | | | | | | | | | | | | | | | | | | | | | |
| **NERVOUS SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Brain Stem | | | | | | | | | | | | | | | | | | | | | | | | |
| **ENDOCRINE SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Thyroid Gland | | | | | | | | | | | | | | | | | | | | | | | | |
| Parathyroid, Malignant | | | | | | | | | | | | | | | | | | | | | | | | |
| Pancreatic Islets | | | | | | | | | | | | | | | | | | | | | | | | |
| Pancreatic Adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| **REPRODUCTIVE SYSTEM** | | | | | | | | | | | | | | | | | | | | | | | | |
| Mammary Gland | | | | | | | | | | | | | | | | | | | | | | | | |
| Prostate | | | | | | | | | | | | | | | | | | | | | | | | |
| Seminal Vesicle | | | | | | | | | | | | | | | | | | | | | | | | |
| **MULTIPLE ORGANS NOS** | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenocarcinoma, Malignant | | | | | | | | | | | | | | | | | | | | | | | | |
| Acinar-Cell Adenoma | | | | | | | | | | | | | | | | | | | | | | | | |
| **SPECIAL TUMORS** | | | | | | | | | | | | | | | | | | | | | | | | |
| Multiple Organs | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenocarcinoma, Malignant | | | | | | | | | | | | | | | | | | | | | | | | |
| Adenosis | | | | | | | | | | | | | | | | | | | | | | | | |

### Notes:
- Tissue examined microscopically: **X**
- Tissue not examined microscopically: **N**
- Necropsy, no histology due to protocol: **C**
- Necropsy, no histology due to protocol: **H**
- Necropsy, no autolysis, no microscopic examination: **A**
- Necropsy, no autolysis, no microscopic examination: **M**
- Necropsy, no autolysis: **N**
- Necropsy performed: **P**

---

Propyl Gallate 70
<table>
<thead>
<tr>
<th>ANIMAL STUDY</th>
<th>SKIN</th>
<th>LUNG AND BRONCHUS</th>
<th>TRACHEA</th>
<th>NEPHROTIC SYSTEM</th>
<th>DIGESTIVE SYSTEM</th>
<th>CIRCULATORY SYSTEM</th>
<th>RESPIRATORY SYSTEM</th>
<th>LENS AND EYELID</th>
<th>OTHER SYSTEMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Table A3.

## Individual Animal Tumor Pathology Tables of Male Rats in the 2-Year Study of Propyl Gallate

### Low Dose

<table>
<thead>
<tr>
<th>Animal Number</th>
<th>Weeks on Study</th>
<th>Integumentary System</th>
<th>Skin</th>
<th>Basal-Cell Tumor</th>
<th>Sebaceous Adenoma</th>
<th>Seborrhoea</th>
<th>Hairless Mammal</th>
<th>Malignant</th>
<th>( \text{N} )</th>
<th>( \text{X} )</th>
<th>( \text{C} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animal Number</th>
<th>Weeks on Study</th>
<th>Respiratory System</th>
<th>Lungs and Bronchi</th>
<th>Metastatic</th>
<th>Miscellaneous</th>
<th>Tumors</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animal Number</th>
<th>Weeks on Study</th>
<th>Digestive System</th>
<th>Salivary Gland</th>
<th>Liver</th>
<th>Acute-Phase Node</th>
<th>Bile Duct</th>
<th>Gallbladder &amp; Common Bile Duct</th>
<th>Pancreas</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Animal Number | Weeks on Study | Circulatory System | Heart | | | | | | | |
|---------------|----------------|-------------------|------|---|---|---|---|---|
|               | 1              |                   |      |   |   |   |   |   |

| Animal Number | Weeks on Study | Urogenital System | Kidney | Tubular-Cell Adenoma | Urinary Bladder | | | | |
|---------------|----------------|------------------|------|----------------------|-----------------|---|---|---|
|               | 1              |                   |      |                      |                  |   |   |   |

| Animal Number | Weeks on Study | Reproductive System | Hypothalamic | Tumors | | | | | |
|---------------|----------------|---------------------|-------------|--------|---|---|---|
|               | 1              |                     |             |        |   |   |   |

| Animal Number | Weeks on Study | Nervous System | Brain | | | | | | |
|---------------|----------------|--------------|------|---|---|---|---|
|               | 1              |              |      |   |   |   |   |

<table>
<thead>
<tr>
<th>Animal Number</th>
<th>Weeks on Study</th>
<th>Other Systems</th>
<th>Multiple Organs</th>
<th>Tissues Examined Microscopically</th>
<th>No Tissue Information Submitted</th>
<th>Necropsy, No Histology Due to Protocol</th>
<th>Necropsy, No Tissue Examined Microscopically</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Propyl Gallate

72
<table>
<thead>
<tr>
<th>Tissue System</th>
<th>Interim #</th>
<th>Week #</th>
<th>Total Tissues</th>
<th>Tumor Ancy.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Integumentary System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SKIN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal-Cell Tumor</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sebaceous Adenoma</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Tissue</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIBROMA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIBROSARCOMA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEURILEMOMA, MALIGNANT</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNGS AND BRONCHI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurilemoma, Metastatic</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TRACHEA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hepatic System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LIVER</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEOPLASTIC MUCOSA</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Digestive System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urinary System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KIDNEY</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TUBULAR-CELL ADENOMA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urogenital System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROSTATE</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Reproductive System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALEXY, GLOM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TESTIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INTERSTITIAL-CELL TUMOR</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nervous System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRAIN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Spleen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lymph Nodes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thymus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Circulatory System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heart</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Connective System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intestine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Muscular System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neural System</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other Systems</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ANIMALS NECROSISED
+ TISSUE EXAMINED MICROSCOPICALLY
- TISSUE NOT EXAMINED MICROSCOPICALLY
X TUMOR INCIDENCE
U TUMOR INCIDENCE, NO HISTOLOGY DUE TO PROTOCOL
C NO TISSUE INFORMATION SUBMITTED
N NO HISTOLOGY PERFORMED
M NO HISTOLOGY PERFORMED

Propyl Gallate
### TABLE A3.

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

#### HIGH DOSE

<table>
<thead>
<tr>
<th>ANIMAL NUMBER</th>
<th>WEEK ON STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30</td>
</tr>
<tr>
<td></td>
<td>31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58</td>
</tr>
</tbody>
</table>

**INTEGUMENTARY SYSTEM**

- **SUBCUTANEOUS TISSUE**
  - Fibroma
  - Fibrosarcoma

**RESPIRATORY SYSTEM**

- **LUNGS AND BRENCHI**
  - Adenocarcinoma
  - Adenocystic carcinoma

**HYPOTHALAMIC SYSTEM**

- **BONE MARROW**
  - Megakaryocytes

**HEMATOPOIETIC SYSTEM**

- **BONE MARROW**
  - Megakaryocytes

**CIRCULATORY SYSTEM**

- **ARTERIES**
  - Adenoma

**ENDOCRINE SYSTEM**

- **PITUITARY**
  - Macroadenoma
  - Adenoma
  - Adenocystic carcinoma
  - Carcinoma

**REPRODUCTIVE SYSTEM**

- **Testes**
  - Carcinoma
  - Adenoma

**NERVOUS SYSTEM**

- **BRAIN**

**SPECIAL TISSUE GROUPS**

- **ZYGOMATIC GLAND**
  - Adenoma

**BODY CAVITIES**

- **Mesorhizone**

**ALL OTHER SYSTEMS**

- **MULTIPLE ORGANS**

<table>
<thead>
<tr>
<th>TISSUE EXAMINED MICROSCOPICALLY</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
<th>TISSUE EXAMINED MICROSCOPICALLY DUE TO PROTOCOL</th>
<th>AUTOLYSIS</th>
<th>NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION</th>
<th>NECROPSY PERFORMED</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

**Propyl Gallate**

74
TABLE A3. MALE RATS: TUMOR PATHOLOGY (CONTINUED)  HIGH DOSE

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Tumors</th>
<th>Total Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integumentary System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fimbria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs and Bronchi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVEOLAR-EPITHELIAL CARCINOMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trachea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematopoietic System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Marrow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph Nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thymus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circulatory System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digestive System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral Cavity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary Gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile Duct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallbladder &amp; Common Bile Duct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ureter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urethra</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special Sense Organs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zymbal's Gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serosal Adenocarcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Cavities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesentery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesothelioma Benign</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Other Systems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Organs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head MS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous Cell Carcinoma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Animals Necropsied:
A: Tissue Examined Microscopically
B: Necropsy, no histology due to protocol
C: Necropsy, no histology submitted
D: Tumor Incidence
E: Necropsy, no autopsy, no microscopic examination

75

Propyl Gallate
**TABLE A4.**

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

**CONTROL**

<table>
<thead>
<tr>
<th>ORGAN SYSTEM</th>
<th>TUMORS REPORTED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LUNG AND BRONCHI</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>TRACHEA</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>HEMATOPOIETIC SYSTEM</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>BONE MARROW</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>SPLEEN</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>LYMPH NODES</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>THYMUS</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>HEART</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>SALIVARY GLAND</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>LIVER</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>BILE DUCT</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>GALLBLADDER &amp; COMMON BILE DUCT</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>PANCREAS</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>ESOPHAGUS</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>STOMACH</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>SMALL INTESTINE</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>LUNG AND BRONCHI</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>TRACHEA</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>HEMATOPOIETIC SYSTEM</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>BONE MARROW</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>SPLEEN</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>LYMPH NODES</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>THYMUS</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>HEART</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>SALIVARY GLAND</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>LIVER</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>BILE DUCT</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>GALLBLADDER &amp; COMMON BILE DUCT</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>PANCREAS</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>ESOPHAGUS</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>STOMACH</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>SMALL INTESTINE</strong></td>
<td>-</td>
</tr>
</tbody>
</table>

* TISSUE EXAMINED MICROSCOPICALLY
** TISSUE EXAMINED MICROSCOPICALLY BUT NOT REPORTED
H HISTOLOGY NOT PERFORMED
X AUTOLYSIS
M MULTIPLE ORGANS NOT REPORTED

<table>
<thead>
<tr>
<th>WEEKS ON STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21  22  23  24  25  26  27  28  29  30  31  32  33  34  35  36  37  38  39  40  41  42</td>
</tr>
<tr>
<td>TUMOR SITE</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
</tr>
<tr>
<td>PANCREAS</td>
</tr>
<tr>
<td>STOMACH</td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
</tr>
<tr>
<td>LIVER</td>
</tr>
<tr>
<td>BLADDER</td>
</tr>
<tr>
<td>KIDNEY</td>
</tr>
<tr>
<td>BLADDER</td>
</tr>
<tr>
<td>PITUITARY</td>
</tr>
<tr>
<td>ADRENAL</td>
</tr>
<tr>
<td>THYROID</td>
</tr>
<tr>
<td>OVARY</td>
</tr>
<tr>
<td>BRAIN</td>
</tr>
<tr>
<td>SPECIAL SENSE ORGANS</td>
</tr>
<tr>
<td>NERVOUS SYSTEM</td>
</tr>
<tr>
<td>PERITONEUM</td>
</tr>
<tr>
<td>ALL OTHER SYSTEMS</td>
</tr>
</tbody>
</table>

* ANIMALS NECROPSIED
  + TISSUE EXAMINED MICROSCOPICALLY
  + TISSUE EXAMINED AND DETERMINED POSITIVEFor microscopic examination
  + TISSUE EXAMINED, BUT NOT DETERMINED POSITIVE for microscopic examination
  + TISSUE NOT EXAMINED MICROSCOPICALLY
  + TISSUE EXAMINED, BUT NOT DETERMINED POSITIVE for microscopic examination
  + NO TISSUE EXAMINED, NO MICROSCOPIC EXAMINATION
  + NO TISSUE EXAMINED, NO HISTOLOGICAL DETERMINATION
  + NO TISSUE EXAMINED, NO HISTOLOGICAL DETERMINATION DUE TO PROTOCOL
  + NO TISSUE EXAMINED, NO HISTOLOGICAL DETERMINATION DUE TO PROTOCOL AND PROTOCOL ANIMAL MISSES
  + NO TISSUE EXAMINED, NO HISTOLOGICAL DETERMINATION DUE TO PROTOCOL, PROTOCOL ANIMAL MISSES
  + NO TISSUE EXAMINED, NO HISTOLOGICAL DETERMINATION DUE TO PROTOCOL, PROTOCOL ANIMAL MISSES
  + NO TISSUE EXAMINED, NO HISTOLOGICAL DETERMINATION DUE TO PROTOCOL, PROTOCOL ANIMAL MISSES
  + NO TISSUE EXAMINED, NO HISTOLOGICAL DETERMINATION DUE TO PROTOCOL, PROTOCOL ANIMAL MISSES

77 Propyl Gallate
<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Female Rats</th>
<th>Male Rats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell papilloma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs and bronchi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trachea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal cavity</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematopoietic system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone marrow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thymus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circulatory system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digestive system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma, metastatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metaplastic nodule</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal bladder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma, nos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma, nos</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Adrenal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical adenoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phaeochromocytoma</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-cell adenoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-cell carcinoma</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Parathyroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma, nos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Preputial/Clitoral gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma, nos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometrial stromal polyp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma, nos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special sense organs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomital's gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL OTHER SYSTEMS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MULTIPLE ORGANS NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undifferentiated leukemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEAD NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma, nos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Tissue examined microscopically
+ Required tissue not examined microscopically
X No tissue information submitted
B: No necropsy performed
A: Autopsy
G: Autolysis
A: Necropsy, no histology due to protocol
H: Tumor incidence
I: Necropsy, no autolysis, no microscopic examination
N: Necropsy performed
**TABLE A4. FEMALE RATS: TUMOR PATHOLOGY (CONTINUED)**

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>ANIMAL NUMBER</th>
<th>TOTAL TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANIMAL NUMBER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RESPIRATORY SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs and Bronchi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trachea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal Cavity</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RENAL SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SALIVARY GLAND</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ENDOCRINE SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parathyroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SKELETAL SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Marrow</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>REPRODUCTIVE SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovaries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NERVOUS SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SPECIAL SENSE ORGANS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ALL OTHER SYSTEMS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Organs, NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NOTE</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Animals examined microscopically* = **
*Animals examined microscopically* = *
*Required tissue not examined microscopically* = +
*Failed to necropsy, no histology due to protocol* = x
*Failed to necropsy, no microscopic examination* = *
*Failed to necropsy, no autopsies, no microscopic examination* = X

79 Propyl Gallate
# TABLE A4.

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

### HIGH DOSE

<table>
<thead>
<tr>
<th>ANIMAL NUMBER</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
<th>19</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERDUETARY SYSTEM</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SUBCUTANEOUS TISSUE</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>RESPIRATORY SYSTEM</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LUNGS AND BRONCHI</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TRACHEA</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HEPATOPOIETIC SYSTEM</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>BONE MARROW</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SPLEEN</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>THYMUS</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CIRCULATORY SYSTEM</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HEART</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>DIGESTIVE SYSTEM</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LIVER</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>BILE DUCT</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LATERAL DUCT</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SPLEEN</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>BONE MARROW</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SPLEEN</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>THYMUS</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CIRCULATORY SYSTEM</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HEART</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>DIGESTIVE SYSTEM</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LIVER</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>BILE DUCT</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LATERAL DUCT</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SPLEEN</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>BONE MARROW</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SPLEEN</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>THYMUS</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Legend:**

- **+** Tissue examined microscopically
- **X** Tissue not examined microscopically
- **C** Necropsy, no histology due to protocol
- **M** Animal missing
- **A** Necropsy, no autopsy, no microscopic examination
- **B** Necropsy performed

---

Propyl Gallate 80
<table>
<thead>
<tr>
<th>Table A4. Female Rats: Tumor Pathology (Continued)</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SYSTEM</strong></td>
<td><strong>WEEKS ON STUDY</strong></td>
</tr>
<tr>
<td>INTERSTITIAL SYSTEM</td>
<td>1 2 3 4 5 6 7 8</td>
</tr>
<tr>
<td>SUBCUTANEOUS TISSUE</td>
<td>*+ + + + + + + + + + N * + + + + + + + + + +</td>
</tr>
<tr>
<td>RESPIRATORY SYSTEM</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>LUNGS AND BRONCHI</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>TRACHEA</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>MACROPHAGE SYSTEM</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>BONE MARROW</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>THYMUS</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>CIRCULATORY SYSTEM</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>HEART</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>DIGESTIVE SYSTEM</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>LIVER</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>BILE DUCT</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>GALLBLADDER &amp; COMMON BILE DUCT</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>PANCREAS</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>ESOPHAGUS</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>STOMACH</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>LARGE INTESTINE</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>URINARY SYSTEM</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>KIDNEY</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>IMMUNE SYSTEM</td>
<td>* + + + + + + + + + +</td>
</tr>
<tr>
<td>PITUITARY</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ADENOCARCINOMA</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>Glandules</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>THYROID</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>PANCREATIC ISLETS</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ISLET-CELL CARCINOMA</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>MAMMARY GLAND</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>PREPUTITAL/COSTAL GLAND</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>UTERUS</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>PREPUTITAL/COSTAL GLAND</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ADENOCARCINOMA</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>NERVOUS SYSTEM</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>BRAIN</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>ALL OTHER SYSTEM</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>MULTIPLE ORGANS NOS</td>
<td>X X X X X X X X X X X X</td>
</tr>
<tr>
<td>UNDIFFERENTIATED LEUKEMIA</td>
<td>X X X X X X X X X X X X</td>
</tr>
</tbody>
</table>

* ANALYSIS PERFORMED
+ TISSUE EXAMINED MICROSCOPICALLY
- REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY
C: NECROPSY, NO HISTOLOGY DUE TO PROTOCOL
M: NECROPSY, NO AUTOLYSIS, NO MICROSCOPIC EXAMINATION
A: ANIMAL MISSING
B: NO NECROPSY PERFORMED

81 Propyl Gallate
APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE FED DIETS CONTAINING PROPYL GALLATE
<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANIMALS INITIALLY IN STUDY</strong></td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td><strong>ANIMALS NECROPSIED</strong></td>
<td>50</td>
<td>49</td>
<td>50</td>
</tr>
<tr>
<td><strong>ANIMALS EXAMINED HISTOPATHOLOGICALLY</strong></td>
<td>50</td>
<td>49</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>INTEGUMENTARY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SKIN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SARCOMA, NOS</td>
<td>5 (10%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>FIBROMA</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEUROLEMOMA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SUBCUT TISSUE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SARCOMA, NOS</td>
<td>5 (10%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>FIBROMA</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIBROSARCOMA</td>
<td>2 (4%)</td>
<td>3 (6%)</td>
<td></td>
</tr>
<tr>
<td>NEUROLEMOMA</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEUROLEMOMA, MALIGNANT</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RESPIRATORY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LUNG/BRONCHIOLE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAPILLARY ADENOMA</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>LUNG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEPATOCELLULAR CARCINOMA, METASTATIC</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>ALVEOULAR/BRONCHIOLAR ADENOMA</td>
<td>3 (6%)</td>
<td>4 (8%)</td>
<td></td>
</tr>
<tr>
<td>ALVEOULAR/BRONCHIOLAR CARCINOMA</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>PHEDOHRAMOCYTOMA, METASTATIC</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HEMATOPOIETIC SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MULTIPLE ORGANS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALIG.LYMHPHOMA, NOS</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>MALIG.LYMHPHOMA, LYMPHOCYTIC TYPE</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALIG.LYMHPHOMA, MIXED TYPE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#MESENTERIC L. NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>MALIG.LYMHPHOMA, LYMPHOCYTIC TYPE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Number of animals with tissue examined microscopically
* Number of animals necropsied

**TABLE B1.**
**SUMMARY OF THE INCIDENCE OF NEOPLASMS OF MALE MICE FED DIETS CONTAINING PROPYL GALLATE**
<table>
<thead>
<tr>
<th>System</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#LIVER</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>#PEYER'S PATCH</td>
<td>(48)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td><strong>URINARY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ENDOCRINE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#ADRENAL</td>
<td>(49)</td>
<td>(47)</td>
<td>(50)</td>
</tr>
<tr>
<td>#THYROID</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
</tbody>
</table>

* Number of animals with tissue examined microscopically
* Number of animals necropsied

---

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

<table>
<thead>
<tr>
<th>System</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#SPLEEN</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#SALIVARY GLAND</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>#LIVER</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>URINARY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ENDOCRINE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#ADRENAL</td>
<td>(49)</td>
<td>(47)</td>
<td>(50)</td>
</tr>
<tr>
<td>#THYROID</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
</tbody>
</table>

* Number of animals with tissue examined microscopically
* Number of animals necropsied

---

Propyl Gallate
<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testis</td>
<td>(49)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>Interstitial-cell tumor</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>NERVOUS SYSTEM</td>
<td>NONE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECIAL SENSE ORGANS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harderian gland</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>Adenoma, NOB</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>MUSCULOSKELETAL SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NONE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BODY CAVITIES</td>
<td>NONE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL OTHER SYSTEMS</td>
<td>NONE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ANIMAL DISPOSITION SUMMARY**

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animals initially in study</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Natural deaths</td>
<td>5</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Moribund sacrifice</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Scheduled sacrifice</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accidentally killed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Terminal sacrifice</td>
<td>31</td>
<td>37</td>
<td>44</td>
</tr>
<tr>
<td>Animal missing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Includes autolyzed animals

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

* NUMBER OF ANIMALS NECROPSIED
<table>
<thead>
<tr>
<th>TUMOR SUMMARY</th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL ANIMALS WITH PRIMARY TUMORS*</td>
<td>29</td>
<td>31</td>
<td>22</td>
</tr>
<tr>
<td>TOTAL PRIMARY TUMORS</td>
<td>38</td>
<td>39</td>
<td>30</td>
</tr>
<tr>
<td>TOTAL ANIMALS WITH BENIGN TUMORS</td>
<td>15</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>TOTAL BENIGN TUMORS</td>
<td>17</td>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>TOTAL ANIMALS WITH MALIGNANT TUMORS</td>
<td>18</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>TOTAL MALIGNANT TUMORS</td>
<td>21</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>TOTAL ANIMALS WITH SECONDARY TUMORS#</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL SECONDARY TUMORS</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGANT</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL UNCERTAIN TUMORS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 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

<table>
<thead>
<tr>
<th>ANIMALS INITIALLY IN STUDY</th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animals necropsied</td>
<td>50</td>
<td>50</td>
<td>49</td>
</tr>
<tr>
<td>Animals examined histopathologically</td>
<td>50</td>
<td>50</td>
<td>49</td>
</tr>
</tbody>
</table>

**INTEGUMENTARY SYSTEM**

<table>
<thead>
<tr>
<th>Subcut Tissue</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhabdomyosarcoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>Fibrous Histiocytoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
</tbody>
</table>

**RESPIRATORY SYSTEM**

<table>
<thead>
<tr>
<th>Lung</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar/Bronchiolar Adenoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>Alveolar/Bronchiolar Carcinoma</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Osteosarcoma, Metastatic</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HEMATOPOIETIC SYSTEM**

<table>
<thead>
<tr>
<th>Multiple Organs</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant Lymphoma, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>Malig. Lymphoma, Lymphocytic Type</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Malig. Lymphoma, Histiocytic Type</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Malignant Lymphoma, Mixed Type</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Leukemia, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Lymphocytic Leukemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Spleen</td>
<td>(50)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>Malignant Lymphoma, Mixed Type</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td># Mesenteric L. Node</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>Malignant Lymphoma, Mixed Type</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td># Liver</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>Leukemia, NOS</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
* Number of animals necropsied
# TABLE B2. FEMALE MICE: NEOPASMS (CONTINUED)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus, Hemangiosarcoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver, Hepatocellular Adenoma</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>Liver, Hepatocellular Carcinoma</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
<td>5 (10%)</td>
</tr>
<tr>
<td><strong>URINARY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney, Adenocarcinoma, NOS, Metastatic</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td><strong>ENDOCRINE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary, Carcinoma, NOS</td>
<td>(48)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>Pituitary, Adenoma, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Adrenal, Pheochromocytoma</td>
<td>(50)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>Adrenal Cortex, Sarcoma, NOS</td>
<td>(50)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>Thyroid, Follicular-Cell Adenoma</td>
<td>(49)</td>
<td>(47)</td>
<td>(48)</td>
</tr>
<tr>
<td>Thyroid, Islet-Cell Adenoma</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>Pancreatic Islets</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
* Number of animals necropsied
<table>
<thead>
<tr>
<th>TABLE 82. FEMALE MICE: NEOPLASMS (CONTINUED)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong># MAMMARY GLAND</strong></td>
</tr>
<tr>
<td><strong>ADENOCARCINOMA, NOS</strong></td>
</tr>
<tr>
<td><strong>MIXED TUMOR, MALIGNANT</strong></td>
</tr>
<tr>
<td><strong># UTERUS</strong></td>
</tr>
<tr>
<td><strong>ENDOMETRIAL STROMAL POLYP</strong></td>
</tr>
<tr>
<td><strong>ENDOMETRIAL STROMAL SARCOMA</strong></td>
</tr>
<tr>
<td><strong># CERVIX UTERI</strong></td>
</tr>
<tr>
<td><strong>SARCOMA, NOS</strong></td>
</tr>
<tr>
<td><strong># UTERUS/ENDOMETRIUM</strong></td>
</tr>
<tr>
<td><strong>CARCINOMA, NOS</strong></td>
</tr>
<tr>
<td><strong>ADENOCARCINOMA, NOS</strong></td>
</tr>
<tr>
<td><strong># OVARY</strong></td>
</tr>
<tr>
<td><strong>PAPILLARY CYSTADENOMA, NOS</strong></td>
</tr>
<tr>
<td><strong># BRAIN</strong></td>
</tr>
<tr>
<td><strong>EPENDYMOMA</strong></td>
</tr>
<tr>
<td><strong>SPECIAL SENSE ORGANS</strong></td>
</tr>
<tr>
<td><strong># HARDERIAN GLAND</strong></td>
</tr>
<tr>
<td><strong>ADENOMA, NOS</strong></td>
</tr>
<tr>
<td><strong>MUSCULOSKELETAL SYSTEM</strong></td>
</tr>
<tr>
<td><strong># LUMBAR VERTEBRA</strong></td>
</tr>
<tr>
<td><strong>OSTEOSARCOMA</strong></td>
</tr>
<tr>
<td><strong># MUSCLE OF BACK</strong></td>
</tr>
<tr>
<td><strong>RABDOMYOSARCOMA</strong></td>
</tr>
<tr>
<td><strong># ABDOMINAL MUSCLE</strong></td>
</tr>
<tr>
<td><strong>FIBROSARCOMA</strong></td>
</tr>
<tr>
<td><strong>BODY CAVITIES</strong></td>
</tr>
<tr>
<td><strong>NONE</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong># NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY</strong></td>
</tr>
<tr>
<td><strong># NUMBER OF ANIMALS NECROPSIED</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(48)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
</tbody>
</table>

Propyl Gallate
### TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL OTHER SYSTEMS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*MULTIPLE ORGANS</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>SARCOMA, NOS</td>
<td>(50)</td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

**ANIMAL DISPOSITION SUMMARY**

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANIMALS INITIALLY IN STUDY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>NATURAL DEATH</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>MORIBUND SACRIFICE</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>SCHEDULED SACRIFICE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACCIDENTALLY KILLED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TERMINAL SACRIFICE</td>
<td>37</td>
<td>33</td>
<td>38</td>
</tr>
<tr>
<td>ANIMAL MISSING</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\* Includes autolyzed animals

**TUMOR SUMMARY**

| TUMORS WITH PRIMARY TUMORS          | 25      | 17       | 22        |
| TOTAL PRIMARY TUMORS                | 32      | 18       | 27        |
| TUMORS WITH BENIGN TUMORS           | 9       | 8        | 9         |
| TOTAL BENIGN TUMORS                 | 10      | 8        | 11        |
| TUMORS WITH MALIGNANT TUMORS        | 20      | 10       | 15        |
| TOTAL MALIGNANT TUMORS              | 22      | 10       | 16        |
| TUMORS WITH SECONDARY TUMORS#       | 1       | 1        |           |
| TOTAL SECONDARY TUMORS              | 1       | 1        |           |
| TUMORS UNCERTAIN-                  |         |          |           |
| BENVENIG OR MALIGNANT              |         |          |           |
| 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

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>TISSUE EXAMINED MICROSCOPICALLY</th>
<th>REQUIRED TISSUE NOT EXAMINED MICROSCOPICALLY</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUNG</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>LIVER</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>STOMACH</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>LARGE INTESTINE</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>KIDNEY</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>SPLEEN</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>THYROID</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>PARATHYROID</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>BRAIN</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>SPECIAL SENSE ORGANS</td>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TISSUE EXAMINED MICROSCOPICALLY</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
<th>NO TISSUE EXAMINED MICROSCOPICALLY</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAMMARY GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROSTATE</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TISSUE EXAMINED MICROSCOPICALLY</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
<th>NO TISSUE EXAMINED MICROSCOPICALLY</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
<th>NO TISSUE INFORMATION SUBMITTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKIN FIBRONA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEURILEMONA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SUBCUTANEOUS TISSUE</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANNICULAR CARCINOMA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVEOLAR-BRONCHIOCARCINOMA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAPILLARY CARCINOMA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAPILLARY ADENOMA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MUCINOUS ADENOMA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MUCINOUS ADENOCARCINOMA</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KIDNEY</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMMON BILE DUCT</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANCREAS</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESOPHAGUS</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STOMACH</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LARGE INTESTINE</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROSTATE</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HORMONAL GLAND</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| HORMONAL GLA...
<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>TUMORS NUMBER</th>
<th>TOTAL TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integumentary System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs and Bronchi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trachea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bio Marrow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chondrosarcoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph Nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoma, Lymphocytic Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thymus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circulatory System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digestive System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary Gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile Duct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallbladder &amp; Common Bile Duct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nodular Adenocarcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urogenital System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovaries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special Sense Organs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urogenital System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male Gland</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Animals Necropsied*

**Tissue Examined Microscopically**

- Required tissue not examined microscopically
- No tissue information submitted
- Necropsy; no histology due to protocol
- Necropsy; no autolysis, no microscopic examination
- Necropsy performed

---

Table B3. Male Mice: Tumor Pathology (Continued)
<table>
<thead>
<tr>
<th>#</th>
<th>INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF PROPYLGALLATE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TABLE 83.</strong></td>
<td><strong>LOW DOSE</strong></td>
</tr>
<tr>
<td><strong>INDIVIDUAL NUMBER</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>WORKS ON INDIVIDUAL NUMBER</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>ORGAN SYSTEM</strong></td>
<td><strong>SKIN</strong></td>
</tr>
<tr>
<td><strong>TUMOR INFORMATION</strong></td>
<td><strong>NECROPSY, NO AUTOLYSIS</strong></td>
</tr>
<tr>
<td><strong>SARCOMA, NOS</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>FIBROMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>FIBROSARCOMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>NEURILEIOMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>LUNGS AND BRONCHI</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>ALVEOLAR/BRONCHIOLAR ADENOMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>ALVEOLAR/BRONCHIOLAR CARCINOMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>PHEOCHROMOCYTOMA, METASTATIC</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>TRACHEA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>HEPATOPOIETIC SYSTEM</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>BONE MARROW</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>SPLEEN</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>HEMANGIOSARCOMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>LYMPH NODES</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>THYMUS</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>HEART</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>SALIVARY GLAND</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>LIVER</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>HEPATOCELLULAR ADENOMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>HEPATOCELLULAR CARCINOMA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>BILE DUCT</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>GALLBLADDER &amp; COMMON BILE DUCT</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>PANCREAS</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>ESOPHAGUS</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>STOMACH</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>DUODENUM</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>SMALL INTESTINE</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>LARGE INTESTINE</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>URETER</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>URETHRA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>REPRODUCTIVE SYSTEM</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>VAGINA</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>OVARY</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>FEMALE REPRODUCTIVE SYSTEM</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>MAMMARY GLAND</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>TESTIS</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>INTERSTITIAL-CELL TUMOR</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>PROSTATE</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>BRAIN</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>HARDERIAN GLAND</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>ADENOMA, NOS</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>ADENOMA, LYMPHOID, LYMPHOCYTIC TYPE</strong></td>
<td>++</td>
</tr>
<tr>
<td><strong>ADENOMA, LYMPHOID, MIXED TYPE</strong></td>
<td>++</td>
</tr>
</tbody>
</table>

Propyl Gallate 94
<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>MAMMARY GLAND</th>
<th>TESTIS</th>
<th>INTERSTITIAL-CELL TUMOR</th>
<th>PROSTATE</th>
<th>BRAIN</th>
<th>SPECIAL SENSE ORGANS</th>
<th>ALL OTHER SYSTEMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKIN</td>
<td>+ + + A + + +</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNGS AND BRONCHI</td>
<td>+ t A + t + t</td>
<td>- + *</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVEOLAR/BRONCHIOLAR ADENOMA</td>
<td>X X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVEOLAR/BRONCHIOLAR CARCINOMA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHEOCHROMOCYTOMA, METASTATIC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LIVER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEOPLASM.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEPAOTCELLULAR ADENOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEPAOTCELLULAR CARCINOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BILE DUCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GALLBLADDER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMMON BILE DUCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANCREAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESOPHAGUS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STOMACH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LARGE INTESTINE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URINARY BLADDER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHEOCHROMOCYTOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THYROID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FOLLICULAR-CELL ADENOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PARATHYROID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROSTAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INTERSTITIAL-CELL TUMOR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRAIN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECIAL SENSE ORGANS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HARDERIAN GLAND</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALIGNANT LYMPHOMA, MIXED TYPE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# TABLE B3.
## INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF MALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

### HIGH DOSE

<table>
<thead>
<tr>
<th>ANIMAL NUMBER</th>
<th>WEEKS ON STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
</tbody>
</table>

**INTESINAL SYSTEM**

- **SUBCUTANEOUS TISSUE**
  - SARCOMA, RMS
  - MEUROBLASTOMA, MALIG.

**RESPIRATORY SYSTEM**

- LUNGS AND BRONCHI
  - HEPATOCELLULAR CARCINOMA, METASTASIS
  - ADENOMA, PAPILLARY, ADENOMA

- TRACHEA

**HEMATOPOIETIC SYSTEM**

- BONE MARROW
- SPLEEN

**DIGESTIVE SYSTEM**

- SALIVARY GLAND
- PAPILLARY ADENOMA

**ENDOCRINE SYSTEM**

- PITUITARY
- ADRENAL
- THYROID
- PARATHYROID

**REPRODUCTIVE SYSTEM**

- MAMMARY GLAND
- TESTIS
- PROSTATE

**NERVOUS SYSTEM**

- BRAIN

**ALL OTHER SYSTEMS**

- MULTIPLE ORGANS, RMS

<table>
<thead>
<tr>
<th>TISSUE EXAMINED</th>
<th>TISSUE EXAMINED</th>
<th>TISSUE EXAMINED</th>
<th>TISSUE EXAMINED</th>
<th>TISSUE EXAMINED</th>
<th>TISSUE EXAMINED</th>
<th>TISSUE EXAMINED</th>
<th>TISSUE EXAMINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- NO TISSUE EXAMINED
  - NO TISSUE EXAMINED
  - NO TISSUE EXAMINED
  - NO TISSUE EXAMINED
  - NO TISSUE EXAMINED
  - NO TISSUE EXAMINED

- TUMOR INCIDENTAL
  - TUMOR INCIDENTAL
  - TUMOR INCIDENTAL
  - TUMOR INCIDENTAL
  - TUMOR INCIDENTAL
  - TUMOR INCIDENTAL

- NEPHROPY, NO AUTOPSY, NO MICROSCOPIC EXAMINATION
  - NEPHROPY, NO AUTOPSY, NO MICROSCOPIC EXAMINATION
  - NEPHROPY, NO AUTOPSY, NO MICROSCOPIC EXAMINATION
  - NEPHROPY, NO AUTOPSY, NO MICROSCOPIC EXAMINATION
  - NEPHROPY, NO AUTOPSY, NO MICROSCOPIC EXAMINATION
  - NEPHROPY, NO AUTOPSY, NO MICROSCOPIC EXAMINATION
### TABLE 83. MALE MICE: TUMOR PATHOLOGY (CONTINUED)  HIGH DOSE

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>TISSUE EXAMINED</th>
<th>TUMOR INCIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INTEGUMENTARY SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SUBCUTANEOUS TISSUE</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Superficial soft tissue, malignant</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td><strong>RESPIRATORY SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs and bronchi</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Hepatocellular carcinoma, metastasis</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td>Alveolar/bronchial adenoma</td>
<td>X</td>
<td>2</td>
</tr>
<tr>
<td>Papillary adenoma</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td><strong>HEMATOPOIETIC SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone marrow</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td><strong>LYMPHATIDIC SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Malignant lymphoma, histiocytic type</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td>Malignant lymphoma, mixed type</td>
<td>X</td>
<td>2</td>
</tr>
<tr>
<td>Thymus</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary gland</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Liver</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Hepatocellular adenoma</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>X</td>
<td>2</td>
</tr>
<tr>
<td>Malignant lymphoma, histiocytic type</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td>Bile duct</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Gallbladder &amp; common bile duct</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Pancreas</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Esophagus</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Stomach</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Small intestine</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Large intestine</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td><strong>URINARY SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td><strong>REPRODUCTIVE SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mammary gland</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Testis</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Interstitial-cell tumor</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Prostate</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td><strong>NERVOUS SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td><strong>SPECIAL SENSE ORGANS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harderian gland</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Adenoma, NOS</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td><strong>ALL OTHER SYSTEMS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple organs, NOS</td>
<td>X</td>
<td>72</td>
</tr>
<tr>
<td>Malignant lymphoma, mixed type</td>
<td>X</td>
<td>1</td>
</tr>
</tbody>
</table>

* Tissue examined microscopically
+ Tissue examined microscopically
- Required tissue not examined microscopically
\* Tissue examination submitted
\+ Tumor incidence
\- Tumor incidence
\^ Necropsy, no histology due to protocol
\$ Necropsy, no autolysis, no microscopic examination
\& Necropsy performed

97 Propyl Gallate
TABLE 84.
INDIVIDUAL ANIMAL TUMOR PATHOLOGY TABLES OF FEMALE MICE IN THE 2-YEAR STUDY OF PROPYL GALLATE

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>CONTROL</th>
<th>PROPYL GALLATE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RESPIRATORY SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNGS AND BRONCHI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchiolar Bronchial Adenoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteosarcoma, Metastatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trachea</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HEMATOPOIETIC SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone Marrow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute Malignant Lymphoma, Mixed Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LYMPH NODES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant Lymphoma, Mixed Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thymus</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CIRCULATORY SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary Gland</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic Cell Carcinoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile Duct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallbladder &amp; Common Bile Duct</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large Intestine</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>URETERAL SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RENAL BLEDDER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ENDOCRINE SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma, NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SKELETAL SYSTEM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ALL OTHER SYSTEMS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Organs NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant Lymphoma, Mixed Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant Lymphoma, Lymphocytic Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant Lymphoma, Mixed Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphatic Leukemia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Tissue Examined Microscopically** |         |                |
| **Required Tissue Not Examined Microscopically** |         |                |
| **Tissue Submission**              |         |                |
| **Animal Missing**                 |         |                |
| **No Necropsy, No Microscopic Examination** |         |                |
| **Tissue Examined Necropsy**       |         |                |
| **Tissue Examined Necropsy**       |         |                |
| **Tissue Examined Necropsy**       |         |                |

Propyl Gallate 98
**TABLE B4. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED)**

<table>
<thead>
<tr>
<th>ANIMAL</th>
<th>WEEKS ON STUDY</th>
<th>TOTAL TISSUES</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESPIRATORY SYSTEM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNGS AND BRONCHI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVEOLAR/BRONCHIOLAR ADENOMA</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>OSTEOSARCOMA, METASTATIC</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>TRACHEA</td>
<td></td>
<td>49</td>
</tr>
<tr>
<td>ADRENAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SENSE MARROW</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>SPLEEN</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>MALIG. LYMPHOMA, MIXED TYPE</td>
<td></td>
<td>49</td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td></td>
<td>47</td>
</tr>
<tr>
<td>DIGESTIVE SYSTEM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td></td>
<td>48</td>
</tr>
<tr>
<td>LIVER</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>HEPATOCELLULAR CARCINOMA</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>BILE DUCT</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>GALLBLADDER &amp; COMMON BILE DUCT</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>PANCREAS</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>ESOPHAGUS</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>STOMACH</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
<td></td>
<td>57</td>
</tr>
<tr>
<td>LARGE INTESTINE</td>
<td></td>
<td>49</td>
</tr>
<tr>
<td>URINARY SYSTEM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KIDNEY</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>URETHRAL BLADDER</td>
<td></td>
<td>48</td>
</tr>
<tr>
<td>ENDOCRINE SYSTEM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PITUITARY</td>
<td></td>
<td>48</td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>ADRENAL</td>
<td></td>
<td>55</td>
</tr>
<tr>
<td>SARCOMA, NOS</td>
<td></td>
<td>49</td>
</tr>
<tr>
<td>THYROID</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>HYPOPHYSIS</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>PARATHYROID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADRENAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADRENAL GLAND</td>
<td></td>
<td>32</td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIXED TUMOR, MALIG.</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>EMENDATIONS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIXED TUMOR, MALIG.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TUMOR, MALIG.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UTERUS</td>
<td></td>
<td>50</td>
</tr>
<tr>
<td>FIBROUS HISTIOCYTIC</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>ENDOMETRIAL STROMAL POLYP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENDOMETRIAL STROMAL SARCOMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIBROUS</td>
<td></td>
<td>48</td>
</tr>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEANDIAL GLAND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADENOMA, NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIXED TUMOR, MALIG.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UTERUS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL OTHER SYSTEMS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL OTHER TUMORS, NOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALIG. LYMPHOMA, MIXED TYPE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALIG. LYMPHOMA, SYSTIC TYPE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MALIG. LYMPHOMA, MIXED TYPE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ANIMALS NECROPTED
  - TISSUE EXAMINED MICROSCOPICALLY
  - TISSUE EXAMINED MICROSCOPICALLY
  - NO TISSUE INFORMATION SUBMITTED
  - TISSUE EXAMINED MICROSCOPICALLY
  - TISSUE EXAMINED MICROSCOPICALLY
  - TISSUE EXAMINED MICROSCOPICALLY
  - TISSUE EXAMINED MICROSCOPICALLY
  - TISSUE EXAMINED MICROSCOPICALLY
  - TISSUE EXAMINED MICROSCOPICALLY

99 Propyl Gallate
**TABLE B4.**

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

**LOW DOSE**

<table>
<thead>
<tr>
<th>ANIMAL NUMBER</th>
<th>WEEKS ON STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0  1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21  22</td>
</tr>
</tbody>
</table>

**NECROPSY SYSTEM**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUNGS AND BRONCHI</td>
<td>ALVEOLAR/BRONCHOLOAL ADENOMA</td>
</tr>
<tr>
<td>BONE MARROW</td>
<td>MALIGNANT LYMPHOMA, MIXED TYPE</td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td></td>
</tr>
<tr>
<td>THYROID</td>
<td></td>
</tr>
</tbody>
</table>

**CIRCULATORY SYSTEM**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DIGESTIVE SYSTEM**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>SALTIVARY GLAND</td>
<td></td>
</tr>
<tr>
<td>LIVER</td>
<td></td>
</tr>
<tr>
<td>BILE DUCT</td>
<td></td>
</tr>
<tr>
<td>PANCREAS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**REPRODUCTIVE SYSTEM**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>KIDNEY</td>
<td></td>
</tr>
<tr>
<td>PITUITARY</td>
<td></td>
</tr>
<tr>
<td>THYROID</td>
<td></td>
</tr>
</tbody>
</table>

**REPRODUCTIVE SYSTEM**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTERUS</td>
<td></td>
</tr>
<tr>
<td>OVARY</td>
<td></td>
</tr>
</tbody>
</table>

**HEART**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SPECIAL SENSE ORGANS**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ANOTHER SYSTEM**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ALL OTHER SYSTEMS**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Malignant Lesion Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Tissue Examination Codes:**

- Tissue Examined Microscopically
- Tissue Not Examined Microscopically
- Tissue Undetermined
- Tumor Incidence
- Necropsy, No Autolysis, No Microscopic Examination
- Necropsy, No Histology Due to Protocol
- No Tissue Information Submitted
- Animal Missing
- Necropsy Performed

---

Propyl Gallate 100
<table>
<thead>
<tr>
<th>ANIMAL NUMBER</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>TOTAL TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>WEEKS ON STUDY</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>RESPIRATORY SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNGS AND BRONCHI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVEOLAR/BRONCHIOLAR ADENOMA</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>58</td>
</tr>
<tr>
<td>TRACHEA</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>49</td>
</tr>
<tr>
<td>RETICULOENDOTHELIAL SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BONE MARROW</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>33</td>
</tr>
<tr>
<td>LYMPH NODES</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>48</td>
</tr>
<tr>
<td>THYMUS</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>49</td>
</tr>
<tr>
<td>CIRCULATORY SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEART</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>58</td>
</tr>
<tr>
<td>DIGESTIVE SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SALIVARY GLAND</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>58</td>
</tr>
<tr>
<td>GIVER</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>58</td>
</tr>
<tr>
<td>MALIGNANT LYMPHOMA</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>34</td>
</tr>
<tr>
<td>THYMUS</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>49</td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>42</td>
</tr>
<tr>
<td>LARGE INTESTINE</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>42</td>
</tr>
<tr>
<td>URINARY SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADRENAL GLAND</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URETER</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>36</td>
</tr>
<tr>
<td>PAPILLARY CYSTADENOMA</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>14</td>
</tr>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UTERUS</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>48</td>
</tr>
<tr>
<td>OVARY</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>48</td>
</tr>
<tr>
<td>RETROPERITONEAL Lymph Nodes</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>48</td>
</tr>
<tr>
<td>ANIMALS NEOPERIC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TISSUE EXAMINED MICROSCOPICALLY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TISSUE NOT EXAMINED MICROSCOPICALLY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TISSUE EXAMINED MACROSCOPICALLY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO TISSUE INFORMATION SUBMITTED</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X: TUMOR INCIDENCE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X: TUMOR INCIDENCE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A: AUTOLYSIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B: NO NEUROPSY PERFORMED</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Type</td>
<td>Animal Number</td>
<td>High Dose</td>
<td>Medium Dose</td>
<td>Low Dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------</td>
<td>---------------</td>
<td>-----------</td>
<td>-------------</td>
<td>----------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous Tissue</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhadamysarcoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lungs and Bronchi</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar/bronchial adenoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar/bronchial carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematopoietic System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone marrow</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymph nodes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thymus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circulatory System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digestive System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salivary gland</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatocellular adenoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukemia, NOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile duct</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallbladder &amp; common bile duct</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pallignant lymphoma, mixed type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large intestine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary gland</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parathyroid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic islet</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mammary gland</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed tumor, Pallignant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney, NOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate, NOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate, mixed type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal System</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All other systems</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple organs, NOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple organs, mixed type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Tissue examined microscopically
+ Tissue information submitted
D Necropsy, no histology due to protocol
M Necropsy, no autolysis, no microscopic examination
B Necropsy performed
A Animal missing
F No necropsy performed
TABLE 84. FEMALE MICE: TUMOR PATHOLOGY (CONTINUED)  HIGH DOSE

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>HIGH DOSE</th>
<th>FIRST</th>
<th>SECOND</th>
<th>THIRD</th>
<th>FOURTH</th>
<th>TOTAL</th>
<th>TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIGESTIVE SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SUBCUTANEOUS TISSUE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RETROPERITONEAL TISSUE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEPATIC CARCINOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANCREAS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BILE DUCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMMON BILE DUCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESOPHAGUS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STOMACH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMALL INTESTINE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LARGE INTESTINE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URINARY SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KIDNEY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URINARY BLADDER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ENDOCRINE SYSTEM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADRENAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THYROID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANCREATIC ISLETS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PANCREATIC ISLET ADENOMA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PARATHYROID Glands</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL OTHER MUSCULAR SYSTEMS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL OTHER SYSTEMS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Abbreviations:
  - T: Tumor incidence
  - N: Normal tissue
  - H: Hematoxylin
  - D: Dye
  - M: Microscopic
  - R: Recorded
  - X: Negative
  - *: No tissue information submitted
  - 1: No tissue information submitted
  - 2: Microscopic examination due to protocol
  - 3: Necropsy, no histology due to protocol
  - 4: Necropsy, no autopsy, no microscopic examination
  - 5: Animal missing
  - 6: 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 |

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANIMALS INITIALLY IN STUDY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS NECROPSIED</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS EXAMINED HISTOPATHOLOGICALLY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>INTEGUMENTARY SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SKIN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYST, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>EPIDERMAL INCLUSION CYST</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>ULCER, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIBROSIS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RESPIRATORY SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNG/BRONCHIOLE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, FOCAL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, ADENOMATOUS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONGESTION, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>CONGESTION, CHRONIC PASSIVE</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>EDEMA, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDEMA, INTERSTITIAL</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BRONCHOPNEUMONIA, ACUTE</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>HYPERPLASIA, ALVEOLAR EPITHELIUM</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>METAPLASIA, OSSSEOUS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LUNG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALVEOLAR EPITHELIUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, ADENOMATOUS</td>
<td>2 (4%)</td>
<td></td>
<td>3 (6%)</td>
</tr>
<tr>
<td>HEMATOPOIETIC SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BONE MARROW</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MYEOFIBROSIS</td>
<td>(49)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>SPLEEN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONGESTION, NOS</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED
TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFLAMMATION, GRANULOMATOUS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>FIBROSIS, FOCAL</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>HEMATOPOIESIS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#MANDIBULAR L. NODE</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, NOS</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>#MESENTERIC L. NODE</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#RENAL LYMPH NODE</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HEMOSIDEROSIS</td>
<td>1 (2%)</td>
<td></td>
<td>4 (8%)</td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#INGUINAL LYMPH NODE</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>FIBROSIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#LUNG</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>LEUKOCYTOSIS, NOS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ERYTHROBLASTOSIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#LIVER</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>LEUKOCYTOSIS, NOS</td>
<td>1 (2%)</td>
<td>3 (10%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>ERYTHROBLASTOSIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEMATOPOIESIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#KIDNEY</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#ADRENAL</td>
<td>(50)</td>
<td>(48)</td>
<td>(50)</td>
</tr>
<tr>
<td>HEMATOPOIESIS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#ADRENAL CORTEX</td>
<td>(50)</td>
<td>(43)</td>
<td>(50)</td>
</tr>
<tr>
<td>HEMATOPOIESIS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#THYMUS</td>
<td>(36)</td>
<td>(38)</td>
<td>(35)</td>
</tr>
<tr>
<td>HYPERPLASIA, NOS</td>
<td>1 (3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CIRCULATORY SYSTEM

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>#HEART/ATRIUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>THROMBOSIS, NOS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#MYOCARDIUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Propyl Gallate
### TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FIBROSIS, FOCAL</strong></td>
<td>18 (36%)</td>
<td>21 (42%)</td>
<td>23 (46%)</td>
</tr>
<tr>
<td><strong>FIBROSIS, DIFFUSE</strong></td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td><strong>#PANCREAS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periarteritis</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>3 (6%)</td>
<td>5 (10%)</td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td><strong>#MESENTRY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periarteritis</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
<td></td>
</tr>
</tbody>
</table>

### DIGESTIVE SYSTEM

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>#PAROTID GLAND</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Atrophy, Focal</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td><strong>#LIVER</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Deformity, NOS</td>
<td>4 (8%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Congestion, NOS</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Inflammation, Focal</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Eosinophilic Infiltrate</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Inflammation, Necrotic</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Degeneration, Cystic</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Necrosis, Central</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Cytoplasmic Vascularization</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Nodular Regeneration</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td><strong>#LIVER/CEPHALOBLADAR</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Necrosis, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Metaplasia Fatty</td>
<td>3 (6%)</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Atrophy, NOS</td>
<td>5 (10%)</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td><strong>#LIVER/HEPATOCEGETES</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Degeneration, Cystic</td>
<td>5 (10%)</td>
<td>3 (6%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Cytoplasmic Vascularization</td>
<td>3 (6%)</td>
<td>20 (40%)</td>
<td>17 (34%)</td>
</tr>
<tr>
<td><strong>#BILE DUCT</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Hyperplasia, NOS</td>
<td>43 (86%)</td>
<td>37 (74%)</td>
<td>29 (58%)</td>
</tr>
<tr>
<td>Hyperplasia, Focal</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>#PANCREATIC ACINUS</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Atrophy, NOS</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Atrophy, Focal</td>
<td>17 (34%)</td>
<td>9 (18%)</td>
<td>13 (26%)</td>
</tr>
<tr>
<td>Hyperplasia, Focal</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>#GASTRIC FUNIDAL GLAND</strong></td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Dilatation, NOS</td>
<td>22 (44%)</td>
<td>22 (44%)</td>
<td>28 (56%)</td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
* Number of animals necropsied
TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HYPERTROPHIA, NOS</strong></td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>HYPERPLASIA, FOCAL</strong></td>
<td>2 (4%)</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>ANGIETASIS</strong></td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td><strong>PEPTIC ULCUS</strong></td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>(49)</td>
</tr>
<tr>
<td><strong>HYPERPLASIA, FOCAL</strong></td>
<td>(50)</td>
<td>(48)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>HYPERPLASIA, NOS</strong></td>
<td>1 (2%)</td>
<td>9 (18%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>HYPERPLASIA, C-CELL</strong></td>
<td>(50)</td>
<td>(48)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>HYPERPLASIA, NOS</strong></td>
<td>(44)</td>
<td>(44)</td>
<td>(48)</td>
</tr>
<tr>
<td><strong>HYPERPLASIA, NOS</strong></td>
<td>2 (5%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
# Number of animals necropsied
<table>
<thead>
<tr>
<th>Tissue System</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nervous System</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain Compression</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Hypothalamus Compression</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Special Sense Organs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Hemorrhage</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Retinopothy</td>
<td>12 (24%)</td>
<td>8 (16%)</td>
<td>35 (70%)</td>
</tr>
<tr>
<td>Cataract</td>
<td>12 (24%)</td>
<td>4 (8%)</td>
<td>35 (70%)</td>
</tr>
<tr>
<td>Harderian Gland Ectopia</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Musculoskeletal System</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
* Number of animals necropsied

Propyl Gallate 110
### TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Body Cavities</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Wall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal Wall Adhesion, Nos</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Abdominal Wall Necrosis, Fat</td>
<td>1 (2%)</td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Peritoneum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritoneum Inflammation, Nos</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Pleura</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleura Inflammation, Nos</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Mesentery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesentery Hemorrhage</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Mesentery Inflammation, Granulomatous Necrosis, Fat</td>
<td>3 (6%)</td>
<td>4 (8%)</td>
<td>8 (16%)</td>
</tr>
</tbody>
</table>

### ALL OTHER SYSTEMS

<table>
<thead>
<tr>
<th>System</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omentum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omentum Necrosis, Fat</td>
<td>2</td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>

### SPECIAL MORPHOLOGY SUMMARY

None

- * Number of animals with tissue examined microscopically
- * Number of animals necropsied


<table>
<thead>
<tr>
<th>TABLE C2.</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS FED DIETS CONTAINING PROPYL GALLATE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANIMALS INITIALLY IN STUDY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS NECROPSIED</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>ANIMALS EXAMINED HISTOPATHOLOGICALLY</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

### INTEGUMENTARY SYSTEM

*Skin

- Inflammation, NOS
  - Ulcer, NOS: 2 (4%)
  - Ulcer, Chronic
- Inflammation, Chronic Focal
- Fibrosis: 1 (2%)

### RESPIRATORY SYSTEM

* Nasal Cavity

- Vegetable Foreign Body
  - Inflammation, Suppurative
  - Inflammation, NOS: 1 (2%)
- Ulcer: 1 (2%)
- Pneumonia, Aspiration: 2 (4%)
- Inflammation, Focal Granulomatous
- Hyperplasia, Alveolar Epithelium: 2 (4%)

* Lung

- Congestion, NOS: 1 (2%)
- Inflammation, Focal
- Hyperplasia, Adenomatous: 1 (2%)

### HEMATOPOIETIC SYSTEM

* Bone Marrow

- Myelofibrosis: 1 (2%)

* Spleen

- Infarct, NOS: 1 (2%)

<table>
<thead>
<tr>
<th># NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY</th>
</tr>
</thead>
<tbody>
<tr>
<td># NUMBER OF ANIMALS NECROPSIED</td>
</tr>
</tbody>
</table>

Propyl Gallate 112
TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEMATOPOIESIS</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>#MANDIBULAR L. NODE</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, NOS</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>HYPERPLASIA, CYSTIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#INGUINAL LYMPH NODE</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#LUNG</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>LEUKOCYTOSIS, NOS</td>
<td>2 (4%)</td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#LIVER</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>LEUKOCYTOSIS, NOS</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#CERVICAL MUCOUS MEMB</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>LEUKOCYTOSIS, NOS</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>CIRCULATORY SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#MYOCARDIUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>INFLAMMATION, FOCAL</td>
<td>2 (4%)</td>
<td></td>
<td>10 (20%)</td>
</tr>
<tr>
<td>FIBROSIS, FOCAL</td>
<td>4 (8%)</td>
<td>10 (20%)</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>PERIARTERITIS</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#MESENTERY</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>PERIARTERITIS</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>DIGESTIVE SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#LIVER</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>DEFORMITY, NOS</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>CONGESTION, NOS</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>CHOLEANGIOPATHY</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>NECROSIS, FOCAL</td>
<td>1 (2%)</td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>METAPHOSIS FATTY</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYTOPLASMIC VACUOLIZATION</td>
<td>3 (6%)</td>
<td></td>
<td>2 (4%)</td>
</tr>
<tr>
<td>BASOPHILIC CYTO CHANGE</td>
<td>3 (8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, NOS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NODULAR REGENERATION</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>#LIVER/CENTRILOBULAR</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>METAPHOSIS FATTY</td>
<td>4 (8%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

* Number of animals necropsied

**Number of animals with tissue examined microscopically

# Number of animals with tissue examined microscopically

Propyl Gallate
### TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATROPHY, NOS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># LIVER/Hepatocytes</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Cytoplasmic Vacuolation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Basophilic Cyto Change</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Bile Duct</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hyperplasia, NOS</strong></td>
<td>13 (26%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Hyperplasia, Focal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Pancreatic Acinus</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Atrophy, Focal</strong></td>
<td>13 (26%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td># Gastric Mucosa</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Inflammation, Suppurative</strong></td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Degeneration, Mucoid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hyperplasia, Basal Cell</strong></td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td># Gastric Fundal Gland</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Dilatation, NOS</strong></td>
<td>26 (52%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
</tbody>
</table>

#### Urinary System

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td># Kidney</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Neprosis, NOS</strong></td>
<td>8 (16%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td># Kidney/Tudule</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Metamorphosis Fatty Pigmentation, NOS</strong></td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td># Urinary Bladder</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Hyperplasia, Epithelial</strong></td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
</tbody>
</table>

#### Endocrine System

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td># Pituitary</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Embryonal Duct Cyst</strong></td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Hemorrhage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hyperplasia, NOS</strong></td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Hyperplasia, Focal</strong></td>
<td>5 (10%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Angiectasis</strong></td>
<td>2 (4%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td># Anterior Pituitary</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Angiectasis</strong></td>
<td>5 (10%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
</tbody>
</table>

* Number of animals with tissue examined microscopically
* Number of animals necropsied

Propyl Gallate 114
TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADRENAL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiectasis</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>ADRENAL CORTEX</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metamorphosis Fatty</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Cytoplasmic Vacuolization Angiectasis</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>ADRENAL MEDULLA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytoplasmic Change, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Hyperplasia, Focal</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>THYROID</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic Follicles</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Degeneration, Cystic</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, C-CELL</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>PARATHYROID</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia, Focal</td>
<td>(45)</td>
<td>(45)</td>
<td>(48)</td>
</tr>
</tbody>
</table>

REPRODUCTIVE SYSTEM

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAMMARY GLAND</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic Ducts</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Inflammation, Suppurative</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Hyperplasia, Cystic</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Adenosis</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Cystic Disease</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>PREPUTIAL GLAND</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation, Suppurative</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Inflammation, Chronic</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, Cystic</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>VAGINA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation, Suppurative</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>VAGINAL MUCOUS MEMBR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyst, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>UTERUS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolapase</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Hydrometra</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
</tbody>
</table>

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

115 Propyl Gallate
TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEMATOMA, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>HEMATOMETRA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, SUPPURATIVE</td>
<td>1 (2%)</td>
<td></td>
<td>2 (4%)</td>
</tr>
<tr>
<td>#UTERUS-ENDOMETRIUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>HYPERPLASIA, CYSTIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, Stromal</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>7 (14%)</td>
</tr>
<tr>
<td>#ENDOMETRIAL GLAND</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>DILATATION, NOS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#OVARY/PAROVARIAN HEMORRHAGE</td>
<td>(49)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>#OVARY FOLLICULAR CYST, NOS</td>
<td>(49)</td>
<td>(50)</td>
<td>3 (6%)</td>
</tr>
</tbody>
</table>

NERVOUS SYSTEM

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>#BRAIN COMPRESSION</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>#INTERNAL CAPSULE GLIOSIS</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>#HYPOTHALAMUS COMPRESSION</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
</tbody>
</table>

SPECIAL SENSE ORGANS

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>#EYE INFLAMMATION, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>RETINOpatY</td>
<td>10 (20%)</td>
<td>1 (2%)</td>
<td>14 (28%)</td>
</tr>
<tr>
<td>CATARACT</td>
<td>8 (16%)</td>
<td>40 (80%)</td>
<td>13 (26%)</td>
</tr>
<tr>
<td>#EYE/CORNEA ULCER, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>#HARDERIAN GLAND ECTOPIA</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>#EXTERNAL EAR ULCER, NOS</td>
<td>(50)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED
TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>All Other Systems</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hyperplasia, Focal</strong></td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Musculoskeletal System</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Skull</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperostosis</td>
<td>1 (2%)</td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>Body Cavities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Mesentery</em></td>
<td></td>
<td>(50)</td>
<td>(50)</td>
</tr>
<tr>
<td>Necrosis, Fat</td>
<td>4 (6%)</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td><strong>Sole of Foot</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Callus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omentum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrosis, Fat</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Infarct Hemorrhagic</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascularization</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANIMALS INITIALLY IN STUDY</strong></td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td><strong>ANIMALS NECROPSIED</strong></td>
<td>50</td>
<td>49</td>
<td>50</td>
</tr>
<tr>
<td><strong>ANIMALS EXAMINED HISTOPATHOLOGICALLY</strong></td>
<td>50</td>
<td>49</td>
<td>50</td>
</tr>
</tbody>
</table>

### INTEGUMENTARY SYSTEM

<table>
<thead>
<tr>
<th><strong>SKIN</strong></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer, Nos</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Ulcer, Focal</td>
<td>10 (20%)</td>
<td>4 (8%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Inflammation, Chronic Focal</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Hyperplasia, Basal Cell</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SUBCUT TISSUE

<table>
<thead>
<tr>
<th><strong>SUBCUT TISSUE</strong></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abscess, Nos</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Inflammation, Acute/Chronic</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Inflammation, Chronic</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation, Chronic Suppurativ</td>
<td>3 (6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess, Chronic</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

### RESPIRATORY SYSTEM

<table>
<thead>
<tr>
<th><strong>LUNG/BRONCHIOLE</strong></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperplasia, Nos</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

### LUNG

<table>
<thead>
<tr>
<th><strong>LUNG</strong></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestion, Nos</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Lymphocytic Inflammatory Infiltr</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation, Granulomatous</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation, Focal Granulomatous</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction, Foreign Body</td>
<td>1 (2%)</td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Cholesterol Deposit</td>
<td>1 (2%)</td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Hyperplasia, Adenomatous</td>
<td>11 (22%)</td>
<td>8 (17%)</td>
<td>7 (14%)</td>
</tr>
<tr>
<td>Hyperplasia, Alveolar Epithelium</td>
<td>1 (2%)</td>
<td></td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

### HEMATOPOIETIC SYSTEM

<table>
<thead>
<tr>
<th><strong>MULTIPLE ORGANS</strong></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperplasia, Lymphoid</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY

# NUMBER OF ANIMALS NECROPSIED

---

Propyl Gallate 120
TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion Description</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>#BONE MARROW</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>ATROPHY, NOS</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, GRANULOCYTIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#SPLEEN</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>FIBROSIS, FOCAL</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>AMYLOIDOSIS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEMATOPOIESIS</td>
<td>3 (6%)</td>
<td>5 (10%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#LYMPH NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#PANCREATIC L. NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#MESENTERIC L. NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>HEMORRHAGE</td>
<td>1 (2%)</td>
<td>4 (8%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEMATOPOIESIS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#RENAL LYMPH NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>INFLAMMATION, GRANULOMATOUS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#AXILLARY LYMPH NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#INGUINAL LYMPH NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#LIVER</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>LEUKOCYTOSIS, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#PEYER'S PATCH</td>
<td>(48)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>HYPERPLASIA, LYMPHOID</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td></td>
</tr>
</tbody>
</table>

CIRCULATORY SYSTEM

<table>
<thead>
<tr>
<th>Lesion Description</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>#MESENTERIC L. NODE</td>
<td>(49)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>THROMBOSIS, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#HEART</td>
<td>(48)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>INFLAMMATION, SUPPURATIVE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROSIED

121  Propyl Gallate
### TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>#AURICULAR APPENDAGE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THROMBUS, MURAL</td>
<td>(48)</td>
<td></td>
<td>(49)</td>
</tr>
<tr>
<td><strong>DIGESTIVE SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>#LIVER</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MINERALIZATION</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>CYST, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, GRANULOMATOUS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NECROSIS, FOCAL</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NECROSIS, COAGULATIVE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NUCLEAR-SIZE ALTERATION</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYTOPLASMIC VACUOLIZATION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FOCAL CELLULAR CHANGE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td>1 (2%)</td>
<td></td>
<td>2 (4%)</td>
</tr>
<tr>
<td><strong>#PANCREAS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytic inflammatory infiltr</td>
<td>(50)</td>
<td>(49)</td>
<td>(48)</td>
</tr>
<tr>
<td><strong>#SMALL INTESTINE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ULCER, FOCAL</td>
<td>(48)</td>
<td></td>
<td>(49)</td>
</tr>
<tr>
<td><strong>#COLON</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEMATODIASIS</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td><strong>URINARY SYSTEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>#KIDNEY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYDRONEPHROSIS</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>PYELONEPHRITIS, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LYMPHOCYTIC INFLAMMATORY INFILTR</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, INTERSTITIAL</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td>4 (3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC FOCAL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEPHROSIS, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>#KIDNEY/PELVIS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NECROSIS, MEDULLARY</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td><strong>#URINARY BLADDER</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td>(50)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
</tbody>
</table>

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

Propyl Gallate 122
**TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)**

<table>
<thead>
<tr>
<th><strong>#</strong></th>
<th><strong>Tissue</strong></th>
<th><strong>Control</strong></th>
<th><strong>Low Dose</strong></th>
<th><strong>High Dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADRENAL CORTEX</strong></td>
<td>HYPERPLASIA, FOCAL</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>ADRENAL MEDULLA</strong></td>
<td>HYPERPLASIA, FOCAL</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>THYROID</strong></td>
<td>FOLLICULAR CYST, NOS</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

**REPRODUCTIVE SYSTEM**

<table>
<thead>
<tr>
<th><strong>#</strong></th>
<th><strong>Tissue</strong></th>
<th><strong>Control</strong></th>
<th><strong>Low Dose</strong></th>
<th><strong>High Dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PREPUTIAL GLAND</strong></td>
<td>CYSTIC DUCTS</td>
<td>3 (6%)</td>
<td>6 (12%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td></td>
<td>INFLAMMATION, SUPPURATIVE</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td></td>
<td>ABSCESS, NOS</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>PROSTATE</strong></td>
<td>INFLAMMATION, SUPPURATIVE</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>SEMINAL VESICLE</strong></td>
<td>INFLAMMATION, ACUTE SUPPURATIVE</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>TESTIS</strong></td>
<td>GRANULOMA, SPERMATIC</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>EPIDIDYMIS</strong></td>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

**NERVOUS SYSTEM**

<table>
<thead>
<tr>
<th><strong>#</strong></th>
<th><strong>Tissue</strong></th>
<th><strong>Control</strong></th>
<th><strong>Low Dose</strong></th>
<th><strong>High Dose</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRAIN/MENINGES</strong></td>
<td>PERIVASCULAR CUFFING</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED
<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECIAL SENSE ORGANS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XEYE</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>PHTHISIS BULBI</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MUSCULOSKELETAL SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NONE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BODY CAVITIES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XMESENTERY</td>
<td>(50)</td>
<td>(49)</td>
<td>(50)</td>
</tr>
<tr>
<td>NECROSIS, FAT</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>ALL OTHER SYSTEMS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NONE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECIAL MORPHOLOGY SUMMARY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO LESION REPORTED</td>
<td>7</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>AUTOLYSIS/NO NECROPSY</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
# NUMBER OF ANIMALS NECOPSYED

Propyl Gallate 124
# TABLE D2.
## SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE FED DIETS CONTAINING PROPYL GALLATE

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANIMALS INITIALLY IN STUDY</strong></td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td><strong>ANIMALS NECROPSIED</strong></td>
<td>50</td>
<td>50</td>
<td>49</td>
</tr>
<tr>
<td><strong>ANIMALS EXAMINED HISTOPATHOLOGICALLY</strong></td>
<td>50</td>
<td>50</td>
<td>49</td>
</tr>
</tbody>
</table>

## INTEGUMENTARY SYSTEM
- **SKIN**
  - Inflammation, Chronic
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)

## RESPIRATORY SYSTEM
- **LUNG**
  - Edema, NOS
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)
  - Inflammation, Suppurative
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)
  - Inflammation, Granulomatous
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)
  - Inflammation, Focal Granulomatous
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)
  - Cholesterol Deposit
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)
  - Hyperplasia, Adenomatous
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)
  - Hyperplasia, Alveolar Epithelium
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)

## HEMATOPOIETIC SYSTEM
- **MULTIPLE ORGANS**
  - Hyperplasia, Lymphoid
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)
  - Myelofibrosis
    - *Number of Animals Tissue Examined Microscopically* (50) (50) (49)

## OTHER SYSTEMS
- **Spleen**
  - Atrophy, NOS
    - *Number of Animals Tissue Examined Microscopically* (50) (49) (49)
  - Angiectasis
    - *Number of Animals Tissue Examined Microscopically* (50) (49) (49)
  - Hyperplasia, Lymphoid
    - *Number of Animals Tissue Examined Microscopically* (50) (49) (49)
  - Hematopoiesis
    - *Number of Animals Tissue Examined Microscopically* (50) (49) (49)

## MANDIBULAR NODES
- **Lymphoid, Hyperplasia**
  - *Number of Animals Tissue Examined Microscopically* (49) (48) (49)

* Number of animals with tissue examined microscopically
* Number of animals necropsied
<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control (49)</th>
<th>Low Dose (48)</th>
<th>High Dose (49)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bronchial Lymph Node</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia, Lymphoid</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mesenteric L. Node</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiectasis</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia, Lymphoid</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td><strong>Renal Lymph Node</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiectasis</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Peyer’s Patch</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia, Lymphoid</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia, Lymphoid</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Hematopoiesis</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td><strong>Thymus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necrosis, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Circulatory System**

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control (49)</th>
<th>Low Dose (50)</th>
<th>High Dose (49)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Myocardium</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation, Suppurative</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation, Chronic</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac Valve</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocarditis, Bacterial</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Uterus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombus, Organized</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thyroid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periarteritis</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Digestive System**

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Control (49)</th>
<th>Low Dose (50)</th>
<th>High Dose (49)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytic Inflammatory Infiltr</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# Number of animals with tissue examined microscopically
* Number of animals necropsied
TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Control</th>
<th>Low Dose</th>
<th>High Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>ABSCES, CHRONIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NECROSIS, COAGULATIVE</td>
<td>1 (2%)</td>
<td></td>
<td>2 (4%)</td>
</tr>
<tr>
<td>NUCLEAR-SIZE ALTERATION</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#PANCREAS</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>CYSTIC DUCTS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC FOCAL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC SUPPURATIVE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#PANCREATIC ACINUS</td>
<td>(49)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>ATROPHY, NOS</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATROPHY, FOCAL</td>
<td></td>
<td></td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#STOMACH</td>
<td>(50)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>ULCER, FOCAL</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#GASTRIC MUCOSA</td>
<td>(50)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>ULCER, FOCAL</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC SUPPURATIVE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URINARY SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#KIDNEY</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>HYDRONEPHROSIS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LYMPHOCYTIC INFLAMMATORY INFLTR</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>PYELONEPHRITIS DIFFUSE</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, INTERSTITAL</td>
<td>4 (8%)</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>INFLAMMATION, SUPPURATIVE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, CHRONIC</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>GLOMERULONEPHRITIS PROLIFERATIVE</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>PERIVASCULAR CUFFING</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>AMYLOIDOSIS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>METAPLASIA, OSSUES</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#KIDNEY/PELVIS</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>LYMPHOCYTIC INFLAMMATORY INFLTR</td>
<td>4 (8%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>ENDOCRINE SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>#PITUITARY</td>
<td>(48)</td>
<td>(48)</td>
<td>(49)</td>
</tr>
<tr>
<td>INFLAMMATION, NOS</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROSIED
### TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPERPLASIA, NOS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, FOCAL</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td></td>
<td>4 (8%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>ADRENAL</td>
<td>(50)</td>
<td>(49)</td>
<td>(49)</td>
</tr>
<tr>
<td>ATROPHY, NOS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANGIECTASIS</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>THYROID</td>
<td>(49)</td>
<td>(47)</td>
<td>(48)</td>
</tr>
<tr>
<td>CYSTIC FOLLICLES</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>LYMPHOCYTIC INFLAMMATORY INFILTR</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>DEGENERATION, CYSTIC</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>HYPERPLASIA, FOLLICULAR-CELL</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>REPRODUCTIVE SYSTEM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAMMARY GLAND</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>CYSTIC DUCTS</td>
<td></td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>#UTERUS</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>PYOMETRA</td>
<td></td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>#UTERUS/ENDOMETRIUM</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>INFLAMMATION, SUPPURATIVE</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>ABSCESS, NOS</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, ACUTE/CHRONIC</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, EPITHELIAL</td>
<td>2 (4%)</td>
<td>4 (82%)</td>
<td></td>
</tr>
<tr>
<td>HYPERPLASIA, CYSTIC</td>
<td></td>
<td>4 (82%)</td>
<td>40 (82%)</td>
</tr>
<tr>
<td>OVARY/OVIDUCT</td>
<td>(50)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>CYST, NOS</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>#OVARY</td>
<td>(48)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>CYSTIC FOLLICLES</td>
<td>2 (4%)</td>
<td>6 (12%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>FOLLICULAR CYST, NOS</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>ABSCESS, NOS</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>INFLAMMATION, SUPPURATIVE</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABSCESS, CHRONIC</td>
<td></td>
<td>2 (4%)</td>
<td></td>
</tr>
<tr>
<td>#OVARY/FOLLICLE</td>
<td>(48)</td>
<td>(50)</td>
<td>(49)</td>
</tr>
<tr>
<td>HEMORRHAGE</td>
<td></td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED
TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

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

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

129
TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

<table>
<thead>
<tr>
<th>Lesion Description</th>
<th>CONTROL</th>
<th>LOW DOSE</th>
<th>HIGH DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation, Chronic Suppurative</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Necrosis, Fat</td>
<td>3 (6%)</td>
<td>3 (6%)</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

### ALL OTHER SYSTEMS

- **Multiple Organs**
  - Inflammation, Suppurative (50) (50) (49)
  - Inflammation, Granulomatous (1) (2%)

- **Head**
  - Inflammation, Suppurative (1)

- **Broad Ligament**
  - Hemorrhagic Cyst (1)

  - Abscess, Chronic (1)

### SPECIAL MORPHOLOGY SUMMARY

- No lesion reported (1)
- Autolysis/No Necropsy (2)
- 1

- **Number of Animals with Tissue Examined Microscopically**
  - Number of Animals Necropsied

---

**Propyl Gallate** 130
APPENDIX E

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

A. ELEMENTAL ANALYSIS

<table>
<thead>
<tr>
<th>Element</th>
<th>C</th>
<th>H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theory</td>
<td>56.60</td>
<td>5.70</td>
</tr>
<tr>
<td>Lot No. 2185:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Determined</td>
<td>56.39</td>
<td>5.72</td>
</tr>
<tr>
<td></td>
<td>56.50</td>
<td>5.61</td>
</tr>
<tr>
<td>Lot No. 831:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Determined</td>
<td>56.92</td>
<td>5.76</td>
</tr>
<tr>
<td></td>
<td>56.77</td>
<td>5.87</td>
</tr>
</tbody>
</table>

B. WATER ANALYSIS (Karl Fisher)

Lot No. 2185:
1.3 ± 0.1(δ)%

Lot No. 831:
0.04 ± 0.02(δ)

C. MELTING POINT

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

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.

Propyl Gallate 132
APPENDIX E

1. Solvent System 1: 95% ethanol/H₂O (90:10)

<table>
<thead>
<tr>
<th>Spot intensity</th>
<th>Rf</th>
<th>Rst</th>
<th>Visualization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Visible Light</td>
</tr>
<tr>
<td>Lot No. 831 (major)</td>
<td>0.70</td>
<td>0.96</td>
<td>beige</td>
</tr>
<tr>
<td>Lot No. 2185 (major)</td>
<td>0.70</td>
<td>0.96</td>
<td>beige</td>
</tr>
<tr>
<td>Reference</td>
<td>0.72</td>
<td>nd</td>
<td>blue</td>
</tr>
<tr>
<td>Gallic acid</td>
<td>0.66</td>
<td>0.91</td>
<td>beige</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Spot intensity</th>
<th>Rf</th>
<th>Rst</th>
<th>Visualization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Visible Light</td>
</tr>
<tr>
<td>Lot No. 831</td>
<td>0.65</td>
<td>0.94</td>
<td>beige</td>
</tr>
<tr>
<td>major</td>
<td></td>
<td></td>
<td>nd</td>
</tr>
<tr>
<td>slight trace</td>
<td>origin</td>
<td>nd</td>
<td>nd</td>
</tr>
<tr>
<td>Lot No. 2185</td>
<td>0.65</td>
<td>0.94</td>
<td>beige</td>
</tr>
<tr>
<td>major</td>
<td></td>
<td></td>
<td>nd</td>
</tr>
<tr>
<td>slight trace</td>
<td>origin</td>
<td>nd</td>
<td>nd</td>
</tr>
<tr>
<td>Reference</td>
<td>0.70</td>
<td>nd</td>
<td>blue</td>
</tr>
<tr>
<td>Gallic acid</td>
<td>0.66</td>
<td>0.95</td>
<td>beige</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>Spot intensity</th>
<th>Rf</th>
<th>Rst</th>
<th>Visualization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Visible Light</td>
</tr>
<tr>
<td>Lot No. 831</td>
<td>0.49</td>
<td>0.94</td>
<td>beige</td>
</tr>
<tr>
<td>major</td>
<td></td>
<td></td>
<td>nd</td>
</tr>
<tr>
<td>slight trace</td>
<td>origin</td>
<td>nd</td>
<td>nd</td>
</tr>
<tr>
<td>Lot No. 2185</td>
<td>0.49</td>
<td>0.94</td>
<td>beige</td>
</tr>
<tr>
<td>major</td>
<td></td>
<td></td>
<td>nd</td>
</tr>
<tr>
<td>slight trace</td>
<td>origin</td>
<td>nd</td>
<td>nd</td>
</tr>
<tr>
<td>Reference</td>
<td>0.51</td>
<td>nd</td>
<td>red</td>
</tr>
<tr>
<td>Gallic acid</td>
<td>0.29</td>
<td>0.56</td>
<td>beige</td>
</tr>
</tbody>
</table>

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°C to 245°C 10°C/min.
Results: One homogeneous peak, retention time 13.4 min.

Propyl Gallate
APPENDIX E

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: υ-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: C18 υ-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 υ-Bondapak C18, 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.

<table>
<thead>
<tr>
<th>Peak No.</th>
<th>Retention Time (min.)</th>
<th>Retention Time (Relative to Major Peak)</th>
<th>Area (Percent of Major Peak)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.25</td>
<td>0.51</td>
<td>0.38</td>
</tr>
<tr>
<td>2</td>
<td>18.25</td>
<td>1.00</td>
<td>100</td>
</tr>
</tbody>
</table>

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.
APPENDIX E

G. SPECTRAL DATA

1. Infrared
   Instrument: Beckman IR-12
   a. Lot 2185
      Cell: 1.2% in potassium bromide pellet
      Results: See Figure 5
   Instrument: Beckman IR-12
   b. Lot 831
      Cell: 1% in potassium bromide pellet
      Results: See Figure 6

2. Ultraviolet/Visible
   Instrument: Cary 118
   a. Lot 2185
      | $\lambda_{\text{max}}$ (nm) | $\epsilon \times 10^{-3}$ |
      | 276                  | 10.51 ± 0.06 (δ) |
      | 218                  | 26.5 ± 0.2 (δ)   |
      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
   b. Lot 831
      | $\lambda_{\text{max}}$ (nm) | $\epsilon \times 10^{-3}$ |
      | 372 (shoulder)         | 0.00157 ± 0.0012 (δ) |
      | 331 (shoulder)         | 1.334 ± 0.042 (δ)   |
      | 277                   | 10.13 ± 0.08 (δ)    |
      | 218                   | 26.01 ± 0.36 (δ)    |
      Solvent: 95% ethanol

3. Nuclear Magnetic Resonance
   Instrument: Varian HA-100
   Solvent: CD3OD with internal tetramethylsilane
   Assignments (See Figures 7 and 8)
   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

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

Literature Values (Sedlacek, 1962)

<table>
<thead>
<tr>
<th>$\lambda_{\text{max}}$ (nm)</th>
<th>$\epsilon \times 10^{-3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>271</td>
<td>8.23</td>
</tr>
<tr>
<td>220</td>
<td>9.89</td>
</tr>
</tbody>
</table>

Solvent: 72% Ethanol

No literature spectrum found
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
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

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Average (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>9.2 ± 0.4</td>
</tr>
<tr>
<td>25</td>
<td>9.4 ± 0.4</td>
</tr>
<tr>
<td>5</td>
<td>9.8 ± 0.4</td>
</tr>
<tr>
<td>-20</td>
<td>10.0 ± 0.4</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Date Mixed</th>
<th>Date Used</th>
<th>6,000 ppm</th>
<th>12,000 ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/15/78</td>
<td>Week of 08/16 and 08/23</td>
<td>6,100</td>
<td>11,900</td>
</tr>
<tr>
<td>09/14/78</td>
<td>Week of 09/15 and 09/22</td>
<td>6,100</td>
<td>11,300</td>
</tr>
<tr>
<td>10/10/78</td>
<td>Week of 10/11 and 10/18</td>
<td>5,900</td>
<td>11,100</td>
</tr>
<tr>
<td>11/08/78</td>
<td>Week of 11/09 and 11/16</td>
<td>6,500</td>
<td>11,800</td>
</tr>
<tr>
<td>12/06/78</td>
<td>Week of 12/07 and 12/14</td>
<td>6,600</td>
<td>11,800</td>
</tr>
<tr>
<td>01/03/79</td>
<td>Week of 01/04 and 01/11</td>
<td>5,600</td>
<td>12,000</td>
</tr>
<tr>
<td>01/31/79</td>
<td>Week of 02/01 and 02/08</td>
<td>5,500</td>
<td>11,300</td>
</tr>
<tr>
<td>02/28/79</td>
<td>Week of 03/01 and 03/08</td>
<td>5,500</td>
<td>11,200</td>
</tr>
<tr>
<td>03/28/79</td>
<td>Week of 03/30 and 04/07</td>
<td>5,500</td>
<td>10,900</td>
</tr>
<tr>
<td>04/25/79</td>
<td>Week of 04/26 and 05/01</td>
<td>5,400</td>
<td>11,100</td>
</tr>
<tr>
<td>05/29/79</td>
<td>Week of 06/01 and 06/08</td>
<td>6,000</td>
<td>12,000</td>
</tr>
<tr>
<td>06/20/79</td>
<td>Week of 06/21 and 06/28</td>
<td>5,600</td>
<td>11,200</td>
</tr>
<tr>
<td>07/18/79</td>
<td>Week of 07/19 and 07/26</td>
<td>5,900</td>
<td>11,800</td>
</tr>
<tr>
<td>08/15/79</td>
<td>Week of 08/16 and 08/23</td>
<td>6,600</td>
<td>11,400</td>
</tr>
<tr>
<td>09/12/79</td>
<td>Week of 09/13 and 09/20</td>
<td></td>
<td>11,400</td>
</tr>
<tr>
<td>10/10/79</td>
<td>Week of 10/11 and 10/18</td>
<td>5,700</td>
<td>11,600</td>
</tr>
<tr>
<td>11/07/79</td>
<td>Week of 11/08 and 11/15</td>
<td>5,500</td>
<td>11,100</td>
</tr>
<tr>
<td>12/05/79</td>
<td>Week of 12/06 and 12/13</td>
<td>5,500</td>
<td>11,200</td>
</tr>
<tr>
<td>01/02/80</td>
<td>Week of 01/03 and 01/10</td>
<td>5,700</td>
<td>11,200</td>
</tr>
<tr>
<td>01/30/80</td>
<td>Week of 02/01 and 02/08</td>
<td>5,400</td>
<td>12,000</td>
</tr>
<tr>
<td>02/27/80</td>
<td>Week of 02/28 and 03/05</td>
<td>5,700</td>
<td>11,200</td>
</tr>
<tr>
<td>03/26/80</td>
<td>Week of 03/27 and 04/03</td>
<td>5,860</td>
<td>11,900</td>
</tr>
<tr>
<td>04/23/80</td>
<td>Week of 04/24 and 05/01</td>
<td>5,700</td>
<td>12,000</td>
</tr>
<tr>
<td>05/21/80</td>
<td>Week of 05/22 and 05/29</td>
<td></td>
<td>11,100</td>
</tr>
<tr>
<td>05/28/80</td>
<td>Week of 05/29 and 06/05</td>
<td>5,950</td>
<td></td>
</tr>
<tr>
<td>06/18/80</td>
<td>Week of 06/19 and 06/26</td>
<td>5,800</td>
<td>11,800</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mean (ppm)</th>
<th>Standard deviation</th>
<th>Coefficient of variation (%)</th>
<th>Range (ppm)</th>
<th>Number of samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5,795</td>
<td>341</td>
<td>5.8</td>
<td>5,400-6,600</td>
<td>28</td>
</tr>
</tbody>
</table>

(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 B6C3F1 MICE IN THE BIOASSAY PROGRAM
### TABLE H1. HISTORICAL INCIDENCE OF THYROID TUMORS IN UNTREATED CONTROL MALE F344/N RATS (a)

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

(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)

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

(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)

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

(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)

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

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

(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)

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

(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 B6C3F1 MICE (a)**

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Histiocytic Lymphoma</th>
<th>All Malignant Lymphoma</th>
<th>Lymphoma or Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battelle</td>
<td>21/348 (6.0%)</td>
<td>45/348 (12.9%)</td>
<td>49/348 (14.1%)</td>
</tr>
<tr>
<td>Dow</td>
<td>4/99 (4.0%)</td>
<td>17/99 (17.2%)</td>
<td>18/99 (18.2%)</td>
</tr>
<tr>
<td>Frederick</td>
<td>7/407 (1.7%)</td>
<td>46/407 (11.3%)</td>
<td>48/407 (11.8%)</td>
</tr>
<tr>
<td>Gulf South</td>
<td>0/48 (0.0%)</td>
<td>6/48 (12.5%)</td>
<td>11/48 (22.9%)</td>
</tr>
<tr>
<td>Hazleton</td>
<td>5/49 (10.2%)</td>
<td>7/49 (14.3%)</td>
<td>7/49 (14.3%)</td>
</tr>
<tr>
<td>Litton</td>
<td>9/507 (1.8%)</td>
<td>44/507 (8.7%)</td>
<td>47/507 (9.3%)</td>
</tr>
<tr>
<td>Mason</td>
<td>12/852 (1.4%)</td>
<td>127/852 (14.9%)</td>
<td>129/852 (15.1%)</td>
</tr>
<tr>
<td>Southern</td>
<td>21/640 (3.3%)</td>
<td>60/640 (9.4%)</td>
<td>65/640 (10.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Historical Range</th>
<th>79/2950 (2.7%)</th>
<th>352/2950 (11.9%)</th>
<th>374/2950 (12.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>5/49</td>
<td>13/39</td>
<td>13/39</td>
</tr>
<tr>
<td>Low</td>
<td>0/50</td>
<td>1/50</td>
<td>1/50</td>
</tr>
</tbody>
</table>

(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 B6C3F1 MICE (a)**

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Adenoma</th>
<th>Carcinoma</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battelle</td>
<td>5/348 (1.4%)</td>
<td>21/348 (6.0%)</td>
<td>25/348 (7.2%)</td>
</tr>
<tr>
<td>Dow</td>
<td>3/98 (3.1%)</td>
<td>5/98 (5.1%)</td>
<td>7/98 (7.1%)</td>
</tr>
<tr>
<td>Frederick</td>
<td>10/431 (2.3%)</td>
<td>13/431 (3.0%)</td>
<td>22/431 (5.1%)</td>
</tr>
<tr>
<td>Gulf South</td>
<td>8/134 (6.0%)</td>
<td>5/134 (3.7%)</td>
<td>13/134 (9.7%)</td>
</tr>
<tr>
<td>Hazleton</td>
<td>1/100 (1.0%)</td>
<td>4/100 (4.0%)</td>
<td>5/100 (5.0%)</td>
</tr>
<tr>
<td>Litton</td>
<td>21/512 (4.1%)</td>
<td>11/512 (2.1%)</td>
<td>32/512 (6.3%)</td>
</tr>
<tr>
<td>Mason</td>
<td>38/859 (4.4%)</td>
<td>40/859 (4.7%)</td>
<td>77/859 (9.0%)</td>
</tr>
<tr>
<td>Southern</td>
<td>18/645 (2.8%)</td>
<td>21/645 (3.3%)</td>
<td>38/645 (5.9%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Historical Range</th>
<th>104/3127 (3.3%)</th>
<th>120/3127 (3.8%)</th>
<th>219/3127 (7.0%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>9/49</td>
<td>7/48</td>
<td>10/49</td>
</tr>
<tr>
<td>Low</td>
<td>0/50</td>
<td>0/50</td>
<td>0/50</td>
</tr>
</tbody>
</table>

(a) Data as of June 15, 1981 for studies of at least 104 weeks. Range is presented for groups of 35 or more animals.
ERRATUM: An error was identified in the NTP Technical Report/Monograph on carcinogenesis bioassay of propyl gallate (CAS NO. 121-79-9) in F344 rats and B6C3F1 mice (feed study) (TR-240). On page 14 there was an error in the text of the first paragraph. The correct synonym for propyl gallate is 3,4,5 trihydroxybenzoic acid propyl ester and not 2,4,5 trihydroxybenzoic acid propyl ester as stated originally in the report/monograph. [February 18, 2014]