NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 424

TOXICOLOGY AND CARCINOGENESIS STUDIES OF *o*-BENZYL-*p*-CHLOROPHENOL

(CAS NO. 120-32-1)

IN F344/N RATS AND B6C3F$_1$ MICE

(GAVAGE STUDIES)

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

FOREWORD

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

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

The studies described in this Technical Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals. The prechronic and chronic studies were conducted in compliance with Food and Drug Administration (FDA) Good Laboratory Practice Regulations, and all aspects of the chronic studies were subjected to retrospective quality assurance audits before being presented for public review.

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

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NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

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NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
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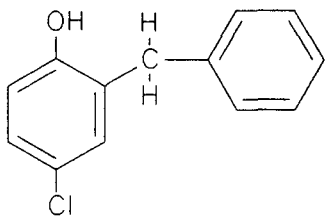
ABSTRACT



o-BENZYL-*p*-CHLOROPHENOL

CAS No. 120-32-1

Chemical Formula: $C_{13}H_{11}ClO$ Molecular Weight: 218.7

Synonyms: 2-benzyl-4-chlorophenol, 4-chloro-2-benzylphenol, 4-chloro-2-(phenylmethyl)phenol, 4-chloro-α-phenol-*o*-cresol, *p*-chloro-*o*-benzylphenol, 2-hydroxy-5-chlorodiphenylmethane

Trade names: Bio-Clave, Chlorophene, Clorofene, Clorophene, Ketolin H, Nipacide BCPR, Preventol BPR, Santophen I, Septiphene

o-Benzyl-*p*-chlorophenol is an aryl halide biocide with widespread use in hospitals and households as a broad-spectrum germicide in disinfectant solutions and soap formulations for general cleaning and disinfecting. Human exposure to *o*-benzyl-*p*-chlorophenol occurs by absorption through the skin and mucous membranes and by ingestion. Toxicity and carcinogenicity studies were conducted by administering *o*-benzyl-*p*-chlorophenol (approximately 97% pure) in corn oil by gavage to male and female F344/N rats and B6C3F$_1$ mice for 16-days, 13-weeks, and 2-years. Clinical pathology parameters were evaluated during the 2-year rat study. Genetic toxicity studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, L5178Y mouse lymphoma cells, and cultured human lymphoblast cells.

16-Day Study in Rats

Groups of five male and five female rats were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 62.5, 125, 250, 500, or 1,000 mg/kg body weight 5 days a week over a 16-day period. Two 1,000 mg/kg female rats died and these deaths were attributed to chemical administration. The mean body weight gains of 1,000 mg/kg males and females were significantly lower than those of the controls. Clinical findings in 1,000 mg/kg males and females included diarrhea and rough hair coat. Absolute and relative kidney and liver weights of 250, 500, and 1,000 mg/kg males and 1,000 mg/kg females were significantly greater than those of the controls. Absolute and relative thymus weights of 500 and 1,000 mg/kg males and 250, 500, and 1,000 mg/kg females were significantly lower than those of the controls. At necropsy, dilatation of the cecum was observed in male and female rats; the incidence generally increased with dose. The dilated cecum of some dosed rats had necrosis of the mucosal epithelium. Mild to moderate nephropathy was observed in all 1,000 mg/kg male and female rats. Minimal nephropathy occurred in one rat receiving 62.5 mg/kg, two rats each from the 125 and 250 mg/kg groups, and seven rats in the 500 mg/kg groups. The incidence and severity of nephropathy increased with dose.

16-Day Study in Mice

Groups of five male and five female mice were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 62.5, 125, 250, 500, or 1,000 mg/kg body weight 5 days a week over a 16-day

period. Deaths occurred only in the 1,000 mg/kg groups, in which three males and all females died. Mean body weight gains of dosed male and female mice were generally similar to those of the controls. Clinical findings in male and female high-dose mice included rough hair coat and postural changes. Absolute and relative liver weights of 500 and 1,000 mg/kg males and 500 mg/kg females (the highest dose group of females surviving) were significantly greater than those of the controls. Necropsy findings included dilatation of the cecum. Nephropathy occurred in 500 and 1,000 mg/kg mice (500 mg/kg, 2/10; 1,000 mg/kg, 6/10).

13-Week Study in Rats

Groups of 10 male and 10 female rats were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 30, 60, 120, 240, or 480 mg/kg body weight 5 days a week for 13 weeks. No deaths were attributed to *o*-benzyl-*p*-chlorophenol administration; however, the deaths of five male rats were attributed to gavage trauma. Mean body weight gains of all dosed rats were generally similar to those of the controls. Clinical findings included yellow-red staining of the urogenital region hair coat of all dosed females. The albumin/globulin ratios in 120, 240, and 480 mg/kg male rats increased with dose and were the result of net decreases in total globulin. Administration of *o*-benzyl-*p*-chlorophenol caused no significant alterations in hematologic or urinalysis parameters. Absolute and relative kidney weights were significantly greater and the absolute and relative thymus weights were significantly lower in 480 mg/kg male and female rats and in 240 mg/kg female rats. No gross lesions related to compound administration were observed at necropsy. Nephropathy of mild to moderate severity occurred in 480 mg/kg male and female rats and in 240 mg/kg male rats. Few or no lesions occurred in other dosed rats and none occurred in controls.

13-Week Studies in Mice

In the first 13-week study, groups of 10 male and 10 female mice were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 30, 60, 120, 240, or 480 mg/kg body weight 5 days a week for 13 weeks. Survival, mean body weight gains, and clinical findings of dosed animals were similar to those of the controls throughout the study. The Pathology Working Group confirmed that no microscopic lesions were observed that could definitively be associated with *o*-benzyl-*p*-chlorophenol administration. On the basis of these findings, a second 13-week study was performed using higher doses.

In the second 13-week study, groups of 15 male and 15 female mice were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 500, 650, 800, or 1,000 mg/kg body weight 5 days a week for up to 13 weeks. Five male and five female mice from each group were evaluated after 2 weeks, with the remainder (up to 10 per sex) evaluated at the end of the study. One 500 mg/kg mouse, three 650 mg/kg mice, 14 mice receiving 800 mg/kg, and 19 mice administered 1,000 mg/kg died before the end of the study. Mean body weight gains of dosed male and female mice that received 500 or 800 mg/kg were lower than those of the controls. Absolute and relative liver weights of 800 mg/kg males and all surviving dosed females were significantly greater than those of the controls. Absolute and relative kidney weights of 500, 650, and 800 mg/kg male mice were slightly lower than those of the controls, and those of female mice were similar to those of the controls. The incidence and severity of nephropathy increased with time and with increasing dose of *o*-benzyl-*p*-chlorophenol. Significant nephropathy was present at all doses, with mild nephropathy present at the 500 mg/kg dose. Acute necrotizing, suppurative inflammation of the olfactory epithelium was noted in all dose groups, with severity increasing with dose. These lesions were considered to be directly related to the caustic nature of *o*-benzyl-*p*-chlorophenol following retrograde exposure after gavage, with the presence of foreign material likely due to retrograde migration of the chemical.

2-Year Study in Rats

Groups of 80 male and 80 female rats were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage 5 days a week for 103 weeks. The doses were 0, 30, 60, or 120 mg/kg body weight for male rats and 0, 60, 120, or 240 mg/kg body weight for female rats. After 3 and 15 months, 7 to 10 male and 8 to 10 female rats were evaluated for organ weights and clinical pathology, and control and high-dose rats were evaluated for histopathology.

Survival, Body Weights, and Clinical Findings
Survival of dosed male and female rats was similar to that of the controls. Mean body weights of dosed rats were generally similar to those of the controls. No chemical-related clinical findings were observed except yellow staining of the urogenital area hair coat in dosed female rats; staining was observed earlier in high-dose female rats.

Pathology Findings
Severe, time- and dose-related nephropathy was observed in male and female rats, occurring as early as 3 months after the beginning of chemical administration (females). In male rats dosed for as long as 2 years, secondary hyperparathyroidism developed, with parathyroid gland hyperplasia, mineralization of the kidney and glandular stomach, and fibrous osteodystrophy occurring in the high-dose group. The severity of these lesions was greater in males. The kidney was the only organ in which chemical-related increased incidences of neoplasms may have occurred. One renal tubule adenoma occurred in a control male rat, one renal tubule adenoma and one transitional cell carcinoma occurred in high-dose female rats, and one transitional cell carcinoma occurred in a mid-dose female. One renal tubule carcinoma was observed in a high-dose male rat.

2-Year Study in Mice

Groups of 70 male and 70 female mice were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 120, 240, or 480 mg/kg body weight 5 days a week for 103 weeks. Ten male and 9 or 10 female mice were evaluated after 3 and 15 months for organ weights and histopathology; the remaining 50 male and 50 female mice were evaluated at the end of the study.

Survival, Body Weights, and Clinical Findings
Survival of high-dose male and female mice was lower than that of the controls, which was associated in part with dose-related increases in the incidence and severity of nephropathy. The final mean body weights of all dosed males and mid- and high-dose females were lower than those of the controls. Chemical-related clinical findings included emaciation, abnormal posture, rough hair coat, and hypoactivity.

Pathology Findings
Nephropathy occurred in most dosed males and females, and the incidence and severity increased with time and dose. Fibrous osteodystrophy of bone, mineralization of the glandular stomach, and squamous hyperplasia of the forestomach occurred in male and female mice. In the standard evaluation, the combined incidence of renal tubule adenoma and carcinoma was increased in 240 mg/kg male mice. Six renal tubule adenomas and three renal tubule carcinomas occurred in dosed male mice. No renal neoplasms occurred in female mice.

Due to the marginal increase in renal neoplasia, and the small size of renal neoplasms, an extended evaluation of the kidney was conducted. No significant alteration in the neoplasm incidences were observed in female mice. However, a dose-related increased trend of renal tubule adenoma was observed in male mice. Combination of the extended evaluation with the original evaluation resulted in an increased incidence of renal tubule adenomas in the 480 mg/kg males and an increased incidence of renal tubule adenomas or carcinomas in both the 240 and 480 mg/kg males.

Genetic Toxicology

o-Benzyl-*p*-chlorophenol did not induce gene mutations in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537 and did not induce sister chromatid exchanges or chromosomal aberrations in cultured Chinese hamster ovary cells. These tests were performed with and without exogenous metabolic activation (S9). Positive results were obtained, however, in gene mutation tests conducted with L5178Y mouse lymphoma cells and TK6 human lymphoblast cells in the absence of S9.

CONCLUSIONS

Under the conditions of these 2-year gavage studies, there was *no evidence of carcinogenic activity** of *o*-benzyl-*p*-chlorophenol in male F344/N rats receiving 30, 60, or 120 mg/kg body weight. There was *equivocal evidence of carcinogenic activity* of *o*-benzyl-*p*-chlorophenol in female F344/N rats based on the occurrence of two rare renal transitional cell carcinomas. There was *some evidence of carcinogenic activity* of *o*-benzyl-*p*-chlorophenol in male B6C3F$_1$ mice based on increased incidences of renal tubule adenoma and renal tubule adenoma or carcinoma (combined). There was *no evidence of carcinogenic activity* of *o*-benzyl-*p*-chlorophenol in female B6C3F$_1$ mice receiving 120, 240, or 480 mg/kg.

o-Benzyl-*p*-chlorophenol was nephrotoxic for male and female F344/N rats and B6C3F$_1$ mice. The severity of nephropathy was increased in male and female rats and the incidence and severity of nephropathy was increased in male and female mice. The incidence and severity of nephropathy increased with length of treatment. Other lesions considered to be associated with the nephropathy and the secondary hyperparathyroidism in male rats and in male and female mice included fibrous osteodystrophy and soft tissue mineralization. Increased incidences of squamous cell hyperplasia of the forestomach were observed in mice.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 11. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 13.

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of *o*-Benzyl-*p*-Chlorophenol

Male F344/N Rats	Female F344/N Rats	Male B6C3F$_1$ Mice	Female B6C3F$_1$ Mice
Doses			
0, 30, 60, or 120 mg/kg body weight in corn oil by gavage	0, 60, 120, or 240 mg/kg body weight in corn oil by gavage	0, 120, 240, or 480 mg/kg body weight in corn oil by gavage	0, 120, 240, or 480 mg/kg body weight in corn oil by gavage
Body weights			
Dosed groups similar to controls	Dosed groups similar to controls	Dosed groups lower than controls	Mid- and high-dose groups lower than controls
2-Year survival rates			
23/48, 24/48, 25/45, 24/46	26/48, 30/49, 28/50, 28/49	45/50, 32/48, 38/50, 30/48	36/50, 40/47, 33/48, 25/51
Nonneoplastic effects			
Kidney: nephropathy (48/50, 48/49, 48/50, 50/50; severity: 2.4, 2.8, 3.0, 3.3); Parathyroid gland: hyperplasia (0/47, 2/47, 5/45, 8/46); Bone: cranial fibrous osteodystrophy (0/50, 0/50, 2/50, 4/51) femur fibrous osteodystrophy (0/50, 0/50, 2/50, 6/51); Glandular stomach: mineralization (2/49, 4/49, 2/49, 9/50)	Kidney: nephropathy (46/50, 47/50, 50/51, 50/50; severity: 1.3, 1.3, 1.5, 2.4)	Kidney: nephropathy (39/50, 48/50, 50/50, 49/50; severity: 1.1, 2.1, 2.4, 2.5); Bone: fibrous osteodystrophy (0/50, 16/50, 25/50, 28/50); Glandular stomach: mineralization (2/50, 6/50, 12/50, 6/50) Forestomach: squamous hyperplasia (4/50, 12/50, 11/50, 9/50)	Kidney: nephropathy (19/50, 38/50, 48/50, 50/52; severity: 1.0, 1.5, 1.9, 2.3); Bone: fibrous osteodystrophy (2/50, 20/50, 33/50, 37/52); Glandular stomach: mineralization (1/50, 6/50, 10/50, 16/52) Forestomach: squamous hyperplasia (3/50, 10/50, 18/50, 20/52)
Neoplastic effects			
None	None	Kidney (standard evaluation): renal tubule adenoma (0/50, 2/50, 2/50, 2/50) renal tubule adenoma or carcinoma (combined) (0/50, 2/50, 4/50, 3/50); Kidney (standard + extended evaluation): renal tubule adenoma (0/50, 2/50, 4/50, 5/50) renal tubule adenoma or carcinoma (combined) (0/50, 2/50, 6/50, 6/50)	None
Uncertain findings			
None	Kidney: transitional cell carcinoma (0/50, 0/50, 1/51, 1/50)	None	None
Level of evidence of carcinogenic activity			
No evidence	Equivocal evidence	Some evidence	No evidence

Summary of the 2-Year Carcinogenesis and Genetic Toxicology Studies of *o*-Benzyl-*p*-Chlorophenol
(continued)

Genetic toxicology	
Salmonella typhimurium gene mutation:	Negative in strains TA98, TA100, TA1535, and TA1537 with and without S9
Mouse lymphoma gene mutation:	Positive without S9
Human lymphoblast gene mutation:	Positive without S9
Sister chromatid exchanges	
Chinese hamster ovary cells *in vitro*:	Negative with and without S9
Chromosomal aberrations	
Chinese hamster ovary cells *in vitro*:	Negative with and without S9

EXPLANATION OF LEVELS OF EVIDENCE OF CARCINOGENIC ACTIVITY

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

Five categories of evidence of carcinogenic activity are used in the Technical Report series to summarize the strength of the evidence observed in each experiment: two categories for positive results (**clear evidence** and **some evidence**); one category for uncertain findings (**equivocal evidence**); one category for no observable effects (**no evidence**); and one category for experiments that cannot be evaluated because of major flaws (**inadequate study**). These categories of interpretative conclusions were first adopted in June 1983 and then revised in March 1986 for use in the Technical Report series to incorporate more specifically the concept of actual weight of evidence of carcinogenic activity. For each separate experiment (male rats, female rats, male mice, female mice), one of the following five categories is selected to describe the findings. These categories refer to the strength of the experimental evidence and not to potency or mechanism.

- **Clear evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy.
- **Some evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a chemical-related increased incidence of neoplasms (malignant, benign, or combined) in which the strength of the response is less than that required for clear evidence.
- **Equivocal evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing a marginal increase of neoplasms that may be chemical related.
- **No evidence** of carcinogenic activity is demonstrated by studies that are interpreted as showing no chemical-related increases in malignant or benign neoplasms.
- **Inadequate study** of carcinogenic activity is demonstrated by studies that, because of major qualitative or quantitative limitations, cannot be interpreted as valid for showing either the presence or absence of carcinogenic activity.

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

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

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS
TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the draft NTP Technical Report on *o*-benzyl-*p*-chlorophenol on December 1, 1992, are listed below. Subcommittee members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, subcommittee members have five major responsibilities in reviewing NTP studies:

- to ascertain that all relevant literature data have been adequately cited and interpreted,
- to determine if the design and conditions of the NTP studies were appropriate,
- to ensure that the Technical Report presents the experimental results and conclusions fully and clearly,
- to judge the significance of the experimental results by scientific criteria, and
- to assess the evaluation of the evidence of carcinogenic activity and other observed toxic responses.

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SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On December 1, 1992, the draft Technical Report on the toxicology and carcinogenesis studies of *o*-benzyl-*p*-chlorophenol received public review by the National Toxicology Program Board of Scientific Counselors Technical Reports Review Subcommittee. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. D.S. Marsman, NIEHS, introduced the studies by discussing the uses of the chemical and rationale of the study, describing the experimental design, reporting on survival and body weight effects, and discussing compound-related neoplasms in female rats and male mice and nonneoplastic lesions in male and female rats and mice. The kidney was the primary target organ for toxicity in both species. Additional step-sections of the kidney were performed in male and female rats and mice. The proposed conclusions were *no evidence of carcinogenic activity* in male F344/N rats, *equivocal evidence of carcinogenic activity* in female F344/N rats, *some evidence of carcinogenic activity* in male $B6C3F_1$ mice, and *no evidence of carcinogenic activity* in female $B6C3F_1$ mice.

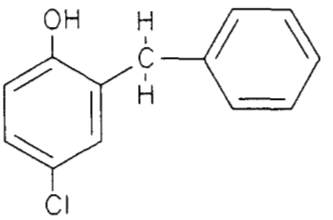
Mr. Beliczky, a principal reviewer, agreed with the proposed conclusions. He questioned whether the testing conducted satisfied concerns regarding consumer safety in household or hospital use. Mr. Beliczky asked if NIOSH could provide data for inclusion on the method of production and encountered health risks. Dr. J. Haartz, NIOSH, said the data cited from the National Occupational Exposure Survey (NOES) reflect potential exposure and not the actual number of workers exposed.

Dr. van Zwieten, the second principal reviewer, agreed with the proposed conclusions. He said that since the rationale for the study included the relationship of the chemical to a known neurotoxin, extra attention should have been given to morphological assessment of the central and peripheral nervous systems. He added that detailed procedures for neurobehavioral testing should be provided. Dr. Marsman said the NTP standard neurobehavioral battery was used and more details would be included. He said had there been any indication that the chemical was a neurotoxin as is hexachlorophene, additional pathology would have been included in the design.

Dr. Ward, the third principal reviewer, agreed with the proposed conclusions in principle. He thought the dose-related increased incidence of renal tubule adenoma or carcinoma (combined) could support *clear evidence of carcinogenic activity* in male mice. He suggested that a sentence be added to the conclusions about the hyperplastic lesions of the forestomach of mice. Dr. Marsman said that the severity of the hyperplasia did not increase in treated animals and was consistent with that observed with chemicals known to be irritants and administered by gavage. Dr. Ward noted that though there was no depression of weight gain in rats, the renal lesions were severe enough to indicate that a maximum tolerated dose was reached.

Mr. Beliczky moved that the technical report on *o*-benzyl-*p*-chlorophenol be accepted with the revisions discussed and the conclusions as written: for male rats and female mice, *no evidence of carcinogenic activity*; for female rats, *equivocal evidence of carcinogenic activity*; and for male mice, *some evidence of carcinogenic activity*. Dr. van Zwieten seconded the motion, which was accepted unanimously with 10 votes.

INTRODUCTION



o-BENZYL-*p*-CHLOROPHENOL

CAS No. 120-32-1

Chemical Formula: $C_{13}H_{11}ClO$ Molecular Weight: 218.7

Synonyms: 2-benzyl-4-chlorophenol, 4-chloro-2-benzylphenol, 4-chloro-2-(phenylmethyl)phenol, 4-chloro-α-phenol-*o*-cresol, *p*-chloro-*o*-benzylphenol, 2-hydroxy-5-chlorodiphenylmethane

Trade names: Bio-Clave, Chlorophene, Clorofene, Clorophene, Ketolin H, Nipacide BCPR, Preventol BPR, Santophen I, Septiphene

CHEMICAL AND PHYSICAL PROPERTIES

o-Benzyl-*p*-chlorophenol is a white to light tan or pink crystal or flake. The melting point is 46.5° to 48° C and the boiling point is 160° to 162° C (*Merck Index*, 1983). *o*-Benzyl-*p*-chlorophenol is essentially insoluble in water, moderately soluble in acetone (100 mg/mL), and freely soluble in ethanol.

USE AND HUMAN EXPOSURE

o-Benzyl-*p*-chlorophenol is a broad spectrum phenolic aryl halide germicide used extensively in hospitals and households throughout the United States in disinfectant solutions and in soap formulations. Approximately 4 million pounds are used annually in the U.S., with the annual U.S. production estimated at 10 million pounds and the extent of potential human exposure estimated at greater than 300,000 workers (NIOSH, 1990). Human exposure can occur by absorption through the skin and mucous membranes or by ingestion. *o*-Benzyl-*p*-chlorophenol applied at a concentration of 10% or greater is a primary irritant to skin and mucous membranes. Prolonged exposure to dilute solutions (0.03%) causes only mild cutaneous irritation (Monsanto).

ENVIRONMENTAL IMPACT

Disposal of *o*-benzyl-*p*-chlorophenol occurs primarily in municipal wastewater treatment plants, where biodegradation removes 95% of the *o*-benzyl-*p*-chlorophenol. Measured influent and effluent concentrations from 16 sites in the U.S. averaged 14.8 μg/L and 0.8 μg/L (Werner *et al.*, 1983). *o*-Benzyl-*p*-chlorophenol is rapidly metabolized by fish and has a low potential for bioconcentration in biota. Biodegradation and photolysis are the principal processes of *o*-benzyl-*p*-chlorophenol transformation in the environment; hydrolysis and volatilization rates are insignificant. Biodegradation of *o*-benzyl-*p*-chlorophenol occurs rapidly in systems such as river water, sewage, and activated sludge (Swisher and Gledhill, 1973); degradation occurs within 6 days in unacclimated river water, 1 day in sewage, and 8 to 24 hours in acclimated sludge.

ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

Experimental Animals

o-Benzyl-*p*-chlorophenol metabolism and distribution studies have been conducted in male Sprague-Dawley rats receiving a single oral dose of either 69 or 206 mg *o*-benzyl-*p*-chlorophenol per kg body weight in corn oil (Ridley *et al.*, 1986). *o*-Benzyl-*p*-chlorophenol was rapidly eliminated and extensively metabolized by male rats, with about half the radioactivity eliminated in the urine and half in the feces 5 days after dosing. Most of the ^{14}C in the feces was unmetabolized and unabsorbed *o*-benzyl-*p*-chlorophenol. Only 0.28% to 0.30% of the radioactivity remained in the body 5 days after dosing; about half of this radioactivity was associated with the liver and kidney. The excretion of *o*-benzyl-*p*-chlorophenol was biphasic, with an initial rapid phase possessing a half-life of 8 to 9 hours and a slower phase with an estimated half-life of 52 to 140 hours. The majority of radioactivity in the urine (41% to 61%) was present as sulfate and/or glucuronide conjugates with sulfate esters as the predominant conjugate. Analysis of the urine and feces identified *o*-benzyl-*p*-chlorophenol and two metabolites with modified benzyl rings.

The distribution and metabolism of *o*-benzyl-*p*-chlorophenol were studied in a series of experiments involving its administration via varying routes (Kao and Birnbaum, 1986). Male F344 rats were administered oral doses of 10, 100, or 1,000 mg/kg of [^{14}C]-labeled *o*-benzyl-*p*-chlorophenol dissolved in corn oil. At the 10 mg/kg dose, almost all the radioactivity had been excreted in the urine and feces after 3 days. At a dose of 100 mg/kg, the rate of fecal excretion decreased and the rate of urinary excretion increased 54%. At the 1,000 mg/kg dose, fecal excretion was increased. Despite differences in routes of excretion, more than 92% of the radioactivity from *o*-benzyl-*p*-chlorophenol was excreted in 3 days by all dosed rats. The increased proportion of radioactivity from *o*-benzyl-*p*-chlorophenol in the feces after oral exposure indicated that [^{14}C]-labeled *o*-benzyl-*p*-chlorophenol was incompletely absorbed.

In a study of cutaneous absorption, *o*-benzyl-*p*-chlorophenol dissolved in acetone was applied to the skin at a total dose of 10 mg/kg body weight (Kao and Birnbaum, 1986). For studies of biliary excretion, *o*-benzyl-*p*-chlorophenol was injected intravenously at doses of 5, 10, or 25 mg/kg body weight (Kao and Birnbaum, 1986). After intravenous administration of a 10 mg/kg dose, 88% of the dose was excreted in 3 days, but when the same dose was applied to the skin, only 59% of the total dose was excreted in this time period. Biliary excretion was affected by dose; excretion 6 hours after administration was 87% of a 5 mg/kg dose, 72% of a 10 mg/kg dose, and 56% of a 25 mg/kg dose. The principal *in vivo* metabolites were glucuronyl conjugates of *o*-benzyl-*p*-chlorophenol and hydroxyl-*o*-benzyl-*p*-chlorophenol. Results of *in vitro* metabolism studies indicated that microsomal oxidation and glutathione and glucuronyl conjugation were major routes of *o*-benzyl-*p*-chlorophenol metabolism. The greatest concentrations of radioactivity from *o*-benzyl-*p*-chlorophenol were in the spleen, kidney, and liver.

Humans

No studies of the metabolism and distribution of *o*-benzyl-*p*-chlorophenol in humans were found in the literature.

TOXICITY

Experimental Animals

The oral LD_{50} in rats has been reported as 2,800 mg/kg body weight (Monsanto). When administered in corn oil by gavage to F344 rats and B6C3F$_1$ mice at doses from 62.5 to 1,000 mg/kg body weight, *o*-benzyl-*p*-chlorophenol produced renal lesions in rats and mice in the higher dose groups (Deskin *et al.*, 1984). Rats were more sensitive to the nephrotoxic activity of *o*-benzyl-*p*-chlorophenol than mice. Renal lesions consistent with nephrosis were observed in rats receiving 480 mg/kg body weight of *o*-benzyl-*p*-chlorophenol for 13 weeks. The incidence and severity of renal lesions increased with increasing dose in rats (Deskin *et al.*, 1984). The effects of *o*-benzyl-*p*-chlorophenol treatment on the activity of drug-metabolizing enzymes in the liver and kidney of male F344 rats have been studied (Kao *et al.*, 1986). Treatment increased cytochrome P-450 activity and decreased aryl hydrocarbon hydroxylase activity in liver and kidney microsomes. In the kidney, treatment of rats with *o*-benzyl-*p*-chlorophenol increased cytochrome *c* reductase and uridine diphosphate glucuronyl transferase activity.

In the kidney, the increases in total cytochrome P-450 and glutathione were minimal. Liver glutathione concentration and glutathione transferase activity were unaltered by treatment with *o*-benzyl-*p*-chlorophenol. La Via and La Via (1979) have reported that phenolic derivatives have some immunodepressive activity in mice. CBA/J male mice were exposed to a disinfectant detergent solution containing three phenolic derivatives including *o*-benzyl-*p*-chlorophenol (4.5%) by being housed in cages washed with dilute solutions of a disinfectant detergent (also containing 5.0% *o*-phenylphenol and 1.0% *p-tert*-amylphenol). After a 4-week exposure, the mice experienced depressed generation of plaque-forming cells when exposed to sheep erythrocytes *in vitro*. This depression was more severe after exposures of as long as 14 weeks.

Humans

o-Benzyl-*p*-chlorophenol used in excess of the recommended concentration as a disinfectant detergent for the cleaning of bassinets and mattresses in hospital nurseries has been linked to multiple cases of idiopathic hyperbilirubinemia in human infants (Wysowski *et al.*, 1978). Some infants required exchange transfusions and some had peak bilirubin concentrations of 23.9 to 42 mg/100 mL. The affected infants had no other illness. After disinfectant detergent use was discontinued, idiopathic hyperbilirubinemia cases ceased. Neither acute hemolysis nor hepatic dysfunction was determined to be the cause of the jaundice. However, the results of *in vitro* studies suggest that enzyme inhibition may have been a factor. A significant inhibition of hepatic bilirubin glucuronyl transferase activity was observed when phenol detergent (containing *o*-benzyl-*p*-chlorophenol) was added at dilutions of 1:128 or less to an *in vitro* assay system for the enzyme (Daum *et al.*, 1976). Signs and symptoms observed in human patients after overexposure to *o*-benzyl-*p*-chlorophenol have included sweating, thirst, nausea, diarrhea, abdominal pain, hyperactivity, convulsions or stupor, low blood pressure, and dyspnea.

Reproductive and Developmental Toxicity

No published studies of the reproductive or developmental toxicity of *o*-benzyl-*p*-chlorophenol in experimental animals were found. No information on the reproductive or developmental toxicity of *o*-benzyl-*p*-chlorophenol in humans was found.

Carcinogenicity

Experimental Animals

o-Benzyl-*p*-chlorophenol was negative as a promoter of cutaneous neoplasms in mouse skin when tested at a 20% concentration in benzene. The initiator, 0.3% 7,12-dimethylbenz(a)anthracene, was applied at a dose of 75 μg/animal. The promoter was applied twice weekly and observations were made for 21 weeks (Boutwell and Bosch, 1959).

Humans

No published studies related to the carcinogenicity of *o*-benzyl-*p*-chlorophenol in humans were found.

Genetic Toxicity

Little data exist on *o*-benzyl-*p*-chlorophenol mutagenicity. The compound did not induce gene mutations in *Salmonella typhimurium*, with or without exogenous metabolic activation (S9) (Mortelmans *et al.*, 1986), but did induce trifluorothymidine resistance in L5178Y mouse lymphoma and TK6 human lymphoblast cells without S9 (Caspary *et al.*, 1988).

Study Rationale

o-Benzyl-*p*-chlorophenol was nominated by the National Cancer Institute for testing because of human exposure, chemical relationship to the known neurotoxin hexachlorophene, and as a representative of a biocide class (Johnson *et al.*, 1984).

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF *O*-BENZYL-*P*-CHLOROPHENOL

o-Benzyl-*p*-chlorophenol was obtained in one lot (KM11195) from McKesson Chemical Company (Kansas City, MO). Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO), and confirmed by the study laboratory (Appendix H).

The chemical, white to pink flakes, was identified as *o*-benzyl-*p*-chlorophenol by infrared, nuclear magnetic resonance, and ultraviolet/visible spectroscopy and gas chromatography. The melting point was 46.5° to 48° C. The purity was found to be approximately 97% by elemental analyses, Karl Fischer water analysis, nonaqueous (phenol) titration, thin-layer chromatography, and gas chromatography. Thin-layer chromatography indicated one major spot. Gas chromatography indicated one major peak and impurities with combined areas of up to 3.1% relative to the major peak. Stability studies performed at the analytical chemistry laboratory indicated that *o*-benzyl-*p*-chlorophenol was stable as a bulk chemical for at least 2 weeks when protected from light at temperatures up to 25° C. The stability of the bulk chemical was monitored periodically at the study laboratory using gas chromatography, nonaqueous titration, and ultraviolet spectroscopy; no change in purity was observed.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

Dose formulations were prepared by mixing *o*-benzyl-*p*-chlorophenol with corn oil (Table H1). The dose formulations were stored at room temperature in amber glass bottles for up to 2 weeks after the date of preparation. Details of preparation and storage of dose formulations are presented in Table H1. Dose formulation volumes for both rats and mice were 5 mL/kg body weight. Doses for the 16-day studies were prepared once; doses for the 13-week studies were prepared once every 2 weeks and discarded after 2 weeks; doses for the 2-year studies were prepared once weekly and discarded after each week. No special handling was required during dosing.

Stability studies of the 40 mg/mL corn oil solutions were conducted by the analytical chemistry laboratory using gas chromatography. The study findings indicated that the dose formulations were stable for 2 weeks in the dark at room temperature and for 3 hours exposed to air and light. Dose formulations were analyzed once during the 16-day studies, a minimum of three times during the 13-week studies, and every 8 weeks during the 2-year studies. All dose formulations for rats and mice were within 10% of the target concentrations throughout the studies (Tables H2 and H3). The peroxide levels of the corn oil vehicle were analyzed periodically by the study laboratory and were within the acceptable limit of 10 mEq/kg. Results of periodic referee analysis performed by the analytical chemistry laboratory indicated agreement with the results obtained for rats and mice (Table H4).

16-DAY STUDIES

Male and female F344/N rats were obtained from Charles River Laboratories (Portage, MI); male and female B6C3F$_1$ mice were obtained from Frederick Cancer Research Center (Frederick, MD). On receipt, the rats were an average of 33 days old and the mice were an average of 44 days old. The animals were quarantined for 19 (rats) or 21 (mice) days before dosing began. During this time, five males and five females of each species were randomly selected for parasite evaluation and gross observation for evidence of disease.

Groups of five male and five female rats and mice were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 62.5, 125, 250, 500, or

1,000 mg/kg body weight 5 days a week for 16 days. Clinical findings were recorded daily. The animals were weighed at study initiation, day 7, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 1.

A necropsy was performed on all rats and mice. The brain, heart, right kidney, liver, lung, right testis, and thymus from all rats and mice were weighed. A complete histopathologic examination was performed on all animals found dead or killed moribund during the study and all high-dose animals. Table 1 lists the tissues and organs routinely examined microscopically.

13-WEEK STUDIES

Male and female F344/N rats were obtained from Charles River Laboratories (Portage, MI); male and female B6C3F$_1$ mice were obtained from Frederick Cancer Research Center (Frederick, MD) for the first and second 13-week mouse studies. On receipt, the rats were an average of 26 days old, the first 13-week study mice were an average of 40 days old, and the second 13-week study mice were an average of 28 days old. The rats were quarantined for 20 to 23 days, the first 13-week study mice for 20 to 22 days, and the second 13-week study mice for 12 to 14 days before dosing began. During this time, five males and five females of each species were randomly selected for parasite evaluation and gross observation for evidence of disease. At the end of the studies, serologic analyses were performed on five male and five female rats and mice using the protocols of the NTP Sentinel Animal Program (Appendix J).

Groups of 10 male and 10 female rats were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 30, 60, 120, 240, or 480 mg/kg body weight. Groups of 10 male and 10 female mice were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 30, 60, 120, 240, or 480 mg/kg body weight in the first 13-week mouse study. Fifteen male and fifteen female mice were administered *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 500, 650, 800, or 1,000 mg/kg body weight in the second 13-week mouse study. Five male and five female mice were designated for interim evaluations after 2 weeks of chemical administration. Rats and mice were housed five per cage; water and feed were available *ad libitum*. Clinical findings were recorded weekly. The animals were weighed at study initiation, weekly, and at the end of the studies. Further details of study design and animal maintenance are summarized in Table 1.

Urine was collected during week 12 from rats for urinalysis. At the end of the 13-week rat study and at day 30 and the end of the first 13-week mouse study, blood was collected from the orbital sinus for hematology profiles and from the vena cava for clinical chemistry evaluations. No clinical pathology evaluations were performed on the mice in the second 13-week study. The clinical pathology parameters measured are listed in Table 1.

Neurobehavioral studies were performed on all rats prior to the start of the 13-week study and immediately following week 13. The neurobehavioral tests conducted were spontaneous motor activity, grip strength, startle response, and analgesia. Spontaneous motor activity was measured using a movement detection apparatus. Eight darkened sound-insulating chambers were used to house individual Plexiglas® test cages. A ventilation fan with baffled air intake and exhaust system was mounted in each cubicle and a 4-inch speaker was used for delivery of 75 dB white noise. A U-shaped photocell/light source holder was placed under the test cages and photo beam detector units were inserted so that infrared photo beams 6 cm apart passed through the test cage just above the cage floor. Animal movement inside the cage interrupted these photo beams and was translated into activity counts by modular signal processing equipment (Coulbourn Instruments). Counts were accumulated over three continuous 5-minute periods and the totals were printed on a microprocessor-based 10-channel printer. One male or female from each dose group was tested at the same time so that there was no bias produced by order, time of day, or other environmental variables. Grip strength was measured using a device and procedure similar to that described by Meyer *et al.*, (1979). Each animal was allowed to grip a triangular ring with its forepaws and was pulled back along a platform until its grip was broken. While the backward motion continued, the animal was allowed to grasp a T-shaped bar with its hindpaws, then forced to release the bar by continued pulling. The maximum strain required to break the forelimb and hindlimb grip was recorded using Chatillin push-pull

strain gauges (Kew Gardens, NY). The average of three valid measurements was taken as the animal's score for either forelimb or hindlimb grip strength. Startle response was measured using a Responder IV Startle Response Monitor (Columbus Instruments, Columbus, OH). Response measurement took place within an Industrial Acoustics sound-isolation cubicle equipped with light, ventilation fan, and one-way viewing window. Four independent startle platforms (transducers) were installed within the cubicle and separated by Plexiglas® partitions. Each platform had a tweeter loudspeaker mounted overhead for delivery of a 4.5 kHz, 200 msec, 120 dB acoustic stimulus at pre-programmed intervals. The startle monitor measured and printed the amplitude and latency of startle response for each platform separately. A pre-pulse, designed to produce a brief hesitation in the spontaneous movement of the animal, was delivered 1.8 seconds prior to each startle stimulus; during that time, the main stimulus was presented. Ten startle stimuli were presented 60 seconds apart. Sensitivity settings used were pre-adjusted to detect both increases and decreases in startle reactivity. For the measurement of analgesia, animals were placed on a heated (55° C) plate (Technilab Instruments). Paw lick latency was recorded up to a maximum allowable period of 60 seconds.

A necropsy was performed on all animals except for mice in the first 13-week study. The brain, heart, right kidney, liver, lung, right testis, and thymus of rats and mice were weighed. Tissues for microscopic examination were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 μm, and stained with hematoxylin and eosin. A complete histopathologic examination was performed on all animals. Table 1 lists the tissues and organs routinely examined microscopically.

2-YEAR STUDIES

Study Design

Groups of 80 male and 80 female rats received *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 30, 60, or 120 mg/kg body weight (males) or 0, 60, 120, or 240 mg/kg body weight (females); groups of 70 male and 70 female mice received *o*-benzyl-*p*-chlorophenol in corn oil by gavage at doses of 0, 120, 240, or 480 mg/kg body weight. A 3-month interim evaluation was included in the 2-year study design due to earlier discrepancies in the 13-week studies. Eight to 10 rats and 9 or 10 mice per group were evaluated after 3 months of chemical administration, 16 to 20 rats and 9 or 10 mice per group were evaluated after 15 months, and the remaining 50 to 55 rats and mice per group were evaluated at the end of the studies.

Source and Specification of Animals

Male and female F344/N rats and B6C3F$_1$ mice were obtained from Frederick Cancer Research Facility (Frederick, MD). Rats were quarantined for 10 days, and mice were quarantined for 21 or 22 days before the beginning of the studies. During this time, five male and five female rats and mice were selected for parasite evaluation and gross observation of disease. Serology samples were collected for viral screening. Rats were approximately 44 days old and mice were approximately 53 days old at the beginning of the studies. The health of the animals was monitored during the studies according to the protocols of the NTP Sentinel Animal Program (Appendix J).

Animal Maintenance

Rats were housed five per cage, and mice were housed individually. Feed and water were available *ad libitum*. Cages and racks were rotated every 2 weeks. Further details of animal maintenance are given in Table 1. Information on feed composition and contaminants is provided in Appendix I.

Clinical Examinations and Pathology

Animals were observed twice daily. Clinical findings were recorded weekly. Animals were weighed at study initiation, weekly for the first 13 weeks, and monthly thereafter. Blood was collected from the orbital sinus of all rats at the 3- and 15-month interim evaluations to determine hematology and clinical chemistry parameters. Urine was collected from all rats at the 3- and 15-month interim evaluations for urinalysis. The clinical pathology parameters are listed in Table 1. The brain, heart, left kidney, right kidney, liver, lung, right testis, and thymus of rats and mice were weighed at the 3- and 15-month interim evaluations.

A complete necropsy was performed on all animals. At necropsy, all organs and tissues were examined for gross lesions, and all major tissues were fixed and

preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 to 6 μm, and stained with hematoxylin and eosin for microscopic examination. Histopathologic examinations were performed on all tissues with grossly visible lesions. Tissues examined are listed in Table 1.

Microscopic evaluations were completed by the study laboratory pathologist, and the pathology data were entered into the Toxicology Data Management System. The microscopic slides, paraffin blocks, and residual wet tissues were sent to the NTP Archive for inventory, slide/block match, and wet tissue audit. The slides, individual animal data records, and pathology tables were evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, the slide and tissue counts were verified, and the histotechnique was evaluated. A quality assessment pathologist reviewed the kidneys of male and female rats and mice for accuracy and consistency of lesion diagnosis.

The quality assessment report and slides were submitted to the NTP Pathology Working Group (PWG) chair, who reviewed the selected slides of tissues and any other tissues when a disagreement in diagnosis between the laboratory and quality assessment pathologists existed. Representative examples of potential chemical-related lesions included neoplasms of the kidney of male and female rats and mice, parathyroid gland of male rats, the pituitary gland of female rats, and the adrenal gland, bone, heart, intestine, liver, and stomach of male and female mice. Examples of disagreements in diagnoses between the laboratory and quality assessment pathologist or lesions of general interest were presented by the chair to the PWG for review. The PWG consisted of the quality assessment pathologist and other pathologists experienced in rodent toxicologic pathology. This group examined the tissues without any knowledge of dose groups or previously rendered diagnoses. When the PWG consensus differed from the opinion of the laboratory pathologist, the diagnosis was changed. Thus, the final diagnoses represent a consensus of contractor pathologists and the PWG. Details of these review procedures have been described, in part, by Maronpot and Boorman (1982) and Boorman *et al.* (1985). For subsequent analyses of the pathology data, the diagnosed lesions for each tissue type were evaluated separately or combined according to the guidelines of McConnell *et al.* (1986).

Due to the small size of renal neoplasms, particularly renal tubule adenomas, relative to the size of the kidney, an extended evaluation of the kidney was conducted. The paraffin blocks were resectioned, and sections were taken at a level at least 4 μm deeper than the level of the original test section. The additional sections were taken (at approximately 1 mm intervals for rats, 0.5 mm intervals for mice) to obtain 3 or 4 additional sections per kidney (6 to 8 additional sections per animal). This extended evaluation was conducted in all animals from all dose groups where chemical-related effects were suspected, and in all control and high-dose animals where no effect was originally observed. The contract pathologist was asked to render a diagnosis on all proliferative lesions observed in these step sections. Subsequently, a special step-section PWG examined representative hyperplastic lesions and all neoplasms identified. The final diagnosis represented a consensus of the contractor pathologist and the step-section PWG. In addition to the reporting of the step-section findings separately, these data were combined with the standard evaluation, with care taken to avoid duplication of data through a slide-by-slide comparison. In the combination analysis, in cases where multiple hyperplasias were identified, the most severe lesion was assigned for each animal.

Statistical Methods

Survival Analyses

The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals were censored from the survival analyses if they were found dead of other than natural causes; animals dying from natural causes were not censored. Statistical analyses for possible dose-related effects on survival used Cox's (1972) method for testing two groups for equality and Tarone's (1975) life table test to identify dose-related trends. All reported P values for the survival analyses are two sided.

Calculation of Incidence

The incidences of neoplasms or nonneoplastic lesions as presented in Tables A1, A5, B1, B5, C1, C5, D1, and D4 are given as the number of animals bearing such lesions at a specific anatomic site and the number of animals with that site examined microscopically. For calculation of statistical significance, the incidences of most neoplasms (Tables A3, B3, C3, and D3) and all nonneoplastic lesions are given as the ratio of the number of affected animals to the number of animals with the site examined microscopically. However, when macroscopic examination was required to detect neoplasms in certain tissues (e.g., skin, intestine, harderian gland, and mammary gland) before microscopic evaluation or when neoplasms had multiple potential sites of occurrence (e.g., leukemia or lymphoma), the denominators consist of the number of animals on which a necropsy was performed.

Analysis of Neoplasm Incidences

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

In addition to logistic regression, other methods of statistical analysis were used, and the results of these tests are summarized in the appendixes. These methods include the life table test (Cox, 1972; Tarone, 1975), appropriate for rapidly lethal neoplasms, and the Fisher exact test and the Cochran-Armitage trend test (Armitage, 1971; Gart *et al.*, 1979), procedures based on the overall proportion of neoplasm-bearing animals.

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

Analysis of Nonneoplastic Lesion Incidences

Because all nonneoplastic lesions in this study were considered to be incidental to the cause of death or not rapidly lethal, the primary statistical analysis used was a logistic regression analysis in which nonneoplastic lesion prevalence was modeled as a logistic function of chemical exposure and time. For lesions detected at the interim evaluation, the Fisher exact test was used, a procedure based on the overall proportion of affected animals.

Analysis of Continuous Variables

Two approaches were employed to assess the significance of pairwise comparisons between dosed and control groups in the analysis of continuous variables. Organ and body weight data, which have approximately normal distributions, were analyzed using the parametric multiple comparison procedures of Dunnett (1955) and Williams (1971, 1972). Clinical chemistry, hematology, and urinalysis data, which have typically skewed distributions, were analyzed using the nonparametric multiple comparison methods of Dunn (1964) and Shirley (1977). Jonckheere's test (Jonckheere, 1954) was used to assess the significance of the dose-response trends and to determine whether a trend-sensitive test (Williams' or Shirley's test) was more appropriate for pairwise comparisons than a test that does not assume a monotonic dose-response trend (Dunnett's or Dunn's test). Average severity values were analyzed for significance using the Mann-Whitney U test (Hollander and Wolfe, 1973).

Historical Control Data

Although the concurrent control group is always the first and most appropriate control group used for evaluation, historical control data can be helpful in the overall assessment of neoplasm incidence in certain instances. Consequently, neoplasm incidences from the NTP historical control database (Haseman *et al.*, 1984, 1985) are included in the NTP reports for neoplasms appearing to be an effect of chemical administration.

Quality Assurance Methods

The 13-week and 2-year studies were conducted in compliance with Food and Drug Administration Good Laboratory Practice Regulations (21 CFR, Part 58). In addition, as records from the 2-year studies were submitted to the NTP Archives, these studies were audited retrospectively by an independent quality assurance contractor. Separate audits covering completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and preliminary review draft of this NTP Technical Report were conducted. Audit procedures and findings are presented in the reports and are on file at NIEHS. The audit findings were reviewed and assessed by NTP staff, so all comments had been resolved or were otherwise addressed during the preparation of this Technical Report.

GENETIC TOXICOLOGY

The genetic toxicity of *o*-benzyl-*p*-chlorophenol was assessed by testing the ability of the chemical to induce mutations in various strains of *Salmonella typhimurium* and chromosomal damage in cultured Chinese hamster ovary cells and mutations *in vitro* in mammalian cells. The protocols for these studies and the results are given in Appendix E.

The genetic toxicity studies of *o*-benzyl-*p*-chlorophenol are part of a larger effort by the NTP to develop a database that would permit the evaluation of carcinogenicity in experimental animals from the structure and the responses of the chemical in short-term *in vitro* and *in vivo* genetic toxicity tests. These genetic toxicity tests were originally developed to study mechanisms of chemically induced DNA damage and to predict carcinogenicity in animals, based on the electrophilic theory of chemical carcinogenesis and the somatic mutation theory (Miller and Miller, 1977; Straus, 1981; Crawford, 1985).

There is a strong correlation between a chemical's potential electrophilicity (structural alert to DNA reactivity), mutagenicity in *Salmonella*, and carcinogenicity in rodents. The combination of electrophilicity and *Salmonella* mutagenicity is highly correlated with the induction of carcinogenicity in rats and mice and/or at multiple tissue sites (Ashby and Tennant, 1991). Other *in vitro* genetic toxicity tests do not correlate well with rodent carcinogenicity (Tennant *et al.*, 1987; Zeiger *et al.*, 1990), although these other tests can provide information on the types of DNA and chromosome effects that can be induced by the chemical being investigated. Data from NTP studies show that a positive response in *Salmonella* is currently the most predictive *in vitro* test for rodent carcinogenicity (89% of the *Salmonella* mutagens were rodent carcinogens), and that there is no complementarity among the *in vitro* genetic toxicity tests. That is, no battery of tests that included the *Salmonella* test improved the predictivity of the *Salmonella* test alone. The predictivity for carcinogenicity of a positive response in bone marrow chromosome aberration or micronucleus tests is not yet defined.

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of *o*-Benzyl-*p*-Chlorophenol

16-Day Studies	13-Week Studies	2-Year Studies
Study Laboratory		
Battelle, Columbus Division (Columbus, OH)	Battelle, Columbus Division (Columbus, OH)	Battelle, Columbus Division (Columbus, OH)
Strain and Species		
Rats: F344/N Mice: $B6C3F_1$	Rats: F344/N Mice: $B6C3F_1$	Rats: F344/N Mice: $B6C3F_1$
Animal Source		
Rats: Charles River Laboratories (Portage, MI) Mice: Frederick Cancer Research Center (Frederick, MD)	Rats: Charles River Laboratories (Portage, MI) Mice: Frederick Cancer Research Center (Frederick, MD)	Frederick Cancer Research Center (Frederick, MD)
Time Held Before Studies		
Rats: 19 days Mice: 21 days	Rats: 20-23 days Mice: First 13-week study, 20-22 days; Second 13-week study 12-14 days	Rats: 10 days Mice: 21-22 days
Average Age When Studies Began		
Rats: 52 days Mice: 65 days	Rats: 55 days Mice: First 13-week study 61 days; Second 13-week study 41 days	Rats: 44 days Mice: 53 days
Date of First Dose		
Rats: 2 March 1982 Mice: 3 March 1982	Rats: 26-27 July 1982 (males) 28-29 July 1982 (females) Mice: First 13-week study 19-20 July 1982 (males) 21-22 July 1982 (females) Second 13-week study 21-22 March 1983 (males) 22-23 March 1983 (females)	Rats: 29-30 October 1984 Mice: 28-29 November 1984
Duration of Dosing		
16 days	Rats: 95 days Mice: 91 days	Rats: 103 weeks Mice: 103 weeks

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of *o*-Benzyl-*p*-Chlorophenol
(continued)

16-Day Studies	13-Week Studies	2-Year Studies
Date of Last Dose		
Rats: 17 March 1982	Rats: 25-26 October 1982 (males) 27-28 October 1983 (females) Mice: First 13-week study 18-19 October 1982 (males) 20-21 October 1982 (females) Second 13-week study 19 June 1983 (males) 20 June 1983 (females)	Rats: 17 October 1986 Mice: 18 November 1986
Necropsy Dates		
Rats: 18 March 1982 Mice: 19 March 1982	Rats: 26-27 October 1982 (males) 28-29 October 1982 (females) Mice: First 13-week study 19-20 October 1982 (males) 21-22 October 1982 (females) Second 13-week study 20-21 June 1983	Rats: 3-month interim - 30-31 January 1985 15-month interim - 27-30 January 1986 Terminal - 27-29 October 1986 Mice: 3-month interim - 28 February to 1 March 1985 15-month interim - 26-27 February 1986 Terminal - 19-26 November 1986
Average Age at Necropsy		
Rats: 69 days Mice: 73 days	Rats: 147 days Mice: First 13-week study, 152 days Second 13-week study, 133 days	Rats: 3-month interim - 21 weeks 15-month interim - 72 weeks Terminal - 111 weeks Mice: 3-month interim - 21 weeks 15-month interim - 73 weeks Terminal - 111 weeks
Size of Study Groups		
5 males and 5 females	First 13-week study 10 males and 10 females Second 13-week study (mice) 15 males and 15 females	Rats: 80 males and 80 females Mice: 70 males and 70 females
Method of Distribution		
Animals randomized from weight classes into cage groups using a table of random numbers; cages randomized into test groups from another table of random numbers	Same as 16-day studies	Same as 16-day studies

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of *o*-Benzyl-*p*-Chlorophenol (continued)

16-Day Studies	13-Week Studies	2-Year Studies
Animals per Cage		
5	5	Rats: 5 Mice: 1
Method of Animal Identification		
Toe clip	Rats: Ear tag Mice: Toe clip	Toe clip
Diet		
NIH-07 open formula pelleted diet (Zeigler Brother, Inc., Gardners, PA), available *ad libitum*	Same as 16-day studies	Same as 16-day studies
Maximum Storage Time for Feed		
90 days post-milling	Same as 16-day studies	Rats: not available Mice: 120 days post-milling
Water		
Automatic watering system (Edstrom Industries, Waterford, WI), available *ad libitum*	Same as 16-day studies	Same as 16-days studies
Cages		
Polycarbonate (Lab Products, Inc., Rochelle Part, NJ), changed twice weekly	Same as 16-day studies	Polycarbonate (Lab Products, Inc., Garfield, NJ), changed twice weekly (rats) or weekly (mice)
Bedding		
Absorb-Dri, hardwood chips (Absorb-Dri, Inc., Rochelle Park, NJ - rats, Garfield, NJ - mice), changed twice weekly	Absorb-Dri, hardwood chips (Absorb-Dri, Inc., Garfield, NJ), changed twice weekly	BetaChips, hardwood chips (Northeastern Products, Inc., Warrensburg, NY), changed twice weekly (rats) or weekly (mice)
Cage Filters		
Spun-bonded polyester filter sheets, DuPont 2024 (Snow Filtration Co., Cincinnati, OH), changed every other week	Same as 16-day studies	Same as 16-day studies
Racks		
Stainless steel (Lab Products, Inc., Garfield, NJ), changed every other week	Same as 16-day studies	Same as 16-day studies

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of *o*-Benzyl-*p*-Chlorophenol
(continued)

16-Day Studies	13-Week Studies	2-Year Studies
Animal Room Environment		
Temperature: 22° ± 1° C Relative humidity: 40% - 60% Fluorescent light: 12 hours/day Room air: minimum of 15 changes/hour	Temperature: 22° ± 1° C Relative humidity: 40% - 63% Fluorescent light: 12 hours/day Room air: minimum of 15 changes/hour	Temperature: rats - 22.5° ± 3° C mice - 22° ± 2° C Relative humidity: rats - 20%-73% mice - 35%-65% Fluorescent light: 12 hours/day Room air: minimum of 10 changes/hour (not available for mice)
Doses		
Rats and mice: 0, 62.5, 125, 250, 500, or 1,000 mg/kg in corn oil by gavage at a dose volume of 5 mL/kg.	Rats: 0, 30, 60, 120, 240, or 480 mg/kg in corn oil by gavage at a dose volume of 5 mL/kg Mice (first 13-week study): 0, 30, 60, 120, 240, or 480 mg/kg in corn oil by gavage at a dose volume of 5 mL/kg Mice (second 13-week study): 0, 500, 650, 800, or 1,000 mg/kg in corn oil by gavage at a dose volume of 5 mL/kg	Rats: 0, 30, 60, or 120 mg/kg (males) or 0, 60, 120, or 240 mg/kg (females) in corn oil by gavage at a dose volume of 5 mL/kg Mice: 0, 120, 240, or 480 mg/kg in corn oil by gavage at a dose volume of 5 mL/kg
Type and Frequency of Observation		
Animals observed twice daily; animals weighed initially, weekly, and at the end of the studies; clinical observations recorded daily	Animals observed twice daily; animals weighed initially, weekly, and at the end of the studies; clinical observations recorded weekly.	Animals observed twice daily; animals weighed initially, weekly for 13 weeks, and monthly thereafter; clinical observations recorded weekly; feed consumption was measured monthly
Method of Sacrifice		
Anesthetization with pentobarbital followed by exsanguination	Anesthetization with pentobarbital followed by exsanguination	Carbon dioxide asphyxiation followed by exsanguination
Necropsy		
Complete necropsy performed on all animals. Organ weights recorded for brain, heart, right kidney, liver, lung, right testis, and thymus	Complete necropsy performed on all animals, except for mice in the first 13-week study. Organ weights recorded for brain, heart, liver, lung, right kidney, right testis, and thymus for rats and for mice in the second 13-week study	Complete necropsy performed on all animals. Organ weights recorded for brain, heart, left kidney, right kidney, liver, lung, right testis, and thymus at the 3- and 15-month interim evaluations and for all animals surviving to the end of the studies

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of *o*-Benzyl-*p*-Chlorophenol
(continued)

16-Day Studies	13-Week Studies	2-Year Studies
Clinical Pathology		
None	Blood was collected from the orbital sinus for hematology and from the vena cava for clinical chemistry. Urine was collected overnight on 19 October 1982 (male rats) and 20 October 1982 (female rats). No clinical pathology evaluations were performed on mice. ***Hematology:*** hematocrit, hemoglobin, erythrocytes, mean erythrocyte volume, leukocyte count and differential, and nucleated erythrocytes ***Clinical Chemistry:*** urea nitrogen, creatinine, total protein, albumin, globulin, albumin/globulin ratio, bilirubin, alanine aminotransferase, aspartate aminotransferase, sorbitol dehydrogenase, cholinesterase ***Urinalysis:*** total volume, specific gravity, and microscopic exam	Blood from the orbital sinus and urine were collected at the 3- and 15-month interim evaluations. No clinical pathology evaluations were performed on mice. ***Hematology:*** (15-month interim only) hematocrit, hemoglobin, erythrocyte, mean erythrocyte volume, mean erythrocyte hemoglobin, mean erythrocyte hemoglobin concentration, platelet morphology, reticulocyte, leukocyte count and differential, and nucleated erythrocytes ***Clinical chemistry:*** urea nitrogen, creatinine, glucose, total protein, albumin, globulin, albumin/globulin ratio, alanine aminotransferase, aspartate aminotransferase ***Urinalysis:*** creatinine, glucose, protein, alkaline phosphatase (15-month interim), galactosidase (15-month interim), lactate dehydrogenase (15-month interim), N-acetyl-ß-glucose aminidase (15-month interim), volume, specific gravity, urea nitrogen ***Porphyrin levels:*** in urine and liver of rats
Histopathology		
Complete histopathology was performed on all animals found dead or killed moribund during the study and all 1,000 mg/kg animals surviving to the end of the studies. In addition to gross lesions and tissue masses, the tissues examined included: adrenal gland, bone (including marrow), brain, esophagus, gallbladder (mice), heart, large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, ileum), kidney, liver, lung, mammary gland, mandibular or mesenteric lymph node, nose, ovary, pancreas, parathyroid gland, pituitary gland, prostate gland, salivary gland, skin, spleen, stomach, testis with epididymis, thymus, thyroid gland, trachea, urinary bladder, and uterus.	Complete histopathology was performed on all animals. In addition to gross lesions and tissue masses, the tissues examined included: adrenal gland, bone (including marrow), brain, esophagus, gallbladder (mice), heart, large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, ileum), kidney, liver, lung, mammary gland, mandibular or mesenteric lymph node, nose, ovary, pancreas, parathyroid gland, pituitary gland, prostate gland, salivary gland, skin, spleen, stomach, testis with epididymis, thymus, thyroid gland, trachea, urinary bladder, and uterus.	Complete histopathology was performed on all rats and mice in the control and high-dose groups at the 3- and 15-month interim evaluations, all animals killed moribund, and those surviving to the end of the studies. The kidneys of low- and mid-dose rats and mice were examined at 3 and 15 months. In addition to gross lesions and tissue masses, the tissues examined included: adrenal gland, brain, clitoral or preputial gland, esophagus, femur, including marrow, gallbladder (mice), large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, and ileum), heart, kidney, liver, lung, (continued)

TABLE 1
Experimental Design and Materials and Methods in the Gavage Studies of o-Benzyl-p-Chlorophenol
(continued)

16-Day Studies	13-Week Studies	2-Year Studies
Histopathology		
		(continued) mammary gland, mandibular or mesenteric lymph node, nose, ovary, pancreas, parathyroid gland, pituitary gland, prostate gland, salivary gland, spleen, stomach, testis with epididymis and seminal vesicle, thymus, thyroid gland, trachea, urinary bladder, and uterus.
Neurobehavioral Studies		
None	Neurobehavioral tests were conducted on all rats before and after 13 weeks of exposure. The tests conducted were spontaneous motor activity, grip strength, startle response, and analgesia.	None

RESULTS

RATS

16-DAY STUDY

Two 1,000 mg/kg female rats died during the study (Table 2). The death of one 62.5 mg/kg male was attributed to a gavage accident. Mean body weight gains of male and female rats receiving 1,000 mg/kg were significantly lower than those of the controls. The final mean body weights of 1,000 mg/kg rats were significantly lower than those of the control groups, with males more severely affected than females. Compound-related clinical findings in 1,000 mg/kg rats included diarrhea and rough hair coat.

Absolute and relative kidney and liver weights of 250, 500, and 1,000 mg/kg males and of 1,000 mg/kg females were significantly greater than those of controls (Table F1). Absolute and relative thymus weights of 500 and 1,000 mg/kg males and of 250,

TABLE 2
Survival and Mean Body Weights of Rats in the 16-Day Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
Male					
0	5/5	213 ± 3	249 ± 3	36 ± 2	
62.5	4/5[c]	212 ± 5	251 ± 6	41 ± 2	101
125	5/5	210 ± 4	247 ± 3	36 ± 2	99
250	5/5	209 ± 4	253 ± 3	44 ± 2	102
500	5/5	211 ± 5	246 ± 4	35 ± 2	99
1,000	5/5	207 ± 5	201 ± 6°°	6 ± 4°°	81
Female					
0	5/5	144 ± 2	165 ± 3	21 ± 2	
62.5	5/5	146 ± 3	164 ± 3	18 ± 1	99
125	5/5	145 ± 3	167 ± 3	22 ± 2	101
250	5/5	144 ± 1	162 ± 2	18 ± 1	98
500	5/5	142 ± 3	159 ± 5	16 ± 2	96
1,000	3/5[d]	143 ± 2	150 ± 0°	8 ± 1°°	90

° Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
°° P≤0.01
[a] Number of animals surviving/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[c] Day of death: 8 due to dosing accident
[d] Day of death: 4, 9

500, and 1,000 mg/kg females were significantly lower than those of the controls. Relative brain and right testis weights of 1,000 mg/kg males were significantly greater in conjunction with the decreased mean body weight at this dose.

Compound-related gross lesions in males and females were confined to a dose-related dilatation of the cecum. Microscopically, multifocal necrosis of the mucosal epithelium of the cecum occurred in a few rats (250 mg/kg, 3/10; 500 mg/kg, 1/10). Mild to moderate nephropathy was observed in all 1,000 mg/kg rats and was characterized by multifocal tubule dilatation and flattening of proximal convoluted tubule epithelium, multifocal epithelial cell necrosis, tubule regeneration, and hyaline cast formation. Severity grades were based on the extent of parenchymal involvement: minimal - less than 10%; mild - 10% to 50%; moderate - 50% to 70%; marked - greater than 70%. The incidence and severity increased with dose (incidence: 62.5 mg/kg, 1/10; 125 mg/kg, 2/10; 250 mg/kg, 2/10; 500 mg/kg, 7/10). Myocardial degeneration occurred in eight 1,000 mg/kg rats.

13-Week Study

No deaths that occurred during the study were attributed to o-benzyl-p-chlorophenol administration; however, the deaths of five male rats were attributed to gavage trauma (Table 3). Mean body weight gains

TABLE 3
Survival and Mean Body Weights of Rats in the 13-Week Gavage Study of o-Benzyl-p-Chlorophenol

Dose (mg/kg)	Survival[a]	Mean Body Weights[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
Male					
0	10/10	129 ± 2	336 ± 5	207 ± 4	
30	9/10[c]	133 ± 2	338 ± 4	204 ± 4	101
60	9/10[d]	128 ± 4	312 ± 10	184 ± 7*	93
120	7/10[e]	132 ± 2	346 ± 4	213 ± 4	103
240	10/10	128 ± 2	327 ± 7	199 ± 6	97
480	9/10[f]	132 ± 3	339 ± 6	206 ± 6	101
Female					
0	10/10	105 ± 2	196 ± 3	91 ± 2	
30	10/10	105 ± 2	195 ± 3	91 ± 2	100
60	10/10	106 ± 2	196 ± 4	89 ± 2	100
120	10/10	106 ± 2	194 ± 3	89 ± 2	99
240	10/10	105 ± 1	200 ± 2	95 ± 2	102
480	10/10	106 ± 2	195 ± 3	89 ± 3	100

* Significantly different (P≤0.01) from the control group by Dunnett's test
[a] Number of animals surviving/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[c] Week of death: 1 due to dosing accident
[d] Week of death: 13 due to unknown causes
[e] Week of death: 1, 1, 1 (all due to dosing accident)
[f] Week of death: 5 due to dosing accident

of dosed rats were generally similar to those of the controls. Clinical findings included a red-yellow staining of the urogenital region hair coat of dosed females, which increased in intensity and in incidence with dose. High-dose males had brown discoloration of the hair coat around the penis (4/10). Alopecia of the head (dosed females only) and transient diarrhea (high-dose males only) were other notable clinical findings.

Neurobehavioral tests indicated no significant differences among the groups for motor activity, startle response, or grip strength. A minor effect on analgesia was noted for female rats in the 480 mg/kg group. The biological significance of this effect is questionable due to the lack of pre-test reference values, a lack of similar effect on males, and the unusually high score noted for control females.

The albumin/globulin ratios in 120, 240, and 480 mg/kg male rats increased with dose (Table G1). The differences were the result of net decreases in total globulin. Other differences in male rat clinical chemistry parameters included reduced bilirubin values and reduced aspartate aminotransferase and alanine aminotransferase enzyme activities. These reductions are unlikely to be of toxicologic significance. Clinical pathology values for female rats were similar to the control values. Urinalysis parameters in dosed rats were similar to those of the controls.

Absolute and relative kidney weights were significantly greater and absolute and relative thymus weights were significantly lower in 480 mg/kg male and female rats and in 240 mg/kg female rats (Table F2). The absolute and relative brain, heart, liver, lung, and right testis weights of dosed rats were not affected by *o*-benzyl-*p*-chlorophenol administration. No gross lesions related to compound administration were found at necropsy.

Microscopically, nephropathy was characterized by tubule dilatation with flattening of tubule epithelium, presence of tubule hyaline casts, and a few foci of mononuclear cells in the renal cortex interstitium. Nephropathy was mild to moderate in severity in 480 mg/kg male and female rats and 240 mg/kg male rats. The incidence and severity were greater in males than in females. Depletion of lymphoid tissue of the thymus occurred in 480 mg/kg females (8/10).

2-YEAR STUDY

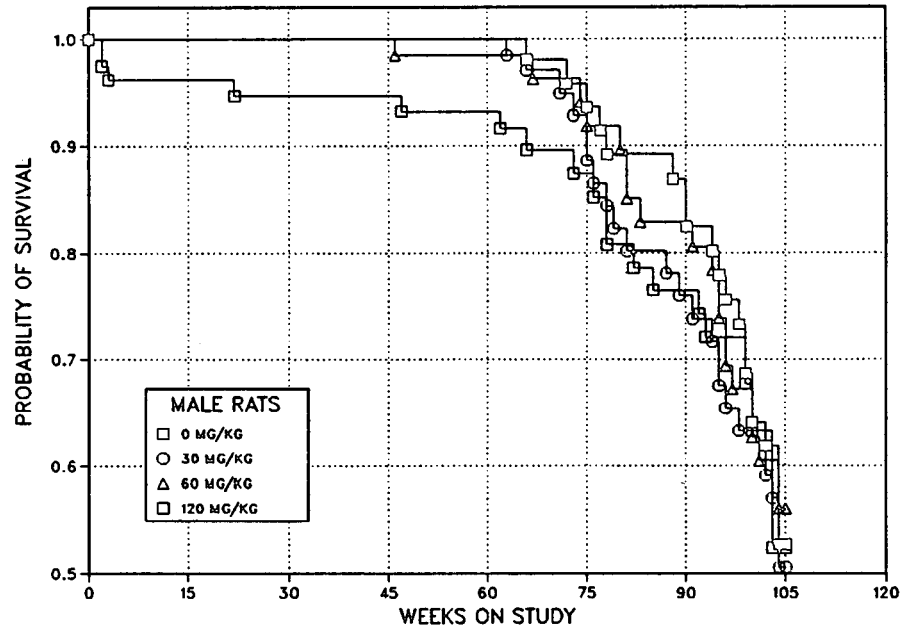
Survival

Estimates of survival probabilities for male and female rats administered *o*-benzyl-*p*-chlorophenol by gavage for 2 years are presented in Table 4 and in the Kaplan-Meier curves in Figure 1. Gavage administration of *o*-benzyl-*p*-chlorophenol had no effect on survival. Survival was similar in all dosed and control groups.

TABLE 4
Survival of Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male				
Animals initially in study[a]	80	80	80	80
3-Month interim evaluation[b]	10	10	10	9
15-Month interim evaluation[b]				
Histopathology evaluation	10	10	10	9
Clinical pathology evaluation	10	10	10	7
Moribund	16	13	14	14
Natural deaths	5	11	6	10
Accidental deaths[b]	6	2	5	7
Animals surviving to study termination	23	24	25	24
Percent probability of survival at end of study[c]	53	51	56	52
Mean survival (days)[d]	526	530	523	493
Survival analysis[e]	P=0.698	P=0.741	P=1.000N	P=0.667
	Vehicle Control	**60 mg/kg**	**120 mg/kg**	**240 mg/kg**
Female				
Animals initially in study[a]	80	80	80	80
3-Month interim evaluation[b]	10	10	8	9
15-Month interim evaluation[b]				
Histopathology evaluation	10	10	9	10
Clinical pathology evaluation	10	10[f]	9	8
Moribund	17	12	15	18
Natural deaths	5	7	8	4
Accidental deaths[b]	2	1	3	3
Animals surviving to study termination	26	30	28	28
Percent probability of survival at end of study[c]	55	61	56	56
Mean survival (days)[d]	533	547	534	543
Survival analysis[e]	P=1.000N	P=0.650N	P=0.961	P=0.911N

[a] Seven to ten of the 80 animals initially in study were evaluated for clinical pathology only.
[b] Censored from survival analyses
[c] Kaplan-Meier determinations
[d] Mean of all deaths (uncensored, censored, and terminal sacrifice)
[e] The result of the life table trend test (Tarone, 1975) is in the control column, and the results of the life table pairwise comparisons (Cox, 1972) with the controls are in the dosed columns. A negative trend or lower mortality in a dose group is indicated by an N.
[f] Includes one animal that died during the scheduled sacrifice period.



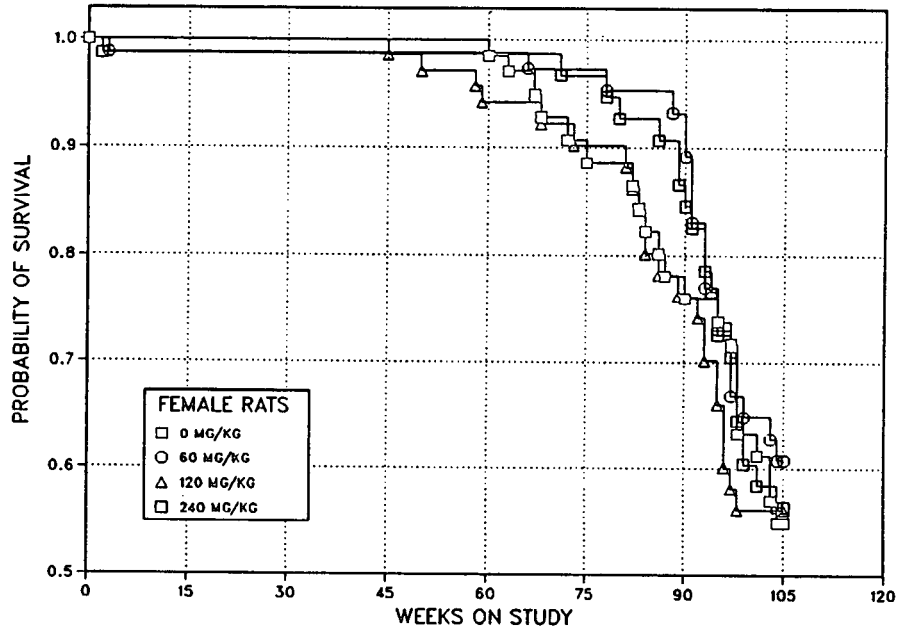


FIGURE 1
Kaplan-Meier Survival Curves for Male and Female F344/N Rats Administered *o*-Benzyl-*p*-Chlorophenol by Gavage for 2 Years

Body Weights and Clinical Findings

Mean body weights of dosed male and female rats were generally similar to those of the controls (Tables 5 and 6 and Figure 2). Yellow staining of the urogenital area hair coat occurred in most dosed female rats and was considered to be chemical related (0 mg/kg, 9/80; 60 mg/kg, 66/80; 120 mg/kg, 69/80; 240 mg/kg, 77/80). Feed consumption was unaffected and no other clinical findings were considered related to *o*-benzyl-*p*-chlorophenol administration.

Clinical Chemistry and Hematology

Hematologic and clinical chemistry parameters were not consistently altered by *o*-benzyl-*p*-chlorophenol administration (Table G3). Urinary alkaline phosphatase values were elevated at 39 and 65 weeks in the 15-month clinical pathology study group, suggesting renal cell damage; in contrast, urinary *N*-acetyl-ß-glucose aminidase and galactosidase levels were lower than those of the controls. These results could be accounted for by significant renal impairment, however urine concentrating ability was not significantly altered by *o*-benzyl-*p*-chlorophenol administration.

Sentinel Animals

Serological titers for *Mycoplasma arthriditis* were positive in one rat each at the 12- and 18-month screenings (Table J1). No clinical or histopathologic evidence of disease caused by this infection was observed.

TABLE 5
Mean Body Weights and Survival of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Weeks on Study	Vehicle Control		30 mg/kg			60 mg/kg			120 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	124	80	124	100	80	125	101	80	125	101	80
2	170	80	171	100	80	171	100	80	172	101	78
3	202	80	202	100	80	203	101	80	205	102	76
4	229	80	228	100	80	229	100	80	233	102	76
5	249	79	248	100	80	249	100	80	253	101	76
6	266	78	265	100	79	266	100	80	270	102	75
7	282	78	281	100	79	281	100	80	288	102	75
8	299	78	298	100	79	300	100	80	306	102	75
9	310	78	309	100	79	312	101	80	317	102	75
10	321	78	321	100	79	322	100	79	329	102	75
11	334	78	331	99	79	334	100	79	340	102	75
12	343	78	340	99	79	343	100	79	347	101	74
13	346	78[b]	343	99	79[b]	346	100	79[b]	351	102	74
17[a]	371	68[b]	368	99	69[b]	370	100	69[b]	377	102	65
21	395	68[b]	394	100	69[b]	395	100	69[b]	404	102	64
25	410	68[b]	404	99	69[b]	405	99	69[b]	409	100	63
29	431	67	428	99	68	432	100	68	424	98	63
33	442	67[b]	440	100	68[b]	439	99	68[b]	433	98	63[b]
37	448	67	441	98	68	448	100	68	445	99	63
41	457	67[b]	449	98	68[b]	451	99	67[b]	446	98	63[b]
45	464	67[b]	461	99	68[b]	461	100	66[b]	451	97	63
49	474	67[b]	467	99	68[b]	472	100	65[b]	460	97	61
53	480	67[b]	475	99	68[b]	479	100	65[b]	468	97	61
57	484	67[b]	475	98	68[b]	484	100	65[b]	474	98	61[b]
61	490	67[b]	480	98	68[b]	491	100	65[b]	479	98	61[b]
65	490	67[b]	488	100	67[b]	497	102	65[b]	484	99	60[b]
69[a]	490	44	483	99	46	494	101	44	479	98	41
73	493	43	487	99	45	492	100	43	482	98	40
77	493	41	486	99	41	493	100	41	479	97	39
81	497	40	490	99	38	498	100	39	483	97	36
85	492	40	479	97	38	505	103	37	475	96	36
89	488	39	477	98	37	489	100	37	475	98	35
90	481	39	480	100	36	488	101	37	473	98	35
93	483	36	467	97	35	480	99	36	468	97	34
97	473	33	456	96	31	469	99	31[b]	463	98	33
101	467	28	441	95	30	455	98	27	445	95	29
104	448	26	428	95	26	429	96	26	421	94	24
Mean for weeks											
1-13	267		266	100		268	100		272	102	
14-52	432		428	99		430	100		428	99	
53-104	483		473	98		483	100		470	97	

[a] Interim evaluations occurred during weeks 14 and 66.
[b] The number of animals weighed for this week is fewer than the number of animals surviving.

TABLE 6
Mean Body Weights and Survival of Female Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol

Weeks on Study	Vehicle Control		60 mg/kg			120 mg/kg			240 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	102	80	103	100	80	103	100	80	101	99	79
2	130	80	130	100	80	131	100	80	128	98	79
3	147	80	145	99	79	145	99	80	143	97	77
4	155	79[b]	155	100	79[b]	154	99	79[b]	152	98	77
5	164	79	162	99	79	162	98	79	161	98	77
6	171	79	169	99	79	170	100	79	168	98	77
7	179	79	176	98	79	178	99	79	174	97	77
8	187	79	184	98	79	186	99	79	183	98	77
9	189	79	187	99	79	188	99	79	185	98	77
10	194	79	193	100	79	193	99	79	191	98	77
11	198	79	196	99	79	197	100	79	195	98	77
12	198	79	195	99	78	196	99	77	192	97	77
13	199	79	196	98	78	196	99	77	193	97	77
17[a]	207	69	203	98	68	205	99	69	200	96	68
21	215	69[b]	213	99	68[b]	212	99	69[b]	207	96	68
25	218	69[b]	215	99	68	213	98	69	206	95	68
29	230	69	229	100	68	224	97	69	218	95	68
33	233	69[b]	229	98	68[b]	228	98	69[b]	222	95	68
37	236	69[b]	234	99	68[b]	228	97	69[b]	222	94	68
41	239	69	239	100	68	233	97	69	228	95	68
45	246	69	243	99	68	238	97	68	234	95	68
49	253	68	250	99	68	246	97	68	241	95	68
53	264	68[b]	260	98	68[b]	258	98	67[b]	250	95	68
57	268	68	265	99	68[b]	263	98	67[b]	255	95	68
61	276	67[b]	271	98	68[b]	269	97	65[b]	265	96	68[b]
65	284	66[b]	277	98	68[b]	276	97	65[b]	272	96	68
69[a]	287	44	281	98	48	282	98	46	276	96	49
73	294	43	287	98	48	290	99	46	285	97	48
77	300	42	295	98	48	291	97	45	286	95	48
81	305	42	300	98	47	297	97	44	296	97	46
85	309	39	303	98	47	298	97	40	298	97	46
89	311	37	302	97	46	297	95	39	298	96	44
93	307	36	302	98	40	301	98	36	302	98	41
97	303	35[b]	298	98	35	302	100	30[b]	305	101	36
101	309	29	299	97	32	306	99	28	306	99	30
104	306	27	299	98	31	306	100	28	305	100	29
Mean for weeks											
1-13	170		169	99		169	99		167	98	
14-52	231		228	99		225	97		220	95	
53-104	295		289	98		288	98		286	97	

[a] Interim evaluations occurred during weeks 14 and 66.
[b] The number of animals weighed for this week is fewer than the number of animals surviving.

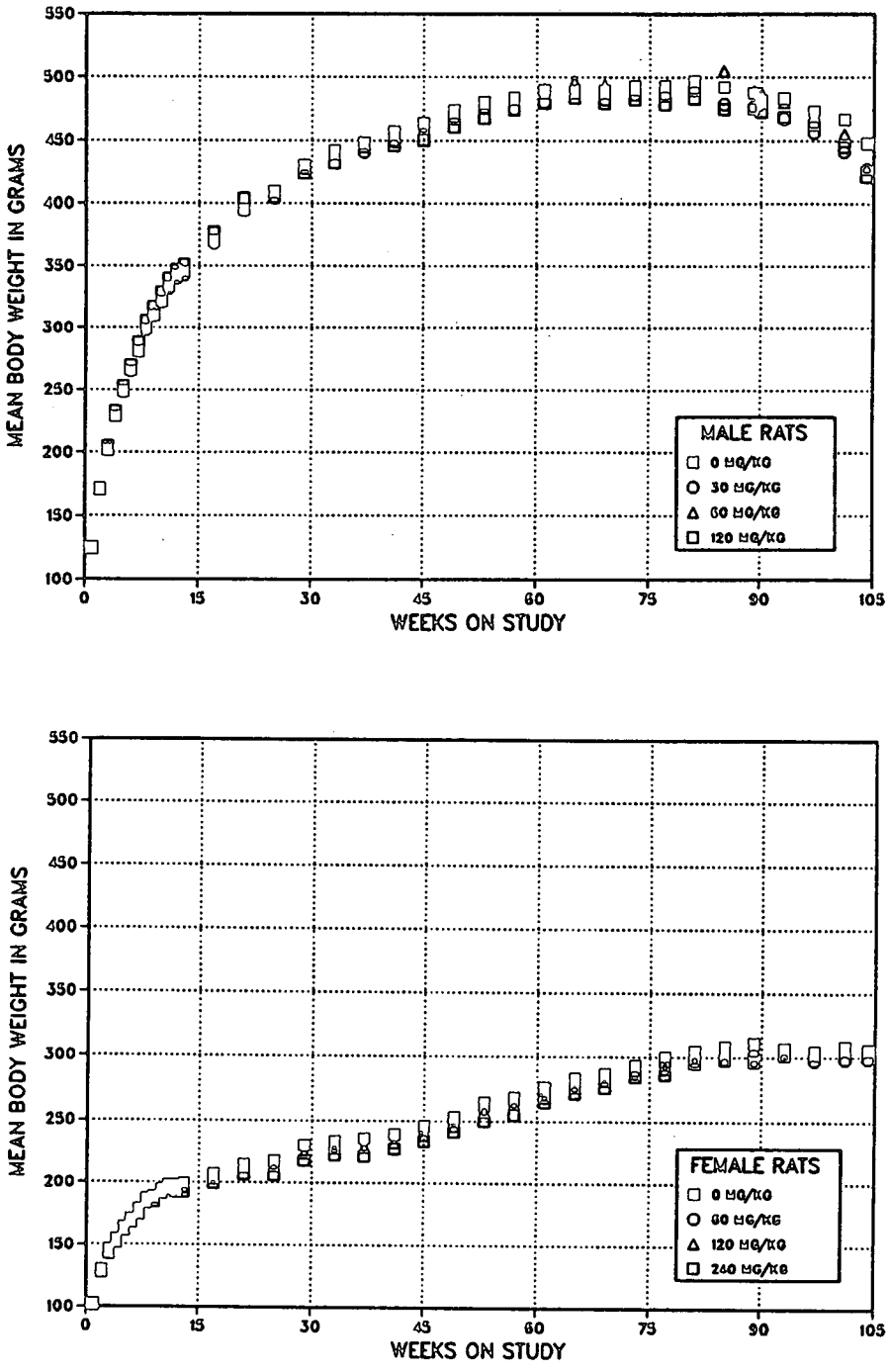


FIGURE 2
Growth Curves for Male and Female F344/N Rats Administered *o*-Benzyl-*p*-Chlorophenol by Gavage for 2 Years

Pathology and Statistical Evaluation

This section describes the biologically noteworthy differences in the incidences of neoplasms and nonneoplastic lesions of the kidney and miscellaneous organs. No neoplasms were positively identified as attributable to the administration of *o*-benzyl-*p*-chlorophenol. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group, and the historical control incidences of neoplasms related to *o*-benzyl-*p*-chlorophenol administration are presented in Appendixes A for male rats and B for female rats.

Kidney: At the 3-month interim evaluation, absolute and relative kidney weights of males receiving 120 mg/kg and females receiving 240 mg/kg were significantly greater than those of the controls (Table F3). The only microscopic lesion related to compound administration at the 3-month evaluation was nephropathy in female rats, for which the incidence and severity increased with dose (Table 7b and Figure 3). At the 15-month interim evaluation, absolute kidney weights were greater in all dosed male groups and absolute and relative kidney weights were significantly greater in mid- and high-dose females than in the controls (Table F4). Nephropathy was present in essentially all rats after 15 months of chemical administration; however, nephropathy increased in severity with dose and was more severe in male than in female rats (Tables 7a and 7b and Figure 3). At the end of the study, nephropathy occurred in most male and female dosed and control rats with a dose-related increase in severity. The histologic changes associated with nephropathy in dosed rats were similar to those of the controls and were similar to those of the aged F344/N rat; the severity was greater in dosed rats, and greater in males than in females as occurs with spontaneous nephropathy.

The nephropathy was characterized by tubule dilatation, flattening of the tubule epithelium, and the presence of regenerative tubules surrounded by a thickened basement membrane. With increased severity, the prominent dilated tubules contained hyaline casts and cellular debris. More advanced lesions were characterized by additional alterations of interstitial fibrosis, multiple interstitial foci of mononuclear cells, foci of mineralization, and degenerative changes with sclerosis of glomeruli. The dose-related increase in severity was particularly striking in high-dose female rats because of the usual minimal severity of spontaneous nephropathy in control female rats.

The Pathology Working Group (PWG) evaluated the compound-related increase in the severity of the nephropathy in males and females, the increased incidence of renal pelvic mineralization, and the increased incidence of hyperplasia of the parathyroid gland in treated male rats. The PWG confirmed that the principal chemical-related nonneoplastic finding was the dose-related increase in severity of the nephropathy. This increased severity was particularly evident in treated female rats, because spontaneous nephropathy is generally of minimal severity in control female rats. Small foci of mineralization found at the corticomedullary junction and in the renal pelvis were not considered treatment related and were not severe enough to obstruct urine flow or induce proliferation of renal pelvic epithelium. The PWG did confirm the presence of one transitional cell carcinoma in the 120 mg/kg females and one in the 240 mg/kg females (Table B1). None occurred in male rats. Transitional cell carcinomas were not found in control female rats in a search of the historical database (Table B4). The PWG confirmed the increased incidence of hyperplasia of the parathyroid gland in male rats (Table A5). These lesions were attributed to renal secondary hyperparathyroidism. Most of the rats with parathyroid gland hyperplasia had severe nephropathy.

Incidences of proliferative lesions occurred in the kidney of some rats (Tables 7a and 7b). Renal tubule hyperplasia is characterized by tubule lumens filled with proliferated cells and by tubule diameters varying from slightly larger than normal to three times larger. The hyperplastic tubule cells form solid clusters, are moderately large, have round to ovoid, palely basophilic nuclei with a prominent nucleolus, and have moderately abundant eosinophilic granular to foamy cytoplasm. Renal tubule adenomas consist of epithelial cells like those found in tubule

TABLE 7a
Evaluation of Nephropathy and Extended Evaluation of Renal Proliferative Lesions of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	0		30		60		120	
3-Month Interim Evaluation								
Kidney[a]	10		10		10		9	
Nephropathy[b]	10	(1.0)[c]	8	(0.8)	9	(1.0)	8	(0.9)
15-Month Interim Evaluation								
Kidney	10		10		10		9	
Nephropathy	10	(1.7)	10	(2.1)*	10	(2.1)*	9	(2.2)*
2-Year Evaluation								
Kidney	50		49		50		50	
Nephropathy	48	(2.3)	48	(2.8)*	48	(2.9)**	50	(3.3)**
Single Sections (Standard Evaluation)								
Kidney	50		49		50		50	
Renal Tubule Hyperplasia	0		2		0		2	
Renal Tubule Adenoma	1		0		0		0	
Renal Tubule Carcinoma	0		0		0		1	
Renal Tubule Adenoma or Carcinoma[d]	1		0		0		1	
Step Sections (Extended Evaluations)								
Kidney	50		49		50		50	
Renal Tubule Hyperplasia	3		7		6		17**	
Renal Tubule Adenoma	0		1		2		1	
Renal Tubule Carcinoma	0		0		0		1	
Renal Tubule Adenoma or Carcinoma	0		1		2		2	
Single and Step Sections combined								
Kidney	50		49		50		50	
Renal Tubule Hyperplasia	3		9		6		17**	
Renal Tubule Adenoma	1		1		2		1	
Renal Tubule Carcinoma	0		0		0		1	
Renal Tubule Adenoma or Carcinoma	1		1		2		2	

* Significantly different ($P \leq 0.05$) from control group by Fisher exact test; severity significantly different by Mann-Whitney U test
** $P \leq 0.01$
[a] Number of animals with kidney examined microscopically
[b] Number of animals with lesion
[c] Average severity grade of lesion in all animals: 0=none, 1=minimal, 2=mild, 3=moderate, 4=marked
[d] Historical incidence for 2-year corn oil gavage studies with vehicle control groups: 12/1,069 (1.1% ± 1.4%); range 0%-4%

TABLE 7b
Evaluation of Nephropathy and Extended Evaluation of Renal Proliferative Lesions of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	0		60		120		240	
3-Month Interim Evaluation								
Kidney[a]	10		10		8		9	
Nephropathy[b]	1	(0.1)[c]	3	(0.3)	3	(0.4)	7**	(1.2)**
15-Month Interim Evaluation								
Kidney	10		10		10		10	
Nephropathy	9	(0.9)	10	(1.2)	9	(1.1)	10	(1.8)**
2-Year Evaluation								
Kidney	50		50		51		50	
Nephropathy	46	(1.2)	47	(1.2)	50	(1.5)*	50	(2.4)**
Single Sections (Standard Evaluation)								
Kidney	50		50		51		50	
Renal Tubule Hyperplasia	0		0		0		1	
Renal Tubule Adenoma[d]	0		0		0		1	
Transitional Cell Carcinoma[e]	0		0		1		1	
Step Sections (Extended Evaluations)								
Kidney	50		–[f]		–		50	
Renal Tubule Hyperplasia	2		–		–		2	
Single and Step Sections combined								
Kidney	50		–		–		50	
Renal Tubule Hyperplasia	2		–		–		3	
Renal Tubule Adenoma	0		–		–		1	
Transitional Cell Carcinoma	0		–		–		1	

* Significantly different (P≤0.05) from control group by Fisher exact test; severity significantly different by Mann-Whitney U test
** P≤0.01
[a] Number of animals with kidney examined microscopically
[b] Number of animals with lesion
[c] Average severity grade of lesion in all animals: 0=none, 1=minimal, 2=mild, 3=moderate, 4=marked
[d] Historical incidence for 2-year corn oil gavage studies with vehicle control groups: 2/1,068 (1.9% ± 0.2%); range 0%-2%
[e] Historical incidence: 0/1,068
[f] Animals not examined in extended or combined evaluations

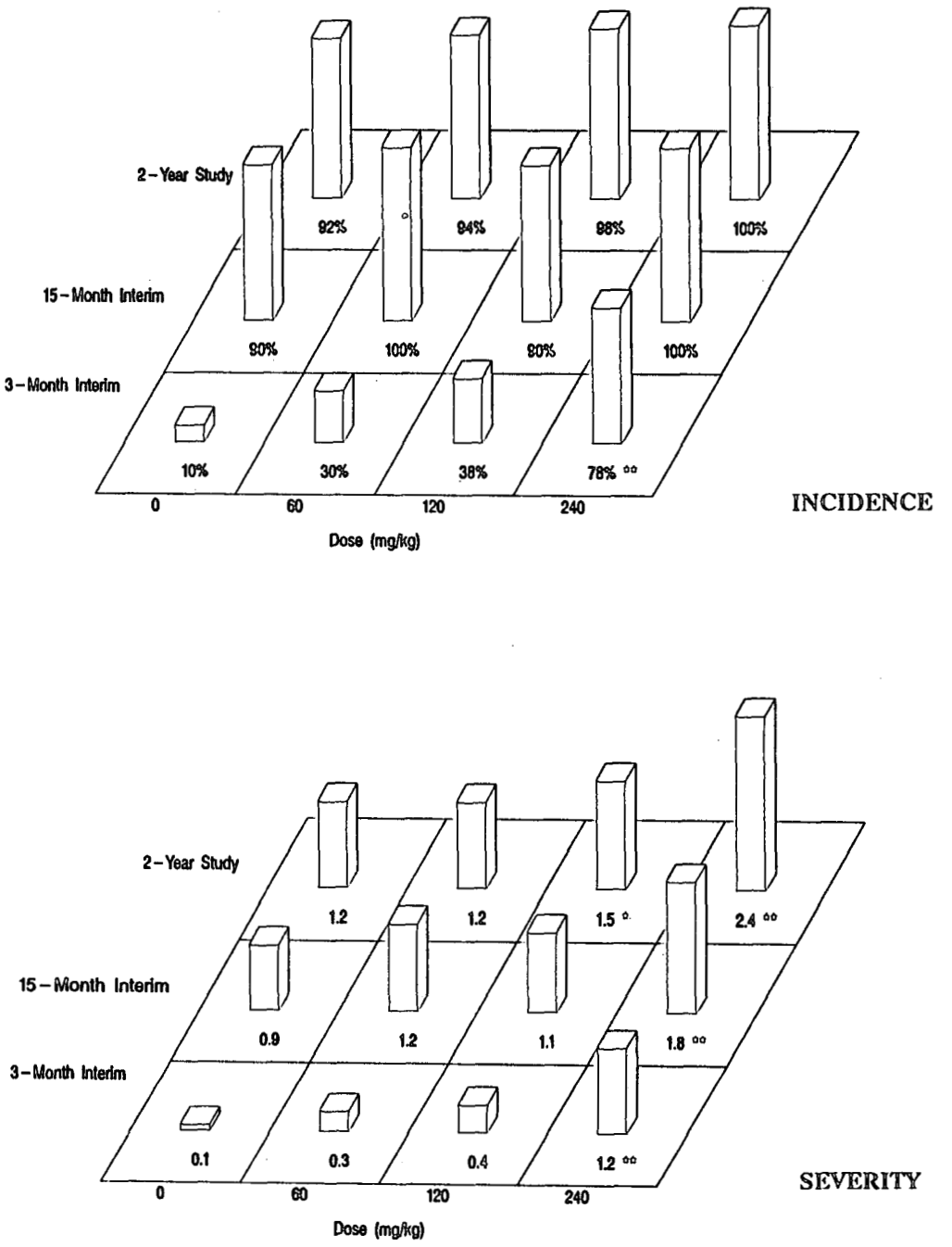


FIGURE 3
Incidences and Severity of Nephropathy in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol. [Incidences are significantly different from the control group (* = P≤0.05; ** = P≤0.01) by the Fisher exact test (3- and 15-month interim evaluations) or the logistic regression test (2-year study). Severity values are significantly different from the control group by the Mann-Whitney U test.]

hyperplasias but are larger than hyperplasias (usually five or more tubule diameters) and have a more complex structure. Some adenomas are composed of multiple, variably sized tubule structures and others consist of solid nests of epithelial cells separated by fine strands of fibrous connective tissue. A renal tubule carcinoma is larger than an adenoma, is less circumscribed, has a more prominent blood supply, and has more cellular anaplasia and atypia. Hemorrhages, necrosis, and locally invasive growth are often features of a renal tubule carcinoma. Transitional cell hyperplasia occurs in the renal pelvis epithelium as a component of some cases of severe nephropathy. Hyperplasia may be diffuse, but small nodular structures several cell layers thick extending into the pelvis are more common. Due to the detection of two rare transitional cell carcinomas in female rats, a review was conducted to specifically evaluate the transitional cell hyperplasia. This review of high-dose and vehicle control rats from the 15-month interim evaluation and 2-year study was limited to the transitional epithelium lining, the renal pelvis, and papilla. An increased incidence of transitional cell hyperplasia was detected in both high-dose males (vehicle control, 5/59, 9%; 120 mg/kg, 26/59, 44%) and females (vehicle control, 4/60, 7%; 240 mg/kg, 17/59, 29%). Transitional cell carcinomas tend to fill and expand the pelvis and invade the adjacent kidney. Carcinomas often have a lobular pattern, some degree of cellular atypia, areas of necrosis, and foci of hemorrhages. Cells may be spindle-shaped in some transitional cell carcinomas.

Miscellaneous organs: Increased incidences of fibrous osteodystrophy occurred in male rats (cranial fibrous osteodystrophy: 0/50, 0/50, 2/50, 4/51; femur fibrous osteodystrophy: 0/50, 0/50, 2/50, 6/51; Table A5). Fibrous osteodystrophy was characterized by bone resorption, increased numbers of osteoclasts, atrophy of osseous trabeculae, and proliferation of fibrous connective tissues. The lesions were ascribed to and correlated with the increased severity of the nephropathy and the development of secondary renal hyperparathyroidism, with lesions primarily restricted to male rats, in which the nephropathy was more severe [parathyroid gland hyperplasia: males 0/47, 2/47 (2.0), 5/45 (2.2), 8/46 (2.5)].

MICE

16-DAY STUDY

Three males and five females in the 1,000 mg/kg groups died during the study (Table 8). Mean body weight gains of dosed mice were generally similar to those of the controls. Clinical findings included rough hair coat and abnormal posture in the 1,000 mg/kg mice.

The only chemical-related differences in organ weights were increases in liver weights. Absolute and relative liver weights of 500 and 1,000 mg/kg males and of 500 mg/kg females (the highest dose group of females surviving) were significantly greater than those of the controls (Table F5).

Dilatation of the cecum occurred in a few mice at all but the lowest dose. Nephropathy characterized by multifocal tubule dilatation and flattening of the proximal convoluted tubule epithelium, tubule regeneration, and minimal focal epithelial cell necrosis occurred in two 500 mg/kg and six 1,000 mg/kg male and female mice.

TABLE 8
Survival and Mean Body Weights of Mice in the 16-Day Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	Survival[a]	Mean Body Weights[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
Male					
0	5/5	25.0 ± 0.7	27.0 ± 0.7	2.0 ± 0.1	
62.5	5/5	24.6 ± 0.8	25.5 ± 1.0	0.9 ± 0.4	95
125	5/5	24.2 ± 0.7	26.9 ± 0.9	2.7 ± 0.4	100
250	5/5	24.6 ± 0.7	26.7 ± 1.3	2.1 ± 0.7	99
500	5/5	24.6 ± 0.5	26.9 ± 0.4	2.3 ± 0.3	100
1,000	2/5[c]	25.0 ± 0.7	27.8 ± 0.1	1.8 ± 1.1	103
Female					
0	5/5	17.4 ± 0.4	19.6 ± 0.2	2.2 ± 0.3	
62.5	5/5	17.4 ± 0.6	19.4 ± 0.7	2.0 ± 0.4	99
125	5/5	17.4 ± 0.5	19.6 ± 0.6	2.2 ± 0.3	100
250	5/5	17.6 ± 0.5	20.0 ± 0.4	2.4 ± 0.2	102
500	5/5	17.8 ± 0.4	20.5 ± 0.5	2.7 ± 0.1	105
1,000	0/5[d]	18.2 ± 0.4	–[e]	–	–

[a] Number of animals surviving/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study. Differences from the control group are not significant by Williams' or Dunnett's test.
[c] Day of death: 3, 4, 4
[d] Day of death: 2, 3, 3, 3, 4
[e] No data calculated due to 100% mortality in this group.

13-WEEK STUDIES

All animals survived to the end of the first 13-week mouse study, with the exception of two mice that were accidentally killed (Table 9). Mean body weight gains and final mean body weights of dosed animals were similar to those of the controls. No clinical findings or gross lesions at necropsy were attributed to *o*-benzyl-*p*-chlorophenol administration. All organ weights were similar to those of the controls. The Pathology Working Group (PWG) confirmed that no microscopic lesions were noted that could be definitely associated with chemical treatment. On the basis of these findings, a second 13-week study was designed, using higher doses of 0, 500, 650, 800, or 1,000 mg/kg.

TABLE 9
Survival and Mean Body Weights of Mice in the First 13-Week Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	Survival[a]	Mean Body Weights[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
Male					
0	10/10	25.9 ± 0.5	33.4 ± 0.5	7.5 ± 0.5	
30	10/10	25.8 ± 0.4	34.3 ± 0.8	8.5 ± 0.7	103
60	10/10	25.7 ± 0.5	32.3 ± 0.8	6.6 ± 0.6	97
120	10/10	25.5 ± 0.5	33.1 ± 0.9	7.6 ± 0.5	99
240	9/10[c]	26.4 ± 0.5	35.1 ± 1.0	8.8 ± 1.1	105
480	10/10	26.4 ± 0.6	33.2 ± 0.8	6.8 ± 0.5	99
Female					
0	9/10[c]	19.4 ± 0.5	27.8 ± 0.4	8.2 ± 0.4	
30	10/10	19.5 ± 0.3	27.7 ± 0.5	8.2 ± 0.6	100
60	10/10	20.1 ± 0.4	28.9 ± 0.3	8.8 ± 0.4	104
120	10/10	20.2 ± 0.4	28.9 ± 0.6	8.7 ± 0.4	104
240	10/10	20.6 ± 0.5*	28.1 ± 0.6	7.5 ± 0.3	101
480	10/10	20.7 ± 0.3*	28.0 ± 0.3	7.3 ± 0.3	101

* Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test.
[a] Number of animals surviving/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[c] Accidental death

In the second 13-week study, survival decreased with dose and most animals in the two highest dose groups died (Table 10). Decreased mean body weight gains occurred in all dosed male groups and in females receiving 500 or 800 mg/kg. Compound-related clinical findings in mice receiving doses of 650 mg/kg or higher of *o*-benzyl-*p*-chlorophenol included hypoactivity and a rough or oily hair coat.

Absolute and relative liver weights of 800 mg/kg male mice and of 500, 650, and 800 mg/kg female mice were significantly greater than those of the controls (Table F6). Absolute and relative kidney weights of 500, 650, and 800 mg/kg male mice were lower than those of the controls. No gross lesions attributable to chemical administration were found at necropsy.

Significant microscopic lesions observed in all dosed groups included a time- and dose-related increased incidence and severity of nephropathy, which consisted of renal tubule cell necrosis, luminal casts, tubule regeneration, and mononuclear inflammatory cells in the renal cortical interstitium. The PWG confirmed significant increases in the incidence and severity of nephropathy, even at the lowest dose tested (500 mg/kg). Nasal lesions, considered to be caused by the caustic nature of *o*-benzyl-*p*-chlorophenol following retrograde exposure after gavage, consisted of an acute, necrotizing, suppurative inflammation of the olfactory epithelium. Because doses of 500 mg/kg were considered potentially life-threatening but had no effect in the second 13-week study, a high dose of 480 mg/kg was chosen for the 2-year study.

TABLE 10
Survival and Mean Body Weights of Mice in the Second 13-Week Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	Survival[a]	Mean Body Weights[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
Male					
0	10/10	20.3 ± 0.3	35.7 ± 0.7	15.4 ± 0.6	
500	10/10	19.8 ± 0.5	29.8 ± 0.9°°	10.0 ± 0.8°°	83
650	8/10[c]	20.1 ± 0.5	30.0 ± 1.1°°	9.9 ± 0.7°°	84
800	4/10[d]	20.4 ± 0.5	30.5 ± 1.2°°	9.0 ± 1.2°°	85
1,000	1/10[e]	20.3 ± 0.5	30.0[f]	7.0	84
Female					
0	10/10	15.7 ± 0.30	24.0 ± 0.5	8.3 ± 0.3	
500	9/10[g]	16.1 ± 0.3	23.0 ± 0.4	6.9 ± 0.2°	96
650	9/10[h]	15.5 ± 0.2	23.9 ± 0.6	8.4 ± 0.6	100
800	2/10[i]	16.1 ± 0.2	23.5 ± 1.5	7.5 ± 0.5	98
1,000	0/10[j]	15.6 ± 0.2	–[k]	–	–

° Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test.
°° P≤0.01
[a] Number of animals surviving/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[c] Week of death: 5, 11
[d] Week of death: 1, 2, 3, 7, 9, 11
[e] Week of death: 1, 1, 2, 2, 3, 6, 7, 7, 8, 10
[f] No standard errors were calculated for groups with high mortality.
[g] Week of death: 8
[h] Week of death: 11
[i] Week of death: 1, 1, 1, 1, 4, 7, 7, 11
[j] Week of death: 1, 1, 1, 1, 1, 1, 1, 1, 3, 6
[k] No final mean body weights or body weight changes were calculated for groups with 100% mortality.

2-YEAR STUDY

Survival

Estimates of survival probabilities for male and female mice administered *o*-benzyl-*p*-chlorophenol by gavage for 2 years are presented in Table 11 and in the Kaplan-Meier curves in Figure 4. Decreased survival trends were noted for both male and female mice. The probability of survival for dosed male mice was lower than that of controls and varied from 64% to 81% (control, 90%). The probability of survival for female mice in the highest dose group (51%) was significantly lower than that of the controls (control, 74%). In both sexes, the number of natural deaths was increased in the high-dose groups (males, 10; females, 14). Even with the decreased survival in dosed groups, the number of mice surviving to the end of the study was considered adequate for evaluation of chronic toxicity and carcinogenicity. Renal disease was considered a significant factor in the decreased survival of dosed male and female mice.

Body Weights and Clinical Findings

Final mean body weights of all dosed males and mid- and high-dose females were lower than those of the controls (Tables 12 and 13 and Figure 5). The lengths of time to a 10% lower mean body weight than controls were 84, 68, and 28 weeks for 120, 240, and 480 mg/kg male mice. For female mice, the lengths of time to a 10% lower mean body weight than controls were 93 and 26 weeks for the 240 and 480 mg/kg groups. Clinical findings attributed to *o*-benzyl-*p*-chlorophenol administration in male and female mice included emaciation, abnormal posture, rough hair coat, and hypoactivity. These findings were most frequent in the 480 mg/kg groups but also occurred as a significant dose-related trend. Other abnormalities in dosed male and female mice were considered spontaneous and unrelated to treatment either because of the low incidences or because incidences were similar to those in controls. No effect on feed consumption was observed.

Sentinel Animals

Significant titers were observed for two viruses (Table J1). Four of ten mice at the end of the study had positive titers for Reovirus 3. Several mice had positive titers for the virus of epizootic diarrhea of infant mice: 6/10 at 6 months, 7/10 at 12 months, 4/10 at 18 months, 10/10 at the end of the study. These viruses produce disease in infant mice and these titers in adult mice had no adverse affect on the study.

TABLE 11
Survival of Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Male				
Animals initially in study	70	70	70	70
3-Month interim evaluation[a]	10	10	10	10
15-Month interim evaluation[a]	10	10	10	10
Moribund	2	12	7	8
Natural deaths	3	4	5	10
Accidental deaths[a]		2		2
Animals surviving to study termination	45	32	38	30
Percent probability of survival at end of study[b]	90	69	81	64
Mean survival (days)[c]	591	551	572	530
Survival analysis[d]	P=0.007	P=0.014	P=0.222	P=0.002
Female				
Animals initially in study	70	70	70	70
3-Month interim evaluation[a]	10	10	10	9
15-Month interim evaluation[a]	10	10	10	9
Moribund	9	4	10	12
Natural deaths	5	3	5	14
Accidental deaths[a]		3	2	1
Animals surviving to study termination	36	40	33	25
Percent probability of survival at end of study[b]	74	85	69	51
Mean survival (days)[c]	583	554	551	520
Survival analysis[d]	P<0.001	P=0.314N	P=0.665	P=0.007

[a] Censored from survival analyses
[b] Kaplan-Meier determinations
[c] Mean of all deaths (uncensored, censored, and terminal sacrifice)
[d] The result of the life table trend test (Tarone, 1975) is in the control column, and the results of the life table pairwise comparisons (Cox, 1972) with the controls are in the dosed columns. A lower mortality in a dose group is indicated by N.

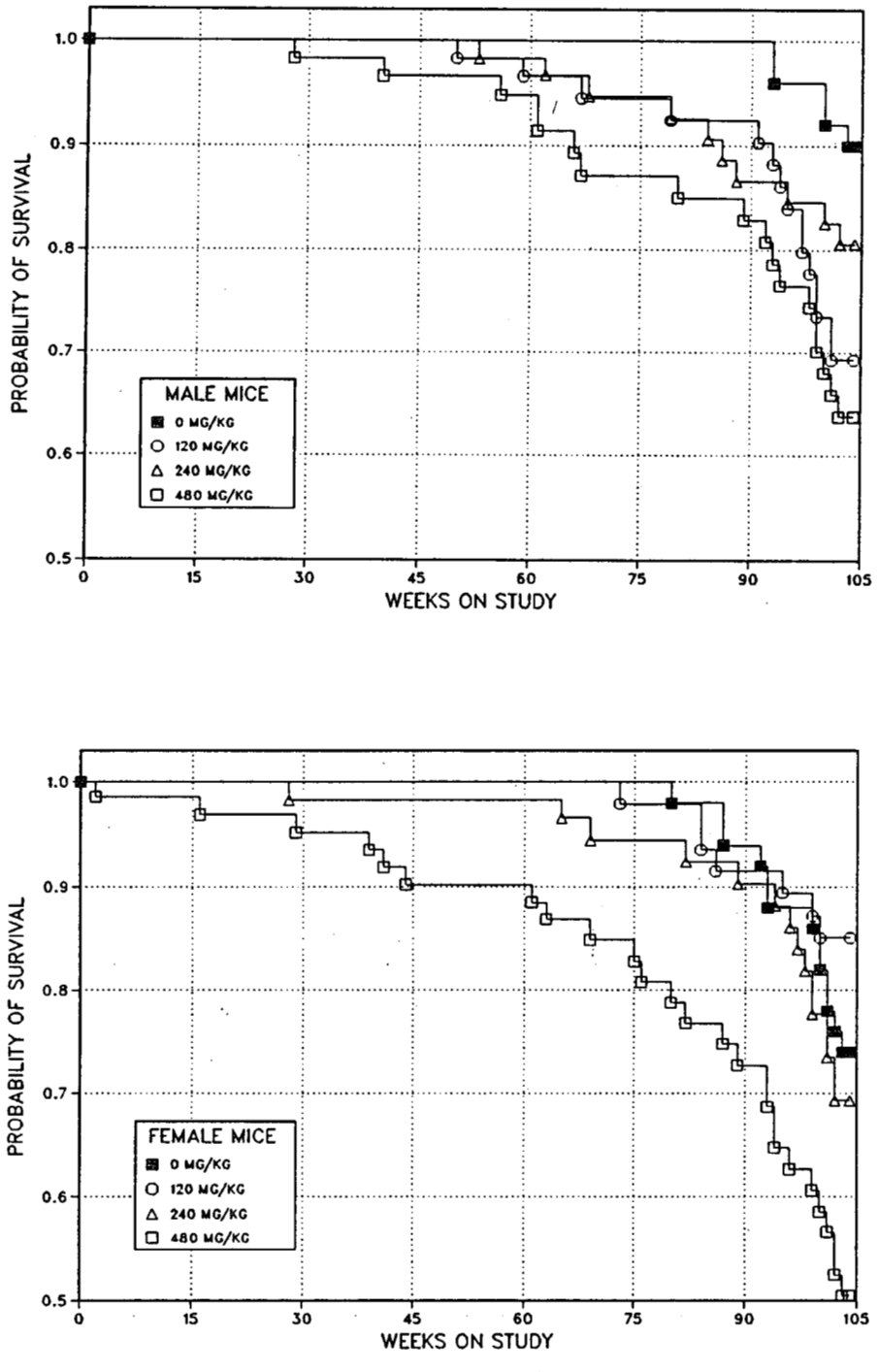


FIGURE 4
Kaplan-Meier Survival Curves for Male and Female B6C3F$_1$ Mice Administered *o*-Benzyl-*p*-Chlorophenol by Gavage for 2 Years

TABLE 12
Mean Body Weights and Survival of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Weeks on Study	Vehicle Control		120 mg/kg			240 mg/kg			480 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	22.4	70	22.5	100	70	22.5	100	70	22.6	101	70
2	24.2	70	24.1	100	69	24.1	100	70	24.2	100	68
3	25.1	70	25.0	100	69	25.1	100	70	25.2	100	68
4	25.5	70	25.3	99	68	25.5	100	70	25.4	100	68
5	26.6	70	26.3	99	68	26.3	99	70	26.3	99	68
6	27.3	70	27.2	100	68	27.2	100	70	27.1	99	68
7	27.6	70	27.6	100	68	27.4	99	70	27.3	99	68
8	28.2	70	28.1	100	68	27.8	99	70	27.6	98	68
9	29.1	70	29.0	100	68	28.7	99	70	28.2	97	68
10	29.5	70	29.2	99	68	29.0	98	70	28.2	96	68
11	30.6	70	30.4	99	68	29.6	97	70	28.6	94	68
12	30.6	70	30.2	99	68	29.9	98	70	28.9	94	68
13	32.1	70	32.1	100	68	31.7	99	70	30.2	94	68
17[a]	34.1	60	34.3	101	58	33.2	97	60	31.8	93	58
21	36.6	60	36.7	100	58	35.4	97	60	33.2	91	58
25	38.2	60	38.5	101	58	36.3	95	60	34.2	90	58
29	40.4	60	39.7	98	58	38.5	95	60	34.0	84	57[b]
33	39.7	60	39.2	99	58	37.7	95	60	33.8	85	57
37	43.0	60	42.6	99	58	41.3	96	60	35.7	83	57
41	45.5	60	45.0	99	58	43.5	96	60	37.1	82	56[b]
45	44.2	60	44.1	100	58	42.9	97	60	37.0	84	56
49	46.2	60	46.6	101	58	44.7	97	60	37.6	81	56
53	48.2	60	47.5	99	57	45.5	94	59	38.2	79	56[b]
57	49.0	60	48.0	98	57	45.8	94	59[b]	38.0	78	55[b]
61	49.3	60	47.9	97	56	45.3	92	59	37.4	76	53[b]
65[a]	50.5	60	47.9	95	56	45.4	90	58[b]	36.8	73	53
69	50.2	50	47.7	95	45	43.0	86	47[b]	35.2	70	41[b]
73	50.0	50	47.0	94	45	42.8	86	47[b]	35.2	70	41
77	50.8	50	46.7	92	45	42.8	84	47	36.6	72	41
81	49.8	50	45.5	91	44[b]	41.5	83	46[b]	36.1	73	40
85	50.4	50	43.9	87	44	40.6	81	45	35.6	71	40
89	51.3	50	44.0	86	44	39.9	78	43	35.4	69	39
93	51.3	48	41.7	81	43[b]	37.9	74	43	34.7	68	37
97	52.0	48	41.3	79	39[b]	38.2	74	42	34.3	66	36
101	49.6	46	38.4	77	35	36.4	73	41[b]	32.2	65	32
103	48.6	46	38.9	80	33	35.4	73	40	32.0	66	30
Mean for weeks											
1-13	27.6		27.5	100		27.3	99		26.9	97	
14-52	40.9		40.7	100		39.3	96		34.9	85	
53-103	50.1		44.7	89		41.5	83		35.6	71	

[a] Interim evaluations occurred during weeks 13 and 65.
[b] The number of animals weighed for this week is fewer than the number of animals surviving.

TABLE 13
Mean Body Weights and Survival of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Weeks on Study	Vehicle Control		120 mg/kg			240 mg/kg			480 mg/kg		
	Av. Wt. (g)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors	Av. Wt. (g)	Wt. (% of controls)	No. of Survivors
1	18.9	70	18.6	98	70	18.7	99	70	18.8	100	70
2	20.3	70	20.3	100	69	20.5	101	68	20.7	102	68
3	21.3	70	21.1	99	67	21.4	101	68	21.6	101	68
4	21.5	70	21.2	99	67	21.6	101	68	21.8	101	68
5	22.2	70	22.0	99	67	22.3	101	68	22.4	101	68
6	23.5	70	23.1	98	67	23.5	100	68	23.7	101	68
7	23.8	70	23.4	98	67	23.8	100	68	23.8	100	68
8	24.1	70	23.8	99	67	23.8	99	68	23.8	99	68
9	25.1	70	24.7	98	67	24.4	97	68	24.5	98	68
10	25.3	70	24.9	98	67	25.0	99	68	24.9	98	68
11	25.9	70	25.5	99	67	25.5	99	68	25.3	98	68
12	25.8	70	25.5	99	67	25.5	99	68	25.2	98	68
13	27.3	70	27.1	99	67	26.8	98	68	26.4	97	68
17[a]	29.1	60	28.9	99	57	28.3	97	58	27.2	94	58
21	30.4	60	30.1	99	57	29.7	98	58	28.0	92	58
26	32.8	60[b]	33.4	102	57[b]	31.7	97	58[b]	28.9	88	58[b]
30	34.7	60[b]	34.9	101	57[b]	33.4	96	57[b]	30.1	87	57[b]
33	34.7	60	35.7	103	57	34.3	99	57	30.4	88	57
37	37.5	60	38.4	102	57	36.4	97	57	32.0	85	57
41	39.1	60	40.2	103	57	38.4	98	57	33.3	85	55
45	39.2	60	40.1	102	57	38.2	97	57	33.3	85	54
49	40.5	60	41.6	103	57	40.2	99	57	34.7	86	54
53	42.3	60	43.2	102	57	41.6	98	57	35.9	85	54
57	43.6	60	45.4	104	57	43.5	100	57	36.4	84	54
61	44.3	60	45.4	103	57	43.6	98	57	35.3	80	53
65	45.5	60	46.6	102	57	44.3	97	56	35.5	78	52
69[a]	46.0	50	48.2	105	47	44.7	97	45	36.2	79	42
73	46.6	50	48.2	103	46	45.6	98	45	38.5	83	42
77	48.0	50	48.8	102	46	45.5	95	45	38.4	80	40
81	47.9	49	49.1	103	46	45.2	94	44	37.8	79	39[b]
85	48.6	49	50.2	103	44	45.2	93	44	37.5	77	38
89	49.5	47	49.7	100	43	45.1	91	43	36.1	73	36
93	49.5	44	49.0	99	43	44.0	89	43	36.0	73	35
97	49.8	44	49.4	99	42	43.7	88	41	35.3	71	31
101	48.1	40	48.3	100	40	41.0	85	36	34.5	72	29
103	47.6	37	46.3	97	40	41.2	87	33	33.3	70	25
Mean for weeks											
1-13	23.5		23.2	99		23.3	99		23.3	99	
14-52	35.3		35.9	102		34.5	98		30.9	88	
53-103	47.0		47.7	101		43.9	93		36.2	77	

[a] Interim evaluations occurred during weeks 13 and 65.
[b] The number of animals weighed for this week is fewer than the number of animals surviving.

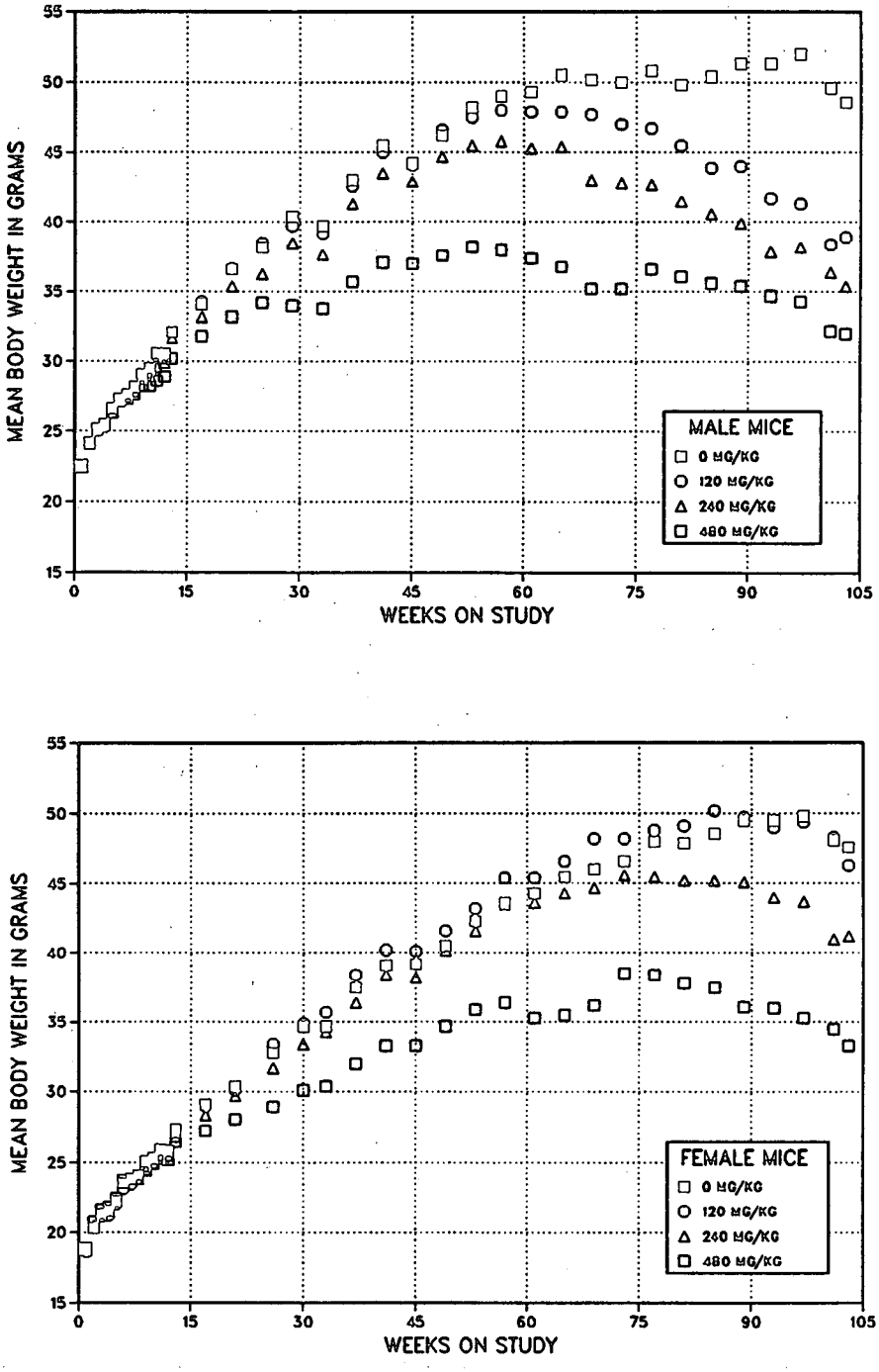


FIGURE 5
Growth Curves for Male and Female B6C3F$_1$ Mice Administered *o*-Benzyl-*p*-Chlorophenol by Gavage for 2 Years

Pathology and Statistical Evaluation

This section describes the statistically significant or biologically noteworthy differences in the incidences of neoplasms and nonneoplastic lesions in the kidney and in miscellaneous organs. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group, and the historical control incidences of neoplasms related to *o*-benzyl-*p*-chlorophenol administration are presented in Appendixes C for male mice and D for female mice.

Kidney: At the 3-month interim evaluation, the incidence and severity of nephropathy were dose-related and more severe in male than female mice (Tables 14a and 14b and Figures 6 and 7). Severity grades were based on the extent of parenchymal involvement: minimal - less than 10%; mild - 10% to 50%; moderate - 50% to 70%; marked - greater than 70%. Chemical-related microscopic lesions were confined to the kidney and included multiple foci of dilated tubules with a flattened epithelium, a few tubules with hyaline casts, regenerated tubules with basophilic epithelium, a few necrotic tubules with neutrophils and debris in the lumen, and foci of mononuclear cells in the renal cortical interstitium.

At the 15-month interim evaluation, because the incidence of spontaneous nephropathy was increased in control males, incidences in dosed males were similar to those of the controls; the incidence of nephropathy in dosed female mice increased. However, a dose-related increase in severity occurred in dosed males and females. Absolute kidney weights of high-dose males were lower than those of the controls at the 3-month interim evaluation (Table F7). Absolute and relative kidney weights of dosed male mice were lower than those of the controls, as were the absolute kidney weights of dosed females at the 15-month interim evaluation. Gross lesions related to compound administration were found in the kidney, particularly in male mice. Affected kidneys were pale, tan, and/or granular. The microscopic lesions were designated nephropathy and consisted of multifocal dilatation of renal tubules with flattening of the tubule epithelium, luminal hyaline casts and cellular debris, thickened tubule basement membranes, tubule cell necrosis, regeneration of tubule cells, and infiltrates of mononuclear cells in the renal cortical interstitium.

At the end of the 2-year study, compound-related nephropathy occurred in both sexes but was more severe in male mice and was characterized by a spectrum of lesions that varied in severity, including interstitial fibrosis, multifocal dilated tubules with flattening of the renal tubule epithelium, regenerative tubules with basophilic epithelium, thickened basement membranes, and hyaline casts. Severe cases were characterized by loss of nephrons in a wedge-shaped pattern and replacement by fibrous tissue with only a few atrophied and sclerosed glomeruli remaining. Grossly, these kidneys were smaller than those of the controls, had increased renal pelvis size, and decreased renal cortex width. The PWG confirmed a compound-related, time- and dose-dependent nephropathy that was more severe in male than in female mice.

At the end of the 2-year study, the only organ with a significant incidence of proliferative lesions was the kidney (Tables 14a and 14b). These proliferative lesions included renal tubule hyperplasia as well as renal tubule adenoma and carcinoma and only occurred in dosed males. In the standard evaluation the incidence of adenoma and carcinoma (combined) was significantly increased in 240 mg/kg males (Table C3). Most of the neoplasms were identified at necropsy as masses and round to oval lesions, well-delineated from adjacent renal tissue, and were variable in size but much smaller than the host kidney. Neoplasms were located mostly in the subcapsular cortex and displaced the capsule outward. Renal tubule hyperplasia occurred in mid- and high-dose males. Renal tubule hyperplasia, as a spontaneous focal hyperplasia of tubule epithelial cells, is characterized by a tubule two to three times the size of a normal tubule, filled with stratified layers of polygonal tubule epithelial cells. These hyperplasias are not associated with tubule regeneration and generally do not have a thickened basement membrane typically present in regenerative tubules of chronic nephropathy. Renal tubule adenomas are circumscribed, solid areas of epithelial cells with

TABLE 14a
Evaluation of Nephropathy and Extended Evaluation of Renal Proliferative Lesions of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	0		120		240		480	
3-Month Interim Evaluation								
Kidney[a]	10		10		10		10	
Nephropathy[b]	1	(0.1)[c]	3	(0.3)	10°°	(1.2)°°	10°°	(2.2)°°
15-Month Interim Evaluation								
Kidney	10		10		10		10	
Nephropathy	9	(0.9)	10	(2.7)°°	10	(2.7)°°	10	(2.7)°°
2-Year Evaluation								
Kidney	50		50		50		50	
Nephropathy	39	(0.8)	48°°	(2.0)°°	50°°	(2.4)°°	49°°	(2.4)°°
Single Sections (Standard Evaluation)								
Kidney	50		50		50		50	
Renal Tubule Hyperplasia	0		0		3		6°°	
Renal Tubule Adenoma[d]	0		2		2		2	
Renal Tubule Carcinoma[e]	0		0		2		1	
Renal Tubule Adenoma or Carcinoma[f]	0		2		4°		3	
Step Sections (Extended Evaluations)								
Kidney	50		50		50		50	
Renal Tubule Hyperplasia	9		16°		13		9	
Renal Tubule Adenoma	0		1		2		3	
Renal Tubule Carcinoma	0		0		1		0	
Renal Tubule Adenoma or Carcinoma	0		1		3		3	
Single and Step Sections Combined								
Kidney	50		50		50		50	
Renal Tubule Hyperplasia	9		16°		14		13	
Renal Tubule Adenoma	0		2		4		5°	
Renal Tubule Carcinoma	0		0		2		1	
Renal Tubule Adenoma or Carcinoma	0		2		6°°		6°°	

° Significantly different (P≤0.05) from control group by Fisher exact test; severity significantly different by Mann-Whitney U test
°° P≤0.01
[a] Number of animals with kidney examined microscopically
[b] Number of animals with lesion
[c] Average severity grade of lesion in all animals: 0=none, 1=minimal, 2=mild, 3=moderate, 4=marked
[d] Historical incidence for 2-year corn oil gavage studies with vehicle control groups (mean ± standard deviation): 4/949 (0.8% ± 1.0%); range 0%-2%
[e] Historical incidence: 0/949
[f] Historical incidence: 4/949 (0.8% ± 1.0%); range 0%-2%

TABLE 14b
Evaluation of Nephropathy and Extended Evaluation of Renal Proliferative Lesions of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

Dose (mg/kg)	0	120	240	480
3-Month Interim Evaluation				
Kidney	10	10	10	9
Nephropathy	0	2 (0.2)	8** (0.9)**	7** (0.9)**
15-Month Interim Evaluation				
Kidney	10	10	10	9
Nephropathy	0	9** (1.0)**	10** (1.5)**	9** (2.6)**
2-Year Evaluation				
Kidney	50	50	50	52
Nephropathy	19 (0.4)	38** (1.1)**	48** (1.8)**	50** (2.2)**
Single Sections (Standard Evaluation)				
Kidney	50	50	50	52
Renal Tubule Hyperplasia	0	0	0	0
Step Sections (Extended Evaluation)				
Kidney	50	–[d]	–	52
Renal Tubule Hyperplasia	0	–	–	1
Single and Step Sections Combined				
Kidney	50			52
Renal Tubule Hyperplasia	0	–	–	1

* Significantly different (P≤0.05) from control group by Fisher exact test; severity significantly different by Mann-Whitney U test
** P≤0.01
[a] Number of animals with kidney examined microscopically
[b] Number of animals with lesion
[c] Average severity grade of lesion in all animals: 0=none, 1=minimal, 2=mild, 3=moderate, 4=marked
[d] Animals not examined in extended and combined evaluations

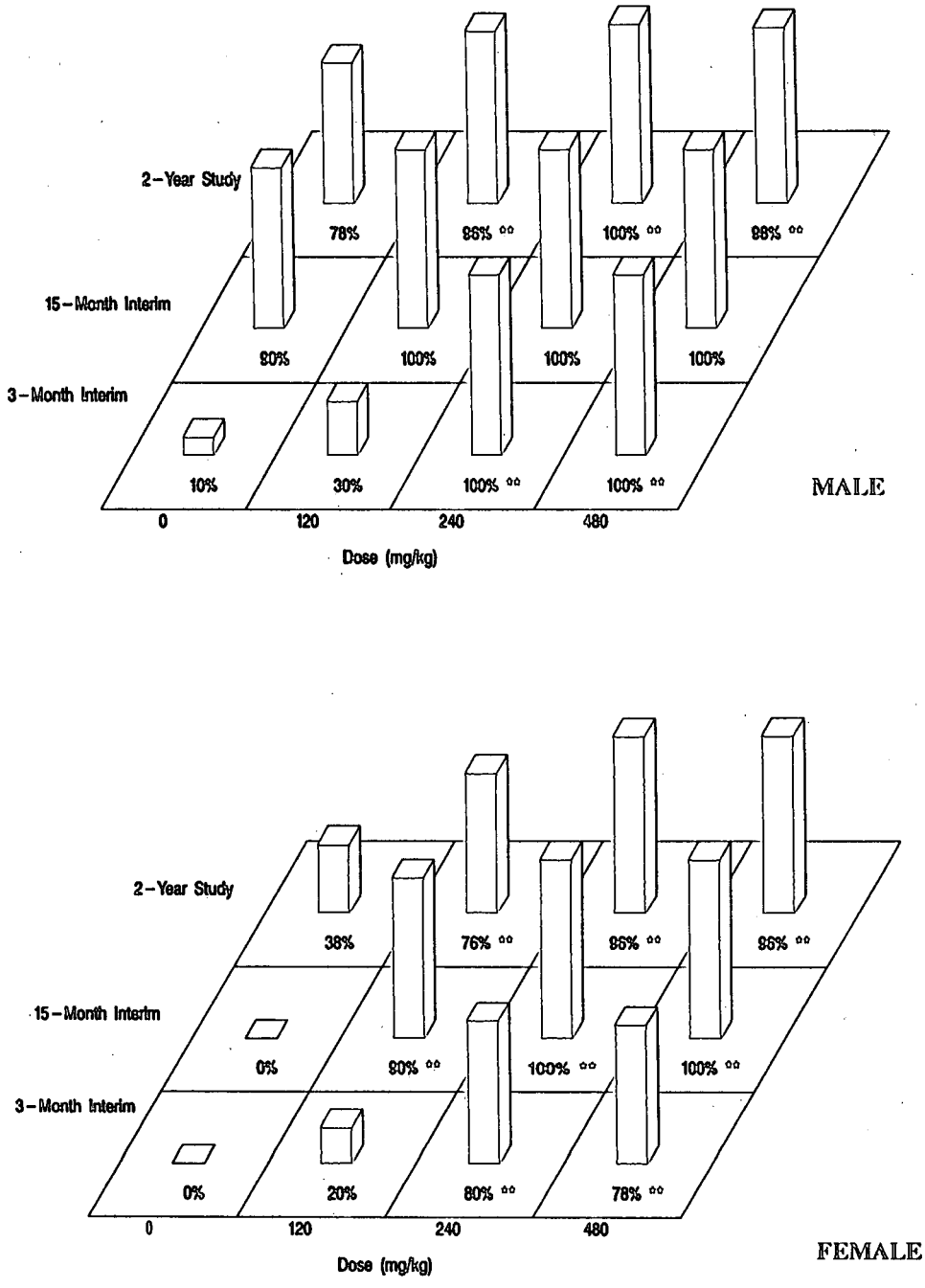
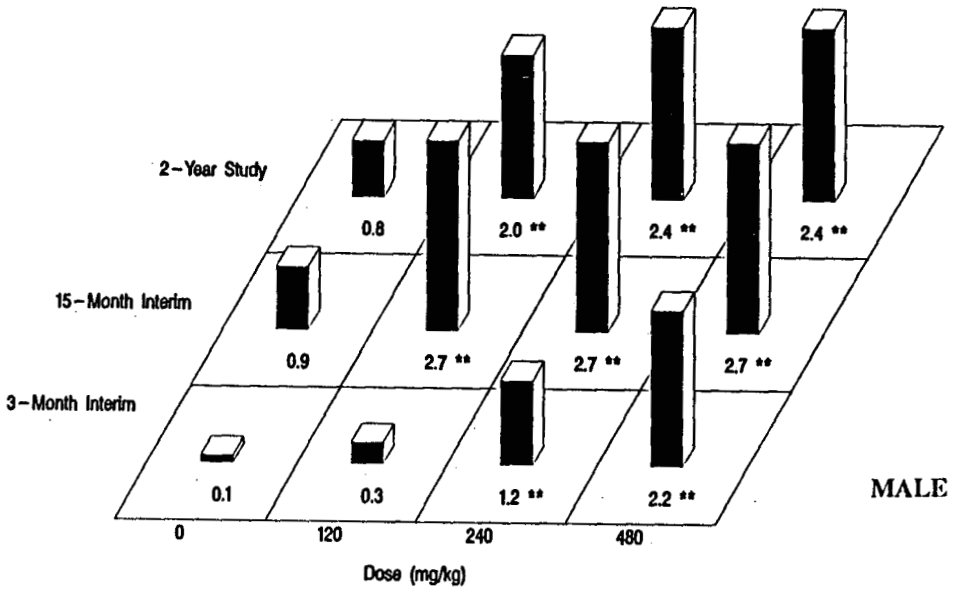


FIGURE 6
Incidences of Nephropathy in Male and Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol. [Incidences are significantly different (** = P≤0.01) from the control group by the Fisher exact test (3- and 15-month interim evaluations) or by the logistic regression test (2-year study).]



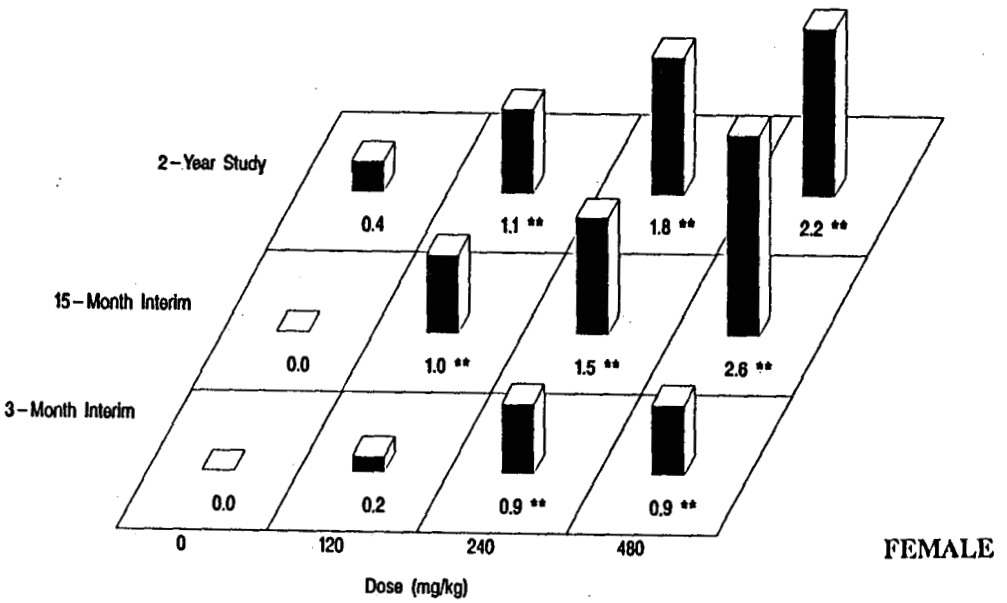


FIGURE 7
Severity of Nephropathy in Male and Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol. [Severity values are significantly different (= P≤0.01) from the control group by the Mann-Whitney U test.]**

scant amounts of stroma and vessels and without definite tubule structures. The adenoma cells are uniform, are round to polygonal, and have well-defined plasma membranes and round to oval nuclei.

Renal tubule carcinomas are differentiated from adenomas by larger size, by less demarcation from adjacent parenchyma, and by the presence of invasion and cellular anaplasia and atypia. The presence of proliferative lesions in dosed male mice was confirmed by the PWG and lesions included renal tubule hyperplasia, tubule adenoma, and tubule carcinoma. The historical incidence of renal neoplasms in the (corn oil gavage) control male mice standard section database is adenoma (4/949) and carcinoma (0/949) (Table C4).

Because of the low incidence and small average size of the renal neoplasms observed, a step-section review of the kidney was requested and reviewed by the PWG. The findings of this review extended the significant increased incidence of renal neoplasms in both the mid- (240 mg/kg) and high-dose (480 mg/kg) groups of male mice (0/50, 2/50, 6/50, and 6/50). These findings confirm the low incidences observed in the original diagnoses, providing additional evidence that this response is chemical related. This increased incidence of neoplasia was attributable to detection of a dose-related increase in the incidence of benign renal tubule adenomas.

Liver: Significantly increased absolute and relative liver weights were observed in high-dose male mice at the 3-month interim evaluation and in high-dose female mice at the 3- and 15-month interim evaluations (Tables F8 and F9). Absolute liver weights generally increased with dose in both male and female mice at the 3- and 15-month interim evaluations.

Miscellaneous organs: Dose-related increased incidences of fibrous osteodystrophy occurred in male and female mice (Table 15). Fibrous osteodystrophy was characterized by bone resorption, increased number of osteoclasts, atrophy of osseous trabeculae, and proliferation of fibrous connective tissues. The lesions were ascribed to and correlated with the increased severity of the nephropathy and the development of secondary renal hyperparathyroidism. The incidence of focal adrenal cortical hyperplasia was increased in all dosed males and was compound related. However, this increase was not considered biologically significant since no dose-related pattern in the incidences of the lesion occurred (control, 3/50; 120 mg/kg, 16/50; 240 mg/kg, 8/50; 480 mg/kg, 8/49; Table C5). Increased incidences of hyperplasia of the forestomach occurred in dosed male and female mice (Table 15). Focally, the forestomach squamous epithelium was hyperplastic and thickened, forming a broad-based lesion with moderate hyperkeratosis. The increased incidences were not dose related in male mice but appeared to increase in incidence with dose in female mice. The lesion was probably related to an irritant action of the dosed compound. A compound-related lesion occurring in both sexes was focal mucosal ulceration of the forestomach. The incidence increased with dose in female mice. This lesion could have been a response to the irritant action of the dosed compound or secondary to the nephropathy. Other lesions considered to be secondary to the combined disturbances of nephropathy and the associated secondary hyperparathyroidism included: mineralization of the glandular mucosa with focal gastric and duodenal ulcers (all dosed groups of males and females); myocardial degeneration (mid- and high-dose males); and focal coagulative necrosis of the liver (high-dose females). The PWG confirmed the presence of mineralization and of myocardial degeneration.

Genetic Toxicology

o-Benzyl-*p*-chlorophenol (0.1 to 100 μg/plate) was not mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537 when tested in a preincubation protocol with and without Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9 (Table E1; Mortelmans *et al.*, 1986). However, *o*-benzyl-*p*-chlorophenol (10 to 45 μg/mL) induced gene mutations in L5178Y mouse lymphoma cells and TK6 human lymphoblast cells without S9 activation (Caspary *et al.*, 1988). In cytogenetic tests with cultured Chinese hamster ovary cells, *o*-benzyl-*p*-chlorophenol did not induce sister chromatid exchanges (Table E2) or chromosomal aberrations (Table E3), with or without Aroclor 1254-induced male Sprague-Dawley rat liver S9. The highest non-lethal dose tested in either of these mammalian cell assays was 16 μg/mL. In the chromosomal aberrations test, the second reported trial under each activation condition was a continuation of the cultures harvested in the first trial; the results of this second harvest indicated that cell cycle delay was not a factor in the observed lack of induced chromosomal aberrations following treatment with *o*-benzyl-*p*-chlorophenol.

TABLE 15
Incidences of Selected Nonneoplastic Lesions in Male and Female Mice in the 2-Year Gavage Study of o-Benzyl-p-chlorophenol

Dose (mg/kg)	0	120	240	480
Male				
Forestomach[a]	50	50	50	50
Mucosal Squamous Hyperplasia[b]	4 (1.3)[c]	12* (1.6)	11* (2.0)	9 (1.7)
Mucosal Ulcer	1	6*	9**	6
Glandular Stomach	50	50	50	50
Mucosal Mineralization	2	6	12*	6
Duodenum	50	50	48	47
Ulcer	0	1	1	2
Bone	50	50	50	50
Fibrous Osteodystrophy	0	16**	25**	28**
Heart	49	50	49	50
Myocardial Degeneration	0	0	5*	9**
Female				
Forestomach	50	50	50	52
Mucosal Squamous Hyperplasia	3 (1.7)	10* (1.8)	18** (1.8)	20** (2.0)
Mucosal Ulcer	2	4	12**	13**
Glandular Stomach	50	50	50	52
Mucosal Mineralization	1	6*	10**	16**
Duodenum	49	49	48	52
Ulcer	0	0	4	8**
Bone	50	50	50	52
Fibrous Osteodystrophy	2	20**	33**	37**
Heart	50	50	49	50
Myocardial Degeneration	0	0	1	0

* Trend was significant ($P \leq 0.05$) by logistic regression test; dosed group significantly different from control group
** $P \leq 0.01$
[a] Number of animals with organ examined microscopically
[b] Number of animals with lesion
[c] Average severity grade of affected animals: 1=minimal; 2=mild; 3=moderate; 4=marked

DISCUSSION AND CONCLUSIONS

o-Benzyl-*p*-chlorophenol is an aryl halide biocide used extensively in hospitals and households in the United States in disinfectant preparations and soap formulations. The estimated annual production of *o*-benzyl-*p*-chlorophenol is 4.5×10^6 kg. *o*-Benzyl-*p*-chlorophenol was selected by the National Cancer Institute for toxicity and carcinogenicity studies because of the potential for human exposure, chemical relationship to the known neurotoxin hexachlorophene, and as a representative of a biocide class and the specific subclass of aryl halides. Human exposure to *o*-benzyl-*p*-chlorophenol can occur by absorption through the skin and mucous membranes after contact exposure and by absorption through the gastrointestinal tract mucous membranes following ingestion. Chronic cutaneous exposure results in irritation at the sites of application. Epidemics of infant hyperbilirubinemia have been associated with the use of disinfectant detergents containing *o*-benzyl-*p*-chlorophenol to clean equipment in hospital nurseries (Wysowski *et al.*, 1978). In the present study, dosed rats exhibited bilirubin values similar to (or lower than) control values (Table G1).

Nephropathy characterized by tubule dilatation and flattening of the tubule epithelium, tubule casts, interstitial fibrosis, and mononuclear cell infiltrates occurred in male and female rats and mice in the 13-week and 2-year studies. Kidney disease is a common background lesion in aged rats but is less common in mice. In the 2-year studies, the severity of nephropathy in rats and the incidence and severity of nephropathy in mice was related to the administration of *o*-benzyl-*p*-chlorophenol. The incidence of parathyroid gland hyperplasia associated with the nephropathy increased with increasing dose in male rats (control, 0/47; 30 mg/kg, 2/47; 60 mg/kg, 5/45; 120 mg/kg, 8/46). Parathyroid gland hyperplasia is a manifestation of secondary hyperparathyroidism caused by severe nephropathy. The nephropathy is accompanied by failure of renal function and disruption of calcium and phosphorus homeostasis, leading to stimulation of the parathyroid gland. Other lesions secondary to the disturbed mineral homeostasis of the nephropathy and secondary hyperparathyroidism include fibrous osteodystrophy in male rats and male and female mice and mineralization of tissues such as the gastric mucosa.

The route of *o*-benzyl-*p*-chlorophenol administration in these studies was by gavage. Selection of this route was based on the conclusion that systemic toxicity could not be achieved by cutaneous application because of the strong irritating and corrosive properties of *o*-benzyl-*p*-chlorophenol. The results of cutaneous exposure in rabbits included necrosis, severe desquamation, and hemorrhages at application sites after 15 doses at a concentration of 0.3% in isopropanol at a dosing volume of 2 mL/kg body weight and a dermal dose of 6 mg/kg body weight (Monsanto). Thus, while the exposure of humans is most commonly cutaneous, this route was excluded for the animal studies because of possible cutaneous irritation preventing a dose adequate for systemic toxicity.

Doses for the 16-day gavage studies were set at 0, 62.5, 125, 250, 500, or 1,000 mg/kg body weight. Significantly lower survival and clinical signs of toxicity were confined to high-dose groups of both rats and mice. Nephropathy occurred in rats and mice. Because of the increased incidence and severity of nephropathy, doses selected for the 13-week studies were 0, 30, 60, 120, 240, or 480 mg/kg for rats, 0, 30, 60, 120, 240, or 480 mg/kg for the first 13-week mouse study, and 0, 500, 650, 800, or 1,000 mg/kg for the second 13-week mouse study. The second 13-week mouse study was performed because no toxic level was established in the first 13-week study. Survival in the second 13-week mouse study was lowest in mice receiving doses of 800 or 1,000 mg/kg. Nephropathy was considered the limiting lesion for *o*-benzyl-*p*-chlorophenol administration in rats and mice.

Because the background renal lesions were more severe in males, the doses set for the 2-year study in

rats were 0, 30, 60, or 120 mg/kg body weight for males and 0, 60, 120, or 240 mg/kg body weight for females. The doses chosen for the male rats were half those chosen for the female rats because of the nephrotoxicity of the chemical in the 13-week study and the likelihood that the renal lesions would be more severe in male rats. The highest dose for male rats (120 mg/kg) did not significantly lower survival and mean body weights were slightly lower than controls. However, the severity of nephropathy was increased from 2.4 for control male rats to 3.3 for high-dose male rats. A substantially higher dose probably would have increased the severity of nephropathy to a critical stage, decreasing survival and resulting in an inadequate number of rats for the 2-year evaluation. At the high dose chosen, the deaths of 10 male rats were ascribed to nephropathy. The high dose for female rats did not lower survival and the mean body weights were similar to those of the controls. This dose, although possibly not large enough to equal the minimum lethal dose, did cause an increase in the severity of nephropathy. These renal lesions established a toxic effect in female rats and allowed the conclusion that the doses used for female rats were adequate to determine the chronic toxicity and carcinogenicity of *o*-benzyl-*p*-chlorophenol.

Mice appeared less susceptible to the toxic effects of *o*-benzyl-*p*-chlorophenol and no apparent difference existed between males and females in the second 13-week study. Thus, the doses chosen for the 2-year study in mice were 0, 120, 240, or 480 mg/kg body weight for each sex. Toxicity was produced since body weights of all dosed males and of mid- and high-dose females were lower than those of the controls. Also, survival was reduced in all dosed groups of male mice and high-dose females, with increased numbers of moribund animals and spontaneous deaths. However, in the group with the lowest survival, the high-dose females, 51% survived to the end of the 2-year study and 12 were killed moribund so that adequate numbers were available for histopathologic evaluation. The severity of nephropathy increased with dose in males, and both the incidence and severity of nephropathy increased with dose in females. Thus, these doses demonstrated toxicity and the survival was high enough for evaluation of the chronic toxicity and carcinogenicity of *o*-benzyl-*p*-chlorophenol in mice.

A variety of neoplasms occurred in control and dosed male and female F344/N rats. No neoplasms were considered compound induced. A few renal neoplasms occurred, but the incidences were very low (single incidences of transitional cell carcinoma in female rats receiving 240 and 480 mg/kg). While transitional cell carcinoma has not occurred in control female rats (0/1,068), the lack of an increased incidence after step-section review justified the call of equivocal evidence of carcinogenic activity. A higher incidence of renal neoplasms occurred in the kidney of male mice and included renal tubule adenoma and carcinoma. These incidences in the standard evaluation are outside the range of historical control values (males: adenoma 4/949, range 0% to 2%; carcinoma 0/949) and indicated some evidence of carcinogenic activity, a finding supported by the extended evaluation. The neoplasms were accompanied by renal tubule hyperplasia, supporting the conclusion of a proliferative response of renal tubule epithelium to *o*-benzyl-*p*-chlorophenol administration. No renal neoplasms were found in control mice. In control male mice from five studies to date, no additional renal tubule adenomas or carcinomas were identified through extended step-section review (NTP, 1991; NTP, 1992a,b,c; NTP, 1993). While this database is small, the absence of renal neoplasms in these extended evaluations suggests that renal neoplasms are very rare in control male mice, strengthening the evidence for chemical-induced effects observed in this study.

The mechanism of induction of renal tubule neoplasms is not established and the induction of these neoplasms in male mice is unique among several germicides tested for carcinogenicity. While there was clear evidence of carcinogenicity in male F344/N rats receiving 1,4-dichlorobenzene based on increased incidences of renal tubule carcinomas, no renal neoplasms occurred in female rats or male and female mice (NTP, 1987). Other phenolic disinfectants were negative for induction of renal neoplasms, including phenol in rats and mice (NCI, 1980), *o*-phenylphenol in mice (NTP, 1986), and hexachlorophene in rats (NCI, 1978a). Other compounds considered positive for induction of renal neoplasms in male mice include bromodichloromethane (NTP, 1988), nitrilotriacetic acid (NCI, 1977), tris(2,3-dibromopropyl)phosphate (NCI, 1978b) and 2,4-diaminophenol dihydrochloride (NTP, 1992c).

There was some evidence of carcinogenicity in F344/N rats receiving quercetin based on production of renal tubule adenomas or carcinomas (NTP, 1992a).

The chemicals active as renal tubule carcinogens represent a variety of chemical structures and include both genotoxic and nongenotoxic substances. Thus, both primary and secondary mechanisms probably are operative in the induction of the renal neoplasms. A specific mechanism has not been studied for *o*-benzyl-*p*-chlorophenol, but the chemical is mutagenic in certain test systems and not mutagenic in others. When applied topically, *o*-benzyl-*p*-chlorophenol was active neither as an initiator nor as a complete carcinogen; however, *o*-benzyl-*p*-chlorophenol did weakly promote skin neoplasms following initiation with 7,12-dimethylbenz(a)anthracene (NTP, 1994). Thus, the available evidence suggests that *o*-benzyl-*p*-chlorophenol is at best a weak carcinogen acting through a nongenotoxic mechanism. Cellular proliferative lesions induced by the nephropathy possibly provided a background for genetic mutations, resulting in the low incidence of renal neoplasms in male mice (and possibly female rats). Increased severity of nephropathy in male mice may explain the difference in tumorigenic response between male and female mice. The incidence of other neoplasms was considered usual in type and incidence for the $B6C3F_1$ mouse and within historical control ranges. None were considered related to the administration of *o*-benzyl-*p*-chlorophenol.

CONCLUSIONS

Under the conditions of these 2-year gavage studies, there was *no evidence of carcinogenic activity** of *o*-benzyl-*p*-chlorophenol in male F344/N rats receiving 30, 60, or 120 mg/kg body weight. There was *equivocal evidence of carcinogenic activity* of *o*-benzyl-*p*-chlorophenol in female F344/N rats based on the occurrence of two rare renal transitional cell carcinomas. There was *some evidence of carcinogenic activity* of *o*-benzyl-*p*-chlorophenol in male $B6C3F_1$ mice based on increased incidences of renal tubule adenoma and renal tubule adenoma or carcinoma (combined). There was *no evidence of carcinogenic activity* of *o*-benzyl-*p*-chlorophenol in female $B6C3F_1$ mice receiving 120, 240, or 480 mg/kg.

o-Benzyl-*p*-chlorophenol was nephrotoxic for male and female F344/N rats and $B6C3F_1$ mice. The severity of nephropathy was increased in male and female rats and the incidence and severity of nephropathy was increased in male and female mice. The incidence and severity of nephropathy increased with length of treatment. Other lesions considered to be associated with the nephropathy and the secondary hyperparathyroidism in male rats and in male and female mice included fibrous osteodystrophy and soft tissue mineralization. Increased incidences of squamous cell hyperplasia of the forestomach were observed in mice.

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* Explanation of Levels of Evidence of Carcinogenic Activity is on page 11. A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 13.

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APPENDIX A
SUMMARY OF LESIONS IN MALE RATS IN THE 2-YEAR GAVAGE STUDY OF *o*-BENZYL-*p*-CHLOROPHENOL

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Disposition Summary				
Animals initially in study[b]	80	80	80	80
3-Month interim evaluation[c]	10	10	10	9
15-Month interim evaluation				
Histopathology	10	10	10	9
Clinical pathology	10	10	10	7
Early deaths				
Accidental deaths	6	2	5	7
Moribund	16	13	14	14
Natural deaths	5	11	6	10
Survivors				
Terminal sacrifice	23	24	25	24
Animals examined microscopically	70	70	70	73
15-Month Interim Evaluation				
Alimentary System				
None				
Cardiovascular System				
None				
Endocrine System				
Parathyroid gland	(9)			(7)
Carcinoma	1 (11%)			
Pituitary gland	(10)	(1)		(9)
Pars distalis, adenoma	2 (20%)	1 (100%)		
General Body System				
None				
Genital System				
Preputial gland	(10)	(2)		(9)
Adenoma	1 (10%)	1 (50%)		
Carcinoma		1 (50%)		
Testes	(10)	(1)	(1)	(9)
Sertoli cell tumor benign	1 (10%)			
Bilateral, interstitial cell, adenoma	2 (20%)			1 (11%)
Interstitial cell, adenoma	5 (50%)	1 (100%)		3 (33%)
Hematopoietic System				
None				

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
15-Month Interim Evaluation (continued)				
Integumentary System				
Skin	(10)	(1)		(9)
Basal cell adenoma				1 (11%)
Squamous cell papilloma		1 (100%)		
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Esophagus	(50)	(50)	(50)	(51)
Carcinoma			1 (2%)	
Intestine large, cecum	(48)	(48)	(49)	(48)
Intestine large, colon	(50)	(50)	(49)	(50)
Leiomyosarcoma, metastatic, uncertain primary site		1 (2%)		
Polyp adenomatous		1 (2%)		
Sarcoma, metastatic, uncertain primary site		1 (2%)		
Intestine large, rectum	(50)	(49)	(49)	(49)
Intestine small, duodenum	(49)	(49)	(49)	(50)
Carcinoma, metastatic, uncertain primary site			1 (2%)	
Intestine small, jejunum	(49)	(48)	(48)	(50)
Adenocarcinoma			1 (2%)	
Leiomyosarcoma			1 (2%)	
Leiomyosarcoma, metastatic, uncertain primary site		1 (2%)		

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Liver	(50)	(50)	(50)	(51)
Hepatocellular adenoma		1 (2%)		1 (2%)
Sarcoma, metastatic, skin				1 (2%)
Sarcoma, metastatic, uncertain primary site		1 (2%)		
Mesentery	(10)	(13)	(6)	(6)
Carcinoma, metastatic, uncertain primary site			1 (17%)	
Hemangioma		1 (8%)		
Leiomyosarcoma, metastatic, uncertain primary site		1 (8%)		
Sarcoma, metastatic, uncertain primary site		1 (8%)		
Pancreas	(49)	(47)	(48)	(49)
Carcinoma, metastatic, uncertain primary site			1 (2%)	
Sarcoma, metastatic, uncertain primary site		1 (2%)		
Acinus, adenoma	1 (2%)		2 (4%)	
Acinus, adenoma, multiple		1 (2%)		1 (2%)
Pharynx				(1)
Palate, squamous cell papilloma				1 (100%)
Salivary glands	(50)	(50)	(49)	(49)
Stomach, forestomach	(49)	(50)	(49)	(51)
Carcinoma, metastatic, uncertain primary site			1 (2%)	
Squamous cell papilloma	1 (2%)		1 (2%)	
Stomach, glandular	(49)	(49)	(49)	(50)
Carcinoma, metastatic, uncertain primary site			1 (2%)	
Tooth		(1)		
Mixed tumor NOS		1 (100%)		
Cardiovascular System				
Heart	(50)	(50)	(50)	(51)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(51)
Adenoma			1 (2%)	
Carcinoma, metastatic, uncertain primary site			1 (2%)	
Adrenal gland, medulla	(50)	(50)	(49)	(50)
Pheochromocytoma malignant	1 (2%)	1 (2%)	1 (2%)	1 (2%)
Pheochromocytoma benign	12 (24%)	7 (14%)	6 (12%)	9 (18%)
Bilateral, pheochromocytoma malignant				1 (2%)
Bilateral, pheochromocytoma benign	1 (2%)		3 (6%)	4 (8%)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol
(continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Endocrine System (continued)				
Islets, pancreatic	(49)	(47)	(48)	(50)
Adenoma		1 (2%)		
Carcinoma	2 (4%)		2 (4%)	2 (4%)
Parathyroid gland	(47)	(47)	(45)	(46)
Adenoma		1 (2%)		
Pituitary gland	(48)	(50)	(49)	(51)
Pars distalis, adenoma	16 (33%)	11 (22%)	18 (37%)	13 (25%)
Pars distalis, carcinoma	2 (4%)			
Thyroid gland	(49)	(50)	(47)	(50)
Bilateral, C-cell, adenoma	1 (2%)			
Bilateral, C-cell, carcinoma			1 (2%)	
C-cell, adenoma	8 (16%)	10 (20%)	5 (11%)	4 (8%)
C-cell, carcinoma	3 (6%)		2 (4%)	
Follicular cell, adenoma	2 (4%)	1 (2%)		1 (2%)
Follicular cell, carcinoma	1 (2%)	1 (2%)	1 (2%)	
General Body System				
None				
Genital System				
Epididymis	(50)	(49)	(50)	(51)
Preputial gland	(49)	(48)	(49)	(51)
Adenoma	6 (12%)	3 (6%)	2 (4%)	2 (4%)
Carcinoma	2 (4%)	2 (4%)	3 (6%)	
Prostate	(50)	(50)	(50)	(51)
Seminal vesicle	(50)	(50)	(50)	(51)
Carcinoma, metastatic, uncertain primary site			1 (2%)	
Testes	(50)	(48)	(50)	(51)
Bilateral, interstitial cell, adenoma	33 (66%)	33 (69%)	29 (58%)	31 (61%)
Interstitial cell, adenoma	5 (10%)	8 (17%)	10 (20%)	11 (22%)
Hematopoietic System				
Bone marrow	(50)	(50)	(49)	(51)
Lymph node	(50)	(50)	(50)	(50)
Deep cervical, carcinoma, metastatic, thyroid gland	1 (2%)			
Mediastinal, carcinoma, metastatic, uncertain primary site			1 (2%)	
Mediastinal, carcinoma adenosquamous, metastatic, lung	1 (2%)			
Mediastinal, sarcoma, metastatic, uncertain primary site		1 (2%)		
Lymph node, mandibular	(49)	(50)	(48)	(49)
Lymph node, mesenteric	(49)	(48)	(50)	(49)

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Hematopoietic System (continued)				
Spleen	(50)	(49)	(50)	(50)
Fibrosarcoma		1 (2%)		
Leiomyosarcoma, metastatic, uncertain primary site		1 (2%)		
Sarcoma, metastatic, uncertain primary site		1 (2%)		
Thymus	(45)	(46)	(48)	(47)
Integumentary System				
Mammary gland	(37)	(44)	(44)	(41)
Fibroadenoma	2 (5%)	2 (5%)	2 (5%)	1 (2%)
Skin	(49)	(50)	(50)	(51)
Basal cell adenoma, multiple			1 (2%)	
Basosquamous tumor malignant	1 (2%)	1 (2%)		
Keratoacanthoma	6 (12%)	4 (8%)	2 (4%)	1 (2%)
Squamous cell carcinoma			1 (2%)	
Squamous cell papilloma		4 (8%)	1 (2%)	1 (2%)
Sebaceous gland, adenoma			1 (2%)	
Subcutaneous tissue, fibroma	1 (2%)	1 (2%)	1 (2%)	2 (4%)
Subcutaneous tissue, fibrosarcoma	1 (2%)	1 (2%)	1 (2%)	
Subcutaneous tissue, hemangiosarcoma	1 (2%)			
Subcutaneous tissue, lipoma		1 (2%)	1 (2%)	
Subcutaneous tissue, sarcoma			1 (2%)	1 (2%)
Musculoskeletal System				
Skeletal muscle	(2)	(3)		
Chordoma		1 (33%)		
Fibrosarcoma	1 (50%)			
Leiomyosarcoma, metastatic, uncertain primary site		1 (33%)		
Sarcoma, metastatic, uncertain primary site		1 (33%)		
Nervous System				
Brain	(50)	(50)	(50)	(51)
Astrocytoma benign	1 (2%)			
Astrocytoma malignant		1 (2%)		
Carcinoma, metastatic, pituitary gland	2 (4%)			
Peripheral nerve	(2)	(1)	(1)	
Schwannoma benign		1 (100%)		
Spinal cord	(3)		(1)	
Chordoma	1 (33%)			

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol
(continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Respiratory System				
Lung	(50)	(50)	(50)	(51)
Alveolar/bronchiolar adenoma		1 (2%)		
Alveolar/bronchiolar carcinoma	2 (4%)		1 (2%)	
Carcinoma, metastatic, preputial gland			1 (2%)	
Carcinoma, metastatic, thyroid gland			1 (2%)	
Carcinoma, metastatic, uncertain primary site			1 (2%)	
Carcinoma adenosquamous	1 (2%)			
Chordoma, metastatic, spinal cord	1 (2%)			
Chordoma, metastatic, uncertain primary site	1 (2%)			
Squamous cell carcinoma			1 (2%)	
Squamous cell carcinoma, metastatic, multiple, uncertain primary site			1 (2%)	
Mediastinum, carcinoma, metastatic, thyroid gland			1 (2%)	
Nose	(50)	(50)	(48)	(51)
Papilloma		1 (2%)		
Special Senses System				
Ear	(1)		(1)	(2)
Pinna, squamous cell papilloma	1 (100%)			1 (50%)
Zymbal's gland		(1)	(1)	(2)
Adenoma		1 (100%)		1 (50%)
Carcinoma			1 (100%)	1 (50%)
Urinary System				
Kidney	(50)	(49)	(50)	(50)
Renal tubule, adenoma	1 (2%)			
Renal tubule, carcinoma				1 (2%)
Urinary bladder	(50)	(50)	(50)	(50)
Transitional epithelium, papilloma	1 (2%)			
Systemic Lesions				
Multiple organs[d]	(50)	(50)	(50)	(51)
Leukemia mononuclear	10 (20%)	9 (18%)	10 (20%)	10 (20%)
Mesothelioma benign	4 (8%)	1 (2%)		
Mesothelioma malignant		1 (2%)		

TABLE A1
Summary of the Incidence of Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol
(continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Neoplasm Summary				
Total animals with primary neoplasms[e]				
15-Month interim evaluation	9	4		5
2-Year study	45	48	45	44
Total primary neoplasms				
15-Month interim evaluation	12	5		5
2-Year study	132	116	115	102
Total animals with benign neoplasms				
15-Month interim evaluation	8	4		5
2-Year study	45	48	44	44
Total benign neoplasms				
15-Month interim evaluation	11	4		5
2-Year study	103	96	86	85
Total animals with malignant neoplasms				
15-Month interim evaluation	1	1		
2-Year study	23	17	22	15
Total malignant neoplasms				
15-Month interim evaluation	1	1		
2-Year study	29	19	29	17
Total animals with metastatic neoplasms				
2-Year study	6	2	4	1
Total metastatic neoplasms				
2-Year study	6	12	13	1
Total animals with malignant neoplasms uncertain primary site				
2-Year study	1	2	2	
Total animals with neoplasms uncertain-benign or malignant				
2-Year study		1		
Total uncertain neoplasms				
2-Year study		1		

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Seven or ten of the 80 animals in each dose group were evaluated for clinical pathology only.
[c] No lesions were observed at the 3-month interim evaluation.
[d] Number of animals with any tissue examined microscopically
[e] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control

Number of Days on Study	0 2 5	0 3 7	1 9 7	4 5 7	4 6 5	4 6 7	5 0 0	5 2 1	5 3 3	5 4 3	6 1 0	6 2 4	6 2 4	6 3 8	6 5 5	6 6 0	6 7 0	6 8 3	6 8 7	6 8 7	6 9 5	6 9 6	7 1 1	7 2 2	7 2 3
Carcass ID Number	0 0 7 2	0 0 4 4	0 1 2 5	0 0 5 2	0 0 8 1	0 1 0 3	0 0 2 2	0 0 1 3	0 0 2 4	0 0 3 4	0 0 1 1	0 0 8 2	0 0 9 4	0 1 1 5	0 1 0 4	0 1 9 3	0 0 2 1	0 0 5 5	0 0 7 5	0 0 9 2	0 0 7 3	0 0 1 5	0 0 9 5	0 0 8 3	0 0 5 3
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery							+		+									+			+	+			
Pancreas	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																		X							
Stomach, glandular	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign														X						X					X
Bilateral, pheochromocytoma benign																							X		
Islets, pancreatic	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Parathyroid gland	+	+	A	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma				X				X			X	X	X							X	X	X		X	
Pars distalis, carcinoma																			X						
Thyroid gland	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, C-cell, adenoma																									X
C-cell, adenoma												X			X										
C-cell, carcinoma																									
Follicular cell, adenoma					X																	X			
Follicular cell, carcinoma																					X				
General Body System																									
None																									

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 4	7 2 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 1 1 4	0 1 0 2	0 0 1 2	0 0 1 4	0 0 2 3	0 0 2 5	0 0 3 5	0 0 4 1	0 0 4 2	0 0 4 3	0 0 5 1	0 0 5 4	0 0 6 1	0 0 6 2	0 0 6 5	0 0 7 1	0 0 8 4	0 0 9 1	0 1 0 1	0 1 1 2	0 1 1 3	0 1 1 1	0 1 2 2	0 1 2 3	0 1 2 4	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery				+							+	+										+		+		10
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinus, adenoma										X																1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell papilloma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																X										1
Pheochromocytoma benign	X	X	X		X	X	X	X									X	X								12
Bilateral, pheochromocytoma benign																										1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma	X	X																								2
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	48
Pars distalis, adenoma	X			X	X														X				X	X	X	16
Pars distalis, carcinoma								X																		2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bilateral, C-cell, adenoma																										1
C-cell, adenoma										X			X							X		X		X	X	8
C-cell, carcinoma														X					X	X						3
Follicular cell, adenoma																										2
Follicular cell, carcinoma																										1
General Body System																										
None																										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	0 2 5	0 3 7	1 9 7	4 5 7	4 6 5	4 6 7	5 0 0	5 2 1	5 3 3	5 4 3	6 1 0	6 2 4	6 2 4	6 3 8	6 5 5	6 6 0	6 7 0	6 8 3	6 8 7	6 8 7	6 9 5	6 9 6	7 1 1	7 2 2	7 2 3
Carcass ID Number	0 0 7 2	0 0 4 4	0 1 2 5	0 0 5 2	0 0 8 1	0 1 0 3	0 0 2 2	0 0 1 3	0 0 2 4	0 0 3 4	0 0 1 1	0 0 8 2	0 0 9 4	0 1 1 5	1 1 0 4	0 0 9 3	0 0 2 1	0 0 5 5	0 0 7 5	0 0 9 2	0 0 7 3	0 0 1 5	0 0 9 5	0 0 8 3	0 0 5 3
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+
Adenoma				X							X										X				
Carcinoma										X						X									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma					X				X	X	X		X		X	X	X	X	X						X
Interstitial cell, adenoma							X														X			X	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Deep cervical, carcinoma, metastatic, thyroid gland																									
Mediastinal, carcinoma adenosquamous, metastatic, lung																									
Lymph node, mandibular	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Integumentary System																									
Mammary gland	+	+	M	+	M	M	+	M	+	+	+	M	+	+	+	+	+	+	+	M	+	M	+	+	+
Fibroadenoma																	X								
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basosquamous tumor malignant																									
Keratoacanthoma											X	X						X							
Subcutaneous tissue, fibroma				X																					
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, hemangiosarcoma															X										
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle														+											
Fibrosarcoma																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma benign														X											
Carcinoma, metastatic, pituitary gland																			X						
Peripheral nerve																			+					+	
Spinal cord												+							+					+	
Chordoma																								X	

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 4	7 2 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 1 1 4	0 1 0 2	0 0 1 2	0 0 1 4	0 0 2 3	0 0 2 5	0 0 3 5	0 0 4 1	0 0 4 2	0 0 4 3	0 0 5 1	0 0 5 4	0 0 6 1	0 0 6 2	0 0 6 5	0 0 7 1	0 0 8 4	0 0 9 1	0 1 0 1	0 1 1 2	0 1 1 3	0 1 2 1	0 2 2 2	0 2 2 3	0 2 2 4	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma				X																X		X				6
Carcinoma																										2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				X	X	X	X	33
Interstitial cell, adenoma																			X	X						5
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Deep cervical, carcinoma, metastatic, thyroid gland																			X							1
Mediastinal, carcinoma adenosquamous, metastatic, lung		X																								1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	45
Integumentary System																										
Mammary gland	+	M	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	M	+	M	+	+	M	+	37
Fibroadenoma	X																									2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	49
Basosquamous tumor malignant																						X				1
Keratoacanthoma									X	X	X															6
Subcutaneous tissue, fibroma																										1
Subcutaneous tissue, fibrosarcoma									X																	1
Subcutaneous tissue, hemangiosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle					+																					2
Fibrosarcoma					X																					1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma benign																										1
Carcinoma, metastatic, pituitary gland								X																		2
Peripheral nerve																										2
Spinal cord																										3
Chordoma																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	0	0	1	4	4	4	5	5	5	5	6	6	6	6	6	6	6	6	6	6	6	7	7	7
	2	3	9	5	6	6	0	2	3	4	1	2	2	3	5	6	7	8	8	8	9	9	1	2	2
	5	7	7	7	5	7	0	1	3	3	0	4	4	8	5	0	0	3	7	7	5	6	1	2	3
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	1	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
	7	4	2	5	8	0	2	1	2	3	1	8	9	1	0	9	2	5	7	9	7	1	9	8	5
	2	4	5	2	1	3	2	3	4	4	1	2	4	5	4	3	1	5	5	2	3	5	5	3	3
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																						X			
Carcinoma adenosquamous																									
Chordoma, metastatic, spinal cord																									X
Chordoma, metastatic, uncertain primary site												X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Pinna, squamous cell papilloma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional epithelium, papilloma																		X							
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X		X					X	X		X		X	X	
Mesothelioma benign							X																		X

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 4	7 2 6	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 1 1 4	0 1 0 2	0 0 1 2	0 0 1 4	0 0 2 3	0 0 2 5	0 0 3 5	0 0 4 1	0 0 4 2	0 0 4 3	0 0 5 1	0 0 5 4	0 0 6 1	0 0 6 2	0 0 6 5	0 0 7 1	0 0 8 4	0 0 9 1	0 1 0 1	0 1 1 2	0 1 1 3	0 1 2 1	0 1 2 2	0 1 2 3	0 1 2 4	Total Tissues/ Tumors
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma				X																						2
Carcinoma adenosquamous		X																								1
Chordoma, metastatic, spinal cord																										1
Chordoma, metastatic, uncertain primary site																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																			+							1
Pinna, squamous cell papilloma																			X							1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenoma																							X			1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Transitional epithelium, papilloma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X	X							X																	10
Mesothelioma benign																						X			X	4

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 30 mg/kg

Number of Days on Study	0 3 2	1 5 8	4 3 9	4 5 6	4 9 3	5 0 9	5 2 5	5 2 5	5 2 9	5 4 3	5 4 7	5 6 2	6 0 3	6 2 2	6 3 1	6 5 6	6 5 9	6 6 0	6 6 9	6 8 4	7 1 1	7 1 3	7 1 9	7 2 2	7 2 3
Carcass ID Number	0 2 4 4	0 2 1 1	0 1 8 1	0 2 0 4	0 1 9 4	0 2 1 3	0 2 2 5	0 2 8 4	0 1 7 1	0 2 7 2	0 2 5 4	0 2 6 4	0 2 8 3	0 1 9 2	0 2 5 3	0 2 0 3	0 2 6 2	0 2 6 1	0 2 7 3	0 2 0 5	0 2 7 1	0 2 4 2	0 2 3 5	0 1 9 1	0 2 0 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma, metastatic, uncertain primary site																		X							
Polyp adenomatous																									
Sarcoma, metastatic, uncertain primary site															X										
Intestine large, rectum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma, metastatic, uncertain primary site																		X							
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Sarcoma, metastatic, uncertain primary site															X										
Mesentery												+	+	+	+	+	+		+		+				
Hemangioma																									
Leiomyosarcoma, metastatic, uncertain primary site																		X							
Sarcoma, metastatic, uncertain primary site															X										
Pancreas	+	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, metastatic, uncertain primary site															X										
Acinus, adenoma, multiple																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																	+								
Mixed tumor NOS																	X								
Cardiovascular System																									
Blood vessel																						+			
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign																			X				X		

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 30 mg/kg
(continued)

Number of Days on Study	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 2 7 4	0 1 7 3	0 1 7 4	0 1 7 5	0 1 8 2	0 1 8 3	0 1 8 4	0 1 8 5	0 1 9 3	0 1 9 5	0 2 0 1	0 2 2 1	0 2 2 4	0 2 3 1	0 2 3 3	0 2 3 4	0 2 4 3	0 2 4 5	0 2 5 1	0 2 5 5	0 2 6 3	0 2 6 5	0 2 8 1	0 2 8 2	0 2 8 5	Total Tissues/ Tumors
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma, metastatic, uncertain primary site																									1
Polyp adenomatous																							X		1
Sarcoma, metastatic, uncertain primary site																									1
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leiomyosarcoma, metastatic, uncertain primary site																									1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																						X			1
Sarcoma, metastatic, uncertain primary site																									1
Mesentery						+											+		+				+	+	13
Hemangioma																								X	1
Leiomyosarcoma, metastatic, uncertain primary site																									1
Sarcoma, metastatic, uncertain primary site																									1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Sarcoma, metastatic, uncertain primary site																									1
Acinus, adenoma, multiple			X																						1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Tooth																									1
Mixed tumor NOS																									1
Cardiovascular System																									
Blood vessel				+																					2
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant						X																			1
Pheochromocytoma benign			X			X								X				X						X	7

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 30 mg/kg
(continued)

Number of Days on Study	0 3 2	1 5 8	4 3 9	4 5 6	4 9 3	5 0 9	5 2 5	5 2 5	5 2 9	5 4 3	5 4 7	5 6 2	6 0 3	6 2 2	6 3 1	6 5 6	6 5 9	6 6 0	6 6 9	6 8 4	7 1 1	7 1 3	7 1 9	7 2 2	7 2 3
Carcass ID Number	0 2 4 4	0 2 1 1	0 1 8 1	0 2 0 4	0 1 9 4	0 2 1 3	0 2 2 5	0 2 8 4	0 1 7 1	0 2 7 2	0 2 5 4	0 2 6 4	0 2 8 3	0 1 9 2	0 2 5 3	0 2 0 3	0 2 6 3	0 2 6 1	0 2 7 3	0 2 0 5	0 2 7 1	0 2 4 2	0 2 3 5	0 1 9 1	0 2 0 2
Endocrine System (continued)																									
Islets, pancreatic	+	+	A	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																X									
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																							X		
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma				X				X		X	X	X		X					X						
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma					X								X							X				X	
Follicular cell, adenoma																X									
Follicular cell, carcinoma																					X				
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+
Adenoma																							X		
Carcinoma											X														
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma			X						X	X			X		X	X		X		X	X	X	X	X	X
Interstitial cell, adenoma						X	X										X								
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, sarcoma, metastatic, uncertain primary site															X										
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	M	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma																				X					
Leiomyosarcoma, metastatic, uncertain primary site																		X							
Sarcoma, metastatic, uncertain primary site															X										
Thymus	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+
Integumentary System																									
Mammary gland	M	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	+	+
Fibroadenoma								X																X	

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 30 mg/kg (continued)

Number of Days on Study	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 2 7 4	0 1 7 3	0 1 7 4	0 1 7 5	0 1 8 2	0 1 8 3	0 1 8 4	0 1 8 5	0 1 9 3	0 1 9 5	0 2 0 1	0 2 2 1	0 2 2 4	0 2 3 1	0 2 3 3	0 2 3 4	0 2 4 3	0 2 4 5	0 2 5 1	0 2 5 5	0 2 6 3	0 2 6 5	0 2 8 1	0 2 8 2	0 2 8 5	Total Tissues/ Tumors
Endocrine System (continued)																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																									1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	47
Adenoma																									1
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X					X												X			X		11
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma		X							X						X	X			X		X				10
Follicular cell, adenoma																									1
Follicular cell, carcinoma																									1
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma													X	X											3
Carcinoma															X										2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Bilateral, interstitial cell, adenoma	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X				X	X	X	X		X	33
Interstitial cell, adenoma					X												X	X	X					X		8
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, sarcoma, metastatic, uncertain primary site																									1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Fibrosarcoma																									1
Leiomyosarcoma, metastatic, uncertain primary site																									1
Sarcoma, metastatic, uncertain primary site																									1
Thymus	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Integumentary System																									
Mammary gland	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Fibroadenoma																									2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 30 mg/kg
(continued)

Number of Days on Study	0 3 2	1 5 8	4 3 9	4 5 6	4 9 3	5 0 9	5 2 5	5 2 5	5 2 9	5 4 3	5 4 7	5 6 2	6 0 3	6 2 2	6 3 1	6 5 6	6 5 9	6 6 0	6 6 9	6 8 4	7 1 1	7 1 3	7 1 9	7 2 2	7 2 3
Carcass ID Number	0 2 4 4	0 2 1 1	0 1 8 1	0 2 0 4	0 1 9 4	0 2 1 3	0 2 2 5	0 2 8 4	0 2 7 1	0 2 7 2	0 2 5 4	0 2 6 4	0 2 8 3	0 1 9 2	0 2 5 3	0 2 0 3	0 2 6 2	0 2 6 1	0 2 7 3	0 2 0 5	0 2 7 1	0 2 4 2	0 2 3 5	0 1 9 1	0 2 0 2
Integumentary System (continued)																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basosquamous tumor malignant																									
Keratoacanthoma																									
Squamous cell papilloma														X						X					
Subcutaneous tissue, fibroma																X									
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, lipoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle									+						+			+							
Chordoma									X																
Leiomyosarcoma, metastatic, uncertain primary site																		X							
Sarcoma, metastatic, uncertain primary site															X										
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma malignant					X																				
Peripheral nerve			+																						
Schwannoma benign			X																						
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye		+																+			+				
Zymbal's gland																									
Adenoma																									
Urinary System																									
Kidney	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear													X			X									X
Mesothelioma benign																									
Mesothelioma malignant																				X					

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 30 mg/kg (continued)

Number of Days on Study	7 2 5	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 2 7 4	0 1 7 3	0 1 7 4	0 1 7 5	0 1 8 2	0 1 8 3	0 1 8 4	0 1 8 5	0 1 9 3	0 1 9 5	0 2 0 1	0 2 2 1	0 2 2 4	0 2 3 1	0 2 3 3	0 2 3 4	0 2 4 3	0 2 4 5	0 2 5 1	0 2 5 5	0 2 6 3	0 2 6 5	0 2 8 1	0 2 8 2	0 2 8 5	Total Tissues/ Tumors
Integumentary System (continued)																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basosquamous tumor malignant																							X			1
Keratoacanthoma							X								X	X								X		4
Squamous cell papilloma											X									X						4
Subcutaneous tissue, fibroma																										1
Subcutaneous tissue, fibrosarcoma																								X		1
Subcutaneous tissue, lipoma									X																	1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										3
Chordoma																										1
Leiomyosarcoma, metastatic, uncertain primary site																										1
Sarcoma, metastatic, uncertain primary site																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma malignant																										1
Peripheral nerve																										1
Schwannoma benign																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma									X																	1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma											X															1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye																										3
Zymbal's gland															+											1
Adenoma															X											1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X										X			X				X	X					X		9
Mesothelioma benign																			X							1
Mesothelioma malignant																										1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg

Number of Days on Study	0 6 1	1 9 7	2 7 4	3 0 6	3 1 9	4 6 3	4 9 2	5 1 5	5 2 1	5 5 4	5 6 2	5 6 5	5 7 9	6 3 3	6 5 4	6 6 1	6 6 1	6 6 6	6 7 8	6 9 6	7 9 4	9 0 7	7 1 1	7 3 3	7 2 6
Carcass ID Number	0 4 0 4	0 4 1 5	0 4 0 1	0 4 4 1	0 3 9 5	0 3 3 1	0 3 5 4	0 4 4 5	0 3 6 3	0 4 3 1	0 3 3 2	0 3 6 2	0 3 6 4	0 4 1 4	0 3 9 4	0 3 8 2	0 4 2 2	0 4 2 4	0 4 4 5	0 3 0 5	0 4 7 5	0 3 3 5	0 4 0 2	0 4 3 4	0 3 9 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma					X																				
Intestine large	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site																							X		
Intestine small, ileum	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																X									
Leiomyosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery																				+		+	+		
Carcinoma, metastatic, uncertain primary site																							X		
Pancreas	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site																							X		
Acinus, adenoma																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Stomach	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site																							X		
Squamous cell papilloma															X										
Stomach, glandular	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site																							X		
Cardiovascular System																									
Blood vessel																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma, metastatic, uncertain primary site																							X		
Adrenal gland, medulla	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Pheochromocytoma benign													X												
Bilateral, pheochromocytoma benign																				X					

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 3 3 3	0 3 3 5	0 3 4 2	0 3 4 3	0 3 4 4	0 3 5 1	0 3 5 2	0 3 5 5	0 3 6 1	0 3 6 5	0 3 7 1	0 3 7 3	0 3 8 3	0 3 8 4	0 3 8 5	0 3 9 2	0 3 9 3	0 4 0 3	0 4 1 1	0 4 1 2	0 4 1 3	0 4 3 2	0 4 3 4	0 4 4 2	0 4 4 4	Total Tissues/ Tumors
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																									1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, uncertain primary site																									1
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenocarcinoma																									1
Leiomyosarcoma						X																			1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery							+						+					+							6
Carcinoma, metastatic, uncertain primary site																									1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, uncertain primary site																									1
Acinus, adenoma													X			X									2
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, uncertain primary site																									1
Squamous cell papilloma																									1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, metastatic, uncertain primary site																									1
Cardiovascular System																									
Blood vessel				+																					1
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma			X																						1
Carcinoma, metastatic, uncertain primary site																									1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																		X							1
Pheochromocytoma benign		X												X	X									X	6
Bilateral, pheochromocytoma benign	X															X									3

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg
(continued)

Number of Days on Study	0 6 1	1 9 7	2 7 4	3 0 6	3 1 9	4 6 3	4 9 2	5 1 5	5 2 1	5 5 4	5 6 2	5 6 5	5 7 9	6 3 3	6 5 4	6 6 1	6 6 1	6 6 6	6 6 8	6 7 6	6 9 4	6 9 7	7 0 1	7 2 3	7 2 6
Carcass ID Number	0 4 0 4	0 4 1 5	0 4 0 1	0 4 1 1	0 3 9 5	0 3 3 1	0 3 5 4	0 4 4 5	0 3 6 3	0 4 3 1	0 3 3 2	0 3 6 2	0 3 6 4	0 4 1 4	0 3 9 4	0 3 8 2	0 3 2 2	0 4 2 4	0 3 4 5	0 4 0 5	0 3 7 5	0 4 3 5	0 4 0 2	0 3 3 4	0 3 9 1
Endocrine System (continued)																									
Islets, pancreatic	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																									
Parathyroid gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma								X	X			X	X				X	X	X		X			X	
Thyroid gland	+	A	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Bilateral, C-cell, carcinoma															X										
C-cell, adenoma								X												X					X
C-cell, carcinoma																									
Follicular cell, carcinoma																									
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma											X		X	X											
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, uncertain primary site																							X		
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma						X					X			X	X			X					X	X	
Interstitial cell, adenoma							X			X		X	X			X	X		X		X				
Hematopoietic System																									
Bone marrow	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinal, carcinoma, metastatic, uncertain primary site																							X		
Lymph node, mandibular	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	M	+	+	M	+	+	+	+	+	+	M	M	+	+	M	+	+	+
Fibroadenoma																X									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 3 3 3	0 3 3 5	0 3 4 2	0 3 4 3	0 3 4 4	0 3 5 1	0 3 5 2	0 3 5 5	0 3 6 1	0 3 6 5	0 3 7 1	0 3 7 3	0 3 8 3	0 3 8 4	0 3 8 5	0 3 9 2	0 3 9 3	0 4 0 3	0 4 1 1	0 4 1 2	0 4 1 3	0 4 3 2	0 4 3 4	0 4 4 2	0 4 4 4	Total Tissues/ Tumors
Endocrine System (continued)																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma									X									X							2
Parathyroid gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	45
Pituitary gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma	X	X	X		X	X						X						X		X	X				18
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Bilateral, C-cell, carcinoma																									1
C-cell, adenoma																				X			X		5
C-cell, carcinoma				X					X																2
Follicular cell, carcinoma								X																	1
General Body System																									
None																									
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma							X				X														2
Carcinoma																									3
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, uncertain primary site																									1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, interstitial cell, adenoma	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X		X	X	X	X	29
Interstitial cell, adenoma																		X		X					10
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mediastinal, carcinoma, metastatic, uncertain primary site																									1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Fibroadenoma							X																		2

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg
(continued)

Number of Days on Study	0 6 1	1 9 7	2 7 4	3 0 6	3 1 9	4 6 3	4 9 2	5 1 5	5 2 1	5 5 4	5 6 2	5 6 5	5 7 9	6 3 3	6 5 4	6 6 1	6 6 1	6 6 6	6 6 8	6 7 6	6 9 4	6 9 7	7 0 1	7 2 3	7 2 6
Carcass ID Number	0 4 0 4	0 4 1 5	0 4 0 1	0 4 1 1	0 3 9 5	0 3 3 1	0 3 5 4	0 4 6 5	0 3 3 1	0 4 3 2	0 3 3 2	0 3 6 2	0 3 6 4	0 4 1 4	0 3 9 4	0 3 8 2	0 4 2 2	0 4 2 4	0 3 4 5	0 4 0 5	0 3 7 5	0 4 3 5	0 4 0 2	0 3 3 4	0 3 9 1
Integumentary System (continued)																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell adenoma, multiple																									
Keratoacanthoma																									
Squamous cell carcinoma																									
Squamous cell papilloma																									
Sebaceous gland, adenoma																	X								
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, fibrosarcoma																									
Subcutaneous tissue, lipoma																									
Subcutaneous tissue, sarcoma																									X
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Peripheral nerve																		+							
Spinal cord																		+							
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Carcinoma, metastatic, preputial gland											X														
Carcinoma, metastatic, thyroid gland															X										
Carcinoma, metastatic, uncertain primary site																							X		
Squamous cell carcinoma																						X			
Squamous cell carcinoma, metastatic, multiple, uncertain primary site												X													
Mediastinum, carcinoma, metastatic, thyroid gland															X										
Nose	+	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																			+						
Eye																			+						
Zymbal's gland																									+
Carcinoma																									X
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear								X			X		X											X	

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 3 3 3	0 3 3 5	0 3 4 2	0 3 4 3	0 3 4 4	0 3 5 1	0 3 5 2	0 3 5 5	0 3 6 1	0 3 6 5	0 3 7 1	0 3 7 3	0 3 8 3	0 3 8 4	0 3 8 5	0 3 9 2	0 3 9 3	0 4 0 3	0 4 1 1	0 4 1 2	0 4 1 3	0 4 2 3	0 4 3 2	0 4 3 4	0 4 4 2	0 4 4 4	Total Tissues/ Tumors
Integumentary System (continued)																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Basal cell adenoma, multiple	X																									1
Keratoacanthoma		X															X									2
Squamous cell carcinoma																	X									1
Squamous cell papilloma																X										1
Sebaceous gland, adenoma																										1
Subcutaneous tissue, fibroma									X																	1
Subcutaneous tissue, fibrosarcoma																X										1
Subcutaneous tissue, lipoma						X																				1
Subcutaneous tissue, sarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma															X											1
Carcinoma, metastatic, preputial gland																										1
Carcinoma, metastatic, thyroid gland																										1
Carcinoma, metastatic, uncertain primary site																										1
Squamous cell carcinoma																										1
Squamous cell carcinoma, metastatic, multiple, uncertain primary site																										1
Mediastinum, carcinoma, metastatic, thyroid gland																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Ear																										1
Eye																										1
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear	X		X			X											X			X			X			10

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg

Number of Days on Study	0 1 3	0 8 0	1 2 2	1 5 0	3 2 4	3 2 7	4 3 1	4 5 9	4 5 9	4 6 4	5 0 8	5 2 7	5 4 1	5 4 3	5 6 8	5 9 1	6 4 1	6 4 8	6 8 7	6 8 7	6 9 4	6 9 5	7 1 6	7 1 7	7 1 9
Carcass ID Number	0 6 0 4	0 5 9 5	0 4 9 2	0 5 8 1	0 5 1 2	0 5 1 3	0 5 6 2	0 4 9 4	0 5 8 3	0 5 9 2	0 5 4 5	0 5 4 1	0 5 7 1	0 5 0 3	0 4 9 3	0 5 2 3	0 6 0 2	0 5 8 2	0 5 1 5	0 5 0 2	0 5 8 5	0 5 0 4	0 5 5 5	0 5 5 4	0 5 6 4	0 5 3 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	A	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	A	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Sarcoma, metastatic, skin																							X		
Mesentery																		+					+	+	
Pancreas	A	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+
Acinus, adenoma, multiple																									
Pharynx																									
Palate, squamous cell papilloma																									
Salivary glands	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																	X								
Pheochromocytoma benign																		X			X				
Bilateral, pheochromocytoma malignant																									
Bilateral, pheochromocytoma benign																									X
Islets, pancreatic	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																							X		
Parathyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma								X								X			X		X	X		
Thyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma																									
Follicular cell, adenoma																									
General Body System																									
None																									

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	7 1 9	7 2 0	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 4 1	0 5 2 5	0 5 9 1	0 5 0 1	0 5 0 5	0 5 1 1	0 5 1 4	0 5 1 1	0 5 2 2	0 5 2 4	0 5 3 2	0 5 3 3	0 5 3 4	0 5 3 5	0 5 4 2	0 5 4 3	0 5 6 1	0 5 7 2	0 5 7 3	0 5 7 4	0 5 7 5	0 5 8 4	0 5 9 3	0 5 9 4	0 6 0 1	0 6 0 5	Total Tissues/ Tumors
Alimentary System																											
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hepatocellular adenoma					X																						1
Sarcoma, metastatic, skin																											1
Mesentery								+	+																+		6
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Acinus, adenoma, multiple				X																							1
Pharynx									+																		1
Palate, squamous cell papilloma									X																		1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																											
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																											
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																											1
Pheochromocytoma benign			X	X									X	X		X			X				X				9
Bilateral, pheochromocytoma malignant								X																			1
Bilateral, pheochromocytoma benign	X																	X		X							4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma												X															2
Parathyroid gland	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pars distalis, adenoma					X	X	X					X			X	X	X					X					13
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma							X		X										X	X							
Follicular cell, adenoma			X																								
General Body System																											
None																											

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg
(continued)

Number of Days on Study	0 1 3	0 8 0	1 2 2	1 5 0	3 2 4	3 2 7	4 3 1	4 5 9	4 5 9	4 6 4	5 0 8	5 2 7	5 4 1	5 4 3	5 6 8	5 9 1	6 4 1	6 4 8	6 8 7	6 8 7	6 9 4	6 9 5	7 1 6	7 1 7	7 1 9
Carcass ID Number	0 6 0 4	0 5 9 5	0 4 9 2	0 5 8 1	0 5 1 2	0 5 1 3	0 5 6 2	0 4 9 4	0 5 8 3	0 5 9 2	0 5 4 5	0 5 7 1	0 5 0 3	0 4 9 3	0 5 2 3	0 6 0 2	0 5 8 2	0 5 1 5	0 5 0 2	0 5 8 5	0 5 0 4	0 5 5 5	0 5 5 4	0 5 6 4	0 5 3 1
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, interstitial cell, adenoma										X		X	X	X	X		X	X					X	X	X
Interstitial cell, adenoma							X	X			X					X			X	X	X				
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	M	M	+	+	+	+	+	M	+	M	M	+	+	M	+	+	+	+	+	M	+	+	+
Fibroadenoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Squamous cell papilloma																									
Subcutaneous tissue, fibroma																				X		X			
Subcutaneous tissue, sarcoma																							X		
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Pinna, squamous cell papilloma																									
Eye															+			+							
Zymbal's gland														+	+										
Adenoma														X											
Carcinoma															X										

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg
(continued)

Number of Days on Study	7 1 9	7 2 0	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 4 1	0 5 2 5	0 5 9 1	0 5 0 1	0 5 0 5	0 5 1 1	0 5 1 4	0 5 2 1	0 5 2 2	0 5 2 4	0 5 3 2	0 5 3 3	0 5 3 4	0 5 3 5	0 5 4 2	0 5 4 3	0 5 6 1	0 5 7 2	0 5 7 3	0 5 7 4	0 5 7 5	0 5 8 4	0 5 9 3	0 5 9 4	0 6 0 1	0 6 0 5	Total Tissues/ Tumors
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Preputial gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adenoma																			X		X						2
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Bilateral, interstitial cell, adenoma	X	X	X	X		X	X	X	X	X	X		X	X			X	X	X	X	X		X	X	X	X	31
Interstitial cell, adenoma					X										X	X						X					11
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	M	+	+	M	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	47
Integumentary System																											
Mammary gland	+	+	M	+	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Fibroadenoma							X																				1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Keratoacanthoma																					X						1
Squamous cell papilloma																				X							1
Subcutaneous tissue, fibroma																											2
Subcutaneous tissue, sarcoma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																											
Ear								+										+									2
Pinna, squamous cell papilloma																		X									1
Eye									+								+	+				+					6
Zymbal's gland																											2
Adenoma																											1
Carcinoma																											1

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg
(continued)

Number of Days on Study	0	0	1	1	3	3	4	4	4	4	5	5	5	5	5	6	6	6	6	6	7	7	7	
	1	8	2	5	2	2	3	5	5	6	0	2	4	4	6	9	4	4	8	8	9	9	1	1	1
	3	0	2	0	4	7	1	9	9	4	8	7	1	3	8	1	1	8	7	7	4	5	6	7	9
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	6	5	4	5	5	5	5	4	5	5	5	5	5	4	5	6	5	5	5	5	5	5	5	5	5
	0	9	9	8	1	1	6	9	8	9	4	7	0	9	2	0	8	1	0	8	0	5	5	6	3
	4	5	2	1	2	3	2	4	3	2	5	1	3	3	3	2	2	5	2	5	4	5	4	4	1
Urinary System																									
Kidney	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, carcinoma																									X
Urinary bladder	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear											X	X				X					X				

TABLE A2
Individual Animal Tumor Pathology of Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg
(continued)

Number of Days on Study	7 1 9	7 2 0	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 5 4 1	0 5 2 5	0 5 9 1	0 5 0 1	0 5 0 5	0 5 1 1	0 5 1 4	0 5 1 1	0 5 2 2	0 5 2 2	0 5 2 4	0 5 3 2	0 5 3 3	0 5 3 4	0 5 3 5	0 5 4 2	0 5 4 3	0 5 6 1	0 5 7 2	0 5 7 3	0 5 7 4	0 5 7 5	0 5 8 4	0 5 9 3	0 5 9 4	0 6 0 1	0 6 0 5	Total Tissues/ Tumors
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, carcinoma																											1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Leukemia mononuclear								X	X				X			X		X		X						10

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Adrenal Medulla: Benign Pheochromocytoma				
Overall rates[a]	13/50 (26%)	7/50 (14%)	9/49 (18%)	13/50 (26%)
Adjusted rates[b]	44.1%	26.1%	32.2%	45.6%
Terminal rates[c]	7/23 (30%)	5/24 (21%)	7/25 (28%)	9/24 (38%)
First incidence (days)	638	669	579	641
Life table tests[d]	P=0.404	P=0.104N	P=0.203N	P=0.562N
Logistic regression tests[d]	P=0.338	P=0.100N	P=0.247N	P=0.551
Cochran-Armitage test[d]	P=0.382			
Fisher exact test[d]		P=0.105N	P=0.251N	P=0.590N
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rates	14/50 (28%)	7/50 (14%)	10/49 (20%)	15/50 (30%)
Adjusted rates	47.6%	26.1%	35.9%	50.6%
Terminal rates	8/23 (35%)	5/24 (21%)	8/25 (32%)	10/24 (42%)
First incidence (days)	638	669	579	591
Life table tests	P=0.283	P=0.069N	P=0.202N	P=0.523
Logistic regression tests	P=0.216	P=0.064N	P=0.253N	P=0.440
Cochran-Armitage test	P=0.264			
Fisher exact test		P=0.070N	P=0.259N	P=0.500
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	16/48 (33%)	11/50 (22%)	18/49 (37%)	13/51 (25%)
Adjusted rates	46.2%	30.4%	52.4%	42.7%
Terminal rates	6/22 (27%)	4/24 (17%)	9/24 (38%)	8/24 (33%)
First incidence (days)	457	456	521	459
Life table tests	P=0.433N	P=0.197N	P=0.460	P=0.324N
Logistic regression tests	P=0.435N	P=0.152N	P=0.407	P=0.327N
Cochran-Armitage test	P=0.372N			
Fisher exact test		P=0.152N	P=0.445	P=0.262N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rates	18/48 (38%)	11/50 (22%)	18/49 (37%)	13/51 (25%)
Adjusted rates	51.2%	30.4%	52.4%	42.7%
Terminal rates	7/22 (32%)	4/24 (17%)	9/24 (38%)	8/24 (33%)
First incidence (days)	457	456	521	459
Life table tests	P=0.308N	P=0.112N	P=0.539N	P=0.198N
Logistic regression tests	P=0.299N	P=0.073N	P=0.575	P=0.190N
Cochran-Armitage test	P=0.244N			
Fisher exact test		P=0.072N	P=0.552N	P=0.142N
Preputial Gland: Adenoma				
Overall rates	6/49 (12%)	3/48 (6%)	2/49 (4%)	2/51 (4%)
Adjusted rates	19.8%	11.6%	8.0%	8.3%
Terminal rates	3/23 (13%)	2/24 (8%)	2/25 (8%)	2/24 (8%)
First incidence (days)	457	719	729 (T)	729 (T)
Life table tests	P=0.092N	P=0.239N	P=0.127N	P=0.137N
Logistic regression tests	P=0.097N	P=0.251N	P=0.133N	P=0.135N
Cochran-Armitage test	P=0.086N			
Fisher exact test		P=0.254N	P=0.134N	P=0.122N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Preputial Gland: Carcinoma				
Overall rates	2/49 (4%)	2/48 (4%)	3/49 (6%)	0/51 (0%)
Adjusted rates	5.2%	6.5%	7.6%	0.0%
Terminal rates	0/23 (0%)	1/24 (4%)	0/25 (0%)	0/24 (0%)
First incidence (days)	543	543	562	–[e]
Life table tests	P=0.216N	P=0.691	P=0.495	P=0.255N
Logistic regression tests	P=0.179N	P=0.686	P=0.493	P=0.223N
Cochran-Armitage test	P=0.188N			
Fisher exact test		P=0.684	P=0.500	P=0.238N
Preputial Gland: Adenoma or Carcinoma				
Overall rates	8/49 (16%)	5/48 (10%)	5/49 (10%)	2/51 (4%)
Adjusted rates	24.0%	17.7%	15.0%	8.3%
Terminal rates	3/23 (13%)	3/24 (13%)	2/25 (8%)	2/24 (8%)
First incidence (days)	457	543	562	729 (T)
Life table tests	P=0.045N	P=0.278N	P=0.276N	P=0.055N
Logistic regression tests	P=0.037N	P=0.287N	P=0.276N	P=0.046N
Cochran-Armitage test	P=0.034N			
Fisher exact test		P=0.290N	P=0.276N	P=0.040N
Skin: Keratoacanthoma				
Overall rates	6/50 (12%)	4/50 (8%)	2/50 (4%)	1/51 (2%)
Adjusted rates	19.9%	16.7%	8.0%	4.2%
Terminal rates	3/23 (13%)	4/24 (17%)	2/25 (8%)	1/24 (4%)
First incidence (days)	610	729 (T)	729 (T)	729 (T)
Life table tests	P=0.027N	P=0.365N	P=0.130N	P=0.063N
Logistic regression tests	P=0.032N	P=0.373N	P=0.140N	P=0.064N
Cochran-Armitage test	P=0.028N			
Fisher exact test		P=0.370N	P=0.134N	P=0.053N
Skin: Squamous Cell Papilloma				
Overall rates	0/50 (0%)	4/50 (8%)	1/50 (2%)	1/51 (2%)
Adjusted rates	0.0%	13.7%	4.0%	4.2%
Terminal rates	0/23 (0%)	2/24 (8%)	1/25 (4%)	1/24 (4%)
First incidence (days)	–	622	729 (T)	729 (T)
Life table tests	P=0.550N	P=0.066	P=0.517	P=0.508
Logistic regression tests	P=0.572N	P=0.062	P=0.517	P=0.508
Cochran-Armitage test	P=0.548N			
Fisher exact test		P=0.059	P=0.500	P=0.505
Skin: Squamous Cell Papilloma or Squamous Cell Carcinoma				
Overall rates	0/50 (0%)	4/50 (8%)	2/50 (4%)	1/51 (2%)
Adjusted rates	0.0%	13.7%	8.0%	4.2%
Terminal rates	0/23 (0%)	2/24 (8%)	2/25 (8%)	1/24 (4%)
First incidence (days)	–	622	729 (T)	729 (T)
Life table tests	P=0.570N	P=0.066	P=0.256	P=0.508
Logistic regression tests	P=0.595N	P=0.062	P=0.256	P=0.508
Cochran-Armitage test	P=0.569N			
Fisher exact test		P=0.059	P=0.247	P=0.505

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol
(continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Skin: Keratoacanthoma, Basal Cell Adenoma, or Squamous Cell Carcinoma				
Overall rates	6/50 (12%)	8/50 (16%)	4/50 (8%)	2/51 (4%)
Adjusted rates	19.9%	29.4%	16.0%	8.3%
Terminal rates	3/23 (13%)	6/24 (25%)	4/25 (16%)	2/24 (8%)
First incidence (days)	610	622	729 (T)	729 (T)
Life table tests	P=0.051N	P=0.393	P=0.348N	P=0.139N
Logistic regression tests	P=0.061N	P=0.381	P=0.383N	P=0.146N
Cochran-Armitage test	P=0.052N			
Fisher exact test		P=0.387	P=0.370N	P=0.128N
Skin (Subcutaneous Tissue): Fibroma, Fibrosarcoma, or Sarcoma				
Overall rates	2/50 (4%)	2/50 (4%)	3/50 (6%)	3/51 (6%)
Adjusted rates	6.4%	6.9%	11.5%	9.9%
Terminal rates	1/23 (4%)	1/24 (4%)	2/25 (8%)	0/24 (0%)
First incidence (days)	457	656	726	694
Life table tests	P=0.380	P=0.687N	P=0.526	P=0.510
Logistic regression tests	P=0.353	P=0.695	P=0.495	P=0.494
Cochran-Armitage test	P=0.381			
Fisher exact test		P=0.691N	P=0.500	P=0.509
Testes: Adenoma				
Overall rates	38/50 (76%)	41/48 (85%)	39/50 (78%)	42/51 (82%)
Adjusted rates	97.3%	100.0%	97.4%	97.6%
Terminal rates	22/23 (96%)	24/24 (100%)	24/25 (96%)	23/24 (96%)
First incidence (days)	465	439	463	431
Life table tests	P=0.323	P=0.419	P=0.523N	P=0.322
Logistic regression tests	P=0.060	P=0.160	P=0.390	P=0.068
Cochran-Armitage test	P=0.360			
Fisher exact test		P=0.178	P=0.500	P=0.294
Thyroid Gland (C-cell): Adenoma				
Overall rates	9/49 (18%)	10/50 (20%)	5/47 (11%)	4/50 (8%)
Adjusted rates	32.7%	33.4%	16.4%	16.7%
Terminal rates	6/23 (26%)	6/24 (25%)	2/25 (8%)	4/24 (17%)
First incidence (days)	624	493	515	729 (T)
Life table tests	P=0.050N	P=0.518	P=0.177N	P=0.110N
Logistic regression tests	P=0.057N	P=0.497	P=0.218N	P=0.126N
Cochran-Armitage test	P=0.048N			
Fisher exact test		P=0.520	P=0.217N	P=0.109N
Thyroid Gland (C-cell): Carcinoma				
Overall rates	3/49 (6%)	0/50 (0%)	3/47 (6%)	0/50 (0%)
Adjusted rates	13.0%	0.0%	10.6%	0.0%
Terminal rates	3/23 (13%)	0/24 (0%)	2/25 (8%)	0/24 (0%)
First incidence (days)	729 (T)	–	654	–
Life table tests	P=0.157N	P=0.111N	P=0.631N	P=0.111N
Logistic regression tests	P=0.170N	P=0.111N	P=0.644	P=0.111N
Cochran-Armitage test	P=0.163N			
Fisher exact test		P=0.117N	P=0.641	P=0.117N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rates	11/49 (22%)	10/50 (20%)	8/47 (17%)	4/50 (8%)
Adjusted rates	40.6%	33.4%	25.8%	16.7%
Terminal rates	8/23 (35%)	6/24 (25%)	4/25 (16%)	4/24 (17%)
First incidence (days)	624	493	515	729 (T)
Life table tests	P=0.028N	P=0.478N	P=0.268N	P=0.039N
Logistic regression tests	P=0.034N	P=0.506N	P=0.344N	P=0.048N
Cochran-Armitage test	P=0.028N			
Fisher exact test		P=0.479N	P=0.341N	P=0.041N
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rates	3/49 (6%)	2/50 (4%)	1/47 (2%)	1/50 (2%)
Adjusted rates	8.7%	6.0%	4.0%	4.2%
Terminal rates	0/23 (0%)	0/24 (0%)	1/25 (4%)	1/24 (4%)
First incidence (days)	465	631	729 (T)	729 (T)
Life table tests	P=0.206N	P=0.493N	P=0.308N	P=0.315N
Logistic regression tests	P=0.204N	P=0.490N	P=0.320N	P=0.300N
Cochran-Armitage test	P=0.198N			
Fisher exact test		P=0.490N	P=0.324N	P=0.301N
All Organs: Mononuclear Cell Leukemia				
Overall rates	10/50 (20%)	9/50 (18%)	10/50 (20%)	10/51 (20%)
Adjusted rates	29.5%	30.9%	32.1%	33.0%
Terminal rates	1/23 (4%)	5/24 (21%)	6/25 (24%)	6/24 (25%)
First incidence (days)	610	603	515	508
Life table tests	P=0.501	P=0.499N	P=0.576N	P=0.580
Logistic regression tests	P=0.473	P=0.505N	P=0.585	P=0.570
Cochran-Armitage test	P=0.533			
Fisher exact test		P=0.500N	P=0.598N	P=0.579N
All Organs: Benign or Malignant Mesothelioma				
Overall rates	4/50 (8%)	2/50 (4%)	0/50 (0%)	0/51 (0%)
Adjusted rates	14.2%	7.3%	0.0%	0.0%
Terminal rates	2/23 (9%)	1/24 (4%)	0/25 (0%)	0/24 (0%)
First incidence (days)	500	684	–	–
Life table tests	P=0.018N	P=0.331N	P=0.060N	P=0.068N
Logistic regression tests	P=0.019N	P=0.336N	P=0.064N	P=0.065N
Cochran-Armitage test	P=0.017N			
Fisher exact test		P=0.339N	P=0.059N	P=0.056N
All Organs: Benign Neoplasms				
Overall rates	45/50 (90%)	48/50 (96%)	44/50 (88%)	44/51 (86%)
Adjusted rates	97.8%	100.0%	100.0%	100.0%
Terminal rates	22/23 (96%)	24/24 (100%)	25/25 (100%)	24/24 (100%)
First incidence (days)	457	439	463	431
Life table tests	P=0.395N	P=0.428	P=0.402N	P=0.493N
Logistic regression tests	P=0.598	P=0.212	P=0.692N	P=0.525
Cochran-Armitage test	P=0.179N			
Fisher exact test		P=0.218	P=0.500N	P=0.394N

TABLE A3
Statistical Analysis of Primary Neoplasms in Male Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol
(continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
All Organs: Malignant Neoplasms				
Overall rates	24/50 (48%)	20/50 (40%)	24/50 (48%)	15/51 (29%)
Adjusted rates	62.6%	53.8%	63.6%	44.8%
Terminal rates	9/23 (39%)	8/24 (33%)	12/25 (48%)	7/24 (29%)
First incidence (days)	543	493	319	508
Life table tests	P=0.096N	P=0.301N	P=0.514N	P=0.087N
Logistic regression tests	P=0.070N	P=0.264N	P=0.553	P=0.061N
Cochran-Armitage test	P=0.049N			
Fisher exact test		P=0.273N	P=0.579N	P=0.043N
All Organs: Benign or Malignant Neoplasms				
Overall rates	45/50 (90%)	48/50 (96%)	45/50 (90%)	44/51 (86%)
Adjusted rates	97.8%	100.0%	100.0%	100.0%
Terminal rates	22/23 (96%)	24/24 (100%)	25/25 (100%)	24/24 (100%)
First incidence (days)	457	439	319	431
Life table tests	P=0.403N	P=0.428	P=0.463N	P=0.493N
Logistic regression tests	P=0.588N	P=0.212	P=0.566	P=0.525
Cochran-Armitage test	P=0.184N			
Fisher exact test		P=0.218	P=0.630N	P=0.394N

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, epididymis, heart, kidney, larynx, liver, lung, nose, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no neoplasms in animal group

TABLE A4
Historical Incidence of Renal Tubule Neoplasms in Male F344/N Rats Administered Corn Oil by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Battelle-Columbus Division			
Dimethoxane	0/50	0/50	0/50
o-Benzyl-*p*-chlorophenol	1/50	0/50	1/50
Ochratoxin A	1/50	0/50	1/50
Overall Historical Incidence			
Total	8/1.069 (0.7%)	4/1,069 (0.4%)	12/1,069 (1.1%)
Standard deviation	1.0%	1.0%	1.4%
Range	0%-2%	0%-4%	0%-4%

[a] Data as of 20 August 1992

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Disposition Summary				
Animals initially in study[b]	80	80	80	80
3-Month interim evaluation	10	10	10	9
15-Month interim evaluation				
Histopathology	10	10	10	9
Clinical Pathology	10	10	10	7
Early deaths				
Accidental deaths	6	2	5	7
Moribund	16	13	14	14
Natural deaths	5	11	6	10
Survivors				
Terminal sacrifice	23	24	25	24
Animals examined microscopically	70	70	70	73
3-Month Interim Evaluation				
Alimentary System				
Esophagus	(10)			(9)
Muscularis, inflammation, chronic	2 (20%)			1 (11%)
Intestine large, rectum	(10)			(9)
Parasite metazoan	1 (10%)			
Mesentery				(1)
Inflammation, granulomatous				1 (100%)
Cardiovascular System				
Heart	(10)			(9)
Myocardium, degeneration, chronic	9 (90%)			5 (56%)
Endocrine System				
None				
General Body System				
None				
Genital System				
Preputial gland	(10)			(9)
Inflammation, chronic active				1 (11%)
Hematopoietic System				
None				

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
3-Month Interim Evaluation (continued)				
Integumentary System				
None				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)			(9)
Inflammation, chronic active	2 (20%)			2 (22%)
Nose	(10)			(9)
Mucosa, inflammation, suppurative	1 (10%)			
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(9)
Nephropathy	10 (100%)	8 (80%)	9 (90%)	8 (89%)
15-Month Interim Evaluation				
Alimentary System				
Intestine large, colon	(10)			(9)
Parasite metazoan	1 (10%)			
Liver	(10)	(1)	(1)	(9)
Basophilic focus	1 (10%)			1 (11%)
Fatty change	6 (60%)			1 (11%)
Hepatodiaphragmatic nodule	1 (10%)	1 (100%)	1 (100%)	
Inflammation, necrotizing	1 (10%)			
Bile duct, hyperplasia	4 (40%)			3 (33%)
Mesentery	(4)	(1)	(1)	(2)
Hemorrhage	1 (25%)			1 (50%)
Fat, necrosis	3 (75%)	1 (100%)	1 (100%)	1 (50%)
Pancreas	(10)			(9)
Acinus, atrophy	5 (50%)			5 (56%)
Stomach, forestomach	(10)			(9)
Inflammation, necrotizing	1 (10%)			
Stomach, glandular	(10)			(9)
Inflammation, necrotizing				1 (11%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
15-Month Interim Evaluation (continued)				
Cardiovascular System				
Heart	(10)			(9)
Myocardium, degeneration, chronic	10 (100%)			8 (89%)
Endocrine System				
Adrenal gland, cortex	(10)			(9)
Hyperplasia	2 (20%)			
Adrenal gland, medulla	(10)			(9)
Hyperplasia				1 (11%)
Pituitary gland	(10)	(1)		(9)
Pars distalis, hyperplasia	1 (10%)			2 (22%)
Thyroid gland	(9)			(9)
C-cell, hyperplasia				1 (11%)
Follicle, cyst	1 (11%)			
General Body System				
None				
Genital System				
Testes	(10)	(1)	(1)	(9)
Interstitial cell, hyperplasia	8 (80%)			9 (100%)
Seminiferous tubule, atrophy	1 (10%)		1 (100%)	
Hematopoietic System				
None				
Integumentary System				
None				
Musculoskeletal System				
Skeletal muscle	(1)			
Edema	1 (100%)			
Nervous System				
None				

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
15-Month Interim Evaluation (continued)				
Respiratory System				
Lung	(10)			(9)
Inflammation, chronic active	3 (30%)			1 (11%)
Alveolar epithelium, hyperplasia	1 (10%)			
Nose	(10)			(9)
Fungus	1 (10%)			
Mucosa, inflammation, suppurative	2 (20%)			
Special Senses System				
Eye				(1)
Lens, cataract				1 (100%)
Retina, atrophy				1 (100%)
Urinary System				
Kidney	(10)	(10)	(10)	(9)
Nephropathy	10 (100%)	10 (100%)	10 (100%)	9 (100%)
2-Year Study				
Alimentary System				
Esophagus	(50)	(50)	(50)	(51)
Dilatation			1 (2%)	
Foreign body	2 (4%)		1 (2%)	
Inflammation, chronic active	3 (6%)		1 (2%)	
Intestine large, cecum	(48)	(48)	(49)	(48)
Inflammation, necrotizing		1 (2%)		
Intestine large, colon	(50)	(50)	(49)	(50)
Inflammation, necrotizing		1 (2%)		
Intestine large, rectum	(50)	(49)	(49)	(49)
Parasite metazoan	2 (4%)	7 (14%)	4 (8%)	2 (4%)
Intestine small, duodenum	(49)	(49)	(49)	(50)
Inflammation, necrotizing			1 (2%)	1 (2%)
Intestine small, jejunum	(49)	(48)	(48)	(50)
Inflammation, necrotizing	1 (2%)			
Liver	(50)	(50)	(50)	(51)
Basophilic focus	34 (68%)	33 (66%)	25 (50%)	30 (59%)
Clear cell focus	23 (46%)	16 (32%)	21 (42%)	22 (43%)
Degeneration, cystic	6 (12%)	3 (6%)	6 (12%)	
Eosinophilic focus	7 (14%)	6 (12%)	3 (6%)	7 (14%)
Fatty change	1 (2%)	1 (2%)	3 (6%)	
Hepatodiaphragmatic nodule	1 (2%)	3 (6%)	2 (4%)	4 (8%)
Inflammation, granulomatous	3 (6%)		1 (2%)	1 (2%)
Inflammation, necrotizing	1 (2%)		2 (4%)	
Mixed cell focus	1 (2%)	3 (6%)	1 (2%)	1 (2%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Liver (continued)				
Bile duct, hyperplasia	42 (84%)	43 (86%)	42 (84%)	32 (63%)
Centrilobular, necrosis	1 (2%)	9 (18%)		
Mesentery	(10)	(13)	(6)	(6)
Fat, necrosis	10 (100%)	7 (54%)	6 (100%)	6 (100%)
Pancreas	(49)	(47)	(48)	(49)
Basophilic focus	1 (2%)			3 (6%)
Acinus, atrophy	15 (31%)	10 (21%)	12 (25%)	14 (29%)
Acinus, hyperplasia	6 (12%)	11 (23%)	8 (17%)	13 (27%)
Salivary glands	(50)	(50)	(49)	(49)
Inflammation, chronic active				2 (4%)
Stomach, forestomach	(49)	(50)	(49)	(51)
Inflammation, chronic		1 (2%)		3 (6%)
Inflammation, necrotizing	3 (6%)	5 (10%)	5 (10%)	4 (8%)
Mineralization				1 (2%)
Epithelium, hyperplasia		3 (6%)	4 (8%)	1 (2%)
Stomach, glandular	(49)	(49)	(49)	(50)
Inflammation, necrotizing	2 (4%)	7 (14%)	4 (8%)	5 (10%)
Mineralization	2 (4%)	4 (8%)	2 (4%)	9 (18%)
Cardiovascular System				
Blood vessel		(2)	(1)	
Foreign body		1 (50%)		
Inflammation, chronic active		1 (50%)		
Heart	(50)	(50)	(50)	(51)
Inflammation, necrotizing			1 (2%)	1 (2%)
Mineralization		1 (2%)		2 (4%)
Thrombosis		1 (2%)		
Myocardium, degeneration, chronic	45 (90%)	46 (92%)	46 (92%)	46 (90%)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(51)
Accessory adrenal cortical nodule			1 (2%)	
Hemorrhage, chronic	1 (2%)			
Hyperplasia	18 (36%)	12 (24%)	21 (42%)	19 (37%)
Hypertrophy	4 (8%)	1 (2%)	3 (6%)	
Necrosis	1 (2%)			
Adrenal gland, medulla	(50)	(50)	(49)	(50)
Hemorrhage, chronic	1 (2%)			
Hyperplasia	18 (36%)	26 (52%)	17 (35%)	19 (38%)
Islets, pancreatic	(49)	(47)	(48)	(50)
Hyperplasia		4 (9%)	1 (2%)	1 (2%)
Parathyroid gland	(47)	(47)	(45)	(46)
Hyperplasia		2 (4%)	5 (11%)	8 (17%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Endocrine System (continued)				
Pituitary gland	(48)	(50)	(49)	(51)
Pars distalis, ectasia		1 (2%)	1 (2%)	
Pars distalis, hyperplasia	19 (40%)	13 (26%)	15 (31%)	11 (22%)
Pars nervosa, hyperplasia, glandular				1 (2%)
Thyroid gland	(49)	(50)	(47)	(50)
C-cell, hyperplasia	16 (33%)	8 (16%)	7 (15%)	10 (20%)
Follicle, cyst				1 (2%)
Follicular cell, hyperplasia	2 (4%)	3 (6%)	2 (4%)	3 (6%)
General Body System				
None				
Genital System				
Preputial gland	(49)	(48)	(49)	(51)
Hyperplasia		1 (2%)		
Inflammation, chronic active	2 (4%)			2 (4%)
Duct, dilatation		1 (2%)	1 (2%)	
Prostate	(50)	(50)	(50)	(51)
Degeneration, mucoid	1 (2%)			
Dilatation		1 (2%)		
Hyperplasia		2 (4%)		
Inflammation, chronic active	5 (10%)	11 (22%)	7 (14%)	7 (14%)
Seminal vesicle	(50)	(50)	(50)	(51)
Dilatation		1 (2%)		
Mineralization				1 (2%)
Testes	(50)	(48)	(50)	(51)
Degeneration		1 (2%)		
Inflammation, chronic active	1 (2%)		1 (2%)	3 (6%)
Mineralization				1 (2%)
Interstitial cell, hyperplasia	8 (16%)	6 (13%)	13 (26%)	11 (22%)
Seminiferous tubule, atrophy	2 (4%)	4 (8%)	2 (4%)	3 (6%)
Hematopoietic System				
Lymph node, mandibular	(49)	(50)	(48)	(49)
Edema			2 (4%)	
Mineralization				1 (2%)
Sinus, ectasia	1 (2%)			
Spleen	(50)	(49)	(50)	(50)
Fibrosis	4 (8%)	2 (4%)	3 (6%)	7 (14%)
Inflammation, necrotizing		1 (2%)		

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Integumentary System				
Mammary gland	(37)	(44)	(44)	(41)
Hyperplasia				1 (2%)
Inflammation, chronic active				2 (5%)
Skin	(49)	(50)	(50)	(51)
Cyst epithelial inclusion		1 (2%)		
Edema			1 (2%)	
Inflammation, chronic active	1 (2%)	2 (4%)	3 (6%)	4 (8%)
Subcutaneous tissue, fibrosis		1 (2%)		
Musculoskeletal System				
Bone	(50)	(50)	(50)	(51)
Cranium, fibrous osteodystrophy			2 (4%)	4 (8%)
Femur, fibrous osteodystrophy			2 (4%)	6 (12%)
Skeletal muscle	(2)	(3)		
Diaphragm, hemorrhage, chronic	1 (50%)			
Nervous System				
Brain	(50)	(50)	(50)	(51)
Compression	6 (12%)	3 (6%)	5 (10%)	1 (2%)
Degeneration	1 (2%)		1 (2%)	
Respiratory System				
Lung	(50)	(50)	(50)	(51)
Fibrosis	1 (2%)			
Foreign body	3 (6%)	2 (4%)	4 (8%)	3 (6%)
Inflammation, chronic active	6 (12%)	2 (4%)	6 (12%)	3 (6%)
Inflammation, necrotizing	5 (10%)	2 (4%)	4 (8%)	5 (10%)
Mineralization				2 (4%)
Alveolar epithelium, hyperplasia	10 (20%)	10 (20%)	12 (24%)	10 (20%)
Mediastinum, hemorrhage	1 (2%)			1 (2%)
Nose	(50)	(50)	(48)	(51)
Foreign body				1 (2%)
Fungus	1 (2%)			
Mucosa, inflammation, suppurative	12 (24%)	3 (6%)	7 (15%)	6 (12%)
Trachea	(50)	(50)	(50)	(50)
Inflammation, chronic active				1 (2%)
Special Senses System				
Ear	(1)		(1)	(2)
Pinna, inflammation, chronic active				1 (50%)

TABLE A5
Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
2-Year Study (continued)				
Special Senses System (continued)				
Eye		(3)	(1)	(6)
Degeneration			1 (100%)	2 (33%)
Inflammation, chronic active				3 (50%)
Cornea, mineralization				1 (17%)
Lens, cataract		1 (33%)		
Urinary System				
Kidney	(50)	(49)	(50)	(50)
Mineralization	1 (2%)	2 (4%)		3 (6%)
Nephropathy	48 (96%)	48 (98%)	48 (96%)	50 (100%)
Pelvis, inflammation, suppurative				1 (2%)
Renal tubule, hyperplasia		2 (4%)		2 (4%)
Transitional epithelium, hyperplasia		1 (2%)	2 (4%)	1 (2%)
Urinary bladder	(50)	(50)	(50)	(50)
Hemorrhage	1 (2%)	1 (2%)		
Inflammation, chronic active			1 (2%)	
Transitional epithelium, hyperplasia	1 (2%)	1 (2%)		

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Seven or ten of the 80 animals in each dose group were evaluated for clinical pathology only.

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE 2-YEAR GAVAGE STUDY OF *o*-BENZYL-*p*-CHLOROPHENOL

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Dispositon Summary				
Animals initially in study[b]	80	80	80	80
3-Month interim evaluation[c]	10	10	8	9
15-Month interim evaluation				
Histopathology	10	10	9	10
Clinical pathology	10	10[d]	9	8
Early deaths				
Accidental deaths	2	1	3	3
Moribund	17	12	15	18
Natural deaths	5	7	8	4
Survivors				
Terminal sacrifice	26	30	28	28
Animals examined microscopically	70	70	71	72
15-Month Interim Evaluation				
Alimentary System				
None				
Cardiovascular System				
None				
Endocrine System				
Pituitary gland	(10)	(1)	(1)	(10)
Pars distalis, adenoma	1 (10%)			
Thyroid gland	(10)			(10)
C-cell, adenoma				1 (10%)
General Body System				
None				
Genital System				
Uterus	(10)		(2)	(10)
Polyp stromal				1 (10%)
Hematopoietic System				
None				
Integumentary System				
Mammary gland	(10)			(10)
Fibroadenoma				2 (20%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
15-Month Interim Evaluation (continued)				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Esophagus	(50)	(50)	(51)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Intestine large, rectum	(49)	(50)	(51)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Liver	(50)	(50)	(51)	(50)
Hepatocellular adenoma	1 (2%)			
Mesentery	(4)	(3)	(1)	(5)
Liposarcoma				1 (20%)
Osteosarcoma, metastatic, uncertain primary site		1 (33%)		
Pancreas	(50)	(50)	(50)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Osteosarcoma, metastatic, uncertain primary site		1 (2%)		
Stomach, glandular	(49)	(50)	(51)	(50)
Cardiovascular System				
Heart	(50)	(50)	(51)	(50)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(51)	(50)
Adrenal gland, medulla	(50)	(50)	(51)	(50)
Pheochromocytoma malignant		1 (2%)		
Pheochromocytoma benign		3 (6%)	3 (6%)	4 (8%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
2-Year Study (continued)				
Endocrine System (continued)				
Islets, pancreatic	(50)	(50)	(50)	(50)
Adenoma			1 (2%)	
Carcinoma			1 (2%)	
Pituitary gland	(50)	(50)	(50)	(50)
Craniopharyngioma	1 (2%)			
Pars distalis, adenoma	16 (32%)	14 (28%)	13 (26%)	19 (38%)
Pars distalis, adenoma, multiple	3 (6%)			
Pars distalis, carcinoma	2 (4%)			
Thyroid gland	(50)	(50)	(51)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Bilateral, C-cell, adenoma				1 (2%)
C-cell, adenoma	9 (18%)	6 (12%)	6 (12%)	5 (10%)
C-cell, carcinoma	1 (2%)	1 (2%)		1 (2%)
Follicular cell, adenoma	3 (6%)	1 (2%)		2 (4%)
Follicular cell, carcinoma		1 (2%)	1 (2%)	
General Body System				
None				
Genital System				
Clitoral gland	(49)	(48)	(49)	(47)
Adenoma	7 (14%)	7 (15%)	4 (8%)	3 (6%)
Carcinoma	5 (10%)	2 (4%)	2 (4%)	2 (4%)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Bilateral, adenoma	1 (2%)			1 (2%)
Ovary	(50)	(50)	(51)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Uterus	(50)	(50)	(51)	(50)
Leiomyoma		1 (2%)		
Polyp stromal	4 (8%)	5 (10%)	3 (6%)	10 (20%)
Polyp stromal, multiple	1 (2%)	1 (2%)		1 (2%)
Sarcoma stromal	2 (4%)	1 (2%)		
Hematopoietic System				
Bone marrow	(50)	(50)	(51)	(50)
Lymph node	(50)	(50)	(51)	(50)
Lymph node, mandibular	(50)	(50)	(50)	(49)
Squamous cell carcinoma, metastatic, nose		1 (2%)		
Lymph node, mesenteric	(49)	(48)	(51)	(50)
Spleen	(50)	(50)	(51)	(50)
Thymus	(48)	(46)	(46)	(48)
Thymoma benign	1 (2%)			

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
2-Year Study (continued)				
Integumentary System				
Mammary gland	(49)	(50)	(50)	(50)
Adenocarcinoma	2 (4%)		1 (2%)	2 (4%)
Adenoma		2 (4%)		
Fibroadenoma	13 (27%)	10 (20%)	15 (30%)	16 (32%)
Fibroadenoma, multiple		3 (6%)	2 (4%)	3 (6%)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Skin	(50)	(49)	(50)	(50)
Keratoacanthoma		1 (2%)		
Squamous cell carcinoma	1 (2%)			
Squamous cell papilloma			1 (2%)	1 (2%)
Subcutaneous tissue, fibroma	1 (2%)			1 (2%)
Subcutaneous tissue, fibrosarcoma	1 (2%)	1 (2%)		
Subcutaneous tissue, fibrous histiocytoma			1 (2%)	
Subcutaneous tissue, lipoma				1 (2%)
Subcutaneous tissue, sarcoma			1 (2%)	
Musculoskeletal System				
Bone	(50)	(50)	(51)	(50)
Osteosarcoma	1 (2%)			
Nervous System				
Brain	(50)	(50)	(51)	(50)
Astrocytoma benign			1 (2%)	
Carcinoma, metastatic, pituitary gland	2 (4%)			
Oligodendroglioma benign	1 (2%)			
Respiratory System				
Lung	(50)	(50)	(51)	(50)
Alveolar/bronchiolar adenoma		1 (2%)		
Carcinoma, metastatic, kidney				1 (2%)
Carcinoma, metastatic, thyroid gland		1 (2%)		
Osteosarcoma, metastatic, bone	1 (2%)			
Mediastinum, fibrous histiocytoma, metastatic, skin			1 (2%)	
Nose	(50)	(50)	(51)	(50)
Nasolacrimal duct, squamous cell carcinoma		1 (2%)		
Trachea	(50)	(50)	(51)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Special Senses System				
Eye	(2)	(3)	(4)	(6)
Lids, squamous cell carcinoma, metastatic, nose		1 (33%)		
Zymbal's gland		(1)		(1)
Carcinoma				1 (100%)

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
2-Year Study (continued)				
Urinary System				
Kidney	(50)	(50)	(51)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Osteosarcoma, metastatic, uncertain primary site		1 (2%)		
Renal tubule, adenoma				1 (2%)
Transitional epithelium, carcinoma			1 (2%)	1 (2%)
Urinary bladder	(50)	(50)	(51)	(50)
Fibrous histiocytoma, metastatic, skin			1 (2%)	
Transitional epithelium, papilloma	1 (2%)			
Systemic Lesions				
Multiple organs[e]	(50)	(50)	(51)	(50)
Leukemia mononuclear	14 (28%)	16 (32%)	11 (22%)	17 (34%)
Neoplasm Summary				
Total animals with primary neoplasms[f]				
15-Month interim evaluation	1			3
2-Year study	44	40	42	47
Total primary neoplasms				
15-Month interim evaluation	1			4
2-Year study	92	79	68	94
Total animals with benign neoplasms				
15-Month interim evaluation	1			3
2-Year study	36	33	34	41
Total benign neoplasms				
15-Month interim evaluation	1			4
2-Year study	63	55	49	69
Total animals with malignant neoplasms				
2-Year study	24	19	17	22
Total malignant neoplasms				
2-Year study	29	24	19	25
Total animals with metastatic neoplasms				
2-Year study	3	3	1	1
Total metastatic neoplasms				
2-Year study	3	6	11	1
Total animals with malignant neoplasms uncertain primary site				
2-Year study		1		

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] Eight to ten of the 80 animals in each dose group were evaluated for clinical pathology only.
[c] No neoplasms were observed at the 3-month interim evaluation.
[d] Includes one animal that died during the scheduled sacrifice period.
[e] Number of animals with any tissue examined microscopically
[f] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control

Number of Days on Study	0 2 3	3 1 7	4 1 6	4 3 5	4 6 5	4 7 0	5 0 0	5 2 1	5 6 8	5 7 7	5 8 3	5 9 8	6 0 3	6 2 8	6 5 9	6 7 6	6 8 0	6 8 0	6 8 0	6 8 2	7 0 1	7 1 7	7 1 7	7 2 6	7 2 9
Carcass ID Number	0 6 6 3	0 7 2 1	0 6 8 2	0 7 1 5	0 6 8 1	0 6 8 5	0 7 5 4	0 6 9 3	0 6 6 4	0 7 6 4	0 6 5 1	0 7 5 5	0 7 4 3	0 7 4 4	0 7 2 5	0 6 5 5	0 6 5 3	0 7 0 5	0 7 2 2	0 7 3 5	0 7 1 4	0 7 0 1	0 7 5 2	0 6 6 1	0 6 5 2
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									X
Mesentery																			+			+			
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Craniopharyngioma											X														
Pars distalis, adenoma						X				X					X		X		X	X					
Pars distalis, adenoma, multiple																					X				
Pars distalis, carcinoma								X																	
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma															X			X		X					
C-cell, carcinoma																									
Follicular cell, adenoma																									X
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma											X							X							
Carcinoma																			X						X
Bilateral, adenoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal																			X						
Polyp stromal, multiple																									
Sarcoma stromal							X												X						

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 6 6 2	0 6 7 1	0 6 7 2	0 6 7 3	0 6 7 4	0 6 7 5	0 6 8 4	0 6 9 2	0 6 9 5	0 7 0 2	0 7 0 3	0 7 0 4	0 7 1 2	0 7 1 3	0 7 2 4	0 7 3 3	0 7 3 1	0 7 3 2	0 7 3 4	0 7 4 2	0 7 4 5	0 7 5 3	0 7 6 1	0 7 6 2	0 7 6 3	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																										1
Mesentery							+									+										4
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	M	+	+	+	M	+	+	+	+	+	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Craniopharyngioma																										1
Pars distalis, adenoma	X	X	X		X			X			X				X			X	X		X					16
Pars distalis, adenoma, multiple																X							X			3
Pars distalis, carcinoma													X													2
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma		X									X						X		X		X				X	9
C-cell, carcinoma				X																						1
Follicular cell, adenoma															X						X					3
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma		X				X	X				X													X		7
Carcinoma				X				X														X				5
Bilateral, adenoma					X																					1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal				X							X					X										4
Polyp stromal, multiple	X																									1
Sarcoma stromal																										2

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	0 2 3	3 1 7	4 1 6	4 3 5	4 6 5	4 7 0	5 0 0	5 2 1	5 6 8	5 7 7	5 8 3	5 9 8	6 0 3	6 2 8	6 5 9	6 7 6	6 8 0	6 8 0	6 8 0	6 8 2	7 0 1	7 1 7	7 1 7	7 2 6	7 2 9
Carcass ID Number	0 6 6 3	0 7 2 1	0 6 8 2	0 7 1 5	0 6 8 1	0 6 8 5	0 7 5 4	0 6 9 3	0 6 6 4	0 7 6 4	0 6 5 1	0 7 5 5	0 7 4 3	0 7 4 4	0 7 2 5	0 6 5 5	0 6 5 3	0 7 0 5	0 7 2 2	0 7 3 5	0 7 1 4	0 7 0 1	0 7 5 2	0 6 6 1	0 6 5 2
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymoma benign																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																						X		X	
Fibroadenoma											X			X	X	X			X					X	
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, fibrosarcoma																								X	
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma					X																				
Skeletal muscle																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, pituitary gland								X																	
Oligodendroglioma benign				X																					
Peripheral nerve			+																						
Spinal cord			+																						
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, bone					X																				
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye						+						+													
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional epithelium, papilloma								X																	
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X						X			X	X			X		X		X				X	X

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 6 6 2	0 6 7 1	0 6 7 2	0 6 7 3	0 6 7 4	0 6 7 5	0 6 8 4	0 6 9 2	0 6 9 5	0 6 7 2	0 7 0 3	0 7 0 4	0 7 1 2	0 7 1 3	0 7 2 4	0 7 3 3	0 7 3 1	0 7 3 2	0 7 3 4	0 7 4 2	0 7 4 5	0 7 5 3	0 7 6 1	0 7 6 2	0 7 6 3	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	48
Thymoma benign																		X								1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma																										2
Fibroadenoma		X									X	X	X					X	X				X			13
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																		X								1
Subcutaneous tissue, fibroma																	X									1
Subcutaneous tissue, fibrosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma																										1
Skeletal muscle																						+				1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, pituitary gland													X													2
Oligodendroglioma benign																										1
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic, bone																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye																										2
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Transitional epithelium, papilloma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear						X					X								X					X	X	14

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg

Number of Days on Study	0 1 5	0 7 6	5 4 4	6 1 0	6 2 5	6 2 9	6 3 2	6 3 2	6 3 3	6 4 6	6 4 8	6 4 9	6 6 0	6 6 3	6 7 4	6 7 6	6 7 6	6 9 2	7 1 6	7 2 4	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 8 1 4	0 8 2 2	0 8 1 1	0 9 2 3	0 9 2 1	0 8 4 1	0 8 7 1	0 9 0 5	0 8 2 3	0 9 2 5	0 8 6 1	0 8 9 3	0 9 2 2	0 8 4 2	0 9 0 2	0 8 7 2	0 9 2 2	0 8 8 4	0 8 5 3	0 8 7 5	0 8 1 2	0 8 1 3	0 8 1 5	0 8 2 1	0 8 2 4
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery												+						+							
Osteosarcoma, metastatic, uncertain primary site																		X							
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, uncertain primary site																		X							
Pharynx																									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant									X																
Pheochromocytoma benign												X	X												
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma									X				X			X	X			X					X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell, adenoma															X							X			
C-cell, carcinoma																									
Follicular cell, adenoma																									
Follicular cell, carcinoma			X																						
General Body System																									
None																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 8 2 5	0 8 3 1	0 8 3 2	0 8 3 4	0 8 4 3	0 8 4 5	0 8 5 1	0 8 5 4	0 8 5 5	0 8 6 2	0 8 6 4	0 8 6 5	0 8 8 1	0 8 8 2	0 8 8 3	0 8 9 1	0 8 9 4	0 8 9 5	0 9 0 1	0 9 0 3	0 9 0 4	0 9 1 1	0 9 1 2	0 9 1 3	0 9 1 4	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery																	+									3
Osteosarcoma, metastatic, uncertain primary site																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic, uncertain primary site																										1
Pharynx													+													1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma malignant																										1
Pheochromocytoma benign										X																3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	M	+	+	+	+	M	+	+	M	+	+	M	+	+	M	+	+	+	+	+	+	44
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma						X			X	X	X			X				X	X		X					14
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
C-cell, adenoma					X					X													X		X	6
C-cell, carcinoma																			X							1
Follicular cell, adenoma	X																									1
Follicular cell, carcinoma																										1
General Body System																										
None																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	0 1 5	0 7 6	5 4 4	6 1 0	6 2 5	6 2 9	6 3 2	6 3 2	6 3 3	6 4 6	6 4 8	6 4 9	6 6 0	6 6 3	6 7 4	6 7 6	6 7 6	6 9 2	7 1 6	7 2 4	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9
Carcass ID Number	0 8 1 4	0 8 2 2	0 8 1 1	0 9 2 3	0 9 2 1	0 8 4 1	0 8 7 1	0 9 0 5	0 8 2 3	0 9 2 5	0 8 6 1	0 8 9 3	0 9 2 2	0 8 4 2	0 9 0 2	0 8 9 2	0 8 7 2	0 9 2 4	0 8 8 4	0 8 5 3	0 8 7 5	0 8 1 2	0 8 1 3	0 8 1 5	0 8 2 1	0 8 2 4
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma							X				X													X	X	
Carcinoma																					X					
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																										
Polyp stromal			X					X													X					
Polyp stromal, multiple							X																			
Sarcoma stromal									X																	
Vagina																+										
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, nose																										
Lymph node, mesenteric	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																										
Fibroadenoma						X		X	X		X	X														X
Fibroadenoma, multiple																										
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																										
Subcutaneous tissue, fibrosarcoma																					X					
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle																										
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma															X											
Carcinoma, metastatic, thyroid gland																										
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nasolacrimal duct, squamous cell carcinoma																										
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																										
Eye				+																						
Lids, squamous cell carcinoma, metastatic, nose																										
Harderian gland																										
Zymbal's gland																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	729	729	729	729	729	730	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	
Carcass ID Number	08825	08831	08832	08834	08843	08845	08851	08854	08855	08862	08864	08865	08881	08882	08883	08891	08894	08895	09201	09203	09204	09211	09212	09213	09214	Total Tissues/ Tumors
Genital System																										
Clitoral gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma					X	X																	X			7
Carcinoma										X																2
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyoma												X														1
Polyp stromal																			X		X					5
Polyp stromal, multiple																										1
Sarcoma stromal																										1
Vagina																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, nose										X																1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	M	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	46
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma						X				X																2
Fibroadenoma		X											X			X		X								10
Fibroadenoma, multiple	X			X																					X	3
Skin	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Keratoacanthoma														X												1
Subcutaneous tissue, fibrosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle							+																			1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																										1
Carcinoma, metastatic, thyroid gland																			X							1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nasolacrimal duct, squamous cell carcinoma										X																1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye										+							+									3
Lids, squamous cell carcinoma, metastatic, nose										X																1
Harderian gland										+																1
Zymbal's gland							+																			1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	0	0	5	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7
	1	7	4	1	2	2	3	3	3	4	4	4	6	6	7	7	7	9	1	2	2	2	2	2	2
	5	6	4	0	5	9	2	2	3	6	8	9	0	3	4	6	6	2	6	4	9	9	9	9	9
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	8	8	8	9	9	8	8	9	8	9	8	8	9	8	9	8	9	8	8	8	8	8	8	8	8
	1	2	1	2	2	4	7	0	2	2	6	9	2	4	0	7	2	8	5	7	1	1	1	2	2
	4	2	1	3	1	1	1	5	3	5	1	3	2	2	2	2	4	4	3	5	2	3	5	1	4
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Osteosarcoma, metastatic, uncertain primary site																		X							
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X		X		X	X	X			X		X	X		X	X					

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 60 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 8 2 5	0 8 3 1	0 8 3 2	0 8 3 4	0 8 4 3	0 8 4 5	0 8 5 1	0 8 5 4	0 8 5 5	0 8 6 2	0 8 6 4	0 8 6 5	0 8 8 1	0 8 8 2	0 8 8 3	0 8 9 1	0 8 9 4	0 8 9 5	0 9 0 1	0 9 0 3	0 9 0 4	0 9 1 1	0 9 1 2	0 9 1 3	0 9 1 4	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Osteosarcoma, metastatic, uncertain primary site																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear										X			X		X			X	X				X			16

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg

Number of Days on Study	0 1 9	3 0 9	3 4 5	4 0 2	4 7 1	5 0 8	5 6 2	5 6 8	5 7 9	5 8 2	5 8 3	5 9 8	6 2 2	6 4 0	6 4 5	6 4 9	6 6 2	6 6 5	6 6 6	6 7 0	6 7 0	6 7 6	6 8 0	7 2 9	7 2 9
Carcass ID Number	1 0 3 1	1 0 4 5	1 0 6 2	1 0 8 5	1 0 5 1	0 9 8 5	1 0 6 5	1 0 2 3	0 9 9 2	0 9 8 1	1 0 0 2	1 0 0 4	1 0 3 4	1 0 5 5	1 0 2 1	0 9 9 4	1 0 3 5	1 0 3 2	1 0 0 3	1 0 7 2	1 0 8 3	1 0 3 3	0 9 7 2	0 9 7 1	0 9 7 3
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery		+																							
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																							X		
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+
Pars distalis, adenoma										X		X		X	X		X	X						X	X
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
C-cell, adenoma															X								X		X
Follicular cell, carcinoma																									
General Body System																									
Tissue NOS																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 9 7 5	0 9 8 2	0 9 8 3	0 9 8 4	0 9 9 1	0 9 9 3	0 9 9 5	1 0 1 1	1 0 1 2	1 0 1 3	1 0 1 4	1 0 1 5	1 0 2 2	1 0 2 4	1 0 2 5	1 0 4 1	1 0 4 2	1 0 4 4	1 0 5 2	1 0 5 3	1 0 5 4	1 0 7 1	1 0 7 3	1 0 7 4	1 0 7 5	1 0 8 2	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Fibrous histiocytoma, metastatic, skin																										1
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine large, colon	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Fibrous histiocytoma, metastatic, skin																										1
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Mesentery																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, skin																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Pheochromocytoma benign														X					X					X		3
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																							X			1
Carcinoma																										1
Parathyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma			X					X							X								X	X		13
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Fibrous histiocytoma, metastatic, skin																										1
C-cell, adenoma													X						X						X	6
Follicular cell, carcinoma																								X		1
General Body System																										
Tissue NOS																				+						1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	0 1 9	3 0 9	3 4 5	4 0 2	4 7 1	5 0 8	5 6 2	5 6 8	5 7 9	5 8 2	5 8 3	5 9 8	6 2 2	6 4 0	6 4 5	6 4 9	6 6 2	6 6 5	6 7 6	6 7 0	6 7 0	6 7 6	6 8 0	7 2 9	7 2 9
Carcass ID Number	1 0 3 1	1 0 4 5	1 0 6 2	1 0 8 5	1 0 5 1	0 9 8 5	1 0 6 5	1 0 2 3	0 9 9 2	0 9 8 1	0 0 0 2	1 0 0 4	1 0 3 4	1 0 5 5	1 0 2 1	0 0 9 4	1 0 3 5	1 0 3 2	1 0 0 3	1 0 7 2	1 0 8 3	1 0 3 3	0 9 7 2	0 9 7 1	0 9 7 3
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+
Adenoma									X																
Carcinoma																									
Fibrous histiocytoma, metastatic, skin																X									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal													X												
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Adenocarcinoma												X													
Fibroadenoma							X		X								X			X	X				
Fibroadenoma, multiple											X												X		
Fibrous histiocytoma, metastatic, skin																X									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Squamous cell papilloma																									
Subcutaneous tissue, fibrous histiocytoma																X									
Subcutaneous tissue, sarcoma						X																			
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma benign																X									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mediastinum, fibrous histiocytoma, metastatic, skin																X									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
Special Senses System																									
Ear				+																					
Eye				+														+							
Harderian gland																		+							

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 9 7 5	0 9 8 2	0 9 8 3	0 9 8 4	0 9 9 1	0 9 9 3	0 9 9 5	1 0 1 1	1 0 1 2	1 0 1 3	1 0 1 4	1 0 1 5	1 0 2 2	1 0 2 4	1 0 2 5	1 0 4 1	1 0 4 2	1 0 4 4	1 0 5 2	1 0 5 3	1 0 5 4	1 0 7 1	1 0 7 3	1 0 7 4	1 0 7 5	1 0 8 2	Total Tissues/ Tumors
Genital System																											
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma			X																X							X	4
Carcinoma																				X				X			2
Fibrous histiocytoma, metastatic, skin																											1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Fibrous histiocytoma, metastatic, skin																											1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Polyp stromal							X											X									3
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	46
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																											1
Fibroadenoma	X					X		X				X	X							X		X	X	X	X		15
Fibroadenoma, multiple																											2
Fibrous histiocytoma, metastatic, skin																											1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma		X																									1
Subcutaneous tissue, fibrous histiocytoma																											1
Subcutaneous tissue, sarcoma																											1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Astrocytoma benign																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Mediastinum, fibrous histiocytoma, metastatic, skin																											1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Fibrous histiocytoma, metastatic, skin																											1
Special Senses System																											
Ear																											1
Eye													+			+											4
Harderian gland																											1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	0 1 9	3 0 9	3 4 5	4 0 2	4 7 1	5 0 1 8	5 6 2	5 6 8	5 7 9	5 8 2	5 8 3	5 9 8	6 2 2	6 4 0	6 4 5	6 4 9	6 6 2	6 6 5	6 6 6	6 7 0	6 7 0	6 7 6	6 8 0	7 2 9	7 2 9
Carcass ID Number	1 0 3 1	1 0 4 5	1 0 6 2	1 0 8 5	1 0 5 1	0 9 8 5	1 0 6 5	1 0 2 3	1 0 9 2	0 9 8 1	0 9 0 2	1 0 0 4	1 0 3 4	1 0 5 5	1 0 2 1	1 0 9 4	0 9 3 5	1 0 3 2	1 0 3 3	1 0 0 2	1 0 7 3	1 0 8 3	1 0 3 3	0 9 7 2	0 9 7 1	0 9 7 3
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
Transitional epithelium, carcinoma			X																						
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, skin																X									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear				X				X					X						X			X	X		

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	0 9 7 5	0 9 8 2	0 9 8 3	0 9 8 4	0 9 9 1	0 9 9 3	0 9 9 5	1 0 1 1	1 0 1 2	1 0 1 3	1 0 1 4	1 0 1 5	1 0 2 2	1 0 2 4	1 0 2 5	1 0 4 1	1 0 4 2	1 0 4 4	1 0 5 2	1 0 5 3	1 0 5 4	1 0 7 1	1 0 7 3	1 0 7 4	1 0 7 5	1 0 8 2	Total Tissues/ Tumors
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Fibrous histiocytoma, metastatic, skin																										1
Transitional epithelium, carcinoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	5
Fibrous histiocytoma, metastatic, skin																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Leukemia mononuclear	X		X	X										X								X				11

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg

Number of Days on Study	4 7 1	4 9 3	5 4 1	5 5 4	6 0 0	6 1 9	6 2 2	6 2 4	6 3 2	6 4 8	6 4 9	6 5 2	6 5 9	6 6 1	6 7 6	6 8 0	6 8 0	6 8 4	6 8 7	6 9 3	7 0 5	7 2 4	7 2 9	7 2 9	7 2 9
Carcass ID Number	1 1 4 2	1 1 3 4	1 1 5 5	1 1 3 5	1 2 4 3	1 1 7 5	1 1 7 1	1 1 7 2	1 1 8 4	1 1 5 2	1 2 4 4	1 1 6 5	1 2 2 2	2 2 3 3	1 1 7 4	1 1 6 2	2 1 4 2	1 2 4 3	2 2 2 5	2 2 2 3	1 2 8 2	2 1 4 1	1 1 3 1	1 1 3 2	1 1 4 5
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesentery		+																							
Liposarcoma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign														X			X							X	
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma	X		X		X		X	X	X		X		X		X		X						X		
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, C-cell, adenoma																				X					
C-cell, adenoma									X			X										X			
C-cell, carcinoma																									X
Follicular cell, adenoma											X								X						
General Body System																									
None																									
Genital System																									
Clitoral gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+
Adenoma															X										
Carcinoma																									X
Bilateral, adenoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Polyp stromal																	X						X		X
Polyp stromal, multiple																					X				

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	729	729	729	729	729	729	729	730	730	730	730	730	730	730	730	730	731	731	731	731	731	731	731	731	731	
Carcass ID Number	11515	11513	11514	11561	11563	11564	11583	11585	11591	11594	11595	11601	11602	11604	11605	11611	11612	11614	11615	11623	11633	11632	11634	11635	11645	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mesentery							+			+	+														+	5
Liposarcoma							X																			1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma benign																							X			4
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma				X	X		X							X			X	X		X			X			19
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bilateral, C-cell, adenoma																										1
C-cell, adenoma				X																					X	5
C-cell, carcinoma																										1
Follicular cell, adenoma																										2
General Body System																										
None																										
Genital System																										
Clitoral gland	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	47
Adenoma																	X						X			3
Carcinoma					X																					2
Bilateral, adenoma																					X					1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Polyp stromal				X					X	X				X	X			X		X						10
Polyp stromal, multiple																										1

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	4 7 1	4 9 3	5 4 1	5 5 4	6 0 0	6 1 9	6 2 2	6 2 4	6 3 2	6 4 8	6 4 9	6 5 2	6 5 9	6 6 1	6 7 6	6 8 0	6 8 0	6 8 4	6 8 7	6 9 3	7 0 5	7 2 4	7 2 9	7 2 9	7 2 9
Carcass ID Number	1 1 4 2	1 1 3 4	1 1 5 5	1 1 3 5	1 2 4 3	1 1 7 5	1 1 7 1	1 1 7 2	1 1 8 4	1 1 5 2	1 2 4 4	1 1 6 5	1 2 2 2	1 2 3 3	1 1 7 4	1 1 6 2	1 2 4 2	1 1 4 2	1 2 2 3	1 2 2 5	1 1 8 3	1 2 4 1	1 1 3 1	1 1 3 2	1 1 4 5
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma											X														
Fibroadenoma								X		X	X					X							X		
Fibroadenoma, multiple													X				X								X
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell papilloma																									
Subcutaneous tissue, fibroma																									
Subcutaneous tissue, lipoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, kidney															X										
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																			+	+		+			
Zymbal's gland				+																					
Carcinoma				X																					
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																									
Transitional epithelium, carcinoma															X										
Urinary Bladder	+	+	+	+	+	+	+	+	+	+	+	+													
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X			X	X	X					X		X	X			X			X	X			

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 0	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	7 3 1	
Carcass ID Number	1 1 5 1	1 1 5 3	1 1 5 4	1 1 6 1	1 1 6 3	1 1 6 4	1 1 8 3	1 1 8 5	1 1 9 1	1 1 9 4	1 1 9 5	1 2 0 1	1 2 0 2	1 2 0 4	1 2 0 5	1 2 2 1	1 2 2 2	1 2 2 4	1 2 2 5	1 2 3 4	1 2 3 1	1 2 3 2	1 2 3 4	1 2 3 5	1 2 4 5	Total Tissues/ Tumors
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma												X														2
Fibroadenoma	X		X	X				X	X			X	X		X			X	X				X			16
Fibroadenoma, multiple																										3
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell papilloma				X																						1
Subcutaneous tissue, fibroma															X											1
Subcutaneous tissue, lipoma																			X							1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, kidney																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye														+								+		+		6
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenoma																X										1
Transitional epithelium, carcinoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia mononuclear			X		X												X		X	X		X		X		17

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Adrenal Medulla: Benign Pheochromocytoma				
Overall rates[a]	0/50 (0%)	3/50 (6%)	3/51 (6%)	4/50 (8%)
Adjusted rates[b]	0.0%	8.3%	10.7%	12.2%
Terminal rates[c]	0/26 (0%)	1/30 (3%)	3/28 (11%)	2/28 (7%)
First incidence (days)	–[e]	649	729 (T)	661
Life table tests[d]	P=0.086	P=0.143	P=0.133	P=0.074
Logistic regression tests[d]	P=0.087	P=0.124	P=0.133	P=0.072
Cochran-Armitage test[d]	P=0.077			
Fisher exact test[d]		P=0.121	P=0.125	P=0.059
Adrenal Medulla: Benign or Malignant Pheochromocytoma				
Overall rates	0/50 (0%)	4/50 (8%)	3/51 (6%)	4/50 (8%)
Adjusted rates	0.0%	10.5%	10.7%	12.2%
Terminal rates	0/26 (0%)	1/30 (3%)	3/28 (11%)	2/28 (7%)
First incidence (days)	–	633	729 (T)	661
Life table tests	P=0.128	P=0.083	P=0.133	P=0.074
Logistic regression tests	P=0.127	P=0.063	P=0.133	P=0.072
Cochran-Armitage test	P=0.114			
Fisher exact test		P=0.059	P=0.125	P=0.059
Clitoral Gland: Adenoma				
Overall rates	8/49 (16%)	7/48 (15%)	4/49 (8%)	4/47 (9%)
Adjusted rates	28.1%	21.1%	12.8%	13.6%
Terminal rates	6/25 (24%)	5/29 (17%)	3/28 (11%)	3/27 (11%)
First incidence (days)	583	632	582	676
Life table tests	P=0.093N	P=0.387N	P=0.144N	P=0.146N
Logistic regression tests	P=0.097N	P=0.439N	P=0.173N	P=0.148N
Cochran-Armitage test	P=0.119N			
Fisher exact test		P=0.518N	P=0.178N	P=0.199N
Clitoral Gland: Carcinoma				
Overall rates	5/49 (10%)	2/48 (4%)	2/49 (4%)	2/47 (4%)
Adjusted rates	18.5%	6.6%	7.1%	7.4%
Terminal rates	4/25 (16%)	1/29 (3%)	2/28 (7%)	2/27 (7%)
First incidence (days)	680	724	729 (T)	729 (T)
Life table tests	P=0.172N	P=0.173N	P=0.188N	P=0.189N
Logistic regression tests	P=0.179N	P=0.175N	P=0.213N	P=0.194N
Cochran-Armitage test	P=0.197N			
Fisher exact test		P=0.226N	P=0.218N	P=0.235N
Clitoral Gland: Adenoma or Carcinoma				
Overall rates	13/49 (27%)	9/48 (19%)	6/49 (12%)	6/47 (13%)
Adjusted rates	44.9%	26.9%	19.8%	20.8%
Terminal rates	10/25 (40%)	6/29 (21%)	5/28 (18%)	5/27 (19%)
First incidence (days)	583	632	582	676
Life table tests	P=0.033N	P=0.142N	P=0.041N	P=0.042N
Logistic regression tests	P=0.034N	P=0.161N	P=0.056N	P=0.042N
Cochran-Armitage test	P=0.050N			
Fisher exact test		P=0.251N	P=0.062N	P=0.075N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Mammary Gland: Fibroadenoma				
Overall rates	13/50 (26%)	13/50 (26%)	17/51 (33%)	19/50 (38%)
Adjusted rates	38.8%	35.0%	48.5%	54.3%
Terminal rates	7/26 (27%)	8/30 (27%)	11/28 (39%)	13/28 (46%)
First incidence (days)	583	629	562	624
Life table tests	P=0.120	P=0.441N	P=0.308	P=0.222
Logistic regression tests	P=0.111	P=0.521N	P=0.269	P=0.210
Cochran-Armitage test	P=0.082			
Fisher exact test		P=0.590N	P=0.278	P=0.142
Mammary Gland: Adenoma or Fibroadenoma				
Overall rates	13/50 (26%)	15/50 (30%)	17/51 (33%)	19/50 (38%)
Adjusted rates	38.8%	40.9%	48.5%	54.3%
Terminal rates	7/26 (27%)	10/30 (33%)	11/28 (39%)	13/28 (46%)
First incidence (days)	583	629	562	624
Life table tests	P=0.153	P=0.569	P=0.308	P=0.222
Logistic regression tests	P=0.147	P=0.494	P=0.269	P=0.210
Cochran-Armitage test	P=0.111			
Fisher exact test		P=0.412	P=0.278	P=0.142
Mammary Gland: Adenoma, Fibroadenoma, or Carcinoma				
Overall rates	14/50 (28%)	15/50 (30%)	18/51 (35%)	19/50 (38%)
Adjusted rates	40.9%	40.9%	49.8%	54.3%
Terminal rates	7/26 (27%)	10/30 (33%)	11/28 (39%)	13/28 (46%)
First incidence (days)	583	629	562	624
Life table tests	P=0.196	P=0.511N	P=0.314	P=0.290
Logistic regression tests	P=0.189	P=0.589	P=0.275	P=0.285
Cochran-Armitage test	P=0.144			
Fisher exact test		P=0.500	P=0.283	P=0.198
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	19/50 (38%)	14/50 (28%)	13/50 (26%)	19/50 (38%)
Adjusted rates	56.0%	39.3%	36.2%	46.8%
Terminal rates	12/26 (46%)	9/30 (30%)	7/28 (25%)	9/28 (32%)
First incidence (days)	470	633	582	471
Life table tests	P=0.510	P=0.122N	P=0.136N	P=0.460N
Logistic regression tests	P=0.507	P=0.124N	P=0.139N	P=0.523N
Cochran-Armitage test	P=0.449			
Fisher exact test		P=0.198N	P=0.142N	P=0.582N
Pituitary Gland (Pars Distalis): Adenoma or Carcinoma				
Overall rates	21/50 (42%)	14/50 (28%)	13/50 (26%)	19/50 (38%)
Adjusted rates	60.1%	39.3%	36.2%	46.8%
Terminal rates	13/26 (50%)	9/30 (30%)	7/28 (25%)	9/28 (32%)
First incidence (days)	470	633	582	471
Life table tests	P=0.433N	P=0.060N	P=0.071N	P=0.318N
Logistic regression tests	P=0.435N	P=0.063N	P=0.067N	P=0.371N
Cochran-Armitage test	P=0.490N			
Fisher exact test		P=0.104N	P=0.069N	P=0.419N

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol
(continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Thyroid Gland (C-cell): Adenoma				
Overall rates	9/50 (18%)	6/50 (12%)	6/51 (12%)	6/50 (12%)
Adjusted rates	29.8%	19.0%	19.5%	17.5%
Terminal rates	6/26 (23%)	5/30 (17%)	4/28 (14%)	2/28 (7%)
First incidence (days)	659	674	645	632
Life table tests	P=0.257N	P=0.215N	P=0.276N	P=0.248N
Logistic regression tests	P=0.238N	P=0.212N	P=0.280N	P=0.229N
Cochran-Armitage test	P=0.274N			
Fisher exact test		P=0.288N	P=0.274N	P=0.288N
Thyroid Gland (C-cell): Adenoma or Carcinoma				
Overall rates	10/50 (20%)	7/50 (14%)	6/51 (12%)	7/50 (14%)
Adjusted rates	33.3%	22.2%	19.5%	20.6%
Terminal rates	7/26 (27%)	6/30 (20%)	4/28 (14%)	3/28 (11%)
First incidence (days)	659	674	645	632
Life table tests	P=0.252N	P=0.213N	P=0.195N	P=0.252N
Logistic regression tests	P=0.234N	P=0.213N	P=0.199N	P=0.231N
Cochran-Armitage test	P=0.271N			
Fisher exact test		P=0.298N	P=0.195N	P=0.298N
Thyroid Gland (Follicular Cell): Adenoma				
Overall rates	3/50 (6%)	1/50 (2%)	0/51 (0%)	2/50 (4%)
Adjusted rates	11.5%	3.3%	0.0%	5.5%
Terminal rates	3/26 (12%)	1/30 (3%)	0/28 (0%)	0/28 (0%)
First incidence (days)	729 (T)	729 (T)	–	649
Life table tests	P=0.430N	P=0.254N	P=0.107N	P=0.465N
Logistic regression tests	P=0.426N	P=0.254N	P=0.107N	P=0.462N
Cochran-Armitage test	P=0.443N			
Fisher exact test		P=0.309N	P=0.118N	P=0.500N
Thyroid Gland (Follicular Cell): Adenoma or Carcinoma				
Overall rates	3/50 (6%)	2/50 (4%)	1/51 (2%)	2/50 (4%)
Adjusted rates	11.5%	5.3%	3.6%	5.5%
Terminal rates	3/26 (12%)	1/30 (3%)	1/28 (4%)	0/28 (0%)
First incidence (days)	729 (T)	544	729 (T)	649
Life table tests	P=0.386N	P=0.436N	P=0.277N	P=0.465N
Logistic regression tests	P=0.386N	P=0.476N	P=0.277N	P=0.462N
Cochran-Armitage test	P=0.402N			
Fisher exact test		P=0.500N	P=0.301N	P=0.500N
Uterus: Stromal Polyp				
Overall rates	5/50 (10%)	6/50 (12%)	3/51 (6%)	11/50 (22%)
Adjusted rates	17.9%	15.6%	9.5%	36.3%
Terminal rates	4/26 (15%)	2/30 (7%)	2/28 (7%)	9/28 (32%)
First incidence (days)	680	544	622	680
Life table tests	P=0.063	P=0.592	P=0.334N	P=0.108
Logistic regression tests	P=0.063	P=0.532	P=0.353N	P=0.101
Cochran-Armitage test	P=0.052			
Fisher exact test		P=0.500	P=0.346N	P=0.086

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Uterus: Stromal Polyp or Stromal Sarcoma				
Overall rates	6/50 (12%)	7/50 (14%)	3/51 (6%)	11/50 (22%)
Adjusted rates	19.7%	17.6%	9.5%	36.3%
Terminal rates	4/26 (15%)	2/30 (7%)	2/28 (7%)	9/28 (32%)
First incidence (days)	500	544	622	680
Life table tests	P=0.133	P=0.598	P=0.225N	P=0.180
Logistic regression tests	P=0.130	P=0.508	P=0.234N	P=0.187
Cochran-Armitage test	P=0.111			
Fisher exact test		P=0.500	P=0.234N	P=0.143
All Organs: Mononuclear Cell Leukemia				
Overall rates	14/50 (28%)	16/50 (32%)	11/51 (22%)	17/50 (34%)
Adjusted rates	38.7%	38.9%	30.7%	42.7%
Terminal rates	6/26 (23%)	6/30 (20%)	5/28 (18%)	7/28 (25%)
First incidence (days)	416	625	402	493
Life table tests	P=0.421	P=0.555	P=0.328N	P=0.448
Logistic regression tests	P=0.380	P=0.440	P=0.303N	P=0.344
Cochran-Armitage test	P=0.359			
Fisher exact test		P=0.414	P=0.302N	P=0.333
All Organs: Benign Neoplasms				
Overall rates	36/50 (72%)	33/50 (66%)	34/51 (67%)	41/50 (82%)
Adjusted rates	89.7%	78.0%	80.6%	89.0%
Terminal rates	22/26 (85%)	21/30 (70%)	20/28 (71%)	23/28 (82%)
First incidence (days)	435	544	562	471
Life table tests	P=0.252	P=0.151N	P=0.356N	P=0.433
Logistic regression tests	P=0.191	P=0.189N	P=0.341N	P=0.361
Cochran-Armitage test	P=0.105			
Fisher exact test		P=0.333N	P=0.358N	P=0.171
All Organs: Malignant Neoplasms				
Overall rates	24/50 (48%)	20/50 (40%)	17/51 (33%)	22/50 (44%)
Adjusted rates	59.8%	46.8%	42.5%	53.1%
Terminal rates	11/26 (42%)	8/30 (27%)	7/28 (25%)	10/28 (36%)
First incidence (days)	416	544	345	493
Life table tests	P=0.367N	P=0.185N	P=0.140N	P=0.321N
Logistic regression tests	P=0.407N	P=0.255N	P=0.097N	P=0.421N
Cochran-Armitage test	P=0.410N			
Fisher exact test		P=0.273N	P=0.097N	P=0.421N
All Organs: Benign or Malignant Neoplasms				
Overall rates	44/50 (88%)	41/50 (82%)	42/51 (82%)	47/50 (94%)
Adjusted rates	93.5%	87.2%	87.5%	94.0%
Terminal rates	23/26 (88%)	24/30 (80%)	22/28 (79%)	25/28 (89%)
First incidence (days)	416	544	345	471
Life table tests	P=0.405	P=0.145N	P=0.366N	P=0.521N
Logistic regression tests	P=0.246	P=0.207N	P=0.296N	P=0.355
Cochran-Armitage test	P=0.154			
Fisher exact test		P=0.288N	P=0.303N	P=0.243

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol
(continued)

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, salivary gland, spleen, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no neoplasms in animal group

TABLE B4a
Historical Incidence of Renal Tubule Neoplasms in Female F344/N Rats Administered Corn Oil by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Battelle-Columbus Division			
Dimethoxane	0/50	0/50	0/50
o-Benzyl-*p*-chlorophenol	0/50	0/50	0/50
Ochratoxin A	0/50	0/50	0/50
Overall Historical Incidence			
Total	2/1,068 (0.2%)	0/1,068 (0.0%)	2/1,068 (0.2%)
Standard deviation	0.6%		0.6%
Range	0%-2%		0%-2%

[a] Data as of 20 August 1992

TABLE B4b
Historical Incidence of Transitional Cell Neoplasms in Female F344/N Rats Administered Corn Oil by Gavage[a]

Study	Incidence in Controls	
	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Battelle-Columbus Division		
Dimethoxane	0/50	0/50
o-Benzyl-*p*-chlorophenol	0/50	0/50
Ochratoxin A	0/50	0/50
Overall Historical Incidence		
Total	0/1,068 (0.0%)	0/1,068 (0.0%)

[a] Data as of 20 August 1992

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Disposition Summary				
Animals initially in study[b]	80	80	80	80
3-Month interim evaluation	10	10	8	9
15-Month interim evaluation				
Histopathology	10	10	9	10
Clinical pathology	10	10[c]	9	8
Early deaths				
Accidental deaths	2	1	3	3
Moribund	17	12	15	18
Natural deaths	5	7	8	4
Survivors				
Terminal sacrifice	26	30	28	28
Animals examined microscopically	70	70	71	72
3-Month Interim Evaluation				
Alimentary System				
Esophagus	(10)			(9)
Muscularis, inflammation, chronic	1 (10%)			1 (11%)
Intestine large, rectum	(10)			(8)
Parasite metazoan	1 (10%)			
Pancreas	(10)			(9)
Inflammation, chronic	1 (10%)			
Cardiovascular System				
Heart	(10)			(9)
Myocardium, degeneration, chronic	3 (30%)			2 (22%)
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
Bone marrow	(10)			(9)
Femoral, hyperplasia, reticulum cell	1 (10%)			1 (11%)
Integumentary System				
None				

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
3-Month Interim Evaluation (continued)				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)			(9)
Inflammation, chronic active	2 (20%)			2 (22%)
Special Senses System				
Eye	(1)		(1)	(1)
Lens, cataract	1 (100%)		1 (100%)	1 (100%)
Retina, atrophy	1 (100%)			1 (100%)
Harderian gland	(1)			(1)
Inflammation, chronic active	1 (100%)			1 (100%)
Urinary System				
Kidney	(10)	(10)	(8)	(9)
Nephropathy	1 (10%)	3 (30%)	3 (38%)	7 (78%)
Corticomedullary junction, concretion	1 (10%)			
Corticomedullary junction, mineralization	5 (50%)	6 (60%)	3 (38%)	1 (11%)
15-Month Interim Evaluation				
Alimentary System				
Esophagus	(10)		(1)	(10)
Foreign body			1 (100%)	
Inflammation, chronic active			1 (100%)	
Intestine large, colon	(10)			(10)
Parasite metazoan	3 (30%)			
Intestine large, rectum	(10)			(10)
Parasite metazoan	1 (10%)			
Liver	(10)	(4)	(1)	(10)
Basophilic focus	2 (20%)			3 (30%)
Hepatodiaphragmatic nodule	1 (10%)	4 (100%)	1 (100%)	
Bile duct, hyperplasia	1 (10%)			
Pancreas	(10)			(10)
Acinus, atrophy	2 (20%)			1 (10%)
Stomach, forestomach	(10)		(1)	(10)
Cyst			1 (100%)	

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
15-Month Interim Evaluation (continued)				
Cardiovascular System				
Heart	(10)			(10)
Myocardium, degeneration, chronic	5 (50%)			2 (20%)
Endocrine System				
Adrenal gland, cortex	(10)			(10)
Hyperplasia	1 (10%)			
Pituitary gland	(10)	(1)	(1)	(10)
Pars distalis, hyperplasia	2 (20%)	1 (100%)	1 (100%)	2 (20%)
Thyroid gland	(10)			(10)
C-cell, hyperplasia	1 (10%)			1 (10%)
General Body System				
None				
Genital System				
Clitoral gland	(10)		(1)	(9)
Duct, dilatation	1 (10%)		1 (100%)	
Ovary	(10)	(2)		(10)
Periovarian tissue, cyst	1 (10%)	1 (50%)		
Hematopoietic System				
None				
Integumentary System				
Mammary gland	(10)			(10)
Hyperplasia	1 (10%)			
Skin	(10)	(1)		(10)
Subcutaneous tissue, edema		1 (100%)		
Musculoskeletal System				
None				
Nervous System				
Brain	(10)			(10)
Developmental malformation	1 (10%)			
Respiratory System				
Lung	(10)			(9)
Inflammation, chronic active	1 (10%)			

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
15-Month Interim Evaluation (continued)				
Special Senses System				
Eye		(1)	(3)	
Lens, cataract		1 (100%)	3 (100%)	
Retina, atrophy		1 (100%)	3 (100%)	
Urinary System				
Kidney	(10)	(10)	(9)	(10)
Nephropathy	9 (90%)	10 (100%)	9 (100%)	10 (100%)
2-Year Study				
Alimentary System				
Esophagus	(50)	(50)	(51)	(50)
Inflammation, chronic active			1 (2%)	
Inflammation, necrotizing				1 (2%)
Intestine large, cecum	(48)	(50)	(51)	(50)
Inflammation, necrotizing				1 (2%)
Intestine large, rectum	(49)	(50)	(51)	(50)
Parasite metazoan	2 (4%)	6 (12%)	3 (6%)	1 (2%)
Intestine small, duodenum	(50)	(50)	(51)	(50)
Inflammation, necrotizing	2 (4%)			1 (2%)
Liver	(50)	(50)	(51)	(50)
Basophilic focus	39 (78%)	43 (86%)	41 (80%)	40 (80%)
Clear cell focus	6 (12%)	10 (20%)	9 (18%)	16 (32%)
Degeneration, cystic			1 (2%)	2 (4%)
Eosinophilic focus	1 (2%)	2 (4%)	3 (6%)	2 (4%)
Fatty change	1 (2%)	4 (8%)	1 (2%)	1 (2%)
Hepatodiaphragmatic nodule	7 (14%)	5 (10%)	8 (16%)	8 (16%)
Inflammation, granulomatous	8 (16%)	9 (18%)	5 (10%)	2 (4%)
Inflammation, necrotizing			1 (2%)	2 (4%)
Mixed cell focus		3 (6%)		
Bile duct, hyperplasia	34 (68%)	37 (74%)	33 (65%)	25 (50%)
Centrilobular, necrosis		3 (6%)		
Mesentery	(4)	(3)	(1)	(5)
Fibrosis			1 (100%)	
Hemorrhage				1 (20%)
Fat, necrosis	4 (100%)	2 (67%)		3 (60%)
Pancreas	(50)	(50)	(50)	(50)
Acinus, atrophy	9 (18%)	12 (24%)	8 (16%)	15 (30%)
Acinus, hyperplasia	4 (8%)	1 (2%)	1 (2%)	
Pharynx		(1)		
Inflammation, suppurative		1 (100%)		
Salivary glands	(50)	(50)	(50)	(50)
Inflammation, chronic active	1 (2%)			1 (2%)
Inflammation, suppurative				1 (2%)

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Stomach, forestomach	(50)	(50)	(51)	(50)
Inflammation, chronic	1 (2%)			2 (4%)
Inflammation, necrotizing	2 (4%)	2 (4%)	1 (2%)	5 (10%)
Epithelium, hyperplasia	1 (2%)	2 (4%)		
Stomach, glandular	(49)	(50)	(51)	(50)
Inflammation, necrotizing	1 (2%)	3 (6%)		3 (6%)
Mineralization	3 (6%)	2 (4%)		2 (4%)
Cardiovascular System				
Heart	(50)	(50)	(51)	(50)
Mineralization				1 (2%)
Thrombosis		1 (2%)		
Myocardium, degeneration, chronic	35 (70%)	43 (86%)	42 (82%)	42 (84%)
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(51)	(50)
Hyperplasia	14 (28%)	14 (28%)	10 (20%)	26 (52%)
Hypertrophy	1 (2%)	2 (4%)	4 (8%)	2 (4%)
Necrosis	1 (2%)	2 (4%)	1 (2%)	
Adrenal gland, medulla	(50)	(50)	(51)	(50)
Hyperplasia	8 (16%)	4 (8%)	3 (6%)	10 (20%)
Islets, pancreatic	(50)	(50)	(50)	(50)
Hyperplasia		1 (2%)		
Parathyroid gland	(46)	(44)	(46)	(47)
Hyperplasia		1 (2%)		1 (2%)
Pituitary gland	(50)	(50)	(50)	(50)
Pars distalis, ectasia		1 (2%)		1 (2%)
Pars distalis, hyperplasia	25 (50%)	21 (42%)	29 (58%)	26 (52%)
Pars intermedia, hyperplasia	1 (2%)		1 (2%)	1 (2%)
Thyroid gland	(50)	(50)	(51)	(50)
C-cell, hyperplasia	18 (36%)	8 (16%)	11 (22%)	21 (42%)
Follicular cell, hyperplasia	5 (10%)	1 (2%)	1 (2%)	4 (8%)
General Body System				
None				
Genital System				
Clitoral gland	(49)	(48)	(49)	(47)
Hyperplasia	1 (2%)	2 (4%)	5 (10%)	1 (2%)
Inflammation, chronic active	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Duct, dilatation			1 (2%)	
Ovary	(50)	(50)	(51)	(50)
Cyst	2 (4%)	4 (8%)	3 (6%)	1 (2%)

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
2-Year Study (continued)				
Genital System (continued)				
Uterus	(50)	(50)	(51)	(50)
Dilatation			2 (4%)	1 (2%)
Vagina		(1)		
Inflammation, acute		1 (100%)		
Hematopoietic System				
Lymph node	(50)	(50)	(51)	(50)
Mediastinal, edema			1 (2%)	
Lymph node, mesenteric	(49)	(48)	(51)	(50)
Edema	1 (2%)			
Spleen	(50)	(50)	(51)	(50)
Fibrosis		1 (2%)		
Hematopoietic cell proliferation	1 (2%)		1 (2%)	
Thymus	(48)	(46)	(46)	(48)
Cyst		1 (2%)		
Integumentary System				
Mammary gland	(49)	(50)	(50)	(50)
Hyperplasia			2 (4%)	
Skin	(50)	(49)	(50)	(50)
Inflammation, chronic active	2 (4%)	1 (2%)		1 (2%)
Musculoskeletal System				
Skeletal muscle	(1)	(1)		
Hemorrhage		1 (100%)		
Nervous System				
Brain	(50)	(50)	(51)	(50)
Compression	5 (10%)	2 (4%)	1 (2%)	6 (12%)
Infarct	1 (2%)			
Inflammation, granulomatous	1 (2%)			
Respiratory System				
Lung	(50)	(50)	(51)	(50)
Foreign body	1 (2%)	2 (4%)		
Inflammation, chronic active	7 (14%)	1 (2%)	1 (2%)	4 (8%)
Inflammation, necrotizing	2 (4%)	1 (2%)	1 (2%)	
Mineralization				2 (4%)
Alveolar epithelium, hyperplasia	4 (8%)	8 (16%)	2 (4%)	7 (14%)
Nose	(50)	(50)	(51)	(50)
Mucosa, inflammation, suppurative	2 (4%)	3 (6%)	6 (12%)	4 (8%)
Nasolacrimal duct, inflammation, suppurative		1 (2%)		

TABLE B5
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
2-Year Study (continued)				
Special Senses System				
Eye	(2)	(3)	(4)	(6)
Degeneration		1 (33%)	2 (50%)	3 (50%)
Inflammation, chronic active				2 (33%)
Lens, cataract		1 (33%)		1 (17%)
Harderian gland		(1)	(1)	
Inflammation, chronic active			1 (100%)	
Zymbal's gland		(1)		(1)
Cyst		1 (100%)		
Urinary System				
Kidney	(50)	(50)	(51)	(50)
Atrophy				1 (2%)
Calculus micro observation only				2 (4%)
Infarct		1 (2%)		
Mineralization				1 (2%)
Nephropathy	46 (92%)	47 (94%)	50 (98%)	50 (100%)
Pelvis, inflammation, suppurative	1 (2%)		1 (2%)	2 (4%)
Pelvis, mineralization	3 (6%)	2 (4%)	2 (4%)	16 (32%)
Renal tubule, hyperplasia				1 (2%)
Urinary bladder	(50)	(50)	(51)	(50)
Transitional epithelium, hyperplasia	1 (2%)			1 (2%)

[a] Number of animals examined at site and number of animals with lesion
[b] Eight to ten of the eighty animals in each dose group were evaluated for clinical pathology only.
[c] Includes one animal that died during the scheduled sacrifice period.

APPENDIX C
SUMMARY OF LESIONS IN MALE MICE IN THE 2-YEAR GAVAGE STUDY OF *o*-BENZYL-*p*-CHLOROPHENOL

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Disposition Summary				
Animals initially in study	70	70	70	70
3-Month interim evaluation[b]	10	10	10	10
15-Month interim evaluation	10	10	10	10
Early deaths				
Accidental deaths		2		2
Moribund	2	12	6	8
Natural deaths	3	3	4	10
Survivors				
Died last week of study		1	2	
Terminal sacrifice	45	32	38	30
Animals examined microscopically	70	70	70	70
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(1)	(1)	(10)
Hepatocellular carcinoma				1 (10%)
Hepatocellular adenoma		1 (100%)		2 (20%)
Hepatocellular adenoma, multiple			1 (100%)	
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
None				
Integumentary System				
None				
Musculoskeletal System				
None				

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
15-Month Interim Evaluation (continued)				
Nervous System				
None				
Respiratory System				
Lung	(10)	(2)		(10)
Alveolar/bronchiolar adenoma	1 (10%)	2 (100%)		2 (20%)
Hepatocellular carcinoma, metastatic, liver				1 (10%)
Special Senses System				
Harderian gland				(1)
Adenoma				1 (100%)
Urinary System				
None				
2-Year Study				
Alimentary System				
Intestine large, cecum	(50)	(50)	(48)	(44)
Leiomyosarcoma			1 (2%)	
Intestine small, jejunum	(49)	(50)	(48)	(45)
Hemangiosarcoma	1 (2%)			
Liver	(50)	(50)	(50)	(50)
Hemangioma, multiple	1 (2%)			
Hemangiosarcoma	2 (4%)		1 (2%)	1 (2%)
Hemangiosarcoma, multiple	1 (2%)			1 (2%)
Hepatocellular carcinoma	7 (14%)	11 (22%)	9 (18%)	4 (8%)
Hepatocellular carcinoma, multiple		1 (2%)	2 (4%)	
Hepatocellular adenoma	8 (16%)	12 (24%)	15 (30%)	11 (22%)
Hepatocellular adenoma, multiple	13 (26%)	5 (10%)	4 (8%)	2 (4%)
Mesentery	(3)	(6)	(2)	(4)
Hemangiosarcoma				1 (25%)
Squamous cell carcinoma, metastatic, stomach		1 (17%)		
Pancreas	(50)	(50)	(49)	(50)
Squamous cell carcinoma, metastatic		1 (2%)		
Salivary glands	(50)	(50)	(50)	(50)
Hemangioma	1 (2%)			
Stomach, forestomach	(50)	(50)	(50)	(50)
Papilloma squamous	1 (2%)		2 (4%)	2 (4%)
Squamous cell carcinoma	1 (2%)	1 (2%)		

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Stomach, glandular	(50)	(50)	(50)	(50)
Hemangiosarcoma				1 (2%)
Tooth	(2)		(2)	
Adamantinoma benign	1 (50%)			
Cardiovascular System				
Heart	(49)	(50)	(49)	(50)
Hemangiosarcoma				1 (2%)
Endocrine System				
Adrenal gland	(50)	(50)	(50)	(49)
Capsule, adenoma	1 (2%)	1 (2%)	4 (8%)	1 (2%)
Adrenal gland, cortex	(50)	(50)	(50)	(49)
Adenoma	1 (2%)	1 (2%)		1 (2%)
Adrenal gland, medulla	(49)	(50)	(49)	(48)
Pheochromocytoma malignant			1 (2%)	
Pheochromocytoma benign	1 (2%)			
Thyroid gland	(50)	(50)	(50)	(50)
Follicle, adenoma	1 (2%)	2 (4%)		
General Body System				
None				
Genital System				
Prostate	(50)	(50)	(49)	(50)
Squamous cell carcinoma, metastatic, stomach		1 (2%)		
Seminal vesicle	(50)	(50)	(48)	(50)
Squamous cell carcinoma, metastatic, stomach		1 (2%)		
Hematopoietic System				
Bone marrow	(49)	(50)	(50)	(50)
Hemangioma				1 (2%)
Hemangiosarcoma			1 (2%)	1 (2%)
Lymph node	(49)	(50)	(48)	(49)
Squamous cell carcinoma, metastatic, stomach		1 (2%)		
Lumbar, hemangiosarcoma				1 (2%)
Lymph node, mandibular	(48)	(49)	(47)	(48)
Carcinoma, metastatic, nose	1 (2%)			
Lymph node, mesenteric	(49)	(44)	(44)	(41)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Hematopoietic System (continued)				
Spleen	(50)	(50)	(49)	(50)
Hemangiosarcoma	1 (2%)		2 (4%)	1 (2%)
Thymus	(42)	(38)	(41)	(41)
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Subcutaneous tissue, fibrosarcoma				1 (2%)
Subcutaneous tissue, hemangiosarcoma		2 (4%)	1 (2%)	
Musculoskeletal System				
Skeletal muscle		(1)		
Squamous cell carcinoma, metastatic		1 (100%)		
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Alveolar/bronchiolar adenoma	12 (24%)	9 (18%)	5 (10%)	4 (8%)
Alveolar/bronchiolar adenoma, multiple		1 (2%)	1 (2%)	
Alveolar/bronchiolar carcinoma	1 (2%)	2 (4%)	1 (2%)	1 (2%)
Alveolar/bronchiolar carcinoma, multiple	1 (2%)	1 (2%)		
Carcinoma, metastatic, nose	1 (2%)			
Hepatocellular carcinoma, metastatic, liver	2 (4%)	4 (8%)	2 (4%)	
Mediastinum, hemangiosarcoma			1 (2%)	
Nose	(50)	(50)	(50)	(50)
Carcinoma	1 (2%)			
Special Senses System				
Harderian gland	(3)	(4)	(4)	(2)
Adenoma	3 (100%)	2 (50%)	4 (100%)	1 (50%)
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Squamous cell carcinoma, metastatic, stomach		1 (2%)		
Renal tubule, adenocarcinoma			2 (4%)	1 (2%)
Renal tubule, adenoma		2 (4%)	2 (4%)	2 (4%)

TABLE C1
Summary of the Incidence of Neoplasms in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Systemic Lesions				
Multiple organs[c]	(50)	(50)	(50)	(50)
Lymphoma malignant mixed	1 (2%)			1 (2%)
Lymphoma malignant undifferentiated cell	1 (2%)			
Neoplasm Summary				
Total animals with primary neoplasms[d]				
15-Month interim evaluation	1	3	1	4
2-Year study	38	33	37	28
Total primary neoplasms				
15-Month interim evaluation	1	3	1	6
2-Year study	62	53	59	41
Total animals with benign neoplasms				
15-Month interim evaluation	1	3	1	4
2-Year study	30	24	27	24
Total benign neoplasms				
15-Month interim evaluation	1	3	1	5
2-Year study	44	35	37	25
Total animals with malignant neoplasms				
15-Month interim evaluation				1
2-Year study	17	16	17	10
Total malignant neoplasms				
15-Month interim evaluation				1
2-Year study	18	18	22	16
Total animals with secondary neoplasms				
15-Month interim evaluation				1
2-Year study	3	5	2	
Total secondary neoplasms				
15-Month interim evaluation				1
2-Year study	4	11	2	

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] No neoplasms were observed at the 3-month interim evaluation.
[c] Number of animals with any tissue examined microscopically
[d] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control

Number of Days on Study	6 4 6	6 5 0	6 9 4	6 9 9	7 2 1	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7
Carcass ID Number	0 1 0 1	0 5 4 1	0 2 9 1	0 3 8 1	0 6 7 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	0 0 7 1	0 0 9 1	0 1 1 1	0 1 2 1	0 1 3 1	0 1 4 1	0 1 6 1	0 1 7 1	0 1 8 1	0 1 9 1	0 2 0 1	0 2 1 1	0 2 2 1	0 2 3 1	0 2 5 1	0 2 7 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma, multiple																	X								
Hemangiosarcoma																									
Hemangiosarcoma, multiple													X												
Hepatocellular carcinoma		X			X				X			X					X								
Hepatocellular adenoma	X							X								X						X			
Hepatocellular adenoma, multiple						X	X										X						X		
Mesentery				+		+																			
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangioma																									
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																		X							
Squamous cell carcinoma																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth																				+					
Adamantinoma benign																				X					
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																									X
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Adrenal gland, medulla	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma benign																									
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	728	728	728	728	728	728	728	728	728	728	728	728	728	729	729	729	729	729	729	729	729	729	729	729	729	
Carcass ID Number	02811	03011	03111	03211	03311	03411	03511	03611	04011	04411	04311	04411	04511	04611	04711	04911	05111	05311	05511	05611	05711	05911	06511	06611	06811	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	M	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma																							X			1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma, multiple																										1
Hemangiosarcoma									X								X									2
Hemangiosarcoma, multiple																										1
Hepatocellular carcinoma													X					X								7
Hepatocellular adenoma								X					X					X							X	8
Hepatocellular adenoma, multiple	X	X	X				X		X	X	X				X				X							13
Mesentery								+																		3
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma						X																				1
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous																										1
Squamous cell carcinoma																			X							1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth															+											2
Adamantinoma benign																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma																										1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma											X															1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma benign		X																								1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	6 4 6	6 5 0	6 9 4	6 9 9	7 2 1	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7
Carcass ID Number	0 1 0 1	0 5 4 1	0 2 9 1	0 3 8 1	0 6 7 1	0 0 2 1	0 0 4 1	0 0 5 1	0 0 6 1	0 0 7 1	0 0 9 1	0 1 1 1	1 1 2 1	1 1 3 1	1 1 4 1	1 1 6 1	1 1 7 1	1 1 8 1	1 1 9 1	1 2 0 1	2 2 1 1	2 2 2 1	2 2 3 1	2 2 5 1	2 2 7 1
Endocrine System (continued)																									
Parathyroid gland	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicle, adenoma																X									
General Body System																									
Tissue NOS																				+					
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland						+	+		+						+						+		+		+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, nose			X																						
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Thymus	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M	M	M	M	M	M	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma				X			X			X						X	X					X			
Alveolar/bronchiolar carcinoma																									
Alveolar/bronchiolar carcinoma, multiple																									
Carcinoma, metastatic, nose			X																						
Hepatocellular carcinoma, metastatic, liver												X													
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma			X																						
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	0 2 8 1	0 3 0 1	0 3 1 1	0 3 2 1	0 3 3 1	0 3 4 1	0 3 5 1	0 3 6 1	0 3 0 1	0 4 1 1	0 4 3 1	0 4 4 1	0 4 5 1	0 4 6 1	0 4 7 1	0 4 9 1	0 5 1 1	0 5 3 1	0 5 5 1	0 5 6 1	0 5 7 1	0 5 9 1	0 6 5 1	0 6 6 1	0 6 8 1	Total Tissues/ Tumors
Endocrine System (continued)																											
Parathyroid gland	+	+	+	+	+	+	+	+	M	M	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Pituitary gland	M	+	M	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicle, adenoma																											1
General Body System																											
Tissue NOS																											1
Genital System																											
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland		+	+				+									+	+	+	+	+			+				16
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mandibular	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, metastatic, nose																											1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma									X																		1
Thymus	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	M	M	+	+	M		42
Integumentary System																											
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M		2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Alveolar/bronchiolar adenoma			X			X	X						X					X				X				12
Alveolar/bronchiolar carcinoma	X																										1
Alveolar/bronchiolar carcinoma, multiple								X																			1
Carcinoma, metastatic, nose																											1
Hepatocellular carcinoma, metastatic, liver													X														2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50
Carcinoma																											1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	4	5	9	9	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	6	0	4	9	1	2	2	2	2	4	4	4	4	7	7	7	7	7	7	7	7	7	7	7	7
Carcass ID Number	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1	5	2	3	6	0	0	0	0	0	0	1	1	1	1	1	1	1	1	2	2	2	2	2	2
	0	4	9	8	7	2	4	5	6	7	9	1	2	3	4	6	7	8	9	0	1	2	3	5	7
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Special Senses System																									
Eye		+									+														
Harderian gland		+									+														
Adenoma		X									X														
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant mixed																									
Lymphoma malignant undifferentiated cell type				X																					

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	0 2 8 1	0 3 0 1	0 3 1 1	0 3 2 1	0 3 3 1	0 3 4 1	0 3 5 1	0 3 6 1	0 3 0 1	0 4 1 1	0 4 3 1	0 4 4 1	0 4 5 1	0 4 6 1	0 4 7 1	0 4 9 1	0 5 1 1	0 5 3 1	0 5 5 1	0 5 6 1	0 5 7 1	0 5 9 1	0 6 5 1	0 6 6 1	0 6 8 1	Total Tissues/ Tumors
Special Senses System																										
Eye																										2
Harderian gland													+													3
Adenoma													X													3
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed														X												1
Lymphoma malignant undifferentiated cell type																										1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol: 120 mg/kg

Number of Days on Study	0 1 0	0 2 4	3 4 9	4 1 2	4 6 4	5 5 2	6 3 1	6 5 0	6 5 7	6 6 1	6 7 3	6 7 7	6 8 2	6 8 7	6 9 3	7 0 6	7 0 7	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 3
Carcass ID Number	0 8 6 1	0 7 4 1	0 9 6 1	0 7 7 1	1 1 4 1	1 3 5 1	1 2 0 1	0 7 5 1	1 0 0 1	1 1 9 1	1 1 7 1	0 7 9 1	1 2 7 1	0 7 2 1	0 9 0 1	1 1 1 1	1 3 9 1	0 7 3 1	0 7 6 1	0 8 0 1	0 8 1 1	0 8 4 1	0 8 7 1	0 8 8 1	1 2 5 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	+	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma								X	X				X		X	X	X								X
Hepatocellular carcinoma, multiple														X											
Hepatocellular adenoma					X							X						X		X			X		
Hepatocellular adenoma, multiple													X												
Mesentery											+					+								+	
Squamous cell carcinoma, metastatic, stomach											X														
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic											X														
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma											X														
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																									
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicle, adenoma																									
General Body System																									
None																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	724	724	724	724	724	724	724	727	727	727	727	727	727	728	728	728	728	729	729	729	729	729	729	729	
Carcass ID Number	08911	09111	09931	09941	09951	09971	09981	09991	10021	10031	10041	10061	10071	10121	11161	11181	11221	11261	11291	11311	11331	11341	11371	11381	11401	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma															X			X	X				X			11
Hepatocellular carcinoma, multiple																										1
Hepatocellular adenoma						X	X						X		X		X		X		X					12
Hepatocellular adenoma, multiple										X	X							X				X				5
Mesentery	+															+			+							6
Squamous cell carcinoma, metastatic, stomach																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic																										1
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma[c]							X																			1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma																			X							1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicle, adenoma																					X	X				2
General Body System																										
None																										

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	0 1 0	0 2 4	3 4 9	4 1 2	4 6 4	5 5 2	6 3 1	6 5 0	6 5 7	6 6 1	6 7 3	6 7 7	6 8 2	6 8 7	6 9 3	7 0 6	7 0 7	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 3
Carcass ID Number	0 8 6 1	0 7 4 1	0 9 6 1	0 7 7 1	1 1 4 1	1 3 5 1	1 2 0 1	0 7 5 1	1 0 0 1	1 1 9 1	1 1 7 1	0 7 9 1	1 2 7 1	0 7 2 1	0 9 0 1	1 1 1 1	1 3 9 1	0 7 3 1	0 7 6 1	0 8 0 1	0 8 1 1	0 8 4 1	0 8 7 1	0 8 8 1	1 2 5 1
Genital System																								
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland								+	+		+		+	+			+	+		+	+			+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach											X													
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach											X													
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach											X													
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+
Lymph node, mesenteric	M	M	+	+	+	+	M	+	M	M	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	M	+	+	M	+	+	M	+	+	M	+	M	+	+	+	+	M	+	+	+	M
Integumentary System																								
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangiosarcoma												X											X	
Musculoskeletal System																								
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skeletal muscle											+													
Squamous cell carcinoma, metastatic											X													
Nervous System																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																								
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma							X						X						X					
Alveolar/bronchiolar adenoma, multiple																								
Alveolar/bronchiolar carcinoma														X										
Alveolar/bronchiolar carcinoma, multiple																								
Hepatocellular carcinoma, metastatic, liver														X		X								
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	0 8 9 1	0 9 1 1	0 9 3 1	0 9 4 1	0 9 5 1	0 9 7 1	0 9 8 1	0 9 9 1	1 0 2 1	1 0 3 1	1 0 4 1	1 0 6 1	1 0 7 1	1 1 2 1	1 1 6 1	1 1 8 1	1 2 1 1	1 2 2 1	1 2 6 1	1 3 1 1	1 3 3 1	1 3 4 1	1 3 7 1	1 3 8 1	1 4 0 1	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Preputial gland	+	+	+	+		+	+			+					+					+	+	+	+			22
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach																										1
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach																										1
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	M	+	+	M	+	+	M	+	+	+	M	+	+	+	+	M	+	+	38
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, hemangiosarcoma																										2
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										1
Squamous cell carcinoma, metastatic																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma									X	X		X		X			X	X								9
Alveolar/bronchiolar adenoma, multiple								X																		1
Alveolar/bronchiolar carcinoma											X															2
Alveolar/bronchiolar carcinoma, multiple																			X							1
Hepatocellular carcinoma, metastatic, liver																		X					X			4
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	0	0	3	4	4	5	6	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7
	1	2	4	1	6	5	3	5	5	6	7	7	8	8	9	0	0	2	2	2	2	2	2	2	2
	0	4	9	2	4	2	1	0	7	1	3	7	2	7	3	6	7	2	2	2	2	2	2	2	3
Carcass ID Number	0	0	0	0	1	1	1	0	1	1	1	0	1	0	0	1	1	0	0	0	0	0	0	0	1
	8	7	9	7	1	3	2	7	0	1	1	7	2	7	9	1	3	7	7	8	8	8	8	8	2
	6	4	6	7	4	5	0	5	0	9	7	9	7	2	0	1	9	3	6	0	1	4	7	8	5
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Special Senses System																									
Eye																									
Harderian gland				+																					
Adenoma																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma, metastatic, stomach											X														
Renal tubule, adenoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	724	724	724	724	724	724	724	727	727	727	727	727	727	728	728	728	728	729	729	729	729	729	729	729	
Carcass ID Number	08991	09911	09931	09941	09951	09971	09981	09991	10211	10031	10041	10061	10071	10121	10261	10681	11211	11221	11261	11331	11341	11371	11381	11401	Total Tissues/ Tumors
Special Senses System																									
Eye																		+		+					2
Harderian gland									+									+		+					4
Adenoma																		X		X					2
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Squamous cell carcinoma, metastatic, stomach																									1
Renal tubule, adenoma	X					X																			2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg

Number of Days on Study	3 7 0	4 3 3	4 7 2	5 4 7	5 8 8	6 0 2	6 1 5	6 5 9	6 9 9	7 1 3	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4
Carcass ID Number	1 6 3 1	2 0 5 1	1 4 3 1	2 0 9 1	1 8 2 1	1 9 6 1	1 5 9 1	2 0 1 1	2 0 3 1	1 7 0 1	1 4 2 1	1 4 4 1	1 4 5 1	1 4 6 1	1 4 9 1	1 5 0 1	1 5 2 1	1 5 3 1	1 5 7 1	1 7 8 1	1 5 8 1	1 6 0 1	1 6 2 1	1 6 4 1	1 6 7 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	A	A	+	+	+	M	A	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma						X																			
Intestine large, colon	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	I	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Hepatocellular carcinoma	X					X		X		X					X					X	X			
Hepatocellular carcinoma, multiple			X																						
Hepatocellular adenoma		X		X	X			X							X			X					X	
Hepatocellular adenoma, multiple			X						X																
Mesentery																									
Pancreas	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous																									
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tooth						+								+											
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Capsule, adenoma																	X								
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma malignant																									
Islets, pancreatic	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	M	+
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
General Body System																									
None																									

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	1 6 8 1	1 7 1 1	1 7 2 1	1 7 3 1	1 7 4 1	1 7 6 1	1 7 7 1	1 8 0 1	1 8 8 1	1 8 8 1	1 8 8 1	1 8 8 1	1 8 8 1	1 8 8 1	1 8 8 1	1 9 0 1	1 9 9 1	1 9 9 1	2 0 0 1	2 0 0 1	2 0 0 1	2 0 0 1	2 0 0 1	2 0 0 1	2 0 1 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Leiomyosarcoma																										1
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																									X	1
Hepatocellular carcinoma									X											X						9
Hepatocellular carcinoma, multiple											X															2
Hepatocellular adenoma		X	X	X		X											X			X			X		X	15
Hepatocellular adenoma, multiple					X									X												4
Mesentery	+																	+								2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous							X														X					2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tooth																										2
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Capsule, adenoma		X	X																				X			4
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pheochromocytoma malignant																				X						1
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	3 7 0	4 3 3	4 7 2	5 4 7	5 7 8	6 0 2	6 1 5	6 5 9	6 9 9	7 1 3	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4
Carcass ID Number	1 6 3 1	2 0 5 1	1 4 3 1	2 0 9 1	1 8 2 1	1 9 6 1	1 5 9 1	2 0 1 1	2 0 3 1	1 7 0 1	1 4 2 1	1 4 4 1	1 4 5 1	1 4 6 1	1 4 9 1	1 5 0 1	1 5 2 1	1 5 3 1	1 5 7 1	1 7 8 1	1 5 8 1	1 6 0 1	1 6 2 1	1 6 4 1	1 6 7 1
Genital System																									
Epididymis	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial gland											+			+											
Prostate	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Testes	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph node	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	M	+	+	+	+	+	M	+	+	+	+	+		+	+	+	+	+	+	+	+
Lymph node, mesenteric	A	M	+	+	M	M	M	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+
Spleen	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma							X																		
Thymus	+	+	M	+	M	+	+	M	M	M	+	+	+	+	M	+	+	+	+	+	M	+	+	M	+
Integumentary System																									
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	+	M	M	M	M
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, hemangiosarcoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma											X														X
Alveolar/bronchiolar adenoma, multiple																									
Alveolar/bronchiolar carcinoma					X																				
Hepatocellular carcinoma, metastatic, liver						X				X															
Mediastinum, hemangiosarcoma																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	1 6 8 1	1 7 1 1	1 7 2 1	1 7 3 1	1 7 4 1	1 7 6 1	1 7 7 1	1 8 0 1	1 8 1 1	1 8 3 1	1 8 9 1	1 8 4 1	1 8 6 1	1 8 7 1	1 8 8 1	1 9 0 1	1 9 8 1	1 9 9 1	1 9 0 1	2 0 0 2 1	2 0 0 4 1	2 0 0 6 1	2 0 0 7 1	2 0 0 8 1	2 0 1 0 1	Total Tissues/ Tumors
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Preputial gland				+			+	+	+			+		+	+					+			+		+	12
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma															X											1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma															X											2
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	41
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, hemangiosarcoma															X											1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma																	X		X				X			5
Alveolar/bronchiolar adenoma, multiple														X												1
Alveolar/bronchiolar carcinoma																										1
Hepatocellular carcinoma, metastatic, liver																										2
Mediastinum, hemangiosarcoma														X												1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	3	4	4	5	5	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	7	3	7	4	8	0	1	5	9	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	0	3	2	7	8	2	5	9	9	3	2	2	2	2	2	2	2	2	2	2	4	4	4	4	4
Carcass ID Number	1	2	1	2	1	1	1	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	6	0	4	0	8	9	5	0	0	7	4	4	4	4	4	5	5	5	5	7	5	6	6	6	6
	3	5	3	9	2	6	9	1	3	0	2	4	5	6	9	0	2	3	7	8	8	0	2	4	7
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Special Senses System																									
Ear																	+								
Eye				+																					
Harderian gland		+		+																					
Adenoma		X		X																					
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenocarcinoma																									
Renal tubule, adenoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	1 6 8 1	1 7 1 1	1 7 2 1	1 7 3 1	1 7 4 1	1 7 6 1	1 7 7 1	1 8 0 1	1 8 1 1	1 8 3 1	1 8 9 1	1 8 4 1	1 8 6 1	1 8 7 1	1 8 8 1	1 8 0 1	1 9 0 1	1 9 8 1	1 9 9 1	2 0 0 1	2 0 2 1	2 0 4 1	2 0 6 1	2 0 7 1	2 0 8 1	2 1 0 1	Total Tissues/ Tumors
Special Senses System																										
Ear																										1
Eye																			+							2
Harderian gland																			+	+						4
Adenoma																			X	X						4
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenocarcinoma									X								X									2
Renal tubule, adenoma																							X		X	2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg

Number of Days on Study	0 0 1 2 3 4 4 4 4 5 6 6 6 6 6 6 7 7 7 7 7 7 7 7 0 0 9 7 8 2 2 6 6 5 1 4 5 5 8 8 9 0 0 1 2 2 2 2 2 9 9 4 5 7 1 4 1 5 8 9 3 1 7 0 7 2 0 6 3 2 2 2 2 2
Carcass ID Number	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 3 4 2 7 7 3 8 1 6 6 3 4 5 2 6 4 3 3 4 7 1 1 1 1 1 0 9 3 2 0 3 0 1 1 8 6 4 4 5 2 2 7 4 3 1 5 6 7 8 9 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Alimentary System	
Esophagus	+ +
Gallbladder	+ A A A + + A + + + + + + + + + + + A + + + + + +
Intestine large	+ A + + + + + + + + + + + + + + + + A + + + + + +
Intestine large, cecum	A A + A + + + A + + + + + + A + + + A + + + + + +
Intestine large, colon	+ A + + + + + + + + + + + + + + + + A + + + + + +
Intestine large, rectum	+ A + + + + + + + + + + + + A + + + A + + + + + +
Intestine small	+ + A +
Intestine small, duodenum	A A A +
Intestine small, ileum	+ A A A + + + + + + + M + + A M + + A + + + + + +
Intestine small, jejunum	+ + A A + + + + + + + M + + A + + + A + + + + + +
Liver	+ +
Hemangiosarcoma	X
Hemangiosarcoma, multiple	X
Hepatocellular carcinoma	X X X
Hepatocellular adenoma	X X X X X
Hepatocellular adenoma, multiple	
Mesentery	+ + + +
Hemangiosarcoma	X
Pancreas	+ +
Salivary glands	+ +
Stomach	+ +
Stomach, forestomach	+ +
Papilloma squamous	
Stomach, glandular	+ +
Hemangiosarcoma	X
Cardiovascular System	
Heart	+ +
Hemangiosarcoma	
Endocrine System	
Adrenal gland	+ + + + + M + + + + + + + + + + + + + + + + + +
Capsule, adenoma	
Adrenal gland, cortex	+ + + + + M + + + + + + + + + + + + + + + + + +
Adenoma	
Adrenal gland, medulla	+ + + + + M + + + + + + + + + + + + + + + + + +
Islets, pancreatic	+ + M +
Parathyroid gland	+ + + + + M M + + + + + + + + + + + + + + + + + +
Pituitary gland	+ + M + + M + + + + + M + + + + M + + + + + + + +
Thyroid gland	+ +
General Body System	
None	
Genital System	
Epididymis	+ +
Penis	+
Preputial gland	+

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg (continued)

Number of Days on Study	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 2 0 1	2 2 4 1	2 2 9 1	2 3 1 1	2 3 5 1	2 3 8 1	2 3 9 1	2 4 5 1	2 4 7 1	2 4 8 1	2 5 3 1	2 5 5 1	2 5 6 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 0 1	2 6 5 1	2 6 6 1	2 6 7 1	2 7 4 1	2 7 5 1	2 7 6 1	2 7 7 1	2 7 8 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Hemangiosarcoma, multiple																										1
Hepatocellular carcinoma																										4
Hepatocellular adenoma				X								X						X			X	X			X	11
Hepatocellular adenoma, multiple										X													X			2
Mesentery																								+		4
Hemangiosarcoma																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous																		X		X						2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																				X						1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Capsule, adenoma							X																			1
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma													X													1
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	48
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										
Genital System																										
Epididymis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Penis																										1
Preputial gland																										1

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg (continued)

Number of Days on Study	0 0 1 2 3 4 4 4 4 5 6 6 6 6 6 6 7 7 7 7 7 7 7 7 0 0 9 7 8 2 2 6 6 5 1 4 5 5 8 8 9 0 0 1 2 2 2 2 2 9 9 4 5 7 1 4 1 5 8 9 3 1 7 0 7 2 0 6 3 2 2 2 2 2
Carcass ID Number	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 3 4 2 7 7 3 8 1 6 6 3 4 5 2 6 4 3 3 4 7 1 1 1 1 1 0 9 3 2 0 3 0 1 1 8 6 4 4 5 2 2 7 4 3 1 5 6 7 8 9 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Genital System (continued)	
Prostate	+ +
Seminal vesicle	+ +
Testes	+ +
Hematopoietic System	
Bone marrow	+ +
Hemangioma	
Hemangiosarcoma	X
Lymph node	+ + + + + M + + + + + + + + + + + + + + + + + +
Lumbar, hemangiosarcoma	X
Lymph node, mandibular	+ + + + + M + + + + + M + + + + + + + + + + + +
Lymph node, mesenteric	M M A M M M + + + + + M M + + + + + M + + + + + +
Spleen	+ +
Hemangiosarcoma	X
Thymus	+ + + + + + M + + I + + M M M + + + + M + + + M +
Integumentary System	
Mammary gland	+ M M M M M M + M M M M M M M M M M M M M M M M M
Skin	+ +
Subcutaneous tissue, fibrosarcoma	
Musculoskeletal System	
Bone	+ +
Nervous System	
Brain	+ +
Respiratory System	
Lung	+ +
Alveolar/bronchiolar adenoma	
Alveolar/bronchiolar carcinoma	
Nose	+ +
Trachea	+ +
Special Senses System	
Harderian gland	+
Adenoma	X
Urinary System	
Kidney	+ +
Renal tubule, adenocarcinoma	
Renal tubule, adenoma	X
Urinary bladder	+ +
Systemic Lesions	
Multiple organs	+ +
Lymphoma malignant mixed	

TABLE C2
Individual Animal Tumor Pathology of Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg (continued)

Number of Days on Study	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 2 0 1	2 2 4 1	2 2 9 1	2 3 1 1	2 3 5 1	2 3 8 1	2 3 9 1	2 4 5 1	2 4 7 1	2 4 8 1	2 5 3 1	2 5 5 1	2 5 6 1	2 5 7 1	2 5 8 1	2 5 9 1	2 6 0 1	2 6 5 1	2 6 6 1	2 6 7 1	2 7 4 1	2 7 5 1	2 7 6 1	2 7 7 1	2 7 8 1	Total Tissues/ Tumors
Genital System (continued)																										
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Testes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangioma											X															1
Hemangiosarcoma																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lumbar, hemangiosarcoma																										1
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	41
Integumentary System																										
Mammary gland	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	2
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma												X														1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma			X		X												X	X								4
Alveolar/bronchiolar carcinoma																						X				1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Harderian gland								+																		2
Adenoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Renal tubule, adenocarcinoma										X																1
Renal tubule, adenoma																								X		2
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant mixed																							X			1

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Adrenal Gland (Capsule): Adenoma				
Overall rates[a]	1/50 (2%)	1/50 (2%)	4/50 (8%)	1/49 (2%)
Adjusted rates[b]	2.2%	3.0%	10.0%	3.3%
Terminal rates[c]	1/45 (2%)	1/33 (3%)	4/40 (10%)	1/30 (3%)
First incidence (days)	722 (T)	722 (T)	722 (T)	722 (T)
Life table tests[d]	P=0.396	P=0.691	P=0.146	P=0.669
Logistic regression tests[d]	P=0.396	P=0.691	P=0.146	P=0.669
Cochran-Armitage test[d]	P=0.518			
Fisher exact test[d]		P=0.753N	P=0.181	P=0.747
Harderian Gland: Adenoma				
Overall rates	3/50 (6%)	2/50 (4%)	4/50 (8%)	1/50 (2%)
Adjusted rates	6.4%	6.1%	8.9%	3.2%
Terminal rates	2/45 (4%)	2/33 (6%)	2/40 (5%)	0/30 (0%)
First incidence (days)	650	722 (T)	433	713
Life table tests	P=0.413N	P=0.623N	P=0.448	P=0.443N
Logistic regression tests	P=0.273N	P=0.544N	P=0.573N	P=0.354N
Cochran-Armitage test	P=0.292N			
Fisher exact test		P=0.500N	P=0.500	P=0.309N
Kidney (Renal Tubule): Adenoma or Carcinoma[e]				
Overall rates	0/50 (0%)	2/50 (4%)	4/50 (8%)	3/50 (6%)
Adjusted rates	0.0%	6.1%	10.0%	9.4%
Terminal rates	0/45 (0%)	2/33 (6%)	4/40 (10%)	2/30 (7%)
First incidence (days)	–[f]	722 (T)	722 (T)	692
Life table tests	P=0.054	P=0.173	P=0.049	P=0.064
Logistic regression tests	P=0.061	P=0.173	P=0.049	P=0.080
Cochran-Armitage test	P=0.113			
Fisher exact test		P=0.247	P=0.059	P=0.121
Liver: Hemangiosarcoma				
Overall rates	3/50 (6%)	0/50 (0%)	1/50 (2%)	2/50 (4%)
Adjusted rates	6.7%	0.0%	2.5%	5.3%
Terminal rates	3/45 (7%)	0/33 (0%)	1/40 (3%)	0/30 (0%)
First incidence (days)	722 (T)	–	722 (T)	651
Life table tests	P=0.563	P=0.181N	P=0.348N	P=0.653N
Logistic regression tests	P=0.608N	P=0.181N	P=0.348N	P=0.562N
Cochran-Armitage test	P=0.556N			
Fisher exact test		P=0.121N	P=0.309N	P=0.500N
Liver: Hepatocellular Adenoma				
Overall rates	21/50 (42%)	17/50 (34%)	19/50 (38%)	13/50 (26%)
Adjusted rates	45.6%	46.6%	40.9%	36.5%
Terminal rates	20/45 (44%)	14/33 (42%)	13/40 (33%)	9/30 (30%)
First incidence (days)	646	464	433	387
Life table tests	P=0.377N	P=0.453	P=0.558	P=0.442N
Logistic regression tests	P=0.119N	P=0.431N	P=0.315N	P=0.144N
Cochran-Armitage test	P=0.073N			
Fisher exact test		P=0.268N	P=0.419N	P=0.069N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Liver: Hepatocellular Carcinoma				
Overall rates	7/50 (14%)	12/50 (24%)	11/50 (22%)	4/50 (8%)
Adjusted rates	14.8%	29.7%	24.0%	10.0%
Terminal rates	5/45 (11%)	5/33 (15%)	6/40 (15%)	0/30 (0%)
First incidence (days)	650	650	370	465
Life table tests	P=0.342N	P=0.058	P=0.165	P=0.478N
Logistic regression tests	P=0.134N	P=0.111	P=0.413	P=0.250N
Cochran-Armitage test	P=0.140N			
Fisher exact test		P=0.154	P=0.218	P=0.262N
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rates	25/50 (50%)	25/50 (50%)	26/50 (52%)	16/50 (32%)
Adjusted rates	52.0%	59.3%	52.9%	41.4%
Terminal rates	22/45 (49%)	16/33 (48%)	17/40 (43%)	9/30 (30%)
First incidence (days)	646	464	370	387
Life table tests	P=0.352N	P=0.137	P=0.312	P=0.455N
Logistic regression tests	P=0.054N	P=0.400	P=0.430N	P=0.093N
Cochran-Armitage test	P=0.034N			
Fisher exact test		P=0.579N	P=0.500	P=0.052N
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	12/50 (24%)	10/50 (20%)	6/50 (12%)	4/50 (8%)
Adjusted rates	26.1%	27.9%	15.0%	13.3%
Terminal rates	11/45 (24%)	8/33 (24%)	6/40 (15%)	4/30 (13%)
First incidence (days)	699	631	722 (T)	722 (T)
Life table tests	P=0.061N	P=0.476	P=0.152N	P=0.141N
Logistic regression tests	P=0.043N	P=0.573N	P=0.154N	P=0.115N
Cochran-Armitage test	P=0.013N			
Fisher exact test		P=0.405N	P=0.096N	P=0.027N
Lung: Alveolar/bronchiolar Carcinoma				
Overall rates	2/50 (4%)	3/50 (6%)	1/50 (2%)	1/50 (2%)
Adjusted rates	4.4%	8.6%	2.2%	3.3%
Terminal rates	2/45 (4%)	2/33 (6%)	0/40 (0%)	1/30 (3%)
First incidence (days)	722 (T)	687	588	722 (T)
Life table tests	P=0.383N	P=0.366	P=0.537N	P=0.640N
Logistic regression tests	P=0.312N	P=0.426	P=0.421N	P=0.640N
Cochran-Armitage test	P=0.279N			
Fisher exact test		P=0.500	P=0.500N	P=0.500N
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rates	14/50 (28%)	13/50 (26%)	7/50 (14%)	5/50 (10%)
Adjusted rates	30.4%	35.5%	16.8%	16.7%
Terminal rates	13/45 (29%)	10/33 (30%)	6/40 (15%)	5/30 (17%)
First incidence (days)	699	631	588	722 (T)
Life table tests	P=0.046N	P=0.328	P=0.122N	P=0.132N
Logistic regression tests	P=0.025N	P=0.488	P=0.099N	P=0.108N
Cochran-Armitage test	P=0.007N			
Fisher exact test		P=0.500N	P=0.070N	P=0.020N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol
(continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
All Organs: Hemangiosarcoma				
Overall rates	4/50 (8%)	2/50 (4%)	4/50 (8%)	3/50 (6%)
Adjusted rates	8.9%	5.5%	9.6%	8.5%
Terminal rates	4/45 (9%)	1/33 (3%)	3/40 (8%)	1/30 (3%)
First incidence (days)	722 (T)	677	615	651
Life table tests	P=0.476	P=0.479N	P=0.576	P=0.614
Logistic regression tests	P=0.566	P=0.408N	P=0.629	P=0.597N
Cochran-Armitage test	P=0.519N			
Fisher exact test		P=0.339N	P=0.643N	P=0.500N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	6/50 (12%)	2/50 (4%)	4/50 (8%)	4/50 (8%)
Adjusted rates	13.3%	5.5%	9.6%	11.6%
Terminal rates	6/45 (13%)	1/33 (3%)	3/40 (8%)	2/30 (7%)
First incidence (days)	722 (T)	677	615	651
Life table tests	P=0.529	P=0.250N	P=0.446N	P=0.613N
Logistic regression tests	P=0.524N	P=0.195N	P=0.401N	P=0.507N
Cochran-Armitage test	P=0.430N			
Fisher exact test		P=0.134N	P=0.370N	P=0.370N
All Organs: Benign Tumors				
Overall rates	30/50 (60%)	26/50 (52%)	28/50 (56%)	25/50 (50%)
Adjusted rates	62.4%	65.9%	60.6%	66.6%
Terminal rates	27/45 (60%)	20/33 (61%)	22/40 (55%)	18/30 (60%)
First incidence (days)	646	10	433	194
Life table tests	P=0.236	P=0.285	P=0.479	P=0.211
Logistic regression tests	P=0.344N	P=0.342N	P=0.384N	P=0.408N
Cochran-Armitage test	P=0.228N			
Fisher exact test		P=0.273N	P=0.420N	P=0.211N
All Organs: Malignant Tumors				
Overall rates	17/50 (34%)	16/50 (32%)	17/50 (34%)	11/50 (22%)
Adjusted rates	34.7%	38.0%	35.9%	30.0%
Terminal rates	13/45 (29%)	7/33 (21%)	10/40 (25%)	6/30 (20%)
First incidence (days)	650	650	370	465
Life table tests	P=0.418N	P=0.309	P=0.432	P=0.510N
Logistic regression tests	P=0.150N	P=0.547	P=0.385N	P=0.233N
Cochran-Armitage test	P=0.111N			
Fisher exact test		P=0.500N	P=0.583N	P=0.133N
All Organs: Benign or Malignant Tumors				
Overall rates	38/50 (76%)	34/50 (68%)	38/50 (76%)	29/50 (58%)
Adjusted rates	76.0%	75.4%	76.0%	70.1%
Terminal rates	33/45 (73%)	22/33 (67%)	28/40 (70%)	18/30 (60%)
First incidence (days)	646	10	370	194
Life table tests	P=0.371	P=0.183	P=0.280	P=0.341
Logistic regression tests	P=0.092N	P=0.367N	P=0.461N	P=0.131N
Cochran-Armitage test	P=0.046N			
Fisher exact test		P=0.252N	P=0.592N	P=0.044N

TABLE C3
Statistical Analysis of Primary Neoplasms in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, epididymis, gallbladder, heart, kidney, larynx, liver, lung, nose, pancreas, parathyroid gland, pituitary gland, preputial gland, prostate gland, salivary gland, spleen, testes, thyroid gland, and urinary bladder; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Does not include data collected during the extended, step-section evaluation.
[f] Not applicable; no neoplasms in animal group

TABLE C4
Historical Incidence of Renal Tubule Neoplasms in Male B6C3F$_1$ Mice Administered Corn Oil by Gavage[a]

Study	Incidence in Controls		
	Adenoma	Carcinoma	Adenoma or Carcinoma
Historical Incidence at Battelle-Columbus			
Dimethoxane	1/50	0/50	1/50
o-Benzyl-*p*-chlorophenol	0/50	0/50	0/50
Overall Historical Incidence			
Total	4/949 (0.4%)	0/949 (0.0%)	4/949 (0.4%)
Standard deviation	0.8%		0.8%
Range	0%-2%		0%-2%

[a] Data as of 20 August 1992

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Disposition Summary				
Animals initially in study	70	70	70	70
3-Month interim evaluation	10	10	10	10
15-Month interim evaluation	10	10	10	10
Early deaths				
Accidental deaths		2		2
Moribund	2	12	6	8
Natural deaths	3	3	4	10
Survivors				
Died last week of study		1	2	
Terminal sacrifice	45	32	38	30
Animals examined microscopically	70	70	70	70
3-Month Interim Evaluation				
Alimentary System				
Liver	(10)			(10)
Inflammation, necrotizing	3 (30%)			2 (20%)
Pancreas	(10)			(10)
Inflammation, chronic	2 (20%)			
Necrosis	1 (10%)			
Stomach, glandular	(10)			(10)
Inflammation, suppurative	1 (10%)			
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
Thymus	(10)			(10)
Depletion lymphoid				1 (10%)
Integumentary System				
None				

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
3-Month Interim Evaluation (continued)				
Musculoskeletal System				
Bone	(10)			(10)
Hyperostosis				1 (10%)
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Nephropathy	1 (10%)	3 (30%)	10 (100%)	10 (100%)
15-Month Interim Evaluation				
Alimentary System				
Liver	(10)	(1)	(1)	(10)
Fatty change	5 (50%)			
Mesentery		(1)		
Fat, necrosis		1 (100%)		
Pancreas	(10)	(1)		(10)
Cyst	1 (10%)			
Stomach, forestomach	(10)	(3)	(1)	(10)
Hyperplasia, squamous				1 (10%)
Inflammation, necrotizing				1 (10%)
Ulcer		1 (33%)		
Stomach, glandular	(10)	(2)	(1)	(10)
Mucosa, mineralization	3 (30%)		1 (100%)	
Cardiovascular System				
None				
Endocrine System				
Adrenal gland, cortex	(10)	(2)		(10)
Hyperplasia	1 (10%)	1 (50%)		1 (10%)
Hypertrophy, focal		1 (50%)		

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
15-Month Interim Evaluation (continued)				
General Body System				
None				
Genital System				
Preputial gland	(1)	(1)	(3)	
Inflammation, chronic active			1 (33%)	
Duct, dilatation	1 (100%)	1 (100%)	2 (67%)	
Hematopoietic System				
None				
Integumentary System				
None				
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(10)	(2)		(10)
Alveolar epithelium, hyperplasia	1 (10%)			1 (10%)
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(10)
Metaplasia, osseous			2 (20%)	
Nephropathy	9 (90%)	10 (100%)	10 (100%)	10 (100%)
Renal tubule, hyperplasia		1 (10%)	1 (10%)	
2-Year Study				
Alimentary System				
Intestine small, duodenum	(50)	(50)	(48)	(47)
Ulcer		1 (2%)	1 (2%)	2 (4%)

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Liver	(50)	(50)	(50)	(50)
Cyst	1 (2%)			1 (2%)
Degeneration, cystic				1 (2%)
Hepatodiaphragmatic nodule			1 (2%)	
Hyperplasia	5 (10%)	4 (8%)	5 (10%)	3 (6%)
Inflammation, chronic		2 (4%)		2 (4%)
Necrosis, coagulative	4 (8%)	4 (8%)	7 (14%)	5 (10%)
Mesentery	(3)	(6)	(2)	(4)
Foreign body				2 (50%)
Inflammation, necrotizing				2 (50%)
Fat, necrosis	2 (67%)	5 (83%)	1 (50%)	1 (25%)
Pancreas	(50)	(50)	(49)	(50)
Basophilic focus			1 (2%)	
Inflammation, chronic		2 (4%)	2 (4%)	
Salivary glands	(50)	(50)	(50)	(50)
Inflammation, chronic			1 (2%)	1 (2%)
Stomach, forestomach	(50)	(50)	(50)	(50)
Cyst epithelial inclusion	1 (2%)			
Hyperplasia, squamous	4 (8%)	12 (24%)	11 (22%)	9 (18%)
Ulcer	1 (2%)	6 (12%)	9 (18%)	6 (12%)
Stomach, glandular	(50)	(50)	(50)	(50)
Ulcer	1 (2%)	5 (10%)	1 (2%)	1 (2%)
Mucosa, mineralization	2 (4%)	6 (12%)	12 (24%)	6 (12%)
Tooth	(2)		(2)	
Developmental malformation	1 (50%)			
Inflammation, chronic active			2 (100%)	
Cardiovascular System				
Heart	(49)	(50)	(49)	(50)
Bacterium				1 (2%)
Artery, inflammation, necrotizing		2 (4%)	2 (4%)	
Atrium, thrombus			1 (2%)	1 (2%)
Myocardium, degeneration			5 (10%)	9 (18%)
Myocardium, mineralization			1 (2%)	
Pericardium, inflammation, subacute	1 (2%)			
Valve, inflammation, chronic active				1 (2%)
Endocrine System				
Adrenal gland	(50)	(50)	(50)	(49)
Capsule, hyperplasia	5 (10%)	1 (2%)	7 (14%)	6 (12%)
Adrenal gland, cortex	(50)	(50)	(50)	(49)
Degeneration, fatty, focal			1 (2%)	
Hyperplasia	3 (6%)	16 (32%)	8 (16%)	8 (16%)
Hypertrophy, focal	5 (10%)	3 (6%)	4 (8%)	4 (8%)
Adrenal gland, medulla	(49)	(50)	(49)	(48)
Hyperplasia	1 (2%)			2 (4%)

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Endocrine System (continued)				
Islets, pancreatic	(50)	(50)	(49)	(49)
Hyperplasia	2 (4%)			
Pituitary gland	(47)	(48)	(47)	(46)
Pars distalis, hyperplasia	2 (4%)	1 (2%)	3 (6%)	1 (2%)
Thyroid gland	(50)	(50)	(50)	(50)
Follicle, hyperplasia	5 (10%)	3 (6%)		1 (2%)
General Body System				
None				
Genital System				
Preputial gland	(16)	(22)	(12)	(1)
Inflammation, chronic active		3 (14%)		
Duct, dilatation	16 (100%)	22 (100%)	12 (100%)	1 (100%)
Seminal vesicle	(50)	(50)	(48)	(50)
Inflammation, chronic	1 (2%)	1 (2%)		1 (2%)
Hematopoietic System				
Bone marrow	(49)	(50)	(50)	(50)
Hyperplasia, mast cell		1 (2%)		
Myelofibrosis			1 (2%)	
Lymph node	(49)	(50)	(48)	(49)
Mediastinal, hyperplasia		1 (2%)		
Lymph node, mandibular	(48)	(49)	(47)	(48)
Hyperplasia, mast cell		1 (2%)		
Lymph node, mesenteric	(49)	(44)	(44)	(41)
Ectasia		1 (2%)		
Hyperplasia, lymphoid			1 (2%)	
Sinus, ectasia			2 (5%)	
Spleen	(50)	(50)	(49)	(50)
Depletion lymphoid	2 (4%)	2 (4%)	3 (6%)	6 (12%)
Hematopoietic cell proliferation	5 (10%)	7 (14%)	2 (4%)	1 (2%)
Hyperplasia, lymphoid	2 (4%)	1 (2%)	6 (12%)	
Inflammation, chronic		1 (2%)		
Integumentary System				
Skin	(50)	(50)	(50)	(50)
Edema	1 (2%)			
Inflammation, chronic		1 (2%)		
Ulcer				1 (2%)
Hair follicle, atrophy				1 (2%)

TABLE C5
Summary of the Incidence of Nonneoplastic Lesions in Male Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Musculoskeletal System				
Bone	(50)	(50)	(50)	(50)
Fibrous osteodystrophy		16 (32%)	25 (50%)	28 (56%)
Nervous System				
None				
Respiratory System				
Lung	(50)	(50)	(50)	(50)
Foreign body		2 (4%)		3 (6%)
Inflammation, chronic			1 (2%)	3 (6%)
Inflammation, subacute	1 (2%)			
Nose	(50)	(50)	(50)	(50)
Foreign body		1 (2%)		2 (4%)
Inflammation, suppurative		1 (2%)		
Special Senses System				
Eye	(2)	(2)	(2)	
Cataract			1 (50%)	
Phthisis bulbi	1 (50%)		1 (50%)	
Cornea, inflammation, chronic		2 (100%)	1 (50%)	
Harderian gland	(3)	(4)	(4)	(2)
Hyperplasia		1 (25%)		1 (50%)
Inflammation, suppurative		1 (25%)		
Urinary System				
Kidney	(50)	(50)	(50)	(50)
Nephropathy	39 (78%)	48 (96%)	50 (100%)	49 (98%)
Renal tubule, hyperplasia			3 (6%)	6 (12%)
Renal tubule, hyperplasia, adenomatous		1 (2%)		

[a] Number of animals examined microscopically at site and number of animals with lesion

APPENDIX D
SUMMARY OF LESIONS IN FEMALE MICE IN THE 2-YEAR GAVAGE STUDY OF *o*-BENZYL-*p*-CHLOROPHENOL

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Disposition Summary				
Animals initially in study	70	70	70	70
3-Month interim evaluation[b]	10	10	10	9
15-Month interim evaluation	10	10	10	9
Early deaths				
Accidental deaths		3	2	1
Moribund	9	4	10	12
Natural deaths	4	3	5	14
Survivors				
Died last week of study	1			
Terminal sacrifice	36	40	33	25
Animals examined microscopically	70	70	70	70

15-Month Interim Evaluation

Alimentary System
None

Cardiovascular System
None

Endocrine System
None

General Body System
None

Genital System

Ovary	(10)			(9)
Teratoma	1 (10%)			

Hematopoietic System
None

Integumentary System
None

Musculoskeletal System
None

Nervous System
None

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
15-Month Interim Evaluation (continued)				
Respiratory System				
Lung	(10)			(9)
Alveolar/bronchiolar adenoma				1 (11%)
Special Senses System				
None				
Urinary System				
None				
2-Year Study				
Alimentary System				
Gallbladder	(47)	(47)	(48)	(45)
Intestine large, cecum	(50)	(50)	(50)	(52)
Intestine large, rectum	(49)	(50)	(50)	(52)
Intestine small, duodenum	(49)	(49)	(48)	(52)
Intestine small, ileum	(50)	(48)	(48)	(52)
Intestine small, jejunum	(50)	(48)	(48)	(52)
Liver	(50)	(50)	(50)	(52)
Carcinoma, metastatic, islets, pancreatic			1 (2%)	
Fibrous histiocytoma, metastatic, ear		1 (2%)		
Hepatocellular carcinoma	2 (4%)	1 (2%)	3 (6%)	2 (4%)
Hepatocellular carcinoma, multiple				1 (2%)
Hepatocellular adenoma	9 (18%)	9 (18%)	11 (22%)	10 (19%)
Hepatocellular adenoma, multiple	2 (4%)	5 (10%)	4 (8%)	4 (8%)
Mast cell tumor malignant, metastatic, mesentery		1 (2%)		
Mesentery	(5)	(8)	(2)	
Hemangioma		1 (13%)		
Hemangiosarcoma		1 (13%)		
Mast cell tumor malignant		1 (13%)		
Pancreas	(50)	(50)	(50)	(52)
Salivary glands	(50)	(50)	(50)	(52)
Stomach	(50)	(50)	(50)	(52)
Adenocarcinoma		1 (2%)		
Stomach, forestomach	(50)	(50)	(50)	(52)
Papilloma squamous		3 (6%)	2 (4%)	1 (2%)
Stomach, glandular	(50)	(50)	(50)	(52)
Cardiovascular System				
Heart	(50)	(50)	(49)	(52)
Hemangiosarcoma		1 (2%)		

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Endocrine System				
Adrenal gland	(50)	(50)	(50)	(52)
Adrenal gland, cortex	(50)	(50)	(50)	(52)
Islets, pancreatic	(50)	(50)	(50)	(52)
Carcinoma			1 (2%)	
Pituitary gland	(47)	(50)	(47)	(49)
Pars distalis, adenoma	8 (17%)	4 (8%)	5 (11%)	1 (2%)
Pars intermedia, adenoma			1 (2%)	
Thyroid gland	(49)	(50)	(50)	(52)
Follicle, adenoma	1 (2%)	1 (2%)		1 (2%)
General Body System				
None				
Genital System				
Ovary	(49)	(49)	(49)	(51)
Granulosa cell tumor benign	2 (4%)			
Hemangioma				1 (2%)
Hemangiosarcoma	1 (2%)			
Thecoma benign	1 (2%)			
Bilateral, hemangiosarcoma		1 (2%)		
Uterus	(50)	(50)	(50)	(52)
Hemangiosarcoma	1 (2%)	1 (2%)		
Leiomyoma	1 (2%)	1 (2%)	1 (2%)	
Leiomyosarcoma		2 (4%)		1 (2%)
Polyp stromal	1 (2%)	2 (4%)		
Vagina			(1)	(1)
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(52)
Hemangiosarcoma			1 (2%)	
Mast cell tumor malignant, metastatic, mesentery		1 (2%)		
Lymph node	(49)	(50)	(48)	(52)
Lymph node, mandibular	(46)	(47)	(46)	(51)
Carcinoma, metastatic, islets, pancreatic			1 (2%)	
Fibrous histiocytoma, metastatic, ear		1 (2%)		

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Lymph node, mesenteric	(44)	(48)	(46)	(45)
Mast cell tumor malignant, metastatic, mesentery		1 (2%)		
Spleen	(50)	(50)	(50)	(52)
Hemangiosarcoma		2 (4%)	1 (2%)	1 (2%)
Mast cell tumor malignant, metastatic, mesentery		1 (2%)		
Thymus	(45)	(44)	(44)	(44)
Thymoma malignant	1 (2%)			
Integumentary System				
Mammary gland	(47)	(49)	(47)	(46)
Skin	(50)	(50)	(50)	(52)
Subcutaneous tissue, fibrosarcoma	3 (6%)			1 (2%)
Subcutaneous tissue, fibrous histiocytoma		1 (2%)		
Subcutaneous tissue, hemangioma	1 (2%)			
Subcutaneous tissue, neurofibrosarcoma	1 (2%)			
Musculoskeletal System				
Bone	(50)	(50)	(50)	(52)
Hemangiosarcoma			1 (2%)	
Skeletal muscle	(2)			
Rhabdomyosarcoma	1 (50%)			
Nervous System				
Brain	(50)	(50)	(50)	(52)
Meningioma malignant			1 (2%)	
Osteosarcoma, metastatic, bone				1 (2%)
Respiratory System				
Lung	(49)	(50)	(50)	(52)
Alveolar/bronchiolar adenoma	3 (6%)	1 (2%)		3 (6%)
Alveolar/bronchiolar carcinoma	2 (4%)	2 (4%)	1 (2%)	1 (2%)
Hepatocellular carcinoma, metastatic, liver			1 (2%)	2 (4%)
Rhabdomyosarcoma, metastatic, skeletal muscle	1 (2%)			
Special Senses System				
Ear		(1)		
Pinna, fibrous histiocytoma		1 (100%)		
Harderian gland	(5)	(3)	(3)	(3)
Adenoma	4 (80%)	1 (33%)	2 (67%)	3 (100%)

TABLE D1
Summary of the Incidence of Neoplasms in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Urinary System				
Kidney	(50)	(50)	(50)	(52)
Urinary bladder	(50)	(50)	(50)	(52)
Systemic Lesions				
Multiple organs[c]	(50)	(50)	(50)	(52)
Lymphoma malignant histiocytic		3 (6%)	4 (8%)	3 (6%)
Lymphoma malignant lymphocytic	2 (4%)	1 (2%)		
Lymphoma malignant mixed	5 (10%)	1 (2%)	3 (6%)	1 (2%)
Lymphoma malignant undifferentiated cell	2 (4%)	4 (8%)	3 (6%)	
Neoplasm Summary				
Total animals with primary neoplasms[d]				
15-Month interim evaluation	1			1
2-Year study	39	35	29	28
Total primary neoplasms				
15-Month interim evaluation	1			1
2-Year study	54	52	45	35
Total animals with benign neoplasms				
15-Month interim evaluation	1			1
2-Year study	28	25	22	22
Total benign neoplasms				
15-Month interim evaluation	1			1
2-Year study	33	28	26	24
Total animals with malignant neoplasms				
2-Year study	18	16	15	10
Total malignant neoplasms				
2-Year study	21	24	19	11
Total animals with secondary neoplasms				
2-Year study	1	2	2	3
Total secondary neoplasms				
2-Year study	1	6	3	3

[a] Number of animals examined microscopically at site and number of animals with lesion
[b] No neoplasms were observed at the 3-month interim evaluation.
[c] Number of animals with any tissue examined microscopically
[d] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control

Number of Days on Study	5 6 6 6 6 6 6 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
	6 0 0 4 4 5 9 9 9 0 0 1 1 2 2 2 2 2 2 2 2 2 2 2
	0 3 5 0 5 0 2 4 9 6 7 3 9 2 2 2 2 4 4 4 4 5 7 7 7
Carcass ID Number	3 3 2 3 3 3 3 3 3 3 3 3 3 2 2 2 2 2 2 2 2 3 2 2 2
	4 1 9 3 3 1 1 0 1 0 3 0 2 8 8 8 8 8 8 9 9 3 9 9 9
	3 3 6 9 6 7 2 5 6 8 8 7 1 2 3 4 5 6 8 1 2 3 3 4 5
	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Alimentary System	
Esophagus	+ +
Gallbladder	A + + + + M + + + + + + + + + + + + + + + + + + +
Intestine large	+ +
Intestine large, cecum	+ +
Intestine large, colon	A +
Intestine large, rectum	A +
Intestine small	+ +
Intestine small, duodenum	A +
Intestine small, ileum	+ +
Intestine small, jejunum	+ +
Liver	+ +
Hepatocellular carcinoma	X
Hepatocellular adenoma	X X
Hepatocellular adenoma, multiple	X X
Mesentery	+ + +
Pancreas	+ +
Salivary glands	+ +
Stomach	+ +
Stomach, forestomach	+ +
Stomach, glandular	+ +
Cardiovascular System	
Heart	+ +
Endocrine System	
Adrenal gland	+ +
Adrenal gland, cortex	+ +
Adrenal gland, medulla	+ + + + + + + + + + + + M + + + + + + + + + + + +
Islets, pancreatic	+ +
Parathyroid gland	+ + + M + + + + + M + + + M M + M + + + + + + + M
Pituitary gland	+ + + M + + + + + + + M + + + + + + + + + + + + +
Pars distalis, adenoma	X X X X
Thyroid gland	+ +
Follicle, adenoma	
General Body System	
None	

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 9 7 1	2 9 8 1	2 9 9 1	3 0 1 1	3 0 3 1	3 0 6 1	3 1 0 1	3 1 4 1	3 1 8 1	3 1 9 1	3 2 0 1	3 2 2 1	3 2 6 1	3 2 7 1	3 2 9 1	3 3 0 1	3 3 2 1	3 3 5 1	3 4 0 1	4 4 1 1	4 4 2 1	4 4 6 1	4 4 7 1	4 4 8 1	4 4 9 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma		X																								2
Hepatocellular adenoma	X					X			X						X	X					X		X		9
Hepatocellular adenoma, multiple																										2
Mesentery		+								+																5
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	43
Pituitary gland	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma	X										X						X						X			8
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	49
Follicle, adenoma																						X				1
General Body System																										
None																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	5 6 6 6 6 6 6 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 6 0 0 4 4 5 9 9 9 0 0 1 1 2 2 2 2 2 2 2 2 2 2 2 0 3 5 0 5 0 2 4 9 6 7 3 9 2 2 2 2 4 4 4 5 7 7 7
Carcass ID Number	3 3 2 3 3 3 3 3 3 3 3 3 3 2 2 2 2 2 2 2 2 3 2 2 2 4 1 9 3 3 1 1 0 1 0 3 0 2 8 8 8 8 8 8 9 9 3 9 9 9 3 3 6 9 6 7 2 5 6 8 8 7 1 2 3 4 5 6 8 1 2 3 3 4 5 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Genital System	
Ovary	+ +
Granulosa cell tumor benign	X
Hemangiosarcoma	X
Thecoma benign	
Uterus	+ +
Hemangiosarcoma	X
Leiomyoma	
Polyp stromal	X
Hematopoietic System	
Bone marrow	+ +
Lymph node	+ M + + +
Lymph node, mandibular	M + + + + + + + + + + M + + + + + + + + + M M + +
Lymph node, mesenteric	M + + M + + + + + + + + + + + + + + + + + M + + +
Spleen	+ +
Thymus	+ + + + + + M + + + + + + M M + + + + + + M + + +
Thymoma malignant	
Integumentary System	
Mammary gland	+ + M + + + + + + + + + + M + + + + + + + + + + +
Skin	+ +
Subcutaneous tissue, fibrosarcoma	X X X
Subcutaneous tissue, hemangioma	
Subcutaneous tissue, neurofibrosarcoma	X
Musculoskeletal System	
Bone	+ +
Skeletal muscle	+ +
Rhabdomyosarcoma	X
Nervous System	
Brain	+ +
Respiratory System	
Lung	+ +
Alveolar/bronchiolar adenoma	X
Alveolar/bronchiolar carcinoma	X X
Rhabdomyosarcoma, metastatic, skeletal muscle	X
Nose	+ +
Trachea	+ +

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 9 7 1	2 9 8 1	2 9 9 1	3 0 1 1	3 0 3 1	3 0 6 1	3 1 0 1	3 1 4 1	3 1 8 1	3 1 9 1	3 2 0 1	3 2 2 1	3 2 6 1	3 2 7 1	3 2 9 1	3 3 0 1	3 3 2 1	3 3 5 1	3 4 0 1	3 4 1 1	3 4 2 1	3 4 6 1	3 4 7 1	3 4 8 1	3 4 9 1	Total Tissues/ Tumors
Genital System																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	49
Granulosa cell tumor benign																									X	2
Hemangiosarcoma																										1
Thecoma benign					X																					1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Leiomyoma																		X								1
Polyp stromal																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Lymph node, mesenteric	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	M	+	44
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	45
Thymoma malignant	X																									1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrosarcoma																										3
Subcutaneous tissue, hemangioma																						X				1
Subcutaneous tissue, neurofibrosarcoma																										1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Skeletal muscle																										2
Rhabdomyosarcoma																										1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	49
Alveolar/bronchiolar adenoma							X					X														3
Alveolar/bronchiolar carcinoma																										2
Rhabdomyosarcoma, metastatic, skeletal muscle																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	5	6	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	6	0	0	4	4	5	9	9	9	0	0	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2
	0	3	5	0	5	0	2	4	9	6	7	3	9	2	2	2	2	4	4	4	4	5	7	7	7	7
Carcass ID Number	3	3	2	3	3	3	3	3	3	3	3	3	3	2	2	2	2	2	2	2	2	3	2	2	2	2
	4	1	9	3	3	1	1	0	1	0	3	0	2	8	8	8	8	8	8	9	9	3	9	9	9	9
	3	3	6	9	6	7	2	5	6	8	8	7	1	2	3	4	5	6	8	1	2	3	3	4	1	5
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Special Senses System																										
Eye			+																	+						
Harderian gland			+				+																			
Adenoma			X				X																			
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant lymphocytic				X	X																					
Lymphoma malignant mixed						X		X						X					X							
Lymphoma malignant undifferentiated cell type																										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: Vehicle Control (continued)

Number of Days on Study	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	2 9 7 1	2 9 8 1	2 9 9 1	3 0 1 1	3 0 3 1	3 0 6 1	3 1 0 1	3 1 4 1	3 1 8 1	3 1 9 1	3 2 0 1	3 2 2 1	3 2 6 1	3 2 7 1	3 2 9 1	3 3 0 1	3 3 2 1	3 3 5 1	3 4 0 1	4 4 1 1	4 4 2 1	4 4 6 1	4 4 7 1	4 4 8 1	4 4 9 1	Total Tissues/ Tumors
Special Senses System																										
Eye																										2
Harderian gland	+				+			+																		5
Adenoma	X							X																		4
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant lymphocytic																										2
Lymphoma malignant mixed																			X							5
Lymphoma malignant undifferentiated cell type																					X	X				2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg

Number of Days on Study	0 1 0	0 1 4	0 1 7	5 1 0	5 8 8	5 8 8	6 0 0	6 6 4	6 9 2	6 9 7	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4
Carcass ID Number	3 6 7 1	4 0 3 1	3 6 0 1	3 7 9 1	3 9 6 1	4 1 5 1	3 8 1 1	3 7 8 1	3 8 3 1	3 5 5 1	3 5 3 1	3 5 4 1	3 5 6 1	3 6 3 1	3 6 4 1	3 6 5 1	3 6 6 1	3 7 1 1	3 7 2 1	3 7 3 1	3 7 4 1	3 7 5 1	3 7 7 1	3 8 0 1	3 8 4 1
Alimentary System																									
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder	+	M	+	+	+	+	A	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, ileum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Intestine small, jejunum	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrous histiocytoma, metastatic, ear																									
Hepatocellular carcinoma													X												
Hepatocellular adenoma											X											X			
Hepatocellular adenoma, multiple															X		X	X					X		
Mast cell tumor malignant, metastatic, mesentery																					X				
Mesentery				+					+						+						+				
Hemangioma																									
Hemangiosarcoma															X										
Mast cell tumor malignant																					X				
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma																									
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma squamous							X																		X
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma				X																					
Endocrine System																									
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pars distalis, adenoma											X								X						
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicle, adenoma														X											

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	724	727	727	727	727	727	727	727	727	728	728	728	728	728	728	728	729	729	729	729	729	729	729	729	
Carcass ID Number	38551	38711	38811	39211	39311	39411	39511	39711	39811	39911	40011	40111	40411	40811	40911	41011	41111	41211	41311	41411	41611	41711	41811	41911	42011	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	49
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	49
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibrous histiocytoma, metastatic, ear																						X				1
Hepatocellular carcinoma																										1
Hepatocellular adenoma									X			X			X			X	X		X				X	9
Hepatocellular adenoma, multiple																		X								5
Mast cell tumor malignant, metastatic, mesentery																										1
Mesentery	+			+								+								+						8
Hemangioma																				X						1
Hemangiosarcoma																										1
Mast cell tumor malignant																										1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma																					X					1
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous						X																				3
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																										1
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Parathyroid gland	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pars distalis, adenoma							X												X							4
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicle, adenoma																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	0 1 0	0 1 4	0 1 7	5 1 0	5 8 8	5 8 8	6 0 0	6 6 4	6 9 2	6 9 7	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4
Carcass ID Number	3 6 7 1	4 0 3 1	3 6 0 1	3 7 9 1	3 9 6 1	4 1 5 1	3 8 1 1	3 7 8 1	3 8 3 1	3 5 5 1	3 5 3 1	3 5 4 1	3 5 6 1	3 6 3 1	3 6 4 1	3 6 5 1	3 6 6 1	3 6 1 1	3 7 2 1	3 7 3 1	3 7 4 1	3 7 5 1	3 7 7 1	3 8 0 1	3 8 4 1
General Body System																									
None																									
Genital System																									
Clitoral gland																	+								
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bilateral, hemangiosarcoma				X																					
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Leiomyoma																									
Leiomyosarcoma											X														
Polyp stromal				X				X																	
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mast cell tumor malignant, metastatic, mesentery																				X					
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	M	+	+
Fibrous histiocytoma, metastatic, ear																									
Lymph node, mesenteric	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mast cell tumor malignant, metastatic, mesentery																				X					
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma															X										
Mast cell tumor malignant, metastatic, mesentery																				X					
Thymus	+	+	+	+	+	M	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue, fibrous histiocytoma																									
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																									
Alveolar/bronchiolar carcinoma															X										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	3 8 5 1	3 8 7 1	3 8 8 1	3 9 2 1	3 9 3 1	3 9 4 1	3 9 5 1	3 9 7 1	3 9 8 1	3 9 9 1	4 0 0 1	4 0 1 1	4 0 4 1	4 0 8 1	4 0 9 1	4 1 0 1	4 1 1 1	4 1 2 1	4 1 3 1	4 1 4 1	4 1 6 1	4 1 7 1	4 1 8 1	4 1 9 1	4 2 0 1	Total Tissues/ Tumors
General Body System																										
None																										
Genital System																										
Clitoral gland																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	49
Bilateral, hemangiosarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																							X			1
Leiomyoma											X															1
Leiomyosarcoma				X																						2
Polyp stromal																										2
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Mast cell tumor malignant, metastatic, mesentery																										1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Fibrous histiocytoma, metastatic, ear																							X			1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Mast cell tumor malignant, metastatic, mesentery																										1
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma														X												2
Mast cell tumor malignant, metastatic, mesentery																										1
Thymus	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	44
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue, fibrous histiocytoma																							X			1
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X																			1
Alveolar/bronchiolar carcinoma																									X	2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	0	0	0	5	5	5	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	1	1	1	1	8	8	0	6	9	9	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	0	4	7	0	8	8	0	4	2	7	2	2	2	2	2	2	2	2	4	4	4	4	4	4	4
Carcass ID Number	3	4	3	3	3	4	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	6	0	6	7	9	1	8	7	8	5	5	5	5	6	6	6	6	7	7	7	7	7	7	8	8
	7	3	0	9	6	5	1	8	3	5	3	4	6	3	4	5	6	1	2	3	4	5	7	0	4
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Respiratory System (continued)																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Ear																									
Pinna, fibrous histiocytoma																									
Harderian gland					+																				+
Adenoma					X																				
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic						X															X				
Lymphoma malignant lymphocytic									X																
Lymphoma malignant mixed										X															
Lymphoma malignant undifferentiated cell type											X				X										

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 120 mg/kg (continued)

Number of Days on Study	724	727	727	727	727	727	727	727	727	728	728	728	728	728	728	728	728	729	729	729	729	729	729	729	
Carcass ID Number	38515	38711	38811	38921	39031	39941	39951	39971	39981	39901	40011	40041	40081	40091	40101	40121	40131	40141	40161	40171	40181	40191	40211	40201	Total Tissues/ Tumors
Respiratory System (continued)																									
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																									
Ear																						+			1
Pinna, fibrous histiocytoma																						X			1
Harderian gland							+																		3
Adenoma																									1
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																							X		3
Lymphoma malignant lymphocytic																									1
Lymphoma malignant mixed																									1
Lymphoma malignant undifferentiated cell type							X					X													4

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol: 240 mg/kg

Number of Days on Study	0 0 1 4 4 5 6 6 6 6 6 6 6 7 7 7 7 7 7 7 7 7 7 7
	0 0 9 4 8 6 2 5 6 7 8 9 9 0 0 1 1 2 2 2 2 2 2 2
	7 7 6 9 2 9 2 2 8 8 5 1 2 6 7 4 4 2 2 2 2 2 2 4
Carcass ID Number	4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
	6 6 6 6 2 8 9 6 4 6 4 6 7 5 2 4 4 2 2 2 3 3 3 3
	0 5 2 6 4 2 0 4 1 3 8 7 1 8 8 0 5 1 5 7 9 0 1 2 3
	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Alimentary System	
Esophagus	+ +
Gallbladder	+ + + + + + + + + + M + + + + + + + + + + + +
Intestine large	+ +
Intestine large, cecum	+ +
Intestine large, colon	+ +
Intestine large, rectum	+ +
Intestine small	+ + + + + + + + + + + + M + + + + + + + + + + +
Intestine small, duodenum	+ + + + + + + + + + + + M + + + + + + + + + + +
Intestine small, ileum	+ + + + + + + + + + + + M + + + + + + + + + + +
Intestine small, jejunum	+ + + + + + + + + + + + M + + + + + + + + + + +
Liver	+ +
Carcinoma, metastatic, islets, pancreatic	X
Hepatocellular carcinoma	X X X
Hepatocellular adenoma	X X
Hepatocellular adenoma, multiple	X X X
Mesentery	+ +
Pancreas	+ +
Salivary glands	+ +
Stomach	+ +
Stomach, forestomach	+ +
Papilloma squamous	
Stomach, glandular	+ +
Cardiovascular System	
Heart	+ +
Endocrine System	
Adrenal gland	+ +
Adrenal gland, cortex	+ +
Adrenal gland, medulla	+ +
Islets, pancreatic	+ +
Carcinoma	X
Parathyroid gland	+ + + + M + + + + + + + + + + + + + + M + + + + + +
Pituitary gland	+ + + + + + M + + + + + + + + + + M + + M + + + + +
Pars distalis, adenoma	X
Pars intermedia, adenoma	X
Thyroid gland	+ +
General Body System	
None	

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	4 3 4 1	4 3 8 1	4 3 9 1	4 4 2 1	4 4 9 1	4 5 1 1	4 5 4 1	4 5 5 1	4 5 7 1	4 5 9 1	4 6 8 1	4 6 9 1	4 7 0 1	4 7 2 1	4 7 3 1	4 7 4 1	4 7 5 1	4 7 7 1	4 7 9 1	4 8 1 1	4 8 4 1	4 8 6 1	4 8 7 1	4 8 8 1	4 8 9 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	48
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	48
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	48
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	48
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, metastatic, islets, pancreatic																										1
Hepatocellular carcinoma																										3
Hepatocellular adenoma	X			X	X					X						X	X	X	X		X					11
Hepatocellular adenoma, multiple															X											4
Mesentery																										2
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Papilloma squamous		X					X																			2
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	49
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma																										1
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	M	+	46
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Pars distalis, adenoma	X														X		X	X								5
Pars intermedia, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
General Body System																										
None																										

Table D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	007	007	196	449	482	569	622	652	668	678	685	691	692	706	707	714	714	722	722	722	722	722	722	722	724
Carcass ID Number	4601	4651	4621	4661	4241	4821	4901	4641	4411	4631	4481	4671	4711	4581	4281	4401	4451	4211	4251	4271	4291	4301	4311	4321	4331
Genital System																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																									
Vagina											+														
Hematopoietic System																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph node	+	+	M	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph node, mandibular	+	+	M	+	+	+	+	M	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, islets, pancreatic																X									
Lymph node, mesenteric	+	+	M	+	+	+	+	+	M	+	+	M	+	+	+	M	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Thymus	+	+	+	+	+	+	+	+	+	+	+	M	M	+	+	M	M	+	+	+	+	+	+	+	+
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Musculoskeletal System																									
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Nervous System																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Meningioma malignant																X									
Peripheral nerve					+																				
Spinal cord					+																				
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Hepatocellular carcinoma, metastatic, liver																	X								
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
Eye																		+							
Harderian gland			+								+							+							
Adenoma											X							X							

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	4 3 4 1	4 3 8 1	4 3 9 1	4 4 2 1	4 4 9 1	4 5 1 1	4 5 4 1	4 5 5 1	4 5 7 1	4 5 9 1	4 6 8 1	4 6 9 1	4 7 0 1	4 7 2 1	4 7 3 1	4 7 4 1	4 7 5 1	4 7 7 1	4 7 9 1	4 8 1 1	4 8 4 1	4 8 6 1	4 8 7 1	4 8 8 1	4 8 9 1	Total Tissues/ Tumors
Genital System																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyoma																								X		1
Vagina																										1
Hematopoietic System																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																							X			1
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Carcinoma, metastatic, islets, pancreatic																										1
Lymph node, mesenteric	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																							X			1
Thymus	+	+	+	+	M	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	44
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	47
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Musculoskeletal System																										
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma																							X			1
Nervous System																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Meningioma malignant																										1
Peripheral nerve																										1
Spinal cord																										1
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma																		X								1
Hepatocellular carcinoma, metastatic, liver																										1
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Special Senses System																										
Eye																										1
Harderian gland																										3
Adenoma																										2

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	0	0	1	4	4	5	6	6	6	6	6	6	6	7	7	7	7	7	7	7	7	7	7	7
	0	0	9	4	8	6	2	5	6	7	8	9	9	0	0	1	1	2	2	2	2	2	2	2
	7	7	6	9	2	9	2	2	8	8	5	1	2	6	7	4	4	2	2	2	2	2	2	4
Carcass ID Number	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	6	6	6	6	2	8	9	6	4	6	4	6	7	5	2	4	4	2	2	2	2	3	3	3	3
	0	5	2	6	4	2	0	4	1	3	8	7	1	8	8	0	5	1	5	7	9	0	1	2	3
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymphoma malignant histiocytic				X							X														
Lymphoma malignant mixed						X												X							
Lymphoma malignant undifferentiated cell type																								X	

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 240 mg/kg (continued)

Number of Days on Study	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	4 3 4 1	4 3 8 1	4 3 9 1	4 4 2 1	4 4 9 1	4 5 1 1	4 5 4 1	4 5 5 1	4 5 7 1	4 5 7 1	4 5 9 1	4 6 8 1	4 6 9 1	4 7 0 1	4 7 2 1	4 7 3 1	4 7 4 1	4 7 5 1	4 7 7 1	4 7 9 1	4 8 1 1	4 8 4 1	4 8 6 1	4 8 7 1	4 8 8 1	4 8 9 1	Total Tissues/ Tumors
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymphoma malignant histiocytic																			X		X						4
Lymphoma malignant mixed									X																		3
Lymphoma malignant undifferentiated cell type																		X		X							3

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg

Number of Days on Study	0 0 1 1 2 2 3 4 4 4 5 5 5 5 6 6 6 6 6 6 6 6 7 7 7 0 0 1 9 6 8 0 2 3 8 2 3 5 7 0 1 4 5 5 5 6 8 9 0 1 1 8 8 0 7 9 2 3 2 7 2 1 2 4 0 8 8 7 1 2 8 6 9 9 7 4 4
Carcass ID Number	5 5 5 4 5 5 5 5 5 5 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 2 4 1 9 3 4 3 1 3 0 9 5 1 5 1 5 2 1 2 3 0 6 3 2 0 5 4 7 4 2 4 8 6 2 5 4 1 8 8 4 0 6 8 9 3 2 0 0 8 1 8 3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Alimentary System	
Esophagus	+ +
Gallbladder	+ + + M A + A A + + + + + + M + + + + + + + + + A +
Intestine large	+ +
Intestine large, cecum	+ +
Intestine large, colon	+ +
Intestine large, rectum	+ +
Intestine small	+ +
Intestine small, duodenum	+ +
Intestine small, ileum	+ +
Intestine small, jejunum	+ +
Liver	+ +
Hepatocellular carcinoma	X
Hepatocellular carcinoma, multiple	X
Hepatocellular adenoma	X
Hepatocellular adenoma, multiple	X
Pancreas	+ +
Salivary glands	+ +
Stomach	+ +
Stomach, forestomach	+ +
Papilloma squamous	X
Stomach, glandular	+ +
Cardiovascular System	
Heart	+ +
Endocrine System	
Adrenal gland	+ +
Adrenal gland, cortex	+ +
Adrenal gland, medulla	+ +
Islets, pancreatic	+ +
Parathyroid gland	+ +
Pituitary gland	+ + + + + + + + + + + + M + M + + + + + + + + + M
Pars distalis, adenoma	X
Thyroid gland	+ +
Follicle, adenoma	
General Body System	
None	
Genital System	
Ovary	+ + + + + + + + + + M + + + + + + + + + + + + +
Hemangioma	
Uterus	+ +
Leiomyosarcoma	
Vagina	+

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg (continued)

Number of Days on Study	7 2 0	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	4 9 9 1	4 9 6 1	4 9 7 1	5 0 2 1	5 0 5 1	5 0 7 1	5 1 1 1	5 1 5 1	5 1 6 1	5 1 7 1	5 2 2 1	5 2 7 1	5 3 0 1	5 3 7 1	5 3 9 1	5 4 0 1	5 4 2 1	5 4 3 1	5 4 4 1	5 4 6 1	5 4 9 1	5 5 0 1	5 5 1 1	5 5 5 1	5 5 7 1	5 5 9 1	Total Tissues/ Tumors
Alimentary System																										
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Gallbladder	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Intestine large	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, cecum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, colon	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine large, rectum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, duodenum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, ileum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Intestine small, jejunum	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hepatocellular carcinoma									X																	2
Hepatocellular carcinoma, multiple																										1
Hepatocellular adenoma			X							X				X				X	X	X		X	X		X	10
Hepatocellular adenoma, multiple									X		X					X										4
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Salivary glands	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Stomach, forestomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Papilloma squamous																										1
Stomach, glandular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Cardiovascular System																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Endocrine System																										
Adrenal gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adrenal gland, cortex	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Adrenal gland, medulla	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Islets, pancreatic	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Parathyroid gland	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	M	+	+	+	+	+	+	+	50
Pituitary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Pars distalis, adenoma																										1
Thyroid gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Follicle, adenoma			X																							1
General Body System																										
None																										
Genital System																										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Hemangioma															X											1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Leiomyosarcoma																	X									1
Vagina																										1

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg (continued)

Number of Days on Study	0 0 1 1 2 2 3 4 4 4 5 5 5 5 6 6 6 6 6 6 6 6 7 7 7 0 0 1 9 6 8 0 2 3 8 2 3 5 7 0 1 4 5 5 5 6 8 9 0 1 1 8 8 0 7 9 2 3 2 7 2 1 2 4 0 8 8 7 1 2 8 6 9 9 7 4 4
Carcass ID Number	5 5 5 4 5 5 5 5 5 5 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 2 4 1 9 3 4 3 1 3 0 9 5 1 5 1 5 2 1 2 3 0 6 3 2 0 5 4 7 4 2 4 8 6 2 5 4 1 8 8 4 0 6 8 9 3 2 0 0 8 1 8 3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Hematopoietic System	
Bone marrow	+ +
Lymph node	+ +
Lymph node, mandibular	+ + + + + + + + + + + + + + + + + M + + + + + + +
Lymph node, mesenteric	+ + + + + M M + + M + + + + + M + + + + + + M + + +
Spleen	+ +
Hemangiosarcoma	X
Thymus	+ + + + + + + + + M M M + M + + + + + M + + + + M M
Integumentary System	
Mammary gland	+ + M + + + + + + M M + + + M + + + + + + + + + M +
Skin	+ +
Subcutaneous tissue, fibrosarcoma	
Musculoskeletal System	
Bone	+ +
Nervous System	
Brain	+ +
Osteosarcoma, metastatic, bone	X
Respiratory System	
Lung	+ +
Alveolar/bronchiolar adenoma	X X
Alveolar/bronchiolar carcinoma	
Hepatocellular carcinoma, metastatic, liver	X
Nose	+ +
Trachea	+ +
Special Senses System	
Eye	+
Harderian gland	+ +
Adenoma	X X
Urinary System	
Kidney	+ +
Urinary bladder	+ +
Systemic Lesions	
Multiple organs	+ +
Lymphoma malignant histiocytic	X X X
Lymphoma malignant mixed	X

TABLE D2
Individual Animal Tumor Pathology of Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol: 480 mg/kg (continued)

Number of Days on Study	7 2 0	7 2 2	7 2 2	7 2 2	7 2 2	7 2 2	7 2 4	7 2 4	7 2 4	7 2 4	7 2 4	7 2 7	7 2 7	7 2 7	7 2 7	7 2 7	7 2 8	7 2 8	7 2 8	7 2 8	7 2 8	7 2 9	7 2 9	7 2 9	7 2 9	7 2 9	
Carcass ID Number	4 9 9 1	4 9 6 1	4 9 7 1	5 0 2 1	5 0 5 1	5 0 7 1	5 1 1 1	5 1 5 1	5 1 6 1	5 1 7 1	5 2 2 1	5 2 7 1	5 3 0 1	5 3 7 1	5 3 9 1	5 4 0 1	5 4 2 1	5 4 3 1	5 4 4 1	5 4 6 1	5 4 9 1	5 5 0 1	5 5 1 1	5 5 5 1	5 5 7 1	5 5 9 1	Total Tissues/ Tumors
Hematopoietic System																											
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymph node, mandibular	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	51
Lymph node, mesenteric	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	45
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Hemangiosarcoma																											1
Thymus	+	+	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Integumentary System																											
Mammary gland	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Subcutaneous tissue, fibrosarcoma						X																					1
Musculoskeletal System																											
Bone	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Nervous System																											
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Osteosarcoma, metastatic, bone																											1
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Alveolar/bronchiolar adenoma																		X									3
Alveolar/bronchiolar carcinoma																						X					1
Hepatocellular carcinoma, metastatic, liver									X																		2
Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Special Senses System																											
Eye					+																						2
Harderian gland					+																						3
Adenoma					X																						3
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	52
Lymphoma malignant histiocytic																											3
Lymphoma malignant mixed																											1

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Harderian Gland: Adenoma				
Overall rates[a]	4/50 (8%)	1/50 (2%)	2/50 (4%)	3/52 (6%)
Adjusted rates[b]	9.5%	2.2%	5.5%	9.8%
Terminal rates[c]	2/37 (5%)	0/40 (0%)	1/33 (3%)	1/25 (4%)
First incidence (days)	605	588	685	658
Life table tests[d]	P=0.469	P=0.189N	P=0.392N	P=0.623
Logistic regression tests[d]	P=0.563N	P=0.156N	P=0.346N	P=0.556N
Cochran-Armitage test[d]	P=0.524N			
Fisher exact test[d]		P=0.181N	P=0.339N	P=0.478N
Liver: Hepatocellular Adenoma				
Overall rates	11/50 (22%)	14/50 (28%)	15/50 (30%)	14/52 (27%)
Adjusted rates	27.3%	35.0%	42.3%	50.5%
Terminal rates	8/37 (22%)	14/40 (35%)	13/33 (39%)	12/25 (48%)
First incidence (days)	694	722 (T)	668	437
Life table tests	P=0.030	P=0.395	P=0.159	P=0.062
Logistic regression tests	P=0.095	P=0.294	P=0.164	P=0.137
Cochran-Armitage test	P=0.362			
Fisher exact test		P=0.322	P=0.247	P=0.365
Liver: Hepatocellular Carcinoma				
Overall rates	2/50 (4%)	1/50 (2%)	3/50 (6%)	3/52 (6%)
Adjusted rates	5.4%	2.5%	8.1%	9.4%
Terminal rates	2/37 (5%)	1/40 (3%)	1/33 (3%)	1/25 (4%)
First incidence (days)	722 (T)	722 (T)	678	554
Life table tests	P=0.167	P=0.473N	P=0.455	P=0.346
Logistic regression tests	P=0.252	P=0.473N	P=0.461	P=0.458
Cochran-Armitage test	P=0.319			
Fisher exact test		P=0.500N	P=0.500	P=0.519
Liver: Hepatocellular Adenoma or Carcinoma				
Overall rates	13/50 (26%)	15/50 (30%)	17/50 (34%)	16/52 (31%)
Adjusted rates	32.3%	37.5%	46.7%	53.3%
Terminal rates	10/37 (27%)	15/40 (38%)	14/33 (42%)	12/25 (48%)
First incidence (days)	694	722 (T)	668	437
Life table tests	P=0.021	P=0.497	P=0.160	P=0.056
Logistic regression tests	P=0.086	P=0.385	P=0.163	P=0.146
Cochran-Armitage test	P=0.344			
Fisher exact test		P=0.412	P=0.257	P=0.377
Lung: Alveolar/bronchiolar Adenoma				
Overall rates	3/49 (6%)	1/50 (2%)	0/50 (0%)	3/52 (6%)
Adjusted rates	7.4%	2.5%	0.0%	8.6%
Terminal rates	2/36 (6%)	1/40 (3%)	0/33 (0%)	1/25 (4%)
First incidence (days)	560	722 (T)	--[e]	482
Life table tests	P=0.402	P=0.286N	P=0.140N	P=0.525
Logistic regression tests	P=0.576	P=0.291N	P=0.102N	P=0.584N
Cochran-Armitage test	P=0.548			
Fisher exact test		P=0.301N	P=0.117N	P=0.632N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Lung: Alveolar/bronchiolar Adenoma or Carcinoma				
Overall rates	5/49 (10%)	3/50 (6%)	1/50 (2%)	4/52 (8%)
Adjusted rates	12.3%	7.5%	3.0%	12.4%
Terminal rates	3/36 (8%)	3/40 (8%)	1/33 (3%)	2/25 (8%)
First incidence (days)	560	722 (T)	722 (T)	482
Life table tests	P=0.526	P=0.325N	P=0.131N	P=0.583
Logistic regression tests	P=0.448N	P=0.362N	P=0.100N	P=0.463N
Cochran-Armitage test	P=0.412N			
Fisher exact test		P=0.346N	P=0.098N	P=0.462N
Pituitary Gland (Pars Distalis): Adenoma				
Overall rates	8/47 (17%)	4/50 (8%)	5/47 (11%)	1/49 (2%)
Adjusted rates	21.3%	10.0%	15.1%	2.9%
Terminal rates	7/36 (19%)	4/40 (10%)	4/32 (13%)	0/25 (0%)
First incidence (days)	692	722 (T)	714	652
Life table tests	P=0.061N	P=0.136N	P=0.358N	P=0.060N
Logistic regression tests	P=0.044N	P=0.165N	P=0.343N	P=0.040N
Cochran-Armitage test	P=0.017N			
Fisher exact test		P=0.149N	P=0.276N	P=0.013N
Skin (Subcutaneous Tissue): Fibrosarcoma				
Overall rates	3/50 (6%)	0/50 (0%)	0/50 (0%)	1/52 (2%)
Adjusted rates	6.9%	0.0%	0.0%	4.0%
Terminal rates	0/37 (0%)	0/40 (0%)	0/33 (0%)	1/25 (4%)
First incidence (days)	645	–	–	722 (T)
Life table tests	P=0.324N	P=0.131N	P=0.142N	P=0.428N
Logistic regression tests	P=0.269N	P=0.116N	P=0.116N	P=0.356N
Cochran-Armitage test	P=0.239N			
Fisher exact test		P=0.121N	P=0.121N	P=0.294N
Skin (Subcutaneous Tissue): Neurofibrosarcoma or Fibrosarcoma				
Overall rates	4/50 (8%)	0/50 (0%)	0/50 (0%)	1/52 (2%)
Adjusted rates	9.4%	0.0%	0.0%	4.0%
Terminal rates	1/37 (3%)	0/40 (0%)	0/33 (0%)	1/25 (4%)
First incidence (days)	645	–	–	722 (T)
Life table tests	P=0.185N	P=0.068N	P=0.081N	P=0.298N
Logistic regression tests	P=0.146N	P=0.063N	P=0.064N	P=0.234N
Cochran-Armitage test	P=0.120N			
Fisher exact test		P=0.059N	P=0.059N	P=0.169N
Stomach (Forestomach): Squamous Cell Papilloma				
Overall rates	0/50 (0%)	3/50 (6%)	2/50 (4%)	1/52 (2%)
Adjusted rates	0.0%	7.2%	6.1%	3.6%
Terminal rates	0/37 (0%)	2/40 (5%)	2/33 (6%)	0/25 (0%)
First incidence (days)	–	600	722 (T)	714
Life table tests	P=0.418	P=0.126	P=0.213	P=0.439
Logistic regression tests	P=0.499	P=0.119	P=0.213	P=0.442
Cochran-Armitage test	P=0.570			
Fisher exact test		P=0.121	P=0.247	P=0.510

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
All Organs: Hemangiosarcoma				
Overall rates	1/50 (2%)	4/50 (8%)	1/50 (2%)	1/52 (2%)
Adjusted rates	2.7%	9.5%	3.0%	3.6%
Terminal rates	1/37 (3%)	3/40 (8%)	1/33 (3%)	0/25 (0%)
First incidence (days)	722 (T)	510	722 (T)	714
Life table tests	P=0.515N	P=0.197	P=0.736	P=0.681
Logistic regression tests	P=0.408N	P=0.180	P=0.736	P=0.689
Cochran-Armitage test	P=0.358N			
Fisher exact test		P=0.181	P=0.753N	P=0.743N
All Organs: Hemangioma or Hemangiosarcoma				
Overall rates	2/50 (4%)	5/50 (10%)	1/50 (2%)	2/52 (4%)
Adjusted rates	5.4%	11.9%	3.0%	7.4%
Terminal rates	2/37 (5%)	4/40 (10%)	1/33 (3%)	1/25 (4%)
First incidence (days)	722 (T)	510	722 (T)	714
Life table tests	P=0.552N	P=0.242	P=0.540N	P=0.555
Logistic regression tests	P=0.440N	P=0.208	P=0.540N	P=0.567
Cochran-Armitage test	P=0.354N			
Fisher exact test		P=0.218	P=0.500N	P=0.676N
All Organs: Malignant Lymphoma and Histiocytic Sarcoma				
Overall rates	9/50 (18%)	9/50 (18%)	10/50 (20%)	3/52 (6%)
Adjusted rates	20.9%	20.8%	26.5%	8.3%
Terminal rates	5/37 (14%)	6/40 (15%)	7/33 (21%)	0/25 (0%)
First incidence (days)	640	588	449	437
Life table tests	P=0.199N	P=0.574N	P=0.406	P=0.176N
Logistic regression tests	P=0.061N	P=0.577	P=0.500	P=0.059N
Cochran-Armitage test	P=0.045N			
Fisher exact test		P=0.602N	P=0.500	P=0.053N
All Organs: Benign Neoplasms				
Overall rates	28/50 (56%)	25/50 (50%)	22/50 (44%)	23/52 (44%)
Adjusted rates	63.3%	56.6%	59.0%	66.1%
Terminal rates	21/37 (57%)	21/40 (53%)	18/33 (55%)	14/25 (56%)
First incidence (days)	560	510	668	437
Life table tests	P=0.207	P=0.270N	P=0.338N	P=0.295
Logistic regression tests	P=0.440N	P=0.444N	P=0.278N	P=0.483N
Cochran-Armitage test	P=0.135N			
Fisher exact test		P=0.344N	P=0.159N	P=0.161N
All Organs: Malignant Neoplasms				
Overall rates	18/50 (36%)	16/50 (32%)	15/50 (30%)	11/52 (21%)
Adjusted rates	40.4%	36.2%	37.6%	32.3%
Terminal rates	11/37 (30%)	12/40 (30%)	9/33 (27%)	4/25 (16%)
First incidence (days)	640	510	449	437
Life table tests	P=0.410N	P=0.375N	P=0.479N	P=0.412N
Logistic regression tests	P=0.124N	P=0.472N	P=0.388N	P=0.175N
Cochran-Armitage test	P=0.056N			
Fisher exact test		P=0.417N	P=0.335N	P=0.074N

TABLE D3
Statistical Analysis of Primary Neoplasms in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
All Organs: Benign or Malignant Neoplasms				
Overall rates	39/50 (78%)	35/50 (70%)	29/50 (58%)	29/52 (56%)
Adjusted rates	81.1%	74.5%	72.1%	75.7%
Terminal rates	28/37 (76%)	28/40 (70%)	22/33 (67%)	16/25 (64%)
First incidence (days)	560	510	449	437
Life table tests	P=0.371	P=0.207N	P=0.175N	P=0.442
Logistic regression tests	P=0.104N	P=0.387N	P=0.066N	P=0.184N
Cochran-Armitage test	P=0.009N			
Fisher exact test		P=0.247N	P=0.026N	P=0.015N

(T)Terminal sacrifice
[a] Number of neoplasm-bearing animals/number of animals examined. Denominator is number of animals examined microscopically for adrenal gland, bone marrow, brain, clitoral gland, gallbladder, heart, kidney, larynx, liver, lung, nose, ovary, pancreas, parathyroid gland, pituitary gland, salivary gland, spleen, thyroid gland, urinary bladder, and uterus; for other tissues, denominator is number of animals necropsied.
[b] Kaplan-Meier estimated neoplasm incidence at the end of the study after adjustment for intercurrent mortality
[c] Observed incidence at terminal kill
[d] Beneath the control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between the controls and that dosed group. The life table analysis regards neoplasms in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The logistic regression tests regard these lesions as nonfatal. The Cochran-Armitage and Fisher exact tests compare directly the overall incidence rates. For all tests, a negative trend or a lower incidence in a dose group is indicated by N.
[e] Not applicable; no neoplasms in animal group

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Disposition Summary				
Animals initially in study	70	70	70	70
3-Month interim evaluation	10	10	10	9
15-Month interim evaluation	10	10	10	9
Early deaths				
Accidental deaths		3	2	1
Moribund	9	4	10	12
Natural deaths	4	3	5	14
Survivors				
Died last week of study	1			
Terminal sacrifice	36	40	33	25
Animals examined microscopically	70	70	70	70
3-Month Interim Evaluation				
Alimentary System				
Liver	(10)			(9)
Inflammation, necrotizing	6 (60%)			3 (33%)
Salivary glands	(10)			(9)
Inflammation, chronic	1 (10%)			
Stomach, forestomach	(10)			(9)
Inflammation, chronic active				1 (11%)
Cardiovascular System				
None				
Endocrine System				
Thyroid gland	(10)			(9)
C-cell, hyperplasia	1 (10%)			
General Body System				
None				
Genital System				
None				
Hematopoietic System				
None				
Integumentary System				
None				

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
3-Month Interim Evaluation (continued)				
Musculoskeletal System				
None				
Nervous System				
Brain	(10)			(9)
Cyst epithelial inclusion	1 (10%)			
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(9)
Nephropathy		2 (20%)	8 (80%)	7 (78%)
Urinary bladder	(10)			(9)
Inflammation				1 (11%)
15-Month Interim Evaluation				
Alimentary System				
Pancreas	(10)			(9)
Basophilic focus				1 (11%)
Acinus, hyperplasia	1 (10%)			1 (11%)
Stomach, forestomach	(10)	(1)		(9)
Hyperplasia, squamous				2 (22%)
Stomach, glandular	(10)	(1)		(9)
Mucosa, mineralization		1 (100%)		1 (11%)
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
15-Month Interim Evaluation (continued)				
Genital System				
Ovary	(10)			(9)
Cyst				2 (22%)
Uterus	(10)	(2)	(6)	(9)
Cyst	1 (10%)			
Endometrium, hyperplasia		2 (100%)	6 (100%)	
Hematopoietic System				
None				
Integumentary System				
Skin	(10)			(8)
Inflammation, chronic active	1 (10%)			
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
None				
Special Senses System				
None				
Urinary System				
Kidney	(10)	(10)	(10)	(9)
Amyloid deposition				1 (11%)
Nephropathy		9 (90%)	10 (100%)	9 (100%)
2-Year Study				
Alimentary System				
Esophagus	(50)	(50)	(50)	(52)
Foreign body		1 (2%)		
Inflammation, chronic		1 (2%)		
Intestine small, duodenum	(49)	(49)	(48)	(52)
Inflammation, chronic		1 (2%)		
Ulcer			4 (8%)	8 (15%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Liver	(50)	(50)	(50)	(52)
Foreign body				1 (2%)
Hyperplasia	3 (6%)	8 (16%)	7 (14%)	4 (8%)
Inflammation, chronic			1 (2%)	5 (10%)
Necrosis, coagulative	1 (2%)	3 (6%)	3 (6%)	18 (35%)
Mesentery	(5)	(8)	(2)	
Inflammation, chronic		1 (13%)		
Fat, necrosis	3 (60%)	2 (25%)	1 (50%)	
Pancreas	(50)	(50)	(50)	(52)
Inflammation, chronic	2 (4%)	2 (4%)	2 (4%)	4 (8%)
Necrosis, coagulative	1 (2%)			
Acinus, atrophy		2 (4%)		
Salivary glands	(50)	(50)	(50)	(52)
Ectasia		1 (2%)		
Stomach, forestomach	(50)	(50)	(50)	(52)
Hyperplasia, squamous	3 (6%)	10 (20%)	18 (36%)	20 (38%)
Ulcer	2 (4%)	4 (8%)	12 (24%)	13 (25%)
Stomach, glandular	(50)	(50)	(50)	(52)
Inflammation, chronic	1 (2%)		2 (4%)	
Ulcer		1 (2%)	1 (2%)	1 (2%)
Mucosa, mineralization	1 (2%)	6 (12%)	10 (20%)	16 (31%)
Cardiovascular System				
Heart	(50)	(50)	(49)	(52)
Artery, inflammation, necrotizing	1 (2%)			
Atrium, thrombus	1 (2%)	1 (2%)		1 (2%)
Myocardium, degeneration			1 (2%)	
Myocardium, mineralization			2 (4%)	1 (2%)
Valve, inflammation, chronic active	1 (2%)			
Endocrine System				
Adrenal gland, cortex	(50)	(50)	(50)	(52)
Hyperplasia	4 (8%)	4 (8%)	4 (8%)	2 (4%)
Adrenal gland, medulla	(49)	(50)	(50)	(52)
Hyperplasia		2 (4%)		2 (4%)
Islets, pancreatic	(50)	(50)	(50)	(52)
Hyperplasia	1 (2%)	1 (2%)		
Pituitary gland	(47)	(50)	(47)	(49)
Cyst		1 (2%)		
Pars distalis, hyperplasia	4 (9%)	7 (14%)	4 (9%)	1 (2%)
Pars intermedia, hyperplasia				1 (2%)
Thyroid gland	(49)	(50)	(50)	(52)
Inflammation, chronic	1 (2%)			
Follicle, hyperplasia	8 (16%)	3 (6%)	4 (8%)	3 (6%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
General Body System				
None				
Genital System				
Clitoral gland		(1)		
Duct, dilatation		1 (100%)		
Ovary	(49)	(49)	(49)	(51)
Cyst	19 (39%)	17 (35%)	18 (37%)	11 (22%)
Infarct	2 (4%)		2 (4%)	2 (4%)
Inflammation, chronic active				1 (2%)
Inflammation, suppurative	1 (2%)			
Uterus	(50)	(50)	(50)	(52)
Dilatation			1 (2%)	
Hemorrhage	2 (4%)	1 (2%)		
Inflammation, suppurative	1 (2%)		1 (2%)	1 (2%)
Artery, inflammation, chronic active			1 (2%)	
Endometrium, hyperplasia	44 (88%)	41 (82%)	36 (72%)	32 (62%)
Vagina			(1)	(1)
Inflammation, suppurative				1 (100%)
Hematopoietic System				
Bone marrow	(50)	(50)	(50)	(52)
Myelofibrosis	16 (32%)	3 (6%)	2 (4%)	
Lymph node	(49)	(50)	(48)	(52)
Mediastinal, hyperplasia, lymphoid		1 (2%)		
Lymph node, mandibular	(46)	(47)	(46)	(51)
Infiltration cellular, histiocyte	1 (2%)			
Lymph node, mesenteric	(44)	(48)	(46)	(45)
Ectasia			2 (4%)	
Infiltration cellular, histiocyte	1 (2%)			
Spleen	(50)	(50)	(50)	(52)
Amyloid deposition	1 (2%)		1 (2%)	1 (2%)
Depletion lymphoid		1 (2%)	1 (2%)	8 (15%)
Hematopoietic cell proliferation	7 (14%)	3 (6%)	7 (14%)	12 (23%)
Hyperplasia, lymphoid	9 (18%)	5 (10%)	6 (12%)	12 (23%)
Infiltration cellular, histiocyte	1 (2%)			
Inflammation, granulomatous			1 (2%)	
Thymus	(45)	(44)	(44)	(44)
Atrophy		1 (2%)	1 (2%)	1 (2%)
Cyst				1 (2%)
Integumentary System				
Skin	(50)	(50)	(50)	(52)
Hyperkeratosis				1 (2%)
Inflammation, chronic			1 (2%)	
Ulcer			1 (2%)	1 (2%)

TABLE D4
Summary of the Incidence of Nonneoplastic Lesions in Female Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
2-Year Study (continued)				
Musculoskeletal System				
Bone	(50)	(50)	(50)	(52)
Fibrous osteodystrophy	2 (4%)	20 (40%)	33 (66%)	37 (71%)
Nervous System				
Brain	(50)	(50)	(50)	(52)
Hypothalamus, compression	1 (2%)	3 (6%)		1 (2%)
Respiratory System				
Lung	(49)	(50)	(50)	(52)
Foreign body		3 (6%)	2 (4%)	2 (4%)
Inflammation, chronic	2 (4%)	1 (2%)	2 (4%)	2 (4%)
Thrombus		1 (2%)		1 (2%)
Alveolus, infiltration cellular, histiocyte	1 (2%)			
Nose	(50)	(50)	(50)	(52)
Foreign body		3 (6%)	2 (4%)	
Special Senses System				
Eye	(2)		(1)	(2)
Phthisis bulbi				1 (50%)
Cornea, inflammation, chronic	1 (50%)		1 (100%)	1 (50%)
Cornea, inflammation, necrotizing	1 (50%)			
Harderian gland	(5)	(3)	(3)	(3)
Hyperplasia	1 (20%)	1 (33%)		
Inflammation, suppurative			1 (33%)	
Urinary System				
Kidney	(50)	(50)	(50)	(52)
Hydronephrosis		1 (2%)		
Nephropathy	19 (38%)	38 (76%)	48 (96%)	50 (96%)
Renal tubule, mineralization	1 (2%)			
Urinary bladder	(50)	(50)	(50)	(52)
Inflammation, necrotizing	1 (2%)			1 (2%)
Transitional epithelium, hyperplasia		1 (2%)		

[a] Number of animals examined microscopically at site and number of animals with lesion

APPENDIX E
GENETIC TOXICOLOGY

GENETIC TOXICOLOGY

SALMONELLA TYPHIMURIUM MUTAGENICITY TEST PROTOCOL

Testing was performed as reported by Mortelmans *et al.* (1986). *o*-Benzyl-*p*-chlorophenol was sent to the laboratory as a coded aliquot from Radian Corporation (Austin, TX). *o*-Benzyl-*p*-chlorophenol was incubated with the *Salmonella typhimurium* tester strains (TA98, TA100, TA1535, and TA1537) either in buffer or S9 mix (metabolic activation enzymes and cofactors from Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver) for 20 minutes at 37° C. Top agar supplemented with *l*-histidine and *d*-biotin was added, and the contents of the tubes were mixed and poured onto the surfaces of minimal glucose agar plates. Histidine-independent mutant colonies arising on these plates were counted following incubation for 2 days at 37° C.

Each trial consisted of triplicate plates of concurrent positive and negative controls and at least five doses of *o*-benzyl-*p*-chlorophenol. The high dose was limited by toxicity. All trials were repeated.

In this assay, a positive response is defined as a reproducible, dose-related increase in histidine-independent (revertant) colonies in any one strain/activation combination. An equivocal response is defined as an increase in revertants that is not dose related, not reproducible, or is of not of sufficient magnitude to support a determination of mutagenicity. A negative response is obtained when no increase in revertant colonies is observed following chemical treatment. No minimum percentage or fold increase is required for a chemical to be judged positive or weakly positive.

CHINESE HAMSTER OVARY CELL CYTOGENETICS PROTOCOLS

Testing was performed as reported by Galloway *et al.* (1987). *o*-Benzyl-*p*-chlorophenol was sent to the laboratory as a coded aliquot by Radian Corporation. *o*-Benzyl-*p*-chlorophenol was tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchanges (SCEs) and chromosomal aberrations (Abs), both in the presence and absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least four doses of *o*-benzyl-*p*-chlorophenol. A single flask per dose was used.

Sister Chromatid Exchange Test: In the SCE test without S9, CHO cells were incubated for 26 hours with *o*-benzyl-*p*-chlorophenol in McCoy's 5A medium supplemented with fetal bovine serum, *l*-glutamine, and antibiotics. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 26 hours, the medium containing *o*-benzyl-*p*-chlorophenol was removed and replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for as long as 2 hours. Cells were then harvested by mitotic shake-off, fixed, and stained with Hoechst 33258 and Giemsa. In the SCE test with S9, cells were incubated with *o*-benzyl-*p*-chlorophenol, serum-free medium, and S9 for 2 hours. The medium was then removed and replaced with medium containing serum and BrdU and no *o*-benzyl-*p*-chlorophenol and incubation proceeded for an additional 26 hours, with Colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9. All slides were scored blind and those from a single test were read by the same person. Fifty second-division metaphase cells were scored for frequency of SCEs/cell from each dose level.

Statistical analyses were conducted on the slopes of the dose-response curves and the individual dose points (Galloway *et al.*, 1987). An SCE frequency 20% above the concurrent solvent control value was chosen as a statistically conservative positive response. The probability of this level of difference occurring by chance at one dose point is less than 0.01; the probability for such a chance occurrence at two dose points is less than 0.001. An increase of 20% or greater at any single dose was considered weak evidence of activity; increases at two or more doses resulted in a determination that the trial was positive. A

statistically significant trend ($P \leq 0.05$) in the absence of any responses reaching 20% above background led to a call of equivocal.

Chromosomal Aberrations Test: In the Abs test without S9, cells were incubated in McCoy's 5A medium with *o*-benzyl-*p*-chlorophenol for 10 hours; Colcemid was added and incubation continued for 2 hours. The cells were then harvested by mitotic shake-off, fixed, and stained with Giemsa. The second trial was a continuation of the culture harvested in the first trial. The harvest time was extended to 21 hours to provide sufficient metaphases at harvest time. For the Abs test with S9, cells were treated with *o*-benzyl-*p*-chlorophenol and S9 for 2 hours, after which the treatment medium was removed and the cells were incubated for 12.5 hours in fresh medium, with Colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9. The second trial was a continuation of the culture harvested in the first trial. The harvest time was extended to 18 hours to provide sufficient metaphases at harvest time.

Cells were selected for scoring on the basis of good morphology and completeness of karyotype (21 ± 2 chromosomes). All slides were scored blind and those from a single test were read by the same person. One hundred first-division metaphase cells were scored at each dose level. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocations), and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

Chromosomal aberration data are presented as percentage of cells with aberrations. Statistical analyses were conducted on both the dose-response curve and individual dose points. For a single trial, a statistically significant ($P \leq 0.05$) difference for one dose point and a significant trend ($P \leq 0.015$) are considered weak evidence for a positive response; significant differences for two or more doses indicate the trial is positive. A positive trend test in the absence of a statistically significant increase at any one dose results in an equivocal call (Galloway *et al.*, 1987).

RESULTS

o-Benzyl-*p*-chlorophenol (0.1 to 100 μg/plate) was not mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537 when tested in a preincubation protocol with or without Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9 (Table E1; Mortelmans *et al.*, 1986). However, *o*-benzyl-*p*-chlorophenol (10 to 45 μg/mL) induced gene mutations in mouse lymphoma L5178Y cells and human lymphoblast TK6 cells without S9 activation (Caspary *et al.*, 1988). In cytogenetic tests with cultured Chinese hamster ovary cells, *o*-benzyl-*p*-chlorophenol did not induce sister chromatid exchanges (Table E2) or chromosomal aberrations (Table E3), with or without Aroclor 1254-induced male Sprague-Dawley rat liver S9. The highest non-lethal dose tested in either of these mammalian cell assays was 16 μg/mL. In the Abs test, the second reported trial under each activation condition was a continuation of the cultures harvested in the first trial; the results of this second harvest indicated that cell cycle delay was not a factor in the observed lack of induced Abs following treatment with *o*-benzyl-*p*-chlorophenol.

TABLE E1
Mutagenicity of *o*-Benzyl-*p*-Chlorophenol in *Salmonella typhimurium*[a]

Strain	Dose (μg/plate)	Revertants/plate[b] -S9 Trial 1	-S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
Study performed at SRI, International							
TA100	0.0	99 ± 5.7	103 ± 4.0	123 ± 6.8	108 ± 5.4	125 ± 13.6	121 ± 7.0
	0.1	142 ± 9.7	133 ± 3.5				
	0.3	126 ± 13.1	124 ± 7.3				
	1.0	130 ± 3.8	114 ± 5.4	125 ± 10.3	107 ± 5.0	156 ± 3.9	129 ± 12.8
	3.0	140 ± 9.4	138 ± 5.4	111 ± 16.1	105 ± 4.3	158 ± 3.2	141 ± 9.1
	10.0	151 ± 8.1	133 ± 2.3	115 ± 5.2	109 ± 4.2	114 ± 10.5	135 ± 3.5
	33.0			125 ± 0.9	109 ± 9.4	115 ± 8.7	129 ± 3.8
	66.0						116 ± 10.1
	100.0			117 ± 13.0	84 ± 9.9[c]	41 ± 20.7[c]	
Trial summary		Equivocal	Negative	Negative	Negative	Negative	Negative
Positive control[d]		433 ± 17.5	281 ± 6.9	1,617 ± 71.3	1,112 ± 18.2	533 ± 44.5	572 ± 32.9
TA 1535	0.0	23 ± 2.8	22 ± 2.0	10 ± 3.3	10 ± 0.9	7 ± 0.3	11 ± 2.4
	0.1	34 ± 7.7	32 ± 5.8				
	0.3	44 ± 3.2	35 ± 3.7				
	1.0	42 ± 3.2	37 ± 2.4	14 ± 1.2	5 ± 0.3	11 ± 2.7	11 ± 3.3
	3.0	48 ± 1.3	31 ± 1.8	11 ± 1.0	6 ± 1.0	9 ± 2.5	11 ± 2.2
	10.0	45 ± 0.9	38 ± 5.2	7 ± 1.5	9 ± 1.9	10 ± 1.2	10 ± 3.2
	33.0			14 ± 1.2	9 ± 2.8	8 ± 2.2	8 ± 3.9
	66.0						13 ± 0.3
	100.0			7 ± 2.1	4 ± 0.3[c]	2 ± 1.2[c]	
Trial summary		Equivocal	Negative	Negative	Negative	Negative	Negative
Positive control		488 ± 6.0	295 ± 1.7	458 ± 12.6	312 ± 11.7	208 ± 5.8	129 ± 17.6
TA1537	0.0	6 ± 1.2	4 ± 1.0	5 ± 1.0	8 ± 1.2	4 ± 0.9	6 ± 0.9
	0.1	6 ± 0.0	6 ± 1.9				
	0.3	4 ± 0.7	4 ± 1.5				
	1.0	4 ± 1.2	6 ± 0.9	7 ± 0.9	6 ± 0.9	6 ± 1.7	8 ± 1.0
	3.0	5 ± 0.3	6 ± 1.5	9 ± 2.1	7 ± 0.3	4 ± 1.2	10 ± 1.2
	10.0	4 ± 0.3	5 ± 1.2	8 ± 0.6	4 ± 1.0	7 ± 0.6	7 ± 1.8
	33.0			9 ± 1.9	6 ± 0.3	7 ± 1.2	6 ± 0.9
	66.0						7 ± 0.7
	100.0			5 ± 1.7	2 ± 0.3[c]	2 ± 2.0[c]	
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		161 ± 6.7	329 ± 59.5	328 ± 6.2	335 ± 37.6	168 ± 4.7	146 ± 6.4
TA98	0.0	16 ± 1.8	16 ± 0.3	31 ± 3.6	26 ± 4.0	32 ± 0.6	24 ± 0.3
	0.1	16 ± 0.9	16 ± 1.0				
	0.3	17 ± 3.5	18 ± 1.0				
	1.0	15 ± 0.7	18 ± 3.8	32 ± 2.2	30 ± 3.5	30 ± 6.2	24 ± 2.4
	3.0	11 ± 4.0	14 ± 1.5	27 ± 1.8	24 ± 2.3	31 ± 2.6	31 ± 1.5
	10.0	14 ± 2.4	15 ± 2.1	22 ± 4.7	25 ± 2.6	28 ± 1.7	29 ± 1.7
	33.0			26 ± 1.9	19 ± 4.6	27 ± 2.2	32 ± 0.7
	66.0						27 ± 1.8
	100.0			19 ± 1.2	0 ± 0.0[c]	0 ± 0.0[c]	
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		908 ± 46.9	472 ± 27.7	1,438 ± 97.8	774 ± 37.1	535 ± 16.8	446 ± 24.0

TABLE E1
Mutagenicity of *o*-Benzyl-*p*-Chlorophenol in *Salmonella typhimurium* (continued)

Strain	Dose (μg/plate)	Revertants/plate -S9 Trial 1	-S9 Trial 2	-S9 Trial 3	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% hamster S9 Trial 3	+10% rat S9 Trial 1	+10% rat S9 Trial 2
Study performed at EG&G Mason Research Corporation									
TA100	0.0	181 ± 13.2	143 ± 4.8	151 ± 10.7	242 ± 5.9	128 ± 8.0	149 ± 10.7	133 ± 6.7	148 ± 11.2
	0.3	197 ± 4.5	143 ± 6.1	141 ± 4.8					
	1.0	190 ± 7.0	140 ± 5.9	146 ± 5.8	245 ± 4.1	118 ± 7.1	138 ± 11.2	124 ± 4.1	129 ± 8.6
	3.3	204 ± 2.3	143 ± 13.1	162 ± 3.8	241 ± 5.5	116 ± 6.7	138 ± 7.0	142 ± 11.0	135 ± 8.5
	10.0	199 ± 3.3	166 ± 7.7	174 ± 3.4	244 ± 4.6	135 ± 9.5	140 ± 4.6	149 ± 4.4	139 ± 4.2
	33.0	Toxic	138 ± 1.5[c]	Toxic	207 ± 7.0	124 ± 11.3	145 ± 3.5	141 ± 5.2	136 ± 3.0
	100.0				118 ± 19.6[c]	122 ± 3.6[c]	121 ± 15.0[c]	148 ± 2.1[c]	117 ± 5.1[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Positive control		890 ± 26.9	1,330± 22.3	1,503 ± 24.3	1,116 ± 91.9	1,017 ± 31.0	1,247 ± 26.8	700 ± 36.5	1,029 ± 47.4
TA1535	0.0	38 ± 1.2	30 ± 1.0	24 ± 2.0	48 ± 1.7	9 ± 1.0	10 ± 2.2	9 ± 0.3	11 ± 2.0
	0.3	35 ± 4.6	38 ± 1.7	28 ± 3.8					
	1.0	43 ± 2.6	36 ± 8.5	25 ± 3.9	49 ± 0.9	10 ± 2.1	11 ± 2.4	9 ± 1.5	9 ± 0.9
	3.3	38 ± 1.5	33 ± 2.9	30 ± 2.5	46 ± 0.6	10 ± 1.9	14 ± 1.5	8 ± 1.3	11 ± 0.9
	10.0	36 ± 5.5	30 ± 2.9	33 ± 2.0	46 ± 2.0	13 ± 0.6	12 ± 2.9	8 ± 0.9	11 ± 2.2
	33.0	14 ± 4.3[c]	34 ± 0.7[c]	Toxic	47 ± 3.1	10 ± 1.2	11 ± 2.0	6 ± 0.9	11 ± 2.1
	100.0				8 ± 2.7[c]	9 ± 2.1[c]	7 ± 1.9[c]	9 ± 0.7[c]	7 ± 1.8[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Positive control		694 ± 10.3	1,030 ± 31.7	1,207 ± 54.6	128 ± 17.6	86 ± 2.3	95 ± 6.1	73 ± 5.2	85 ± 1.8

Strain	Dose (μg/plate)	Revertants/plate -S9 Trial 1	-S9 Trial 2	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% rat S9 Trial 1	+10% rat S9 Trial 2
Study performed at EG&G Mason Research Corporation							
TA1537	0.0	7 ± 0.6	6 ± 1.2	6 ± 2.3	5 ± 0.6	6 ± 2.9	11 ± 2.9
	0.3	7 ± 1.5	5 ± 2.2				
	1.0	4 ± 1.2	4 ± 0.6	8 ± 1.7	8 ± 1.7	6 ± 0.7	6 ± 1.8
	3.3	4 ± 0.9	8 ± 0.3	8 ± 1.8	9 ± 0.6	8 ± 0.7	7 ± 0.6
	10.0	4 ± 0.3	4 ± 1.0	5 ± 0.7	2 ± 0.3	8 ± 1.0	8 ± 1.0
	33.0	Toxic	Toxic	8 ± 2.0	6 ± 1.5	6 ± 2.2	6 ± 0.9
	100.0			3 ± 0.6[c]	7 ± 0.6[c]	3 ± 1.0[c]	9 ± 0.3[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		132 ± 29.2	340 ± 21.8	96 ± 0.7	111 ± 0.9	65 ± 5.2	68 ± 4.5

TABLE E1
Mutagenicity of *o*-Benzyl-*p*-Chlorophenol in *Salmonella typhimurium* (continued)

Strain	Dose (μg/plate)	Revertants/plate -S9 Trial 1	-S9 Trial 2	-S9 Trial 3	+10% hamster S9 Trial 1	+10% hamster S9 Trial 2	+10% hamster S9 Trial 3
Study performed at EG&G Mason Research Corporation							
TA98	0.0	19 ± 3.3	17 ± 1.0	16 ± 0.3	32 ± 2.0	29 ± 1.3	31 ± 5.1
	0.3	19 ± 2.1	12 ± 1.5	15 ± 1.2			
	1.0	13 ± 0.6	15 ± 2.0	17 ± 1.8	24 ± 4.6	32 ± 3.8	30 ± 4.1
	3.3	15 ± 3.0	20 ± 0.7	18 ± 1.8	22 ± 1.5	26 ± 3.6	24 ± 1.8
	10.0	13 ± 2.0	19 ± 1.5	16 ± 3.8	20 ± 2.5	29 ± 2.6	30 ± 2.7
	33.0	3 ± 0.0[c]	12 ± 1.2[c]	Toxic	24 ± 2.3	25 ± 1.5	33 ± 3.5
	100.0				12 ± 1.8[c]	24 ± 2.8[c]	19 ± 1.8[c]
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		1,439 ± 47.5	1,122 ± 47.7	1,363 ± 38.7	1,045 ± 46.0	842 ± 44.7	915 ± 27.3

Strain	Dose (μg/plate)	Revertants/plate +10% rat S9 Trial 1	+10% rat S9 Trial 2	+10% rat S9 Trial 3
TA98	0.0	23 ± 1.7	25 ± 5.2	25 ± 4.3
	0.3	19 ± 2.0	30 ± 2.7	25 ± 3.5
	1.0	24 ± 0.6	29 ± 4.2	24 ± 0.6
	3.3	31 ± 3.5	26 ± 4.0	28 ± 1.9
	10.0	30 ± 2.2	25 ± 2.9	20 ± 5.0
	33.0	14 ± 1.2[c]	24 ± 4.5[c]	18 ± 0.3[c]
Trial summary		Negative	Negative	Negative
Positive control		723 ± 31.8	550 ± 25.4	724 ± 31.1

[a] The detailed protocol and these data are presented in Mortelmans *et al.* (1986).
[b] Revertants are presented as mean ± the standard error from three plates.
[c] Slight toxicity
[d] 2-aminoanthracene was used on all strains in the presence of S9. In the absence of metabolic activation, 4-nitro-*o*-phenylenediamine was tested on TA98, sodium azide was tested on TA100 and TA1535, and 9-aminoacridine was tested on TA1537.

TABLE E2
Induction of Sister Chromatid Exchanges in Chinese Hamster Ovary Cells by *o*-Benzyl-*p*-Chlorophenol[a]

Compound	Dose μg/mL	Total Cells	No. of Chromosomes	No. of SCEs	SCEs/ Chromosome	SCEs/ Cell	Hrs in BrdU	Relative SCEs/ Chromosome[b] %
-S9								
Summary: Negative								
Dimethylsulfoxide		50	1,035	493	0.47	9.9	26.5	
Mitomycin-C	0.01	50	1,043	1,898	1.81	38.0	26.5	282.04
o-Benzyl-*p*-chlorophenol	0.5	50	1,038	525	0.50	10.5	26.5	6.18
	1.6	50	1,033	506	0.48	10.1	26.5	2.84
	5.0	50	1,041	550	0.52	11.0	26.5	10.92
	16.0	50	1,047	511	0.48	10.2	26.5	2.46
								P=0.255[c]
+S9								
Summary: Negative								
Dimethylsulfoxide		50	1,041	581	0.55	11.6	26.0	
Cyclophosphamide	2.0	50	1,047	3,165	3.02	63.3	26.0	441.64
o-Benzyl-*p*-chlorophenol	0.05	50	1,049	552	0.52	11.0	26.0	–5.72
	0.16	50	1,035	501	0.48	10.0	26.0	–13.27
	0.50	50	1,039	509	0.48	10.2	26.0	–12.22
	1.60	50	1,046	501	0.47	10.0	26.0	–14.18
	5.00	50	1,042	504	0.48	10.1	26.0	–13.34
	16.00	50	1,044	554	0.53	11.1	26.0	–4.92
								P=0.931

[a] Study performed at Environmental Health Research & Testing. SCE=sister chromatid exchange; BrdU=bromodeoxyuridine. A detailed description of the SCE protocol is presented by Galloway *et al.* (1987).
[b] SCEs/chromosome of culture exposed to *o*-benzyl-*p*-chlorophenol relative to those of culture exposed to solvent
[c] Significance of percent cells with SCEs tested by the linear regression trend test vs. log of the dose

TABLE E3
Induction of Chromosomal Aberrations in Chinese Hamster Ovary Cells by *o*-Benzyl-*p*-Chlorophenol[a]

–S9					+S9				
Dose (μg/mL)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells w/Abs	Dose (μg/mL)	Total Cells	No. of Abs	Abs/ Cell	Percent Cells w/Abs
Trial 1 – Harvest time: 12.0 hours Summary: Negative					**Trial 1** – Harvest time: 14.5 hours Summary: Negative				
Dimethylsulfoxide					Dimethylsulfoxide				
	100	1	0.01	1.0		100	2	0.02	2.0
Mitomycin-C					Cyclophosphamide				
0.50	100	45	0.45	34.0	50.0	100	120	1.2	60.0
o-Benzyl-*p*-chlorophenol					*o*-Benzyl-*p*-chlorophenol				
0.16	100	0	0.00	0.0	0.5	100	0	0.00	0.0
0.50	100	5	0.05	2.0	1.6	100	2	0.02	2.0
1.60	100	3	0.03	3.0	5.0	100	2	0.02	2.0
5.00	100	0	0.00	0.0	16.0	100	4	0.04	3.0
16.00	100	2	0.02	2.0					
				P=0.265[b]					P=0.171
Trial 2 – Harvest time: 21.0 hours[c] Summary: Negative					**Trial 2** – Harvest time: 18.0 hours[c] Summary: Negative				
Dimethylsulfoxide					Dimethylsulfoxide				
	100	0	0.00	0.0		100	0	0.00	0.0
Mitomycin-C					Cyclophosphamide				
0.25	100	8	0.08	8.0	50.0	100	108	1.08	57.0
0.50	100	8	0.08	7.0					
o-Benzyl-*p*-chlorophenol					*o*-Benzyl-*p*-chlorophenol				
0.5	100	0	0.00	0.0	0.5	100	0	0.00	0.0
1.6	100	0	0.00	0.0	1.6	100	0	0.00	0.0
5.0	100	0	0.00	0.0	5.0	100	0	0.00	0.0
16.0	100	0	0.00	0.0	16.0	100	0	0.00	0.0
				P=0.500					P=0.500

[a] Study performed at Environmental Health Research & Testing. Abs=aberrations. A detailed presentation of the technique for detecting chromosomal aberrations is found in Galloway *et al.* (1987).
[b] Significance of percent cells with aberrations tested by the linear regression trend test vs. log of the dose
[c] Because *o*-benzyl-*p*-chlorophenol induced significant cell cycle delay, incubation time prior to addition of Colcemid was lengthened to provide sufficient metaphases at harvest.

APPENDIX F
ORGAN WEIGHTS AND ORGAN-WEIGHT-TO-BODY-WEIGHT RATIOS

TABLE F1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 16-Day Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	62.5 mg/kg	125 mg/kg	250 mg/kg	500 mg/kg	1,000 mg/kg
Male						
n	5	4	5	5	5	5
Necropsy body weight	249 ± 3	251 ± 6	247 ± 3	253 ± 3	246 ± 4	200 ± 6**
Brain						
Absolute	1.866 ± 0.020	1.826 ± 0.017	1.836 ± 0.010	1.800 ± 0.027	1.825 ± 0.014	1.838 ± 0.024
Relative	7.49 ± 0.08	7.29 ± 0.11	7.45 ± 0.11	7.12 ± 0.18	7.44 ± 0.18	9.22 ± 0.29**
Heart						
Absolute	0.877 ± 0.028	0.847 ± 0.034	0.834 ± 0.032	0.829 ± 0.026	0.811 ± 0.028	0.687 ± 0.026**
Relative	3.52 ± 0.13	3.39 ± 0.20	3.39 ± 0.16	3.28 ± 0.10	3.30 ± 0.11	3.44 ± 0.09
R. Kidney						
Absolute	0.944 ± 0.031	0.944 ± 0.024	1.043 ± 0.011*	1.084 ± 0.036**	1.082 ± 0.029**	1.047 ± 0.020**
Relative	3.78 ± 0.10	3.77 ± 0.11	4.23 ± 0.09**	4.28 ± 0.11**	4.40 ± 0.08**	5.25 ± 0.17**
Liver						
Absolute	11.064 ± 0.240	10.941 ± 0.237	11.105 ± 0.190	13.224 ± 0.293**	13.547 ± 0.284**	12.076 ± 0.586**
Relative	44.39 ± 0.86	43.69 ± 1.43	45.05 ± 0.58	52.25 ± 1.01**	55.13 ± 0.40**	60.27 ± 1.41**
Lung						
Absolute	1.384 ± 0.103	1.313 ± 0.053	1.302 ± 0.067[b]	1.369 ± 0.044	1.359 ± 0.091	1.156 ± 0.053
Relative	5.55 ± 0.41	5.23 ± 0.15	5.29 ± 0.32[b]	5.41 ± 0.18	5.52 ± 0.29	5.78 ± 0.19
R. Testis						
Absolute	1.357 ± 0.020	1.347 ± 0.022	1.386 ± 0.024	1.349 ± 0.028	1.353 ± 0.013	1.247 ± 0.016**
Relative	5.45 ± 0.10	5.37 ± 0.08	5.63 ± 0.13	5.33 ± 0.07	5.51 ± 0.08	6.25 ± 0.13**
Thymus						
Absolute	0.382 ± 0.026	0.384 ± 0.023	0.342 ± 0.017	0.348 ± 0.020	0.268 ± 0.011**	0.173 ± 0.019**
Relative	1.53 ± 0.10	1.53 ± 0.09	1.38 ± 0.06	1.38 ± 0.09	1.09 ± 0.03**	0.87 ± 0.10**

TABLE F1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 16-Day Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	62.5 mg/kg	125 mg/kg	250 mg/kg	500 mg/kg	1,000 mg/kg
Female						
n	5	5	5	5	5	3
Necropsy body weight	165 ± 3	164 ± 3	167 ± 3	162 ± 2	159 ± 5	150 ± 0°
Brain						
Absolute	1.739 ± 0.021	1.705 ± 0.027	1.740 ± 0.027	1.725 ± 0.012	1.763 ± 0.028	1.678 ± 0.029
Relative	10.53 ± 0.18	10.39 ± 0.18	10.46 ± 0.15	10.65 ± 0.12	11.16 ± 0.36	11.22 ± 0.21
Heart						
Absolute	0.611 ± 0.025	0.618 ± 0.029	0.627 ± 0.028	0.630 ± 0.007	0.553 ± 0.029	0.528 ± 0.002
Relative	3.70 ± 0.12	3.76 ± 0.13	3.76 ± 0.15	3.89 ± 0.08	3.48 ± 0.10	3.53 ± 0.02
R. Kidney						
Absolute	0.631 ± 0.019	0.654 ± 0.011	0.663 ± 0.028	0.654 ± 0.015	0.689 ± 0.017°	0.737 ± 0.020°°
Relative	3.82 ± 0.06	3.99 ± 0.06	3.98 ± 0.14	4.04 ± 0.09	4.36 ± 0.12°°	4.93 ± 0.13°°
Liver						
Absolute	6.208 ± 0.424	6.415 ± 0.327	6.489 ± 0.194	6.743 ± 0.328	6.862 ± 0.381	7.771 ± 0.279°°
Relative	37.61 ± 2.63	39.01 ± 1.60	38.96 ± 0.89	41.61 ± 1.92	43.14 ± 1.08°	51.95 ± 1.78 °°
Lung						
Absolute	1.131 ± 0.058	1.047 ± 0.049	1.111 ± 0.025	1.051 ± 0.026	1.057 ± 0.033	1.132 ± 0.008
Relative	6.86 ± 0.38	6.38 ± 0.30	6.68 ± 0.17	6.49 ± 0.21	6.71 ± 0.38	7.57 ± 0.07
Thymus						
Absolute	0.344 ± 0.017	0.319 ± 0.021	0.336 ± 0.019	0.276 ± 0.013°	0.220 ± 0.029°°	0.187 ± 0.020°°
Relative	2.08 ± 0.11	1.94 ± 0.12	2.01 ± 0.10	1.70 ± 0.07°	1.38 ± 0.14°°	1.25 ± 0.13°°

° Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
°° $P \leq 0.01$
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error)
[b] n=4

TABLE F2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg	240 mg/kg	480 mg/kg
Male						
n	10	9	9	7	10	9
Necropsy body weight	338 ± 6	331 ± 9	307 ± 15*	348 ± 4	323 ± 5	330 ± 5
Brain						
Absolute	1.892 ± 0.021	1.896 ± 0.013	1.928 ± 0.016	1.933 ± 0.025	1.878 ± 0.017	1.882 ± 0.020
Relative	5.60 ± 0.09	5.76 ± 0.15	6.41 ± 0.32**	5.56 ± 0.11	5.82 ± 0.09	5.71 ± 0.08
Heart						
Absolute	0.993 ± 0.028	1.018 ± 0.023	0.976 ± 0.032	1.015 ± 0.022	0.933 ± 0.018	0.916 ± 0.014*
Relative	2.94 ± 0.09	3.08 ± 0.07	3.24 ± 0.19	2.91 ± 0.06	2.89 ± 0.03	2.78 ± 0.03
R. Kidney						
Absolute	1.118 ± 0.025	1.111 ± 0.022	1.087 ± 0.026	1.210 ± 0.013	1.139 ± 0.029	1.280 ± 0.036**
Relative	3.30 ± 0.05	3.37 ± 0.06	3.62 ± 0.21	3.48 ± 0.03	3.52 ± 0.06	3.87 ± 0.09**
Liver						
Absolute	14.399 ± 0.421	13.173 ± 0.658	12.870 ± 0.428	14.308 ± 0.516	13.593 ± 0.333	15.176 ± 0.514
Relative	42.48 ± 0.58	39.60 ± 1.28	42.51 ± 1.96	41.10 ± 1.40	42.06 ± 0.72	45.91 ± 1.14
Lung						
Absolute	1.729 ± 0.067	1.622 ± 0.070	1.682 ± 0.058	1.793 ± 0.074	1.585 ± 0.048	1.733 ± 0.054
Relative	5.11 ± 0.19	4.92 ± 0.23	5.61 ± 0.39	5.16 ± 0.25	4.92 ± 0.18	5.25 ± 0.13
R. Testis						
Absolute	1.431 ± 0.026	1.402 ± 0.022	1.379 ± 0.027	1.424 ± 0.017	1.322 ± 0.032*	1.380 ± 0.020*
Relative	4.23 ± 0.06	4.26 ± 0.13	4.57 ± 0.20	4.10 ± 0.09	4.09 ± 0.09	4.18 ± 0.07
Thymus						
Absolute	0.270 ± 0.014	0.289 ± 0.022	0.279 ± 0.019	0.304 ± 0.015	0.260 ± 0.015	0.208 ± 0.018*
Relative	0.80 ± 0.05	0.87 ± 0.05	0.93 ± 0.09	0.87 ± 0.04	0.80 ± 0.04	0.63 ± 0.06*

TABLE F2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg	240 mg/kg	480 mg/kg
Female						
n	10	10	10	10	10	10
Necropsy body weight	193 ± 3	192 ± 5	187 ± 3	193 ± 4	193 ± 3	181 ± 4
Brain						
Absolute	1.766 ± 0.025	1.758 ± 0.020	1.740 ± 0.027	1.750 ± 0.013	1.767 ± 0.005	1.758 ± 0.035
Relative	9.15 ± 0.10	9.20 ± 0.16	9.33 ± 0.11	9.08 ± 0.17	9.17 ± 0.14	9.76 ± 0.21°
Heart						
Absolute	0.644 ± 0.013	0.591 ± 0.022	0.615 ± 0.013	0.644 ± 0.010	0.615 ± 0.017	0.619 ± 0.021
Relative	3.33 ± 0.06	3.08 ± 0.08	3.30 ± 0.04	3.34 ± 0.05	3.19 ± 0.09	3.43 ± 0.11
R. Kidney						
Absolute	0.631 ± 0.017	0.670 ± 0.029	0.649 ± 0.010	0.670 ± 0.016	0.715 ± 0.019°°	0.724 ± 0.012°°
Relative	3.27 ± 0.06	3.49 ± 0.12	3.48 ± 0.05	3.46 ± 0.06	3.70 ± 0.07°°	4.02 ± 0.08°°
Liver						
Absolute	7.566 ± 0.246	7.253 ± 0.297	6.921 ± 0.136	7.639 ± 0.366	7.143 ± 0.243	6.894 ± 0.208
Relative	39.12 ± 0.83	37.73 ± 0.89	37.17 ± 0.94	39.37 ± 1.26	36.96 ± 0.94	38.15 ± 0.76
Lung						
Absolute	1.156 ± 0.031[b]	1.190 ± 0.093	1.148 ± 0.039[b]	1.199 ± 0.036	1.198 ± 0.036	1.154 ± 0.030
Relative	5.99 ± 0.16[b]	6.17 ± 0.40	6.13 ± 0.19[b]	6.22 ± 0.21	6.20 ± 0.16	6.39 ± 0.09
Thymus						
Absolute	0.229 ± 0.008	0.231 ± 0.009	0.216 ± 0.007	0.212 ± 0.006	0.177 ± 0.009°°	0.123 ± 0.006°°
Relative	1.19 ± 0.04	1.21 ± 0.03	1.16 ± 0.04	1.10 ± 0.03	0.91 ± 0.04°°	0.68 ± 0.02°°

° Significantly different ($P \leq 0.05$) from the control group by Williams' or Dunnett's test
°° $P \leq 0.01$
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error)
[b] n=9

TABLE F3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 3-Month Interim Evaluation in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male				
n	10	10	10	9
Necropsy body weight	343 ± 7	337 ± 5	343 ± 7	342 ± 5
Brain				
Absolute	1.971 ± 0.021	1.925 ± 0.021	1.900 ± 0.021*	1.925 ± 0.018
Relative	5.77 ± 0.11	5.71 ± 0.05	5.55 ± 0.10	5.64 ± 0.07
Heart				
Absolute	1.035 ± 0.033	1.000 ± 0.021	1.049 ± 0.024	1.044 ± 0.033
Relative	3.02 ± 0.08	2.96 ± 0.04	3.06 ± 0.05	3.06 ± 0.10
L. Kidney				
Absolute	1.170 ± 0.028	1.201 ± 0.016	1.234 ± 0.038	1.317 ± 0.036**
Relative	3.42 ± 0.03	3.56 ± 0.04	3.59 ± 0.04	3.86 ± 0.09**
R. Kidney				
Absolute	1.155 ± 0.032	1.195 ± 0.021	1.209 ± 0.035	1.286 ± 0.033**
Relative	3.37 ± 0.06	3.54 ± 0.05	3.52 ± 0.04	3.77 ± 0.09**
Liver				
Absolute	12.974 ± 0.472	12.634 ± 0.296	13.196 ± 0.446	13.931 ± 0.429
Relative	37.78 ± 0.80	37.45 ± 0.74	38.40 ± 0.86	40.81 ± 1.20*
Lung				
Absolute	1.988 ± 0.049	1.942 ± 0.031	2.055 ± 0.057	1.973 ± 0.082
Relative	5.82 ± 0.18	5.77 ± 0.15	6.00 ± 0.17	5.78 ± 0.22
R. Testis				
Absolute	1.514 ± 0.026	1.492 ± 0.030	1.475 ± 0.029	1.538 ± 0.023[b]
Relative	4.43 ± 0.07	4.42 ± 0.06	4.30 ± 0.08	4.52 ± 0.07[b]
Thymus				
Absolute	0.320 ± 0.008	0.297 ± 0.013	0.276 ± 0.011*	0.290 ± 0.009*
Relative	0.94 ± 0.03	0.88 ± 0.03	0.80 ± 0.03*	0.85 ± 0.02*

TABLE F3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 3-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female				
n	10	10	8	9
Necropsy body weight	198 ± 3	198 ± 3	194 ± 3	191 ± 4
Brain				
Absolute	1.806 ± 0.015	1.804 ± 0.015	1.769 ± 0.019	1.789 ± 0.025
Relative	9.13 ± 0.12	9.11 ± 0.11	9.11 ± 0.13	9.41 ± 0.18
Heart				
Absolute	0.688 ± 0.012	0.675 ± 0.020	0.654 ± 0.015	0.647 ± 0.015
Relative	3.48 ± 0.07	3.40 ± 0.08	3.37 ± 0.09	3.40 ± 0.05
L. Kidney				
Absolute	0.729 ± 0.011	0.735 ± 0.014	0.758 ± 0.015	0.776 ± 0.017°
Relative	3.68 ± 0.05	3.71 ± 0.07	3.90 ± 0.07°	4.08 ± 0.05°°
R. Kidney				
Absolute	0.724 ± 0.012	0.747 ± 0.012	0.755 ± 0.018	0.797 ± 0.018°°
Relative	3.66 ± 0.05	3.77 ± 0.06	3.89 ± 0.06°	4.19 ± 0.06°°
Liver				
Absolute	6.271 ± 0.137	6.856 ± 0.123°	6.829 ± 0.170°	6.617 ± 0.175
Relative	31.71 ± 0.76	34.59 ± 0.55°°	35.15 ± 0.75°°	34.73 ± 0.66°°
Lung				
Absolute	1.243 ± 0.034	1.327 ± 0.031	1.319 ± 0.024	1.301 ± 0.038
Relative	6.27 ± 0.12	6.69 ± 0.13	6.79 ± 0.12°	6.85 ± 0.24°
Thymus				
Absolute	0.236 ± 0.009	0.229 ± 0.012	0.210 ± 0.005	0.201 ± 0.013°
Relative	1.19 ± 0.05	1.15 ± 0.05	1.08 ± 0.03	1.05 ± 0.06

° Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
°° P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=8

TABLE F4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male				
n	10	10	10	9
Necropsy body weight	482 ± 15	508 ± 9	503 ± 7	501 ± 9
Brain				
Absolute	2.085 ± 0.018	2.097 ± 0.019	2.055 ± 0.026	2.078 ± 0.023
Relative	4.36 ± 0.13	4.14 ± 0.07	4.09 ± 0.04	4.16 ± 0.08
Heart				
Absolute	1.168 ± 0.039	1.204 ± 0.020	1.172 ± 0.022	1.211 ± 0.023
Relative	2.43 ± 0.05	2.37 ± 0.03	2.33 ± 0.04	2.42 ± 0.05
L. Kidney				
Absolute	1.403 ± 0.045	1.560 ± 0.036*	1.546 ± 0.049*	1.554 ± 0.032**
Relative	2.91 ± 0.05	3.08 ± 0.08	3.07 ± 0.08	3.11 ± 0.04
R. Kidney				
Absolute	1.413 ± 0.046	1.558 ± 0.026*	1.538 ± 0.036*	1.581 ± 0.034**[b]
Relative	2.94 ± 0.07	3.08 ± 0.06	3.06 ± 0.06	3.13 ± 0.07[b]
Liver				
Absolute	16.539 ± 0.875	17.739 ± 0.530	17.189 ± 0.648	16.473 ± 0.278
Relative	34.21 ± 1.33	34.99 ± 1.06	34.18 ± 1.25	32.92 ± 0.33
Lung				
Absolute	2.398 ± 0.090	2.393 ± 0.133	2.456 ± 0.096	2.322 ± 0.082
Relative	4.99 ± 0.17	4.76 ± 0.35	4.88 ± 0.17	4.64 ± 0.14
R. Testis				
Absolute	1.600 ± 0.040[c]	1.642 ± 0.041	1.606 ± 0.027[c]	1.651 ± 0.035
Relative	3.37 ± 0.08[c]	3.24 ± 0.08	3.22 ± 0.06[c]	3.31 ± 0.09
Thymus				
Absolute	0.228 ± 0.018	0.202 ± 0.021	0.231 ± 0.019	0.194 ± 0.018
Relative	0.47 ± 0.03	0.40 ± 0.04	0.46 ± 0.04	0.39 ± 0.04

TABLE F4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female				
n	10	10	9	10
Necropsy body weight	287 ± 8	275 ± 6	274 ± 7	279 ± 6
Brain				
Absolute	1.861 ± 0.032	1.903 ± 0.020	1.883 ± 0.025	1.899 ± 0.018
Relative	6.51 ± 0.19	6.94 ± 0.15	6.90 ± 0.15	6.84 ± 0.13
Heart				
Absolute	0.785 ± 0.016	0.756 ± 0.019	0.772 ± 0.012	0.758 ± 0.008
Relative	2.75 ± 0.07	2.75 ± 0.07	2.83 ± 0.06	2.73 ± 0.05
L. Kidney				
Absolute	0.890 ± 0.018	0.878 ± 0.023	0.985 ± 0.028°	0.968 ± 0.024°
Relative	3.11 ± 0.08	3.20 ± 0.08	3.60 ± 0.07°°	3.48 ± 0.06°°
R. Kidney				
Absolute	0.866 ± 0.018	0.868 ± 0.027	0.981 ± 0.036°	0.945 ± 0.020°
Relative	3.03 ± 0.08	3.16 ± 0.08	3.57 ± 0.07°°	3.39 ± 0.05°°
Liver				
Absolute	9.552 ± 0.276	8.950 ± 0.356	9.583 ± 0.500	9.346 ± 0.246
Relative	33.39 ± 1.12	32.55 ± 1.06	34.81 ± 1.04	33.63 ± 1.00
Lung				
Absolute	1.601 ± 0.035	1.575 ± 0.077	1.653 ± 0.072	1.582 ± 0.048
Relative	5.62 ± 0.23	5.73 ± 0.26	6.04 ± 0.24	5.70 ± 0.20
Thymus				
Absolute	0.178 ± 0.012	0.127 ± 0.007°	0.138 ± 0.015°	0.126 ± 0.015°°
Relative	0.62 ± 0.04	0.47 ± 0.03°	0.51 ± 0.06	0.45 ± 0.05°

° Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
°° P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=8
[c] n=9

TABLE F5
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male				
n	23	24	25	24
Necropsy body weight	449 ± 7	424 ± 9*	420 ± 9*	414 ± 10**
Brain				
Absolute	2.160 ± 0.016	2.142 ± 0.020	2.131 ± 0.019	2.147 ± 0.016
Relative	4.84 ± 0.11	5.11 ± 0.12	5.14 ± 0.13	5.25 ± 0.13*
Heart				
Absolute	1.804 ± 0.039	1.923 ± 0.052	1.953 ± 0.062	2.119 ± 0.069**
Relative	4.02 ± 0.08	4.56 ± 0.11**	4.66 ± 0.12**	5.14 ± 0.15**
R. Kidney				
Absolute	1.798 ± 0.040	1.888 ± 0.053	1.976 ± 0.059*	2.135 ± 0.080**
Relative	4.01 ± 0.09	4.48 ± 0.11*	4.72 ± 0.12**	5.18 ± 0.17**
Liver				
Absolute	16.894 ± 0.382	16.946 ± 0.522	17.431 ± 0.541	18.698 ± 0.579*
Relative	37.59 ± 0.59	40.07 ± 1.07	41.67 ± 1.16*	45.38 ± 1.43**

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female				
n	26	29	27	28
Necropsy body weight	305 ± 5	306 ± 4	308 ± 4	312 ± 7
Brain				
Absolute	1.932 ± 0.013	1.935 ± 0.013	1.956 ± 0.013	1.944 ± 0.013
Relative	6.36 ± 0.11	6.36 ± 0.07	6.40 ± 0.09	6.32 ± 0.14
Heart				
Absolute	1.169 ± 0.020	1.229 ± 0.022	1.240 ± 0.019*	1.382 ± 0.031**
Relative	3.85 ± 0.09	4.03 ± 0.07	4.06 ± 0.07	4.45 ± 0.06**
R. Kidney				
Absolute	1.147 ± 0.017	1.203 ± 0.019	1.239 ± 0.018**	1.374 ± 0.030**
Relative	3.78 ± 0.09	3.94 ± 0.06	4.05 ± 0.06**	4.43 ± 0.06**
Liver				
Absolute	11.781 ± 0.475	11.804 ± 0.311	11.480 ± 0.267	11.933 ± 0.319
Relative	38.80 ± 1.70	38.70 ± 1.02	37.48 ± 0.80	38.33 ± 0.59

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).

TABLE F6
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 16-Day Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	62.5 mg/kg	125 mg/kg	250 mg/kg	500 mg/kg	1,000 mg/kg
Male						
n	5	5	5	5	5	2
Necropsy body weight	27.0 ± 0.7	25.5 ± 1.0	26.9 ± 0.9	26.7 ± 1.3	26.9 ± 0.4	27.8 ± 0.1
Brain						
Absolute	0.467 ± 0.008	0.461 ± 0.008	0.464 ± 0.010	0.469 ± 0.008	0.463 ± 0.010	0.439 ± 0.016
Relative	17.33 ± 0.36	18.17 ± 0.74	17.37 ± 0.79	17.78 ± 0.97	17.23 ± 0.33	15.82 ± 0.55
Heart						
Absolute	0.138 ± 0.008	0.156 ± 0.016	0.143 ± 0.005	0.138 ± 0.012	0.133 ± 0.005	0.146 ± 0.016
Relative	5.13 ± 0.23	6.08 ± 0.43	5.36 ± 0.27	5.15 ± 0.28	4.94 ± 0.14	5.24 ± 0.55
R. Kidney						
Absolute	0.226 ± 0.017	0.221 ± 0.015	0.217 ± 0.008	0.215 ± 0.016	0.228 ± 0.018	0.245 ± 0.003
Relative	8.33 ± 0.46	8.62 ± 0.32	8.10 ± 0.20	8.05 ± 0.27	8.45 ± 0.60	8.83 ± 0.09
Liver						
Absolute	1.519 ± 0.080	1.394 ± 0.096	1.528 ± 0.055	1.586 ± 0.114[b]	1.922 ± 0.059°°	2.255 ± 0.003°°
Relative	56.22 ± 1.82	54.44 ± 1.92	56.96 ± 1.65	58.37 ± 1.45[b]	71.50 ± 2.33°°	81.24 ± 0.06°°
Lung						
Absolute	0.218 ± 0.015	0.204 ± 0.013	0.211 ± 0.010	0.200 ± 0.007	0.207 ± 0.012	0.236 ± 0.017
Relative	8.08 ± 0.43	8.01 ± 0.42	7.90 ± 0.50	7.57 ± 0.34	7.68 ± 0.37	8.49 ± 0.58
R. Testis						
Absolute	0.112 ± 0.005	0.115 ± 0.005	0.108 ± 0.003	0.116 ± 0.005	0.113 ± 0.005	0.112 ± 0.004
Relative	4.17 ± 0.15	4.51 ± 0.12	4.04 ± 0.21	4.39 ± 0.27	4.20 ± 0.16	4.04 ± 0.15
Thymus						
Absolute	0.036 ± 0.002	0.046 ± 0.006	0.048 ± 0.003	0.040 ± 0.004	0.050 ± 0.009	0.043 ± 0.006
Relative	1.36 ± 0.11	1.78 ± 0.19	1.79 ± 0.17	1.51 ± 0.15	1.89 ± 0.37	1.53 ± 0.20
Female						
n	5	5	5	5	5	0
Necropsy body weight	19.6 ± 0.2	19.4 ± 0.7	19.6 ± 0.6	20.0 ± 0.4	20.5 ± 0.5	–[c]
Brain						
Absolute	0.446 ± 0.009	0.436 ± 0.012	0.448 ± 0.015	0.452 ± 0.007	0.467 ± 0.007	–
Relative	22.76 ± 0.36	22.56 ± 0.31	22.81 ± 0.56	22.66 ± 0.34	22.82 ± 0.66	–
Heart						
Absolute	0.114 ± 0.006	0.110 ± 0.005	0.112 ± 0.007	0.122 ± 0.007	0.127 ± 0.007	–
Relative	5.83 ± 0.26	5.70 ± 0.25	5.69 ± 0.32	6.14 ± 0.50	6.18 ± 0.32	–
R. Kidney						
Absolute	0.145 ± 0.008	0.139 ± 0.011	0.138 ± 0.007	0.147 ± 0.006	0.154 ± 0.006	–
Relative	7.39 ± 0.37	7.13 ± 0.32	7.01 ± 0.18	7.37 ± 0.24	7.52 ± 0.15	–
Liver						
Absolute	1.154 ± 0.030	1.170 ± 0.063	1.208 ± 0.053	1.312 ± 0.041°	1.567 ± 0.035°°	–
Relative	58.90 ± 1.10	60.36 ± 1.87	61.48 ± 1.76	65.71 ± 2.00°	76.52 ± 1.89°°	–
Lung						
Absolute	0.177 ± 0.017	0.186 ± 0.019	0.181 ± 0.011	0.189 ± 0.011	0.198 ± 0.011	–
Relative	9.04 ± 0.84	9.53 ± 0.61	9.20 ± 0.45	9.48 ± 0.59	9.65 ± 0.54	–
Thymus						
Absolute	0.057 ± 0.005	0.066 ± 0.005	0.054 ± 0.003	0.056 ± 0.007	0.058 ± 0.004	–
Relative	2.90 ± 0.24	3.38 ± 0.20	2.76 ± 0.16	2.85 ± 0.40	2.81 ± 0.16	–

° Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
°° P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error)
[b] n=4
[c] No measurements taken due to 100% mortality in this group.

TABLE F7
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	500 mg/kg	650 mg/kg	800 mg/kg	1,000 mg/kg
Male					
n	10	10	8	4	1
Necropsy body weight	36.3 ± 0.7	30.4 ± 0.9**	31.7 ± 0.8**	31.0 ± 1.4**	31.1[b]
Brain					
Absolute	0.468 ± 0.009	0.444 ± 0.008*	0.426 ± 0.008**	0.449 ± 0.011*	0.435
Relative	12.94 ± 0.36	14.68 ± 0.49*	13.47 ± 0.38	14.61 ± 0.78	13.99
Heart					
Absolute	0.176 ± 0.009	0.149 ± 0.007	0.154 ± 0.021	0.173 ± 0.013	0.104
Relative	4.86 ± 0.28	4.87 ± 0.15	4.81 ± 0.62	5.57 ± 0.34	3.34
R. Kidney					
Absolute	0.341 ± 0.010	0.269 ± 0.009**	0.273 ± 0.011**	0.258 ± 0.031**	0.300
Relative	9.42 ± 0.23	8.85 ± 0.21	8.61 ± 0.19*	8.28 ± 0.70*	9.65
Liver					
Absolute	2.106 ± 0.082	1.967 ± 0.073	2.288 ± 0.036	2.588 ± 0.085**	2.988
Relative	58.02 ± 1.83	64.55 ± 1.03*	72.52 ± 2.39**	84.05 ± 4.25**	96.08
Lung					
Absolute	0.246 ± 0.012	0.227 ± 0.009[c]	0.227 ± 0.014	0.247 ± 0.021	0.236
Relative	6.77 ± 0.25	7.39 ± 0.25[c]	7.13 ± 0.38	8.02 ± 0.71	7.59
R. Testis					
Absolute	0.108 ± 0.008	0.104 ± 0.004	0.100 ± 0.012	0.115 ± 0.015	0.108
Relative	2.96 ± 0.21	3.42 ± 0.14	3.17 ± 0.37	3.67 ± 0.37	3.47
Thymus					
Absolute	0.036 ± 0.005	0.032 ± 0.003	0.031 ± 0.011	0.039 ± 0.009	0.064
Relative	0.99 ± 0.11	1.07 ± 0.10	0.97 ± 0.36	1.29 ± 0.32	2.06
Female					
n	10	9	9	2	0
Necropsy body weight	24.7 ± 0.8	24.7 ± 0.5	24.2 ± 0.4	24.3 ± 1.2	–[d]
Brain					
Absolute	0.466 ± 0.006	0.447 ± 0.005*	0.446 ± 0.006*	0.446 ± 0.016	–
Relative	18.99 ± 0.44	18.15 ± 0.40	18.42 ± 0.28	18.38 ± 0.23	–
Heart					
Absolute	0.125 ± 0.006	0.122 ± 0.004	0.121 ± 0.005	0.123 ± 0.004	–
Relative	5.08 ± 0.26	4.97 ± 0.16	4.99 ± 0.17	5.07 ± 0.38	–
R. Kidney					
Absolute	0.174 ± 0.009	0.185 ± 0.006	0.183 ± 0.008	0.188 ± 0.005	–
Relative	7.03 ± 0.18	7.48 ± 0.16	7.52 ± 0.28	7.76 ± 0.16	–
Liver					
Absolute	1.270 ± 0.061	1.605 ± 0.049**	1.721 ± 0.042**	1.937 ± 0.082**	–
Relative	51.31 ± 1.47	64.98 ± 1.44**	70.95 ± 1.14**	79.88 ± 0.43**	–
Lung					
Absolute	0.183 ± 0.009	0.212 ± 0.005*	0.200 ± 0.007*	0.202 ± 0.004	–
Relative	7.43 ± 0.28	8.60 ± 0.24*	8.23 ± 0.25*	8.33 ± 0.54	–
Thymus					
Absolute	0.044 ± 0.004	0.046 ± 0.003	0.049 ± 0.002	0.049 ± 0.003	–
Relative	1.76 ± 0.14	1.86 ± 0.11	2.02 ± 0.09	2.01 ± 0.20	–

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] No standard error calculated due to high mortality in this group.
[c] n=9
[d] No measurements taken due to 100% mortality in this group.

TABLE F8
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 3-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Male				
n	10	10	10	10
Necropsy body weight	32.0 ± 0.9	32.0 ± 1.0	31.2 ± 0.8	30.2 ± 0.4
Brain				
Absolute	0.455 ± 0.006	0.461 ± 0.005	0.453 ± 0.005	0.458 ± 0.004
Relative	14.31 ± 0.45	14.56 ± 0.39	14.61 ± 0.42	15.18 ± 0.15
Heart				
Absolute	0.159 ± 0.006	0.159 ± 0.007	0.156 ± 0.006	0.145 ± 0.004
Relative	4.96 ± 0.14	4.97 ± 0.12	5.01 ± 0.21	4.81 ± 0.11
L. Kidney				
Absolute	0.284 ± 0.011	0.262 ± 0.005	0.252 ± 0.006*	0.257 ± 0.011*
Relative	8.89 ± 0.25	8.27 ± 0.20	8.09 ± 0.16	8.52 ± 0.39
R. Kidney				
Absolute	0.297 ± 0.010	0.277 ± 0.006	0.273 ± 0.008	0.269 ± 0.012*
Relative	9.29 ± 0.20	8.70 ± 0.12	8.77 ± 0.21	8.91 ± 0.39
Liver				
Absolute	1.467 ± 0.058	1.485 ± 0.038	1.570 ± 0.034	1.838 ± 0.061**
Relative	45.75 ± 0.89	46.80 ± 1.40	50.51 ± 1.25*	60.82 ± 1.55**
Lung				
Absolute	0.247 ± 0.010	0.247 ± 0.008	0.249 ± 0.008	0.250 ± 0.016
Relative	7.73 ± 0.25	7.77 ± 0.24	8.04 ± 0.31	8.27 ± 0.53
R. Testis				
Absolute	0.114 ± 0.002	0.117 ± 0.002	0.115 ± 0.002	0.115 ± 0.002
Relative	3.57 ± 0.09	3.68 ± 0.08	3.69 ± 0.09	3.81 ± 0.08
Thymus				
Absolute	0.043 ± 0.002	0.045 ± 0.002[b]	0.040 ± 0.002[b]	0.039 ± 0.003
Relative	1.34 ± 0.03	1.42 ± 0.05[b]	1.30 ± 0.06[b]	1.29 ± 0.10

TABLE F8
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 3-Month Interim Evaluation in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Female				
n	10	10	10	9
Necropsy body weight	27.8 ± 1.0	25.8 ± 0.4	26.8 ± 0.4	27.5 ± 0.7
Brain				
Absolute	0.482 ± 0.008	0.472 ± 0.003	0.476 ± 0.004	0.487 ± 0.006
Relative	17.48 ± 0.47	18.31 ± 0.33	17.82 ± 0.37	17.74 ± 0.35
Heart				
Absolute	0.137 ± 0.008	0.137 ± 0.003	0.132 ± 0.003	0.141 ± 0.005
Relative	4.91 ± 0.14	5.30 ± 0.11	4.93 ± 0.16	5.12 ± 0.14
L. Kidney				
Absolute	0.189 ± 0.007	0.178 ± 0.004	0.186 ± 0.004	0.194 ± 0.004
Relative	6.81 ± 0.12	6.91 ± 0.14	6.94 ± 0.18	7.05 ± 0.14
R. Kidney				
Absolute	0.205 ± 0.007	0.193 ± 0.004	0.196 ± 0.004	0.209 ± 0.005
Relative	7.41 ± 0.21	7.49 ± 0.15	7.32 ± 0.15	7.62 ± 0.15
Liver				
Absolute	1.373 ± 0.050	1.328 ± 0.034	1.463 ± 0.028	1.736 ± 0.048**
Relative	49.42 ± 0.70	51.44 ± 0.99	54.66 ± 1.02**	63.21 ± 1.78**
Lung				
Absolute	0.272 ± 0.022	0.264 ± 0.014	0.246 ± 0.014	0.269 ± 0.008
Relative	9.76 ± 0.64	10.24 ± 0.56	9.20 ± 0.55	9.80 ± 0.37
Thymus				
Absolute	0.056 ± 0.003	0.053 ± 0.003	0.054 ± 0.002	0.051 ± 0.003
Relative	2.04 ± 0.09	2.05 ± 0.09	2.03 ± 0.08	1.84 ± 0.09

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9

TABLE F9
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Male				
n	10	10	10	10
Necropsy body weight	51.3 ± 0.8	46.3 ± 1.9**	45.2 ± 1.2**	37.3 ± 1.1**
Brain				
Absolute	0.466 ± 0.006	0.473 ± 0.008	0.469 ± 0.008	0.471 ± 0.008
Relative	9.10 ± 0.21	10.37 ± 0.43*	10.46 ± 0.38**	12.69 ± 0.27**
Heart				
Absolute	0.211 ± 0.005	0.183 ± 0.006**	0.189 ± 0.006**	0.186 ± 0.007**
Relative	4.12 ± 0.07	4.00 ± 0.14	4.19 ± 0.11	5.01 ± 0.17**
L. Kidney				
Absolute	0.407 ± 0.014	0.302 ± 0.014**	0.281 ± 0.010**	0.245 ± 0.009**
Relative	7.94 ± 0.28	6.58 ± 0.27**	6.26 ± 0.25**	6.63 ± 0.32**
R. Kidney				
Absolute	0.426 ± 0.012	0.309 ± 0.014**	0.283 ± 0.007**	0.265 ± 0.009**
Relative	8.32 ± 0.27	6.73 ± 0.26**	6.29 ± 0.23**	7.13 ± 0.19**
Liver				
Absolute	2.167 ± 0.086	1.825 ± 0.069	1.988 ± 0.065	2.305 ± 0.163
Relative	42.12 ± 1.24	39.61 ± 0.90	44.04 ± 1.21	62.22 ± 5.02**
Lung				
Absolute	0.377 ± 0.019	0.289 ± 0.011**	0.300 ± 0.014**	0.289 ± 0.010**[b]
Relative	7.31 ± 0.28	6.35 ± 0.38	6.63 ± 0.23	7.91 ± 0.38[b]
R. Testis				
Absolute	0.122 ± 0.002	0.122 ± 0.003	0.119 ± 0.002[b]	0.117 ± 0.002
Relative	2.38 ± 0.03	2.68 ± 0.14*	2.65 ± 0.06*[b]	3.17 ± 0.11**
Thymus				
Absolute	0.061 ± 0.005	0.042 ± 0.004**	0.039 ± 0.003**[b]	0.031 ± 0.003**
Relative	1.18 ± 0.09	0.90 ± 0.08**	0.88 ± 0.05**[b]	0.82 ± 0.07**

TABLE F9
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice at the 15-Month Interim Evaluation in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol (continued)

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Female				
n	10	10	10	9
Necropsy body weight	44.9 ± 1.8	43.6 ± 1.5	43.8 ± 2.1	35.9 ± 1.2**
Brain				
Absolute	0.493 ± 0.007	0.484 ± 0.006	0.478 ± 0.004	0.485 ± 0.007
Relative	11.20 ± 0.57	11.22 ± 0.42	11.19 ± 0.64	13.61 ± 0.32**
Heart				
Absolute	0.165 ± 0.005	0.156 ± 0.004	0.157 ± 0.005	0.164 ± 0.011
Relative	3.79 ± 0.31	3.61 ± 0.15	3.63 ± 0.15	4.62 ± 0.36*
L. Kidney				
Absolute	0.267 ± 0.010	0.227 ± 0.004*	0.243 ± 0.009*	0.226 ± 0.010**
Relative	6.13 ± 0.56	5.24 ± 0.13	5.66 ± 0.33	6.34 ± 0.34
R. Kidney				
Absolute	0.287 ± 0.013	0.240 ± 0.006**	0.253 ± 0.010**	0.249 ± 0.007**
Relative	6.62 ± 0.66	5.53 ± 0.14	5.88 ± 0.34	6.98 ± 0.30
Liver				
Absolute	1.729 ± 0.088	1.638 ± 0.059	1.893 ± 0.064	2.088 ± 0.076**
Relative	39.89 ± 4.21	37.58 ± 0.65	43.74 ± 1.61	58.39 ± 1.96**
Lung				
Absolute	0.323 ± 0.015	0.288 ± 0.012	0.297 ± 0.019	0.283 ± 0.010
Relative	7.34 ± 0.47	6.63 ± 0.25	6.89 ± 0.47	7.88 ± 0.12
Thymus				
Absolute	0.055 ± 0.005	0.041 ± 0.003*	0.043 ± 0.004*	0.034 ± 0.003**
Relative	1.22 ± 0.09	0.93 ± 0.07*	0.99 ± 0.07*	0.94 ± 0.06*

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9

TABLE F10
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	120 mg/kg	240 mg/kg	480 mg/kg
Male				
n	45	32	38	30
Necropsy body weight	48.0 ± 1.0	39.1 ± 0.9**	35.5 ± 0.7**	32.6 ± 0.7**
Brain				
Absolute	0.453 ± 0.004	0.465 ± 0.005	0.473 ± 0.008*	0.469 ± 0.005*[b]
Relative	9.66 ± 0.24	12.08 ± 0.27**	13.48 ± 0.32**	14.51 ± 0.29**[b]
L. Kidney				
Absolute	0.399 ± 0.008	0.263 ± 0.005**	0.253 ± 0.006**	0.267 ± 0.007**
Relative	8.45 ± 0.22	6.80 ± 0.15**	7.20 ± 0.21**	8.26 ± 0.25
R. Kidney				
Absolute	0.415 ± 0.006	0.280 ± 0.005**	0.266 ± 0.006**	0.281 ± 0.005**
Relative	8.80 ± 0.20	7.24 ± 0.15**	7.57 ± 0.21**	8.71 ± 0.23
Liver				
Absolute	2.424 ± 0.117	2.398 ± 0.202	1.949 ± 0.078*	2.113 ± 0.056*
Relative	51.25 ± 2.73	64.56 ± 7.14	55.66 ± 2.80	65.35 ± 1.95*
Female				
n	36	40	33	25
Necropsy body weight	47.2 ± 1.3	44.9 ± 1.2	40.4 ± 1.2**	33.7 ± 0.9**
Brain				
Absolute	0.477 ± 0.004	0.473 ± 0.003	0.465 ± 0.003*	0.462 ± 0.005*
Relative	10.39 ± 0.32	10.85 ± 0.31	11.88 ± 0.39**	13.94 ± 0.44**
L. Kidney				
Absolute	0.277 ± 0.004	0.261 ± 0.005	0.231 ± 0.004**	0.206 ± 0.014**
Relative	5.99 ± 0.17	5.96 ± 0.20	5.90 ± 0.21	6.35 ± 0.72
R. Kidney				
Absolute	0.291 ± 0.005	0.276 ± 0.005*	0.250 ± 0.005**	0.214 ± 0.006**
Relative	6.29 ± 0.16	6.29 ± 0.20	6.38 ± 0.22	6.43 ± 0.22
Liver				
Absolute	1.970 ± 0.077	2.223 ± 0.123	2.208 ± 0.090	2.121 ± 0.089
Relative	42.38 ± 1.66	52.14 ± 4.24*	56.67 ± 3.53**	63.13 ± 2.34**

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] n=29

APPENDIX G
HEMATOLOGY, CLINICAL CHEMISTRY, AND URINALYSIS RESULTS

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 13-Week Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg	240 mg/kg	480 mg/kg
Male						
Hematology						
n	10	9	8	7	10	9
Hematocrit (%)	49.0 ± 0.6	50.7 ± 0.4*	49.3 ± 2.3*	50.9 ± 1.2	52.3 ± 1.0**	52.0 ± 0.7**
Hemoglobin (g/dL)	15.6 ± 0.1	16.1 ± 0.2*	15.7 ± 0.7*	16.1 ± 0.3	16.4 ± 0.3*	16.3 ± 0.2*
Erythrocytes ($10^6/\mu L$)	9.56 ± 0.09	10.03 ± 0.10**	9.57 ± 0.46*	10.12 ± 0.32	10.55 ± 0.32**	10.19 ± 0.13**
Mean cell volume (fL)	51.2 ± 0.2	50.7 ± 0.2	51.5 ± 0.3	51.1 ± 0.3	50.9 ± 0.2	51.2 ± 0.3
Leukocytes ($10^3/\mu L$)	10.59 ± 0.75	7.11 ± 0.32**	8.34 ± 0.51[b]	8.37 ± 0.70	8.59 ± 0.37	10.32 ± 0.61
Segmented neutrophils ($10^3/\mu L$)	1.39 ± 0.11	1.08 ± 0.09	1.21 ± 0.20	1.05 ± 0.13	1.42 ± 0.26	1.51 ± 0.18
Lymphocytes ($10^3/\mu L$)	8.92 ± 0.70	5.96 ± 0.34**	7.93 ± 1.01	7.17 ± 0.63	7.07 ± 0.32	8.69 ± 0.54
Monocytes ($10^3/\mu L$)	0.05 ± 0.02	0.00 ± 0.00	0.02 ± 0.02	0.01 ± 0.01	0.04 ± 0.03	0.05 ± 0.03
Eosinophils ($10^3/\mu L$)	0.22 ± 0.04	0.07 ± 0.03*	0.16 ± 0.03	0.14 ± 0.04	0.07 ± 0.02**	0.05 ± 0.03**
Nucleated erythrocytes ($10^3/\mu L$)	0.03 ± 0.02	0.02 ± 0.01	0.34 ± 0.34	0.01 ± 0.01	0.02 ± 0.01	0.01 ± 0.01
Clinical Chemistry						
n	10	9	9	7	10	9
Blood urea nitrogen (mg/dL)	27.4 ± 0.6	22.7 ± 0.5**	20.9 ± 1.1**	24.6 ± 0.4**	23.4 ± 1.3**	21.7 ± 0.6**
Creatinine (mg/dL)	0.58 ± 0.02	0.52 ± 0.03	0.54 ± 0.03	0.54 ± 0.05	0.63 ± 0.03	0.68 ± 0.04*
Total protein (g/dL)	6.5 ± 0.1	6.4 ± 0.1	6.4 ± 0.1	6.5 ± 0.0	6.4 ± 0.1	6.4 ± 0.1
Albumin (g/dL)	4.4 ± 0.0	4.4 ± 0.1	4.2 ± 0.1	4.4 ± 0.1	4.6 ± 0.0	4.7 ± 0.1**
Globulin (g/dL)	2.1 ± 0.1	2.0 ± 0.0	2.1 ± 0.1	2.1 ± 0.0	1.9 ± 0.1**	1.8 ± 0.1**
A/G ratio	2.0 ± 0.1	2.2 ± 0.1	2.0 ± 0.1	2.2 ± 0.1	2.5 ± 0.1**	2.7 ± 0.1**
Total bilirubin (mg/dL)	0.4 ± 0.0	0.3 ± 0.0**	0.3 ± 0.0**	0.3 ± 0.0**	0.3 ± 0.0**	0.3 ± 0.0**
Alanine aminotransferase (IU/L)	73 ± 7	52 ± 2*	52 ± 5**	40 ± 2**	47 ± 5**	54 ± 2**
Aspartate aminotransferase (IU/L)	140 ± 12	95 ± 3**	99 ± 7**	84 ± 4**	89 ± 6**	84 ± 3**
Sorbitol dehydrogenase (IU/L)	32 ± 3	22 ± 1**	20 ± 2**	19 ± 2**	24 ± 4**	20 ± 2*
Cholinesterase (IU/L)	809 ± 30	776 ± 23	769 ± 15	809 ± 27	800 ± 39	774 ± 20
Urinalysis						
n	10	9	10	7	10	9
Urine volume (mL/16 hr)	8.2 ± 2.1	6.4 ± 1.2	8.8 ± 1.8	7.9 ± 1.5	7.5 ± 1.8	8.5 ± 1.7
Specific gravity	1.037 ± 0.006	1.037 ± 0.005	1.033 ± 0.005	1.034 ± 0.005	1.040 ± 0.006	1.035 ± 0.006

TABLE G1
Hematology, Clinical Chemistry, and Urinalysis Data for Rats in the 13-Week Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg	240 mg/kg	480 mg/kg
Female						
n	10	10	10	10	10	10
Hematology						
Hematocrit (%)	50.5 ± 0.4	48.8 ± 0.7	49.3 ± 1.0	49.4 ± 0.6	49.3 ± 0.4	50.6 ± 0.8
Hemoglobin (g/dL)	16.4 ± 0.1	15.6 ± 0.3*	15.7 ± 0.3	15.8 ± 0.2	15.9 ± 0.1	16.2 ± 0.3
Erythrocytes ($10^6/\mu L$)	9.17 ± 0.06	8.89 ± 0.11	8.97 ± 0.19	8.99 ± 0.11	8.98 ± 0.07	9.30 ± 0.15
Mean cell volume (fL)	55.0 ± 0.0	54.9 ± 0.2	54.9 ± 0.1	55.1 ± 0.2	54.9 ± 0.2	54.2 ± 0.2**
Leukocytes ($10^3/\mu L$)	8.78 ± 0.41	8.06 ± 0.60	8.21 ± 0.28	7.51 ± 0.54	7.81 ± 0.21	9.23 ± 0.31
Segmented neutrophils ($10^3/\mu L$)	1.47 ± 0.18	1.40 ± 0.17	1.21 ± 0.13	1.11 ± 0.15	1.49 ± 0.13	1.71 ± 0.19
Lymphocytes ($10^3/\mu L$)	7.15 ± 0.39	6.50 ± 0.56	6.88 ± 0.22	6.26 ± 0.48	6.16 ± 0.23	7.37 ± 0.27
Monocytes ($10^3/\mu L$)	0.05 ± 0.03	0.06 ± 0.04	0.03 ± 0.01	0.03 ± 0.01	0.04 ± 0.02	0.09 ± 0.03
Eosinophils ($10^3/\mu L$)	0.12 ± 0.06	0.11 ± 0.03	0.10 ± 0.02	0.11 ± 0.03	0.13 ± 0.02	0.06 ± 0.02
Nucleated erythrocytes ($10^3/\mu L$)	0.07 ± 0.02	0.06 ± 0.03	0.04 ± 0.02	0.03 ± 0.02	0.05 ± 0.03	0.07 ± 0.03
Clinical Chemistry						
Blood urea nitrogen (mg/dL)	25.3 ± 0.6	23.1 ± 0.6	18.7 ± 0.8**	22.5 ± 0.6	20.5 ± 0.7**	24.8 ± 0.7
Creatinine (mg/dL)	0.80 ± 0.05	0.62 ± 0.03	0.58 ± 0.04*	0.70 ± 0.04	0.62 ± 0.03*	0.87 ± 0.05
Total protein (g/dL)	6.1 ± 0.1	6.1 ± 0.1	6.3 ± 0.1	6.2 ± 0.2	6.1 ± 0.1	6.0 ± 0.1
Albumin (g/dL)	4.3 ± 0.1	4.4 ± 0.1	4.5 ± 0.1	4.4 ± 0.1	4.4 ± 0.0	4.3 ± 0.1
Globulin (g/dL)	1.8 ± 0.0	1.7 ± 0.1	1.8 ± 0.1	1.7 ± 0.1	1.7 ± 0.0	1.7 ± 0.1
A/G ratio	2.4 ± 0.0	2.6 ± 0.1	2.5 ± 0.1	2.5 ± 0.1	2.5 ± 0.1	2.6 ± 0.1
Total bilirubin (mg/dL)	0.3 ± 0.0	0.2 ± 0.0	0.3 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	0.3 ± 0.0
Alanine aminotransferase (IU/L)	40 ± 3	37 ± 2	35 ± 3	38 ± 3	34 ± 1	56 ± 3*
Aspartate aminotransferase (IU/L)	87 ± 4	79 ± 9	66 ± 9	86 ± 4	92 ± 6	100 ± 7
Sorbitol dehydrogenase (IU/L)	23 ± 3	20 ± 1	17 ± 2	25 ± 4	20 ± 2	22 ± 2
Cholinesterase	2566 ± 70	2960 ± 132	3181 ± 140*	2803 ± 197	3048 ± 111	2453 ± 96
Urinalysis						
Urine volume (mL/16 hr)	9.0 ± 1.5	4.3 ± 1.0	5.1 ± 0.8	6.1 ± 1.7	5.9 ± 0.8	8.2 ± 1.0
Specific gravity	1.016 ± 0.003	1.033 ± 0.006*	1.022 ± 0.003	1.035 ± 0.009	1.020 ± 0.004	1.019 ± 0.005

* Significantly different ($P \leq 0.05$) from the control group by Dunn's or Shirley's test
** $P \leq 0.01$
[a] Mean ± standard error; A/G ratio = albumin/globulin ratio
[b] n=7

TABLE G2
Clinical Chemistry and Urinalysis Data for Rats at the 3-Month Interim Evaluation in the 2-Year Gavage Study of o-Benzyl-p-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male				
n	10	10	10	9
Clinical Chemistry				
Blood urea nitrogen (mg/dL)				
2 days	17.0 ± 0.8	18.1 ± 0.8	14.8 ± 0.7	16.4 ± 0.6
14 days	19.7 ± 0.9	15.9 ± 0.4**	17.8 ± 0.5	18.9 ± 1.1
30 days	15.6 ± 0.8	17.6 ± 0.7	18.7 ± 0.4*	13.2 ± 1.1
60 days	14.6 ± 0.8	16.2 ± 1.1	15.5 ± 1.0	16.2 ± 0.6
13 weeks	18.0 ± 1.1	20.8 ± 1.5	20.1 ± 1.3	16.8 ± 1.7
Creatinine (mg/dL)				
2 days	0.77 ± 0.12	0.64 ± 0.05	0.64 ± 0.04	0.64 ± 0.03
14 days	0.72 ± 0.10	0.81 ± 0.06	0.73 ± 0.06	0.63 ± 0.03
30 days	0.69 ± 0.07	0.66 ± 0.09	0.60 ± 0.03	0.68 ± 0.08
60 days	0.78 ± 0.06	0.92 ± 0.08	0.75 ± 0.10	0.76 ± 0.04
13 weeks	0.66 ± 0.05	0.83 ± 0.12	0.57 ± 0.10	0.61 ± 0.12
Glucose (mg/dL)				
2 days	151 ± 5	153 ± 6	154 ± 6	172 ± 7[b]
14 days	155 ± 8	156 ± 4	156 ± 5	162 ± 4
30 days	164 ± 6	173 ± 9	159 ± 2	188 ± 4**
60 days	200 ± 6	212 ± 10	205 ± 4	194 ± 7
13 weeks	114 ± 4	109 ± 4	114 ± 4	106 ± 5
Total protein (g/dL)				
2 days	6.1 ± 0.2	5.9 ± 0.1	6.1 ± 0.1	6.2 ± 0.1[b]
14 days	6.9 ± 0.3	6.5 ± 0.1	6.7 ± 0.1	7.0 ± 0.1
30 days	7.0 ± 0.2	7.5 ± 0.3	6.8 ± 0.2	7.7 ± 0.2
60 days	9.2 ± 0.4	9.4 ± 0.4	8.7 ± 0.3	8.3 ± 0.3
13 weeks	7.2 ± 0.2	7.3 ± 0.2	7.4 ± 0.2	7.2 ± 0.2
Albumin (g/dL)				
2 days	4.4 ± 0.1	4.4 ± 0.1	4.4 ± 0.1	4.6 ± 0.1[b]
14 days	4.2 ± 0.2	4.2 ± 0.1	4.2 ± 0.1	4.3 ± 0.1
30 days	4.2 ± 0.1	4.4 ± 0.1	4.2 ± 0.1	4.5 ± 0.1
60 days	5.4 ± 0.2	5.5 ± 0.3	5.1 ± 0.2	4.9 ± 0.2
13 weeks	4.4 ± 0.1	4.4 ± 0.1	4.3 ± 0.1	4.3 ± 0.2
Globulin (g/dL)				
2 days	1.7 ± 0.1	1.5 ± 0.0	1.6 ± 0.1	1.6 ± 0.1[b]
14 days	2.7 ± 0.1	2.4 ± 0.1*	2.5 ± 0.1	2.7 ± 0.1
30 days	2.8 ± 0.1	3.0 ± 0.1	2.6 ± 0.1	3.2 ± 0.1
60 days	3.8 ± 0.3	3.9 ± 0.2	3.6 ± 0.2	3.4 ± 0.2
13 weeks	2.8 ± 0.1	2.9 ± 0.1	3.0 ± 0.1	2.9 ± 0.1
A/G ratio				
2 days	2.7 ± 0.1	3.0 ± 0.1	2.8 ± 0.1	2.9 ± 0.1[b]
14 days	1.6 ± 0.0	1.8 ± 0.1*	1.7 ± 0.1	1.6 ± 0.1
30 days	1.5 ± 0.0	1.5 ± 0.0	1.6 ± 0.0	1.4 ± 0.0
60 days	1.4 ± 0.1	1.4 ± 0.1	1.4 ± 0.1	1.5 ± 0.1
13 weeks	1.6 ± 0.1	1.6 ± 0.0	1.5 ± 0.1	1.5 ± 0.1
Alanine aminotransferase (IU/L)				
2 days	24 ± 1	24 ± 1	23 ± 1	25 ± 1[b]
14 days	22 ± 1[c]	23 ± 1	23 ± 1[c]	25 ± 2
30 days	21 ± 1	22 ± 2	19 ± 1	22 ± 1
60 days	31 ± 2	30 ± 2	27 ± 1	26 ± 2
13 weeks	33 ± 2	31 ± 1	31 ± 1	30 ± 2

TABLE G2
Clinical Chemistry and Urinalysis Data for Rats at the 3-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male (continued)				
n	10	10	10	9
Clinical Chemistry (continued)				
Aspartate aminotransferase (IU/L)				
2 days	87 ± 7	86 ± 7	73 ± 6	78 ± 6[b]
14 days	93 ± 6[c]	94 ± 7	82 ± 6[c]	100 ± 15
30 days	60 ± 1	75 ± 9	58 ± 3	61 ± 4
60 days	57 ± 6	53 ± 4	54 ± 4	62 ± 6
13 weeks	82 ± 3	87 ± 6	91 ± 7	82 ± 3[d]
Urinalysis				
Creatinine (mg/dL)				
2 days	34.27 ± 4.27	25.54 ± 4.58	25.80 ± 4.09	34.95 ± 3.59[b]
14 days	22.74 ± 2.54	30.58 ± 4.23	22.48 ± 3.27	36.99 ± 4.40°°
30 days	43.97 ± 6.32	45.34 ± 5.03	42.84 ± 7.83	65.54 ± 11.43
60 days	70.18 ± 10.94	68.59 ± 7.78	52.86 ± 5.81	99.99 ± 18.64
13 weeks	123.8 ± 15.4	102.9 ± 13.2	108.6 ± 8.8	123.7 ± 13.8[d]
Glucose (mg/dL)				
2 days	23 ± 4	22 ± 3	20 ± 3	29 ± 3[b]
14 days	16 ± 2	20 ± 2	19 ± 3	37 ± 7°°
30 days	23 ± 4	22 ± 3	24 ± 4	42 ± 9
60 days	31 ± 5	26 ± 3	22 ± 2	42 ± 5
13 weeks	46 ± 4	43 ± 6	40 ± 5	53 ± 8
Protein (mg/dL)				
2 days	54 ± 12	47 ± 10[c]	47 ± 9	92 ± 15°[b]
14 days	87 ± 10	80 ± 10	81 ± 10	136 ± 14°
30 days	139 ± 11	134 ± 15	160 ± 19	284 ± 60°°
60 days	145 ± 18	123 ± 12	113 ± 11	198 ± 25
13 weeks	160 ± 12	167 ± 19	168 ± 23	139 ± 29
Volume (mL/16 hr)				
2 days	7.8 ± 0.9	10.3 ± 1.5	8.9 ± 1.4[c]	6.0 ± 0.5[b]
14 days	10.2 ± 0.9	11.9 ± 0.9	11.0 ± 0.9	7.0 ± 0.6°
30 days	8.5 ± 1.1	9.8 ± 1.0	9.6 ± 1.5	6.6 ± 1.0
60 days	6.8 ± 1.0	8.1 ± 0.8	8.1 ± 0.8	4.9 ± 0.7
13 weeks	4.2 ± 0.6	5.0 ± 0.6	6.1 ± 0.9	4.2 ± 0.8
Specific gravity				
2 days	1.090 ± 0.003[d]	1.077 ± 0.004[c]	1.085 ± 0.004[e]	1.093 ± 0.007[d]
14 days	1.080 ± 0.004[e]	1.076 ± 0.004[c]	1.083 ± 0.004[c]	1.081 ± 0.004
30 days	1.083 ± 0.003[d]	1.089 ± 0.004[e]	1.082 ± 0.002	1.085 ± 0.003[f]
60 days	1.094 ± 0.002[d]	1.083 ± 0.004[d]	1.095 ± 0.004[g]	1.098 ± 0.002
13 weeks	1.078 ± 0.009[h]	1.044 ± 0.019[h]	1.065 ± 0.002[h]	1.075 ± 0.001[h]
Urea nitrogen (mg/dL)				
2 days	803 ± 110	600 ± 78	592 ± 81	800 ± 70[b]
14 days	496 ± 59	425 ± 39	518 ± 62	808 ± 102°
30 days	670 ± 83	658 ± 61	649 ± 120	1095 ± 242
60 days	989 ± 149	807 ± 116	657 ± 72	1418 ± 270
13 weeks	1463 ± 187	1508 ± 188	1361 ± 122	1549 ± 235

TABLE G2
Clinical Chemistry and Urinalysis Data for Rats at the 3-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male (continued)				
n	10	10	10	9
Urinalysis (continued)				
Urinary uroporphyrin (nmol/mL)				
13 weeks	0.071 ± 0.012	0.057 ± 0.007	0.063 ± 0.010	0.051 ± 0.012[d]
Urinary coproporphyrin (nmol/mL)				
13 weeks	0.182 ± 0.021	0.179 ± 0.036	0.371 ± 0.041**	0.379 ± 0.039**[e]
Urine coproporphyrin (nmol/mg creatinine)				
13 weeks	0.137 ± 0.017[c]	0.221 ± 0.068	0.348 ± 0.027**	0.409 ± 0.082**[d]
Urine uroporphyrin (nmol/mg creatinine)				
13 weeks	0.062 ± 0.009	0.064 ± 0.014	0.058 ± 0.007	0.056 ± 0.021[d]

Female	**Vehicle Control**	**60 mg/kg**	**120 mg/kg**	**240 mg/kg**
n	10	10	10	9
Clinical Chemistry				
Blood urea nitrogen (mg/dL)				
2 days	18.1 ± 0.8	17.1 ± 1.0	16.7 ± 0.9	15.7 ± 0.7[b]
14 days	16.6 ± 0.8	15.1 ± 0.5	15.4 ± 0.9	15.8 ± 0.9
30 days	17.1 ± 0.7	18.0 ± 0.6	13.9 ± 0.8*	15.3 ± 0.7
60 days	15.0 ± 0.8	19.1 ± 1.0*	15.1 ± 1.0	15.1 ± 0.5
13 weeks	17.6 ± 1.1	18.0 ± 1.2	17.4 ± 1.6[d]	15.6 ± 2.2
Creatinine (mg/dL)				
2 days	0.75 ± 0.05	0.66 ± 0.05	0.80 ± 0.08	0.77 ± 0.06[b]
14 days	0.81 ± 0.05[c]	0.79 ± 0.06	0.78 ± 0.07	0.79 ± 0.05
30 days	0.63 ± 0.04	0.62 ± 0.06	0.74 ± 0.04	0.78 ± 0.06*
60 days	0.79 ± 0.06	0.74 ± 0.03	0.83 ± 0.07	0.82 ± 0.03
13 weeks	0.57 ± 0.07	0.65 ± 0.07	0.53 ± 0.08[d]	0.53 ± 0.11
Glucose (mg/dL)				
2 days	139 ± 4	149 ± 5	148 ± 5	162 ± 5**[b]
14 days	144 ± 4	155 ± 3	145 ± 3	150 ± 6
30 days	149 ± 3	150 ± 3	161 ± 4*	164 ± 3**
60 days	172 ± 5	161 ± 6	170 ± 7	159 ± 3
13 weeks	107 ± 4	111 ± 4	108 ± 5[d]	100 ± 3
Total protein (g/dL)				
2 days	5.7 ± 0.1	5.9 ± 0.2	5.7 ± 0.2	6.2 ± 0.2[b]
14 days	6.3 ± 0.1	6.3 ± 0.1	6.4 ± 0.1	6.6 ± 0.1
30 days	7.0 ± 0.1	6.6 ± 0.1	6.9 ± 0.1	7.1 ± 0.2
60 days	7.5 ± 0.2	7.4 ± 0.2	7.3 ± 0.2	7.6 ± 0.1
13 weeks	7.2 ± 0.1	7.0 ± 0.2	7.1 ± 0.1[d]	6.9 ± 0.2

TABLE G2
Clinical Chemistry and Urinalysis Data for Rats at the 3-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female (continued)				
n	10	10	10	9
Clinical Chemistry (continued)				
Albumin (g/dL)				
2 days	4.2 ± 0.1	4.3 ± 0.1	4.1 ± 0.1	4.6 ± 0.2°[b]
14 days	4.1 ± 0.1	4.1 ± 0.1	4.2 ± 0.1	4.2 ± 0.1
30 days	4.3 ± 0.1[c]	4.2 ± 0.1	4.2 ± 0.0	4.3 ± 0.2
60 days	4.5 ± 0.1	4.5 ± 0.1	4.5 ± 0.1	4.6 ± 0.1
13 weeks	4.5 ± 0.1	4.4 ± 0.1	4.4 ± 0.1[d]	4.3 ± 0.1
Globulin (g/dL)				
2 days	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1[b]
14 days	2.2 ± 0.1	2.2 ± 0.1	2.3 ± 0.1	2.4 ± 0.1
30 days	2.6 ± 0.1[c]	2.5 ± 0.1	2.7 ± 0.1	2.9 ± 0.1
60 days	3.0 ± 0.2	2.9 ± 0.1	2.9 ± 0.1	3.0 ± 0.1
13 weeks	2.7 ± 0.1	2.6 ± 0.1	2.7 ± 0.1[d]	2.6 ± 0.1
A/G ratio				
2 days	2.7 ± 0.1	2.7 ± 0.1	2.6 ± 0.1	2.8 ± 0.1[b]
14 days	1.9 ± 0.1	1.9 ± 0.1	1.9 ± 0.1	1.8 ± 0.1
30 days	1.7 ± 0.1[c]	1.7 ± 0.1	1.6 ± 0.0	1.5 ± 0.1°
60 days	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.5 ± 0.1
13 weeks	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1[d]	1.7 ± 0.1
Alanine aminotransferase (IU/L)				
2 days	23 ± 1	24 ± 1	24 ± 1	32 ± 2°°[b]
14 days	23 ± 1	25 ± 2	25 ± 2	30 ± 3
30 days	19 ± 1	19 ± 1	20 ± 1	21 ± 2
60 days	28 ± 2	23 ± 1	25 ± 1	26 ± 3
13 weeks	28 ± 1	27 ± 1	27 ± 1[d]	26 ± 1
Aspartate aminotransferase (IU/L)				
2 days	96 ± 8	85 ± 6	86 ± 7	77 ± 7[b]
14 days	87 ± 7	96 ± 11	88 ± 9	92 ± 12[d]
30 days	67 ± 4	58 ± 2	59 ± 2	61 ± 3
60 days	69 ± 2	61 ± 7°	67 ± 6	72 ± 11
13 weeks	94 ± 7	91 ± 5	78 ± 3[d]	95 ± 6
Urinalysis				
Creatinine (mg/dL)				
2 days	26.59 ± 4.55	15.61 ± 1.89[c]	17.93 ± 1.51[c]	27.96 ± 2.86[e]
14 days	31.75 ± 3.66	22.16 ± 3.64	16.38 ± 4.20°°	18.06 ± 2.72°
30 days	41.78 ± 8.63	25.09 ± 3.67	33.46 ± 8.05	31.53 ± 6.23
60 days	51.50 ± 7.97	46.79 ± 7.75	42.99 ± 4.50	43.04 ± 8.40
13 weeks	62.64 ± 10.4	62.83 ± 11.44	67.15 ± 12.89[d]	46.43 ± 7.20
Glucose (mg/dL)				
2 days	14 ± 3	10 ± 1	13 ± 1	25 ± 2°°
14 days	16 ± 2	14 ± 3	14 ± 2	12 ± 2
30 days	22 ± 5	15 ± 4	17 ± 4	19 ± 4
60 days	19 ± 4	16 ± 3	17 ± 2	15 ± 2
13 weeks	20 ± 2	23 ± 3	20 ± 2[d]	15 ± 2

TABLE G2
Clinical Chemistry and Urinalysis Data for Rats at the 3-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female (continued)				
n	10	10	10	9
Urinalysis (continued)				
Protein (mg/dL)				
2 days	14 ± 1	15 ± 2	16 ± 2	36 ± 5**
14 days	16 ± 1	15 ± 2	16 ± 3	18 ± 4
30 days	24 ± 4	34 ± 21	25 ± 5	39 ± 8
60 days	22 ± 3	20 ± 3	26 ± 4	30 ± 6
13 weeks	17 ± 3	21 ± 3	20 ± 1[d]	21 ± 5
Volume (mL/16 hr)				
2 days	10.6 ± 1.8	11.6 ± 1.2	11.1 ± 1.8	6.4 ± 1.0*
14 days	7.2 ± 1.1	9.2 ± 1.1	11.3 ± 1.5	11.0 ± 1.5*
30 days	6.7 ± 0.9	10.0 ± 1.3	8.4 ± 1.4	8.7 ± 1.6
60 days	5.9 ± 0.6	6.3 ± 0.8	6.2 ± 1.2	6.9 ± 1.2
13 weeks	4.6 ± 0.6	4.1 ± 0.4	5.2 ± 0.8[d]	7.3 ± 1.1
Specific gravity				
2 days	1.081 ± 0.008[e]	1.076 ± 0.003[c]	1.081 ± 0.005[c]	1.075 ± 0.002[d]
14 days	1.075 ± 0.004[e]	1.072 ± 0.003[c]	1.070 ± 0.003	1.060 ± 0.006*[e]
30 days	1.078 ± 0.002[i]	1.072 ± 0.006[g]	1.066 ± 0.007[d]	1.068 ± 0.002[d]
60 days	1.096 ± 0.011[i]	1.088 ± 0.005[g]	1.096 ± 0.003[e]	1.073 ± 0.004[e]
13 weeks	[j]	1.063 ± 0.007[g]	1.079[k]	1.068[k]
Urea nitrogen (mg/dL)				
2 days	471 ± 79	413 ± 18	499 ± 48	713 ± 72*
14 days	597 ± 50	390 ± 51*[c]	422 ± 76*	414 ± 73*
30 days	844 ± 153	542 ± 54	655 ± 151	615 ± 130
60 days	776 ± 108	725 ± 138	755 ± 76	727 ± 142
13 weeks	900 ± 86	915 ± 146	1,019 ± 168d	725 ± 126
Urinary coproporphyrin (nmol/mL)				
13 weeks	0.113 ± 0.014	0.127 ± 0.023	0.131 ± 0.022[e]	0.157 ± 0.031
Urinary uroporphyrin (nmol/mL)				
13 weeks	0.031 ± 0.005	0.049 ± 0.013	0.035 ± 0.007[d]	0.038 ± 0.009
Urine coproporphyrin (nmol/mg creatinine)				
13 weeks	0.211 ± 0.027	0.240 ± 0.054	0.275 ± 0.045[d]	0.367 ± 0.060
Urine uroporphyrin (nmol/mg creatinine)				
13 weeks	0.055 ± 0.009	0.094 ± 0.028	0.065 ± 0.021[d]	0.096 ± 0.025

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] No measurements were taken for males receiving 240 mg/kg or females receiving 30 mg/kg. Mean ± standard error; A/G ratio = albumin/globulin ratio
[b] n=10
[c] n=9
[d] n=8
[e] n=7
[f] n=6
[g] n=4
[h] n=2
[i] n=3
[j] n=0
[k] n=1

TABLE G3
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male				
n	10	10	10	7
Hematology				
Hematocrit (%)				
13 weeks	47.1 ± 0.6	46.8 ± 0.6	46.8 ± 0.7	47.4 ± 0.4
39 weeks	52.9 ± 0.8	52.3 ± 1.1	51.9 ± 1.3	50.9 ± 0.9
65 weeks	55.0 ± 0.5	54.6 ± 0.8[b]	54.8 ± 0.8	53.1 ± 1.0
Hemoglobin (g/dL)				
13 weeks	16.1 ± 0.3	15.8 ± 0.2	15.8 ± 0.2	16.1 ± 0.2
39 weeks	16.7 ± 0.3	16.3 ± 0.3	16.1 ± 0.4	15.7 ± 0.3°
65 weeks	15.2 ± 0.1	15.4 ± 0.2[b]	15.4 ± 0.2	14.9 ± 0.3
Erythrocytes ($10^6/\mu L$)				
13 weeks	9.27 ± 0.13	9.04 ± 0.10	9.14 ± 0.14	9.05 ± 0.11
39 weeks	10.16 ± 0.14	10.11 ± 0.17	10.14 ± 0.15	9.95 ± 0.13
65 weeks	10.34 ± 0.10	10.33 ± 0.15[b]	10.35 ± 0.17	9.85 ± 0.20
Mean cell volume (fL)				
13 weeks	50.7 ± 0.2	51.9 ± 0.4°	51.5 ± 0.4	52.6 ± 0.4°°
39 weeks	52.1 ± 0.6	51.9 ± 0.6	51.2 ± 0.7	51.0 ± 0.5
65 weeks	53.2 ± 0.3	52.7 ± 0.4[b]	53.1 ± 0.2	54.0 ± 0.2
Mean cell hemoglobin (pg)				
13 weeks	17.4 ± 0.2	17.5 ± 0.1	17.4 ± 0.1	17.8 ± 0.1
39 weeks	16.4 ± 0.3	16.2 ± 0.1	15.7 ± 0.1°	15.8 ± 0.2°
65 weeks	14.7 ± 0.1	14.9 ± 0.1[b]	14.9 ± 0.1	15.1 ± 0.1°°
Mean cell hemoglobin concentration (g/dL)				
13 weeks	34.2 ± 0.3	33.8 ± 0.2	33.7 ± 0.4	34.0 ± 0.2
39 weeks	31.5 ± 0.4	31.2 ± 0.3	30.7 ± 0.4	30.9 ± 0.3
65 weeks	27.7 ± 0.1	28.3 ± 0.3[b]	28.1 ± 0.2	28.0 ± 0.1
Platelets ($10^3/\mu L$)				
13 weeks	812.7 ± 36.4	786.6 ± 25.0	777.0 ± 35.3	836.9 ± 60.2
39 weeks	750.5 ± 30.4	761.5 ± 20.5	758.2 ± 28.8	770.9 ± 19.6
65 weeks	664.4 ± 13.2	636.7 ± 31.1[c]	751.4 ± 45.2[c]	688.9 ± 16.4[d]
Reticulocytes ($10^6/\mu L$)				
13 weeks	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
39 weeks	0.1 ± 0.0	0.2 ± 0.0	0.1 ± 0.0	0.1 ± 0.0°[e]
65 weeks	0.1 ± 0.0[b]	0.1 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
Leukocytes ($10^3/\mu L$)				
13 weeks	6.41 ± 0.37	8.46 ± 0.43°°	8.66 ± 0.63°°	8.93 ± 0.42°°
39 weeks	7.06 ± 0.47	6.64 ± 0.77	8.08 ± 0.54	8.47 ± 0.72
65 weeks	4.24 ± 0.33	5.49 ± 0.66[b]	4.81 ± 0.44	4.17 ± 0.54
Segmented neutrophils ($10^3/\mu L$)				
39 weeks	2.58 ± 0.27	2.08 ± 0.25	2.24 ± 0.24	2.50 ± 0.52
65 weeks	1.70 ± 0.16	2.29 ± 0.55	1.84 ± 0.25	1.54 ± 0.23
Lymphocytes ($10^3/\mu L$)				
39 weeks	4.39 ± 0.56	4.44 ± 0.56	5.71 ± 0.39	5.76 ± 0.43
65 weeks	2.43 ± 0.34	3.02 ± 0.25[b]	2.79 ± 0.28	2.44 ± 0.40
Monocytes ($10^3/\mu L$)				
65 weeks	0.04 ± 0.01	0.09 ± 0.03[b]	0.06 ± 0.05	0.08 ± 0.04
Eosinophils ($10^3/\mu L$)				
39 weeks	0.09 ± 0.02	0.12 ± 0.02	0.13 ± 0.03	0.21 ± 0.05°
65 weeks	0.06 ± 0.02	0.09 ± 0.02[b]	0.12 ± 0.03	0.10 ± 0.03
Nucleated erythrocytes ($10^3/\mu L$)				
39 weeks	0.05 ± 0.02	0.01 ± 0.01	0.03 ± 0.01	0.00 ± 0.00°

TABLE G3
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male (continued)				
n	10	10	10	7
Clinical Chemistry				
Blood urea nitrogen (mg/dL)				
13 weeks	20.2 ± 0.7	17.9 ± 0.8	22.1 ± 0.9	15.9 ± 1.5
39 weeks	15.2 ± 0.9	18.6 ± 0.7**	18.3 ± 0.6*	19.9 ± 1.1**
65 weeks	17.1 ± 0.7	15.5 ± 0.7	15.4 ± 0.5	17.7 ± 0.6
Creatinine (mg/dL)				
13 weeks	0.54 ± 0.07	0.53 ± 0.05	0.49 ± 0.05	0.40 ± 0.08
39 weeks	0.58 ± 0.02	0.62 ± 0.02	0.52 ± 0.03	0.54 ± 0.03
65 weeks	0.60 ± 0.04	0.55 ± 0.03	0.56 ± 0.03	0.60 ± 0.02
Glucose (mg/dL)				
13 weeks	191 ± 11	167 ± 13	157 ± 8*	191 ± 6
39 weeks	163 ± 11	151 ± 10	138 ± 2	140 ± 5
65 weeks	233 ± 24	194 ± 20	218 ± 20	193 ± 15
Total protein (g/dL)				
13 weeks	7.3 ± 0.2	6.8 ± 0.2	7.3 ± 0.2	7.0 ± 0.4
39 weeks	6.6 ± 0.3	7.3 ± 0.1**	7.3 ± 0.1**	7.2 ± 0.1*
65 weeks	6.3 ± 0.1	6.2 ± 0.1	6.4 ± 0.1	6.0 ± 0.1
Albumin (g/dL)				
13 weeks	4.0 ± 0.1	3.8 ± 0.2	4.0 ± 0.1	3.9 ± 0.2
39 weeks	4.2 ± 0.2	4.6 ± 0.1	4.7 ± 0.1*	4.7 ± 0.1*
65 weeks	3.5 ± 0.1	3.5 ± 0.1	3.6 ± 0.1	3.3 ± 0.1
Globulin (g/dL)				
13 weeks	3.3 ± 0.2	3.0 ± 0.1	3.3 ± 0.1	3.0 ± 0.2
39 weeks	2.4 ± 0.1	2.8 ± 0.1*	2.5 ± 0.1	2.5 ± 0.1
65 weeks	2.9 ± 0.1	2.7 ± 0.1	2.8 ± 0.2	2.7 ± 0.1
A/G ratio				
13 weeks	1.3 ± 0.1	1.3 ± 0.1	1.2 ± 0.0	1.3 ± 0.1
39 weeks	1.7 ± 0.1	1.7 ± 0.1	1.9 ± 0.1	1.9 ± 0.1
65 weeks	1.2 ± 0.1	1.3 ± 0.1	1.3 ± 0.1	1.2 ± 0.1
Alanine aminotransferase (IU/L)				
13 weeks	38 ± 3	42 ± 7	33 ± 4*	31 ± 2
39 weeks	40 ± 3	38 ± 4	29 ± 2*	28 ± 0*
65 weeks	41 ± 3	42 ± 7	34 ± 3	29 ± 2**
Aspartate aminotransferase (IU/L)				
13 weeks	62 ± 7[b]	74 ± 12	62 ± 7	52 ± 4
39 weeks	78 ± 5	81 ± 8	62 ± 3*	51 ± 2**
65 weeks	80 ± 15	67 ± 5	64 ± 5	63 ± 4
Urinalysis				
Creatinine (mg/dL)				
13 weeks	95.8 ± 13.4	115.4 ± 13.2	122.5 ± 12.3	110.9 ± 15.1
39 weeks	119.3 ± 11.4	136.1 ± 8.8	127.2 ± 12.3	135.7 ± 4.7
65 weeks	187.5 ± 25.7	172.8 ± 15.3	281.7 ± 46.0	180.9 ± 6.5
Glucose (mg/dL)				
13 weeks	37 ± 7	39 ± 4	45 ± 4	40 ± 4
39 weeks	20 ± 3	21 ± 2	21 ± 2	22 ± 2
65 weeks	26 ± 3	23 ± 2	32 ± 3	22 ± 2

TABLE G3
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male (continued)				
n	10	10	10	7
Urinalysis (continued)				
Protein (mg/dL)				
13 weeks	122 ± 17	137 ± 13	106 ± 18	113 ± 24
39 weeks	129 ± 12	163 ± 11	157 ± 19	150 ± 36
65 weeks	256 ± 41	276 ± 44	643 ± 118°°	731 ± 111°°
Alkaline phosphatase (IU/L)				
13 weeks	3 ± 0[f]	2 ± 0[f]	4 ± 0[f]	4 ± 0[g]
39 weeks	2 ± 0	3 ± 0°	4 ± 0°°	5 ± 0°°
65 weeks	7 ± 1	9 ± 1[b]	13 ± 2°°	16 ± 2°°
Lactate dehydrogenase (IU/L)				
13 weeks	17 ± 5[f]	17 ± 3[f]	16 ± 2[f]	20 ± 1[g]
39 weeks	10 ± 1	12 ± 1	11 ± 1	10 ± 2
65 weeks	14 ± 1	14 ± 1	14 ± 2	3 ± 2°°
N-acetyl-β-glucose aminidase (IU/L)				
13 weeks	18.6 ± 4.0[f]	13.8 ± 1.2[f]	12.6 ± 2.0[f]	11.7 ± 0.3[g]
39 weeks	18.1 ± 3.3	18.5 ± 1.4	13.2 ± 1.0	9.7 ± 2.0°
65 weeks	24.2 ± 3.0	20.3 ± 1.8[b]	24.2 ± 2.9	13.0 ± 0.8°°
Volume (mL/16 hr)				
13 weeks	7.0 ± 0.8	6.3 ± 0.6	5.1 ± 0.4	6.0 ± 0.6
39 weeks	6.7 ± 0.7	5.7 ± 0.6	6.3 ± 0.5	5.6 ± 0.5
65 weeks	5.2 ± 0.6	4.9 ± 0.5	3.2 ± 0.6	4.7 ± 0.3
Specific gravity				
13 weeks	1.075 ± 0.004[f]	1.104 ± 0.012[f]	1.099 ± 0.013[e]	1.092 ± 0.006[g]
39 weeks	1.075 ± 0.006[e]	1.076 ± 0.003[f]	1.091 ± 0.006[h]	1.075 ± 0.001[h]
65 weeks	1.071 ± 0.004[h]	1.074 ± 0.014[i]	1.085 ± 0.007[e]	1.042 ± 0.027[i]
Urea nitrogen (mg/dL)				
13 weeks	1,254 ± 147	1,256 ± 118	1,310 ± 138	1,482 ± 181
39 weeks	1,218 ± 130	1,722 ± 134°	1,539 ± 119	1,783 ± 108°
65 weeks	1,827 ± 238	1,814 ± 190	2,486 ± 302	1,974 ± 184
Galactosidase (IU/L)				
13 weeks	12.40 ± 3.14[f]	7.60 ± 1.29[f]	9.40 ± 1.33[f]	3.67 ± 0.33°[g]
39 weeks	14.30 ± 1.86	15.10 ± 1.22	9.60 ± 1.36	7.29 ± 1.94°
65 weeks	24.80 ± 2.86	21.90 ± 2.38	20.40 ± 2.12	11.71 ± 2.45°°
Coproporphyrin (nmol/ml)				
65 weeks	0.141 ± 0.011[b]	0.253 ± 0.017°°	0.352 ± 0.037°°[e]	0.453 ± 0.028°°
Uroporphyrin (nmol/ml)				
65 weeks	0.131 ± 0.014[b]	0.128 ± 0.009	0.152 ± 0.014[e]	0.126 ± 0.006
Coproporphyrin (nmol/mg creatinine)				
65 weeks	0.087 ± 0.007[b]	0.154 ± 0.013°°	0.198 ± 0.016[e]°°	0.249 ± 0.011°°
Uroporphyrin (nmol/mg creatinine)				
65 weeks	0.078 ± 0.004[b]	0.076 ± 0.003	0.085 ± 0.006[e]	0.069 ± 0.003

TABLE G3
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female				
n	10	10	10	8
Hematology				
Hematocrit (%)				
13 weeks	48.0 ± 1.2	45.8 ± 0.8	46.1 ± 1.2	44.9 ± 0.9
39 weeks	49.1 ± 1.1	49.8 ± 0.7	49.6 ± 0.6	49.3 ± 0.9
65 weeks	53.2 ± 0.5	53.5 ± 0.6[c]	51.8 ± 0.5[c]	51.6 ± 1.4[d]
Hemoglobin (g/dL)				
13 weeks	15.9 ± 0.5	15.1 ± 0.2	15.2 ± 0.4	14.8 ± 0.3
39 weeks	15.5 ± 0.3	15.2 ± 0.1	15.1 ± 0.2	15.1 ± 0.2
65 weeks	15.2 ± 0.2	15.0 ± 0.2[c]	14.7 ± 0.1*[c]	14.6 ± 0.4*[d]
Erythrocytes (10^6/μL)				
13 weeks	8.54 ± 0.21	8.28 ± 0.14	8.20 ± 0.22	7.97 ± 0.16
39 weeks	8.74 ± 0.21	8.87 ± 0.08	8.77 ± 0.09	8.76 ± 0.12
65 weeks	9.03 ± 0.08	9.09 ± 0.12[c]	8.81 ± 0.10[c]	8.82 ± 0.23[d]
Mean cell volume (fL)				
13 weeks	56.0 ± 0.4	55.3 ± 0.4	56.0 ± 0.4	56.4 ± 0.3
39 weeks	56.3 ± 0.4	56.2 ± 0.7	56.6 ± 0.5	56.1 ± 0.7
65 weeks	59.1 ± 0.7	58.9 ± 0.4[c]	59.0 ± 0.3[c]	58.4 ± 0.2[d]
Mean cell hemoglobin (pg)				
13 weeks	18.6 ± 0.1	18.3 ± 0.1	18.5 ± 0.1	18.6 ± 0.1
39 weeks	17.8 ± 0.2	17.1 ± 0.1**	17.3 ± 0.1**	17.2 ± 0.0**
65 weeks	16.9 ± 0.2	16.5 ± 0.1*[c]	16.6 ± 0.1[c]	16.6 ± 0.1[d]
Mean cell hemoglobin concentration (g/dL)				
13 weeks	33.2 ± 0.3	33.0 ± 0.2	32.1 ± 1.0	33.1 ± 0.2
39 weeks	31.6 ± 0.4	30.5 ± 0.4	30.6 ± 0.3	30.6 ± 0.4
65 weeks	28.6 ± 0.3	28.0 ± 0.1[c]	28.2 ± 0.2[c]	28.4 ± 0.2[d]
Platelets (10^3/μL)				
13 weeks	833.3 ± 17.4	851.7 ± 43.4	837.6 ± 24.6	887.1 ± 44.6
39 weeks	604.4 ± 83.0	677.3 ± 33.6	679.8 ± 69.7	805.0 ± 27.7*
65 weeks	650.8 ± 18.9	638.3 ± 14.5[c]	583.5 ± 81.7[c]	706.9 ± 39.0[d]
Reticulocytes (10^6/μL)				
13 weeks	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
39 weeks	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
65 weeks	0.1 ± 0.0	0.1 ± 0.0[c]	0.2 ± 0.0*[c]	0.2 ± 0.0*[d]
Leukocytes (10^3/μL)				
13 weeks	6.95 ± 0.48	6.34 ± 0.48	7.40 ± 0.28	6.14 ± 0.22
39 weeks	4.03 ± 0.26	5.04 ± 0.41	5.55 ± 0.66	4.61 ± 0.49
65 weeks	2.90 ± 0.29	2.76 ± 0.27[c]	3.19 ± 0.53[c]	2.79 ± 0.21[d]
Segmented neutrophils (10^3/μL)				
39 weeks	1.10 ± 0.10	1.34 ± 0.13	1.35 ± 0.20	1.06 ± 0.14
65 weeks	0.87 ± 0.09	0.91 ± 0.15	0.91 ± 0.18	0.91 ± 0.1
Lymphocytes (10^3/μL)				
39 weeks	2.83 ± 0.22	3.63 ± 0.44	4.11 ± 0.50	3.50 ± 0.39
65 weeks	1.97 ± 0.23	1.77 ± 0.23[c]	2.21 ± 0.41[c]	1.79 ± 0.15[d]
Monocytes (10^3/μL)				
65 weeks	0.02 ± 0.01	0.02 ± 0.01[c]	0.02 ± 0.01[c]	0.02 ± 0.01[d]
Eosinophils (10^3/μL)				
39 weeks	0.10 ± 0.01	0.07 ± 0.02	0.09 ± 0.03	0.05 ± 0.02
65 weeks	0.04 ± 0.02	0.06 ± 0.02[c]	0.06 ± 0.03[c]	0.07 ± 0.02[d]
Nucleated erythrocytes (10^3/μL)				
39 weeks	0.03 ± 0.02	0.03 ± 0.01	0.03 ± 0.01	0.02 ± 0.01

TABLE G3
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female (continued)				
n	10	10	10	8
Clinical Chemistry				
Blood urea nitrogen (mg/dL)				
13 weeks	19.7 ± 1.0	20.8 ± 1.1	19.8 ± 1.6	22.1 ± 1.1
39 weeks	20.9 ± 0.7	20.6 ± 1.5	21.0 ± 0.8	22.9 ± 1.3
65 weeks	15.9 ± 0.9	15.9 ± 0.6[b]	16.0 ± 0.9[b]	16.8 ± 0.7
Creatinine (mg/dL)				
13 weeks	0.59 ± 0.07[b]	0.52 ± 0.05	0.50 ± 0.06	0.73 ± 0.10
39 weeks	0.61 ± 0.02	0.58 ± 0.03	0.60 ± 0.03	0.70 ± 0.04
65 weeks	0.57 ± 0.03	0.59 ± 0.02[b]	0.57 ± 0.04[b]	0.54 ± 0.03
Glucose (mg/dL)				
13 weeks	148 ± 6	141 ± 3	151 ± 5	154 ± 5
39 weeks	150 ± 4	135 ± 3°	144 ± 6	134 ± 4°
65 weeks	184 ± 13	189 ± 8[b]	204 ± 24[b]	199 ± 10
Total protein (g/dL)				
13 weeks	6.7 ± 0.3	7.1 ± 0.2	7.0 ± 0.2	7.3 ± 0.1
39 weeks	7.6 ± 0.1	7.1 ± 0.1°°	7.2 ± 0.1°°	7.1 ± 0.1°°
65 weeks	6.7 ± 0.2	6.4 ± 0.2[b]	6.7 ± 0.2[b]	6.2 ± 0.1
Albumin (g/dL)				
13 weeks	4.0 ± 0.2	4.2 ± 0.1	4.3 ± 0.1	4.3 ± 0.1
39 weeks	4.9 ± 0.1	4.6 ± 0.1	4.6 ± 0.1	4.6 ± 0.1
65 weeks	3.9 ± 0.1	3.8 ± 0.2[b]	4.0 ± 0.1[b]	3.7 ± 0.1
Globulin (g/dL)				
13 weeks	2.8 ± 0.2	2.9 ± 0.1	2.8 ± 0.1	3.1 ± 0.1
39 weeks	2.7 ± 0.1	2.5 ± 0.0°	2.6 ± 0.1	2.5 ± 0.0
65 weeks	2.8 ± 0.1	2.6 ± 0.1[b]	2.8 ± 0.1[b]	2.6 ± 0.1
A/G ratio				
13 weeks	1.5 ± 0.0	1.5 ± 0.1	1.6 ± 0.1	1.5 ± 0.1
39 weeks	1.8 ± 0.1	1.9 ± 0.0	1.8 ± 0.1	1.9 ± 0.0
65 weeks	1.4 ± 0.1	1.5 ± 0.1[b]	1.5 ± 0.1[b]	1.4 ± 0.1
Alanine aminotransferase (IU/L)				
13 weeks	28 ± 1	27 ± 2	29 ± 2	27 ± 1
39 weeks	34 ± 2	32 ± 3	32 ± 4	27 ± 1°
65 weeks	43 ± 5	37 ± 5[b]	29 ± 2[b]	25 ± 1°°
Aspartate aminotransferase (IU/L)				
13 weeks	61 ± 7	69 ± 5	74 ± 9	67 ± 4
39 weeks	80 ± 8	70 ± 6	73 ± 17°	57 ± 1°
65 weeks	84 ± 9	80 ± 11[b]	64 ± 6[b]	54 ± 3°°
Urinalysis				
Creatinine (mg/dL)				
13 weeks	72.88 ± 8.32	66.73 ± 13.99	61.70 ± 11.46	57.55 ± 12.49
39 weeks	71.94 ± 7.92	63.90 ± 6.80	68.01 ± 8.30	51.43 ± 3.75[d]
65 weeks	100.94 ± 17.25	94.42 ± 12.74	75.24 ± 8.39[b]	76.10 ± 6.85[d]
Glucose (mg/dL)				
13 weeks	26 ± 4	22 ± 4	23 ± 4	27 ± 4
39 weeks	13 ± 1	11 ± 2	8 ± 2°	10 ± 2[d]
65 weeks	14 ± 2	13 ± 2	10 ± 1[b]	10 ± 2[d]

TABLE G3
Hematology, Clinical Chemistry, and Urinalysis Data for Rats at the 15-Month Interim Evaluation in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol (continued)

	Vehicle Control	60 mg/kg	120 mg/kg	240 mg/kg
Female (continued)				
n	10	10	10	8
Urinalysis (continued)				
Protein (mg/dL)				
13 weeks	17 ± 2	22 ± 3	21 ± 3	28 ± 7
39 weeks	15 ± 2	25 ± 8	32 ± 7*	46 ± 4**[d]
65 weeks	39 ± 9	40 ± 9[b]	56 ± 13[b]	47 ± 8[d]
Alkaline phosphatase (IU/L)				
13 weeks	3 ± 0[f]	3 ± 1[f]	3 ± 0[f]	3 ± 0[f]
39 weeks	1 ± 0	2 ± 0**	2 ± 0**	2 ± 0**[d]
65 weeks	3 ± 0	3 ± 0[b]	3 ± 0[b]	4 ± 0*[d]
Lactate dehydrogenase (IU/L)				
13 weeks	9 ± 1[g]	13 ± 5[f]	11 ± 3[f]	13 ± 3[f]
39 weeks	7 ± 1	7 ± 1[b]	7 ± 1	7 ± 1[d]
65 weeks	8 ± 1	8 ± 1	7 ± 1[b]	8 ± 1[d]
N-acetyl-β-glucose aminidase (IU/L)				
13 weeks	13.8 ± 2.1[f]	8.6 ± 2.8[f]	5.4 ± 1.5*[f]	5.0 ± 1.3*[f]
39 weeks	11.6 ± 1.3	6.9 ± 1.4*	3.8 ± 0.9**	4.4 ± 0.8**[d]
65 weeks	11.9 ± 1.2[b]	5.7 ± 0.8**	4.7 ± 0.9**[b]	3.0 ± 0.7**[d]
Volume (mL/16 hr)				
13 weeks	4.4 ± 0.4	5.4 ± 1.2	5.2 ± 0.9	4.4 ± 0.7
39 weeks	5.2 ± 0.6	5.0 ± 0.8	4.1 ± 0.5	4.4 ± 0.7
65 weeks	4.2 ± 0.5	4.3 ± 0.8	4.6 ± 0.5	4.9 ± 0.4
Specific gravity				
13 weeks	1.080 ± 0.013[f]	1.067 ± 0.002[g]	1.091 ± 0.004[i]	1.095 ± 0.016[g]
65 weeks	1.066 ± 0.007[f]	1.044 ± 0.006[d]	1.050 ± 0.006[g]	1.051 ± 0.008[d]
Urea nitrogen (mg/dL)				
13 weeks	1,166 ± 109	1,071 ± 229	989 ± 172	1,127 ± 177
39 weeks	1,127 ± 106	1,111 ± 108	1,059 ± 111	869 ± 33[d]
65 weeks	1,383 ± 204	1,352 ± 220	1,135 ± 136[b]	1,297 ± 130[d]
Galactosidase (IU/L)				
13 weeks	12.20 ± 3.43[f]	5.80 ± 3.35[f]	1.80 ± 0.97*[f]	1.20 ± 0.49*[f]
39 weeks	10.80 ± 1.31	4.20 ± 0.92**	1.00 ± 0.26**	1.57 ± 0.72**[d]
65 weeks	11.22 ± 1.12[b]	4.70 ± 1.38**	2.89 ± 0.86**[b]	2.14 ± 0.55**[d]
Urinary uroporphyrin (nmol/ml)				
65 weeks	0.060 ± 0.011[b]	0.059 ± 0.010[b]	0.058 ± 0.010[b]	0.053 ± 0.008
Urinary coproporphyrin (nmol/ml)				
65 weeks	0.128 ± 0.017[b]	0.160 ± 0.022[b]	0.166 ± 0.021[b]	0.218 ± 0.023**
Urine coproporphyrin (nmol/mg creatinine)				
65 weeks	0.144 ± 0.014[b]	0.190 ± 0.029[b]	0.220 ± 0.014**[b]	0.301 ± 0.014**[d]
Urine uroporphyrin (nmol/mg creatinine)				
65 weeks	0.063 ± 0.006[b]	0.064 ± 0.006[b]	0.072 ± 0.006[b]	0.067 ± 0.006[d]

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] No measurements were taken for males receiving 240 mg/kg or females receiving 30 mg/kg. Mean ± standard error
[b] n=9; [c] n=8; [d] n=7; [e] n=6; [f] n=5; [g] n=3; [h] n=4

TABLE G4
Liver Porphyrin Data for Rats at the 3- and 15-Month Interim Evaluations in the 2-Year Gavage Study of *o*-Benzyl-*p*-Chlorophenol[a]

	Vehicle Control	30 mg/kg	60 mg/kg	120 mg/kg
Male				
n	10	10	10	9
Liver porphyrin (nmol/g liver)				
13 weeks	0.228 ± 0.023	0.161 ± 0.015	0.238 ± 0.035	0.240 ± 0.021
Liver porphyrin (nmol/g liver)				
65 weeks	1.549 ± 0.175	0.474 ± 0.041**	0.474 ± 0.026**	0.590 ± 0.059**[b]
Female	**Vehicle Control**	**60 mg/kg**	**120 mg/kg**	**240 mg/kg**
n	10	10	10	10
Liver porphyrin (nmol/g liver)				
13 weeks	0.149 ± 0.015	0.111 ± 0.009	0.131 ± 0.020[c]	0.139 ± 0.017[d]
Liver porphyrin (nmol/g liver)				
65 weeks	0.535 ± 0.077	0.444 ± 0.041[d]	0.428 ± 0.043[d]	0.381 ± 0.012*[c]

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error
[b] n=7
[c] n=8
[d] n=9

APPENDIX H
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

PROCUREMENT AND CHARACTERIZATION OF *o*-BENZYL-*p*-CHLOROPHENOL

o-Benzyl-*p*-chlorophenol was obtained from McKesson Chemical Company (Kansas City, MO) in one lot (KM11195), which was used throughout the studies. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO), and confirmed by the study laboratory. Reports on analyses performed in support of the *o*-benzyl-*p*-chlorophenol studies are on file at the National Institute of Environmental Health Sciences.

The chemical, white to pink flakes with a melting point of 46.5° to 48° C, was identified as *o*-benzyl-*p*-chlorophenol by infrared, nuclear magnetic resonance, and ultraviolet/visible spectroscopy and gas chromatography. All spectra were consistent with those expected for the structure and with the literature spectra of *o*-benzyl-*p*-chlorophenol, as shown in Figures H1 and H2 (*Sadtler Standard Spectra*).

The purity was determined by elemental analysis, Karl Fischer water analysis, nonaqueous (phenol) titration, and thin-layer chromatography (TLC) and gas chromatography. Nonaqueous titration was accomplished by dissolving samples of *o*-benzyl-*p*-chlorophenol in N,N-dimethylformamide and titrating with 0.1 N tetrabutylammonium hydroxide. The titration was monitored potentiometrically with a glass indicating electrode and a calomel reference electrode filled with methanolic 1 M tetrabutylammonium chloride. TLC was performed on silica gel 60 F-254 plates with two solvent systems: 1) toluene:methanol:0.1 N glacial acetic acid (90:5:5); and 2) hexanes:acetone:0.1 N glacial acetic acid (60:35:5). The plates were sprayed with 0.4% 2,6-dichloroquinone-4-chloroimide and 10% aqueous sodium carbonate and examined with ultraviolet light (254 nm). ß-Naphthol (1 μL of a 10 μg/μL solution in acetone) was used as the reference standard. Gas chromatography was performed with a flame ionization detector and a nitrogen carrier gas at 70 mL/minute with methylene chloride as the solvent, with two systems:

A) 1% SP-1000 on 100/120 Supelcoport, 1.8m × 4mm ID, glass, oven temperature program of 50° C for 5 minutes, then progressing from 50° to 225° C at 10° C per minute, and
B) 3% SP-2100 on 100/120 Supelcoport, 1.8m × 4mm ID, glass, oven temperature program of 50° C for 5 minutes, then progressing from 50° to 250° C at 10° C per minute.

Elemental analyses for chlorine were slightly high and those for carbon and hydrogen were in agreement with the theoretical values. Karl Fischer water analysis indicated the presence of less than 0.05% water. Titration of the phenolic group indicated a purity of 102.9% ± 0.7%. TLC analysis using system 1 indicated one major spot, two minor spots, and one trace spot; using system 2 one major spot, one minor spot, and one trace spot were observed. Gas chromatography using system A resolved a major peak and six impurity peaks, the largest of which eluted after the major peak and had an area of 1.6% relative to the major peak area. On the basis of mass spectral and synthesis considerations the impurity was identified as *o*-chloro-*p*-benzylphenol. The remaining five impurities, which eluted before the major peak, had a combined area of 1.5% relative to the major peak area. Gas chromatography using system B indicated a major peak and four impurities, the largest of which eluted after the major peak and had an area of 1.1% relative to the major peak area. The remaining three impurities, which eluted before the major peak, had a combined area of 0.6% relative to the major peak area. The overall purity was determined to be approximately 97%.

Stability studies were performed with gas chromatography using system B described for the purity analyses, but at a constant oven temperature of 190° C. *n*-Hexadecane was used as an internal standard. The results indicated that *o*-benzyl-*p*-chlorophenol was stable as a bulk chemical when stored protected from light for 2 weeks at temperatures up to 25° C. Samples stored at 60° C underwent decomposition. The

study laboratory stored the bulk chemical at 4° C protected from light. During the 13-week and 2-year studies, the stability of the bulk chemical was monitored by the study laboratory using gas chromatography with system B described for the purity analyses and nonaqueous titration. Ultraviolet spectroscopy was also used to monitor stability during the 2-year studies. Analyses were performed at the study laboratory four times during the 13-week studies and nine times during the 2-year studies; no degradation of the study material was seen.

Preparation and Analysis of Dose Formulations

The dose formulations were prepared by mixing *o*-benzyl-*p*-chlorophenol with Mazola® corn oil (CPC International, Inc., Englewood, NJ) to give the required concentrations (Table H1). The dose formulations were stored at room temperature in amber glass bottles for up to 2 weeks after the date of preparation.

Stability analyses of 40 mg/mL corn oil solutions were conducted by the analytical chemistry laboratory. Gas chromatography was employed using system B described in the purity analyses, but with a flow rate of 30 mL/minute, eicosane as an internal standard, and an oven temperature of 170° C. Stability of the dose formulation was established for 2 weeks in the dark at room temperature and for 3 hours exposed to air and light.

Periodic analyses of the dose formulations of *o*-benzyl-*p*-chlorophenol were conducted at the study laboratory and at the analytical chemistry laboratory using ultraviolet spectroscopy (286 nm). Dose formulations were analyzed at least three times for rats and three times for mice during the 13-week studies; all results of dose analyses were within 10% of target concentrations (Table H2). Formulations were analyzed at least once every 8 weeks during the 2-year studies; all dose formulations for rats and mice were within 10% of target concentrations. Results of the dose formulation analyses for the 2-year studies are presented in Table H3. Periodic analyses of the corn oil vehicle by the study laboratory demonstrated peroxide levels within the acceptable limit of 10 mEq/kg. Results of periodic referee analyses performed by the analytical chemistry laboratory indicated good agreement with the results obtained for both rats and mice (Table H4).

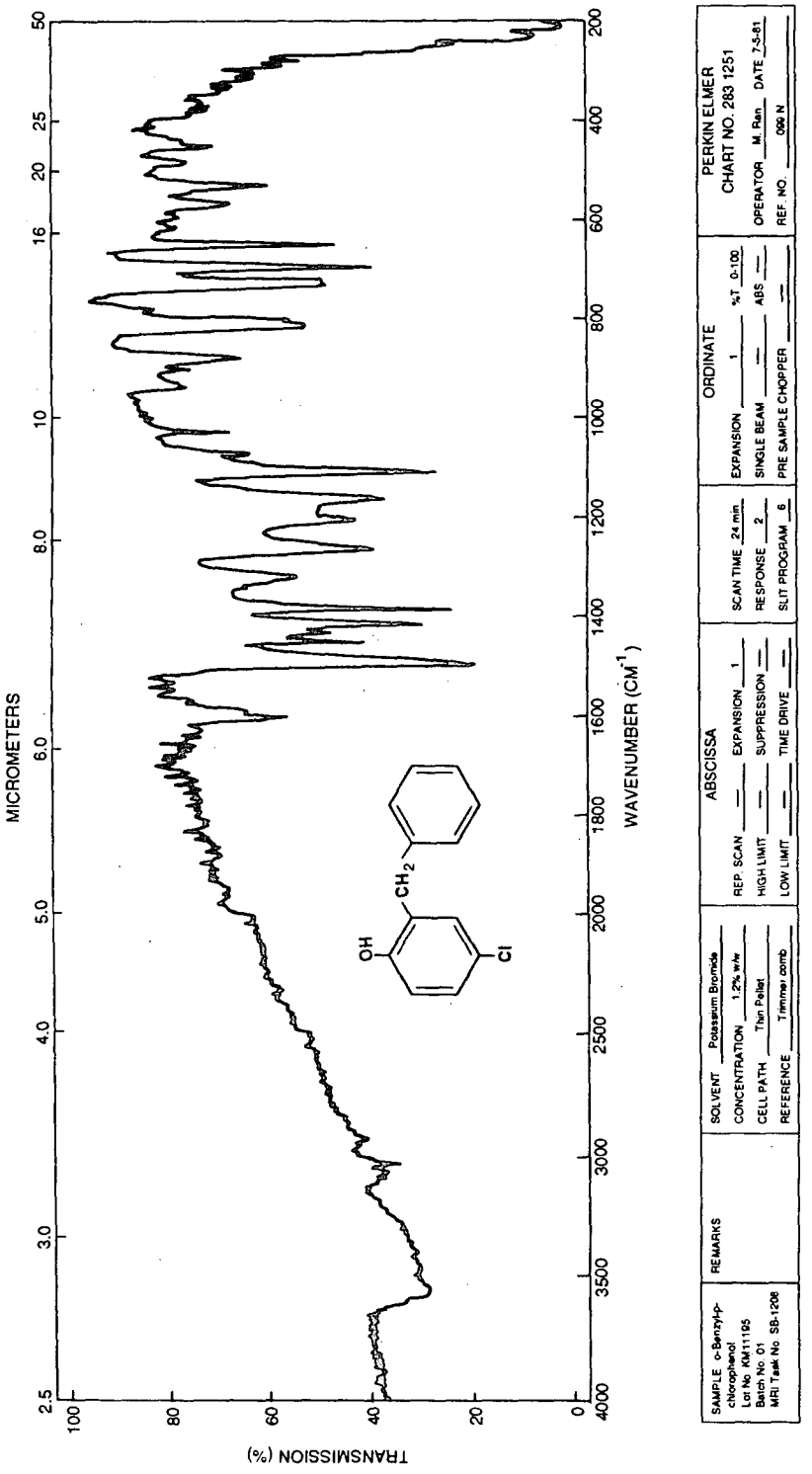

FIGURE H1
Infrared Absorption Spectrum of *o*-Benzyl-*p*-Chlorophenol

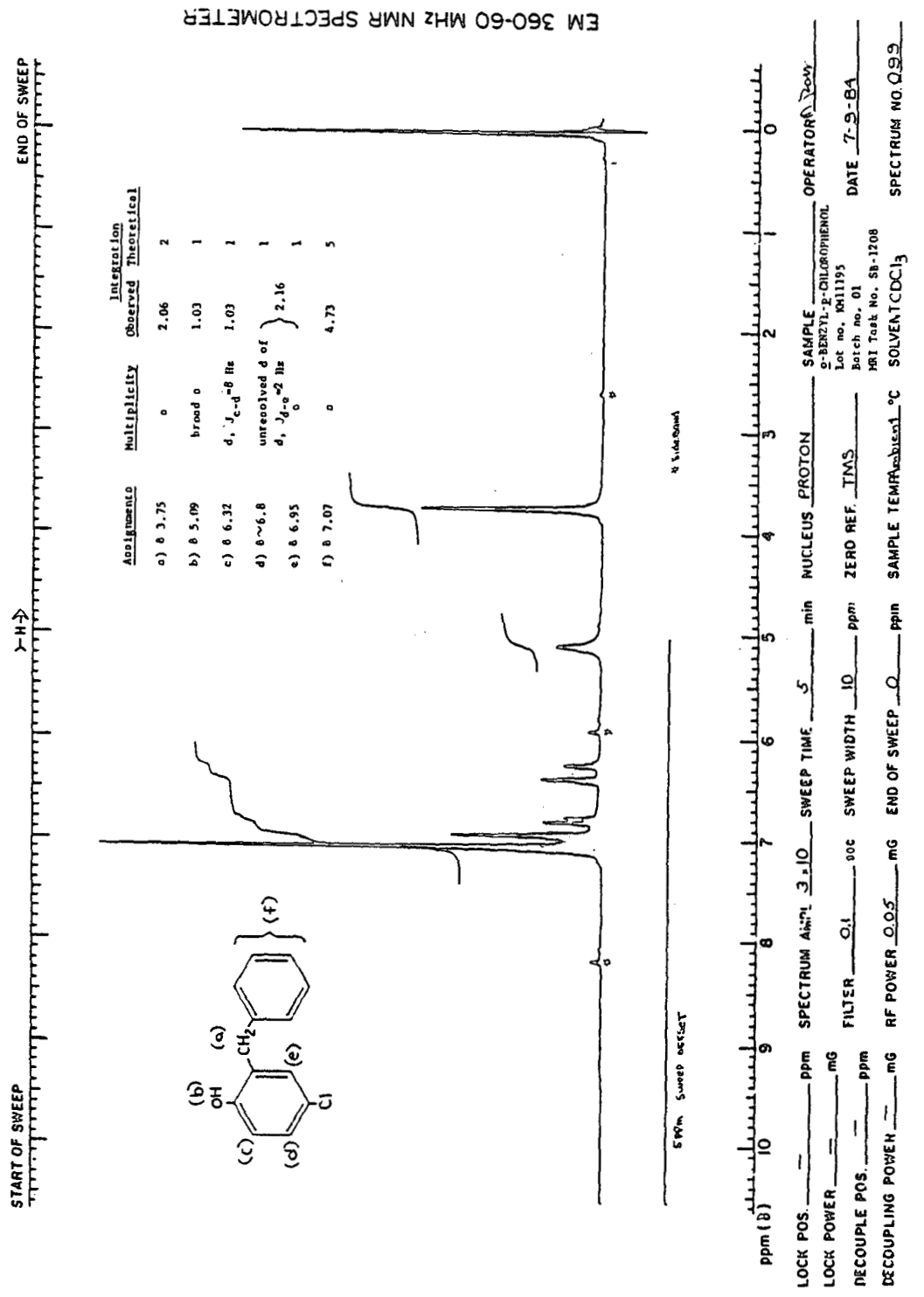

FIGURE H2
Nuclear Magnetic Resonance Spectrum of *o*-Benzyl-*p*-Chlorophenol

TABLE H1
Preparation and Storage of Dose Formulations in the Gavage Studies of *o*-Benzyl-*p*-Chlorophenol

16-Day Studies	13-Week Studies	2-Year Studies
Preparation		
o-Benzyl-*p*-chlorophenol was dissolved in corn oil by mixing with a magnetic stirrer for approximately 30 minutes.	Same as 16-day studies	Same as 16-day studies
Chemical Lot Number		
KM11195	Same as 16-day studies	Same as 16-day studies
Maximum Storage Time		
14 days from date of preparation	Same as 16-day studies	Same as 16-day studies
Storage Conditions		
Stored at room temperature in amber glass bottles	Same as 16-day studies	Same as 16-day studies
Study Laboratory		
Battelle Columbus Division	Same as 16-day studies	Same as 16-day studies
Referee Laboratory		
Midwest Research Institute, Kansas City, MO	Same as 16-day studies	Same as 16-day studies

TABLE H2
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 13-Week Gavage Studies of *o*-Benzyl-*p*-Chlorophenol

Date Prepared	Date Analyzed	Target Concentration[a] (mg/mL)	Determined Concentration[b] (mg/mL)	% Difference from Target
Rats				
14 July 1982	15 July 1982	6	6.3	+5
		12	12.4	+3
		24	24.6	+3
		48	47.1	–2
		96	90.8	–5
20 August 1982	24 August 1982	6	6.1	+2
		12	11.2	–7
		24	24.6	+3
		48	49.8	+4
		96	97.0	+1
8 October 1982	12 October 1982	6	5.7	–6
		12	11.1	–8
		24	21.9	–9
		48	47.1	–2
		96	91.7	–4
Mice				
11 March 1983	15 March 1983	100	101.2	+1
		130	129.9	0
		160	159.9	0
		200	209.4	+5
	28 March 1983[c]	100	101.5	+2
		130	129.2	–1
		160	160.2	0
		200	199.7	0
29 April 1983	2 May 1983	100	99.9	0
		130	127.2	–2
		160	151.9	–5
		200	189.1	–5
	16 May 1983[c]	100	100.2	0
		130	127.2	–2
		160	151.9	–5
		200	197.5	–1
10 June 1983	14 June 1983	100	104.5	+5
		130	136.8	+5
		160	160.3	0
		200	202.8	+1

[a] Rats: Dosing volume = 5 mL/kg; 6 mg/mL = 30 mg/kg; 12 mg/mL = 60 mg/kg; 24 mg/mL = 120 mg/kg; 48 mg/mL = 240 mg/kg; 96 mg/mL = 480 mg/kg
Mice: Dosing volume = 5 mL/kg; 100 mg/mL = 500 mg/kg; 130 mL/kg = 650 mg/kg; 160 mL/kg = 800 mg/kg; 200 mL/kg = 1,000 mg/kg
[b] Results of duplicate analyses
[c] Samples taken from the animal room

TABLE H3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Gavage Studies of *o*-Benzyl-*p*-Chlorophenol

Date Prepared	Date Analyzed	Target Concentration[a] (mg/mL)	Determined Concentration[b] (mg/mL)	% Difference from Target
Rats				
23 October 1984	24 October 1984	6	5.8	+3
		12	13.0	–8
		24	24.4	+2
		48	50.0	+4
	7 November 1984[c]	6	6.4	+7
		12	12.6	+5
		24	23.5	0
		48	47.7	+1
11 December 1984	13 December 1984	6	5.8	–3
		12	12.0	0
		24	23.3	–3
		48	47.7	–1
29 January 1985	1 February 1985	6	5.9	–2
		12	12.1	0
		24	26.0	+8
		48	48.9	+2
27 March 1985	29 March 1985	6	6.1	–1
		12	11.9	–1
		24	25.4	+6
		48	49.0	+2
	11 April 1985[c]	6	6.1	–2
		12	12.2	+2
		24	25.1	+4
		48	48.7	+2
23 May 1985	24 May 1985	6	5.8	–4
		12	12.0	0
		24	24.0	0
		48	46.6	–3
	5 June 1985[c]	6	6.2[d]	+4
		12	12.4	+3
		24	22.7	–5
		48	46.2	–4
17 July 1985	19 July 1985	6	5.5	–8
		12	11.6	–4
		24	24.1	0
		48	48.1	0
11 September 1985	12 September 1985	6	6.2	+3
		12	12.4	+4
		24	25.4	+6
		48	50.3	+5

TABLE H3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Gavage Studies of *o*-Benzyl-*p*-Chlorophenol (continued)

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration (mg/mL)	% Difference from Target
Rats (continued)				
11 September 1985	24 September 1985[c]	6	6.4	+7
		12	10.9	−10
		24	25.3	+5
		48	48.6	+1
7 November 1985	8 November 1985	6	6.1	+1
		12	11.9	−1
		24	22.5	−6
		48	49.4	+3
	18 November 1985[c]	6	5.9	−2
		12	12.6	+5
		24	24.0	0
		48	47.6	−1
31 December 1985	2 January 1986	6	5.5	−8
		12	11.4	−5
		24	22.5	−6
		48	45.1	−6
26 February 1986	27 February 1986	6	6.0	0
		12	11.5	−4
		24	23.3	−3
		48	44.4	−8
23 April 1986	24 April 1986	6	6.0	+1
		12	12.1	+1
		24	23.2	−3
		48	48.1	0
	9 May 1986[c]	6	6.1	+1
		12	12.1	0
		24	23.3	−3
		48	45.3	−6
18 June 1986	19 June 1986	6	5.8	−3
		12	12.2	+2
		24	24.6	+3
		48	49.3	+3
15 August 1986	15 August 1986	6	5.8[e]	−4
		12	11.4	−5
		24	24.6	+3
		48	47.2	−2
8 October 1986	9 October 1986	6	5.9	−2
		12	12.3	+3
		24	24.2	+1
		48	47.2	−2
	21 October 1985[c]	6	5.9	−2
		12	12.0	0
		24	24.1	+1
		48	49.0	+2

TABLE H3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Gavage Studies of o-Benzyl-p-Chlorophenol (continued)

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration (mg/mL)	% Difference from Target
Mice				
20 November 1984	21 November 1984	12	11.6	–3
		24	23.9	–1
		48	46.8	–2
	5 December 1984[c]	12	11.5	–4
		24	24.7	+3
		48	47.0	–2
29 January 1985	1 February 1985	12	12.4	+3
		24	25.2	+5
		48	48.2	0
27 March 1985	29 March 1985	12	12.4	+4
		24	24.7	+3
		48	49.1	+2
23 May 1985	24 May 1985	12	12.1	0
		24	24.0	0
		48	48.2	0
	5 June 1985[c]	12	12.2	+2
		24	23.1	–4
		48	46.1	–4
17 July 1985	19 July 1985	12	11.6	–4
		24	24.0	0
		48	48.4	+1
11 September 1985	12 September 1985	12	11.6	–3
		24	25.0	+4
		48	51.4	+7
6 November 1985	8 November 1985	12	11.5	–4
		24	22.2	–7
		48	49.5	+3
	18 November 1985[c]	12	12.1	+1
		24	24.5	+2
		48	47.4	–1
31 December 1985	2 January 1986	12	11.6	–3
		24	23.2	–3
		48	45.4	–5
26 February 1986	27 February 1986	12	11.0	–8
		24	22.8	–5
		48	46.8	–2

TABLE H3
Results of Analysis of Dose Formulations Administered to Rats and Mice in the 2-Year Gavage Studies of *o*-Benzyl-*p*-Chlorophenol (continued)

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration (mg/mL)	% Difference from Target
Mice (continued)				
23 April 1986	25 April 1986	12	12.2	+1
		24	24.4	+1
		48	48.1	0
	9 May 1986[c]	12	11.6	−3
		24	22.7	−5
		48	52.2	+9
18 June 1986	19 June 1986	12	12.1	+1
		24	24.3	+1
		48	48.1	0
13 August 1986	15 August 1986	12	11.9	−1
		24	23.8	−1
		48	47.9	0
8 October 1986	9 October 1986	12	11.9	−1
		24	23.9	−1
		48	46.7	−3
	21 October 1986[c]	12	12.3	+3
		24	24.5	+2
		48	48.2	0

[a] Dosing volume = 5 mL/kg; 6 mg/mL = 30 mg/kg; 12 mg/mL = 60 mg/kg; 24 mg/mL = 120 mg/kg; 48 mg/mL = 240 mg/kg
[b] Results of duplicate analyses
[c] Samples taken from the animal room
[d] Results of quadruplicate analyses
[e] Results of triplicate analyses

TABLE H4
Results of Referee Analysis of Dose Formulations in the 2-Year Gavage Studies of *o*-Benzyl-*p*-Chlorophenol

Date Mixed	Target Concentration[a] (mg/mL)	Determined Concentration (mg/mL)	
		Study Laboratory[b]	Referee Laboratory[c]
Rats			
11 September 1985	12	12.4	11.7 ± 0.1
	24	25.4	23.5 ± 0.0
	12	10.9	11.8 ± 0.0
23 April 1986	6	6.0	5.77 ± 0.03
Mice			
8 October 1986	12	11.9	12.3 ± 0.06

[a] Dosing volume = 5 mL/kg; 6 mg/mL = 30 mg/kg; 12 mg/mL = 60 mg/kg; 24 mg/mL = 120 mg/kg
[b] Results of duplicate analyses
[c] Results of triplicate analyses. Mean ± standard deviation

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

TABLE I1
Ingredients of NIH-07 Rat and Mouse Ration[a]

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

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

TABLE I2
Vitamins and Minerals in NIH-07 Rat and Mouse Ration[a]

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

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

TABLE I3
Nutrient Composition of NIH-07 Rat and Mouse Ration

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Protein (% by weight)	22.21 ± 0.51	21.1–23.5	22
Crude Fat (% by weight)	5.73 ± 0.46	4.7–6.5	22
Crude Fiber (% by weight)	3.47 ± 0.49	2.7–5.4	22
Ash (% by weight)	6.45 ± 0.25	6.1–7.0	22
Amino Acids (% of total diet)			
Arginine	1.308 ± 0.606	1.210–1.390	8
Cystine	0.306 ± 0.084	0.181–0.400	8
Glycine	1.150 ± 0.047	1.060–1.210	8
Histidine	0.576 ± 0.024	0.531–0.607	8
Isoleucine	0.917 ± 0.029	0.881–0.944	8
Leucine	1.946 ± 0.055	1.850–2.040	8
Lysine	1.270 ± 0.058	1.200–1.370	8
Methionine	0.448 ± 0.128	0.306–0.699	8
Phenylalanine	0.987 ± 0.140	0.665–1.110	8
Threonine	0.877 ± 0.042	0.824–0.940	8
Tryptophan	0.236 ± 0.176	0.107–0.671	8
Tyrosine	0.676 ± 0.105	0.564–0.794	8
Valine	1.103 ± 0.040	1.050–1.170	8
Essential Fatty Acids (% of total diet)			
Linoleic	2.393 ± 0.258	1.830–2.570	7
Linolenic	0.280 ± 0.040	0.210–0.320	7
Vitamins			
Vitamin A (IU/kg)	9,190 ± 2,815	4,700–15,000	22
Vitamin D (IU/kg)	4,450 ± 1,382	3,000–6,300	4
α-Tocopherol (ppm)	37.95 ± 9.406	22.5–48.9	8
Thiamine (ppm)	20.41 ± 1.74	17.0–23.0	22
Riboflavin (ppm)	7.92 ± 0.87	6.10–9.00	8
Niacin (ppm)	103.4 ± 26.59	65.0–150.0	8
Pantothenic Acid (ppm)	29.54 ± 3.60	23.0–34.0	8
Pyridoxine (ppm)	9.55 ± 3.48	5.60–14.0	8
Folic Acid (ppm)	2.25 ± 0.73	1.80–3.70	8
Biotin (ppm)	0.254 ± 0.042	0.19–0.32	8
Vitamin B12 (ppb)	38.45 ± 22.01	10.6–65.0	8
Choline (ppm)	3,089 ± 328.69	2,400–3,430	8
Minerals			
Calcium (%)	1.12 ± 0.08	0.95–1.27	22
Phosphorus (%)	0.91 ± 0.05	0.73–0.99	22
Potassium (%)	0.883 ± 0.078	0.772–0.971	6
Chloride (%)	0.526 ± 0.092	0.380–0.635	8
Sodium (%)	0.313 ± 0.390	0.258–0.371	8
Magnesium (%)	0.168 ± 0.010	0.151–0.181	8
Sulfur (%)	0.280 ± 0.064	0.208–0.420	8
Iron (ppm)	360.5 ± 100	255.0–523.0	8
Manganese (ppm)	92.0 ± 6.01	81.70–99.40	8
Zinc (ppm)	54.72 ± 5.67	46.10–64.50	8
Copper (ppm)	11.06 ± 2.50	8.090–15.39	8
Iodine (ppm)	3.37 ± 0.92	1.52–4.13	6
Chromium (ppm)	1.79 ± 0.36	1.04–2.09	8
Cobalt (ppm)	0.681 ± 0.14	0.490–0.780	4

TABLE I4
Contaminant Levels in NIH-07 Rat and Mouse Ration

	Mean ± Standard Deviation[a]	Range	Number of Samples
Contaminants			
Arsenic (ppm)	0.75 ± 0.16	0.32–1.07	22
Cadmium (ppm)	0.10		22
Lead (ppm)	0.53 ± 0.28	0.05–1.32	22
Mercury (ppm)	<0.05		22
Selenium (ppm)	0.34 ± 0.09	0.17–0.48	22
Aflatoxins (ppb)	<5.0		22
Nitrate nitrogen (ppm)[b]	14.96 ± 4.03	6.30–22.0	22
Nitrite nitrogen (ppm)[b]	0.30 ± 0.59	<0.10–2.60	22
BHA (ppm)[c]	2.45 ± 1.01	<2.00–5.00	22
BHT (ppm)[c]	2.09 ± 1.15	<1.00–4.00	22
Aerobic plate count (CFU/g)[d]	30,498 ± 39,611	770–130,000	22
Coliform (MPN/g)[e]	16.54 ± 50.6	<3.00–2400	22
E. coli (MPN/g)[f]	3.04 ± 0.21	<3.00–4.00	22
Total nitrosoamines (ppb)[g]	7.22 ± 3.01	3.80–16.00	22
N-Nitrosodimethylamine (ppb)[g]	6.19 ± 3.01	2.80–15.00	22
N-Nitrosopyrrolidine (ppb)[g]	1.02 ± 0.11	1.00–1.50	22
Pesticides (ppm)			
α-BHC	<0.01		22
β-BHC	<0.02		22
γ-BHC	<0.01		22
δ-BHC	<0.01		22
Heptachlor	<0.01		22
Aldrin	<0.01		22
Heptachlor epoxide	<0.01		22
DDE	<0.01		22
DDD	<0.01		22
DDT	<0.01		22
HCB	<0.01		22
Mirex	<0.01		22
Methoxychlor	<0.05		22
Dieldrin	<0.01		22
Endrin	<0.01		22
Telodrin	<0.01		22
Chlordane	<0.05		22
Toxaphene	<0.1		22
Estimated PCBs	<0.2		22
Ronnel	<0.01		22
Ethion	<0.02		22
Trithion	<0.05		22
Diazinon	<0.1		22
Methyl parathion	<0.02		22
Ethyl parathion	<0.02		22
Malathion[h]	0.21 ± 0.67	0.05 – 3.20	22
Endosulfan I	<0.01		22
Endosulfan II	<0.01		22
Endosulfan sulfate	<0.03		22

TABLE I4
Contaminant Levels in NIH-07 Rat and Mouse Ration (continued)

[a] For values less than the limit of detection, the detection limit is given for the mean.
[b] Sources of contamination: alfalfa, grains, and fish meal
[c] Sources of contamination: soy oil and fish meal
[d] CFU=colony forming units
[e] MPN=most probable number
[f] The lot milled 17 October 1982 contained 4.0 MPN; all others lots were less than or equal to the detection limit.
[g] All values were corrected for percent recovery
[h] One lot contained more than 0.50 ppm.

APPENDIX J
SENTINEL ANIMAL PROGRAM

SENTINEL ANIMAL PROGRAM

METHODS

Rodents used in the Carcinogenesis Program of the National Toxicology Program are produced in optimally clean facilities to eliminate potential pathogens that may affect study results. The Sentinel Animal Program is part of the periodic monitoring of animal health that occurs during the toxicologic evaluation of chemical compounds. Under this program, the disease state of the rodents is monitored via serology on sera from extra (sentinel) animals in the study rooms. These animals and the study animals are subject to identical environmental conditions. The sentinel animals come from the same production source and weanling groups as the animals used for the studies of chemical compounds.

Rats

At the end of the 13-week study, samples for viral screening were collected from five male and five female vehicle control rats. These samples were processed appropriately and submitted to Microbiological Associates (Bethesda, MD) for viral titer screening. The following tests were performed on the sera:

Method of Analysis	Time of Analysis
Complement Fixation	
RCV (ratcorona virus)	Study termination
Sendai	Study termination
Hemagglutination Inhibition	
H-1 (Toolan's H-1 virus)	Study termination
KRV (Kilham rat virus)	Study termination
PVM (pneumonia virus of mice)	Study termination

Prior to the beginning of the 2-year study, blood was collected twice (during two separate quarantine screenings) from five male and five female rats. Serum samples were also collected from five male and five female rats at the following intervals: 6, 12, and 18 months into the study and from five male and five female high-dose rats at the end of the study (24 months). Blood from each collection was processed appropriately, shipped to Microbiological Associates, and screened for the following:

Method of Analysis	Time of Analysis
Hemagglutination Inhibition	
H-1	6, 12, 18, and 24 months
KRV	1st and 2nd quarantines, 6, 12, 18, and 24 months
ELISA	
Mycoplasma arthritidis	6, 12, 18, and 24 months
Mycoplasma pulmonis	1st and 2nd quarantines, 6, 12, 18, and 24 months
PVM	1st and 2nd quarantines, 6, 12, 18, and 24 months
RCV	24 months
RCV/SDA	
(rat coronavirus/sialodacrydoadenitis virus)	1st and 2nd quarantines, 6, 12, and 18 months
Sendai	1st and 2nd quarantines, 6, 12, 18, and 24 months

Mice

At the end of the 13-week study, samples for viral screening were collected from 10 female vehicle control mice. These samples were processed appropriately and submitted to Microbiological Associates (Bethesda, MD) for viral titer screening. The following tests were performed on the sera:

Method of Analysis	Time of Analysis
Complement Fixation	
LCM (lymphocytic choriomeningitis virus)	Study termination
Mouse adenoma virus	Study termination
ELISA	
MHV (mouse hepatitis virus)	Study termination
M. pulmonis	Study termination
Hemagglutination Inhibition	
Ectromelia virus	Study termination
GDVII (mouse encephalomyelitis virus)	Study termination
MVM (minute virus of mice)	Study termination
PVM	Study termination
Polyoma virus	Study termination
Reovirus 3	Study termination
Sendai	Study termination

Prior to the beginning of the 2-year study, blood was collected twice (during two separate quarantine screenings) from five male and five female mice. Serum samples were also collected from five males and five females at the following intervals: 6, 12, and 18 months into the study and from five male and five female high-dose mice at the end of the study (24 months). In addition, an unscheduled screening for the mouse hepatitis virus was conducted at about 7 months into the study. Blood from each collection was processed appropriately, shipped to Microbiological Associates, and screened for the following:

Method of Analysis	Time of Analysis
Complement Fixation	
LCM	6, 12, and 18 months
ELISA	
Ectromelia virus	6, 12, 18, and 24 months
GDVII	6, 12, 18, and 24 months
Mouse adenoma virus	6, 12, 18, and 24 months
MHV	1st and 2nd quarantines, 6, 7, 12, 18, and 24 months
M. arthriditis	6, 12, 18, and 24 months
M. pulmonis	1st and 2nd quarantines, 6, 12, 18, and 24 months
PVM	1st and 2nd quarantines, 6, 12, 18, and 24 months
Reovirus 3	6, 12, 18, and 24 months
Sendai	1st and 2nd quarantines, 6, 12, 18, and 24 months
Immunofluorescence Assay	
EDIM (epizootic diarrhea of infant mice)	6, 12, 18, and 24 months
LCM	24 months
MHV	7 months
Reovirus 3	24 months

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TR No.	CHEMICAL
201	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Dermal)
206	1,2-Dibromo-3-chloropropane
207	Cytembena
208	FD & C Yellow No. 6
209	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Gavage)
210	1,2-Dibromoethane
211	C.I. Acid Orange 10
212	Di(2-ethylhexyl)adipate
213	Butyl Benzyl Phthalate
214	Caprolactam
215	Bisphenol A
216	11-Aminoundecanoic Acid
217	Di(2-Ethylhexyl)phthalate
219	2,6-Dichloro-p-phenylenediamine
220	C.I. Acid Red 14
221	Locust Bean Gum
222	C.I. Disperse Yellow 3
223	Eugenol
224	Tara Gum
225	D & C Red No. 9
226	C.I. Solvent Yellow 14
227	Gum Arabic
228	Vinylidene Chloride
229	Guar Gum
230	Agar
231	Stannous Chloride
232	Pentachloroethane
233	2-Biphenylamine Hydrochloride
234	Allyl Isothiocyanate
235	Zearalenone
236	*D*-Mannitol
237	1,1,1,2-Tetrachloroethane
238	Ziram
239	Bis(2-chloro-1-Methylethyl)ether
240	Propyl Gallate
242	Diallyl Phthalate (Mice)
243	Trichlorethylene (Rats and Mice)
244	Polybrominated Biphenyl Mixture
245	Melamine
246	Chrysotile Asbestos (Hamsters)
247	L-Ascorbic Acid
248	4,4′-Methylenedianiline Dihydrochloride
249	Amosite Asbestos (Hamsters)
250	Benzyl Acetate
251	2,4- & 2,6-Toluene Diisocyanate
252	Geranyl Acetate
253	Allyl Isovalerate
254	Dichloromethane (Methylene Chloride)
255	1,2-Dichlorobenzene
257	Diglycidyl Resorcinol Ether
259	Ethyl Acrylate
261	Chlorobenzene
263	1,2-Dichloropropane
266	Monuron
267	1,2-Propylene Oxide
269	Telone II® (1,3-Dichloropropene)
271	HC Blue No. 1
272	Propylene
273	Trichloroethylene (Four Rat Strains)
274	Tris(2-ethylhexyl)phosphate
275	2-Chloroethanol
276	8-Hydroxyquinoline
277	Tremolite
278	2,6-Xylidine
279	Amosite Asbestos
280	Crocidolite Asbestos
281	HC Red No. 3
282	Chlorodibromomethane
284	Diallylphthalate (Rats)
285	C.I. Basic Red 9 Monohydrochloride
287	Dimethyl Hydrogen Phosphite
288	1,3-Butadiene
289	Benzene
291	Isophorone
293	HC Blue No. 2
294	Chlorinated Trisodium Phosphate
295	Chrysotile Asbestos (Rats)
296	Tetrakis(hydroxymethyl) phosphonium Sulfate & Tetrakis(hydroxymethyl) phosponium Chloride
298	Dimethyl Morpholinophosphoramidate
299	C.I. Disperse Blue 1
300	3-Chloro-2-methylpropene
301	*o*-Phenylphenol
303	4-Vinylcyclohexene
304	Chlorendic Acid
305	Chlorinated Paraffins (C_{23}, 43% chlorine)
306	Dichloromethane (Methylene Chloride)
307	Ephedrine Sulfate
308	Chlorinated Pariffins (C_{12}, 60% chlorine)
309	Decabromodiphenyl Oxide
310	Marine Diesel Fuel and JP-5 Navy Fuel
311	Tetrachloroethylene (Inhalation)
312	*n*-Butyl Chloride
313	Mirex
314	Methyl Methacrylate
315	Oxytetracycline Hydrochloride
316	1-Chloro-2-methylpropene
317	Chlorpheniramine Maleate
318	Ampicillin Trihydrate
319	1,4-Dichlorobenzene
320	Rotenone
321	Bromodichloromethane
322	Phenylephrine Hydrochloride
323	Dimethyl Methylphosphonate
324	Boric Acid
325	Pentachloronitrobenzene
326	Ethylene Oxide
327	Xylenes (Mixed)
328	Methyl Carbamate
329	1,2-Epoxybutane
330	4-Hexylresorcinol
331	Malonaldehyde, Sodium Salt
332	2-Mercaptobenzothiazole
333	*N*-Phenyl-2-naphthylamine
334	2-Amino-5-nitrophenol
335	C.I. Acid Orange 3

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TR No.	CHEMICAL
336	Penicillin VK
337	Nitrofurazone
338	Erythromycin Stearate
339	2-Amino-4-nitrophenol
340	Iodinated Glycerol
341	Nitrofurantoin
342	Dichlorvos
343	Benzyl Alcohol
344	Tetracycline Hydrochloride
345	Roxarsone
346	Chloroethane
347	D-Limonene
348	α-Methyldopa Sesquihydrate
349	Pentachlorophenol
350	Tribromomethane
351	*p*-Chloroaniline Hydrochloride
352	N-Methylolacrylamide
353	2,4-Dichlorophenol
354	Dimethoxane
355	Diphenhydramine Hydrochloride
356	Furosemide
357	Hydrochlorothiazide
358	Ochratoxin A
359	8-Methoxypsoralen
360	N,N-Dimethylaniline
361	Hexachloroethane
362	4-Vinyl-1-Cyclohexene Diepoxide
363	Bromoethane (Ethyl Bromide)
364	Rhodamine 6G (C.I. Basic Red 1)
365	Pentaerythritol Tetranitrate
366	Hydroquinone
367	Phenylbutazone
368	Nalidixic Acid
369	Alpha-Methylbenzyl Alcohol
370	Benzofuran
371	Toluene
372	3,3-Dimethoxybenzidine Dihydrochloride
373	Succinic Anhydride
374	Glycidol
375	Vinyl Toluene
376	Allyl Glycidyl Ether
377	*o*-Chlorobenzalmalononitrile
378	Benzaldehyde
379	2-Chloroacetophenone
380	Epinephrine Hydrochloride
381	*d*-Carvone
382	Furfural
384	1,2,3-Trichloropropane
385	Methyl Bromide
386	Tetranitromethane
387	Amphetamine Sulfate
388	Ethylene Thiourea
389	Sodium Azide
390	3,3′-Dimethylbenzidine Dihydrochloride
391	Tris(2-chloroethyl) Phosphate
392	Chlorinated Water and Chloraminated Water
393	Sodium Fluoride
394	Acetaminophen
395	Probenecid
396	Monochloroacetic Acid
397	C.I. Direct Blue 15
398	Polybrominated Biphenyls
399	Titanocene Dichloride
400	2,3-Dibromo-1-propanol
401	2,4-Diaminophenol Dihydrochloride
402	Furan
403	Resorcinol
404	5,5-Diphenylhydantoin
405	C.I. Acid Red 114
406	γ-Butyrolactone
407	C.I. Pigment Red 3
408	Mercuric Chloride
409	Quercetin
410	Naphthalene
411	C.I. Pigment Red 23
412	4,4-Diamino-2,2-stilbenedisulfonic Acid
413	Ethylene Glycol
414	Pentachloroanisole
415	Polysorbate 80
416	*o*-Nitroanisole
417	*p*-Nitrophenol
418	*p*-Nitroaniline
419	HC Hellow 4
420	Triamterene
421	Talc
422	Coumarin
423	Dihydrocoumarin
425	Promethazine Hydrochloride
428	Manganese (II) Sulfate Monohydrate
427	Turmeric Oleoresin
431	Benzyl Acetate
434	1,3-Butadiene
443	Oxazepam

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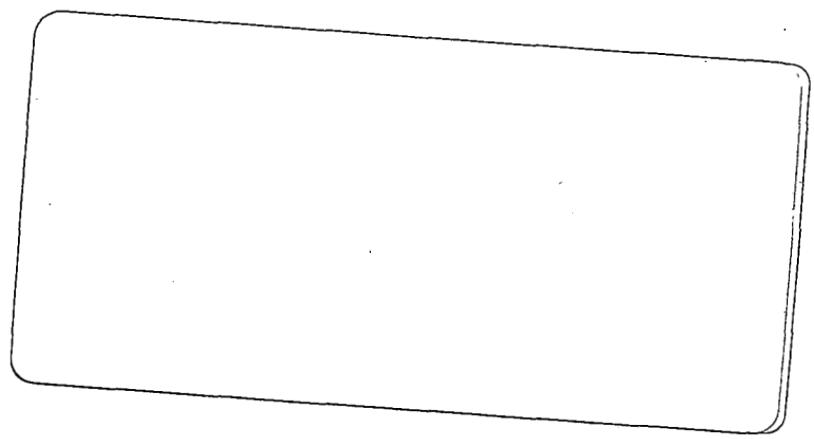

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